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INNOVATIVE INTEGRATED TRAINING IN HEALING PLANTS BUSINESS

Innovative Intergrated Training

in Healing Palnts Business

IO3

The Total Business Plants Training Material

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Introduction

People have been using medicinal plants from ancient time and research workers are constantly bringing to light additional information on the relationship between plants and man.
Medicinal plants play a significant role in the life of human beings and are present in innumerable forms. These plants are used as raw materials for medicines, cosmetics, perfumery, as insecticides, and in various industries. A number of medicinal plants also produce essential oils and are being used for perfumery.
In broad context, MEDICINAL PLANTS could be considered as *"plants producing elements like roots, stem, bark, leaves, flowers, fruits and seeds. The chemical substances derived from these parts either individually or collectively are used in different systems of medicine, especially for their curative properties".* Recently, medicinal plants are also defined as *"all higher plants that have been alleged to have medicinal properties"*. Such effects are related to health or have been admitted as useful drugs by western standards, or which contain constituents that are used in drugs.
Demand for medicinal plants is increasing due to growing recognition of natural products, being non-narcotic, having no side effects, easily available at affordable prices and sometime the only source of health care. Consequently, the need for cultivation of medicinal plants is progressively becoming more and more apparent to satisfy the medicinal, economic, and social needs of people.
Harvest and post-harvest treatment of medicinal plants are considered critical stages regarding their impact to the final product. The procedures included in harvest and post-harvest treatment can be as simple as hand harvest and a typical drying, but also they can be complicated, with specialized equipment and sophisticated distillation and extraction methods. In every step of those procedures, there are parameters that must be considered, so that a fine final product can be guaranteed. Those parameters can be environmental, biological, mechanical, chemical factors that can alter the final product, with direct impact to its market value. Therefore, all the necessary specifications must be respected, in order to achieve the best quality and quantity of the final product.
The knowledge of the development of ideas related to the usage of medicinal plants, as well as the evolution of awareness has increased the ability of pharmacists and physicians to respond to the challenges that have emerged with the spreading of professional services in facilitation of man's life. Quarter of all modern medicines are derived either directly or indirectly from higher plants. This, in addition to the increasing use of medicinal plants, has led to an increase in concern for their safe use and quality standards from many health authorities, pharmaceutical companies and their end user, the public. Thus, it is quite important to understand why quality control and quality assurance is essential when dealing with medicinal plants. It is of paramount importance for safety, effectiveness, and acceptability of the product and it is a crucial operation of the pharmaceutical industry.
For everyone who wants and sees the need of creating Start-Up in medicinal plants sector it is important to understand the meaning of Start-Up and Medicinal Plants. Therefore, those two concepts are described and interrelated stressing on topics like: first business steps, medicinal plants possibilities, skills, preparation, challenges, tools needed, interest of medicinal plants,

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requirements, costumers, target groups, marketing plan, business model, legislations, internationalization and globalization.

Medical prescriptions that are based on substances derived from plants or plant-derived synthetic analogs generally represent 25% of all the prescriptions. Over the past 40 years, research on medicinal plants indicates that they act in a different way than modern drugs: the effect does not derive from one single compound of an herb, but is a synergetic result from many components acting against many targets. Chemical studies of herbal medicines provide fundamental substances for further studies on their biological and pharmacological activity. Pharmaceutical incompatibilities and pharmacodynamics interactions are important issues due to the common practice of prescribing herbs as an addition to essential medications. In already developed societies, people redefine the values and conformity of traditional treatments, and thus the use of medicinal plants as an effective way to improve their everyday life and their general health status.

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INNOVATIVE INTEGRATED TRAINING IN
HEALING PLANTS
BUSINESS

Module No. 1

“Organic cultivation of medicinal plants”

Sofia University “St. Kliment Ohridski”

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Unit 1: Organic cultivation of medicinal plants - agromelioration conditions

1.1 MP classification

Of the 250 000 higher plant species on earth more than 80 000 species are reported to have at least some medicinal value and around 5 000 species have specific therapeutic value. They are classified according to the part used, habit, habitat, therapeutic value, etc., in addition to the common botanical classification.

1.2 Terms related to MP cultivation and collection activities

The definitions explained below have been adapted from the terms included in the glossary collected by the Food and Agriculture Organization of the United Nations (FAO). The glossary can be found at http://www.fao.org/glossary/

Erosion: the process through which water or wind moves soil from one site to another.

Integrated pest management (IPM): the cautious integration of available pest-control techniques used to depress pest-population development and maintain pesticides and other interventions to levels that are economically justifiable and harmless for human health and the environment

Landrace: an early, cultivated form of a crop species, evolved from a wild population, and generally composed of a heterogeneous mixture of genotypes.

Plant genetic resources: the reproductive or vegetative propagating plant material

Propagule: any structure capable of giving rise to a new plant by asexual or sexual reproduction, including bulbils, leaf buds, etc.

Standard operating procedure (SOP): an authorized written procedure providing instructions for performance operation and sustainable use.

1.3 Terms relating to herbal medicines:

Contamination: the undesired introduction of impurities of a chemical or microbiological nature, or of foreign matter, into or on to a starting material or intermediate during production, sampling, packaging or repackaging, storage or transport.

Cross-contamination: contamination of a starting material, intermediate product or finished product by another starting material or product during production.

1.4 The products of herbal medicine

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Herbal medicines comprise herbs, herbal materials, herbal preparations and finished herbal products.

Herbs: comprise crude plant material, i.e. different plant parts, such as leaves, roots, rhizomes, bark, wood, stems, seed, fruit, and flowers, either entire, fragmented or powdered.

Herbal materials: consist of, together with herbs, fresh juices, gums, fixed oils, essential oils, resins and dry powders of herbs. In some countries, local procedures, such as steaming, roasting, or stir-baking with honey, alcoholic beverages or other materials are applied for processing of these materials.

Herbal preparations: represent the basis for preparation of finished herbal products. They include comminuted or powdered herbal materials, extracts, tinctures or fatty oils of herbal materials. Herbal preparations are produced by physical or biological processes, including extraction, fractionation, purification, concentration, etc. They also include

- Finished herbal products: consist of herbal preparations made from one or more herbs. If more than one herb is used, the term mixed herbal product can also be used. Finished herbal products and mixed herbal products may contain excipients in addition to the active ingredients.
- Medicinal plant materials. a plant (wild or cultivated) used for medicinal purposes.

1.5 **Organic cultivation of MP: the essentials**

The MP components are used fresh, dried or processed for diagnosis, treatment, prevention, as well as to help maintain the health of humans or animals and their physiological functions. The substantial role of MP in different industries, leads to increasing production of biomass. The application of organic farming methods for improvement of the yield and quality of MP seems to be very effective.

During the last decade, agricultural production, obtained through application of chemical fertilizers is causing environmental problems. The solution of this problem is called organic agriculture (OA), which represents an integrated system based on ecological principles.

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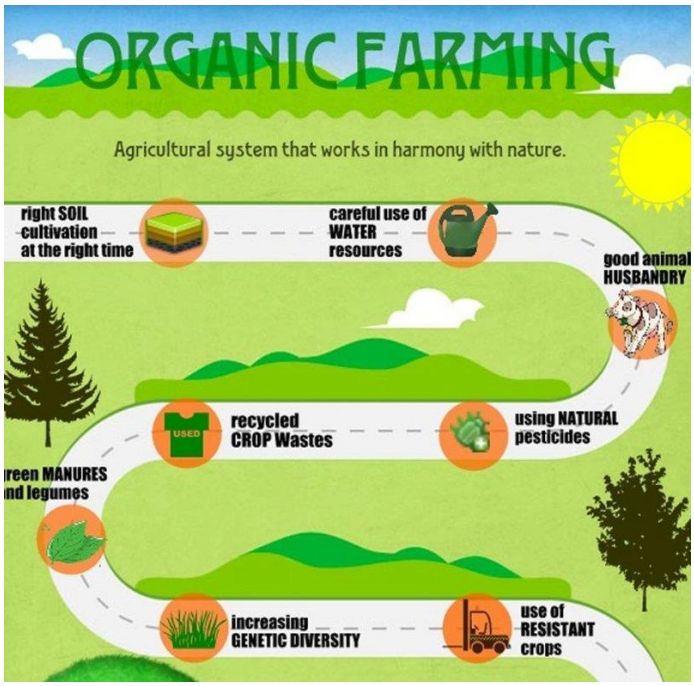

Organic agriculture is a farming system which proposes healthful and quality products. The organic agriculture is a manufacturing system, which denies or excludes the use of synthetic preparations: artificial fertilizers, pesticides, growth accelerators and fodder additives. As an option to these tools, OA applies a number of up-to date warning methods to sustain the natural soil fertility and non-chemical control of weeds, pests and diseases, such as:

- Rotating sowing of crops (with leguminous crops inclusive)
- Proper use of manure
- Activation the populations of useful insects (entomophagy's and pathogens for the pests)
- Vegetation associations (mixed cultivation of two or more crops in one and the same place)
- Weed control with mechanical methods
- Application of well-adapted sustainable plant varieties and livestock breeds in relevant environmental conditions.

1.6 **Organic farming produces high quality MP**

Organic farming, pastoral and wild harvest systems should fit the cycles and ecological balances in nature. Organic management must be adapted to local conditions, ecology, culture and scale.

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The use of bio fertilizers is an ecological way to keep active growth of plants and soil in organic farming systems. In addition to furnishing fully consistent nutrients with the natural feeding of plants, affording to substantially biodiversity. Thus, the application of bio fertilizers edges critical activities improves the quality and maintains the overall health of the environment.

However, there are some negative aspects in OA:

- The yields of crop from OA usually are lower than those of conventional (industrial) agriculture;
- The conventional agriculture organic products are costly than those of industrial agriculture (IFOAM, 2007).

1.7 **Organic cultivation of MP - agro melioration conditions**

Soil requirements:

As per definition, soil is the surface layer of the earth, shaped by weathering of rocks. The soil is formed because of joint action of climate factors like plants and microorganisms. The soil should contain suitable amounts of nutrients, organic matter and other elements to ensure optimal MP growth and quality. Optimal soil conditions, including soil type, drainage, moisture retention, fertility and pH, depend on the chosen medicinal plant species and/or target medicinal plant part.

Plants depend on soil for nutrients, water supply and anchorage. Soil influences germination of seeds, plant capacity to remain erect, stem form, vigor and woodiness, depth of root system, number of flowers per plant, drought and frost resistance, etc.

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Maintenance of natural soil fertility for MP cultivation

Organic agriculture practitioners can enhance efficiency and increase productivity, but this should not be done at the risk of people health and well-being. For this reason, any harmful action towards plants cultivation should be stopped.

The two most important factors influencing the physical and chemical properties of the MP are climate and soil conditions. Medicinal plants require different climatic conditions to grow depending on their origin. The majority of MP require sunny, aerated places sheltered from strong winds and late winter frosts. In addition, the soil for cultivation of MP must be reach of nutrients. It has to contain Na, P, Cu, minerals, organic and other elements required for growth in the necessary amounts and combination.

The soil composting

Composting represents a biological process that includes bioconversion of organic biodegradable wastes into healthy, humus-rich product (compost) for application as a soil conditioner and an organic fertilizer. Its constituents are reused to provide biological control against various plant pathogens. Aqueous extracts of compost can replace synthetic fungicides.

The use of compost to improve soil structure, fertility for growth and productivity of MP were studied in several cases.

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Vermicomposting influence MP yield and secondary metabolite synthesis

Vermicompost comprises the majority of nutrients in plant-available forms, such as nitrates, phosphates, and exchangeable calcium and soluble potassium. Vermicompost is characterizes by a large surface area having many micro-sites for the microbial activity and preservation of nutrients. It contains different microbial populations - fungi, bacteria and actinomycetes, plant growth regulators and other growth-promoting substances, produced by a large diversity of microorganisms. Other products like cytokines and auxins produced by earthworms are taking place in organic wastes. There are also large amounts of humic compounds in vermicompost and their effect on plant growth is similar to that of soil-applied plant growth regulators or hormones.

The most valued nutrients are exchangeable calcium and soluble potassium, which cause an increase in plant growth and crop yield. The beneficial effects of vermicompost have been shown also in horticultural and agronomical crops. Vermicompost is rich in macro- and micro-elements, which are responsible for increased qualitative and quantitative yields of many crops. Other important compounds are phenolic ones, representing a large group of plant secondary metabolites.

Bio-fertilizers influence MP essential oil content and yield

a) Mycorrhizal fungi

Mycorrhizal fungi are beneficial microorganisms that have been considered as bio fertilizer. The terrestrial plants' growth, health, and establishment depend strongly on mycorrhiza, which promotes their realization. The improved productivity of AM (AM=VAM: Vesicular Arbuscular Mycorrhiza) plants was due to facilitated uptake of immobile nutrients like phosphorus, zinc, and

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copper. It is believed that resistance against biotic and abiotic stress factors is linked to the effects of AM fungi on inducing plant hormones production.

b) Phosphate solubilizing microorganisms

Another type of bio-fertilizers, which have the ability to solubilize organic and inorganic phosphorus compounds by producing organic acid or phosphatase enzyme are phosphate solubilizing microorganisms. These bacteria have a synergistic effect with mycorrhiza fungi and co-inoculation of them leads to more absorption of water and soil minerals and increases the growth of host plant. It is found that plants at vegetative growth stage possessed more VAM root colonization abilities in comparison to those at flowering and fruiting stages. Herbaceous plants showed more root colonization in comparison with shrubby and woody plants as well. Thus, the effects of mycorrhizae association on the concentration and composition of essential oil in medicinal plants showed that VAM inoculation increased the concentration of the essential oil in seeds, and improves essence quality.

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c) Bacterial bio-fertilizers

Some bacteria benefit plants with growth promoting compounds and play a major role in phosphate solubilization. The activity of these microorganisms is related to the plant requirements to phosphorus at the root region. The inoculation of soil with bacterial mixtures ensures balanced nutrition for plants. In this way, an improvement of the root uptake of nitrogen and phosphorus takes place due to the main mechanism of interaction between phosphate solubilizing and nitrogen-fixing bacteria.

Studies on the symbiotic relationship between bacteria and plants are provided mainly on cereals and grassy plants. There are limited data regarding this phenomenon in medicinal plants. However, inoculation of *Azotobacter* in *Rosmarinus officinalis* increased the concentration of plant essence. Use of bio-fertilizers *Azospirillum* and *Azotobacter* in the medicinal plant of *Salvia officinalis* increase the plant height and shoot dry and wet weights. In another study, plant biomass and alkaloids levels of *Catharanthus roseus* were enhanced as plantlets were inoculated with *Pseudomonas florescence* bacteria under water stress. In addition, use of biological fertilizers made a significant increase in the plant growth of *Thymus vulgaris.* Moreover, the increase of growth of MP might be because phosphate solubilizing bacteria help plants to absorb nutrients from solution at faster rates than un-inoculated plants resulting in accumulation of more N, P, and K in the leaves. The inoculation of Hibiscus sabdariffa with a mixture of bio-fertilizers improved the growth characteristics of the plant. Similar results were observed on some other MP such as Nigella sativa, *Ammi visnaga* and *Salvia officinalis*.

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The highest essential oil and kamauzolen yield per hectare of chamomile were obtained in phosphate solubilizing bacteria (8 600 g) and nitroxin (923 g) treatments. This result proves that bio-fertilizers can be considered as a replacement for chemical fertilizers in chamomile production. Similar results are reported for the effect of *Azospirillum* and *Azotobacter*, and phosphate solubilizing bacteria on the medicinal plant *Majorana hortensis*. The similar positive effect is reported for the germination indexes, such as percentage and speed of germination, viability, and the length of roots and stems of *Ocimum sanctum* and *Withania somniferum*. Many studies have mentioned the positive effects of microorganisms on improving the growth and performance of MP. In addition to nitrogen fixation, *Azospirillum* improves root growth through generation of stimulating compounds causing an increase in water and nutrients uptake and plant performance. Thus, the most important growth stimulating bacteria are *Azospirillum, Azotobacter*, and *Pseudomonas*. They, in addition to biological nitrogen fixation and solubilizing of soil phosphate, considerably affect synthesis of plant growth regulators like auxin, gibberellin, and cytokine and improve the plant performance. *Azotobacter* is also able to produce antifungal compounds that fight plant diseases and increase viability and germination of the plantlets and in this way improve the overall plant growth.

Medicinal plants intercropping

The “intercropping” represents a special cropping system characterized by the simultaneous growth of two or more plant species. This phenomenon is a useful approach for enhancing yields for one or all the species, thanks to the ability of this system to reduce weeds and pests. Therefore, the intercropping technique is able to minimize the risks of production. This system can give an advantage for mutualistic relationship within partners.

However, intercropping between MP are rare. The evaluation of yields and quality during cultivation in various agroforestry systems showed that introduction of herbs into agroforestry systems may promote biodiversity and improve the income.

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An additional concern for the potential role of MP in intercropping systems is due to the use of sustainable approach for the cultivation of such species. An attempt is made to utilize for this purpose some aromatic oil-bearing plants, namely *Artemisia annua* L., *Coriandrum sativum* L., *Chamomilla recutita* R., *Foeniculum vulgare* M. and *Anethum sowa* Kurtz.

Use of plants cover

In this farming method, plants in a field are grown on the remains of the previous harvest. With the implementation of such a method of weedy grass growth is decreased.

1.8 Effect of organic and bio fertilizer on secondary metabolites of medicinal plants

Investigations on MP show that maximum yield and best quality of secondary metabolites is obtained with the use of organic fertilizers. The results indicate that the use of phosphate solubilizing bacteria and nitrogen fixation in Marjoram herbs lead to increase the essential oil yield. These bacteria increase the oil content of the plant due to the increase in the number of gland secretion and biosynthesis of monoterpenes. The results show that increase in available phosphorus in the soil can significantly increase the concentration of chlorophyll A (28%) and total chlorophyll (19%).

The medicinal plant Vinca (*Caharanthus* roseus) inoculated with the bacterium *Pseudomonas flurescence* increased biomass production and the alkaloid content of the plant was under stress conditions.

The content of organic matter, increased soil water holding capacity, improved plant hormone-like activity, increased nutrient uptake by plants, and generally improved chemical and physical structure of plant litter, including the reasons for increasing the yield of organic fertilizers have been reported.

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Unit 2: Environmental factors influencing the organic cultivation of MP – ecological tolerance

2.1 Light:

Light, in addition to the energy of the chemical bonds in the chemical compounds, is the second major type of usable energy and the only external one that provides for maintenance of life on our planet. For plants – it is the only one source. Light influences photosynthesis, opening and closing of stomata, plant movements, seed germination, flowering and vegetative growth like tuber formation. In addition to these basic physiological processes, light stimulates the accumulation of important MP ingredients. For instance, dry sunny weather increases the proportion of glycosides in Digitalis and of alkaloids in Belladonna.

2.2 Temperature:

Temperature is the major factor influencing the cultivation of the MP. Significant fluctuations from the optimal growth temperature in both directions may cause serious injuries even death of the MP cells. For instance, the decrease of the temperature to values around the zero, especially the sudden one, causes the formation of the ice crystals in intercellular spaces of the plant. As a result, water comes out of the cells and ultimately plants die due to drought and desiccation. The ice crystals also mechanical injure the cells. Water absorption decreases at low temperatures and the insufficient free water in the cell threatened the normal metabolic processes in it.

On the other hand, the moderate increase in the temperature stimulates the growth of seedlings and elevates the rate of photosynthesis. The rate of respiration increases with increase in temperature as well.

2.3 Atmosphere humidity:

By definition, the water vapors in the air are called atmospheric humidity. The visible forms of humidity are clouds and fog. The major sources of water vapors in the atmosphere are evaporation of water from earth surface and transpiration from plants. Humidity imposes a major effect on plant life and climate. Evaporation of water, its condensation and precipitation depend upon relative humidity and humidity affects structure, form, and transpiration in all plants, including MP.

2.4 Altitude:

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The altitude is the most important factor influencing cultivation of MP. In fact, the altitude restricts the growth of MP. With the increase of the altitude, the temperature, and atmospheric pressure decreases while the wind velocity, relative humidity and light intensity increase.

Some MP can be adapted to grow at high altitudes: these are valerian, angelica, mint, sweet balm, St John's wort, Great burdock, Coneflower. Low altitude, especially under the Mediterranean influence, is very convenient for cultivating species such as thyme, salve, lavender, and rosemary. In such altitude, the extracted essential oil is of better quality and yield.

Thus, the altitude is an environmental factor that interrelates various indices that determine the climatic conditions in an ecological niche.

2.5 Rainfall:

The rainfalls are also an important factor influencing cultivation of MP. The main source of water for the soil is rainwater. Rainfall and snowfall have a large effect on the climate condition. The water from rainfall flows into the rivers and lakes percolates into the soil to form groundwater, and remaining is evaporated. The minerals in the soil get dissolved in water and are then absorbed by plants. Water influences morphological characteristics, as well as the physiology of MP. Continuous rain, can lead to a loss of water-soluble substance from leaves and root by leaching; this is known to apply to some plants producing glycosides and alkaloids.

2.6 Water supply:

The place for cultivation is very important for the growth of a given culture as well as for the proper irrigation. It is substantial to avoid the formation of swamps or stagnant waters. MP cannot be cultivated in heavy and water retaining soils.

Depending on water supply, different types of soil exist:

- High water supply: irrigated land (sprinklers) or big volume of rainfall,
- Low water supply: dry land (trickle irrigation).

The adequate soil for the cultivation of MP is the one in the dry zones. It is proven that in such type of soil, the quality and abundance of essential oils in plant biomass is higher than in the irrigated soil. For instance, such tendency is found during cultivation of lavender, thyme, rosemary and St John's wort. In addition, good yields have been registered with cumin, fennel and aniseed.

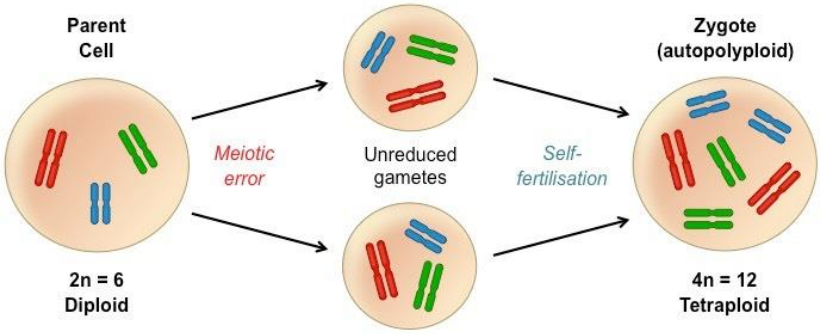
The irrigated soil is suitable for cultivation of a number of species like mint, basil, peppermint, valerian, used as a whole plant either their leaves or root.

2.7 Plants polyploidy significance – ecological considerations

Plants cells that contain two sets of chromosomes, derived at fertilization from the union of one set from the pollen and one set from the egg cells, are named diploids and denoted by “2n”. The term polyploidy is applied to plants with more than two sets of chromosomes in the cells; when four sets are present, the plants are described as tetraploids and denoted by “4n”.

Tetraploidy is induced by treatment with colchicine, which inhibits spindle formation during cell division so that the divided chromosomes are unable to separate and pass to the daughter cells. The two sets of chromosomes remain in one cell and this process results in tetraploid plants.

Treatment with colchicine may be applied in different ways. Besides, all the treatments depend on the effects they produced in the meristem tissue. For instance, the seeds may be soaked in a dilute solution of colchicine. Alternatively, the seedlings, the soil around the seedling or the young shoots may be treated with colchicine solution. The tetraploid condition is designated by the increased size of the pollen grains and stomata, and by chromosome counts in root-tip preparations. These robust and healthy tetraploid plants represent ecological advantages, since they are easily grown with good harvest yields.



2.8 Heredity, variability and ecology

Mutation:

Any heritable change in the structure of a gene on a chromosome or change in the chromosome number is denoted as mutation. Plant mutations can be classified by their way of induction (spontaneous and induced mutations); the time of their phenotypic appearance (recessive and dominant mutations); the type of cells they affect (somatic and germinal mutations); the type of genetic material they affect (chromosomal, genomic and point mutations), and mechanisms of action (forward, back and suppressor mutation).

Certain agents, called mutagens or mutagenic agents can artificially produce induced mutations. The basic types of mutagens are classified as physical mutagens and chemical mutagens.

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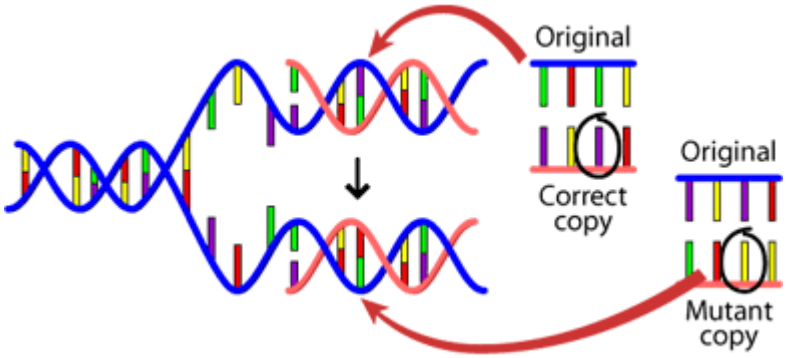

Hybridization:

A hybrid is the resultant of mating or crossing two genetically dissimilar plants with desired genes or genotypes that are brought together into one individual. Hybridization is the process through which hybrids are formed. A hybrid is an organism, which results from crossing of two species or varieties differing at least in one set of features.

Hybridization between homozygous strains, which have been inbred for a number of generations, introduces a heterozygosis effect that results in better vigor or plant dimensions and in other characteristic of the plants.

The procedure for obtaining hybrids, including from MP encompasses the following steps:

1. Choice of parents: between the two parents to be selected, at least one should be as well adopted and proven locally variety.

2. Emasculation: the process of removal of stamens or anthers, or killing the pollen grains of a flower without affecting the female reproductive organs. Emasculation is essential in bisexual flowers.

3. Bagging: immediately after emasculation, the flowers or inflorescences are enclosed in bags of suitable sizes to prevent random cross-pollination.

4. Pollination: mature, fertile, and viable pollens are placed on a receptive stigma.

5. Raising F1 (first-generation) plants: pollination is followed by fertilization. Fertilization results in the formation of seeds. Mature seeds of F1 generation are harvested, dried and stored. These seeds are grown to produce F1 hybrids - robust and healthy.

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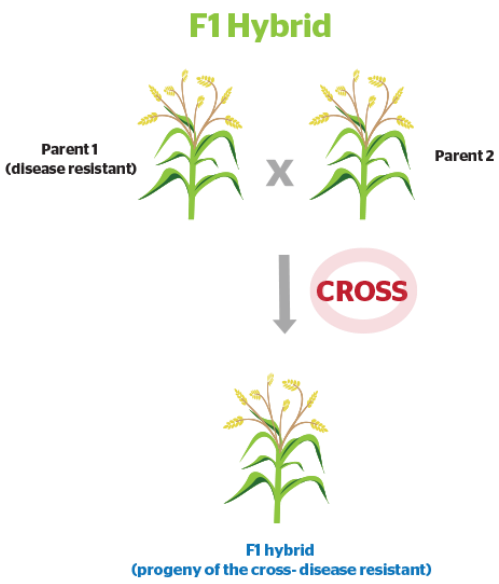
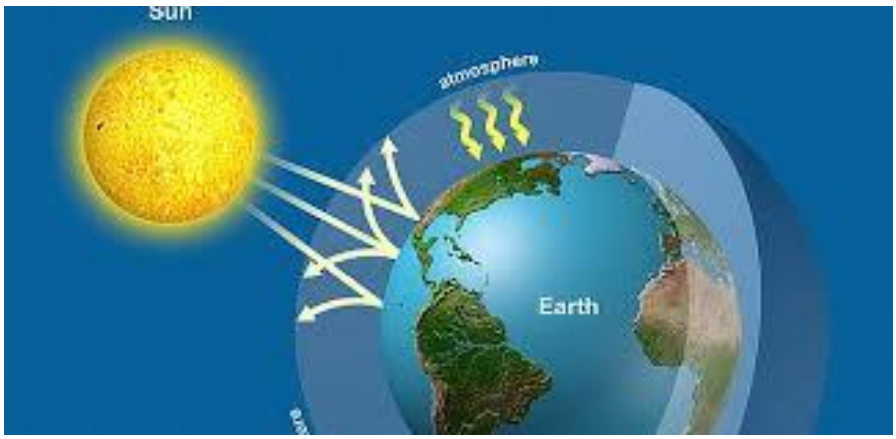


2.9 Greenhouse effect:

In norma, sunrays reach the earth and the heat is radiated back into space. However, when carbon dioxide concentration increases in the atmosphere, it forms a thick cover and prevents the heat from being re-radiated. As a consequence, the atmosphere gets heated and the temperature elevates. This is called greenhouse effect. In the recent pass, amount of carbon dioxide has increased from 290 ppm to 330 ppm due to the cutting of forests and excessive burning of fossil fuels. The rate at which the amount of carbon dioxide in the atmosphere is increasing, it is expected to cause the rise in global temperature. The so-called global warming by two or three degrees would cause polar ice caps to melt, floods in coastal areas, change in the hydrologic cycle and islands would get submerged. The gases producing greenhouse effect are carbon dioxide, sulfur dioxide, oxides of nitrogen, chlorofluorocarbons, etc.



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Unit 3: Introduction of protected and endangered MPs into cultivation – impact on biodiversity

3.1 Introduction

Medicinal Plants (MP) are useful natural resources, which over-exploitation can cause shortage of various herbs and suppression of the development of several species in nature. To meet the rising quest for these plants, it becomes very substantial to conserve the above mentioned species either by a way of large-scale cultivation or through forest conservation measures for their sustainable use. The accent should be on the cultivation of the medical plants as regular crops, instead of collecting them from the wild in order to guarantee the botanical identity, genetic improvement, quality and continuity in supply.

3.2 Wild or cultivated plants

From the beginnings of agriculture, the opinion for medicinal efficacy of wild plants is diminished or absent after cultivation is performed. The question about wild versus cultivated seems as old as the practice of agriculture itself. By theory, the cultivation of wild plant species is linked with gene pool diminution, sometimes drastically. In fact, depending on the mode of the plant reproduction and the number of individuals produced during original selection from the wild, the plant's ability for adaptation to variation of conditions and to withstand healthy may be compromised.

The biodiversity also could be affected and can influence the plant quality. In general, the wild ecosystem is used as a model for establishment agricultural conditions. The majority of conventional agricultural practices diminish the numbers and varieties of soil microorganisms. As the plant nutrition depend strongly on the metabolic byproducts of millions of other (micro) organisms living in this environment, a reduction in microflora biodiversity in the environment will affect plant health.

3.3 The influence of Bad Cultivation Practices

The "wild or cultivated" problem runs very deep and dues to alter the perception of the relationship with nature. In case of human population, activity has influenced wild habitat, many medicinal plants have become sparse or peril and many people consider the cultivation of medicinal plants as an ecological problem.

Throughout the development of this process of cultivation, a spectrum of practices has been introduced, from pre-agricultural gathering to high-tech industrial agriculture. During this process, the biodiversity in the agricultural ecosystem does not correlate to the degree of

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industrialization. If a crop possesses minimal genetic diversity it can easily be wiped out by a single type of predator.

The human trend to make, in order to save labor, a profit, and thus neglecting nature principles, works against people over the long term. All these practices devoted to quick profits in industrial agriculture are not reasonable. These are pedigree breeding and monoculture, systematic elimination of microorganisms due to the use of unnatural fertilizers, herbicides, and fungicides; genetic engineering, etc. In addition, the seed companies' merger caused continuous loss of biodiversity over the past century. In order to repair this damage, it is necessary to learn the natural requirements for plants cultivation. This challenge comprises a new awareness and respect for natural processes and can be realized through implementation of scientific advances.

3.4 Cultivation of MP on commercial farmlands and private land

The cultivation of MP on community lands is well established. There is also good processing and marketing expertise available. The easy access to resources as well as to international and traditional markets is organized. Additionally, the robust nature of some of these crops to stand testing weather conditions contributes to the positive income of these activities. However, the cultivation of MP on commercial farmlands is not that large as needed.

The demand for medicinal plants is large and increasing at a fast rate. The provision of such plant material is not as much as is required by the pharmaceutical industry. The supply is not adequate and it is considered that a useful approach to enlarge and strengthen this supply is to provide cultivation of medicinal crops on private land. Besides, many pharmaceutical companies have started to contract the cultivators directly by providing planting material and know-how.

The cultivation of medicinal plant species by farmers on private land was considered as useful in many regions because it brings increase in both the income and the employment. The cultivation process is performed for indigenous plant species, as well as for completely new crops for these districts of land.

Various case studies with farmers and manufacturers indicated important factors that justify cultivation of medicinal crops on a commercial scale. The major ones are as follow:

- Remarkable range of the demands and stable economic forecasting for growing demands;
- Culturally well-embedded cultivation practices;
- Better relative income for the farmers from MP cultivation in comparison with other crops;
- Better output in cultivation of MP in comparison with other crops, since the cultivation of the former requires fewer resources and is relatively easy;
- MP provide guaranteed markets and prices;

- MP generate larger employment than the seasonal crops; however, specific investments are often essential to start production and the return on investment is less predictable.

It is obvious that the cultivation of MP on both commercial farmlands and private land is necessary to cover the provision of quality raw material to the industry on one hand and to conserve the species identity on the other. MP producers and processors generally agree that marketing opportunities do exist but there are many problems to be solved and increased governmental support is clearly needed.

The main problems are:

- Lack of commercially manufactured specialized machinery;
- Lack of suitable storage and drying facilities;
- Lack of commercially available seeds of high quality (high-yielding cultivars)
- Lack of knowledge on crop-specific management (especially fertilizer requirements;
- Lack of approved herbicides/pesticides and harvesting techniques;
- Commercial problems sometimes outweigh the feasibility of cultivation projects due to marketing reasons.

3.5 Conservation methods

Different methods are used to avoid potential danger and existing threats to MP species. These are *in situ* and *ex situ* conservation techniques. The conservation method is determined by the biological peculiarities of the species and their sources of raw material. According to the source of raw material, MP species have been divided into three groups: sufficient, limited and insufficient.

- The species with sufficient sources of raw material are exploited like common species.
- Widespread species are characterized by a large phenotypic diversity but with low sources of raw material. Wild populations of these species are not endangered in their natural habitats. Nevertheless, sampling of their diversity has been initiated to ensure their further use in breeding.
- Species with low sources of raw material and narrow ecological adaptation are difficult to introduce into cultivation. This group of species includes rare and endangered plants.

3.6 Challenges in conservation of medicinal plants

3.6.1 Improving the conservation of medical plants through agriculture

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The industrial agriculture spread intensively during the 20th century, and consequently, the understanding about the necessary changes in the natural policy context. The development of ecology in the second half of the 20th century contributed to the changing views of humans in nature. The work of the ecological scientists and created innovators in ecological agriculture offers a series of practices known as Nature Farming.

A special attention was given to the cultivation of perennial plants for food called Permaculture ("permanent agriculture"). The Permaculture and other ecological practices, consider wildness as an essential feature in preserving biodiversity and the capacity of the system in adaptation to changing conditions.

Wildness can be created in small scales like hedgerows dividing fields or in bio-strips among rows in a mixed cropping system. Meanwhile, the re-creation of wildness has become the tool for amazing innovation in the current times.

3.6.2 The conservation and the re-creation of wildness

The recent years highlight the concept of the value of wildness and biodiversity to help for understanding about how individual species contribute to the whole. It became apparent that the interactions of a wide variety of species create a dynamic, self-regulating system that takes on a life of its own. Thus, life seems to attract life. The presence of the "pests", do not influence the healthy plants and the balance of the particular ecosystem approximates that of the wild. Therefore, the existed destruction of MP habitat as well as other related worldwide threats, pose the question of how to preserve the conservation avoiding further breakdown?

Therefore, the existed destruction of MP habitats as well as other related worldwide threats, pose the question of how to preserve the conservation avoiding further breakdown? It is necessary to assign the value of a threatened species in order to save it because it will be easier than further to develop value. Nevertheless, the so-called "wild-simulated" or "wild-cultivated" methods are even more closely related to nature.

3.6.3 Conservation through protection

Conservation of MP can be influenced by their protection status. There are two important factors that must be taken into consideration: the harvesting restriction laws concerning certain species; and the amount of material needed for propagation, cultivation, and sustainable harvesting. In some cases, the conservation of MP species by protection is working well. In protected areas, the species come under less threat from illegal harvesting by MP gatherers. There is also less evidence of ring-barked medicinal plants, in protected than in unprotected places. Successful conservation through the protection of species has been implemented in some important places like the Kruger National Park, Hluhluwe Game Reserve, and Mkhambathi Nature Reserve. However, this approach cannot be effectively implemented everywhere, as it shows some drawbacks for MP gatherers. For this reason, a continuum model of managing MP that starts from the wild, without

cutting or stepping, was worked out by communities. This model requires no labor in managing the plant species. On the contrary, it is grounded on the assumption that if the species is of people concern, weeding can take place while the species is in the wild. Although, this requires energy input, weeding of protected MP enables management in their own growing environment and thus, contributes to their conservation.

MP conservation through protection has also social perspective. Traditionally, women are the main player in medicinal plants-based activities of micro-enterprises as they fit easily within their work schedules. These activities often represent the collection and transportation of MP raw materials to the market.

On the other hand, these small businesses help to the preservation of traditional knowledge and give an opportunity to enterprises to employ youth and poor rural people.

The significance of traditional plant knowledge is obvious by the need for 'bioprospecting' including recruiting of native people in order to recognize the uses of local flora as well as the need to protect intellectual rights. There are social beliefs that 'facilitate' medicinal plant conservation. However, there is some decrease in the utilization of traditional food, because their use was associated with poverty. Many households rely on commercial food to avoid the stigma of being considered as poor due to relying on traditional food plants.

3.6.4 Conservation through management of genetic resources and genetic stability/variability

The modern approaches in determining genetic variability most commonly use three types of genetic markers– morphological, biochemical and molecular.

- Morphological markers (e.g. plant height, leaf shape, color, etc.) are the oldest and most widely applied in the determination of genetic stability/variability. However, they lack specificity because gene expression under various environmental conditions may lead to great variability of phenotypic characters in individuals.
- Biochemical markers (e.g. albumin content, isozyme profiles or content of essential oil in an individual organism) are also regarded as non-specific because biochemical characters are quite variable and strongly influenced by an individual's environment.
- Molecular markers are on the playground since the 1980s together with the development of recombinant DNA technologies. Molecular markers comprise a modern tool for determining genetic variability. The represent variability among individuals on the DNA level, which is absolute and not influenced by the environmental conditions.

Molecular markers exploited for confirmation of genetic stability/variability possess different properties, among which various advantages and disadvantages. Thus, they can be classified as dominant and co-dominant markers; markers with different genome coverage; markers with different specificity, cost, ease of analytical interpretation of the resulting data, etc.

Despite this abundance, molecular markers are all highly informative about genetic variability among individuals, populations, and cultivars. Thus, their use is universal for not only plants but also for all living organisms.

Within this context, molecular markers can be considered as essential tools in MP for:

- Cultivar identification (DNA typing) and genome mapping;
- Research and evaluation of genetic stability, variability, and relationships;
- Management of genetic resources and biodiversity;
- Study of phylogenetic relationships.

Among these practical applications, the management of genetic resources and their conservation are considered of crucial importance.

The main objective of the management of genetic resources is to ensure conservation of the existing genetic diversity of species as much as possible. The effectiveness of this process depends largely on the genetic information available on the germplasm under study.

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Molecular markers provide direct genetic information for *ex-situ* and *in-situ* conservation. For *ex-situ* conservation, the acquisition of data on the diversity of collections is important. For these purposes, molecular markers can be used to:

- Recognize valuable genetic variation that is under-represented in a collection sample;
- Identify duplicate accessions and to monitor changes in genetic structure as accessions are generated;
- Assess the available genetic diversity for each species;
- Provide precise and detailed information compared to that obtained by classical phenotypic data analyses;
- Identify traits and types quickly.

From fundamental point of view, the information about molecular markers may lead to further identification of useful genes contained in a collection.

Molecular data on biodiversity provide essential information to establish core sites that accurately represent the entire collection.

For *ex-situ* conservation, molecular markers are used in:

- Determination of identity and/or similarity of accessions or individuals;
- Measurement of the structure of diversity among individuals, accessions, populations and species; and the detection of a particular allele or nucleotide sequences in a taxon, gene-bank succession or *in-situ* population.

3.6.5 Conservation through sustainable harvesting

Another method of conserving medicinal plants is sustainable harvesting of their parts, such as sustainable removal of roots and barks when plants are harvested. For instance, it is shown that the barks of the trees are able to regenerate after the harvesters placed mud on the areas where the bark was removed. In fact, this method allows the survival of the species in their own habitat. However, the application of the sustainable harvesting method is difficult, especially in case the MP gatherers intend to generate revenue from selling and gathering the plants. Although

cultivation ensures long-term survival for the species, there are problems that appear through prolonged periods of the process.

In addition, there are also challenges faced by MP sellers with regard to conservation through harvesting. Many people rely seriously on traditional medicine. The reasons causing high rates of unemployment, urbanization, clearing of vegetation for agriculture and land use, and low levels of formal education are all factors leading to high demand for medicinal plants. All these occasions are linked with over-exploitation of medicinal plants, especially for commercial gatherers to receive income. Exploitation of inappropriate methods of harvesting the medicinal plants has led to a decline in many medicinal plant species, while others are the reason for extinction.

The medicinal plant trade is real and important local economic sector, actively used in many countries and overharvesting of MP, particularly of roots and seeds have reduced the regeneration of potential species. High unemployment rates, especially among women, make harvesting and selling of medicinal plants a popular alternative for their families. Hence, the great demand for medicinal plants, eventually exceeding that, which can be supplied by the wild. The bulk of medicinal plants on the markets is harvested from wild populations and in combination with increased pressure from human habitation, has let to numerous local extinctions.

The shortage of popular medicinal plants has increased the market prices. Besides the escalating prices, additional problems like poor quality of the plant materials, insufficient product stabilization, and trading conditions are arising simultaneously. This makes a serious problem and may threaten:

- The health-care services by the problems that can be caused to people using medicinal plants;
- The biodiversity of resources due to the high pressure of harvesting medicinal plants; and
- The livelihoods of people depending on the trade.

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In this way the, sustainability of the medicinal plant business depends on the majority of the medicinal plant sellers using profit from the medicinal plants for their livelihoods. There is a need to introduce special educational programs that enable the medicinal plant sellers to reflect on the issues that challenge their business.

3.6.6 Conservation through legal protection practices and education

In addition to sustainable harvesting and cultivation, legal protection conservation practices also have an influence on MP conservation.

The provided efforts to sustain the populations of medicinal plant species applying national legislation in most cases have been unsuccessful. The reason is the aggressive behavior of the people invading protected areas and causing significant harm to medicinal plants.

Besides the governmental activities to mitigate the effects of threatened medicinal plants, there are measures initiated to restrict the collection of MP in order to prevent the depletion of the wild plants. In fact, a lot of efforts are still necessary to ensure medicinal plant gatherers to respect the regulations preserving medicinal plants from being used up to extinction. Although the Departments of Agriculture in some countries had introduced permits as a control measure against the unsustainable harvesting of some medicinal plants, this still does not stop the illegal removal of the species from the wild population.

Legal restrictions to strengthen the preservation of MP by governing their access and removal have to be in place. Development and implementation of commercial regulations for harvesting and trade of medicinal plants, including requirements for protection of herbs are very important.

The goal in a long-term perspective is to achieve a careful balance between restricting access to plants (to encourage economic opportunity) and to assure biodiversity conservation.

All these facts show that education in the field of conservation is of primary necessity. It could increase awareness regarding the methods that could be used to conserve MP species.

3.7 Production-oriented dynamic preservation of threatened MP

According to a recent study of the commercial importance and the threatened status of MP in Europe, about 150 species were reported to be threatened in at least one European country because of over-collecting from the wild, inappropriate trade and habitat loss. Some of the threatened medicinal plants are cold tolerant. They are particularly suitable for cultivation and possible raw material production.

By producing raw material from controlled farming systems the economic pressure imposed on some threatened plant species will be decreased, and additional income to the growers specialized in herb production will be guaranteed.

The successful schemes for dynamic preservation and conservation of MP results of plot experiments have to be checked in semi-large scale experimental conditions before educating the growers for production of these new medicinal plants.

The trade in European medicinal plants is long established but has been growing rapidly over the past decade. The conservation community, concerned practitioners and the more aware consumer are calling for sustainable herbal products. Unfortunately, at present only few companies are concerned about sustainable and ethical sourcing.

Cultivation is generally seen as the main solution. Indeed, there is much to be said for cultivation both from a commercial as well as conservation point of view. Cultivation cannot be the sole solution in the context of a complex trade in many hundreds of species, predominantly harvested from the wild, providing livelihoods for large numbers of people in numerous European countries.

Efforts of domestication are coupled with measures to achieve sustainable management for controlled wild harvesting.

The potential strategies, aimed at more sustainable sourcing are highlighted and some of the existing initiatives of WWF-UK and WWF-Germany/TRAFFIC Europe Germany are as follows.

- European Plant Conservation Strategy and its specific MP target;
- The Global Strategy for Plant Conservation of the Convention on Biological Diversity (CBD);
- ECP/GP Working Group on Medicinal and Aromatic Plants.

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Unit 4: Organic cultivation of MP – the research, the commercial and the conservation points

4.1 Organic cultivation of MP – current and future research activities

Main trends of investigations on MP are focused on biology, diversity, and population mapping, as well as on breeding, selection, and introduction of wild MP. Additionally, the research in the field of bio-ecology, amelioration and culture technologies for medicinal plants (MP) has an important role in the increase of production of cultivated species.

MP cultivation on scientific bases:

- Assures the necessity of vegetal raw material for the industry of medicines;
- Guarantees a product rich in active compounds and more homogenous, without substitutions and forgeries;
- Allows harvesting to be done at the optimal moment (when the content in active compounds is maximal) followed by drying or processing in fresh state;
- Help acclimatization of new species that do not grow spontaneously in defined region;
- Facilitates protection of the plants, considered monuments of nature, etc.

High productions of raw material rich in active compounds can be obtained only by the application of technologies of differentiated culture, based on the solid knowledge of biology and requirements of plants compared to the factors of vegetation.

The current and future research trends in MP cultivation encompass the following topics:

- Strengthening / establishing local seed production;
- Surveying the distribution of available genetic diversity together with analyses of genetic erosion;
- Investigations throughout the production-consumption chain;
- Identification of improved agronomic and production procedures and application of value-adding strategies
- Analysis of market opportunities;
- Research on nutritional value of the species, and characterization and evaluation work;
- Development of networks;
- Studies to identify MP cultivation policy failures'
- Development of a database on biodiversity conservation;
- Studies of local and foreign ethnobotanical uses, plant toxicity to humans and animals, chemical constituents and pharmacological uses;

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- Evaluation of morphological and chemotaxonomic characteristics of MP;
- Evaluation of MP ecotypes for quantitative and qualitative differences in secondary metabolites with regard to growth and development and/or biological activity;
- Evaluation of susceptibility to environmental stress (drought, low temperature, depleted soils, etc.)

The perspectives in expanding research activities on PM are concentrated on:

- Encouraging the collectors to provide specimens to the national herbarium collections.
- Promotion the collaboration between national programs working on the same plants/groups of plants through facilitated collaboration and coordination of target teams.
- The need for the development of harmonized methodologies/protocols (sampling and conservation techniques, etc.) by the national and international research programs.

4.2 Management of MP cultivation, harvest and post-harvest processes for their commercial uses

In cultivation, the management activities encompass the following processes:

- Preparation
- Sowing and transplanting
- Manures and fertilizers
- Irrigation
- Weeding and intercultural operations

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- Crop protection

The management of harvest and post-harvest processes include:

- Harvesting
- Primary processing
- Packaging, storage and transportation

All these processes when correctly and efficiently performed create added value, which is substantially important for the MP commercial exploitation as well as the medicinal value of the raw drugs. The added value of the medicinal plants can be accomplished directly (**direct added value**) by getting a better quality of the cultivated or collected plant material or indirectly (**indirect added value**) - through quality assurance during processing of the material to valuable products.

Direct Added Value

The about preservation measures of MP materials often is neglected by respective experts. The dangerous conditions can be minimized by proper cleaning, packing and storage. All the processes listed below generate direct added:

- Proper season collection
- Grading and sorting
- Cleaning
- Packaging
- Storage
- Categorization of MP

Indirect Added value

The indirect added value is evaluated by quality testing for purity and strength of MP. It also includes testing for the physical-chemical standards (moisture, FOM, ash content, extractives, etc.):

- Moisture
- Presence of external matter
- Ash Content
- Extracts
- Pesticides residues
- Microorganisms

4.3 Semi-processing of MP to value-added products

The application of semi-processing processes also results in value-added MP products. The semi-processing techniques are simple and fast for performance and add to the value of the MP

material preparations. The resultant products/preparations are offered in the most popular types of formulation: as a powdered substance, tablets, capsules, and extracts.

4.4 Troubles and limitations for MP management

- Lack of information on wild MP and their geographical distribution, and proper utilization;
- Lack of information in the study area on the ways to improve commercial exchange;
- The variation in the local names of one and the same plant or in one and the same country is a restriction in producing helpful information;
- The proper management of MP raw material along the chain from collection to processing requires the cooperation of researchers and technicians of various organizations and institutions;
- The deficiency of research in the development of techniques for propagation and regeneration of MP in their natural habitats.

4.5 Constraints to the development of MP trade

Cultivation of medicinal plants faces a number of problems. Partly, these problems are due to the typically small scale of operation and performance. However, biotechnological, administrative, legislative, social, etc. factors must not be underestimated.

Some key features of the trade with MP, endangered by these problems are connected to the:

- Increasing pressure on the natural resource for the MP that are in greatest demand;

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- Constantly increasing market for the MP materials that are used in health and medical products;
- Expanding international trade with MP.
- Improvement of the regulatory basis;
- Lack of detailed and accurate information available.

The major problems include the following areas:

1. Cultivation and harvest:

- Small land holdings of the MP producers (the majority);
- Shortage of labour in some rural areas, especially those at high altitude;
- Long lag periods between MP growing and harvesting;
- Bureaucratic obstacles in obtaining permits for cultivating restricted/endangered species;
- Difficulties in cultivating MP (especially in high altitude areas) due to lack of technology and technical facilities;
- Poor quality and/or lack of planting material;
- Limited knowledge of plant properties;
- Prices are too low to make cultivation attractive.

2. Post-harvest processing

- Continuing and commonly abandoned problems with packaging, storage, transportation and quality control, even in cases of well-developed technologies;
- Gap between research activities with MP and MP producers' experience and needs. The latter usually are not included in the R & D schemes;
- Weak relationship between research institutes and industry;
- Bad practices in harvest and post-harvest treatment;
- Lack of research on development of high-yielding varieties, domestication, product and process development;
- Inefficient processing techniques leading to low yields and poor quality products.

3. Quality control, marketing and trade

- Poor quality control procedures;

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- Difficulties in marketing;
- Lack of local markets for primary processed products;
- Lack of access to latest technological and market information;
- Lack of knowledge of their supply capabilities;
- Lack of information and mechanisms for protection of IPR.

4.6 Future trends and areas for improvement of MP cultivation

The listed above problematic elements of the complex procedures of cultivation and processing of MP can be overcome through the application of mitigation measures at several stages and directions. Future measures for overcoming these obstacles can include.

- Establishment of a critical mass of cultivable land in order to guarantee larger consistent supply of MP;
- Reduction of the intermediary numbers/stages involved in the distribution and marketing chain;
- Increase the intermediary role of the producers and collectors.
- Making improvements at post-collection handling, value addition, and product presentation stages;
- Promoting R & D activities on the chemical composition and elimination of the effect from bad practices on the active ingredients of the selected species;
- Development of efficient strategies and corresponding action plans by the country authorities to support improved cultivation, quality controls systems;
- Provision of high-quality planting materials and encouragement of investments in new technologies;
- Performance in-depth global overview of the demand / supply of MP, MP products, and MP drugs in order to clarify market status, to forecast, and to consider more effective solutions;
- Promotion of sustainable cultivation of MP and entering markets at the early stages of the value chain by better supply of manufacturers with unprocessed raw materials;

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- Encouragement of sustainable commercial development and industrial processing of preliminarily identified MP products, which would be most amenable to in the supplying entities;
- Value-addition through processing;
- Stimulation the more equitably sharing of the benefits from the expanded interest in MP;
- Improving the MP marketing.

4.7 Constraints for the economic expansion of MP

- Needs of field studies on the cultivation of MP;
- Inadequate knowledge of the export companies and personnel about standards restrictions. This results in low prices for medicinal herbs and drugs;
- Lack of technologies for MP management and supplies;
- Lack of marketing information regarding the international organizations dealing with MP for capturing world market share.

4.8 Suggestions

- Development of strategies for collecting, surveying and identification of MP, their habitats and field studies for their regeneration;
- Development of a state level R&D centers for MP;
- Encouragement of SMEs to supply the local markets with medicinal and aromatic commodities;

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- Introduction and cultivation of non-native (exotic) medicinal plants under the different climatic and edaphic conditions of the area.
- Encouragement and financing of research programs on regeneration and management of important MP.

4.9 Ecological perspectives of medicinal plant preservation

Land degradation and forest conservation caused reduction of medicinal plant availability. It is known that turning natural forests into agricultural fields has changed the number of medicinal plant species and their distribution in timber plantations. The inadequate information on ecological productivity, growth forms, life history and conservation of the various species complicates harvesting levels of medicinal plants by medicinal plant gatherers.

In fact, the ecology of the species can help a particular species to survive over-exploitation. Such event is described for some MP living in dormancy in certain seasons, particularly winter, and that becomes more readily available in rainy seasons such as summer and spring.

Another important ecological factor is the difficulty of collecting plants, which are visibly present.

There is also another factor that defines the medicinal plants' existence is ecological processes performed by humans, such as herbage fires.

Anthropogenic factors can decline the native medicinal plant species and must be protected through the collaborative activity of all the stakeholders included since MP possess vital importance for society.

4.9 Cultural practices in medicinal plant conservation

The usage of wild plants, including medicinal plants, is connected to cultural peculiarities of all nations. It is known that wild plants are a major source of edible fruits, leafy vegetables, and traditional herbs. They are especially important for food security and keeping the balance of people's diets.

Wild plants are very important for human survival especially in the time of starvation and they have different functions: to prevent the need for cash expenditure and to ensure a source of income to cash-poor households.

Due to alterations in the usage of land for commercial crops, the plant numbers diminish from their natural environment. In addition, the over-harvesting for marketing purposes and clearance of vegetation for industrial development, made the cultured practices associated with the plants to fail away.

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The modern culture and development of modern medicine have also change the alignment and extent of local knowledge and use of medicinal plants in the societies. It has been found that indigenous knowledge is declining in Europe because of technology and modern commercial food. The credibility of the elders has been given through documenting the identification and use of medicinal plants. They are concerned because the youth people are losing the native knowledge that could be utilized to cure diseases. Thus, rapid social change can also affect local knowledge of MP and the interest in their use.

In order to promote conservation, livelihood security, healthcare and local culture, educational documentation of MP and their functions is recommended. The native knowledge has always been looked down upon and being secret. For instance, if someone had knowledge about a special herb able to cure a serious disease, one's grandfather might appear in a dream to tell one who should be given the privileged information about how the herb should be used.

Unlike native medicinal practitioners, scientists are characterized by both cooperation and competition. They performed one another's claims to careful scrutiny by repeating experiments to verify the results of others. This represents a system of quality assurance. The same cannot be said of the native practice.

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Unit 5: Benefits and social impact of MP organic cultivation – success stories

Summary

In Unit 5 the benefits and social impact of MP organic cultivation are discussed with an exemplary success story related to MP cultivation. The characteristic features of organic cultivation of MP and its economic and social advantages as well as the opportunities for MP organic cultivation are presented. The success story of *Aloe vera* cultivation is given as an example for positive social and economic benefit.

Learning outcome descriptors

By the end of the Unit, the trainee should be able to:

- ✓ **Knowledge, understanding and professional skills:**
  1. Specify the characteristic features of organic cultivation of MP and its economic and social advantages
  2. Outline the opportunities for MP organic cultivation
  3. List the benefits and social impact of MP organic cultivation
- ✓ **General and transferable skills:**
  1. Plan a research task.
  2. Work independently or with a minimal guidance where appropriate.
  3. Work in team with minimal guidance where appropriate.
  4. Show good written and oral communication skills.
  5. Demonstrate computer literacy
  6. Perform online (computer) search to develop information technology skills in order to retrieve information from a variety of sources.

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5.1 Introduction

Herbal medicines are widespread and their consumption considerably increases. However, their harvesting from the wild plant populations, which are the main source of raw material, can cause loss of genetic diversity and habitat destruction. Domestic cultivation is a vital alternative and gives an opportunity to overcome the problems that are inherent in herbal extracts: misidentification, genetic and phenotypic variability, extract variability and instability, toxic components and contaminants. The control of the environmental conditions can help to overcome cultivation difficulties and could be a tool to change phenotypic variation in bioactive compounds and toxins. Conventional plant-breeding methods can improve both agronomic and medicinal traits, and molecular marker-assisted selection will be used increasingly. There has been significant progress in the use of tissue culture and genetic transformation techniques to alter pathways for the biosynthesis of target Medicinal Plants (MP) metabolites. Obstacles to bringing MP into successful commercial cultivation include the difficulty of predicting which extracts will remain marketable and the likely market preference for what is seen as naturally sourced extracts.

5.2 The advantages of organic cultivation of medicinal plants

The advantages of organic cultivation can be briefed as follows:

- It ensures the high quality and purity of medicinal plants. The crude drugs are recognized on the basis of the presence of the chemical contents in them and on their purity. The collection of crude drugs from cultivated MP gives a better yield and therapeutic quality. However, it requires some skills and professional expertise. Such practice can let to collecting drugs with higher therapeutic quality and yield. For example, these are the collection of latex from poppy capsules, oleo-resins from *Pinus* species, preservation of green color of *Senna* leaves and minimizing the deterioration of cardiac glycosides in freshly collected leaves of *Digitalis*.
- If in the process of cultivation, all the operations are uniformly maintained, a drug with the highest purity can be achieved like ginger, turmeric, and licorice.
- In the cultivation of rhizomes, an adequate supply of irrigation and fertilizers is necessary. Systemic cultivation can yield crops with higher purity.
- Cultivation ensures a regular supply of crude drugs and minimizes the problem of shortage of raw material by properly planning a crop-cultivation.
- The substantial result of the cultivation of MP is a greater extent of industrialization. For example, cultivation of coffee and cocoa has given rise to several cottage industries. The very important consequence is that cultivation of MP permits application of modern technological aspects such as mutation, polyploidy, and hybridization.

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The major disadvantages of organic cultivation include the high cost of drugs as compared to wild varieties and loss due to ecological disturbances like storms, earthquakes, floods, droughts, etc.

5.3 Opportunities for Medicinal Plants organic cultivation

There is a variety of prospects for MP cultivation from biological, medicinal, economic, etc. viewpoints. The most promising among them are focused on the:

- Extensive use of alternative medicine. Contemporary medicine is integrative - it combines conventional and alternative treatments, for which there is evidence of safety and effectiveness.
- Preference for natural products and chemicals from herbs. In the pharmaceutical industry, where the active medicinal substances cannot be synthesized economically, the product must be obtained from the cultivation of plants. Planned preservation and large-scale cultivation of the respected MP are of great interest. The versatility of biological actions can be attributed to the huge amount and wide variety of secondary metabolites in plant organisms, belonging to several chemical classes as alkaloids, coumarins, flavonoids, tannins, terpenoids, xanthones, etc.
- Dwindling of forest cover, reduced supplies from natural habitats, and threatened biodiversity. The majority of MP, even today, are collected from wild. The continued commercial exploitation of these plants has caused fading the population of many species in their natural habitat. There is some lack in the supply of raw plant materials necessary for the pharmaceutical industry and for the traditional practitioners. Thus, the cultivation of these plants has to ensure immediately their availability to the industry as well as to persons engaged with traditional medicine.
- Availability of markets (global/national). Market demands on MP are stabile according to the economy statistics and forecasts (Eurostat). Apparently, cultivation of medicinal plants could only be promoted if there is a continuous market demand for the raw materials. On the other hand, it is equally important to prepare genetically stable planting material to ensure its uniformity and desired quality.
- Availability of high yielding varieties. Before beginning a regulated cultivation of MP, high yielding varieties have to be selected. When the wild plants are used, they need attentive refinement work. Varieties giving high yields also have to be prepared using selective breeding or clonally micro-propagation.
- Availability of agro-technologies. The regulated cultivation called for specific cultural practices and agronomic demands. They include specific plant strains as well as conditions depending upon soil, water and climatic circumstances. Taking into account the demands of the selected plants, a specific agro-technological package has to be prepared in order

to match the existing infrastructural facilities. The necessary research and development work need to be performed in order to define Good Agricultural Practices (GAP).

- Availability of processing technologies. Cultivation and processing go hand in hand. Smart processing technologies and small-scale processing units have to be established to guarantee the sale of the raw material (cultivation product) and the supply of the processed goods.
- Profitable returns on sustainable basis. The resolution of the use of a closed scale of MP from wild sources has to stand on accurate schedule regarding the kinds of plant resources, abundance, feasibility of harvesting, and preserving the ecosystems.

5.4 **Characteristic features of modern cultivation**

When a cultivation process for MP production is initiated, it is important to take into consideration several parameters: production target, selection of suitable seed, yield and quality.

The management approaches, especially irrigation, fertilization and control against weeds, pests and diseases are also very important. In fact, the MP producers are obliged to apply specialized procedures for selection, harvesting as well as processing and commercialization. All these procedures and schedules should be linked to the requirements of the industry.

Quality of the product

The type of agriculture practices (conventional or organic agriculture) influences product quality. For instance, **organic agriculture production** is characterized with bypassing or excluding the application of synthetic ingredients like artificial fertilizers, pesticides, growth accelerators and fodder additives. Organic cultivation demands more manual and mechanical workforce that usually results in higher price of the final product.

Selection of species

The species selection strongly influences the future success of the MP use. For this reason, it is important to consider not only the climate and soil conditions but also disposable equipment, workforce and facilities, as a tool to obtain maximal yield and efficiency.

Market requirements

The industrial cultivation determines the types of species that are accepted since the MP production is linked to pharmacy, herbal industry, cosmetics and perfumery, as well as nutritional industry.

After admission of all necessary data and selection of suitable species, vegetal material must be obtained for performance of cultivation with technical and specific farm machinery, and afterwards processing of harvested material must be done.

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5.5 Guidelines for harvesting and processing of MP

General guidelines

- Collect only mature parts.
- Do not collect the herbs from Roadsides, Sea Shores, Anthills, near Sewerage etc.
- Start drying process immediately after collection.
- Ensure complete drying before packing and storage.
- Dry aromatic herbs, delicate fruits etc. in shade.
- Store the herbs in properly constructed stores to minimize losses on storage.

Guidelines for collection of different parts of MP

I. Underground Parts & Whole Plants:

- Collect the whole plants after seed shedding.
- Collect underground parts when the mother plant is fully mature.
- Dry fleshy parts before packing and storing. Cut large parts into smaller pieces.

II. Bark and Stem

- Do not harvest from immature Plants.
- Collect from the Branches instead of Main Trunk.
- Strip the bark longitudinally & not all over the circumference of Trunk/Branches.
- Cut into small pieces to facilitate complete drying.
- Harvest only mature branches or stem.

III. Leaves Flowers, Fruits, Seeds and Floral Parts etc.:

- Harvest only mature parts.
- Do not collect from unhealthy plants.
- Do not collect parts manifested with insects, fungi etc.
- Dry flowers and floral parts in the shade. Fleshy flowers may be dried on Sun.
- Rotten and diseased fruits should be segregated from rest of the supply.

IV. Gums, Oils, Resins, Galls etc.:

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- Make vertical incisions only on some portions of the tree. Do not collect the gums or resins from a tree continuously. Collect the gum/resin in the right season.

General requirements in storage of raw drugs

1. Convenient and well-designed space – dry and free from dampness or humidity;
2. Safeguard from rodents, insects, birds, etc.
3. Particular space for diverse grade of raw drugs, e.g. hygroscopic, volatile materials, etc.;
4. Particular space should permit free working of people and equipment;
5. Independent division for “approved”, “rejected” and “untested” raw drugs;
6. Specialized of physically alike looking raw drugs so that identity does not get mixed up.
7. Stamping the raw drugs as follow:
8. Preserve original samples as “reference standards” for each drug in stores;
9. Use raw drugs on a ‘first in - first out basis’ (FIFO);
10. Place packed raw drugs on wooden or plastic pallets; keep one raw drug in one pallet;
11. Use appropriate packing material for storing raw drugs.

5.6 Success story of *Aloe vera*

Cultivation

Aloe vera (Aloe barbadensis) is a popular medicinal plant. It belongs to *Liliaceae* family. It is a perennial plant. Its leaves are long and thick, juicy with a wheel like phyllotaxy. The two sides of the leaves have thorny structure with a thorny tip. The inner substance of the leaves is jelly like, with bad odor and bitter in taste.

It flowers during October to January and the long inflorescence has a large number of small pink flowers all around. Fruits are developed during February to April.

It is normally propagated vegetatively - the propagation is easy and convenient.

World trade of *Aloe vera* is about 80 million US$ dollars exists now and this is likely to increase by 35-40 percent within 5 years. USA dominates the market (65%) other countries have a share of few percent, which could be enhanced by its commercial cultivation.

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Soil and Climate

Aloe vera is growing in hot humid and high rainfall conditions. It is grown in all kind of soils, but well drained one with high organic matter, is most suitable. It grows well in bright sun light. Shady conditions results in disease infestation It is highly sensitive to water stagnation. Therefore, well drained high land should be selected for its cultivation. A rainfall ranging from 1000 – 1200 mm is ideal for *Aloe vera* cultivation.

Seedling Preparation and Planting

Seedlings are normally raised from the plants' roots. Sucker itself can be used as seedlings as well. Rainy season is ideal for sucker plantation.

Land Preparation

About 2-3 ploughings and laddering are done to make the soil weed free and friable. Land leveling is then followed. Along the slope, 45-40 cm apart drainage are made.

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Application of Plant Nutrients

Before the last ploughing, 35 kg N, 70 kg P_2 O5, and 70 kg K_2O/ha are added. In September – October about 35-40 kg N as top dressing may be applied. If the soil is rich in organic matter, N dose can be reduced.

Irrigation and Interculture

After 40 days weeding and earthling up are done. Earthling up is also practiced after top dressing of a fertilizer. *Aloe vera* is slightly tolerant to drought, but very sensitive to water stagnation. Therefore, proper drainage is more important than irrigation. As per need light irrigation during drought is enough.

Plant Protection

Aloe vera is infested by various insects and pests. Special care is needed for their control since *Aloe vera* juice of the leaves is directly taken as medicine. Clean cultivation, interculture operation, regular irrigation, and irrigation on demand, application of adequate organic manure, treatment of sucker before planting, and cultivation of *Aloe vera* in sunny conditions are conducive for the healthy growth of the *Aloe vera* crop. Use of organic materials for plant protection like raw garlic juice, neem oil (10,000 ppm) 2-3 ml / lit, tobacco extractant 20 ml/lit gave the good result.

Yield

In a hot climate, harvesting of leaves starts after 7-8 months of planting. Sharp knife is used for harvesting. Efforts have to be taken to reduce the loss of juice from the cut parts. If harvesting is done once in a year, October – November is the best period. Second-year gives maximum yield and for about 4-5 years, good yield could be harvested. After harvesting leaves, they are dried in shade and then in sun before storage. Flowers are collected in December – January and preserved after proper drying. Yearly 100 – 115 quintals raw leaves and 350 – 400 kg flowers/ha are obtained.

Medicinal Quality

Both the juice of leaves and flowers are used as medicine, but medicines are prepared from leaves. Intake of the juice of leaves improves hunger

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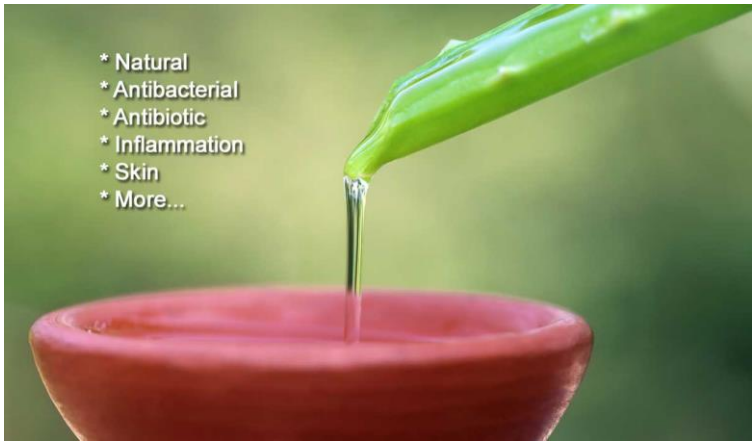
and helps in digestion. Juice when mixed with sugar cures cough and cold. It also cures nervous weakness, asthma, Jaundice, etc. The leaf flesh (about 7-8 g) mixed with honey, taken in morning and evening cures constipation. It contains various organic compounds of therapeutic value. Of these, the main use is alone. Besides, these it contains 12 types of vitamin, 20 kinds of amino acids, 20 kinds of minerals, 200 different types of polysaccharides, and various kinds of glycol proteins, which are used for human health.



Economics

Expenditure to be incurred for *Aloe vera* cultivation normally amounts to a sum that after investment in cultivation provides a good net profit. In addition to monetary benefit, social benefit is very big as well. Better management can results in higher income and net profit.

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Success story of an *Aloe vera* farmer

Three people with a family farm of about 3 ha.

To meet crop needs they used organic manures / vermicompost, etc. prepared by them.

Convinced about the profitability of *Aloe vera* cultivation, they decided to grow this crop. After a year of cultivation, they could get a good amount of profit. The produce is purchased by the local university, which provides technological advice for the cultivation of medicinal plants and their agro-processing. Since produce is purchased by the university, they have virtually no problem of marketing. They plan to start agro-processing unit of their own in future.

The method of cultivation adopted:

1. Land Preparation.

2. Application of about 8 tones vermicompost / ha during last plough.

3. No fertilizer or chemical was applied.

4. The application of ½ kg vermicompost / sucker was applied after establishment of the sucker. The application was again repeated.

5. Hand weeding was followed.

6. Proper drainage facility was provided.

7. Irrigations were provided as and when needed.

8. Number of plants / ha - 2625.

9. Harvesting started after 8 months of planting.

10. In first year three cuttings were given.

11. Yield / ha was 39.4 tons of leaves.

12. From 2nd year on ward 5 cutting were expected.

13. In three years 13 cuttings are expected

14. In three years 170.62 tons of yield per ha is estimated.

5.7 The perspectives

Medicinal plants and their various products can be viewed as important commodity items for sustainable economic development of the country. There is also need for organized marketing and trade of medicinal plants and their various products. To meet the internal and international

demands, it has now become imperative to produce the quality raw materials in significant quantities. This can only be achieved to promote the domestication and cultivation of medicinal plants, which have internal demand in large quantity and have export and import potential.

Pharmaceutical industry includes plant medicines for different kind of diseases and it is now steered up at global level because of its unique approach without side effects. Considerable countries are interested in herbal medicines and they are predicted to have promising future.

Two objectives can be achieved:

i) Utilization of land for additional gain;

ii) Conserving the important plant species, which are now neglected and under extinction due to deforestation. Future generation can be benefited by this kind of action. Some species are on the verge of extinction due to heavy exploitation by pharmaceutical industries. Deforestation resulted in losing the important treasure of unique medicinal plants. It needs now to be cultivated for harmless medicines.

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INNOVATIVE INTEGRATED TRAINING IN
HEALING PLANTS
BUSINESS

Module No. 2

“Methods for harvest treatment”

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Unit 1: Pre-harvest consideration

- Summary

Unit 1 discusses in general about the factors that can affect the product's quality and what a producer should have in mind, even before starting cultivation, (from choosing the right plant to proper storage facilities) in order to achieve the best possible outcome.

- Learning outcome descriptors

- **Knowledge, understanding and professional skills**

1. Specify the main factors that should be taken into consideration before starting the cultivation
2. Plan the different steps of the production in order to keep in line with the needs of the specific plant and final product

- **General and transferable skills:**

1. Plan a research task
2. Work independently or with a minimal guidance where appropriate
3. Work in team with minimal guidance where appropriate
4. Show good written and oral communication skills
5. Demonstrate computer literacy
6. Perform online (computer) search to develop information technology skills in order to retrieve information from a variety of sources

1. Pre-harvest Considerations

It is in light of a legitimate concern for the producer, and the business, to produce a high quality product that will attract a premium market price. Pre-harvest operations involve the preparation of the facilities for the harvest material, which will guarantee the crop is stored and dried (when necessary) rapidly under sterile conditions. The primary explanations behind low quality product are harvesting the crop when it is not developed, poor drying systems where there is a high risk of moisture retention and microbial contamination and successive rain amid the drying procedure, which disturbs the drying procedure. The existence of buildings or structures or of a common facility for drying and curing products, near the harvesting area, is necessary. Numerous producers of herbs utilize conventional techniques and high moisture retention, microbial contamination, and contamination with extraneous matter are regular preparing issues. Measures for protection in order to prevent dangers from additives, contaminants, toxins or

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harmful organisms in food, are taken from international sanitary and phytosanitary agreements. Specifically, there are issues with mildew, high moisture contents and aflatoxin substance. Troubles in diminishing these issues to a low level are because of poor climate conditions at harvest related with low cost preparing innovation, poor storerooms and small-scale production units. Poor storage facilities and unhygienic and improper storage strategies additionally help the contamination with mammalian and other excreta, and also mildew or other microbes. So as to defeat these issues totally, capital venture is fundamental, especially for mechanized handling after harvest. All personnel (counting field workers) required in the propagation, cultivation, harvest and post-harvest preparing phases of plant production ought to maintain appropriate personal hygiene and receive training regarding their hygiene responsibilities.

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1. UNIDO and FAO (2005). Herb, spices and essential oils. Post-harvest operations in developing countries.

Unit 2: Harvesting of healing/medicinal plants

Harvesting medicinal and aromatic plants, is the initial phase in primary processing the plant product, and makes it prepared for use in different ventures. Harvesting ought to be completed such that both quality and health of the product are kept up. Ideal states of harvesting are essential for acquiring a raw material of high quality and increased processing efficiency. There are various elements that they may influence the harvesting conditions, from climate and gear to species or part of the plant specific parameters. Careful consideration for ideal harvesting conditions is a pivotal stride for a high quality harvest.

Quality issues in completed products can be because of: use of the wrong species, absence of organ specificity, harvesting at a non-optimum phase of development, non-optimum cultivation parameters, for example, soil, light, water, temperature and nutrients, contamination by microbial and chemical agents, non-ideal drying and capacity, non-ideal extraction procedure and long-term finished product storage. Quality issues in completed products are additionally complicated by the way that in many cases the phytochemical constituents in charge of the claimed activity of the plant product are often not known or poorly explained. However, to prepare reproducible phytochemical items effectively, the majority of the above described operations should be directed by specific protocols.

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Unit 3: General guide lines

When to harvest

Reproductive circle are different taking under consideration the species of interest and the ferocity of the collection. Mint or equinaceae might be three years, for instance, thyme, oregano and melissa from 4 to 5 years, lavenders and rosemary from 8 to 9 years. The harvesting period begins in May and can last up to October. Certain species are gathered 3 or 4 times a season, while others can only be gathered once or twice. The moment for harvesting relies upon the part of the plant we will use (leaves, seeds, blossoms, roots, etc.), and we ought to remember that this is a key factor for getting the quality and richness in active ingredients we are searching for. All the more accurately, the blooming tops are gathered exactly toward the start of blossoming, the leaves usually before the blossoming and is prescribed to do it at a young hour in the day, the fruits are gathered when mature, the roots in harvest time or winter or once the plant has given its fruits (to have the seeds), the bark is taken from young shoots and the grasses are gathered when blossoming begins.

Normally, production begins after one year, yet in the event that we plant in fall, numerous species are ready for a first harvest by the following summer. Depending on conditions, we harvest once, twice or three times each year. Thyme, for instance, if irrigated, can be gathered three times each year; oregano once, melissa ,similar to mint, can be gathered three or even four times, the surface parts of equinaceae three times, estragon twice, Salvia officinalis three times, Hypericum perforatum twice if irrigated, lavender once. The rhythm of harvest ought to dependably keep pace with the rhythm of production or transformation. In this manner, the harvesting capacity of the machinery used (hectares per day) should exactly match the capacity of the equipment used for transforming (tons per fresh plant per day), and the working capacity of the workers available and the collection periods of the species in question.

Medicinal plant materials ought to be gathered during the suitable season or time period to guarantee the highest quality of both source materials and finished products (Table 1.). It must be taken underconsideration that the quantitative concentration of biologically active substances differs with the phase of plant development and improvement. The best time for collection

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(quality peak season or time of day) ought to be resolved by the quality and amount of biologically active substances instead of the total vegetative yield of the targeted medicinal plant parts. Harvesting ought not to be completed in wet conditions (dew or rain) or in states of high humidity. At whatever point conceivable, harvesting ought to be done in dry, low humidity conditions. In the event that gathering happens in wet conditions, the reaped material ought to be transported quickly to an indoor drying facility to speed up drying in order to keep any conceivable harmful impacts because of expanded moisture levels, which advance microbial fermentation and mildew.

Harvest season	Yield%	
	Fresh mas	Dried mass
Summer	0.25	0.43
Fall	0.16	0.48
Winter	0.20	0.44
Spring	0.21	0.29

Table 1. Cymbopogon citratus essential oil yield of freshly harvested and dried leaves harvested in different seasons (Maringá, 2012)

What to harvest

Once the crop plants develop, first thing to do is to ensure that it is the right species. Phytochemical constituents are not equally dispersed all through the plant; desirable phytochemicals can be found at deferent parts of the plant, for example, buds, bark, leaves, grass, seeds, roots and so forth respectively for deferent species. Prior knowledge of the particular part or parts of the plant that the desired phytochemicals are found in high concentrations is significant for choosing the suitable technique and equipment to maximize quality and quantity of the product.

Furthermore, the phases of growth and development of the plant affect the concentration of biologically active substances. In order to guarantee ideal amount of biologically active substances in the medicinal plant product, the harvesting ought to be done at suitable development stage. The medicinal plant product ought to be thrashed out from any under or over developed product, which may downsize the overall quality of the lot. For those species where

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right phase of collection is not known, collection administrators may look for direction from the responsible person of the completed product manufacturers for such medicinal species for herbal formulations. The harvesting time according to phenological phase of plant species alongside with dates and months for each medicinal plant must be archived.

Collection of health plants is significant, just healthy individuals of wanted plant species ought to be harvested. Plants, which are infested with insects, pests, fungus, bacteria or virus, ought to be avoided (unless the medicinal value of the species comes from such connection as in the case of insect galls, agar wood and specified parts developed due to pathogens) as such infested plant product may degenerate the entire lot. Additionally, throughout gather, care ought to be taken to guarantee that no toxic plants or weeds can blend with the collected harvest. Also damaged and perished plant parts must be rapidly wiped out.

Another parameter for consideration is how to limit the damage to source plant. While collecting the preferred plant parts, for example, leaves, fruits, flowers, seeds etc. there are measures to be taken to limit the damage to the plant from which these parts are being harvested. Cutting the branches to ease collection of its bearings (fruits, leaves, flowers etc.) should not be attempted.

How to harvest

Precautions must be taken in order to avoid any unwanted mixing of foreign matter with the product of the medicinal plants. There is high probability of soil debris, organic matter like leaves, stems, or timber portions being inadvertently blended with the medicinal plant product at some point of the harvesting and post-harvest management. Collectors have to be vigilant to keep away from such mixing. Cross-infection with different medicinal plant product being harvested or processed concurrently must additionally be avoided. If more than one medicinal plant parts is to be collected, the different plant species or plant materials should be amassed one at a time and transported in separate containers.

Contact with soil ought to be prevented to the quantity feasible with a purpose to limit the microbial load of harvested medicinal plant materials. Cutting devices of harvesters ought to be adjusted in order that the collection of soil particles may be reduced to a minimum. When necessary, massive drop cloths, preferably manufactured from easy muslin, may be used as an interface among the harvested plant life and the soil. If the underground parts (such as the roots) are used, any adhering soil ought to be eliminated from the medicinal plant materials as quickly as they may be harvested. The gathered raw medicinal plant materials should be transported right away in dry, clean conditions. They may be located in clean baskets, dry sacks, trailers, hoppers or other properly-aerated containers and carried to a vital point for shipping to the processing facility.

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Equipment used for digging, cutting, sorting, peeling and any other activity must be suitable for the purpose they are used and should be stored in an uncontaminated, dry facility or area free from birds, rodents, insects and other pests and with no access to farm animals or pets. System must be manufactured from a non-toxic stuff and should be maintained in right running circumstance. It is crucial to ensure that elements of the equipment, which are available in direct touch with the product, are clean and free from any potential contaminant like paint, lubricant and so on. Equipment that is used for cutting, shearing, spilling or peeling ought to be thoroughly cleaned after use to avoid cross contamination with the last residues.

All storage units used at harvest must be kept clean and free from contamination that could be caused by previously harvested medicinal plants and foreign matter. If plastic containers are used, unique attention should be paid to any possible retention of humidity that would lead to the increase of mildew. Whilst containers aren't in use, they should be stored in dry conditions, in an area that is protected from insects, rodents, birds and other pests, and unreachable to farm animals and home animals.

In addition, any mechanical damage or compacting of the raw medicinal plant materials, that can be caused by overfilling or stacking of sacks or bags, that can bring about composting or in any other case diminish quality, have to be prevented. Decomposed medicinal plant materials should be diagnosed and discarded at some point of harvest, post-harvest inspections and processing, so that microbial contamination and loss of product quality will be avoided. Finally, the harvested crop ought to be safeguarded from pests, mice/rodents, farm animals and domestic animals whilst pest manage measures should be documented and the time between the harvesting and the processing of the plant must be very brief, with a purpose to avoid that the product could be damaged in its quality and increase its microbiological content.

Conveyances used for transporting bulk plant materials from the location of production to storage for processing should be cleaned between cargos. Bulk transport, like ship or rail cars, where suitable, must be properly ventilated to deduct humidity from plant materials and to prevent condensation.

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Unit 4. Post-harvest treatment of healing/medicinal plants

The most crucial goals of post-harvest managing are retaining the product cool, avoiding moisture loss and gradual down unwanted chemical adjustments and averting physical damage like bruises, in order to delay spoilage. Sanitation is likewise a vital aspect, to lessen the possibility of pathogens that would be carried by using fresh product, such as residue from contaminated washing water.

After the field, post-harvest processing is commonly endured in a storage house. This may be a simple shed, providing shade and running water, or a big-scale, sophisticated, mechanized facility, with conveyor belts, automated sorting and packing stations, walk-in coolers and other equipment similar to those. In mechanized harvesting, processing can also begin as part of the actual harvest procedure, with initial cleaning and sorting carried out through the harvesting machinery.

Primary post-harvest storage conditions are of high significance in order to retaining quality. Each crop has an ideal range of temperature and humidity, so when stored these rates should be taken into consideration. Additionally, certain plants can't be successfully saved together, as undesirable chemical interactions can result. Diverse techniques of high-speed cooling, and complicated refrigerated and atmosphere-controlled environments, are employed to extend freshness, mainly in huge-scale operations.

Irrespective of the dimensions of harvest, from domestic garden to industrialized farm, the simple principles of post-harvest handling for most crops are identical: treat them with care to keep them away from harm (for example bruising, cutting, crushing), cool them immediately and preserve the conditions cool, remove damaged items.

There are many aromatic, culinary and medicinal plants. Most secondary products in these plants can be altered by means of environmental elements as well as post-harvest managing practices, yet little is known about the stability of these plants and their active substances when they are exposed to either pre- or post-harvest environmental changes. Accelerated use of fresh and dried herbs, aromatic and medicinal plants have increased the call for high quality. Pre-harvest factors, together with cultural system, fertilization, and light exposure impact the yield and high-quality of these plants, however these plants, specifically whilst treated fresh, are very vulnerable to extended post-harvest senescence due to a high rate of metabolism, and viable microbiological issues. The successful marketing of high quality, particularly of fresh materials, requires extreme care and attention to post-harvest management. Some of the quality indicators that may be effortlessly deteriorated after harvest include active components, color, aroma, water loss, plus viable microbiological issues which could cause safety problems. Fresh green herbs (Labiatae

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family) are vulnerable to accelerated senescence due to an excessive price of metabolism which is increased further following harvesting and handling tactics.

Postharvest managing is very crucial to the improvement of material suitable for processing. All of the post-harvest ideas that practice to leafy green tissues practice to the managing of fresh herbs and a few other fresh aromatic and medicinal plants. Nevertheless, the post-harvest managing of those products is very challenging due to their outstanding variety, various components, and diverse utilization. As an instance, improving the quality of Australian echinacea via higher post-harvest handling practices was found to be complicated by the finding that the alkylamides and cichoric acid on occasion respond differently to the various handling operations used.

Drying

Freshly harvested medicinal plants occupy massive volumes and pose issue in transportation and storage. For handling and storage purposes, reducing the water content of freshly harvested medicinal plant is vital. By reducing the water content, the material turns into less difficult to handle and less vulnerable to microbial infection. The water content is typically eliminated via thermal drying. The existing methods for drying medicinal plants can be grouped into two categories, natural and mechanical drying, based on the heat source or energy utilization. In both processes, water present in the interior of the medicinal plant must move to the surface by internal diffusion. A big plant surface area combined with air motion favors brief evaporation of water from the plant's surface. The rate at which water is evaporated from the surface of the plant has to be balanced with the rate at which water is eliminated from the interior. Unbalanced evaporation rates can result in deterioration of the very last product. The reasons for drying grain crops also apply to medicinal plant drying: the intention is to control the moisture content of the medicinal plant crop to an appropriate level, which permits quality delivery of the herb to the place of final use, and probable make sure long-time storage with little deterioration.

Figure1. *Solar drying of oregano (Carlos Bertello, GIZ EnDev Peru)*

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But, natural or mechanical drying may be catastrophic to medicinal plants if not properly performed, as extensive high-temperature drying can cause both physical and chemical changes. In natural drying (Figure 1), exposure to the sun and/or the desiccating impact of air currents promotes the removal of water from the material. That natural air-drying can be easily controlled and rarely damages the material. Natural drying is a common method of medicinal plant drying, constituting the method of choice in areas where maturity and harvesting of the plants concur with the beginning of the dry season, and their phytochemicals are not photosensitive. Cinnamon (*Cinnamonum cassia*) bark is commonly sun-dried after harvesting in July and August, since that is the period when the quality of the bark is high. However, it was reported that the reliance on favorable weather conditions limits the use of natural drying. Solar dryers can counteract in some level the dependence from weather. It was reported that the use of plastic house-type solar dryers, in drying of spices and medicinal plants, was quite successful. Plastic house-type solar dryers (Figure 2) were reported to be more economical and efficient than conventional drying systems, provided that supplementary heating was used. Wisniewski (1997) reported that, in Poland, about 60 commercially cultivated medicinal plants crops were dried in flat-type solar dryers.

Figure 2. *Plastic house-type solar dryer (Carlos Bertello, GIZ EnDev Peru)*

Mechanical drying includes freeze drying, artificial drying, microwave drying, far infrared drying, vacuum drying and spray drying. Lyophilization or sublimation (freeze drying), consists of removing water by ice sublimation without passing through the liquid state. The principle of the method includes that the ice is converted into water vapor, under high vacuum, and removed. That leads the material in a dry state. The above method is ideal for preservation, but it is mostly used to dry high-value products because it is very expensive. Artificial drying uses fuels such as charcoal, natural gases, firewood or electricity to heat incoming air. Both labor and drying time of medicinal plants are minimized, when artificial dryers are in use. Artificial drying systems

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include, among others, plate chamber and conveyor dryers. In plate chamber dryers, warm air blows across plates on which plants are placed and usually has a low handling capacity, but is particularly useful for drying flowers and leaves. Plate chamber-style dryers usually count on manual labor. In conveyor dryers, fresh plants are transferred on a conveyor belt through a countercurrent flow of warm air. Drying times are between 2.5-6 h and drying temperature ranges of 40–80°C. Conveyer dryers may have high output with not too much labor input, but they need high capital and energy amounts. Medicinal plants have to be dried for preservation purposes. However it is necessary for drying protocols to be designed in such a way that they do not cause a decrease in phytochemical concentrations.

Extraction of essential oils

The extraction of essential oils from plant material can be managed by various methods and these are shown in the generalized flow diagram (Figure 3). There are five main methods of extraction:

- Expression
- Hydro or water distillation.
- Water and steam distillation
- Steam distillation
- Solvent extraction

For every technique there can be many versions and refinements and the extraction can be conducted under reduced pressure (vacuum), ambient pressure or excess pressure. The selection of extraction technique will be based on the nature of the material, the stability of the chemical components and the specification of the targeted product.

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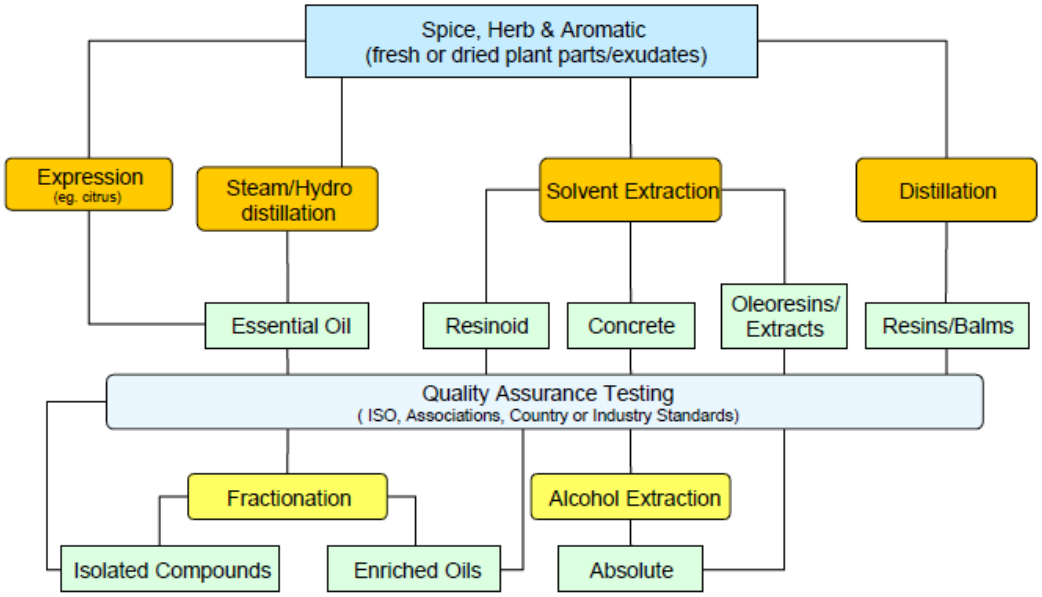

Figure 3. *Extraction processes used and products from spice, herb and aromatic plants*

Flowers are generally solvent-extracted and not steam distilled excluding rose, ylang ylang and orange blossom. In some cases an isolate or essential oil fraction is preferred to the total oil. Some well-known examples of fractionated essential oils with higher quality than the whole oil, are the terpeneless oils and folded citrus oils. Other processing steps can be implemented to lessen instability of certain oils (for example lemon oil which is known to be unstable in soft drinks due to the level of citral). The production of some special oils, oleoresins, absolutes and concretes requires much greater technologically-advanced facilities, labor abilities and safety systems. These processing facilities are commonly past the ability of the small individual producer. The excessive capital cost and the highly-skilled labor requirements of a supercritical carbon dioxide extraction plant additionally limits the widespread application of this extraction process besides for massive flavor, fragrance or pharmaceutical manufacturers. Expression is used solely for the extraction of citrus oil from the fruit peel, due to the fact that the chemical components of the oil are easily damaged by the heat. Citrus oil manufacturing is now a major process of the juice enterprise.

Distillation remains the most low-priced technique of extracting essential oil from spices and aromatic plant material. The principle gain of distillation is that it could commonly be carried out with some quite simple equipment, close to the location of plant production. Distillation requires less intensive labor and less labor skill requirements than solvent extraction. However, using the simplest and lowest-cost extraction technique may be a false financial planning due to low yield, poor or highly variable oil quality and low market value. Water distillation is the simplest of the

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three distillation techniques. The plant material is mixed without delay with water in a still pot. The existence of a perforated grid, above the base of the still pot, is desirable in order to prevent the plant material settling on the bottom and coming in direct contact with the heated base of the still. (Figure 4). Water distillation is probably the most effective and cheapest technique of extracting essential oils, but the quality of the oil has the best capacity to be modified due to the consequences of direct heating and the water contact.

• The plant material will be over-heated and charred, if the water present in the still isn't more than enough to last the duration of the distillation..

• It is very easy for still 'off-notes' to be generated, since some substances of the oil are more sensitive to chemical change and oxygenated components tend to dissolve in the still water that prevents the complete extraction of the oil.

• The plant material will settle in the bottom of the still and the heat will damage it, if it is not kept agitated as the water boils. In order to keep the material scattered in the water, it would be useful to chop it or grind it into fine particles.

• Some plant materials, like cinnamon bark, have high levels of mucilages. When these are leached out the viscosity of the water increases and there is a high risk of charring

• The stills are relatively small and as a result many circles of extraction will be needed in order to produce enough oil amounts. This will increase the possibility of mixing high quality oil with low quality, since each circle may give oil of different quality.

• Water distillation needs more energy, since it is a slower extraction procedure than the other two distillation types

• The main advantage of water distillation is that the cost of the equipment tends to be rather low and the designs of the stills, condensers and oil separator are simple.

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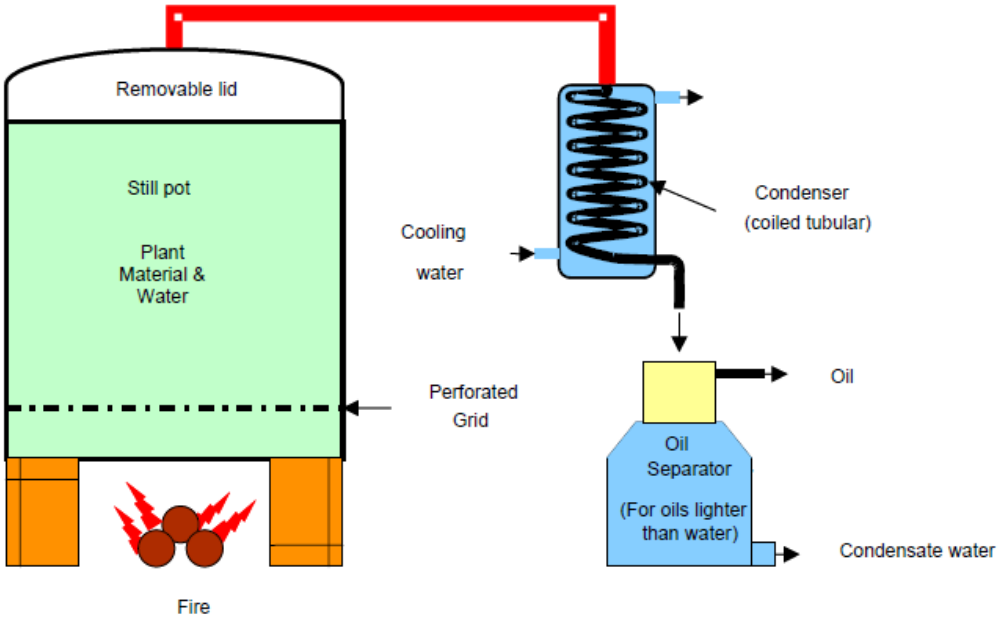

Figure 4. *Diagrammatic representation of water distillation unit where the plant material is suspended in the water*

The water-distilled oils are generally darker in color and have stronger still 'off-note' odors than oils produced via the other techniques, and consequently tend to be of the lowest value. The negative aspects of the water distillation technique might typically outweigh the advantages besides for local market use.

In steam-and-water distillation the basic still layout is quite alike to that of water distillation (Figure 5). The plant material is placed into the still pot that is put on a grill or perforated plate above the boiling water. The capacity of the still pot volume is decreased however it may be possible to achieve high packing density because the plant material is not suspended in water. The benefits of steam and water distillation over water distillation are as follows:

• Higher oil yield.

• Oil component less sensitive to change due to wetness and thermal conductivity of the still from the heat source.

• The effect of refluxing is minimized.

• Reproducible oil quality.

• Faster process

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• Energy efficient

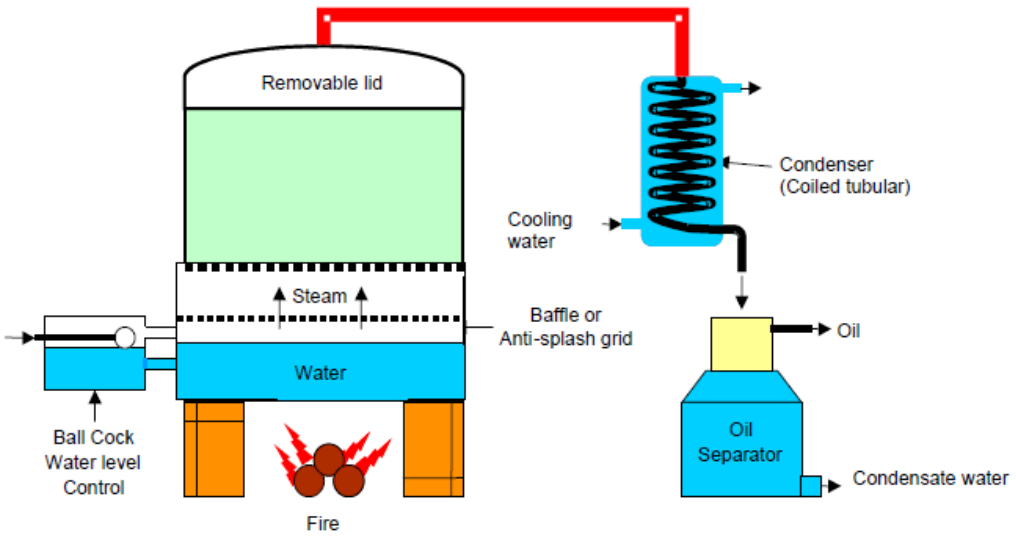

Figure 5. *Diagrammatic representation of a steam and water distillation unit with a baffle, to prevent direct water contact with plant material on the perforated grid.*

The process of distilling plant material with the steam produced outside the still in a stand-alone boiler is called steam distillation (Figure 6). The plant material is supported on a perforated grid above the steam inlet just like in the steam-and-water distillation process. The benefits and disadvantages of steam distillation are as follows:

• The quantity of steam and the quality of the steam can be controlled.

• Less risk of thermal damage as temperature generally not above 100°C.

• Most common process for the extraction of essential oils on a large scale.

• It is the preferable extraction method for the fragrance and flavor supply industry.

• There is a much higher capital requirement and with low-priced oils the payback duration can be over 10 years.

• Demands higher level of technical skill and fabrication

• Higher level of skill, regarding repaining and maintenance

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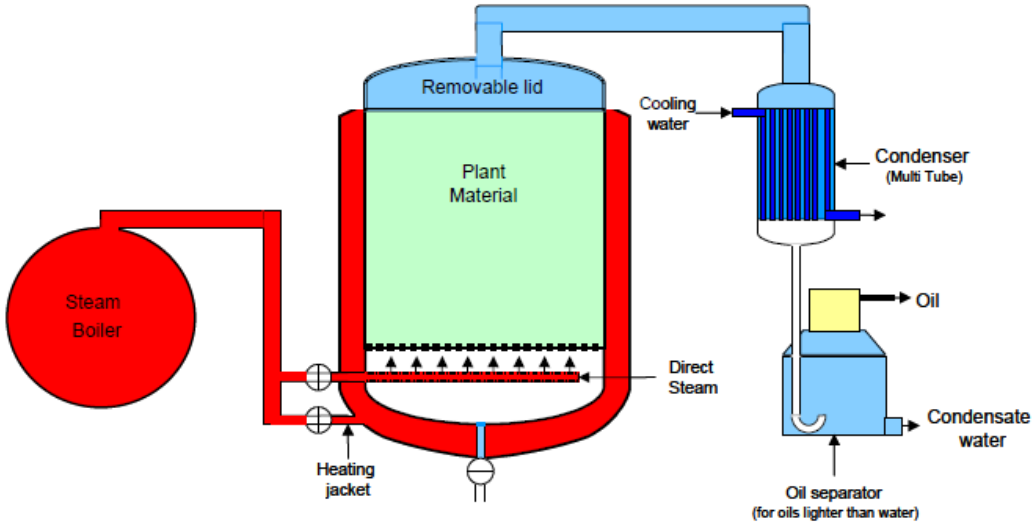

Figure 6. *Diagrammatic representation of steam distillation unit.*

When designing a distillation system, a number of issues must be taken inconsideration:

Site

- Availability of adequate water
- Energy source: electricity, boiler fuel
- Easy transport access
- Skilled and unskilled labor
- Close proximity to plant material
- Access to fabricators and machine shop for repairs
- Environmental zoning and waste management

Distillation Charge

(how much material can be processed in one circle)

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• Still size

• Plant species and oil content

• Oil content

• Daily volume and condition of plant material

• Frequency of material supply

• Preprocess (chopping, crushing, powdering, maceration)

• Time consumed to charge and discharge the still

• Storage capability of plant material before distilling under poor weather conditions

• After distillation waste disposal

Still

• Design based on distillation method; seek professional advice

• Preferably constructed of stainless steel

• Size based on boiler capacity

• Distillation time affected by height of the charge, flow rate and pressure of steam

• Easy to charge and discharge

Boiler

• Must produce sufficient steam to adequately remove the oil from the plant material

• Low pressure (saturated steam) or pressurized (dry steam)

• Seek professional advice on design and access for repairs and maintenance

Condenser

• The role of the condenser is to change the oil and water vapor back to a liquid

• Two main types: coiled tube or multitube

• Multitube hard to make, requires running water, has good heat transfer, effective water use and doesn't build up pressure

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• Coiled tube easy to make, just needs a tank of water and sparse use of running water, but has poor heat transfer, risk of high pressure builds up during distillation and poor use of water

Oil Separator

• Design of separator depends on density of the oil

• Large enough capacity to allow the oil particles to form droplets and readily separate from the water

• Controlling temperature can be used for more efficient separation

• Seek professional advice on design as poor separation affects all the effort of distillation to extract oil

Storage

• System to filter separated oil

• Storage in appropriate containers that shut out light

• Method to remove dissolved water

• Removal of residual still notes and dissolved oxygen

When possible the still vessel condenser and separator must be manufactured from stainless steel. In developing countries access to expert manufacturers, equipment and skills for preservation and repair, must be of prior consideration in the design of the distillation system. The majority of essential oils float on water i.e. their precise gravity is less than 1, but there are some of the wood and root oils which are heavier than water. Separation of oils whose density is near that of water or where the oil includes one major component, whose density is greater than 1, while the other components have density less than 1, is much more difficult. The layout and operation of the separator have to be specific to the oil being extracted. In addition to steam distillation, particular crops, in particular the expensive spices, are now additionally extracted by using solvents and carbon dioxide as this provides standardized extracts of high quality and without contaminants. Super critical fluid or gaseous extraction techniques are getting more common because of the problem of solvent residues in food.

Extraction

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Extraction is a basic function for botanical preparations and refers to the mass diffusion of soluble target substances from an insoluble plant solid into its environment. Briefly, the following steps can describe extraction: transferring the solvent to particles, desorbing compounds from the plant matrices; dissolving the solvents in the solvent and transferring the solutes to the main liquid. Because solutes or phytochemicals are of a different nature, selection of the appropriate solvent and extraction technique is critical for botanical preparations. A variety of techniques are available, such as liquid-solid, supercritical fluid, pressurized fluid and pressurized hot water extraction.

Solid-liquid extraction (SLE)

In industry, conventional methods for solid–liquid extraction (SLE) in industry consist of infusion, decoction, maceration and percolation, which are all commonly performed under atmospheric pressure with organic solvents. In the USA, phytochemicals are extracted with generally regarded as safe (GRAS) solvents, like water, acetone, methanol, methylene glycol, ethyl acetate, ethylene dichloride, isopropyl alcohol, methylene chloride and hexane. Due to their differences in polarity, different solvents show different selectivities toward the target compounds. The choice of the appropriate solvent depends on the solubility and polarity of the target compound in the liquid-solid extraction. If this technique is chosen, all necessary efforts should be made to remove residual organic solvents from the extracts. Extraction of hyperforin from the balm with 50 and 100% ethanol yielded 21 and 64%, respectively, of the total recoverable amount. Hyperforin extraction was not possible when only water was used as a solvent.

Increasing the temperature from 40 to 60°C did not improve the extraction yields. Although no yields are given, flavonol glycosides and terpene trilactones are allegedly extracted from dried Ginkgo biloba leaves with a mixture of acetone and water, before being concentrated, dried and reconstituted with ethanol. The iridoid glycosides, catalpol and aucubin, were extracted from Veronica longifolia leaves with methanol, ethanol, 2-propanol and ether. Catalpol yields of 0.8 ± 0.1, 0.4 ± 0.1, 0.2 ± 0.0 and 0 ± 0.0 mg/g dry weight and aucubin yields of 0.6 ± 0.1, 0.3 ± 0.1, 0.2 ± 0.0 and 0 ± 0.0 mg/g dry weight were obtained with methanol, ethanol, 2-propanol and ether extractions, respectively. The use of ethanol, methanol, acetonitrile and acetone for extracting silybinin A from milk thistle seeds returned 4.0 ± 0.1, 1.5 ± 0.1, 1.5 ± 0.1 and 2.0 ± 0.1 mg/g dry weight, respectively. Gafner and his colleagues reported total saponins recovery from P. quinquefolius roots of 61.7 ± 0.1, 59.4 ± 0.5 and 51.5 ± 0.2 mg/g dry weight for extraction with 50% ethanol, ethanol–glycerin–water (20:40:40) and 65% glycerin solvent systems, respectively. Iridoid glycoside, flavanolignan and saponin recoveries illustrate the importance of solvent selection in SLE processing.

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Supercritical fluid extraction (SFE)

Supercritical fluid extraction (SFE) is primarily based on the solvating power of fluids, which is maintained above their critical point. Supercritical fluids have mass transfer capabilities like gas and solvating strength like liquids. Their very low surface tensions make easy penetration into microporous substances, such as herb matrices. In SFE, density is associated with solvating power. Increases in solvating power can be acquired by manipulating two parameters: temperature and pressure. But, the alternations of these parameters do not always have the result of increased yields. In the phytochemical extraction industry, carbon dioxide is usually the SFE solvent of choice due to low toxicity, chemical inactivity and ease of recovery by venting gaseous CO_2. Nevertheless, two disadvantages ought to be stated: the essential equipment is costly and the technique is not suitable for the extraction of all phytochemicals. Then again, for certain phytochemicals, SFE-CO_2 has determined tremendous use. Total v-3 fatty acids extracted from brown seaweed (Sargassum hemiphyllum) by SFECO2 at 37.9 MPa and 50°C were 16.2 ± 1.3 mg/g dry weight, compared to 13.1 ± 1.3 mg/g dry weight when extracted by Soxhlet with a chloroform–methanol mixture. Similar total vitamin E recoveries of about 22 mg/g dry weight were obtained either with SFE-CO_2 at 27.6 MPa and 40°C, or with SLE with a chloroform–methanol mixture. SFE-CO_2 processes can also include the use of modifiers, where ethanol can be added to CO2 to increase its polarity. In a G. biloba phytochemical preparation, the combination of primary extraction with 70% ethanol, followed by SFE-CO_2 with 5% ethanol modifier at 300 MPa and 60°C, returned 2.1% of the terpenoids and flavonoids, while SLE with chloroform and acetone resulted in a 1.8% yield. However, for certain classes of compounds, the addition of modifier does not increase recovery. For example, hypericin and flavonoids could not be extracted using SFE-CO_2 with modifier from St John'sWort biomass. It has also been reported that SFE-CO_2 with ethanol mixtures could not solvate chichoric or polyphenolics from E. purpurea biomass. Furthermore, the addition of a modifier presents severe drawbacks. The presence of a modifier can result in a higher critical temperature, which may lead to thermal degradation. For example, to remain in the supercritical region of the phase diagram, CO_2 mixed with 10% methanol should be maintained at 7.446 MPa and 60°C. However, when increasing the methanol concentration by 5%, the SFE-CO_2 operating parameters need to be increased to 7.476 MPa and 73.48°C. The increase in temperature may favor the degradation of certain phytochemicals. Moreover, the modifier may condense upon depressurization and leave organic residue, undermining the gain of SFE-CO_2 extraction as an environmentally friendly extraction method.

Pressurized liquid extraction (PLE)

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Pressurized liquid extraction (PLE), also known as accelerated solvent extraction, grew relatively recently and uses organic solvents at pressures of about 14MPa, and extraction temperatures above the solvent boiling point. By pressurizing and operating at or above boiling point solvent temperatures, PLE has the benefit of short extraction times, low solvent consumption and high extraction yields. The improved performance when using PLE happens because of the following reasons: the solubility of solutes increases with increasing solvent temperature ; high solvent temperatures lead to greater diffusion and better solute-solvent interactions. The extraction of hypericin from St John's Wort using PLE at 14 MPa, 60°C and methanol produced 3.5 mg/g dry weight, compared to 2.8 mg/g dry weight by Soxhlet extraction.

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Unit 5. Storage and packaging

Processed plant materials have to be packaged rapidly in order not to allow deterioration of the product and protect the product from pest attacks and other sources of infection. Non-stop in-process quality control measures must be taken to remove substandard materials, contaminants and foreign matter prior to and in the course of the final stages of packaging. Processed plant materials need to be packaged in clean, dry boxes, sacks, bags or different packing containers accordingly to standard operating approaches and national and/or regional regulations of the manufacturer and the end-user countries. Materials used for packaging have to be non-polluting, clean, dry and in undamaged circumstance and have to conform to the quality requirements for the plant substances concerned. Fragile plant substances need to be packaged in stiff packing containers. Reusable packaging material like jute sacks and mesh bags ought to be disinfected and thoroughly dried prior to reuse, as a way to avoid infection by previous contents.

Storage

While storing herbal plant attention must be payed to the following points:

1. Raw material storage.

2. Storage material properties in which the plant material is kept.

3. Proper labeling.

Proper storage of raw herbs after collecting fresh from field should be authenticated first. The personnel should have sufficient training in appropriate fields such as pharmaceutical technology,

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taxonomy botany, phytochemistry, pharmacognosy, hygiene, microbiology. As soon as the herbal material arrives at the processing facility, it should be immediately unloaded and unpacked, while measures should be taken to avoid contact with soil. It should not be exposed directly to the sun. It should be protected from rain and microbiological infection.

Unprocessed drug part such as stem, bark, root, leaves may be contaminated by soil, therefore the dust particle must be removed by high pressure air blower after it passed through clean water once and if require twice. Washing dry herbal material with water is generally not acceptable. When it is necessary to clean them, an air duster or air shower should be employed.

Unprocessed drug if contains volatile oil should be kept in shed. Passing over and over through high pressure air blower must be avoided as it could lead to decrease of percentage of volatile oil. The method of drying herb depends on the active ingredient, for example essential oil and the type of the plant part collected e.g. root, leaf and flower. Drying by direct exposure to sunlight is possible, but without ground contact. Sterilization of raw drug is possible by treating it with ethylene oxide to remove microbes.

Raw herb should have the following information:

1. The botanical name of the plant used according to the binomial system (genus, species, verity and authority) it may also be proper to add the vernacular name and the therapeutic use in the country or region of the origin of the plant.
2. Details of the source of the plant e.g. region from where it is gathered whether it is cultivated or collected from wild, method of cultivation, dates and condition of harvesting, collection procedures, use of pesticides if any then type and quantity of pesticides.
3. Which part of the plants used, for dried plant material, the drying system should be specified.

For each of the processed and cleaned herbs the following information should be given: herb name, arrival date, supplier name, collection's site and time, batch number, stored part (root, stem, bark, leaf, flowers, rhizomes, etc.), inspection status and expire date.

Testing raw herbal material

Storing and preservation are in significant importance for future use of herb in formulation. The assessment of quality, safety and efficiency of formulation in different disease are depending upon storing and preservation condition of herb. When collecting a plant product several factors such as the collection site, collection time, plant growth stage and other environmental factors can affect the chemical composition of the final formulation. Testing of raw material ought to be

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done according to regulations. If the herbal material for processing is not in accordance with its quality specification, rejected herbs are stored separately and disposed accordingly.

Store house

The storage area should be well organized and tidy. Particular attention should be paid to cleanliness and good maintenance. Different plant materials should be stored in different areas. In order to keep the stored material safe and to reduce the risk of pest infestation, its storage time, in unpackaged form, should be reduced to a minimum. Incoming fresh herbal material should be processed, unless specified otherwise, straight away. If the circumstances allow it, they should be stored between 2°C and 8°C, whereas frozen materials should be stored below –18°C. Direct exposure to light, air or microbial organisms that effect on the active component of herb which leads to lower the therapeutic efficacy of drug must be avoided; but if the herb are stored in bulk to minimize the risk of mildew formation or fermentation it is recommended to store them in aerated rooms or container using natural or mechanical aeration and ventilation. Raw drug may be stored under conditions that block contamination and deterioration. There must be adequate space for in-house quality control testing. Approved and discarded herb should be stored with proper arrangement. All herbs should be washed clean, dry (unless a different procedure is required) and placed in order with controlled temperature, humidity in closed room. Temperature should be kept in between 8°C to 25°C.

Storage material

The drug storage methods are to be followed with maximum care as the potency of unprocessed drug has to be retained until we use it in the formulation. Herbal material even when saved in fiber drums, bags or boxes should be stored off the ground and suitably spaced to permit cleaning and inspection. Storage of plants and their products may require special conditions of humidity, temperature and protection from light. Adequate safety measures should be taken when sampling, weighing, analyzing and processing plants so as to facilitate cleaning and avoid contamination from previous batches..

Materials for specialized packing and storage of raw material:

- Stem, heartwood, bark - Gunny bags and woven sacks
- Creepers, leaves – low density plastic woven bags, high strength HMHD bags and high strength polyethylene bags

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- Fruits and roots - High strength HMHD bags, low density plastic woven bags, wooden boxes.
- Flower, anthers, stigma, petals, seed - Corrugated box with polypropylene woven sacks, HDPE containers, Fiber board's liner.
- Herbal extracts and compounds - Air tight HDPE containers, corrugated box with polyethylene woven sacks and fiber board's drums with polyethylene bags.

Different categories of medicinal and aromatic plants, for example fresh herb, dry herb, volatile oil, must be stored separately.

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Unit 6 Specific guidelines examples

Roots (Ginger)

Fresh rhizomes (Figure 7) must be cleaned of foreign materials, stems and roots. When possible, washing under pressure is preferred as it is more effective and tends to reduce bacterial load. Traditionally, the rhizomes are 'killed' by immersion for 10 minutes in boiling water. This procedure can also deactivate the enzymatic processes. After that, they are dried in the sun. Peeling or scratching is recommended to reduce drying time. In addition, it reduces the growth of mold and fermentation. However, while this process minimizes the fiber content, removing the outer layer of the skin, it also tends to remove some oil components, since their concentrations can be higher in the bark. Peeled rhizomes can be bleached in order to gain a better appearance.

Figure 7. *Fresh untreated ginger rhizomes (© Giuseppe Mazza)*

After peeling and washing, the rhizomes are soaked in water for two to three hours. After that, they are placed in a 1.5-2% solution of calcium oxide for six hours. Then, the rhizomes are drained and dried in the sun. This approach is followed when a light, shiny color is wanted.

Cleaning and drying procedures should be done as soon as possible after harvest. The rush is to make sure that the loss that could occur due to microbial contamination, mold growth and fermentation, will be minimized. Mechanical washers, slicers, and solar or hot air driers can help reduce dust contamination throughout post-harvest processes. Undrying peeled ginger takes 7 to 9 days to reach a moisture content of 7.8% to 8.8%. If the ginger is cut into slices, it takes only five to six hours using a cross-flow drier. On the other hand, if the ginger is whole it takes sixteen to eighteen hours under the same conditions. Mechanical drying provides a product that is cleaner and more homogeneous. When drying with hot air, airflow and temperature must be adjusted. Drying should not exceed 60°C in order not to allow discoloration.

Grading and packaging

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A large volume of rhizomes can be stored in jute bags, wooden boxes and covered cartons for transportation. Dried slices or powder are stored in plasticized bags. Storage in a cool and dry environment is of high importance for dry spices.

Storage

Dried spices

Dried rhizomes or slices must be kept in 10-15°C temperatures. When stored at room temperature (23-26°C), losses of up to 20% oleoresin (dry weight) were observed on dry ginger after 3 months, and the content of (6)-gingerol decreased. Is therefore recommended to extract or distill dried ginger rapidly, if cold storage is not available, when oil or oleoresin is the final product. The significance of a dry storage for dried ginger destined for distillation can only be emphasized due to mycotoxins from mildew may be co-distilled with the essential oil. Mildew and bacteria growing on dried rhizomes may be efficiently controlled with Cogamma-irradiation at doses of 5 to 10 kg, with only a few changes in the quality of ginger oil. Also, ethylene oxide can be used for steam disinfection. For both techniques mentioned, special and extremely safe installations are necessary.

Fresh ginger

Fresh ginger must be stored in a humid and low temperature environment. However, low temperature storage may not always be easy near the production area. Fresh ginger rhizome shelf life might be extended by storage at 10-12°C and high humidity.

Drying

Ginger drying involves two stages: peeling of the rhizomes to remove the outer skin and mechanical drying or drying in the sun at acceptable humidity levels. For the production of dry ginger, the harvesting takes place at full maturity. In most areas, the peeled ginger is dried in the sun.But in areas where the weather conditions do not allow the sun drying, improved drying methods with mechanical or solar dryers are also used. In mechanical dryers, 57.2°C is reported to be the highest temperature at which ginger for the spice market could be dehydrated. At higher temperatures, the color tends to lose its brightness.

Traditional method of drying ginger

The method involves placing peeled, cut ginger in clean bamboo or cement surfaces and drying in the sun until the moisture level reaches 10%. Drying can last from seven to fourteen days, according to the weather conditions. Disadvantage of this method is that it cannot be used in rainy conditions.

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Modern method of drying ginger

This method includes the use of a mechanical drier like a hot air tray drier used to make the drying process faster. For drying a whole peeled ginger it takes about sixteen to eighteen hours in a mechanical dryer. It is rather important to monitor the air flow and temperature during drying.

Processing methods

Green (Fresh) Ginger

A significant quantity of green (fresh) ginger is consumed worldwide as vegetable. Ginger for vegetable use should be fleshy with low fiber content and, therefore, harvesting is done from the sixth month onwards.

To prepare the fresh ginger, the clusters are raised carefully with a shovel and then the rhizomes are carefully cut of the plants. The rhizomes are pretty close to each other and their shapes are irregular. This allows the inclusion of dirt in the interspaces, which have to be removed during washing. The adhering roots are also removed. After washing, the ginger is slightly sun-dried before it is placed on the market in this form.

Although there is significant consumption of fresh ginger worldwide, most of the production is altered into dry ginger. Traditionally, the drying of the spice was carried out in highly unsystematic and unhygienic ways, resulting to the often failure of the product to conform to the quality standards of international trade, especially on microbiological grounds. However, modern farmers have acquired considerable awareness on the quality specifications and follow good agricultural practices.

Solvent Extraction of Ginger Oil and Oleoresin

The recovery of the essential oils of ginger depend on kind and origin of the plant as well as the cultivation, moisture at the time of harvest, the methods of extraction and, to some extent, the age of the plant.. Ginger oil is extracted by hydro distillation; water distillation and steam distillation. Extraction of ginger oil is usually achieved by hydro distillation method. Hydro distillation involves the use of water or steam to recover volatile components from the plant. The essential feature of hydro distillation is that it allows the distillation of a compound or a mixture of substances and then the recovery at a much lower temperature than that of the boiling point of the individual components.

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Oleoresin, which is obtained by extraction with volatile solvents, contains the aroma and flavor of the ginger in a highly concentrated form. The procedure essentially contains the following three steps: contacting the powder with the solvent to transfer the ingredients from the spice to the solvent, separating the solution from the powder and distilling the extract to recover the product. The efficiency of oleoresin extraction is affected by factors such as particle size, extraction medium and temperature of extraction.

Mechanical Expression of Juices

Mechanical expression is used widely in the extraction of juices and oils from fruits, vegetables, and oilseeds. They are based on the application of pressure to fluster the plant cells and release the contained juice or oil constituents. The by- products of mechanical expression are solid remnants such as pomace or peels, which are either put in procession to become animal feeds or discarded in the agricultural land..) The benefit of mechanical expression over chemical extraction is that it keeps the liquid free of diluted chemicals and plus that it is a safer procedure.

Seeds (Cardamom)

Harvesting

Harvesting at the right stage of maturity is crucial for a high quality cardamom capsules production. The fruits should only be harvested once they are fully ripe. A mature capsule contains black seeds (Figure 8), while an unripe white. When the capsules are ripe, they can be easily removed from the stem. Harvesting should begin from the base of the stem, moving upwards, removing only the capsules that are easy to cut, while the rest should remain in the plant to mature.

Figure 8. *Mature cardamom capsules and seeds (© 2017 Profexports.com)*

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Cleaning

The crop should be cleaned before processing. The first stage is to take away dust and dirt using a winnowing basket. An experienced worker can clean up to 100kg of cardamom in an eight hour day. Small machines are available for cleaning, but they are not that affective according to their cost.

After winnowing, clean water is used to wash up the capsules. Two or three large plastic buckets (15 litre capacity) are adequate for small amounts but for large quantities, it is usually better to use a sink with a drainage hole. Only water that is safe to drink should be used. It should be changed regularly to block infection.

Drying

Drying is the most important part of the process, since final product's quality is directly affected by it. It is important to dry the cardamom capsules soon enough after harvest to prevent the loss of flavor. As well it is important that the drying process is as short as possible so that mildew does not develop on the capsules and the bright green color is preserved. The drying temperature should not be higher than 50°C as this affects the color and delicate flavor of the final product. In most places, cardamom capsules with a good green color can be sold for a premium price.

A fresh cardamom capsule has about 85% humidity, which must be reduced to 10% in the dried product, in order to store it. If the drying period is too long mildew can start to develop on the cardamom. There are quite a few methods available to the small-scale processor, depending upon the size of the business and the local weather conditions at the time of processing. Each method has its own benefits and drawbacks.

Grinding

Cardamom capsules are sold whole in general, but grinding can be a method to raise the value of the product. However, it is not recommended to grind spices, since they can become more susceptible to spoilage. Compounds that give aroma and flavor are not stable and will soon be lost from the product. The storage life of ground spices has less duration than of the whole spices. It is very difficult for the consumer to estimate the quality of a ground spice. It is also very easy for unprincipled processors to contaminate the ground spice by adding other material. So as a result most consumers, from wholesalers to individual customers, prefer to buy whole spices.

Packaging

Cardamom capsules can be packaged in polythene bags of differ sizes in association with the market demand. The bags must be sealed in order not to let moisture enter. Sealing machines are used for this purpose.The product must have labels that are easily read. The label must have all

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the information that is relevant to the product: the name of the product, trademark (if appropriate), producer's information (name and address), date of production and expiry, weight of the contents, added ingredients (if relevant) plus any other information that the country of origin and of import may require.

Storage

Dried cardamom capsules must be stored in dry containers, without being exposed to direct sunlight. For long term bulk storage, polythene-lined gunny bags (strong sacks made from jute fibers) inside wooden boxes are used. The polythene bags contribute to the preservation of the green color of the pods. Any moisture within the bags will lead to the rotting of the capsules, so it is of highest importance that the capsules are completely dried before they go in the gunny bags. The stored cardamoms must be checked in a regular basis for signs of spoilage or moisture, and when high levels of humidity are detected they must be re-dried until moisture drops to 10%.

The storage house must be clean, dry and cool and pests and insects must not have access to it. Mosquito netting should be fitted on the windows in order not to allow pests and insects from entering the room. Strong smelling foods, detergents and paints should not be stored in the same room as they will spoil the fine aroma and flavor of the cardamom.

Leaves (Stevia)

Harvesting

The harvesting time of stevia is usually affected by growth behavior and accumulation of the steviol glycosides, so the exact harvest time depends on the particular Stevia cultivar used and the growing season. In tropical and subtropical climates, the first harvest generally happens after 4 months of planting and the next harvests are after every three months, but in less warm areas, the number of harvests per year is usually lower. There are some places, particularly in Mainland China, where only one harvest is done in a year.

Harvest usually happens just before flowering, since after flowering, the steviol glycoside content of the leaves is reduced.

For harvesting, stevia plants are cut at approximately 4 inches (10 cm) height from ground. Some specialists recommend cutting at 6 inches (15 cm) height. There is a plethora of manuals and

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mechanized harvesting systems that can be used for stevia harvesting. After harvesting, usually a prophylactic fungicide is used to control fungal infection at the cut end of the stem.

Drying

After the leaves are harvested, they must be dried as quickly as possible to prevent browning and loss of steviol glycoside content. If the leaves are not dried in a proper way and within a specific time window after harvesting, this will may lead to a drastic loss of steviol glycoside and a loss up to half of the primary glycoside content within three days. The initial moisture content of fresh leaves is more or less 80% and they are to be dried to a final moisture level of 10% for long term storage. Therefore, the total loss of weight in drying process is 78%. Higher residual moisture percentage in the leaves during storage results not only in decay of the glycoside content but also mildew growth and decomposition, that would lead to the uselessness of the leaves for glycoside extraction.

Separation of leaves and stems

The stems of Stevia plants include very little steviol glycosides, so their presence in the harvested part decreases the overall glycoside content. Moreover, stems elute a lot of tannin and waxy material during extraction, which messes with the purification of glycosides. So, for making the leaves extraction worthy, the stems are to be separated from the leaves. For very small farms, it can be done by hand, but mechanical procedures are necessary for larger farms. The stems can be separated both before and after drying.

Baling and Packaging

Dried and cleaned stevia leaves (Figure 9) have very low bulk density and are therefore very bulky in nature. For easier and more efficient storing and transport they are compressed into bales and then packaged either in non-woven HDPE bags or in clear LDPE bags. For baling stevia leaves hydraulic horizontal or vertical bailing press is used.

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Figure 9. *Dried stevia leaves*

Flower (Lavender)

Pruning

Flower buds should be pruned off in the first two years so that the plant can grow in the best possible way and create a strong frame. In the years to come, pruning should be carried out as a separate post-harvest process, usually in autumn. The reason for that is because harvesting the plant blossoms for their oil leaves most stalks on the plants. Less frequent pruning will result in crops growing more slowly. Pruning can be done by using machines such as specialized trimmers.

Harvesting

The harvesting of lavender for essential oil should occur when the flowers have grown and the lower half is starting to open. The harvest is usually done at the end of December and early January, depending on the season. The harvest time can be from four to ten days and then the quality will be reduced. Planning the harvest, especially for large plantations, in good weather, is crucial, because the water that comes into contact with the oil during the preheating stage of distillation decreases oil quality and extraction efficiency. Harvesting must also not be performed in too high temperatures and very windy conditions as considerable volumes of oil can be lost through evaporation. Very low temperatures block the development of esters, and harvesting has to be delayed until the weather is warmer. The flower spikes are cut 15 to 20cm below the flowers. It can be hand harvested by means of sickles or shears or by using machines designed for the task. Cutting the flowers to be sold fresh or dried, usually happens a week later than it would be for the production of their essential oil. Flowers are also cut having longer stems.

Steam distillation

Once picked, the lavender is distilled. The value of the oil depends on distillation. If the levels of pressure or temperature are too high, it may result a change to the molecular structure of the molecules responsible for the fragrance, changing the chemical components. The yield of the oil may differ considerably from one season to the next, as the age of the bushes and the weather will influence both the quantity and quality of the product.

Solvent extraction

A smaller quantity of lavender and lavandin concretes is produced by solvent extraction. Concretes are secreted from fresh plant material using solvents like toluene, hexane and petroleum ether. The solvents are evaporated to produce residue called concretes. Concretes are

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used by the perfume industries (mainly soaps) and for further improvement they are blended with ethanol. The mixture is then cooled and filtered. After that the ethanol is evaporated and leaves a wax-free residue called an absolute, which is more widespread in fine perfumery. Usually there is a 50% loss from concrete to absolute.

Dried flowers

After harvesting the flowers, these are put together in bundles and hung up to be dried in the shade (Figure 10). Some flowers are stripped from the spikes after drying and are then stored into boxes or cases lined with paper. Generally, 8 to 10kg of fresh flowers are required to produce 1kg of dry flowers.

Figure 10. *Dried bundles of lavender*

Packaging and storage

Essential oils are volatile and so they must be treated with care. Keep the oils in dark, air-tight glass bottles and do not let them be exposed to heat or heavy metals. Decay begins if the liquid is much darker or thicker than normal. With proper care essential oils remain potent for 6 months to 2 years; if freshness is suspected the oil should be disposed. Dark glass or ceramic containers, as well as the use of fluorinated plastic and processed aluminum, are some other ways of storing. In the context of the value-added market, packaging should be clearly labeled, decent and professional.

Fruit (Fresh Chiles)

Harvest and handling

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In the course of harvest and handling, it is significant to remember that chile fruits soften easily and appear postharvest diseases if they are damaged, bruised, or exposed to high temperatures All types of chile peppers, especially New Mexico green chiles, are particularly sensitive to water loss, sun exposure and high temperature exposure.. These issues are likely to occur if chiles are allowed to sit for more than an hour in direct sunlight. Fresh chile peppers (Figure 11) that are harvested in the summer may have temperatures in their pulp of 32°C or above. For these reasons, they must be collected early in the morning, placed away from direct sunlight and cooled rapidly. If the chiles are not cooled within 1 to 2 hours, they will begin to loose water and soften. Most fresh chili peppers are hand-picked in buckets or sacks and then placed in containers to be transported to a shaded area for packaging or processing. A harvest of field of long green chiles can be harvested in early August and then again in September. A third harvest will typically yield small fruits and may not be worthy.

Figure 11. *New Mexico chile pepper*

Once at the shed, the chile is either dry-dumped onto padded ramps or moving conveyor belts, or wet dumped into a chlorinated wash tank. Wash tanks should be cleaned daily, and the chlorination levels should be checked in regular basis. These sanitation practices are essential due to chiles are quite sensitive to bacterial diseases that could be introduced through the wash tanks. Then the peppers are sorted to remove the infected, overripe, untamed and otherwise defective pieces. After that, classification according to USDA or other market standards can be done. Usually fresh chile peppers are packed in 1 1/4 bushel size corrugated cartons that hold 30 lb. The boxes may be waxed, and should have top and bottom gaps and side slots for airing and cooling. Cartons must be considerably strong to withstand stacking and shipping. Packaging in plastic lined bags (polyethylene) offers an extra protection for peppers from the loss of moisture. Plastic films decrease water loss from the chiles, but may meddle in with cooling efficiency. Small perforations in the plastic will counterbalance for the barrier by improving gas exchange and increasing the airflow during cooling and storage. Chili peppers can also be packed in plastic bags or film-

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wrapped trays when they are to be sold in retail markets for individual consumers. These retail packages can be made at the packing shed or, more commonly, at the delivery center. Both storage temperature and package container affect chile fruit weight loss. Chiles stored in boxes lose weight per day of about 3.5% at 24°C, but only 0.5% at 8°C. In order to reduce fruit weight loss further, plastic wrapped trays or polyethylene bags can be used, especially at lower storage temperatures.

Cooling and storage

Fresh chile is quite spoilable merchandise. Proper cooling expands the shelf life by slowing respiration, water loss, color change, and decomposition. Temperatures higher than 21°C accelerate rippening through breathing and ethylene production.The most preferable cooling methods for chiles are room cooling and forced-air cooling. Cooling and storage are independent operations and for that reason the specific requirements for quick cooling should be considered separately from cold storage needs. In room cooling, where the fresh product is exposed to cold air in a refrigerator, bins or boxes must be stacked properly in order not to prevent airflow between the individual storage units. Room coolers should be divided into sections so that recently harvested chiles with high field heat are kept separate from previously cooled product. Powerful fans and ceiling jets can be used to increase the airflow and, as a result, the cooling efficiency of room coolers. Forced-air cooling is an active cooling procedure and is a much faster way to remove field heat than room cooling. In forced-air cooling, fans send cold air directly into the boxes or bins where the products are stored. Room coolers can be altered into forced-air coolers relatively quickly and without high cost by adding extra fans and partitions. There are quite many variations of forced-air cooling designs; the most common is the forced-air tunnel design. In this system, a series of buckets or pallets are placed on each side of a fan, creating a runway between the two rows. The corridor and the open end are covered with canvas to create a tunnel and the fan creates negative pressure in the tunnel and sends cold air through the stacks to cool the product. The containers must have adequate ventilation so that the air flows properly during cooling. Forced-air evaporative cooling is a system that uses evaporative coolers instead of refrigeration units. This cooling system is practical in areas with dry climate. An evaporative cooler needs less energy than mechanical refrigeration. Furthermore, growers can build their own systems. Forced-air evaporative coolers can reduce product temperature to 16°C and come in use for cooling sensitive products (such as chiles) for a local market.

Storage

The ideal storage conditions for fresh chiles are to 7-10°C and 90 to 95% relative humidity. Chilling injury happens at lower temperatures. The symptoms of chilling injury are softening, pitting, and a raised sensitivity to decomposition. Damage from freezing occurs at 0°C. If the right cool temperature is kept, most fresh chiles can be stored for 2 to 3 weeks. Chiles should be shipped

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on refrigerated trucks, however these vehicles should not be used for pre-cooling because refrigerated trailers do not have sufficient cooling capacity or ventilation to remove field heat fast enough. Transit cooling is intended only to maintain previously cooled product cold during shipping. Inadequate temperature management and ethylene accumulation during storage or transit make the appearance of ripening and decomposition easier. Some fruits and vegetables produce much larger amounts of ethylene than chiles, so chiles should never be stored or shipped with crops like tomatoes, apples, or melons. Storage rooms should be aerated properly to minimize the accumulation of ethylene in the environment. The placement of ethylene scrubbers containing potassium permanganate in the storehouse or transport vehicle may also drop ethylene levels. Preserving a chain of quality from grower through consumer is crucial when handling fresh chiles. The basis of the chain of quality is proper cooling, but reducing mechanical injuries, diseases, and ethylene exposure are also essential for maximum chile quality.

Bark (Cinnamon)

Harvesting

Cinnamon bark is harvested twice a year right after each of the rainy seasons when the moisture makes the bark peel more easily. The first harvest occurs when the trees (Figure 12) are three years old. That is one year after the first pruning. The side stems that are about three years old are taken away and the bark is stripped off. Cinnamon bark can only be acquired from stems that are between 1.2 and 5cm in diameter.

Figure 12. *Peeled cinnamon tree*

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Processing

About 60% of the cost of production of cinnamon goes to processing, since the peeling of bark from the stems is labor strenuous and is usually done by hand, by skilled peelers. Cinnamon's quality depends on how well the bark is separated from the stems, with the larger pieces or quills having higher price in the market than the smaller broken pieces. Drying is also a significant stage of the procedure of cinnamon, since it is one of the factors that influence the quality of the final product.

Processing stages

• Take away the tender stems (with diameters less than 1.2cm) and use them as a fertilizer.

• Stems with diameter greater than 5cm are not used to prepare cinnamon bark, but they can be used for oil distillation.

• Take away the soft outer bark with the use of a good rounded knife with thick rasp.

• Rub the stripped stem with a brass rod to loosen the inner bark. It is essential to use a brass rod so that the bark color does not fade away.

• Drill holes around the stem at intervals of 30cm using a small sharp knife. The knife blade should be stainless steel or brass to avoid staining the bark.

• Make long cuts along the length of the stem, so that the bark can be carefully eased off the stem. Use the pointed knife and the rubbing rod to help ease off the bark.

• The pieces of removed bark are called quills. Put those quills inside one another to create long compound quills (up to 1m long), by using the best whole quills on the outside and fill in the center with broken pieces of bark.

Drying

The compound quills are placed on coir rope racks and dried in the shade to avoid misshaping. After four or five days of drying, the quills are rolled on a board to clinch the filling and then placed in soften sunlight for further drying. In wet climates or during the rainy season, it is necessary to use mechanical driers in order to complete the drying process. There are many types of dryers available to serve different situations (electrical, gas fired, biomass fueled).

Grading

The quality of cinnamon depends on the thickness of the bark, the appearance (broken or entire quills) and the aroma and flavor.

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Grinding

Grinding can be a method of raising the value of a product. However, it is not recommended to grind spices. After grinding, spices are more easily spoiled. The flavor and aroma compounds are unstable and will quickly vanish from ground products, so ground spices have much less storage life than the whole spices. For consumers is difficult to judge the quality of a ground spice. However it is not difficult at all for unethical processors to contaminate the ground spice by adding other material. Consequently most consumers, from wholesalers to individual customers, prefer to buy whole spices.

Cinnamon is sometimes ground to a powder prior to sale. The powder should be packed in moisture-protected packages (polypropylene bags) to keep the flavor.

Packaging

Cinnamon quills (Figure 13) are cut to create pieces up to 10cm in length and packed into n polypropylene bags to be protected from moisture. The bags ought to be sealed to avoid moisture entering. In order to seal the bags, sealing machines can be used. Attractive labels should be applied to the products. The label needs to include all relevant product and legal information – the name of the product, brand name (if appropriate), details of the manufacturer (name and address), date of manufacture, expire date, weight of the contents, added ingredients (if relevant) plus any other information that the country of origin and of import may ask.

Figure 13. Cinnamon quills

Storage

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Dried cinnamon quills should be stored in places protected from moisture and sunlight. The stored cinnamon quills should be frequently checked for signs of decay or moisture. If they have absorbed moisture, they should be re-dried to a moisture content of 10%. The storage room should be clean, dry, cool and pest-free. Mosquito netting should be fitted on the windows in order not to allow pests and insects from entering the room. Strong smelling foods, detergents and paints should not be stored in the same room as they will ruin the delicate aroma and flavor of the cinnamon.

Bulb (Garlic)

Harvesting

Garlic can be harvested at different stages of its development for special markets. However, most of the garlic is harvested after its bulbs mature. Harvest occurs after the tops have fallen and are very dry. Garlic is grown in rich soil, so it is necessary to break over the tops to prevent too much top growth. For the garlic planted early in the fall, a cover crop of oats can be sown at planting time to provide winter protection for the young plants (Figure 14). In cold season, a layer of organic mulch is applied which stabilizes the young plants preventing them from frost heaving, cold injury or premature growth.

Figure 14. Covered garlic field

Post-harvest technologies

Garlic powders

The simplest method of preserving garlic is to dehydrate fresh garlic cloves and grind them. Ground garlic can be used as a flavoring agent for condiments and processed foods. While preparing the powder, garlic cloves are cut in slices, crushed, dried and ground into powder. The

average content of allicin present in garlic is 0.8%, however, raw garlic contains around 3.7 mg/gm of allicin. In India small scale industries use tray drier for drying the garlic cloves. The moisture content of garlic cloves is minimized from initial moisture content of about 60- 65% (wb) to a safe level of 6% (wb). The dehydration of the garlic cloves using tray dryer is both energy strenuous and time consuming procedure. It takes about 9-10 hours to dry garlic cloves in a single stage in a tray dryer at the temperature of 70°C.

Garlic oil

Garlic oil is another significant preparation. It occurs from the distillation process of raw garlic. Steam distillation is the method used to obtain the essential oil of garlic. Garlic cloves' content of essential oil is 0.2-0.5%. It consists a variety of sulfides, like diallyl disulphide and diallyl trisulphide.

Garlic storage

Garlic and its dried products should be stored under low humidity conditions. Sprouting happens if the storage is done at intermediate temperatures. Furthermore, the variety of garlic affects the potential storage life. The conditions to be employed for commercial storage depend on the storage period. Garlic can be stored in good condition for 1-2 months at ambient temperatures (20-30°C) under low relative humidity (< 75%). But under these conditions, bulbs will eventually soften and become spongy and shriveled due to water loss. For long term storage, garlic is best preserved at temperatures of -1°C to 0°C with low relative humidity (60-70%). Also good air flow is essential to avoid moisture accumulation. Under these controlled conditions, garlic's storage life can be increased up to 9 months. Garlic loses dormancy, which is indicated by the sprouting of bulbs. It happens at the storage temperatures of 5-18°C. Also high levels of humidity will favor the mildew development. Moreover, it must be taken under consideration that garlic should be stored separately to avoid the transmission of odor to other products. For bulk storage of garlic, ventilation systems should be designed to supply air into the store room from the bottom at the rate of 2 cubic feet per minutes per cubic feet of production. The rows of containers must be placed parallel to the direction of the air flow and be spaced six to seven inches.

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INNOVATIVE INTEGRATED TRAINING IN
HEALING PLANTS
BUSINESS

Module No. 3

“Quality assurance of the final product (Medicinal plants)”

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Unit 1: Introduction

Medicinal plants, also called medicinal herbs, have been identified and used by many people since the prehistoric times. Plants can produce countless chemical compounds that can be used for biological functions, including defense against insects, fungi and herbivorous mammals. The ingredients that they have can act on the human body just as pharmaceutical drugs without the harmful effects that can be caused from drugs. However, one must be very careful when taking a plant as medicine, because of the many substances that are contained in it. Healing with medicinal plants is as old as humanity itself. The connection between man and his search for drugs in nature dates from the far past, of which there is ample evidence from various sources: written documents, preserved monuments, and even original plant medicines.

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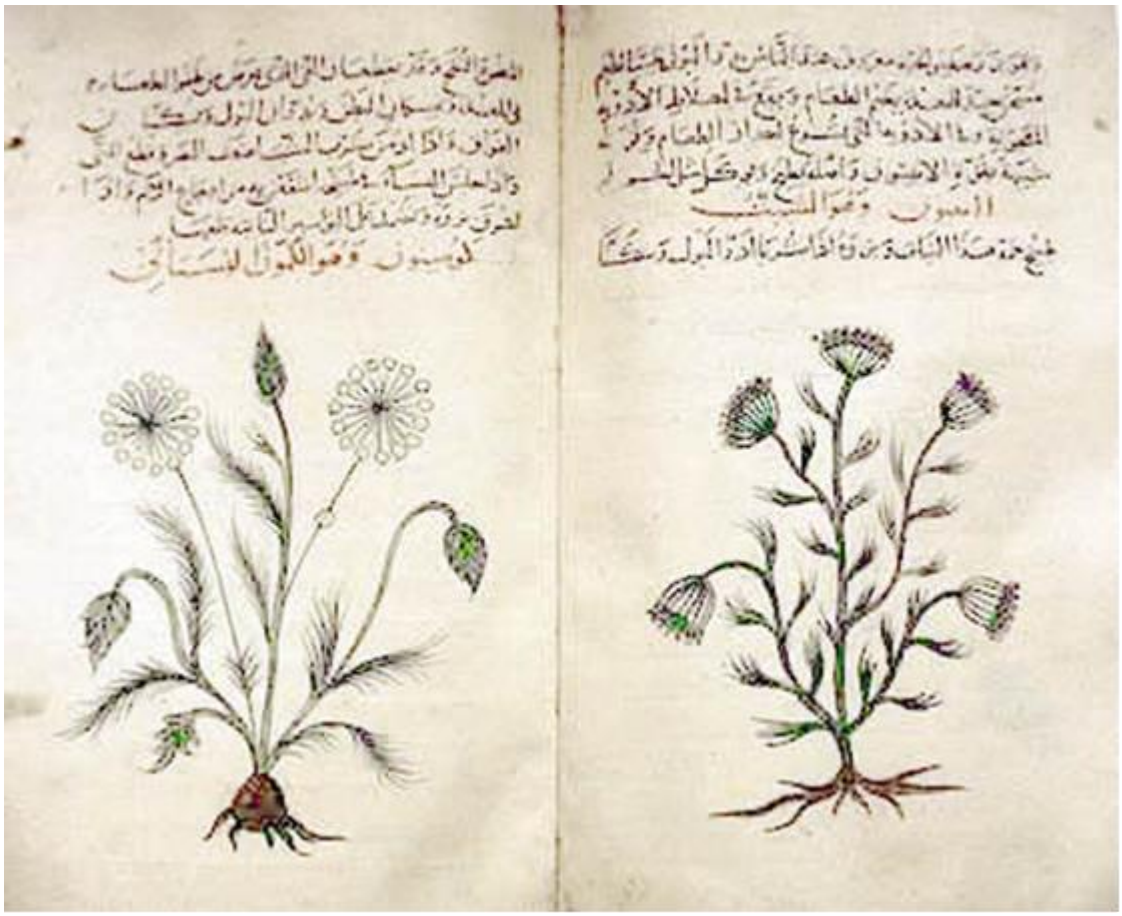

Dioscorides's 1st century De materia medica, seen here in a c. 1334 copy in Arabic, describes some 1000 drug recipes based on over 600 plants.

Those long years that humanity battled serious illnesses and death, led to the rise in awareness of medicinal plant usage and distribution. This helped people all over the world to seek and find useful drugs in seeds, fruits and other parts of a plant. Contemporary science has acknowledged their active action, and it has included in modern pharmacotherapy a range of drugs of plant origin, known by ancient civilizations and used throughout the millennia. The knowledge of the development of ideas related to the usage of medicinal plants as well as the evolution of awareness has increased the ability of pharmacists and physicians to respond to the challenges that have emerged with the spreading of professional services in facilitation of man's life (1). It is very interesting that nowadays, the aberrant use of western drugs has led to their loss of function in about 60% of the patients that use them (2), inevitably leading to the concept of pharmacogenomics or personalized medicine. Personalized medicine means that every human being is a unique creation and that custom tailored treatments can be created for each one of us. These treatments must achieve high efficacy and low to now side effects. We are aware that this

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comes not as new, but personalized medicine has existed in traditional medicine for many years and that traditional and modern medicines can work synergistically and complement each other for the patient's best. In order for all the herbal medicines to be introduced and safely used in western medicine, one must know that standardization, quality control, proof of safety and efficacy are necessary.

25% of all modern medicines are derived either directly or indirectly from higher plants (3, 4). This, in addition to the increasing use of medicinal plants, has led to an increase in concern for their safe use and quality standards from many health authorities, pharmaceutical companies and also their end user, the public. Having said this, it is quite important to understand why quality control and quality assurance is very important when dealing with medicinal or healing plants. According to ISO 9000, quality is a "degree to which a set of inherent characteristics fulfills requirements." Quality control refers to the processes involved directly or indirectly in maintaining the quality and validity of manufactured products. It is of paramount importance for safety, effectiveness, and acceptability of the product and it is an essential operation of the pharmaceutical industry. Drugs must be marketed as safe and with the therapeutically active formulations exhibiting consistent and predictable performance (5).

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Unit 2: Sampling of the final product

Quality assurance on medicinal plants and the final product in general begins with sampling them. Sampling is the procedure in which amounts of product are gathered and packaged accordingly. The form of the final product depends on the starting material and it can be an emulsion, an extract, fine powder, seeds, liquid, flowers or roots. After the opening the first sample taken, you must inspect the contents of the units that are selected for sampling for:

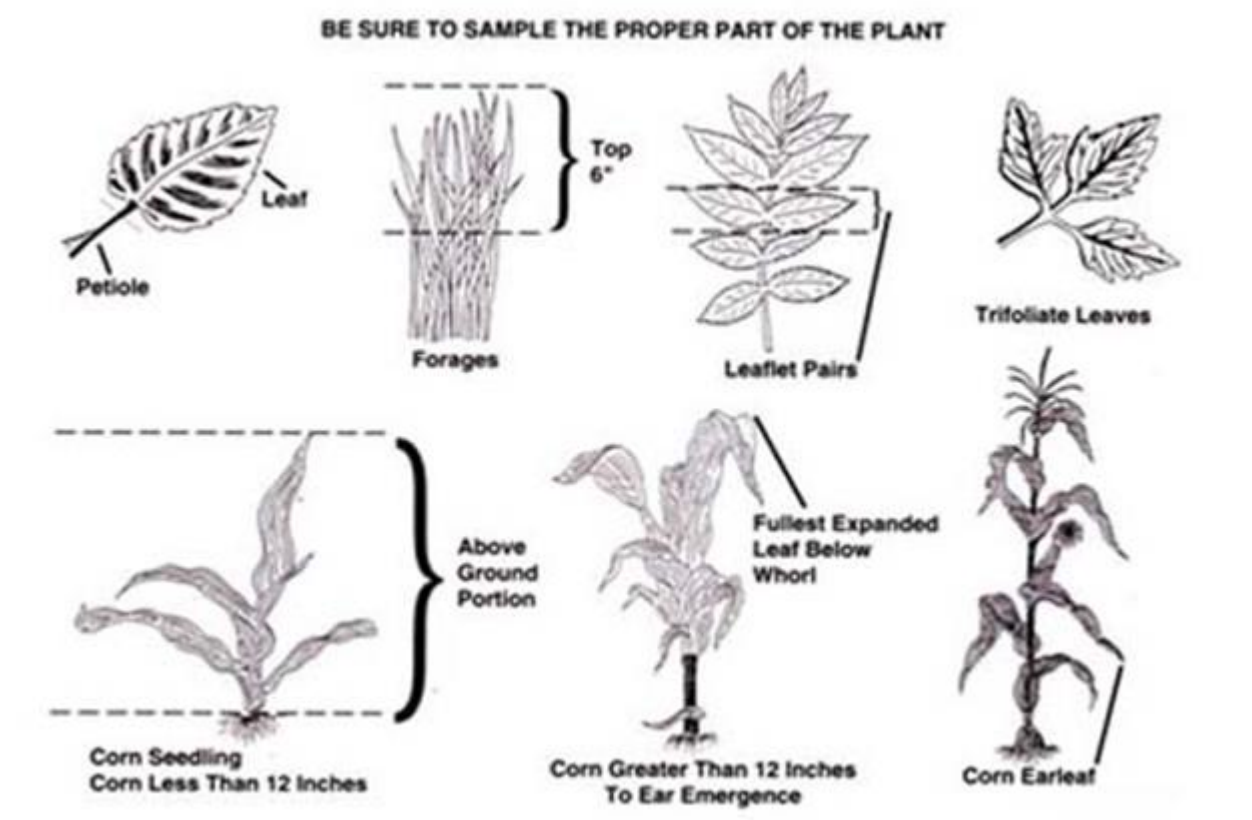
— Organoleptic characteristics (color, texture and odor);

— Presentation of the material (raw, cut, crushed, compressed);

— The presence of admixtures, foreign matter (sand, glass particles, dirt), mold or signs of decay;

— The presence of insects;

— The presence of packaging material originating from poor or degraded containers.



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After this procedure, three samples must be taken from each package. This should be done from the top, the middle and the bottom of the package to ensure uniform gathering. The three original samples should then be combined into a pooled sample, which should be mixed carefully. Then, an average sample needs to be created. This happens via quartering the pooled sample after mixing it. Take two diagonally opposite parts and mix carefully. Repeat the process as necessary until the required quantity, to within ± 10%, is obtained (100– 200 g for flowers and up to 10 kg for certain roots). Any remaining material should be returned to the batch. Using the same procedure that creates quarters, divide the average sample into four final samples, while making sure that each portion is representative of the material as a whole. The final samples are then tested for the following characteristics:

— Degree of fragmentation (sieve test);

— Identity and level of impurities;

— Moisture and ash content;

— Level of active ingredients, where possible.

A portion of each final sample should be retained to serve as reference material, which may also be used for re-test purposes, if necessary (6).

The production of herbal drugs involves three basic steps: (i) identification, (ii) evaluation, and (iii) standardization. Identification of herbs is based on macroscopical and microscopical features. Macroscopical feature involves odor, taste, color, size, shape, and special feature of plant and microscopically involves leaf content, trichome, stomata, and so on. Certain microscopic features and chemical test come under evaluation and standardization of herbal drugs. The term “evaluation of drugs” means the confirmation of their identity, determination of their quality and purity, and detection of any adulteration (7).

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Unit 3: Quality control of medicinal plants/ final product

Despite the fact that herbal products and medicinal plants have gained much popularity nowadays, there is still a problem regarding their acceptance and that is because of the lack of standard quality control profile. Quality of a medicinal plant can be described as the profile of constituents that the final product has. This can cause issues with their safety but also their efficacy. Modern analytical techniques are now able to establish quality control parameters and steps, despite the complex nature of medicinal plants' constituents (8).

It is now established that modern laboratory techniques maintain a high level of quality control for medicinal plants and their final products. There are many techniques that are being used and the most common and successful are among others,

- Determination of foreign matter
- Macroscopic and microscopic examination
- Thin layer chromatography
- Determination of extractable matter
- Determination of pesticide residues
- Determination of arsenic and toxic metals
- Determination of aflatoxins.

Another important step in quality control is the standardization of the medicinal plant (drug) and it involves adjustment of drug preparation to a defined content of a constituent or a group of substances with known therapeutic activity by adding excipients or by mixing herbal drugs or herbal drug preparations. Standardization describes all measures taken during the manufacturing process and quality control, leading to reproducible quality of a particular product that ensures a predefined amount of quantity, quality, and therapeutic effect of ingredients in each dose (9, 10, 11). It is the process of developing and agreeing on technical standards. Specific standards are achieved by experimentation, repetition and observations, which would lead to the process of prescribing a set of characteristics exhibited by the particular herbal medicine. Hence, standardization is a tool in the quality control process (12).

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Therefore, it is vital that the step of standardization is completed successfully in order to ensure reproducibility in the manufacturing of the product. Growing need for standardization and quality control of herbal medicines is recognized by the World Health Organization (WHO). Standardization of botanicals offers many obstacles, and there are several challenges such as controversial identity of various plants and deliberated adulteration of plant material. Therapeutic activity of an herbal formulation depends on its phytochemical constituents (13). The development of authentic analytical methods, which can reliably profile the phytochemical composition, including quantitative analyses of marker/bioactive compounds and other major constituents, is a major challenge to scientists.

Determination of foreign matter (Microscopic/ macroscopic examination)

After the steps of sampling and packaging according to the ways mentioned earlier, the next step for the successful quality assurance of the final products is macroscopic and microscopic examination. This will ensure that the final product will be free of any potentially harmful ingredients. The raw material being used in the preparation of herbal drugs should be pure and free from foreign materials. These exogenous materials could be consisting of parts of medicinal plant materials or materials other than those named with the limits specified for the plant material concerned, any organism, part or product of it, or mineral admixtures not adhering to the medicinal plant materials, such as soils, stones, sand, and dust. Plant materials should be free from any excreta, molds, insects, and chemical residue (14, 15, 16).

Herbal materials should be entirely free from visible signs of contamination by molds, insects, or animal excreta. No abnormal odor, discoloration or signs of deterioration should be detected but is if rarely possible to obtain any plant materials that are free of harmless foreign matter. However, it is obvious that any poison, harmful foreign matter or other residue must not be present.

Macroscopic examination can conveniently be employed for determining the presence of foreign matter in whole or cut plant materials. However, microscopy is indispensable for powdered materials (5).

Limitations regarding the definition of foreign matter should be strict and therefore, the World Health Organization has defined foreign matter as the material that contains:

— Parts of the herbal material or materials other than those named with the limits specified for the herbal material concerned;

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— Any organism, part or product of an organism, other than that named in the specification and description of the herbal material concerned;

— Mineral admixtures not adhering to the herbal materials, such as soil, stones, sand and dust (5).

Macroscopic examination of the final products is probably the easiest way to assess the purity, quality and sometimes quality. It is important that any sample that differs from the standards regarding characteristics such as color, odor or taste should be removed. It is preferred that the same individual carries out the macroscopic examination because of the different judgments of different individuals for the same material. The characteristics that are examined during the macroscopic evaluation of the final products are shape, size, color, surface characteristics, texture, fracture characteristics and appearance of the cut surface.

On the other hand, microscopic examination and evaluation involves the use of a microscope and sometimes the treatment of the final product with a chemical reagent. The features under study include various cellular tissues, trichomes, stomata, starch granules, calcium oxalate crystals, and aleurone grains (17). A complete identification of the final product can be achieved only with the combination of microscopy and other analytical methods.

Physical constants are sometimes considered to evaluate certain drugs. These include moisture content, specific gravity, optical rotation, refractivity, melting point, viscosity, and solubility in different solvents. All these physical properties are useful in identification and detection of constituents present in plants. In addition, they also include foreign matter, total ash, acid-insoluble ash, water soluble ash, swelling and foaming indexes, successive extractive values, moisture content, viscosity, pH, disintegration time, friability, hardness, flow capacity, flocculation, sedimentation, and alcohol content (18).

Macroscopic examination:

- Color: Product should be examined in daylight or in light whose wavelengths similar to those of daylight. The color of the sample should be compared with that of a reference sample.

- Surface characteristics and texture: The sample of the product can be examined with the use of a magnifying glass. The material can be wet with water or reagents, as required, in order to observe the characteristics of a cut surface. The sample should be touched to determine if it is soft or hard; bended and ruptured to obtain information on brittleness and the appearance of the fracture plane — whether it is fibrous, smooth, rough, granular, etc.

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- Odor: A harmless material can be placed on the palm of the hand and the individual can slowly and repeatedly inhale the air over the material. If there is no distinct odor, you crush the sample between your thumb and index finger or between the palms of your hands by utilizing gentle pressure. If the material is known to be dangerous, crush by mechanical means and then pour a small quantity of boiling water onto the crushed sample in a beaker. First, determine the strength of the odor (none, weak, distinct, strong) and then the odor sensation (aromatic, fruity, musty, moldy, rancid, etc.). A direct comparison of the odor with a defined substance is advisable (e.g., peppermint should have an odor similar to menthol, cloves should have an odor similar to eugenol) (5).

Microscopic examination:

The following are required:

— A microscope equipped with lenses providing a wide range of magnification and a sub stage condenser, a graduated mechanical stage, objectives with a magnification of 4×, 10× and 40×, and color filters of ground glass, blue-green; high eye point eyepieces are preferred for wearers of spectacles;

— A lamp, either separate or incorporated into the microscope;

— A set of polarizing filters;

— A stage micrometer and an ocular micrometer to be inserted into a 6x eyepiece and placed on the diaphragm or, preferably, a micrometer eyepiece;

— A set of drawing attachments for the microscope;

— A micro burner (Bunsen type);

— Slides and cover glasses of standard size;

— A set of botanical dissecting instruments.

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Unit 4: Laboratory techniques

Methods for quality control of herbal medicines involve analytical inspection using chromatographic and spectroscopic techniques. They include TLC, HPLC, GC, ultraviolet (UV), Fourier transform infrared (FT-IR), atomic absorption spectroscopy (AAS), fluorimetry, near

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infrared (NIR), and the spectrophotometer. HPLC fingerprinting includes the recording of the chromatograms, the retention time of each individual peak, and the absorption spectra with different mobile phases. Similarly, gas–liquid chromatography (GLC) is used for generating the fingerprint profiles of volatile oils and fixed oils of herbal drugs. Furthermore, the recent approaches of applying hyphenated chromatography and spectrometry such as gas chromatography–mass spectrometry (GC–MS), capillary electrophoresis-diode array detection (CEDAD), high performance liquid chromatography–thin layer chromatography (HPTLC) and high performance liquid chromatography–mass spectroscopy (HPLC–MS), could provide the additional spectral information, which will be very helpful for the qualitative analysis and even for the on-line structural elucidation (4, 19, 20, 21).

There is also a plethora of DNA techniques that are being used as a supplement to methods and techniques of classical botany for plant identification, including RAPD, RFLP, ARMS, CAPS, AFLP, ISSR, hybridization and microarrays (22). A recent technological development is the authentication of medicinal plants by barcode DNA. This method is based on the detection of variable sites of the rDNA internal transcribed spacer (ITS). DNA barcoding provides a powerful tool for the authentication of plants, and is exquisitely suited for quality control of medicinal plants. Research that is currently conducted in this field focuses on the question, how many and which DNA fragments are necessary for the optimal discrimination of different species.

The following is a presentation of each of the aforementioned techniques and the ways they offer quality assurance of the final product.

CHROMATOGRAPHIC/ SPECTROSCOPIC TECHNIQUES

TLC (Thin layer chromatography): Thin-layer chromatography (TLC) is a chromatography technique and it is used for the separation of non-volatile mixtures (23). It uses a sheet of either glass, plastic or aluminum foil that is covered with adsorbent material (silica gel or aluminum oxide) and this is called the stationary phase. Next, the sample is applied on the plate and then the mobile phase (a solvent or solvent mixture) is drawn up the plate through capillary action. The mixture is separated due to the fact that different analytes can ascend a TLC plate at different rates (24). It is important to know that the mobile and stationary phase have different properties and a mobile phase can also be a mixture and this enables any chemist to fine tune the properties of the mobile phase. This, as a result, can be used when performing quality control on mixtures of extracts of medicinal plants and their final products and is a relatively easy method of separating mixtures.

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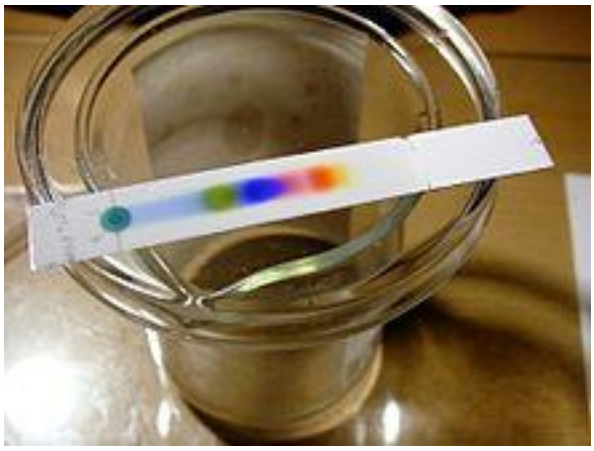

Separation of black ink on a TLC plate

HPLC: High-performance liquid chromatography, is a laboratory technique used on a mixture and it helps to separate, identify, and quantify each component. It utilizes pumps to pass a liquid solvent that is under pressure, containing the sample mixture through a column filled with a solid adsorbent material. It is known that each component that exists the sample, interacts slightly differently with the adsorbent material that is used each time and thus, different flow rates for the different components exist and this is leading to the separation of the components as they flow out the column (25). With this technique, the scientist has total control over operational parameters such as the flow rate of the mobile phase, buffer control of the mobile phase, column oven temperature, etc. In addition, HPLC software is capable of reporting precise and accurate results based on area counts of peaks and this can help on quality assurance of medicinal plants via identification of the elements in a mixture and separate them depending on quality.

An HPLC

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GC: Gas chromatography (GC) is a chromatography technique used for separating and analyzing compounds that can be vaporized. Typical uses of GC include testing the purity of a particular substance (for example our final products of medicinal plants), or separating the different components of a mixture (the relative amounts of such components can also be determined, a useful ability when we need to determine foreign matter in a mixture). In some situations, GC may help in identifying a compound. GC can be used to prepare pure compounds from a mixture (26, 27). Gas chromatography is similar to column chromatography regarding its principles, but has several differences. First, the process of separating the compounds in a mixture is performed between a liquid stationary phase and a gas mobile phase, whereas in column chromatography the stationary phase is a solid and the mobile phase is a liquid. (Hence the full name of the procedure is "Gas–liquid chromatography", referring to the mobile and stationary phases, respectively.) Second, the column through which the gas phase passes is found in an oven where the temperature of the gas can be controlled, whereas column chromatography has no such temperature control (26).

Ultraviolet–visible spectroscopy: Ultraviolet–visible spectroscopy or ultraviolet-visible spectrophotometry (UV-Vis or UV/Vis) is a technique that yields results in the ultraviolet-visible spectrum. This means it uses light in the visible and adjacent spectra. The absorption or reflectance in the visible range can directly affect the color of the chemicals involved. In this region of the electromagnetic spectrum, atoms and molecules undergo electronic transitions. Absorption spectroscopy is complementary to fluorescence spectroscopy, because fluorescence is used for transitions from an excited state to the ground state, while absorption measures transitions from the ground state to an excited state (28). UV/Vis spectroscopy can be utilized for the quantitative determination of different analytes, for example, highly conjugated organic compounds, and biological macromolecules. Spectroscopic analysis is performed in solutions but solids and gases may also be studied.

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Beckman DU640 UV/Vis spectrophotometer.

Fourier transform infrared spectroscopy: Fourier transform infrared spectroscopy (FTIR) is a technique which is used to obtain an infrared spectrum of absorption or emission of a solid, liquid or gas. The fact that an FTIR spectrometer collects high spectral resolution data over a wide spectral range simultaneously, confers a significant advantage over a dispersive spectrometer which measures intensity over a narrow range of wavelengths at a time. The goal of any technique relevant to absorption spectroscopy, is to measure how well a sample absorbs the light at each wavelength. This can be done through shining a monochromatic beam at a sample and then measure light absorption and then repeat these steps for each different wavelength.

Fourier transform spectroscopy can be used to obtain results in a less intuitive way. Rather than shining a monochromatic beam of light at the sample, this technique shines a beam containing many frequencies of light at once, and measures how much of that beam is absorbed by the sample. Next, the beam can be modified in order to contain different combinations of frequencies, giving a second data point. This process is repeated many times. Afterward, a computer takes all this data and works backward to infer what the absorption is at each wavelength (29).

AAS: Atomic absorption spectroscopy (AAS) refers to a spectroanalytical method that is utilized for the quantitative determination of many chemical elements by using the absorption of light by free atoms that exist in the gaseous state. In analytical chemistry, the technique is used to determine the concentration of a particular element (called the analyte) in a sample to be analyzed. AAS is able to determine over 70 different elements existing in a solution or directly in any solid sample that is used in pharmacology, biophysics and toxicology research. AAS is widely used in chemistry, on the analysis of biological fluids, tissues such as blood, saliva etc. It is also

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utilized in the analysis of the final drug product regarding the quantity of the catalyst that remains in it (30).

Flame atomic absorption spectroscopy instrument

Near-infrared spectroscopy: NIRS is a spectroscopic method that uses the near-infrared region of the electromagnetic spectrum (700 nm to 2500 nm). Typical applications include diagnostics and research. Numerous applications in other areas exist as well, such as pharmaceutical, food and agrochemical quality control, something that is of interest to us. Near-infrared spectroscopy is widely applied in agriculture for the determination of the quality of fruits, vegetables, eggs and dairy products, coffee, tea and spices. By utilizing NIRS one can quantify the compositions of those products in a reliable, fast, cheap and non-destructive way (31). So, it is very important to utilize NIRS for the determination of the quality of our final products and mixtures of final products regarding medicinal plants.

Spectrophotometer: A spectrophotometer is used for the measurement of either transmittance or reflectance of solutions and other forms of matter such as transparent or opaque solids, polished glass, or gases. Colorless biochemicals can be converted and be colored in order to be suitable for reactions that form chromogenic compounds and then perform a colorimetric analysis (32). Spectrophotometry is a technique often used for important measurements including those of enzyme activities, determinations of protein concentrations and determinations of enzymatic kinetic constants. Ultimately, when using a spectrophotometer we

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are able to determine, the substances present in a target sample and exactly how much is there, through calculations of the observed wavelengths, something helpful when the target is a mixture of medicinal plants or an extract as well.

GC - MS: Gas chromatography–mass spectrometry (GC-MS) is an analytical method that combines the features of gas-chromatography and mass spectrometry for the identification of different substances within any given sample (33). Of the many applications of GC-MS, some include drug detection, environmental analysis, and identification of unknown samples (useful when we examine a sample from an unknown plant or mixtures). What is even more interesting is that GC - MS can identify trace elements in materials thought to have disintegrated beyond identification through analysis and detection of even the tiniest amounts of a substance. The GC-MS machine is composed of two major blocks: the gas chromatograph and the mass spectrometer. As for the technique, it uses a capillary column which depends on the column's dimensions (length, diameter, film thickness) as well as the phase properties (e.g. 5% phenyl polysiloxane). Separation of the molecules while the sample travels through the length of the column will happen because of the different chemical properties that different molecules in a mixture have. Also, their relative affinity towards the stationary phase of the column is a factor for the separation. The column retains the molecules and then they elute at different times (this is called retention time). This is what allows the mass spectrometer to capture, deflect and detect the ionized molecules each one separately.

Example of a GC-MS instrument

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CEDAD: Capillary electrophoresis (CE) is a method that is performed in capillaries and in micro-fluidic and nano-fluidic channels. The term diode array detection (DAD) when used in capillary electrophoresis (CE) can effectively offer similar advantages as in HPLC, regarding single-wavelength detection. With an optimized optical system, DAD yields sensitivity comparable to that of single or variable wavelength detectors (34). CEDAD is useful when one needs the separation of elements of a mixture in order to next identify them, as in our case, the separation of mixtures of different elements.

HPTCL: High performance thin layer chromatography, is a form of thin layer chromatography that is enhanced with a number of improvements in order to increase the resolution and thus allow more accurate measurements(35). The procedure begins by using a plate that has the samples in it and then we load the first solvent. Then, we rotate the plate by 90° and then it is developed with a second solvent.

HPLC – MS: Liquid chromatography–mass spectrometry (LC-MS) refers to a technique used by analytical chemists and can combine the physical separation capabilities of liquid chromatography with the mass analysis capabilities of mass spectrometry (MS). Systems that couple MS and chromatography are very popular in chemical analysis because the individual capabilities of each technique are enhanced synergistically. The advantage of using HPLC – MS is that while liquid chromatography separates mixtures with multiple components, mass spectrometry can provide is with the structural identities of each of the individual components with both a high molecular specificity but also sensitivity in detection. This is technique that it is usually called a “tandem technique” and it can be used to analyze biochemical, organic, and inorganic compounds that we commonly find in complex samples of environmental and biological origin. Therefore, LC-MS can be applied in a wide range of fields including biotechnology, environmental monitoring, pharmaceutical and agrochemical industries, something of great interest especially when dealing with medicinal plants (36, 37). In addition to the liquid chromatography and mass spectrometry devices, an LC-MS system can contain an interface that can efficiently transfer the separated components from the LC column into the MS ion source (37, 38). LC-MS is frequently used in drug development because it allows the quick confirmation of molecular weight and structure identification of the drug under investigation. These features speed up the process of generating, testing, and validating a discovery starting from a vast array of products with potential application. LC-MS can be applied as a technique for drug development and especially for in vivo drug screening, metabolite identification, impurity identification, quantitative bioanalysis, and quality control (39).

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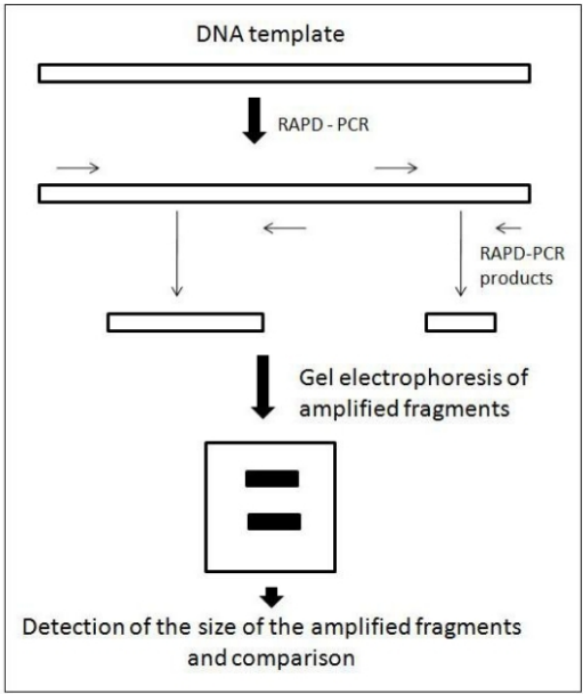
DNA TECHNIQUES

RAPD: RAPD means 'Random Amplification of Polymorphic DNA' (40) and it is a type of PCR reaction, but the amplified DNA segments are random and not specific. The main principle of the technique is the creation of several arbitrary and short primers (8–12 nucleotides), followed by the PCR using a large template of genomic DNA and hoping that some fragments will amplify. The resulting patterns can be resolved and we can obtain a semi – unique profile from this reaction. No knowledge of the DNA sequence of the targeted genome is required, as the primers will bind somewhere in the sequence, but it is not certain exactly where. RAPD is an inexpensive yet powerful typing and identifying method for many bacterial species. It can be used when we need to obtain soil for the creation of a medicinal drug and it needs to be bacteria free. The identification of the different strains can lead to the best strategy for getting rid of them.



The RAPD technique

RFLP: In molecular biology, RFLP, is a technique that uses the variations that exist in homologous DNA sequences. When performing RFLP, the DNA sample must be broken into segments

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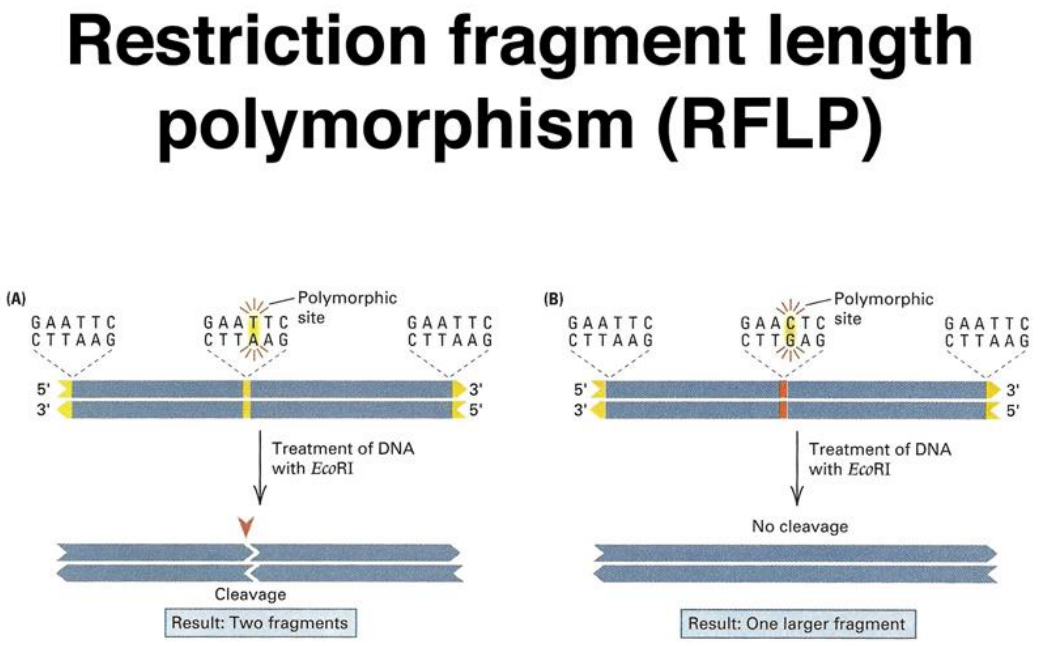
(digested) by known restriction enzymes. Then, those segments are separated according to their length by using gel electrophoresis. This technique is useful when we want to illustrate the differenced between certain DNA samples and also group them according to the digestion patterns. RFLP analysis has been for years the basis for early methods of genetic fingerprinting, useful in the identification of samples often retrieved from crime scenes etc, but also from environmental samples. This helps in the identification of certain rare plants and their byproducts.



The RFLP technique

ARMS: The amplification-refractory mutation system (ARMS) is a simple method used for the detection of mutations called SNPs (Single nucleotide polymorphisms) or very small deletions. The technique principle is based on the use of sequence-specific PCR primers that allow the amplification of the DNA only when the target allele is contained within the sample. After completion of the ARMS reaction, either the presence or absence of a PCR product is indicative of the presence or absence of the target allele. This can help in identification of mutated strains of bacteria of fungi that can be present in the final product and also be useful (for example the Bifidus Actiregularis bacteria).

CAPS: The cleaved amplified polymorphic sequence or CAPS method is a technique in molecular biology for the analysis of genetic markers. It is an addition, or extension to the RFLP method, using polymerase chain reaction (PCR) for faster result analysis. Similar to RFLP, CAPS also exploits

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the fact that differences on individuals can offer new restriction enzyme sites or abolish existing ones. Then, those differences can be detected and analyzed. In the CAPS method, PCR amplification is mainly focused towards the altered restriction site, and the products digested with the restriction enzyme. When agarose or acrylamide gel electrophoresis is performed, the digested PCR products will give distinguishable patterns of bands.

AFLP: AFLP-PCR or just AFLP is a PCR-based technique that is used in genetics research, and in genetic engineering. The method is simple and it utilizes restriction enzymes in order to digest DNA and then, specific adaptors are ligated to the sticky ends that the enzymes have created. A small group of those fragments is selected and amplified. Selection is based on the use of primers that are complementary to the adaptor sequence, the restriction site sequence and a few nucleotides inside the restriction site fragments. After the amplification, the fragments can be separated and then visualized on polyacrylamide gels. The results obtained are referred to as presence – absence polymorphisms (41). The AFLP technology has the capability to detect various polymorphisms in different genomic regions simultaneously. It is also highly sensitive and reproducible. All of the above, make AFLP a suitable tool for the identification of genetic variation in various strains of plants, animals, fungi etc.

ISSR – PCR: ISSR (for inter-simple sequence repeat) is a general term for a genome region between microsatellite loci. The complementary sequences to two neighboring microsatellites are used as PCR primers so that the variable region between them gets amplified. In order to prevent excessive replication of long DNA sequences, there is a limit to the amplification cycles during this type of PCR. This is useful because the resulting DNA strands will be generally short but varying in length. One must pay attention to the fact that this technique is not capable of distinguishing individuals because an ISSR can be a conserved or non-conserved region.

DNA barcoding: DNA barcoding is a method of taxonomy and it uses a short genetic marker in an organism and his DNA in order to identify it and then categorize it as belonging to a specific species (42). It is different that phylogeny because here, the main goal is to identify an unknown sample in terms of a preexisting classification (43). Although barcodes are sometimes used in an effort to identify unknown species, (44) the utility of DNA barcoding for these purposes is subject to debate (45). The most famous commonly used barcoding region for animals is a fragment of approximately 600 bp and it belongs to the mitochondrial gene cytochrome oxidase I (COI). This is different in fungi, where part of Internal Transcribed Spacer 2 (ITS2) between rRNA genes is used, and again in plants, where multiple regions are used.

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Applications of DNA barcoding include, identifying plant leaves even when flowers or fruit are not available, identifying insect larvae, identifying the diet of an animal based on its stomach contents or feces (46) and identifying products in commerce (for example, herbal supplements, wood, or skins and other animal parts) (43). Having a well characterized and standardized locus for DNA barcoding is optimal. It should also be present in the taxa of interest, easily sequenceable (47), short enough (48) and provide large interspecific than intraspecific variation (49). For plants, it is the concatenation of the rbcL and matK chloroplast genes (47, 50). These provide poor resolution for land plants (51, 52) and a call was made for regions to be assessed that could complement rbcL and matK (52). For fungi, the internal transcribed spacer (ITS) region (53). Kress et al. (43) suggest that the use of the COI sequence "is not appropriate for most species of plants because of a much slower rate of cytochrome c oxidase I gene evolution in higher plants than in animals". A series of experiments was then conducted to find a more suitable region of the genome for use in the DNA barcoding of flowering plants (or the larger group of land plants) (48). One 2005 proposal was the nuclear internal transcribed spacer region and the plastid trnH-psbA intergenic spacer; (43) other researchers advocated other regions such as matK (48).

In 2009, it was proposed by a large group of DNA barcode researchers that the following two chloroplast genes (rbcL and matK) should be used as a barcode for plants (47). The addition of the ITS2 region happened in order to provide a better interspecific resolution (54). The search for the best DNA barcodes regarding plants continues with the latest proposal that the ycf1 region belonging in the chloroplast may be suitable (51).

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57. The Marketing Accountability Standards Board (MASB) endorses this definition as part of its ongoing Common Language in Marketing Project

Module No. 4

“Business start-up in the sector of medicinal plants”

FyG Consultores

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Unit 1: Business Start-Up Planning

Social media, internet, newspaper, radio and everywhere around people talk about new challenges, opportunities, business, sectors that are growing and Start-Ups that are growing everywhere from all possible sectors (IT, Marketing, Medicine, Education, Entrepreneurs etc.). The most common small business that are spreading all over the Europe. Find the idea and have an idea is one thing but build the Start-Up is another story. While creating your own business – Start-Up everyone has to know that it's like roller coaster – one moment you are up and feeling like a start but suddenly you can "go down" and fall apart with many issues and doubts about your future. Diversity is good and can cause many positive results. A Start-Up is the opportunity for everyone – there are no limits related to age, generation, sex or nationality. This sector is open and very wide. What's important is to have in mind that while creating a Start-Up it is made for people, for the society in order to change the way that people live their lives.

Short summary about Star-Up:

- young developing company (young doesn't mean it needs to be run by young people)
- most of the time small at the beginning and financed by founds/government support /EU or one individual

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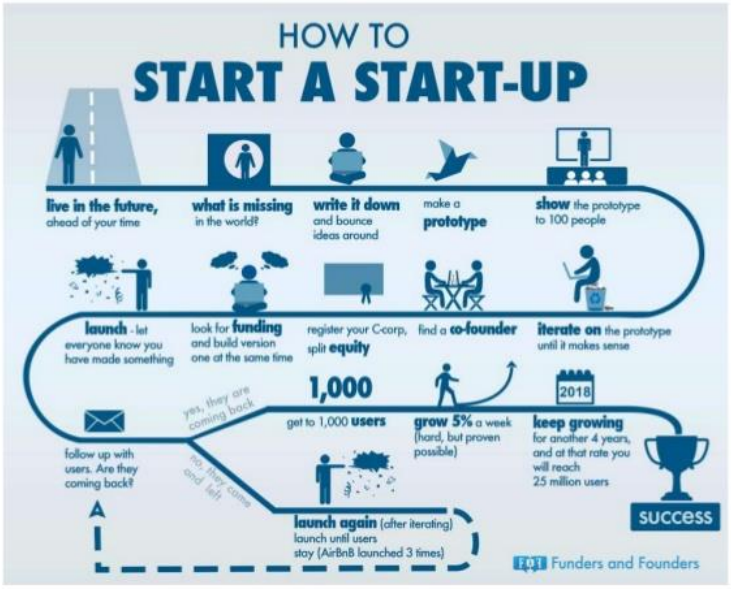
- offering product or service that is new and has the purpose of facilitating life of the others
- offering something that already exist but in an innovative, better and modern way

Important to know that Start-Up is not the same as a Small Business. Start-Up is usually a temporary organization that is following a Business Model and searching for new possibilities and challenges. The idea that's is creating should crash with the current market and have significant impact on it. Start-Ups starts from zero and the support is not the same as fro well known big companies.



Important to know:

- A Start-Up is Temporary; later with time its growing and turning into a big company.

The organizational function of the Start-Up is to search for a repeatable and scalable business model. According to Blank, this means that a Start-Up founder has three main functions:

1. To provide a vision of a product with a set of features

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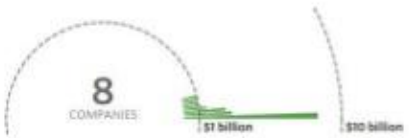
2. To create a series of hypotheses about all the pieces of the business model: Who are the customers? What are the distributions channels? How do we build and finance the company, etc.
3. To quickly validate whether the model is correct, by seeing if customers behave as your model predicts (which he admits they rarely do).

- **A Start-Up Is Funded Differently**

Start-Up and any other small business might start with funds from the founder's savings, family or friends support or a bank loan. If a Start-Up is successful probably will receive additional series of funding from an investor or initial public offering (IPO). The Start-Up founder's equity is eroded but ownership of the company diversifies.

The Eight Most Successful Start-ups in Europe which you might know and use their service



Company	Latest Valuation	Total Equity Funding	Last Valuation
Spotify	$8.5 billion	$1.0 billion	May 2015
Delivery Hero	$3.1 billion	$1.3 billion	June 2015
Powa	$2.7 billion	$156 million	November 2014
Adyen	$1.5 billion	$500 million	December 2014
Home24	$1.0 billion	$20 million	December 2014
Shazam	$1.0 billion	$170 million	January 2015
Farfetch	$1.0 billion	$195 million	March 2015
Funding Circle	$1.0 billion	$273 million	April 2015

Source: http://graphics.wsj.com/billion-dollar-club/

You are probably asking yourself what kind of skills you need to build your Start-Up. Let's be honest:

- You should be patient
- You have to know you might work more than 8 hours per day and probably during the weekends
- You have to be motivated and have positive attitude – with positive attitude everything is possible!

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- You should be open-minded in order to keep your business innovative
- Be creative in order to make your business different and bit your competitor
- Do not be afraid to fail

"Forget about the consequences of failure. Failure is only a temporary change in direction to set you straight for your next success." **Denis Waitley**

"I can accept failure, everyone fails at something. But I can't accept not trying." Michael Jordan

How to start my Start-Up?

First of all, think and have an idea as it´s the basic and very important step. Without any idea, we can´t start. Make a list of your possibilities, advantages, ideas and skills – everything that you have today.

We share with you some features and facts that might help you believe that you can do it because for sure you have one or more from those:

- The idea
- Knowledge about the sector/field/market
- Energy to work
- Motivation – I want to work and earn money
- Have large field
- Love plants and I grow plants
- You work hard
- You have marketing/sales/finance/IT experience
- You have positive attitude
- You very well organized and you go-ahead

As we mentioned, first you need to think about the idea, so what medicinal herbs/plants you would like to grow and what kind of herbs you can grow in your environment – not the same plants can grow in Greece, Italy or Poland. Remember that the market is huge and there are hundreds to choose from.

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Don’t feel like you have to grow everything, it is best to focus on the one that might bring clients and help your business grow! If you start with all kinds of plants at the same time, it might create more headaches and unnecessary hard work than if you just focus on a selected few. That way you’ll become an expert on those ones and you will build a reputation as a medicinal plants/herb expert.

It is very important to know before you start - think carefully about the time when you start (which period of the year). Do you want to start when your plants will grow or maybe before in order to prepare everything?

Opening new Medicinal Plants Business is very similar to any other IT, Marketing, Cosmetics, Sales business. Before you “Go Live” you have to read a lot, learn and be ready for everything that might come. The key for your business is the space and good conditions for your plants which are your power!

Each sector needs other environments in order to succeed, that’s why its critical to have in mind which kind of requirements are related with your area.

Before you decide the plants to cultivate, think about:

- Your climate, soil and irradiation
- Place that you have and space
- Time that you can and want to spend
- Proper equipment that you need
- Delivery service – by car, train, post office?
- Working a lot with nature – do you like it?
- Kind of plants you would like to grow – if you grow something you like you will enjoy it!
- Amount of plants you can afford and you want to sell – do not start with so many as it might be difficult at the beginning. Better go step by step
- What kind of winter and summer temperatures your plants need
- Who will work with you, who will support you – it might be difficult at the beginning
- Who will take care of the plants
- Who will manage the business?
- Who will work with the clients
- Who will be responsible for the marketing and financing part
- Who will sell the plants?
- What’s the way to sell the product?
- Where will you store seeds and plants
- How much space each plant needs
- If you need a greenhouse or not
- Your motivation and involvement – without that it will not work!

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Here are a few popular medicinal herbs to consider growing for profit:

Catnip – Used primarily as a stimulant for cats. Used also for pain and stress relief, as well as helping with cold and flu symptoms.

Chamomile – Can make for a great, soothing tea. Medicinal benefits such as: being a digestive, calming and sleep aid.

Lemon Balm – the strongly scented leaves of this herb can make for a great tea in addition to being an immune booster and beneficial to the digestive tract.

Marshmallow – this herb, also known as Althaea officinalis, used to treat many skin conditions, coughs and bronchitis, helpful for the digestive tract.

Mint-Mentha – Originally used as a medicinal herb to stomach ache and chest pain.

Which are the advantages of creating Business related to Plants?

- ✓ Working with nature – no need to be 8hours watching your PC and stay in the same position for minimum 8 hours
- ✓ Getting back to basic stuff – working with nature which is good for your body and soul
- ✓ Work close to your home as many people dream about the job that allows them to stay at home and "work from home" so they can spend time with family and be closer with them
- ✓ You start with small field and if you see it's growing you make it bigger
- ✓ You can always add or change the plant it you see that there is a need for it

Creating a Start-Up is like going for a trip somewhere where we have never been before. You have the basic knowledge about the place – in this aspect about you have the basic idea and know the sector but there are still missing facts that you will learn while "travelling".

Have a look on 7 Steps you should walk through during your Business Journey:

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1. Manage a personal evaluation

- What's the reason that you want to start a business? What motivates you? Money, different life, changes, dignity or other reason?
- What competences do you have and which ones you can use?
- About which area or sector you know more?
- Will you offer a product or service?
- Do you feel like working part time, full time, weekends or night sheets?

2. Evaluate your industry

As soon as you make a decision on which kind of business you want to have. The one that fits your goals and expectations, you should evaluate your idea in order to make sure that it's a good one and will work out. Who is your customer? Will they buy the product? Do you have competitors, if yes who they are? Don't forget about money – it's important to know how much you need to start.

- How big is the market? Are there other services like mine and people are paying for it? Maybe the idea you have is no longer existing and people won't pay for need as they don't need it anymore. Example: "handwriting classes" is almost anachronism.
- How easy or hard is it to get a customer? How much do I have to spend in order to acquire a new customer?
- How much time, effort and money you need in order to deliver the best profit and service?
- How long will it take for you to get to the market? Is it an easy/small market or on the contrary very difficult one? Is one month, year enough to be recognize and connect with this market?
- What do you have to invest before you start?

3. Remember to work legally

- Check very carefully pros and cons of this specific business
- What papers and perditions you need
- What conditions are required

4. Start the planning process

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"Our goals can only be reached through the vehicle of a plan, in which we must fervently believe, and upon which we must vigorously act. There is no other route to success." – Pablo Picasso

You can start planning process by creating a roadmap – business plan. It will help you chart your progress and at the same time show you missing aspects you have to accomplish in order to achieve specific goal. Business plan is not another paper that later you might throw away, think about it as a document where you can formalize your ideas and intentions. Again, we come back to the topic of travelling, before going somewhere you plan the trip with more or less details but you do it. The same with Start-Up, you need a plan that you will follow or at least you will a based that might be changed. Planning helps to uncover missing parts that you have not thought trough before. Basic planning refers to simple questions, for example: When do I want to start? Where will I work? What do I need? Do I need a team? How much money and equipment I need?

5. Get financed

Depending on the size of your business it's always complicated to find financing help at the beginning. Most of the time people start with their own financing savings. Before you go to the bank of ask you family to support you check all possible governmental or European help for Start-Ups from many different sectors. Maybe it won't cover all your needs but it's always good to receive some extra money.

6. Set up shop

Slowly you are getting there, to the end. Business Plan done, money collected and waiting in the bank, ideas ready to go and get on fire so you are also ready to go. Still there is a long list of tasks to do. From many steps, you still have to take some of them are related to setting the shop. If you decide to sell online and have also a shop think about: location, place, furniture, printer, phone etc. Location is very important as it might dictate the type of customer you attract, what kind of promotions and events you can run. Great location doesn't guarantee a big success but from the other hand a bad location might definitely guarantee failure.

If you are thinking about Shop or sale your products online anyway you have to think about:

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Price – How much people can spend on this product? How much you have to earn to keep working and growing?

Visibility – Is it easy to see your shop? Is your website easy to ready? If you run a promotion, will they see it? Do you have a parking place? Are you in the centre or far away without any access to the public transport?

Competitors –Do you have your competitors close to you? If yes, maybe the location is not the best and you should change it? Who are your competitor and how can you do your business better and provide the service that will attract the customer more than the other.

Local, city, village, rules and regulations—Look into regulations, as areas may be more stringent than others. Make sure there are no restrictions that might limit your operations.

Good to know:

- If you place your products low on shelves that can cost a situation when people are unlikely to see them and therefore unlikely to buy them, whereas placing them at eye-level will mean they're seen first and are therefore probably more likely to reach and be bought.
- Your choice of products and how you decide to price them will create a reputation.
- If you're a service business, build your services in a similar manner, considering your different clients and the value they will get from the different options you offer.

7. Expect to make mistakes

Whether you're starting your first or your third business, always expect to make mistakes. This is natural and at the same time making mistakes means learning and improving.

If you do not make mistakes, you do not learn what to do more and what less. Be open-minded, creative, adapt to the situation, look for opportunities, and above all, enjoy what you do!

The great thing about owning your own business is that you get to decide what you want to do and what direction you want to grow in.

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Unit 2: Market Analysis

Before you go out of your comfort zone you have to check where, how and when should you go and where will you have a chance to succeed. Market analysis is another must for your business – check where is a need, who might buy your product, who is already buying the same product but maybe more expensive, where people are not interested in medicinal plants/herbs – if they are not interested maybe its worthy to check why and start there? Market Analysis can give you a lot of answers for questions related to your future customer.

Nowadays people want to live and have healthy life and pay more attention to what they eat and how they eat. Due to this change, there is a big chance for medicinal plants and herbs to get into the market and attract more clients. Listening about eco-friendly products you might realise that with eco-friendly Medicinal Plants you have a chance to succeed and grow very fast.

If people get what they want and at the same time it's not very expensive but is helpful they are happy and by the time they are willing to pay more for the same product. Making people happy will make you happy.

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Medical research show that there are many herbs which can be used as health alternatives to expensive medicines. It's been reported that in Germany, doctors write seven times as many prescriptions for St John's Wort as they do for Prozac for depression. Because of this fact Medicinal Plans Business is really a good business as people will always get sick and need health support.

Sell my product in the new market. How am I going to do it? How to sell my product now if I have no idea where to go?

Living in 21st century process of selling in not a problem. The issue can be what to sell and how because there is always a way to do it. The market is giving us many channels and due to that fact it's very easy to sell as you can do it online using your online shop/website and at the same time keep selling in your shop or farm. If you run your business at the farm maybe there is a fresh market where your customers go every morning? All eco-friendly events are full of your potential clients as for them their health is very important and they are more likely to try your products. Once the good product will reach to the client it might start an automatic promotion process by "selling" success stories to the neighbours and friends.

There are also many other good news!

- European consumers are becoming more aware of the importance of healthy lifestyles. They take more responsibility for their personal health, integrating mental and physical wellbeing.

- *Euromonitor expects the European food supplements market to grow by 28% from 2013 to 2018. Demand for food supplements is strongest in Western Europe: Germany, France, Italy and the UK. (CBI, Ministry of Foreign Affairs)*

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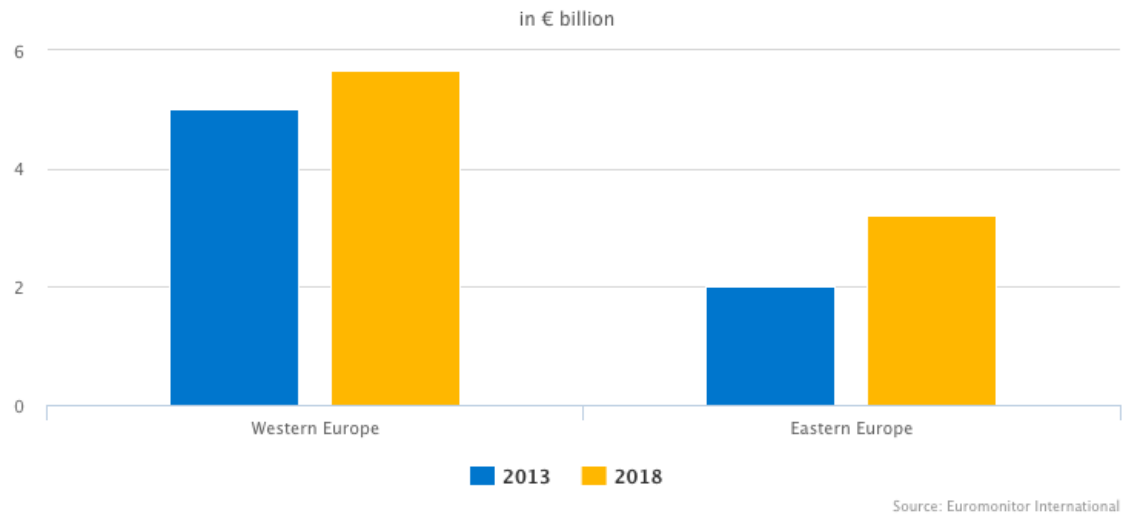
Figure 1: European food supplements markets



- *The strongest growth stems from Eastern European countries, such as Poland, Romania and Slovakia. In 2018, the region is expected to reach a market size of €3.2 billion. Russia makes up around two thirds of that.* (https://www.cbi.eu)
- Very popular trend to live healthy and eco connects with need of healthy products which are safer than synthetic alternatives. Trending natural ingredients include marine ingredients and all that contains Omega-3
- This generated a renewed interest in natural remedies for healthier lives, such as herbal medicinal products
- France and Germany are the region's market leaders in terms of market for herbal medicinal products in Europe.

- In 2015, consumers from Germany spent 1.15 Euro billion (retail prices) on making self-medication herbal products. In 2008, France held a share of 24% of the European market for herbal medicinal products. France is the number-two market in Europe.

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The market for herbal products in the United Kingdom was estimated at *£485 million (€668) in 2012*. This figure also includes food supplements. Spain has a relatively small and declining market of €213 million.

In Eastern Europe, Poland is the main and growing market. A rough estimate of the Polish market is €600 million. (CBI, Ministry of Foreign Affairs)

Interest herbal medicinal products is growing in East European markets, specially Bulgaria, Czech Republic and Romania. Looking outside of the EU, Russia is the main market where we can see that medicinal products market is growing as well.

- Consumer interest in people-helping-people is definitely growing.

This trend of people-helping people is especially strong in the United Kingdom. Consumers are interested in helping others and receiving help or information from others. People are interested in knowing real stories and examples of groups that harvest and produce special ingredients, which later can be used in daily bases.

Due to that phenomenon, you can also document socially sustainable production methods to support and substantiate your marketing story.

By 2050, around 30% of the European population is approximated to be 65 years and older. This is much higher percentage than it was in 2013 – 17%. It's important to have in mind that the senior generation is an important market for natural healthcare products. This target group use

more self-care products than younger easy-going generation and are increasingly interested in natural healthcare offers.

European manufacturers differentiate their marketing target group to specific age groups or segments within the older population, for example menopausal women and people over 70.

In all parts of the world an ageing population has specific health needs different than the young generation. Around 22% of Europe's population is reported to be under long-term treatment for health problems with many areas as: muscles, bones and joints, such as rheumatoid and arthritis. Frequently consumers are looking for natural products that they can use on a daily basis and for a long-term instead of using conventional medicines. Main ingredients that are getting very popular include frankincense, turmeric and capsicum.

Because of that people pay more attention to those who grow their own medical plants and sell them later to the other (People helping People)

- Rising stress level has an impact on medicinal plants market

Nearly four out of fifteen people in Europe are affected by anxiety and depression every year – which is a lot. A major source of stress is work-related aspect. Stress that is work- related is most often reported by workers everywhere that are between 40-54 years old. Moreover, 31% of the Western European population have reported difficulties related to sleep and rest.

Other sources of rising stress levels include:

- Travel
- Pressure
- Sensory overload
- Huge quantities of information

There is an increasing big need for health products to relieve symptoms related to stress (at work, at home, travelling). In Europe, the market offers mood/relaxing food supplements which is the highest in France and Belgium.

In France, this takes up 10% of the total market (€611 million) and in Belgium 10% of a €188-million market. Herbal food supplements that help reduce stress are expected to benefit from the trend towards preventive health care.

- Growing popularity of aromatherapy another chance for medicinal plants market

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There is also a good market for aromatherapy in the United Kingdom and the Netherlands. Here, as in most other Western European countries, aromatherapy products are at the same level as cosmetics. Products are primarily used for relaxation, stress release or preventative care rather than as a form of medication for particular health problem.

- There is more interest in herbal veterinary medicine

The demand of organics (eco-friendly) meat and dairy make many farmers think about changes that they need to apply to the sector of feeding and recovery of the animals. It's observe that there are many opportunities in Western Europe for veterinary natural medicine directed at pets and horses.

At the same time this trend leads us to the conclusion that food and feed supplements for pets can be connected with medicinal/herbal plants. For example: chia seeds are very good for pets, supplements for joint or digestive support or those containing Omega fatty acids or fish oils.

The ingredients used are similar to those used in herbal medicinal products for humans. Examples include rosemary and oregano as raw materials and/or essential oils.

Industry sources warn that in general targeting the herbal feed supplements industry may be difficult at the beginning. The legislative framework is different from human medicine and supplements and can even be stricter, especially for feed additives for industrial production of food, meat, eggs, etc. Because of that it's crucial to make sure you have all needed knowledge in order to sell the product for the Human and not only used.

Wondering where could you start? Would you like to go global? If yes, here are some advices and places where you have a chance to succeed but at the same time there might be more competitors.

- ✓ Countries where you could expand your business and at the same time be aware as they might be your competitors:

- POLAND

Polish growing health market is the largest in Central Europe and it offers opportunities for developing this country. Especially herbal medicine and food supplements make up a considerable share of this market. Local demand for ingredients is focused on plants used in Western herbal medicine, but at the same time there is a growing demand for established tropical species for local consumption and exports to neighbouring countries as Germany, France.

Consumer profile

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Poland represents the largest market in Eastern Europe for (herbal) medicine and food supplements. Polish inhabitants have a strong tradition of collecting, cultivating and using herbs for their health purposes. The knowledge among consumer and interest amount collection communities has changed a lot in recent years, there is still a strong interest in the private sector. There are many meeting and events organised connected with herbal/medical plants topic. The purpose is to build consumer interest in herbal health products in Poland and outside the country.

If we compare Poland with more innovative Western European markets like the UK, Poland still remains traditional, focusing on temperate species with a long-established history of use in the country. Health products in Poland have relatively often been combinations of herbal ingredients with minerals and (synthetic) vitamins.

Good to know and to remember that in Poland, part of the consumption of health products is registered as herbal teas. Herbal teas account for 14% of the €310 million Polish tea market, according to the Ministry of Treasury.

Main suppliers in Poland are from their region. Poland as country is a trade hub for Central and Eastern Europe and has a strong extraction industry. Regional suppliers include several East European countries most of them are: Ukraine (9.7%), Bulgaria (8.6%), Russia (6.4%) and Albania (4.1%). However, Germany is the largest supplier of MAPs to Poland - 37%. Poland's main East European suppliers experienced was growing from 2010 till 2014.

TIPS

- If you are a producer of tropical MAPs, consider your potential for exporting to Poland, as MAPs offer more opportunities for you than temperate species
- Consider establishing a local presence in the Polish market seems as a very good idea. It should be done through a reputable agent or representative and have in mind that price/value remains competitive. Thinking about Poland maybe its worthy to have a partnership with a Polish trading company?
- Very useful market information and interesting companies can be found at PASMI (the Polish Association of the Self Medication Industry) and Polski Komitet Zielarski (the Polish Herbal Committee, website in Polish only).
- Go and show up on the fairs/events related to the herbal market. Trade fairs are excellent venues for finding companies that deal with natural ingredients for health products.

➢ GERMANY

Consumer profile

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Germany for a long time represents the largest market in Europe for (herbal) medicine. In 2013, total (retail) sales of self-medication products, which includes most herbal medicinal products, amounted to € 4.9 billion (AESGP). In 2013, per capital spending on self-medication in Germany amounted to € 61. This is relatively high compared with other European countries. Other countries with high per capital spending include Belgium (€ 71), Switzerland (€ 62) and Austria (€ 71 in 2012). In order to compare with other countries, France and Italy have low per capital spending (€ 35 and € 30, respectively), the same Spain (€ 20) and Poland (€ 19).

Today more than 70% of German physicians prescribe herbs, and St. John's Wort is more commonly used than any other chemical medicine to treat mild to moderate depression.

- Germany has a long tradition of using herbal medicinal products. According to the Institut Für Demoskopie Allensbach (2010), 72% of the German population have used herbal medicinal products at some point in their lives (for their family, at work or their own health care), up from 52% in 1970.

- Germany is the largest and still growing European importer of medicinal and aromatic plants (MAPs). The import volume grew annually by 3% between 2010 and 2014, with the highest growth occurring from 2012 to 2014 (+20%).

- There is a growing role for developing countries in German imports. The developing country share of import volumes increased from 48% in 2010 to 54% in 2014. This is comparable to other main European importers. France (66%) and Spain (59%) have a higher developing country share of imports, while the UK, the Netherlands and Italy have a similar or slightly lower developing country share.

TIPS

- Show understanding of the specific market realities in your promotional materials and communication.
- There is a large market in Germany for established herbal ingredients. The food supplements sector offers greater opportunities for more innovative ingredients.

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- German businesses are comfortable about using English in their communications with potential foreign business relations so do not worry about the language barer.
- Be punctual, as this is highly appreciated in Germany.
- Research the Plant LIBRA Consumer Survey to determine whether your product features in it. Note that the markets for these main products are highly competitive.

➢ THE UNITED KINGDOM

Consumer profile

Interest of natural health products is likely to increase with growing consumer demand for OTC medication and self-medication, as these consumers are more likely to buy natural health options than in other countries. UK sales of over-the-counter (OTC) medication increased by 2.2% between 2012 and 2013. In 2013, OTC sales amounted to £ 2.5 billion (€ 3.2 billion) according to the Proprietary Association of Great Britain (PAGB).

Within the OTC market, the largest product groups in 2013 were:

- pain relief (£ 544 million/€ 687 million)
- coughs/colds/sore throat (£ 444 million/€ 561 million)
- skin treatments (£ 415 million/€ 524 million)

In the UK, the food supplements segment is the one that offers the most opportunities for developing country producers. Consumers are especially interested in natural health products that will increase general wellbeing (They basically want to feel good and healthy). The UK depend mainly on imports of natural ingredients, as local production of raw materials is very limited.

As a result of harmonization of the EU regulatory framework for herbal medicinal products and food supplements, many small shops and sellers have disappeared from the UK market. New

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legislation on herbal medicinal products has affected the UK much more than other European countries, such as Germany, because of the considerable differences between the old UK legislation and the new harmonized framework.

In 2013, product groups with the largest market share were those aimed at:

- Joint health (16%)
- General health (14%); supplements for general welfare and with multiple health benefits
- Heart health (12%)
- Women's health (9.6%); including supplements for pregnant women, menstruation and menopause
- Energy (around 7%)
- Immune system (6.7%)

Consumer trends in natural health products:

General wellbeing, being happy and feel good: Holistic or lifestyle health products are popular in the UK, as are product ranges consisting of several health products or product ranges that go beyond health to include food and cosmetics. The reason for this is that typical UK consumers of natural health products show greater interest in general wellbeing than in specific indications when compared with consumers in other EU countries.

Interest in non- Western health system: This is caused by demand from the UK's large ethnic populations (South Asian, Chinese, African, etc.) and the interest of other UK residents in something different which is non-traditional health options.

Ageing population that want to live healthy: An ageing UK population may lead to growing demand for products such as herbs and medicinal plants. The main reason for this is that UK consumers over 50 years old represent the largest consumer group for vitamins and food supplements, and they are generally more liable to use and buy natural health products as well. Few years ago (around 2013) we could observe that in the UK had a population of 64.5 million, with the 25-54 age group presenting the largest population group (41%). According to the Office for National Statistics (2012), the average age in the UK is expected to rise to 43 by 2037,

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compared with 40 in 2013. The number of people aged 80 or above is projected to double to 6 million by 2037.

Increasing healthcare costs significantly: Rising healthcare costs is another consumer trend that is leading to increased sales of natural health products not only in the UK but in any other country. Herbal medicinal products and, above all, food supplements are seen as low-cost alternatives to conventional drugs especially in the case of prevention or long-term use.

Certified ingredients: You will have more opportunities on the UK food supplements market if you can certify your products as fair trade. As it was mentioned before in the UK, consumers have a particularly strong interest in 'people helping people': consumers want to hear stories and know news from their friends, colleagues or neighbours about their experience and acts related with producing health ingredients. With all changes related to this topic, the requirement for organically certified ingredients in food supplements is also growing, as these are seen as healthier options than non-certified ingredients.

TIPS

- Investigate potential buyers: find out whether they are located in the UK, whether they import MAPs or extracts, and whether these products are sourced directly by them.
- For an overview of legislative requirements for herbal medicinal products and food supplements in Europe, please refer to the CBI EU Buyer Requirements – Natural Ingredients for Health Products
- Reach to the UK if you produce tropical MAPs. This market offers opportunities for tropical species.
- If you produce temperate MAPs, have in mind that the UK may be difficult to access. Although cultivation is small-scale in the UK, many of the species have an established and competitive market owing to production in other countries (continental Europe, Kenya).
- Consider your opportunities to engage in e-marketing. This could be a (niche) opportunity in the UK, particularly with regard to supplying traditional products to immigrant populations or people interested in non-Western nutritional solutions, such as the country's large Indian population.
- As the British are rather formal, always address professionals by their surname, unless they indicated otherwise.
- Be aware that rank is respected and businesspeople like to deal with others at the same professional level. Be punctual, as this is greatly appreciated.

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- SPAIN

Spain has a large market of extracts and imports large quantities of medicinal, aromatic plants and extracts, often from developing countries. Although Spain is still recovering from the crisis, the consumer can still be an interesting target for exporters from developing countries.

People in Spain take a lot of care of their health and at the same time they are looking for low cost products but with high quality.

Consumer profile

Nowadays, consumption of herbal medicine and food supplements is growing, even in the difficult economic situation which is currently affecting many Spanish householders.

Traditionally, herbal products are not very popular health solutions in Spain. Consumption remains limited to a small part of the population. However, Spanish consumers are familiar with herbal health solutions, especially traditional Western herbal medicine based on domestic (temperate) species. One in three Spanish consumers is estimated to have used herbal medicinal products, especially among older generation. Figures are even higher for homeopathy, with 33% of Spanish consumers having used homeopathic products, and an additional 27% using them on occasion or even regularly. Aromatherapy has developed as an important contribution to primary health care in Spain.

Trends in natural health products

Ageing population: Spain's ageing population the same in the other countries will mean higher consumption of health products to (help) remedy the various illnesses associated with age (older age). Moreover, both European expatriates retiring in Spain as well as Spanish elderly more often consume herbal products for their health, especially herbal medicinal products. Important to know that almost 18% of the population is currently over 65 years old, and this is expected to increase to 25% in 2029 and 39% in 2064, one of the highest rates in Europe (INE, 2014).

Increased consumer awareness: There is increased demand for different health product categories, especially food supplements and herbal medicinal products aimed at preventing illnesses. Consumers are looking for healthy options in terms of food, medicines including

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aromatherapy, and cosmetics, due to an increased awareness of general health and wellbeing among Spanish consumers.

Looking for cheap healthcare options: Spanish consumers see herbal medicinal products and, above all, food supplements as low-cost alternatives to conventional drugs, especially when looking at prevention. This is becoming more pertinent as decreasing disposable incomes have affected millions of Spanish households.

Cut-back in reimbursement of prescription drugs: Spanish consumers are increasingly looking at self-medication products and food supplements where, traditionally, they would have mostly considered prescription drugs for their health care. This has changed since the moment when fewer medicinal products are reimbursed by the Spanish government.

TIPS

- Show understanding of market realities in your promotional materials and communication (thanks to that your customers will know that you know their market and economic situation)
- Consider focusing your MAP exports on Spain, as the country plays a major and growing role for developing country suppliers.
- If you produce tropical species, be aware of competition from other places like South American sources, such as Peru and Paraguay.
- Explore your potential for exporting botanical extracts to Spain, as developing country suppliers play a relatively large role in the country's imports.
- Be aware that it is common when doing business with Spanish people that they take the time to get to know you first before deciding on further business relations. They take their time and it is totally normal.
- Preferably approach companies in the Spanish language. Most international companies will have personnel who speak English. It is useful if documentation is translated into Spanish, as English is still not a widespread language

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In order to make it a bit clearer, we present some groups of people that could be your target group:

- ✓ Big companies that care about their stressful employees – they could buy special herbs or plants which reduce the level of stress
- ✓ Owners of animal farms – Some plans or herbs are also for animals
- ✓ Young generation – They care about their healthy lifestyle and also want to buy what is cheaper and good quality. Eco friendly products are a new fashion
- ✓ People who want to lose weight – Some plants might help and work as slimming ingredient
- ✓ People who has difficulties with falling asleep – You know that there are herbs and plants that helps to fall asleep
- ✓ Seniors – they care a lot about their health and not always have enough money to buy expensive medicines
- ✓ People with skin disease/ infections
- ✓ People with depression, without motivation and energy

Another topic and information that you have to know:

- If you want to supply veterinary medicine for pets, go for the Western European market.
- If your natural ingredient has antibiotic properties, consider veterinary medicine as an additional market.
- Obtain organic certification for your ingredients if you want to target the herbal veterinary medicine industry for organic meat production.

- ➢ What with your competitors? They are everywhere but they can't stop you! Learn from their mistakes and do your job better.

Your competitors can be everywhere and they can also help you or harm you but this is totally normal and correct. You have to be aware of your competitors and always check their products, marketing technique and pricing.

Good advice:

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- ✓ Have in mind your competitors from Germany, Eastern European and Egyptian sources if you producer of MAPs (Medicinal and Aromatic Plants)
- ✓ Remember that Germany is the largest European importer of MAPs
- ✓ Germany is the second largest importer of extracts
- ✓ Do not hesitate to check your competitor and try to bit them
- ✓ Each competitor can have something different that can make them better or worse than you

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Unit 3: Building Business Model for Medicinal Plants Sector

What is a business model?

A Business Model allows to describe the base used by a Start-Up/company in order to create, collect and provide value. It is the floor used to manage the company; a very useful strategic management and entrepreneurial tool. Business Model is a based from where the big things are created.

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A Business Model is an essential tool in any Start-Up/company to function correctly. It allows you to set up a map in which you state how your business works. Through the business model, the company creates a plan with the finality of earning profits through its actions, taking into account the costs incurred.

There is no fixed format to follow; the business model can be as simple or complex as the company wants depending on their needs and features.

Business Model might be created today and change any other day but the main structure should be followed. Very important in creating a Business Model is to have in mind that this document should give you the answer for the question "From a customer perspective, why this business should exist?". Creating Business Model its crucial to consider all parts of the business: people, product, service, customer, plan, objectives, challenges etc.

The process of creating a business model is rather very personal action but from the other hand it is possible and required to follow some structures that are more common and make this job easier.

Before you start working - acting you should have at least in mind your Business Plan for the next few months.

Creating Business Plan can start from Start-Up Business Plan which will be used for internal purpose and primarily reflects the needs of each members of the company. This kind of plan, that can be called "draft" is for the creator of the business and his colleagues. We recommend you not to show this kind of "working business plan" to the bank or any other organisation from which you wish to receive any finance support. Inside the plan you should include company's growth or expansion and as well which are the priorities.

The is another plan that could be mentioned here as Strategic Plan – plan that will include your strategy, responsibilities, activities, deadlines, budget and financial plan.

Each kind of plan will be useful during the whole process of preparation and later which you start running your business.

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Summarizing – Everything need a plan but the plan can change. According to the changes that will appear while creating the business, the plan will be modified and adapt to the need. As a result of having a Plan you have that path that you follow and a base from which you can start.

How does a business model relate to business strategy and competitive advantage?

Nonetheless, business models are relatively generic models that can readily be imitated. Therefore, Business strategy complements the model by designing and protecting competitive advantage in imperfect markets. This means business strategy figures out isolating mechanisms that prevent business models from being imitated by competitors.

The VRIN (Valuableness, Rareness, Inimitability and Non-Substitutability) framework offers a tool to examine the (potential) competitive advantage of businesses. When employing a differentiating strategy, businesses can secure higher returns and sustain their competitive advantage.

Four strategic analysis steps are proposed to achieve sustainable business models:

1. Segment the market
2. Create and present a value proposition based on customer needs for each pursued segment – as customers are your future
3. Design and implement mechanisms to capture value from your customers – special segments
4. Figure out and implement isolating mechanisms to hinder imitation by competitors – which will try to deal with you and bit you

Three factors that each person crating Start-Up should follow as they are relevant to impede competitors from imitation:

1. Hard to replicate systems, processes, service, structure, business model.
2. Uncertain imitability – it refers to the action that is creating difficulties for an outsider to understand how the business model is implemented.
3. Break up of existing sales and profits or upsetting business relationships.

What is the role of discovery, learning and adaptation in business model innovation?

The process of innovating and creating a business model requires creativity and insight. Insight into an information about customers, suppliers and competitors – 3 aspects that will follow you for the whole business journey. Creativity goes with capturing value from the deep truths of customers with available sources and at the same time protecting the model from imitation. This primarily is a process of learning, studying and adapting everything step by step that is based on experimentation. One way to do so is by testing the model against the current similar business and see how it might evolve.

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Questions that can be asked about the temporary model include:

- How will the product be used and what customer's problem does it solve? Does it solve any problem? Does it make life easier?
- How much might customers be willing to pay for the delivered value?
- How large is the target group? What is the target group?
- What competitive offers you know?
- How should the product solution be presented and where?
- What are the costs of presenting, delivering and selling this product/service?

Business models are an important part of running a company. One of the most popular and well-known is Business Model Canvas (BMC).

The Business Model Canvas is a strategic management and entrepreneurial tool. It allows you to describe, design, challenge, invent and pivot your business model. It is a visual chart with elements describing a firm's or product's value proposition, infrastructure, customers and finances. The tool is very useful to design, test and innovate our projects´ business model. The very practical approach allows you to highlight the dynamics of the business model and serve as an inspiration to explore new opportunities. As an example AMAZON is a company that uses BMC.

Amazon is a widely used Internet based retailer, which both offers a large diversity of products (from books to jewellery and food) and produces electronic products (like the eBook Kindle or the Fire tablets).

Amazon business model can be analysed using the Business Model Canvas; a visual chart that allows to study the elements that compose a firm.

Please dedicate some minutes of an introductory video that explains the BMC structure:

https://www.youtube.com/watch?v=QoAOzMTLP5s

The Business Model Canvas is used by a different types and sizes of companies. It is also a very important tool for entrepreneurs and Start Ups for business model innovation. It reflects systematically on your business model, as you can map each of the elements of your project or business components. This form of Business design which gives a clear and simple option of knowing every single important part of your business helps you to analyse it properly and

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understand how they connect to each other. If you are ready to turn innovative ideas into action this tool is definitely what you need.

Nowadays the Business Model Canvas (BMC) is one of the popular one that is used as a Business Model by many companies. It allows you to describe, design, challenge, invent, present and pivot your business model. It is a visual chart with elements describing a firm or product's value proposition, infrastructure, customers and finances – all sectors that are related to the business. In order to better understand what a Business Model Canvas is, it is necessary to understand the different elements that it collects. For this reason, let's divide the concept into different stages; which will build the complete picture of the concept.

Component	**Definition**
Customer Segments	A customer segment is considered as the group of people that the company intends to address; it can either be one or many. Since the whole activity of the company will be based on the Customer Segment chosen, this has to be the first decision to make in order to build the business model on the basis of the choice. When deciding which Customer Segment, we should choose/reject, we need to bear in mind how each segment has several characteristics.
Value Proposition	It is the offer made by the company to solve a problem or request from the consumer. It is the combination of products and services a company offers to solve the problem of the concrete segment addressed. There are a lot of types of value that a company can offer through their products/services
Channels.	A channel can be considered as the contact point between the company and the market segment addressed. Market channels have several functions, such as bringing the product to new clients, helping the clients reach the product, allow them to acquire the value proposition, and offer an aftersales service.

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Customer Relationship.	A company can decide the type of relationship for each segment, depending on the outcome it wants to achieve: loyalty, achievement of new clients, increasing sales … depending on the relationship stated with the client, they will have a different opinion of the company.
Revenue Streams	Are collected from the relationship with the segment. We can find two types: • Revenues coming from concrete payments made by the consumer. • Current revenues coming from periodic payments in return for the value proposition given by the company to the consumer.
Key Resources	They are the most important inputs of the company, the ones that allow a business to create the value proposition offered to the consumer. Each Business Model is going to require a different type and amount of these resources.
Key Activities	They are the most important activities necessary for the model to work, and as happened on the previous step, depending on the business model there will be different activities needed.
Key Partners	In other words, it is about the network built by the company with other partners in order to improve their Business Model; the reasons to build a partnership are diverse, such as benefiting from economies of scale, reducing risks or access to determined activities/resources.
Cost Structure	Setting up a business model comes with a lot of costs, and depending on the type they will be higher or lower. We can divide them into two main types: according to costs or according to value. The first one is more focused on reducing costs, while the second prefers to add value to the consumer above all.

As an example, have a look at the BMC used by Apple and Google.

APPLE:

One of the most relatable products of Apple is, undoubtedly, the iPod. Launched in 2001, the machine won over any other mp3 due to the possibility of connecting it to the iTunes platform,

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allowing its users to transfer any content from the computer to the iPod, as well as to buy content through the Apple store.

<table>
<tr>
<td rowspan="2"><u>KEY PARTNERS</u>

Record Labels

Original Equipment Manufacturers</td>
<td><u>KEY ACTIVITIES</u>

Hardware Design

Marketing</td>
<td rowspan="2"><u>VALUE PROPOSITION</u>

Music without interruptions</td>
<td><u>CUSTOMER RELATIONSHIP</u>

Love to the brand

Costs of changing</td>
<td rowspan="2"><u>CUSTOMER SEGMENTS</u>

Mass Market</td>
</tr>
<tr>
<td><u>KEY RESOURCES</u>

People

Content and agreements

Apple brand

iPod Design</td>
<td><u>CHANNEL</u>

Retail Stores

Apple Stores

Apple.com

iTunes Store</td>
</tr>
<tr>
<td colspan="2"><u>COST STRUCTURE</u></td>
<td colspan="3"><u>REVENUE STREAMS</u></td>
</tr>
</table>

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People Manufacturing Marketing and Sales	High revenues from Hardware (selling of iPods) Some revenues from Music (selling music)

GOOGLE

Google's first and best-known service is its search engine, allowing to look for the desired results on the internet. Additionally, the company offers other services such as Gmail, or other applications (Google Calendar, Google Docs…) for free, making money out of the advertising on the internet. However, even if the company has other products (such as their own mobile phones and tablets) the highest amount of revenues is still acquired through the advertising procured in the internet.

KEY PARTNERS	KEY ACTIVITIES	VALUE PROPOSITION	CUSTOMER RELATIONSHIP	CUSTOMER SEGMENTS

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<table>
<tr>
<td rowspan="2">Distribution partners

Open Handset Alliances

Original Equipment Manufacturers</td>
<td>R&D: new products, improvement of products

IT infrastructure</td>
<td rowspan="2">Web Search (browser)

Gmail

Google+

Targeted advertising

Android

Google Chrome

Google Apps

Nexus products</td>
<td>Automation (when possible)

Dedicated sales (large accounts)</td>
<td rowspan="2">Internet Users

Companies wanting to advertise

Google+ Users

Mobile device manufacturers

Developers

Enterprises

Mobile Phone Users</td>
</tr>
<tr>
<td><u>KEY RESOURCES</u>

Datacenter

Google brand</td>
<td><u>CHANNEL</u>

Google Play Store

Global Sales (support teams)

Multi-product sales force</td>
</tr>
<tr>
<td colspan="3"><u>COST STRUCTURE</u>

Traffic Acquisition Costs

R&D Costs

Data Centre Operations

Marketing and Sales</td>
<td colspan="2"><u>REVENUE STREAMS</u>

Revenues from Advertising in websites

Products for enterprises

Nexus Mobile Phones/Tablets</td>
</tr>
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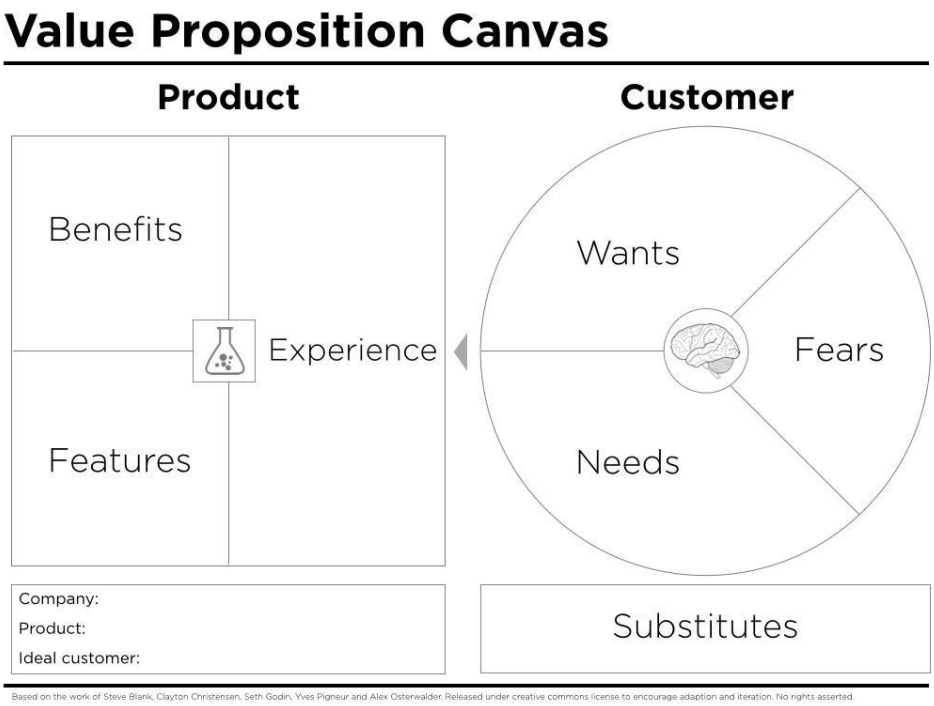

SOURCE: Peter J Thomson, Digital Brand Strategy

EXAMPLE

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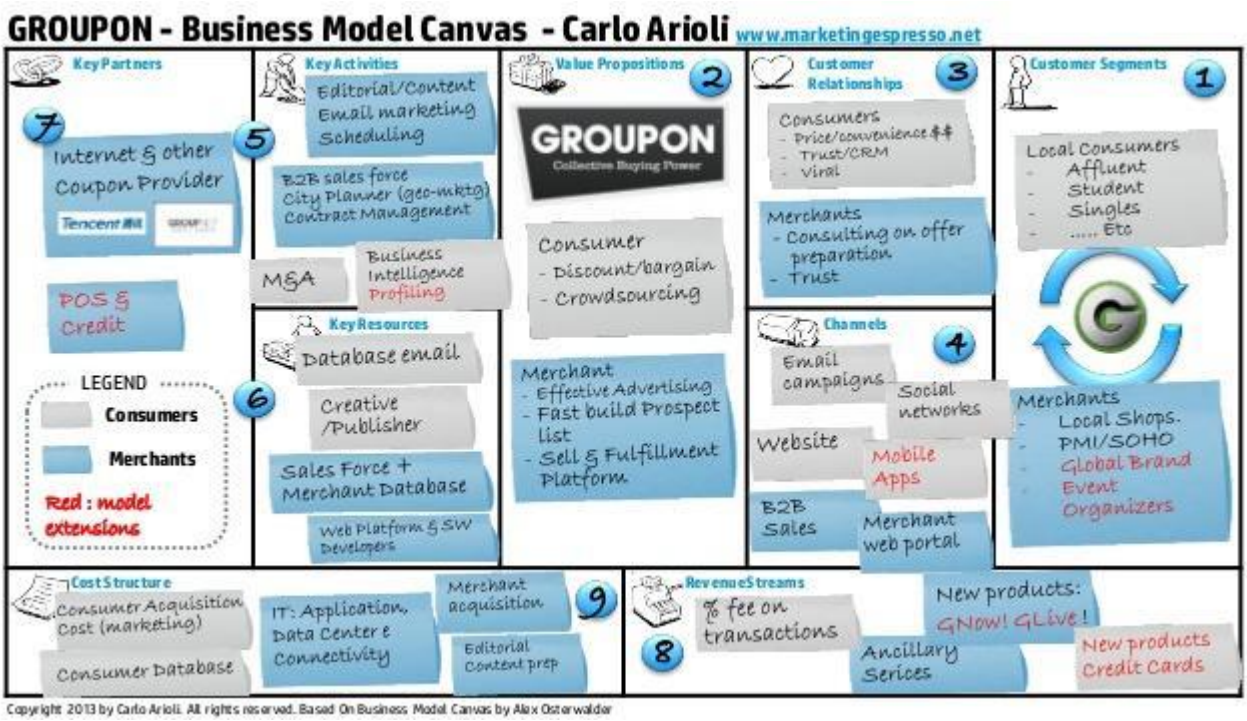

Pattern and example for Medicinal Plants Business Model

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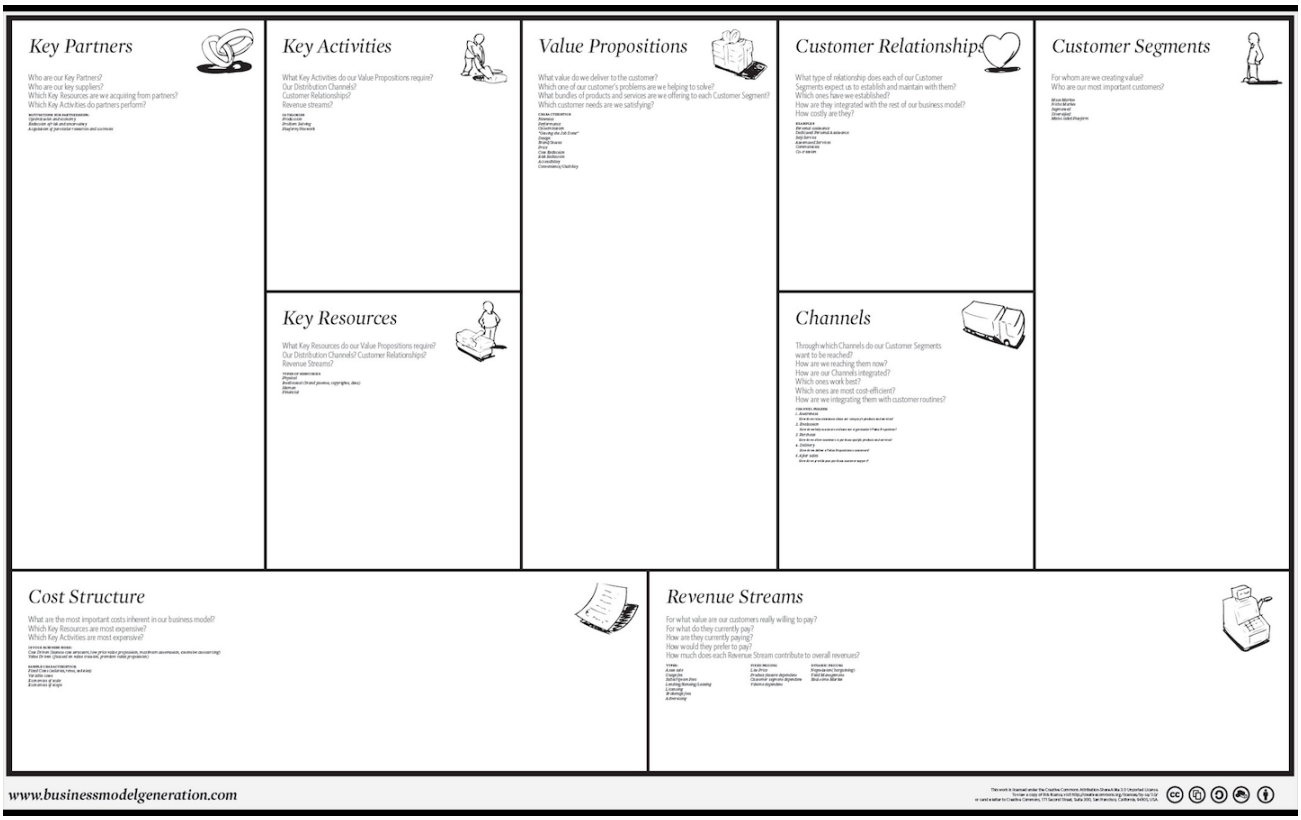

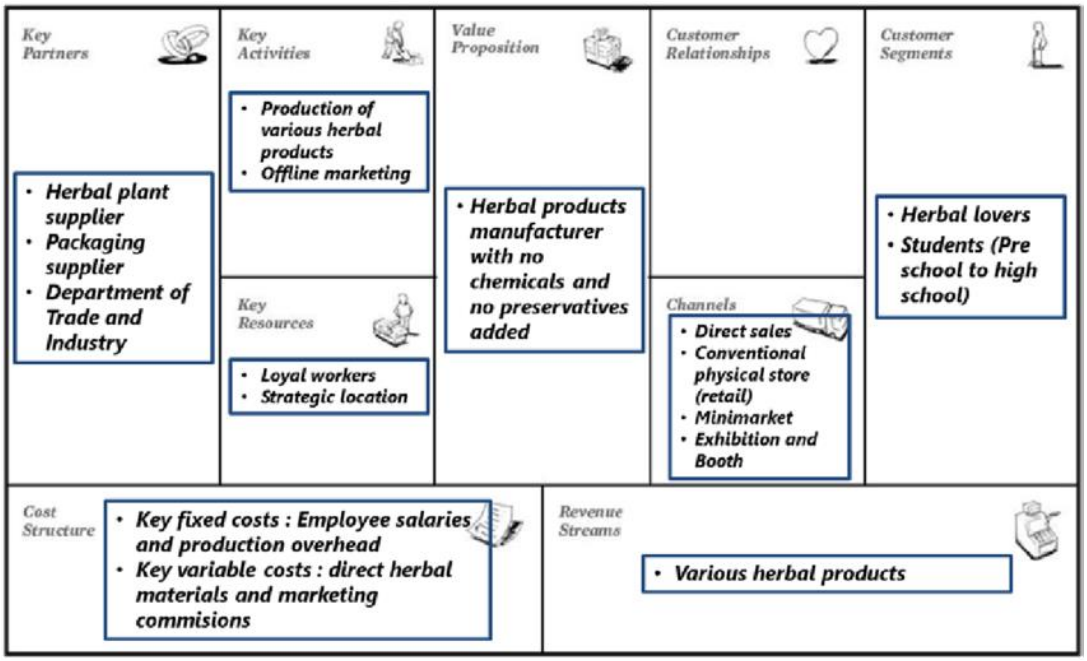

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Unit 4: Marketing Plan

Most people when asked “what is marketing?” they think about promotion, advertising, pictures, comments, billboards, person who is creating another funny commercial etc. Marketing most of the time is connected with big companies and names like Coca Cola, MARS, Red Bull etc., which marketing events are always promoted on each social media channel. The main goal of creating Marketing Plan which includes: event, promotion, meetings, concerts, commercials etc. is to get more customers and get more money. “Profit” is the aspect that everyone follows. As it might seem very “easy going” and friendly sector, marketing is the most critical component of all business plans. Very famous quotes that represents Marketing is “Find a need and fill it”.

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What and where is the importance of Marketing? Why does my business need it? These are reasonable questions: For those that dream of "wealth" in your businesses this is the key and it could not be more significant. Business Plan that was mentioned before can't exist without marketing strategy – as it's a way to get more and more customers and start being popular. Very often people ignore that component resulting in a continued struggle towards their goals. Probably you are wondering why this is so important, people know me and they will buy my product anyway.

Wait a second, before you answer consider this: No matter how innovative, beautiful, useful, new or amazing your product or service is, no one will find it if they do not know that it exists somewhere close or far way. So, because of that marketing is the action to make people know about you.

Well prepared marketing can be beneficial to all kinds and types of businesses. Creating marketing is not an easy process but first of all it's good to know what are the main components of marketing.

Below you can find them:

Advertising

Customer Support

Market Research

Product Planning

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Product Pricing

Sales Strategy

Public Relations

Of course you may face trouble trying to remember or identify all the above mentioned components. Try to think of marketing as everything an organization does in order to build, maintain and boost the business-customer relationship. It is all included there – all the necessary and needed actions taken are just "marketing".

Useful Tips:

- ✓ **Who is your customer? Be aware and clarify your target group.**

Old or young people? Workers or students? People from your village, city, country or from the other culture? Depressed, sick or happy with energy people? Group of people that want to live healthy or want to use something new, cheap or popular?

- ✓ **What is your message? In what way can your product/service facilitate your target group?**

What do you want to share with them? What would you like to present by marketing events? What kind of events you can organize? How would you like them to think about you? What kind of feedback would you like to get? What is your goal in terms of customer perspective?

- ✓ **Redirect your plan to its real business purpose.**

What's the purpose of this marketing plan? What do you want to achieve? What are your expectations? Does this plan match with your vision and idea of the business? Look at it form a business perspective.

- ✓ **Strong customer relationship is the key element** in the effort to growth, stabilize and have a profitable business. Marketing planning is a great way to achieve that.

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✓ **A comprehensive realistic marketing plan can boost the life and well-being of your business in the long term.**

Marketing Benefits:

- Stronger company image
- Ability to attract and retain customers
- Ability to establish partnerships
- Reach to the new group
- Get more clients
- Create a new and better image of the company

Common mistakes related to marketing:

- Spend too many hours and too much effort to design your marketing strategies and never actually following your own great ideas.
- Being unrealistic. Do not think that since the beginning you can create a big marketing event as for example Coca Cola is doing. Know your possibilities and use them.
- Having very high expectations regarding sales. Sales grow slowly at first. It is absolutely normal.
- Always have projections and goals that are conservative so you can meet them.
- Spending too much time and money on a fancy website before getting customers – you can develop it later once you are making profit!

Marketing is the main activity that a company does to acquire customers and maintain a relationship with them. It is based on thinking about business in terms of customer needs and their satisfaction – at this point the customers is number 1. It is not that important to get customers to pay for the product, as it does develop a call for that product and fulfilling the customer's needs. Marketing is a very deep topic, that has many different concepts, techniques, methods and theories. The most known are the 4Ps and 7Ps concept of the marketing mix. The organisation always tends to use marketing mix to create their marketing strategy as effectively as possible. In the 1960s, the American marketer, E. Jerome McCarthy, provided a framework by means of the marketing mix = 4 Ps (McCarthy 1975).

• Product

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The product/service should fit the task consumers want it for, it should work and it should be what the consumers are expecting to get from you.

• Place

The product should be visible and available from where your target consumer finds it easier to shop. This may be a big shop on the main street, small shop in the shopping mall, small market, online shop, e-commerce.

• Price

The product/service should always represent good value for a specific price. This does not necessarily mean it should be the cheapest available or the most expensive; one of the main assumption of the marketing concept is that customers are usually happy to pay a little more for a product or service that works well and last for a long time.

• Promotion

Advertising, Public Relations, Sales Promotion, Personal traditional selling and lately Social Media are all key communication tools for an organisation. These tools should be used to put across the organisation's message to the correct audiences in the manner they would most like to hear. Promotion needs to be adapted to the target group. If your group contains people with 50 or 60+ its most probable that they won't follow you on Facebook or Instagram but maybe they will come to you tend on the market and buy your product directly from you. Promotion events are essential but need to reach to your target group.

Creating Marketing Plan try to use all possible channels and do not miss anything that can bring you closer to your customer. Nowadays technology is the key but at the same time traditional ways of promoting the business works the same efficiently – everything depends on the client and on how well the campaign is prepared.

If you want to reach to young people from the UK you definitely have to think about Social Media channels. Talking about Social Media, have you thought what a well-designed and easy to handle website may offer you? Attracting visitors daily, who are able to see what you purchase and its features online – or even being able to purchase from their homes can be your ally. E Commerce in marketing is the best way to fulfil it.

Examples of Social Media and Traditional marketing channels:

Social Media	Traditional channels
Facebook	Newspaper

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Instagram Pinterest YouTube Twitter Websites Webinars	Promotions (buy 2 get one for free) TV Radio Events related to the topic Fairs related to the topic Advertisements Billboards

- Which market segments should be targeted in Medicinal Plants Business?

Natural ingredients for health products include:

- raw materials, such as medicinal and aromatic plants (MAPs)
- extracts
- active ingredients that are used as starting materials for pharmaceuticals.

The market segments for the natural ingredients for health products are based on:

- their application in the European market (herbal medicinal products vs. food supplement)
- the type of species (tropical, subtropical or temperate).

Which segment you should target depends on how well you can comply with their particular requirements. In order to answer their needs, you have to study the market before you start your marketing plans.

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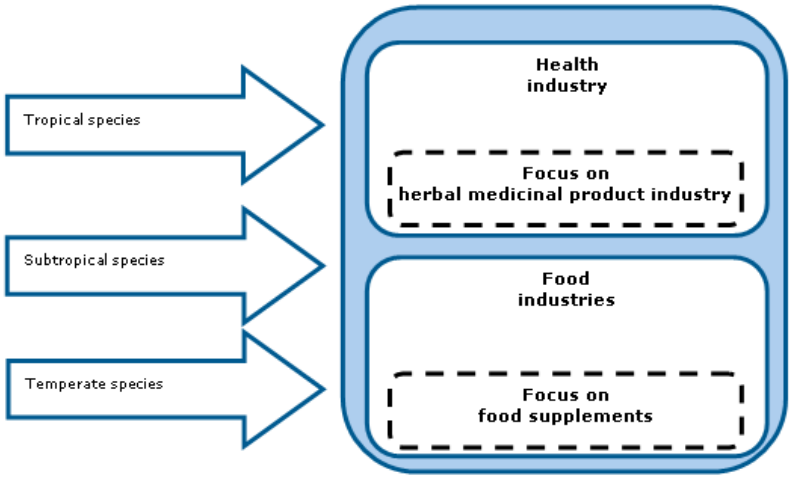

Herbal medicinal products vs. food supplements

There is definitely a clear difference between medicinal products for human use and food supplements. This is because of several borderline issues and at the same time countries classify products differently. For example, a product that contains turmeric (*Curcuma longa*) could be classified as a food supplement, but also as a herbal medicinal product. This is related with active ingredients or compounds it contains and, most importantly, how it is marketed. Only herbal medicinal products can make a medicinal claim.

The most important reason to still categorize these two segments is that there are big differences in related legislation. Because of these legal differences, you need to take a specific way to get to the market and be aware of the difference. Aside from different legal requirements, the route to the market is also different for established and new ingredients. Each specific market also has their own trends and competitor profiles.

You can access the specific market through similar market players, in terms of importers, distributors and processors but it's important to adjust the strategy to the specific consumer.

- Through what channels can you market your natural ingredients for health products?

Major market channels for natural ingredients for health products

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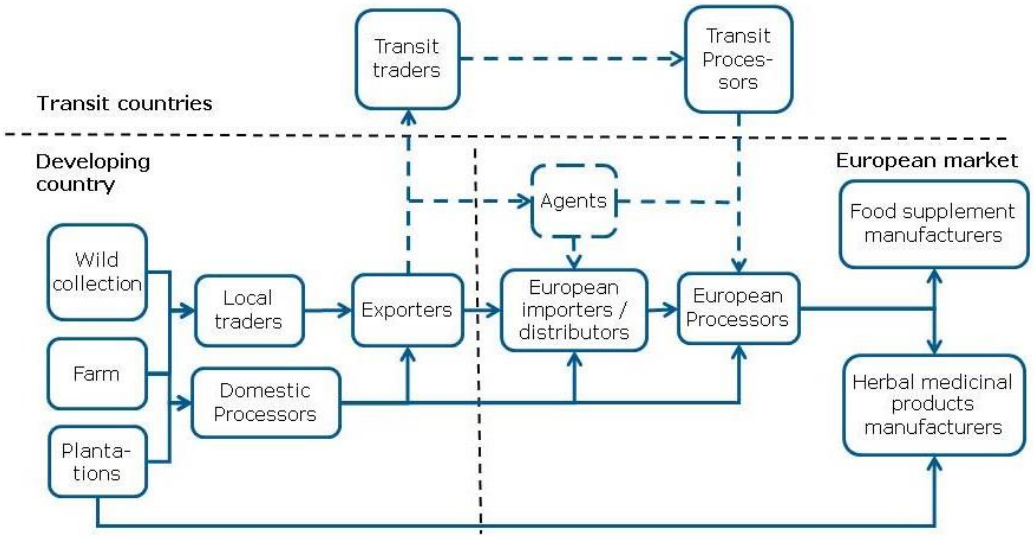

European importers and distributors as the most important entry point

In general, European *importers* and *distributors* are your most important entry point into the market. These can trade in up to 500 species, together with other ingredients and synthetic. Their functions include:

- global sourcing
- analysis and quality control
- rectification
- blending
- product documentation
- sales to processors and end-product manufacturers.

You can commerce your natural ingredients through either general or specialised players. Both types of players can be interesting for you, depending on the:

- size of your company
- type of products you supply
- certification and documentation required.

All over the Europe main importers, distributors and processors are expanding their product range and increasingly work at different levels. The diversification is the result of the merger of

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end-product manufacturers and the high costs to comply with legal requirements. Some of them stock a wide variety of conventional, organic and/or fair-trade ingredient lines to cosmetic, supplements, food and herbal medicinal product manufacturers.

Examples are:

- processors such as Naturex from France, and Indena from Italy
- traders such as the Martin Bauer Group
- distributors such as IMCD.

Have in mind that, if your product is a high-quality product these kinds of companies are at the same time a good connection in order to enter to the market.

Even if nowadays specialisation is becoming less common, there are still members that specialise by:

- direct their sales only to the one sector, for instance: ingredients for food supplements, cosmetics or herbal medicinal products
- limiting their product offers and having less product but with high quality, for example offering a product from a particular region, producing extracts or active principles
- having ingredients which are certified such organic, FairWild and various fair-trade labels.

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Unit 5: Legal issues, funding and networking

Before you start your Medicinal Plants Business you already know you have to prepare many documents, do special research and prepare your business plan. Additionally, of course you have to make sure you are allowed to do your business in this specific sector and in the specific place (city, country etc.)

The European Union legislation for medicinal products is very complex and the base is related to the need of marketing authorization which needs to take place before having the medicines in the market. The main purpose of this is to protect public health by encourage high quality, efficacy and safety. All main requirements and procedures are presented in regulations which are contained in the "Rules Governing Medicinal Products in the European Union". Many figures are included which are supported by other publications such as Good Manufacturing Practice (GMP) guidelines. (www.omicsonline.org)

Medicinal plants have been used for many years in all parts of the world by young people and older generation as well. Even so, strict regulation of herbal medicines in a legal environment was introduced in the 20th century. The EU regulatory framework includes specific requirements for herbal medicinal products (HMP) which are independent from their legal status: traditional herbal medicinal product (THMP) or products based on clinical evidence - well established use (WEU).

Knowing how hard it could be for you, we would like to present some information regarding legal issues and funding.

- Legal issues

The law of European pharmaceutic allocate herbal products as "normal" medicinal products if they claim to prevent illness or if they are conduct with a view to restoring, correcting or modifying physiological functions. Depending on the application and preparation of the product it can be used differently. For example, peppermint tea could be treated as food or medicine. Another example is senna extract, which product need to be declared a medicine by virtue of its pharmacological action.

The component of herbal medicinal products and changes that are happening constantly make an impact on regulatory assessment. Additionally, it is a challenging aspect for health agencies and national authorities.

For long time herbal, medicinal products have been part of cultural heritage and this may be one reason why herbal medicinal products continue to be extensively used in Germany – that is the country where this market is growing very fast.

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Recent studies present that more than 70% of the German population admitted that they used natural herbs/medicines, and apart from that for most of them as a first choice they used herbal medicinal products in the treatment of minor diseases or disorders.

When total European market is 39%, the German one holds the biggest part share by value, followed by France (29%), Italy (7%), Poland (6%) and the United Kingdom (6%). Herbal medicinal products are found among the top 200 of the 2000 most prescribed medicines that were reimbursed by state-supported health insurances in the year 2000. As an example, we can present, a product composed of saccharomyces yeast used for the symptomatic treatment of diarrhoea holds rank 51 with 1.5 million prescriptions, where the most popular brand antidarrhoeal, loperamide, is placed at 145 with 851 000 prescriptions. From the other hand the most important herbals are ginkgo leaves, hypericum, ivy (Hedera helix), mistletoe, hawthorn, saw palmetto and horse chestnut.

Presented data shows that creating a professional herbal medicines plants business you have to have in mind that those are rightly classified as medicinal products because they are used as such. At the same time its crucial to know that there are herbal medicines that may present risks even when properly used. Such risks for humans and animals are mostly moderate and can be avoided by appropriate labelling with description.

The problem that can be observe is that there is a potential interaction between herbal medicinal products with conventional medicines. The most visible example is hypercium. In this case the risk has to be carefully diagnosed. It's critical to balance the potential benefits and clearly labelled the product for consumer and health professionals in order to protect public health.

"These specific challenges were acknowledged at the Eighth International Conference of Drug Regulatory Authorities (ICDRA), in Bahrain in1996. WHO Member States were encouraged to establish groups of experts for herbal medicines in their own countries and regions and to update national legislation in order to allow registration of herbal medicinal products. This was reconfirmed at the Ninth ICDRA in Berlin in 1999". (http://apps.who.int/medicinedocs/en/)

Summarizing all facts, European experience shows that herbal medicinal plants are appropriately assigned to the group of medicinal products. It is caused by the fact that the used is the same as any other medicine. The risk that might appear must be identified and labelled as it is with any other medicine material.

- Funding and networking

European Union every year presents funding in the form of credit and grants for many different sectors. Main areas that can be covered by the EU funds are: education, health, ecosystem, consumer protection, environmental protection, entrepreneurship, agriculture, social and humanitarian aid. All funding programs are managed according to very strict rules and legislations, which help to make sure that there is a control and proper check. The control is mainly addressed to the topic related with funds – how are they used, for who and when. Funds

need to be spent in a transparent way – available for everyone. EU funding process is very complex, as there are various types of programs which are leaded by different parties. Each project has specific target group to which it can be addressed. Projects are divided by subject, age, special target group and location.

More than 76% of the EU budget is managed by the Member States. It includes structural funds that finance regional legislations, trainings, social support, as well as agriculture area (support for farmers as well).

Two main types of funding (www.eubusiness.com)

Grants – it refers to a specific project. Most of the time following a public announcement known as a 'call for proposals'. In this case part of the funding is send by the EU and other part from another source.

Public contracts – Contracts cover a specific area such as: technical assistance and training, consultancy, conference organisation, IT equipment purchases etc. Awarded though calls for tenders.

28 EU Commissioners have an obligation and responsibility to ensure that all funds are spent properly and used in a proper way. There are also many EU funds that are manager at a country level – those are under the national governments control for checks and annual audit.

Beneficiaries of the funds:

- Small businesses
- Non-governmental & civil society organisations
- People that want to create a social entrepreneur
- Groups that have an idea but not enough financial support
- Young or adults with ideas
- Start-Ups
- Niche groups
- Disabled

- Researchers

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In EU budget, more than €53 billion has been made available between 2007 and 2013 for research, principally connected with the seventh plan programme (FP7). Grants are available in the form of co-financing for research related to cooperation, ideas, people, capacities & nuclear research.

- Farmers

Many people that have a farm – farmers are not aware of the benefits that they have. Most of them are eligible to receive a direct payment to support their income. As any other support it requires to follow some rules which are for example: respect standards related to environmental protection, animal welfare and food safety.

Two main types of funding:

- Lifelong Learning Programme – study and learning opportunities through Erasmus, support for students, teachers, induvial / ERASMUS+

- Youth in Action Programme – possibilities to go abroad for work or volunteer action

The market in Europe is very wide – can touch all kind of sectors. Medical sector is connected with herbal medicine plants which is diversified and well documented. The fact is that in Europe, both licensed and unlicensed medicinal plans/herbal products are available for the customer. From the point of view of both the dietary supplements and OTC drugs, the market for HMAP products is considered one of the leading sectors in Europe. In 1994, the annual turnover from the sale of OTC herbal medicines amounted to USD 6 billion which increased to USD 7.5 billion, growing at a rate of between 10 to 15% annum in 1997. The sales volume of the European market for licensed herbal medicines was estimated at higher than USD 475 million in 1997 with three ginkgo (Ginkgo biloba) products attracting the highest sales volume. There has been a drop in the sale of ginkgo products in Germany, one of the most developed herbal markets, in the last 10 years (sales dropped from 9.9 million in 1993 to 8.5 million in 1997). Conversely, some other herbs witnessed increased sales. An example is St. John's wort (*Hypericum perforatum*) which saw sharp sales increases from 2.6 to 8.5 million between 1993 and 1997. The leading herbal products recording the highest sales were derived from ginkgo, ginseng, garlic, St. John's wort, evening primrose and Echinacea.

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Unit 6: Business Start-Up Internationalization and innovation

Innovation and Internationalization

- Is Internationalization and innovation important? Yes it`s very important if you want to make your business well known and growing.

Internationalization - the process through which a firm expands its business outside the national (domestic) market – is pursued because of several reasons

Successful internationalization calls for a careful entry strategy and capacity to cope with various issues

Internationalization of firms may be supported by various public and private organizations – including Chambers of Commerce Abroad.

Easy example: Bob Marley internationalized reggae, making it known throughout the world.

Why should we go international?

- to enter new output markets
- to reduce costs and enhance competitiveness
- to exploit their own core competences in new markets
- to share risks over a larger market
- to take advantage of lower labour cost, lower taxation, cheaper natural resources
- sometimes, because the domestic market is just too small for company growth

Companies in general go international by exporting their product/service first, then by establishing and hiring a sale representatives in the foreign countries, and another step refers to setting up production facilities.

Eventually, international businesses may develop into:

Multinational corporations (MNC): company that carries out its production chain in more than one country. The headquarter office is usually in a place where the company was created (home country) and at the same time in a place that is easy to reach. It is also possible that operations are held in more than one country.

Trans-national corporations (TNC): a MNC that does not identify itself with any specific nation – open for the world, but acquires truly international (i.e., not country-dependent) features and high local responsiveness.

2. Where do companies go international?

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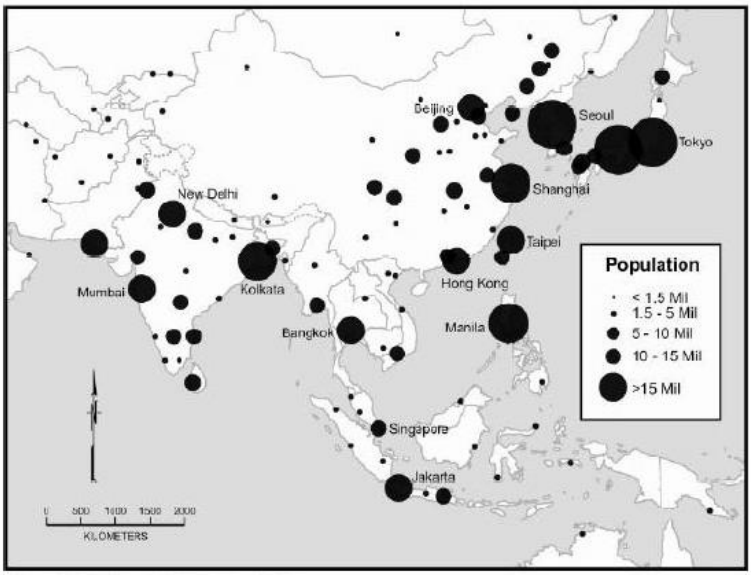

(Source: ESRI, 1998 and World Gazeteer 2005)

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How to go international?

Main strategies that allow you to enter into foreign markets include:

- ✓ Only exporting a company's products into a foreign market, is possibly with the support of trade brokers

- ✓ Licensing a company's production and marketing process, or asking for royalties to be paid for the use of owned assets and resources

- ✓ Franchising a business

- ✓ Directly undertaking production and selling in a foreign country

    a) Through a 'multinational approach' by adapting to local markets

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b) Through a 'global approach' by mass-marketing the same product

- What is Innovation? Is it needed? Do I need it? Yes, and Yes!

"Listen" to the words of Steve Jobs and you'll discover what separates true innovators from everyone else.

It all comes down to dots.

Steve Jobs was an American entrepreneur, businessman, inventor, and industrial designer. Jobs was the chairman, and the chief executive officer (CEO), and a co-founder of Apple Inc. said:

"You can't connect the dots looking forward; you can only connect them looking backwards. So, you have to trust that the dots will somehow connect in your future. You have to trust in something–your gut, destiny, life, karma, whatever. This approach has never let me down, and it has made all the difference in my life." Steve Jobs

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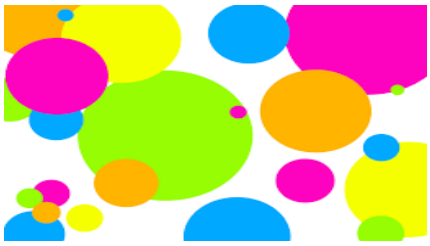

So, what is innovation?

Those other dots, the ones that are missing. The dots people see are not the ones we want you to innovate, the dots that make the world to move forward are the ones which we can call “innovation”. Moving forward is connected with changes and specially with innovative changes.

You have to be innovative and go global. Globally, there are over 100 million new companies (big and small), which are launched every year. Considering the statistics, it translates into roughly 11,000 start-Ups launched every hour, so if one day is only 24 hours can you imagine how many ideas are appearing every day?! In this fast-paced environment, it is essential for start-Ups to keep innovating and be different – original, if they want to survive and keep alive at the market.

With thousands of new companies being launched every day, start-Ups can't afford to rest on their laurels and take the chance to not experiment or innovate. They need to keep their eyes and ears firmly on what is happening around them in the market and keep a check on what their competitors or new players are doing. Considering the pace at which technology gets obsolete today, one new or disruptive technology is all it could take to wipe out a complete business overnight, thus leading to a complete waste of all the resources, time and effort invested in building the business. So, there’s little chance you can count on ‘so-called’ innovative product to keep your start-Up going, if you don’t continue to make innovation your priority on a day-to-day basis.

Innovation can bring many advantages to your business and big companies which were at the beginning consider as Start-Ups knew about it.

Innovation:

- **Gives you a competitive and special peak**

Innovating something that does not exist gives start-Ups an edge over their competition and helps them become and remain a market leader.

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- Think for a moment about the case of Apple Inc., which has remained the industry leader since its launch nine years back. Apple is constantly innovation something new which is different than other smartphones companies. Innovation is a clue in the sector of communication and not only there.

- Another great example is Uber (ordering a car with driver via application where the ride is paid via credit card), which completely disrupted the cab sharing industry, has managed to last a market leader as it is constantly innovating and creating new options for the customer. Right from ride sharing to premium cars, the company has grabbed a foothold in every market it operates in. Now Uber is also creating plane sharing service – is it not a great example of innovation? Many people instead of ordering a taxi they order Uber via application and do not worry about payments via cash as everything is done by credit card.

- **Makes Start-Ups more powerful**

If innovation is the main aspect of your business, it makes it easier to solve problems as well as reach to the big challenges.

Did you know that Google company assigns a special hour or day in each department for everyone for innovation – during this time people experiment and create new possibilities/ideas. It doesn't require from a company any extra cost but due to that it gives a chance to make something new and original.

Many of its innovative products like Hangout, Maps, etc. have all been a part of its in-house born ideas time.

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- **Creates entry barriers for competitors**

Being an innovator or a troublemaker is the best way to stay at the top and become an industry leader. However, one good idea can lead to a thousand followers so think and start your business today. Innovation is the future.

- **Competes with larger well-established companies**

Big companies can out-innovate Start-Ups by adopting a systematic approach to innovation and learning. In order to compete with them, Start-Ups need to be a step or more ahead and adopt a culture of innovation.

- REMEMBER –

Research shows that 95% of Start-Ups fail within their first year due to lack of any new ideas – due to lack of innovation. Customers ask for new application, new updates and new topics so as a person who cares about their needs you have to follow the market and give what they ask for.

It’s very obvious that every Start-Up needs to make steps associated with innovation as a part of its DNA, if the goal is to get ahead of competitors and retain that position.

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Imagine that you have a team of 6 people and if every single person on your team is focused on innovation, there is no way anyone can stop you from reaching the top and keep there as long as possible.

NEW TECHNOLOGY - NEW MARKET – NEW CUSTOMERS – NEW COMPETITORS

Do I have a problem or it's my new challenge? Am I able to make it?

Definitely you have to think that you have new challenges and you will reach your goals.

TECHNOLOGY?

Nowadays almost everything is connected to technology and even if you do not realize you use it every single minute (Computer, Watches, Cars, Phones, TV, Internet, School, Communication, Cooking etc.).

Now you want to start something new and great, your own Start-Up.

Be aware that without Technology it is simply impossible. Asking why?

- ✓ Because you have to act fast! – Emails go faster than letters.
- ✓ Because you might have meetings with people from all over the world – Video conferences are cheaper than flights and you can join the meeting even during the night or early morning.
- ✓ Because you have to keep track on all your money income and outcome. The easiest way to do it is not anymore calculator and peace of paper – now we use Excel.
- ✓ Because you can catch with your co-workers from other city, country or even continent via Skype or Hangouts which is totally free!
- ✓ Because now we all use Apps and people need it as it makes their life easier and can get your product everywhere they are.
    - The total number of mobile app downloads in 2017 – 197 billion (a forecast) (Statista)
    - The total number of iOS app downloads in 2016 – 25+ billion (Source: App Annie)

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What´s important to know:

- **Don’t start with technology, start with people!**

If your workers understand the big picture for the business and its vision for the future, they can more easily comprehend and support the need to adopt new technologies. First of all, explain to you team what’s the new technology and why is it important, after that start implementing the technology.

- **Understand the technology.**

Give yourself and your employee’s time to learn new software, application or way of doing tasks. It can take time and be at the beginning boring or frustrating but you will get there and will be proud of yourself that you made it. Technology is here to help us not to make our life more difficult.

GLOBALIZATION – where to go and how to get there? Use Technology and be noticed out of your comfort zone!

- Find your customer (maybe your customer is in Germany or Italy?)
- Find the niches (Maybe something is still missing in Spain or Hungary?)
- Check all economic advantages and disadvantages in other place as it might be much cheaper there (city, country, and continent)

Globality's mission includes making international commerce more accessible, although the company is too young for its impact to be assessed. From the business perspective, one effect of

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globalization is that of expanded markets. This means that a business that had previously only sold its goods domestically can start selling products to other countries.

One example of expanded markets includes the auto industry. Mercedes, Volkswagen, Ford is knowing everywhere all around the world due to the globalization.

Don't be afraid of failure this is the way to succeed! Don´t be afraid and go Global!

The impact of technology on globalization has been extensively reviewed and will continue to be so for the simple reason that technology is developing faster than globalization. I have chosen two slightly different interpretations of globalization:

Globalization refers to processes that increase world-wide exchanges of national and cultural resources. Advances in transportation and telecommunications infrastructure, including the rise of the Internet, are major factors in globalization, generating further interdependence of economic and cultural activities.

There is a snowball effect when expanding your company internationally - the more countries your company is in, the more potential customers you have. By growing your infrastructure, your company follows.

The act of globalization is an extremely competitive strategy as well. If you are somewhere your competitors aren’t, that is a major business advantage. Simply put, if you want your company to grow, you need to consider globalization as a realistic opportunity.

Of course, you can find people who will say that Globalization is not a good step, but you are the one who make the choice.

For instance, some proponents say globalization creates new markets and wealth, and promotes greater cultural and social integration by eliminating barriers; on the other hand, some critics blame the elimination of barriers for undermining national policies and cultures and destabilizing advanced labour markets in favour of lower-cost wages elsewhere. Similarly, some proponents point to the rising economies of poor countries benefiting from companies there to minimize

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costs; some critics say such moves could lower living standards in developed countries by eliminating jobs.

VERY IMPORTANT!

Know your CUSTOMER – without them you will not succeed as they have to get your service or product!

Where are they from?

What they need?

How old are they?

How much money they can spend at the beginning?

Will they promote your product if they like it?

Will they use it daily, monthly or maybe once per year?

Are they students, workers, families, teenagers, seniors or maybe big companies?

If you don't know how to get more customers we will give you some ideas:

When it comes to your pitch, get out of your comfort zone

If you're having trouble expanding your customer base, you may be inadvertently narrowing your focus—and with that, missing the mark with potential new customers. If you're pitching your business in the same way that you always have, it's no surprise that you're having trouble reaching new customers.

Build a "relationship map"

Build a "relationship map," which will match your strongest relationships with the areas where there is the greatest need for your product or service. This map will help point you in the direction of who you need to reach out to, in order to tap into potential customer bases.

Speak at an event or host an industry gathering

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You have plenty of expertise in your field—why not get involved in the community? By sharing your experience and getting involved in your industry at a local level, you'll have the opportunity to grow your connections, as well as your reputation as a thought leader in your industry.

Try offering free trials, product, service to new customers
Another practical tactic to acquiring new customers? Offer them a free trial of your product. "Free trials are a great way to market, since they attract new customers and garner good reviews and testimonials," says Souny West of CHiC Capital.

Can COMPETITORS help you? Yes, they can! So, don't be afraid of them but be strong enough to bit them!

Use your competitors to know more about the market, customer, offers and changes in your sector.

Looking at who is talking about your competitors can give you incredible insight into what types of customers use similar products to yours. If your product adds more value there's no reason you can't reach out personally to these people & offer a free trial to switch. Facebook allows you to pay $1 to send a message to a non-friend, you can send a tweet to someone, contact them via their blog or if you can get a phone number give them a call.
Competition in a business context is either direct or indirect for any startup or established company. Even if you have a product or business service that is completely niche or unique, it is impossible not to face some competition.

Once a business has set up and is entering the market, the key to success will be competitive advantage. What makes their business better than other people's businesses and what is their USP? You must find a way to differentiate yourself. For example, a soda startup does not have to be daunted by companies such as Coca Cola if they have their own USP, a niche in the market that Coca Cola would not satiate. A small soda company that offers natural ingredients, and branding towards children specifically, will not face direct competition from a huge company because it has a USP. This is the key to entering a busy market – what do you have to offer that sets you apart from the rest?
Don´t be afraid of other Start-ups! You ask why not, because:

- They are guessing, checking and learning just like you … so be faster!
- A lot of them give up and die … You will not!
- Some acquired and stop innovating … You know that innovation is the key!
- Markets can support multiple players … And you play as well so they will support you!
- They also have problems and issues … but for you they are challenging and motivating!

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INNOVATIVE INTEGRATED TRAINING IN
HEALING PLANTS
BUSINESS

Module No. 5

“Medical use of therapeutic plants”

Biognosis

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Unit 1: Therapeutic plants from Antiquity to the end user (Hippocrates, Theophrastos Galenus, others).

Archaeological records and written documents comprise the sources available for the study of the history of using medicinal (as well as nutritional and toxic) plant. Even in mythology we find records of herbal treatments. Master of Herbal Medicine is considered to be the Centaur named Chiron, who lived in Pelion and taught the medical god Asclepius. (Marketos S. 1997)

Apollo delivers Asclepius to Chiron. Goltzius, Hendrick, 1590, etching. Haarlem, Teylers Museum, KG 02499

Remarkable are the references into Homeric epics, reporting the use of herbs for therapeutic purposes or for poisoning. In the Iliad, when Diomedes injures Ares, Zeus calls doctor Peionona, who nourished the angry Mars by using fig milk. In Odyssey, we read about the "nepenthe" that Helen received from Egypt and gave it to Telemachos to forget and not regret the situation with the suitors at his father's home. Witch Circe, used magic drinks, and made Odysseus' comrades forget about their mission, knowing a great deal about herbs and their pharmaceutical effect. Hermes gave Odysseus the “moly” to be able to resist the actions of Chirac's magical drinks (Skaltsa E., 2001).

The history of ethnopharmacology dates back centuries. The first written reference in plant collection for therapeutic purposes was translated from cuneiform writing and attributed to the Sumerians at 4000 BC. Other written reports were discovered in China and Mesopotamia (3000 BC) and Egypt (2500 BC). The first "Botanology" was written in China in 2700 BC. The Chinese healers used 365 medicinal plants. Egyptian papyrus dated around 1700 BC mentions many common herbs used in medicine. In the Ramses III era, cannabis was used for treating eye

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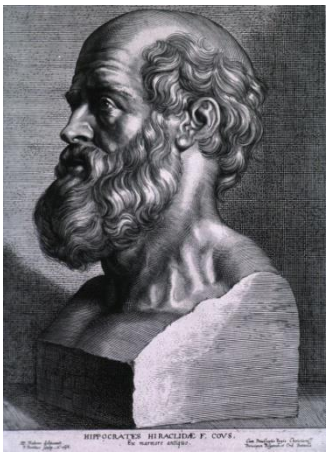
diseases, poppy extract was used to soothe baby crying, and garlic was known for its healing properties. (Benedum J., Loew D., Schiler H. 2006)

Hippocrates, known as the "father of medicine", was born in Kos around 460 BC. He is considered one of the most prominent figures in the history of medicine. The great philosopher studied human nature, body and its function, but also the effect of climate and environment on health. Hippocrates was influenced by the pre-Socrates philosophers, who believed that the world consisted of four elements: fire, water, air and earth, also associated with the basic properties of warm, cold, dry or wet, all four seasons. He categorized all foods and herbs according to their fundamental attributes - warm, cold, dry or wet, and believed that good health is maintained when these properties are in balance.



Engraving by Peter Paul Rubens, 1638

Statue of Hippocrates in Larissa Greece

Hippocrates used plants and herbs in medical applications, because he deeply believed in the healing power of nature. Among approximately 256 plants he used, a lot of them still stand in the basis of modern medicines (Totelin L., 2009).

Theophrastus has been regarded as the founder of botanology. He was born in 372 BC in Eressos, Lesvos, was student of Platon and after his death he followed Aristoteles, as valued him a lot. When in 323 BC Aristotle was accused of disrespect and was forced to flee to Chalkida, donated his library to Theophrastus and entrusted him with the direction of the Peripatetic school. Theophrastus remained in the faculty for 35 years and during that time he taught but also he left many manuscripts. Unfortunately, only two works of botanology have survived from his entire scientific work, of which the first one (chronologically) is titled "On the Causes of Plants". In his work, Theophrastus combined empirical knowledge and philosophical thinking (in terms of methodology). The basic principles of the study of plants were taken by Aristoteles, but he formulated the basic concepts of botanology and described the parts of plants in a very detailed

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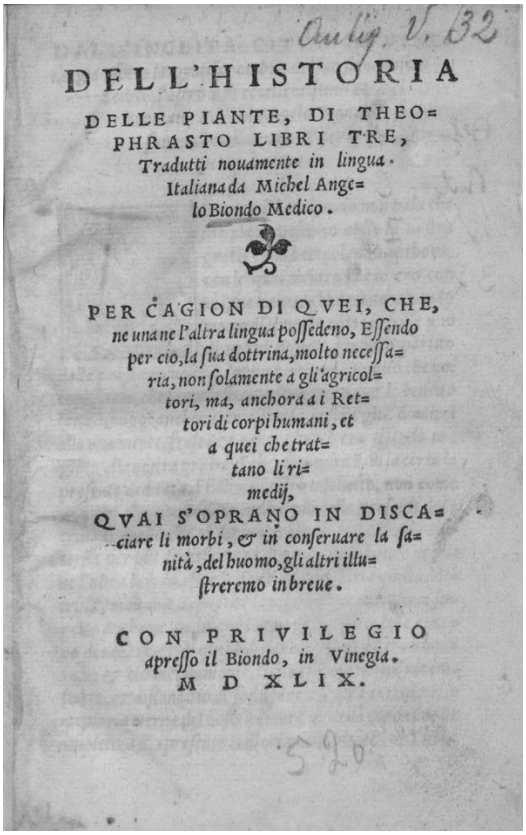
and specific way, paying particular attention to the leaves and roots. Theophrastus' work concerns not only botanology but also phytotherapy, because it also refers to their pharmaceutical uses. (Loeb Classical Library 1980)



DELL'HISTORIA
DELLE PIANTE, DI THEO=
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Tradutti nouamente in lingua
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lo Biondo Medico.

PER CAGION DI QVEI, CHE,
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CON PRIVILEGIO
apresso il Biondo, in Vinegia.
M D XLIX.

Historia plantarum, 1549

Among the precursors of phytotherapy we can mention Heraclides Tarantino, a famous ancient Greek physician, who flourished in the 1st century BC. He was one of the most important representatives of the medical school of empiricists, and Galen called him Heraclides the empiricist. He used plants, especially opium, pepper and balm, and was reported to have experimented with the preparation of antidotes to poisonous plant (hemlock, Hyoscyamus, etc.).

The one that is considered to be the greatest pharmacologist of antiquity is Pedanios Dioskourides (40-90 AD), who was an important physician, pharmacologist and botanist from Anazarbos of Cilicia, known mainly for the five-part work of " De Materia Medica with great Influence on pharmacology until 1600 AD. From his early years he was particularly inclined to study the plants and the herbs, and after the end of his medical studies he investigated the pharmacological properties of many plants, following the Roman army in various Mediterranean countries, serving as a doctor and having the responsibility of treating the wounded. Dioskourides recorded more than 1,000 pharmaceutical substances; the majority of them derived from plants. He knew the

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properties of the mandrake, its therapeutic value and its usefulness in premedication and narcosis (Scarborough J., 1982).

Dioscorides De Materia Medica Spain 12th 13th century

He also observed and described the phenomenon of allergic shock caused by medicament's use. The effect of his work extends over at least until the Renaissance period, and it is generally appreciated that Dioscouride's methods of observation provided strong bases for the evolution of pharmacological science.

Claudius Galen (Pergamos, 129 - Rome, 199) dealt with most medical disciplines. Like Hippocrates, Galen believed that the four liquids - blood, yellow bile, black bile and phlegm, were cold or hot, wet or dry. In order to deal with a disease, a "counter" treatment, of the same intensity, had to be chosen. Thus, diseases that were warm and wet in third degree were treated with a cold and dry treatment in third degree. If the patient was cold and his nose was running, were used medicines and food that heated and dried. By rebalancing the juices, the body returned them to a healthy "neutral" state.

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Mural painting showing Galen and Hippocrates. 12th century; Anagni, Italy

He studied the healing properties of the herbs and produced various complex pharmaceutical formulations known in the literature as "galenical m" and the corresponding pharmacy it is called "galenical pharmacy".

Avickens (980-1037), a famous Muslim philosopher and physician, is considered to be the most systematic representative of Islamic philosophy. Avicken's medical view is also based on the theory of 4 Hippocrates fluids. The most famous of about one hundred books that he wrote is the Cannes of Medicine, which has been a reference point for medical science over centuries. In this book, he describes 764 simple drugs and their pharmaceutical properties, based on the dangers of Dioscourides, Galen and some other Arabic and Indian origins.

In Byzantium, Nicholas Myrepsos was excelled as a leading pharmacist (1222 - 1255 AD), who was a doctor, botanist, and doctor of the court of Ioannis Vatatzes, emperor of Nicaea (13th century). He was deeply acquainted with the medicinal properties of the plants and was the writer of the "Dynameron" work that includes 2656 medical prescriptions. In this work, raw materials, preparatory methods, dosage forms, proportion forms and substitutes were recorded. Also, in this work he tried to create terminology, which was used for centuries by European pharmacists. Until the 18th century this was the official pharmaceutical code of the West and the official textbook of the medical school of Paris. (Marketos S. 2008)

Paracelsus (1493-1541), an amateur alchemist, was the son of a medical doctor from whom he took his first lessons and then studied medicine at the University of Vienna. He was scholar of platonic philosophy and alchemy, and traveled to Egypt, the Holy Land, to Constantinople and other places, seeking the knowledge of the alchemists. He was perspicacious, innovating, and a great revolutionary of his time. He opposed traditional writers like Galenos and Avickens, and was more a fan of Hermetic, Neoplatonic and Pythagorean philosophies. His approach was that there

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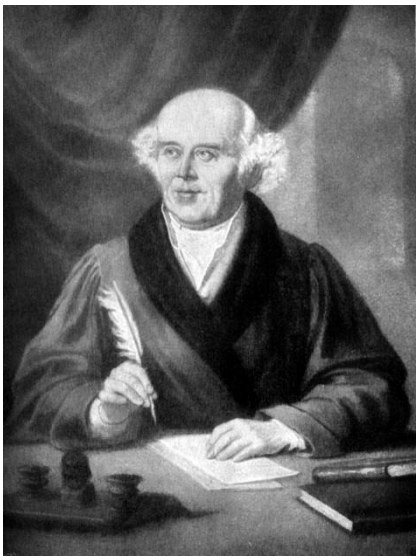
should be a balance of metal elements in the body and that diseases can be cured by the use of chemicals. The basic idea was that vital processes are of a chemical nature and that salvation depends on the balanced composition of fluids, which could be restored by using the appropriate drugs. For this reason, Paracelsus attached great importance to the preparation of drugs, in which study he devoted much of his life, combining experimental observations with alchemical perceptions. He used plants for his therapies and experiments, enriched his knowledge, and helped in discovering the healing properties of many plants. He also introduced herbal tinctures and extracts in medicine (Skaltsa E., 2005).

German physician Christian Friedrich Samuel Hahnemann (1755-1843), who is considered to be the father of homeopathy, was a scholar of Paracelsus's teaching. Hahnemann, by experimenting on himself, noticed that the skin of the cinchona causes a person's fever, and is known to cure sufferers of malaria. He also considered that the reason why the skin of the cinchona heals intermittent fevers is precisely that ability to cause similar symptoms in healthy organisms. For six years, he experimented with other drugs, recording the symptoms they cause in healthy individuals, and by this way he establishes Homeopathy.



Cinchona succirubra ***Christian Friedrich Samuel Hahnemann***

He also gathered all of the previously known elements of toxicology, as he knew Latin, Greek, Arabic, English and French. All this knowledge was the foundations of Materia Medica (Pharmacology) of Homeopathy. Homeopathic pharmacology contains a lot of information on plant properties that have been used so far according to the principles of homeopathy. The study of the action of a plant was the reason for the creation and systematization of a new therapeutic system. Homeopathic remedies originate from plants but not all of them. In contrary to

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homeopathic theraries, phytotherapy uses dried plant material or extracts of plant parts, in certain therapeutic doses so as to treat the disease symptoms, in a way as conventional medicine does. The use of herbal medicines in an evidence- or science-based approach for the treatment and prevention of disease is known as (rational) phytotherapy.

Homeopathy is not the only healing system that came from phytotherapy. Pol Henri's gemmotherapy is a sophisticated field of phytotherapy and was discovered by him in 1965. Unlike phytotherapy, which uses the adult herb, gemmotherapy uses only plant materials that are growing, i.e. plant embryonic tissues such as young roots, eyes, seeds, etc. These natural tissues are rich in growth factors, such as vitamins, trace elements, phyto-hormones and ingredients that are not always found in the mature plant.

The flower remedies were initially discovered and applied by the English physician Edward Bach (1930). The original number produced by Bach has expanded by other therapists. They are made from flowers of plants, bushes or trees. They relieve people of emotional upset such as fear, panic, anxiety, depression, insecurity, lack of self-confidence, jealousy etc. They are based on the theory that every negative physic or mental state affects our defense system and becomes vulnerable to infections and diseases. Therefore the remedy is chosen according to the character, mood and feelings that cause disharmony in the individual.

Although the history of phytotherapy is essentially identical to the history of pharmacy, at least until the Second World War, then begins a short 20 to 30-year decline when the "chemical revolution" dominates in medicine. At this time, the interest of the scientific community is turning to chemical preparations of fragments, and thus neglects phytotherapy. But nowadays people recognize the benefits of phytotherapy and the lack of side effects of phytotherapeutic formulations, as compared to chemical drugs, and more and more scientists are forced to look for natural solutions offered by phytotherapy. That is why we believe that in the coming years, phytotherapy will flourish and regain the place it deserves in sciences.

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Unit 2: Ethnobotanical use and modern Phytotherapy

First findings about the plant's medicinal use in the primitive civilizations have been based on random observation on animal's behavior. It is known from these observations that when an animal is sick, it selects the appropriate herbal remedy based on its instinctive guidance. Over the centuries these recordings were used in mythology, but also have become the basis from which the first records begin and the first phytotherapy books written. Thus, through centuries, a phytotherapeutic tradition has been established and has reached nowadays. Large number of traditional healers still possesses knowledge by their ancestors, which so far has been transferred from one generation to the next. As scientific progress becomes increasingly fundamental, the need for scientific proof of the existence of traditional knowledge has been arisen.

Ethnopharmacology

In modern medicine, the term Ethnopharmacology, describes the specialty of pharmacy, and especially pharmacology, dealing with the thorough investigation of the biologically active substances observed or used in the context of the traditional culture of the peoples (Bruhn & Holmstedt, 1981).

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The term Ethnopharmacology appears in 1967 by Ephron. Ethnopharmacology, although is a specialty of pharmacy, it is rather a transversal science, precisely because it uses, in addition to pharmacology, several methods and techniques, from other sciences such as botany, pharmacology, cognitive anthropology, linguistics, communication, sociology and biostatistics in order to fulfill its purpose.

The goal of Ethnopharmacology is to study the popular therapeutics, in order to provide the laboratory the natural raw material from which the new drug will be developed. For this purpose, ethno-pharmacologists visit the local populations and in the search for this raw material they use anthropological, chemical and botanical methods.

Medicinal plants: Traditions of yesterday and drugs of tomorrow

Plants have formed the basis of traditional medicine systems all over the world. For thousands of years, the herbal kingdom continues to provide mankind with remedies, like Ayurvedic in India, Ancient Greek medicine, Chinese and others. Although, medicinal plant therapy is based on the empirical findings of hundreds and thousands of years, some of the therapeutic properties attributed to plants were not verified. The search for new molecules, nowadays, has taken a slightly different route, where the science of ethnobotany and ethnopharmacognosy are being used as guide leading chemist to different sources and classes of compounds.

As seen in the journals, studies on herbal medicines have been encompassed under several different names, such as plant medicine, phytomedicine, pharmacognosy, and natural products.

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“Natural products” usually refer to products processed or derived from living organisms, including plants, animals, insects, microorganisms, and marine organisms. (Cox P.A 1997)

Residents of a pygman village near Bikoro make baskets Journal of ethnopharmacology

DEFINITION OF TRADITIONAL HERBAL MEDICINES-PHARMACOGNOSY-PHYTOCHEMISTRY

The use of plants for prevention and treatment of diseases is the earliest type of medicine on earth. The practice of traditional medicine developed along with the cultures of ancient Greece, China, India, Egypt, and other places. Different species of plants are used as medicines for treatment in different countries because of the different ecological environments. In countries with long histories and cultures, theories of etiology and pathology, methods for diagnosis, and treatment with herbal medicines or other methods, gradually formed their own complete medical systems finally established. To fully explore the preventative and therapeutic mechanisms of traditional herbal medicines, it is necessary to have a deep understanding of the theories in their corresponding medical systems. (Schultes R.E.1962)

The use of herbal medicines for treatment of diseases was documented several thousand years ago. The vast majority of people on this planet still rely on their traditional Materia Medica (medicinal plants and other materials) for their everyday health care needs.

The profound knowledge of herbal remedies in traditional cultures developed through trial and error over many centuries, and the most important cures were carefully passed on verbally from one generation to another.

According to the World Health Organization (WHO), traditional medicine refers to health practices, approaches, knowledge, and beliefs incorporating plant, animal, and mineral - based medicines, spiritual therapies, manual techniques, and exercises, applied singularly or in

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combination to treat, diagnose, and prevent illnesses or to maintain well-being. If the material is of plant origin, then it is called **traditional herbal medicine (THM**).

Modern allopathic medicine has its roots in ancient medicine, and as it has been up till now, it is likely that many important new remedies will be discovered and commercialized in the future, by following the traditional knowledge and experiences. People, who use traditional remedies, may not understand the scientific rationale behind their medicines, but nowadays we have a better understanding of how the body functions, thus we are in a better position to understand the natural healing powers of plants and their potential as multi-functional chemical entities in treating complicated health issues.

During the 19th century, the most important pharmaceutical discipline and the mother of all present-day pharmaceutical disciplines was pharmacognosy.

Pharmacognosy was for the first time defined as a pharmaceutical discipline in 1815 by Seidler. The definition Pharmacognosy (derived from Greek pharmakon, 'remedy', and gignosco, 'knowledge') is the science of biogenic or nature-derived pharmaceuticals and poisons.

Pharmacognosy deals with all medicinal plants, including those yielding complex mixtures, which are used in the form of crude herbs (comminuted herbal substance) or extracts (phytotherapy), pure compounds such as digoxin, and foods having additional health benefits only in the context of having preventive effects (nutraceuticals).

There are three types of drugs derived from plants:

- Herbal drugs derived from specific parts of a medicinal plants e.g. *Hypericum perforatum*
- Natural products or compounds isolated from nature e.g. digoxin from *Digitalis spp*.
- Nutraceuticals or "functional foods" such as garlic, turmeric e.t.c.

In the 17th and 18th centuries, knowledge about plant-derived drugs expanded, but all attempts to 'distillate' the active ingredients from plants were unsuccessful. The main step came in the early 19th century, when it became clear that the pharmaceutical properties of plants are due to specific molecules that can be isolated and characterized. This led to the development of a field of research now called **natural product chemistry** or, specifically for plants, **phytochemistry**. (Laird S.A, 2002)

Medicinal plants typically contain a mixture of different chemical compounds that may act individually, additively or in synergy to improve health. A single plant may contain different chemicals, such as analgesic compounds and anti-inflammatory compounds that reduce swellings and pain, bitter substances that stimulate digestion, antioxidant compounds, anti-bacterial and

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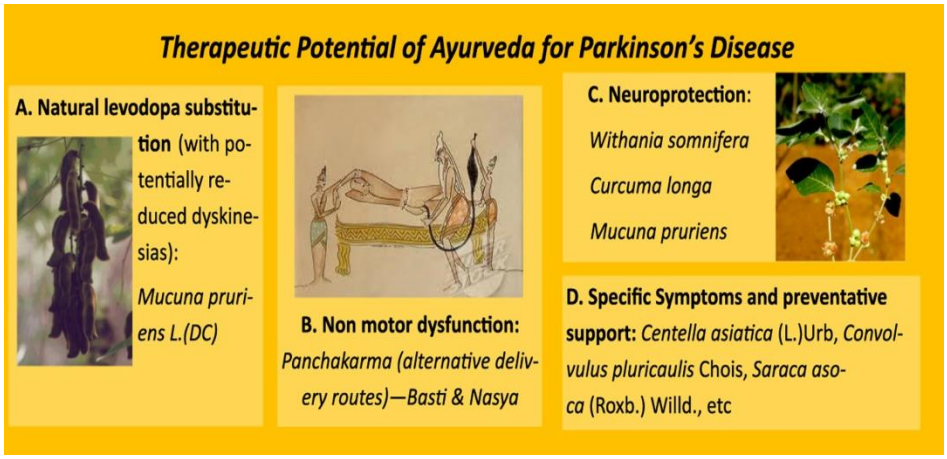
anti-fungal that act as natural antibiotics, but also diuretic substances that enhance the elimination of waste products, and toxins and alkaloids that change the mood and the perception.

Considering that the biological activity may be the result of the combination of several compounds, the isolation process may lead to its loss or reduction (Raskin & Ripoll, 2004), even though modern allopathic medicine usually aims to develop a patentable single compound or a magic bullet to treat specific conditions.

In fact, it is already well known that sometimes the complex mixtures of compounds in herbal medicines-phytocomplexes, have greater effects than isolated compounds (Gomez Castellanos et al., 2009). Herbal medicine often aims to restore balance by using chemically complex plants, or by mixing together several different plants, in order to maximize a synergistic effect or to improve an interaction with a relevant molecular target. It is reasonable to assume that a mixture of compounds (phytochemicals or synthetic) would have greater bioactivity than a single compound because a mixture of bioactive compounds has the ability to affect multiple targets (Schmidt et al., 2008). In most societies today, allopathic and traditional systems of medicine are placed side by side in a complementary way. The former treats serious acute issues, while the latter is used for chronic illnesses, in order to reduce symptoms and improve the quality of life in a cost-effective way.



Namyata Pathak- Gandhi Ashok D.B.Vaidya Journal of Ethnopharmacology 2017

The traditional herbal medicine (TCM) involves botany, chemistry, biology, pharmacology, toxicology, clinical trials, and other disciplines. Chemical composition and biological or biochemical activities of many herbs have been studied by researchers in universities and pharmaceutical companies for investigation purposes or new drug development.

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Although conventional medicine is the mainstream medicine in Western countries, application of traditional medicine, including herbal medicines, is growing worldwide for many reasons, in particular, for the side effects or inefficacy of modern drugs.

Nevertheless, Phytomedicine is not accepted by the medical community and pharmaceutical industry because of a belief that it lacks safety and efficacy validation and regulations, as well as concerns on poor standardization and quality control, mistakes in nomenclature (Houghton, 1998), difficulties in identifying active ingredients and determining their complex modes of action (Raskin & Ripoll, 2004). It's a common belief that, in herbal medicines, the amount of supposedly active constituents is too low to have any relevant therapeutic effect at all. This assumption has led skeptics to dismiss these medicines as placebos (Williamson, 2001). This is not true. In a recent survey on roughly 1000 herbal medicines, only for 156 of them, emerged clinical trials supporting specific pharmacological activities and therapeutic applications. Indeed, the complexity of plant extracts makes the development of an evidence-based herbal medicine a difficult task that requires a huge analytical effort and manufacturing skills to produce well-defined, standardized herbal preparations (Cravotto et al., 2010).

RESEARCH AND DEVELOPMENT OF HERBAL MEDICINES

The herbal medicines and the treatment of diseases began with the use of herbs. For over 1500 years, the classical and most influential book in Europe had been Dioscorides' De materia medica. When the monographs of plants appeared, consisted of an illustration of the healing plant, the botanical name of the plant and its synonyms, its action and the indications for its use. When we consider that the history of classical herbal medicine spans more than 2500 years, we can assume that many of the medicinal herbs used during that period not only have specific actions but also are free of hazardous side effects. We have to estimate all this empirical experience of more than 70 generations of patients and physicians and not accept it as simply a "placebo effect" (Benedum, 1998).

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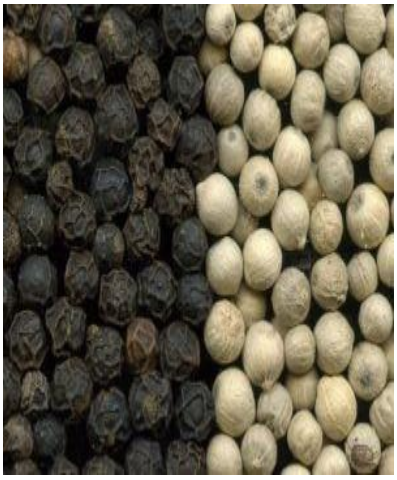
Papaver somniferum

Piper nigrum



Piper nigrum

Phytotherapy as a science today

Phytotherapy is the science of the use of plants in the treatment of diseases. It covers all medicines, from medicinal plants with strong effects such as dactylitis, mandragoras, to those with mild action, such as chamomile, peppermint, etc. Phytotherapy is a complementary or alternative therapeutic practice aimed the holistic treatment of the patient. For the development of phytotherapy as a science, specialists from various research fields have been involved in order to make better use of herbal properties. The herbal medicinal products contain mixtures of active and inactive ingredients derived from different parts of plants, other plant materials, or combinations of them, are defined as dietary supplements or as alternative therapeutic agents.

The following definitions are described for the various forms of phytotherapeutic agents:

An herbal medicinal product is defined as a product containing exclusively as active ingredients one or more herbal substances, or one or more herbal preparations, or one or more combinations of them.

Plant substances are mainly defined as whole, cut or cut plants, parts of plants, algae, fungi, lichens, which are unprocessed, usually in dried form but also sometimes fresh. Certain exudates, which have not undergone special treatment, are also considered as herbal substances. Plant species are precisely determined, by the part of the plant that is used, as well as by the plant's name according to the binomial system (genus, species, variety and author).

Herbal preparations are preparations obtained by subjecting the plant substances to treatments such as extraction, distillation, extrusion, fractionation, purification, condensation or

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fermentation. They include sliced or powdered herbal substances, tinctures, extracts, essential oils, and juices obtained by pressing and treated exudates.

In relation to the efficacy and safety of herbal medicinal products, they are distinguished (http://www.ema.europa.eu) in:

1. Phytotherapeutics with scientifically proven therapeutic safety and/or efficacy (Herbal Medicinal Products HMP)

2. In phytotherapeutics traditionally used in 'popular therapy' (THMP).

In relation to their existing use, herbal medicinal products are distinguished in (Directive 2004/24 / EC - 20/04/2011):

1. Herbal Medicinal Products (HMP) or Well-established Use (Phytotherapeutic Products) with scientifically proven therapeutic safety and/or efficacy.

2. Phytotherapeutic products traditionally used in traditional herbal medicinal products (THMP) or traditional use. This category requires proof of security. To make a product effective and safe, its use should be longer than 30 years.

3. Pure plant substances such as digoxin. In this case, a "complete dossier of proof" is required as for conventional medicines.

In recent years, efforts have been made to apply in phytotherapy the principles of scientific research developed over the last decades to the scientific community. Phytotherapy is the science that implements scientific research to find and confirm the beneficial properties of plants in various daily health problems, with no contraindications and side effects. It is a natural and comprehensive treatment. The modern scientific knowledge of recent decades through extensive clinical research, consistently confirms the great value of the "secrets" of phytotherapy in human health! Almost 80% of the active ingredients of conventional drugs, such as aspirin, morphine and quinine, have their roots in the science of phytotherapy! (Newall, C. A., Anderson, L. A., Phillipson, J. D. 1996).

In order to understand the extent of the science of phytotherapy, we should keep in mind the following:

- 80% of the 30,000 known chemical molecules of natural origin are of plant origin.
- More than 7,000 pharmaceutical preparations of plant origin, which are marketed in the pharmaceutical market, derived from 100 plant species, while 121 prescription drugs are derived from medicinal plants.

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- 75% of the traceable herbal preparations are used, are based on traditional pharmaceuticals (Ravinshankar, 2002).

Principles of phytotherapy

Phytotherapy is based on relationships, such as the relationship between plants and man, and plants and planet. When using plants for healing, we have the opportunity to treat consciously the planet we live in. When we coordinate with the healing power of the planet, our whole bio-life is changing for life. The term "holistic" has been used to describe the "whole", not the "part". Many therapeutic systems are considered holistic because they do not focus on the disease of an organ, but consider humans as a set of organs and functions. We will try to describe the principles on which holistic therapies are based on system theory and applied to phytotherapy. (Volker Schulz, Rudolf Hansel, Mark Blumenthal, Varro Tyler 2004)

Principle of Interaction – Unity

Nature is not a random accumulation of objects and phenomena detached from one another. It is a single set and each part interacts with each other.

The theory of systems uses the term open and closed system. An open system is the system that exchanges materials, actions or information with its environment. Instead, in a closed system there is no exchange with the environment. By using this definition, all organic systems either biologically or socially are open. There are no separate and isolated instruments or functions, but the whole is united to compose a biological reality.

Principle of global change

The universe is in constant motion. Every passing second, the universal occurrence is different from what it was a second ago. This continuous change is kept within limits so that the system is maintained in a controlled balance. Homeostasis becomes possible by using information coming from the external environment and incorporated into the system, in the form of feedback. Feedback expresses the regulator of the system that changes its internal conditions but maintains its steady form. That is why homeostasis is a form of change in which the form is kept stable. Morphogenesis is the type of change in which there is a new form. Thus, while self-protection characterizes homeostasis, self-direction characterizes morphogenesis. Each system uses both of these types in the continuous change process. In daily phytotherapeutic practice, the therapist should keep in mind that the condition of the organs and functions is variable and that he can, at any time, either be directed to heal or worsen to destruction. Therapies of phytotherapy are a constant support and activation of the healing powers of the body.

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Principle of the fight of opposites

Every manifestation of the universe is a phenomenon defined by the equilibrium of two opposing forces. The apparent antagonism of these two forces is in fact a wonderful collaboration, as for example, in the cortex of brain hemispheres. Excitement and inhibition, as essential elements of superior nervous functions, are thus in uninterrupted relationship, and in an apparent rivalry. Another example is the antagonistic cooperation of sympathetic and parasympathetic. The sympathetic nervous system is in charge of the reactions of human organism, in emergency situations, when we are about to make a great effort in the minimum time, using maximum force. The parasympathetic one is designed to generate energy and restore what has been lost. So while seemingly opposing, they work together harmoniously on different levels. The body's hormones and any chemical compound or trace element may be considered, depending on its function, to have sympathicotonic or parasympathetic activity. Thus physiology is studied systemically, based on the principle of interaction and the principle of the struggle of opposites.

Thus, we can distinguish all the chemical compounds of the organism into sympathicotonic and parasympathicotonic. Many compounds are sometimes sympathetic and sometimes parasympathetic.

Principle of action and reaction

When a force is exercised on a system, then a counter force will develop, as a component of the system. When a substance is given, it causes a certain action in the body. This action causes a deviation from the previous equilibrium state. The organism’s self-regulatory system is informed of this change. After substance's action, a counter-action from the self-regulatory system of the organism is mobilized.

What matters most to therapeutic practice, is that the therapist can know which of the patient's symptoms are due to the condition and what the body's attempt to restore balance. This also applies to phytotherapy, the therapist needs to know what the symptoms are due to the disease and what the symptoms are due to the lack of substances.

Principle of cyclical evolution of phenomena

When between two interacting forces one increases too much, then this leads to the ultimate increase also of the opposite one. Then, in healing, the therapist's attention should not be focused on only one symptom, but all of them (Principle of Interaction - Unity). This set of reactions, is not only symptoms of the disease, but also includes symptoms that are the body's efforts to recover, as symptoms that are considered to tend to lead in balance. The healer is not interested in finding the source of symptom but simply follows his current. The organism is faced as a self-regulating system, which tends to achieve its own balance.

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Principle of individuality

In one system there are not two subsystems that are completely identical. There are not two completely identical patients. There are no illnesses but patients. Each person is a unique phenomenon, has his own, distinct personal story. This principle also applies to the use of phytotherapy in practice. Phytotherapy is personalized according to the needs of the individual at each examination. Treatment is most effective when is personalized.

Principle of hierarchy

In each system there is a hierarchy among its members. In human body there is a hierarchy between organs based on their function. There is also a hierarchy between the medical conditions. Certainly different severity has eczema, asthma, or depression on the patient. Understanding the hierarchy of the diseases is very important for the design of the patient's therapeutic scheme. It is better the therapist not to refer to other specialist for each new medical symptom, but to try to estimate its significance as a part of the patient's condition at the time. Treatment in any case should not focus on local symptoms but on the overall picture displayed by the patient.

Understanding of the hierarchy of the disease in relation to time is also significant in planning of therapeutic scheme.

Principle of conversion of quantity into quality

The process of development is not a simple growth process, where quantitative changes do not result in qualitative changes. It is a continuous development that goes through insignificant and latent quantitative changes to obvious and radical changes that are qualitative changes. In the clinical practice of phytotherapy, this is also the case. When a treatment regime is applied, that aims to eliminate constitutional sensitivities of the individual, the person may not see any improvement for weeks and consider that the treatment may not work. But when he thinks there is stagnation, suddenly there is a period of rapid recession of the symptoms.

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Unit 3: Medical use of therapeutic plants: indications, proved pharmacological action of known constituents.

According to the definition in Research Guidelines for Evaluating the Safety and Efficacy of Herbal Medicines of the World Health Organization (WHO), issued in 1994, herbal medicine is a plant-derived material or preparation with therapeutic or other human health benefits, which contains either raw or processed ingredients from one or more plants. Although inorganic and animal materials are also used in treatment of diseases in some countries, herbs always dominate in traditional medicines.

The number of different higher plant species on the surface of the earth has been estimated to be at least 250,000 species plants (*Pimm SL, Science 1995, Lewis NG, 1994),* but so far only about 5-10% of them have been investigated for their constituent natural products *(Kinghorn AD. 2001*). With the development of chemical, biological and molecular biotechnological techniques that have become available for nature products research, there is an increasing demand for extraction and isolation of compounds from herbs, for the purpose of screening bioactive chemical molecules in new drug development, exploring therapeutic and preventative mechanism of

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herbs, as well as establishing quality control and standardization of herbs and herbal products (*Bohlin, L., Bruhn, J.G. (Eds.), 1999).*

There are many purposes and significance to carrying out pharmacological research in traditional herbal medicines:

1. To scientifically ensure the safety and reveal the efficacy of traditional herbs, and elucidate their mechanisms by a modern medicine research system.

2. To validate the efficacy of a new combination of herbal medicines or a new herbal product, and to establish their therapeutic doses, or to evaluate a new indication, or a new administration route for existing herbal products.

3. To evaluate the pharmacological effect of purified or semi-purified compounds isolated or derived from herbal medicine.

4. To discover new pharmacologically active plant materials.

Pharmacological research plays an important role in the modernization of traditional herbal medicines, because the experimental method is the most fundamental method of modern science. Information that cannot be obtained from human beings can be obtained through animal experiments.

All the substances in the universe, including plants, are composed of chemical compounds. First of all, in order to study an herbal medicine, should be isolated the major bioactive chemical components. Before the isolation of an herbal medicine, the material should first be identified by using current methods and techniques, such as all kinds of chromatography and spectrometry, to ensure that it is the right species and was collected and stored properly. Only after the biological compounds of herbs are correctly extracted, isolated, and identified, the biochemical, biological, or pharmacological studies can be performed scientifically. Isolation of chemical compounds from herbs is an important step for a systematic study of herbal medicine. It provides compounds not only for structural identification or elucidation and standards for quantitative and qualitative analysis for quality control of herbal extracts or products, but also for *in vitro* bioassay screen and *in vivo* pharmacological and toxicological study, and clinical trials.

Chemical studies on herbal medicines provide fundamental substances for further studies of biological and pharmacological activity. Chemical studies on plants, during the earlier decades of the 1800s, could only be performed on active compounds that were highly concentrated and isolated into a relatively pure form by techniques such as distillation or extraction with water, acid, base, or alcohol. Extraction and isolation should be carried out based on knowledge of the sample.

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The interest in using nature as a source of potential chemotherapeutic agents continues. Natural products and their derivatives represent more than 50% of all drugs in clinical use in the world. Data from the WHO show that 25% of modern medicines are made from plants that were first used traditionally. During the last 40 years, at least a dozen of effective drugs have been derived from plants like: morphine-analgesic from opium poppy (*Papaver somniferum*), quinine-antimalarial from cinchona bark (*Cinchona succirubra* and others), diosgenin derived from *Dioscorea spp*. -an ovulatory contraceptive agent, reserpine and other anti-hypertensive and tranquilizing alkaloids from Rauwolfia species; pilocarpine to treat glaucoma and "dry mouth'' derived from a group of South American trees (*Pilocarpus spp*.) in the Citrus family; two powerful anti-cancer agents from the Rosy Periwinkle (Catharanthus Roseus); laxative agents from Cassia sp. and as a cardiotonic agent to treat heart failure from Digitalis species. Other examples include atropine, ephedrine, warfarin, aspirin, digoxin, vinblastine vincristine, taxol, hyoscine and huperzine A.

Dioscorea villosa-Wild Yam

Secondary plant metabolites in drug discovery

The chemicals in plants can be divided into primary metabolites and secondary metabolites based on the range of molecular weight, distributions in species, and their biological roles in plants. The ubiquitous macromolecules of primary metabolism in plants, for example, polysaccharides, proteins, lipids, and nucleic acids, are called primary metabolites. They provide nutrients, and thus are essential for growth and survival. In contrast to primary metabolites, small organic compounds are often produced by a particular species, usually possessing important biological activity. They are not necessary for growth and survival, and are called secondary metabolites.

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The roles of secondary metabolites in plants are different. They serve as chemical messengers and defensive chemicals, and play significant biological and ecological roles. There is a growing interest in the study of them, as they represent a tremendous library of potentially useful leading compounds in new drug development. The secondary metabolites comprise a range of chemically diverse compounds. Based on the chemical structure features, they are classified as: alkaloids, flavonoids, coumarins, lignans, quinones, terpenoids, and so on (Rahman, A.U. 1995) (Rahman, A.U.1998).

COMPOUNDS IN PLANTS AND THEIR STRUCTURES AND PROPERTIES

Alkaloids

Alkaloids are one of the major groups of plants constituents used in medicine. Constitute a large class of nitrogen-containing secondary metabolites of plants, microbes, or mammals. Alkaloids are famous for their diverse pharmacological activities. Since the discovery of morphine from the opium poppy, *Papaver somniferum,* in 1806, more than 10,000 alkaloids have been purified and identified from natural resources. Many modern drugs are produced by naturally occurring alkaloids or their synthetic analogs.

Papaver somniferum

Biological Activities of Alkaloids

Alkaloids are a group of substances with diverse structures and a wide range of biological activities, such as antibacterial (e.g., berberine), anti-malaria (e.g., quinine), analgesia (e.g.,

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morphine), anesthesia (e.g., cocaine), anticancer (e.g., vincrinstine), antihypertention (e.g., resepine), cholinomimeric action (e.g., galatamine), relieving cough (e.g., codeine), spasmolysis (e.g., atropine), vasodilatation (e.g., vincamine), anti-arhythmia (e.g., quinidine), and anti-asthma (e.g., ephedrine). To date, over 12,000 plant-derived alkaloids have been reported. For example, the morphine alkaloids are powerful pain relievers and narcotics, and vincristine, isolated from *Vinca rosea* (now *Catharanthus roseus*), is one of the most potent anti-leukemic drugs in use today (Hostettmann, K., Lea, P.J. 1987).

Atropa belladonna

Catharanthus roseus

Flavonoids

Flavonoids are polyphenolic compounds. It is one of the most important groups of secondary plant metabolites. To date, more than 6.000 flavonoid compounds have been purified and identified, many of which exist in fruits, vegetables, and beverages. Flavonoids are responsible for many of the plant colors that dazzle us with their brilliant shades of yellow, orange, or red, and have high ecological importance in nature as color attractants to insects and birds, and aid in plant pollination (Rahman, A.U. 1995-1998).

Blueberries are a source of dietary anthocyanidins

White cauliflower *has anthoxanthin pigments*

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Biological Activities of Flavonoids

Flavonoids have recently attracted considerable interest because of their potential beneficial effects on human health. Flavonoids are most commonly known for their antioxidant activity. The capacity of flavonoids acting as antioxidants depends upon their molecular structures. Therefore, foods rich in flavonoids, such as quercetin-the most abundant dietary flavone, have been proposed to be important in ameliorating diseases such as cancer and heart disease. Components of milk thistle (*Silybum marianum*), in particular silybin and silymarin, are antihepatotoxins and they are used to reduce the effects of poisoning by fungi of the genus Amanita. It has been discovered that flavonoids also provide other important biological activities such as antibacterial, antiviral, antiallergic, antiplatelet, anti-inflammatory and antitumor activities. The antiviral function of flavonoids has been demonstrated with the HIV virus, and also with HSV-1, a herpes simplex virus.

Coumarins

Coumarins are a group that mainly exists in higher plants. Coumarins serve as growth inhibitors (anti-auxins), as well as defense compounds in plants. Coumarins are more concentrated in the families of *Apiaceae*, parsley - fennel family, *Leguminoseae* (bean family), *Rutaceae* (citrus family), and *Umbelliferae*.

Tonka bean or coumarou, one of the sources from which coumarin was first isolated as a natural product in 1820.

Biological Activities of Coumarins

Coumarins have been reported to have multi-biological activities such as anti-HIV, antitumor, antihypertension, anti-arrhythmia, anti-inflammation, anti-osteoporosis, pain relief, and prevention of asthma and antisepsis. Coumarin derivatives are used widely as anticoagulants for the treatment of excessive or undesirable blood clotting. The parent compound coumarin (M1) is found in sweet clover (*Melilotus alba*, *Leguminosae*). Coumarins are also used in sunscreen cosmetics to absorb ultraviolet (UV) rays, and in synthesis of anticancer drugs.

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Lignans

Lignans are widely occurring compounds in plants and are closely related to lignin. This class of compound is common in the plant kingdom, especially in the heartwood and leaves, and as major constituents of resinous exudates from roots and bark.

Biological Activities of Lignans

The lignans are reported to have strong antibacterial activity. Lignans belong to a class of substances known as non-steroidal phyto-oestrogens. They are structurally and functionally similar to oestradiol and related sex hormones. The lignans are capable of binding to estrogen receptors and interfering with the cancer-promoting effects of estrogen on breast tissue, thus they may inhibit the growth of breast, prostate, and colon cancer, and improve bone density. The well-known lignan podophyllotoxin is a mitotic inhibitor that was first isolated from *Podophyllum Peltatum,* with strong anti-neoplastic activity. Etoposide is a podophyllotoxin derivative now used to treat lung cancer, testicular cancer, and acute lymphocytic leukemia. Lignans are also known as good antioxidants. Lignans are found in flax seeds, pumpkin seeds, rye, soybeans, broccoli, some berries, and many traditional Chinese herbs such as *Magnolia Officinalis*, *Schizandra Chinensis,* and *Podophyllum Peltatum*.

Podophyllum peltatum

Quinones

Quinones occur as pigments in bacteria, fungi, and certain higher plants. A number of quinone derivatives (anthraquinones, phenanthraquinones, anthrones and dianthrones) are found in many species of Rheum (q.v.), Rumex and Polygonum juglone in unripe walnuts, spinulosin from the mold *Penicillium Spinuhsum*, arnebinone and arnebifuranone from *Arnebia Euchroma*,

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tanshinone derivatives from *Salvia Miltiorrhiza*, and sennoside A – D from *Rheum palmatum* (Rahman, A.U. 1995-1998).

Biological Activities of Quinones

Quinones containing phenolic hydroxyl groups usually present beautiful colors such as yellow, orange, and red. Anthraquinones are an important group of quinones with purgative actions (e.g.,sennosides), antimicrobacterial (e.g.rhein and saprorthoquinone). They also possess other biological activities, such as antitumor (e.g. emodin and juglone), inhibition of PGE 2 biosynthesis (e.g. arnebinone and arnebifuranone), and anti-cardiovascular disease (e.g. tanshinone II A). Coenzyme Q_{10} is benazoquinone derivative that is used in treatment of cardiovascular diseases, hypertension, and cancer in clinics. Vitamin K compounds like K_1 and K_2 belong to naphthoquinones. They can promote blood coagulation, and thus are used in treatment of natal bleeding.

Senna Alexandrina

<u>Terpenoids</u>

Terpenoids are isoprene oligomers $(C_5H_8)n$ and their derivatives. Terpenoids are widely distributed in nature, mainly in plants. The total number of terpenoids discovered has been over 22,000, and many of them have become important clinical drugs or have been used as leading compounds in new drug development.

Monoterpenes are a class of terpenes that consist of two isoprene units and have the molecular formula $C_{10}H_{16}$. Examples from this class include camphor, menthol, thujone, thymol, nerol, linalool, limonene, geraniol, and perillyl alcohol, found in citrus peels, mint leaves, lavender, and thyme. Among them, menthol is a useful topical pain reliever and anti-puretic; thujone is a toxic agent found in wormwood (*Artemisia absinthium*), from which the liqueur and absinthe are made; borneol is derived from pine oil and is used as a disinfectant and deodorant; camphor is used as a counterirritant, anesthetic, expectorant, and antipruritic, among many other uses.

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Lavender flower

Artemisia abrotanum

One of the most well known medicinally valuable diterpene is paclitaxel (Taxol ®). Another example of the important medicinally diterpenoids are ginkgolides discovered from *Ginkgo biloba,* which show strong bioactivity against the aggregation of platelet. Other examples include nerolidol, farnesol, and ylangene in neroli, mints, sandalwood, ginger, and German chamomile. These phytochemicals commonly have antiallergen and anti-inflammatory properties. Artemisinin is the most valuable medicinal sesquiterpenoids that was first isolated from traditional Chinese herb *Artemisia annua*, with strong anti-malaria activity.

Taxus baccata (European yew)

Triterpenoids are known as cancer chemopreventive, antiulcer, and antidiabetic agents, inhibitors of angiogenesis and eukaryotic DNA polymerases, and so on. They are the biological active components such as glycyrrhetic acid found in liquorice and the limonoids (e.g. limonin), which are highly oxidized bitter principles present in the Citrus plant family (*Rutaceae*). Arbruside E, a

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relatively nontoxic triterpene, was isolated from the extreme toxic jequerity (*Arbrus precatorius*), as a potential sugar substitute because it is 30-100 times sweeter than sucrose (Fullas F.et al.1990). Triterpenes are also components of resins and resinous exudates from plants (e.g. frankincense and myrrh); myrrh is derived from the Arabic word for bitter, a characteristic which many triterpenes display.

The triterpenes include some very important molecules, such as the steroids, which are degraded triterpenes with many important functions in mammals, notably as sex hormones. Recent chemical investigation and pharmacological studies reveal various biological roles such as anti-inflammation, anticancer, anti-cardiovascular, hypoglycemic, and antifungal activities of steroidal compounds in plants. The widely distributed lipid-soluble pigments and essential dietary required carotenoids belong to this group of chemicals. Lycopene is another bioactive carotenoid found in tomatoes and other red fruits, and has been considered a potential agent for prevention of some types of cancers.

Cardiac Glycosides

Cardiac glycosides (also called cardenolides) are named from the impact of this group of compounds on the heart. Many plants contain cardioactive or cardiac glycosides, which have a profound effect on heart rhythm. The most widely studied plant that contains these compounds is the foxglove (*Digitalis purpurea*) of the plant family *Scrophulariaceae*, which was used as long ago as the 18th century in the treatment of heart disease described as 'dropsy'. The basis of this use was well founded as this plant contains the medicinal agents digoxin and digitoxin. Cardiac glycosides are used in the treatment of cardiac failure in clinic.

Making Medicines Safer by Isolating and Modifying Plant Constituents.

A well - known example is the story of aspirin. According to records about willow leaves as an antipyretic treatment in Ebers papyrus, and following the same application of teas made from willow bark as an English herb, chemists and pharmacists successfully isolated salicin from the bark of the white willow, *Salix Alba,* between 1825 and 1826. The compound responsible for the remedy was subsequently converted to salicylic acid via hydrolysis and oxidation, and proved as such a successful antipyretic (fever reducer) that it was actively manufactured and used worldwide. Due to severe gastrointestinal toxicity, salicylic acid was converted into acetylsalicylic acid via acetylation by scientists at Bayer. It was given its trade name of aspirin in 1899. Today, aspirin is still the most widely used analgesic and antipyretic drug in the world.

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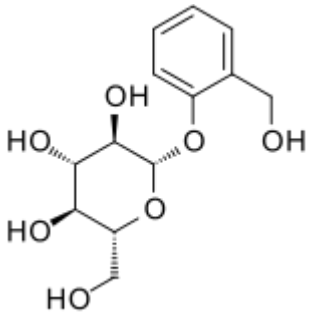
Salix Alba leaves



Salicin

However, the process of finding new drug candidates from herbs in drug development is no longer as easy as the story of aspirin. The story of taxol is that of a difficult journey of a trace compound from a plant becoming a powerful new drug. Taxol is one of the most well-known diterpenes with a very complex steroid structure and anticancer activity. The extract of the bark of Pacific yew (*Taxus Brevifolia*) was first found to be cytotoxic in a cellular assay in 1964. The active ingredient was isolated in 1966 with a very low amount, and the structure was published in 197 (*Goodman, J. and Walsh, V. 2001).* By 1969, 28 kg of crude extract had been isolated from almost 1200 kg of bark, but yielded only 10 g of pure material. By the late 1980s, its value as an anticancer drug had been determined by various clinical studies. Paclitaxel and its analog docetaxel (Taxotere ®) have been approved by U.S. FDA to treat various cancers, including non - small - cell lung cancer, small - lung cancer, ovarian cancer, breast cancer, and head and neck cancers. The research result showed that it acts to stabilize the mitotic apparatus in cells, causing them to act as normal cells rather than undergo rapid proliferation as they do in cancer.

Many people mistakenly believe that herbal products are safe. Although most herbal medicines are relatively safe in comparison with modern drugs, results from toxicological studies show that this is not always true. To a large extent, the safety of herbs depends on dosage and period of administration. It is necessary to mention that purification of some herbal extracts may increase their toxicity. This is because, while the active components are concentrated, the concentration of toxic compounds may also be increased. Sometimes, the active components are also toxic. In this case, while the therapeutic effect is enhanced, the toxicity is also increased. Examples include ephedra extract and herbal extracts from the *Aristolochia* family. Studies of aristolochic acid found in several herbs in Aristolochia family have shown its significant carcinogenic and mutagenic effects and poisoning of the kidney (*Arlt, V.M., et al. 2002) (Debelle, F.D., et al. 2008) (Schmeiser, H.H. , et al. 2009).* In TCM, processing of raw herbal materials with different methods, such as extended heating with steaming or boiling to decompose the chemical bonds of toxic ester or glycoside compounds in herbs, has been long applied to reduce the toxicity of Chinese herbs. Examples include aconitine in radix Aconiti and sennosides in rhubarb.

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Cardiac glycosides of the digitalis type (from foxglove leaf. *Digitalis Purpurea* and *D. lanata*) have a very narrow range of therapeutic dosages. Exceeding the full medicinal dose by just about 50 % can produce toxic effects. The dosage problem is compounded by the large qualitative and quantitative variations that occur in the crude plant material. Depending on its origin, the crude drug may contain a predominance of gitoxin, which is not very active when taken orally, or it may carry a high concentration of the very active compound digitoxin.

Digitalis Purpurea

Thus, isolating the active constituents from herbs with a narrow therapeutic range (Table 1) and administering the pure compounds is not simply an end in itself. This is a scientific method of medicinal plant research, by which very potent constituents can be processed into safe medicinal products (*Withering W., 1885).* The goal is not to concentrate the key active component but to obtain a pharmaceutical product that has a consistent, uniform composition. Then, processing the isolated constituent into pills, tablets, or capsules results in a product were the constituent is diluted by pharmaceutical excipients. For example, the concentration of digitoxin in a digitoxin tablet is approximately 10 times lower than in the original digitalis leaf.

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Constiuent/Drug	Plant	Action
Atropine	Belladonna leaves.& roots	Parasympatholytic
Caffeine	Coffee shrub	Analeptic, CNS stimulant
Cocaine	Coca leaves	Local anesthetic
Colchicine	Autumn crocus bulb	Gout remedy, antiinflammatory
Digoxin	Digitalis/Foxglove leaves	Cardiac remedy (positive inotropic)
Emetine	Ipecac root	Emetic
Ephedrine	Ephedra herb	Antihypotensive
Kawain	Kava root/.rhizome	Anxiolytic
Morphine	Opium poppy exudate	Analgesic
Physostigmine	Calabar bean	Cholinesterase inhibitor
Pilocarpine	Jaborandi leaves	Glaucoma remedy
Quinidine	Cinchona bark	Antiarrhythmic
Quinine	Cinchona bark	Antimalarial
Reserpine	Rauwolfia/Indian snakeroot	Antihypertensive
Salicin	Willow bark	Anti-inflammatory
Scopolamine	Datura spp./Jimson weed	Antispasmodic
Taxol®	Pacific yew bark	Cytostatic
Theophylline	Tea leaves	Bronchodilator

Table 1. Examples of plant constituents that is isolated for medicinal use. Naturally these constituents do not occur alone in plants but as fractions accompanied by related chemical compounds. The isolated substances, which generally have strong, immediate actions, are not considered phytomedicines in the strict sense (Volker Schulz, Rudolf Hansel, Mark Blumenthal, Varro Tyler Rational Phytotherapy 5th edition 2004).

With the development of the natural sciences and the use of scientific methods in medicine, in the early 19th century, herbal remedies became an object of scientific analysis. The isolation of morphine from opium (1803-1806) marked the first time that relatively modern chemical and analytic methods which were used to extract the active principle from an herb. Then, it became possible to perform pharmacological and toxicological studies on the effects of morphine in animals and humans. Various substances isolated from opium, including morphine, codeine, and papaverine, are still in therapeutic use today. In other cases, efforts have been made to improve the natural substance by enhancing its desired properties and minimizing its adverse side effects. Modifying the reserpine molecule (from the traditional Ayurvedic sedative plant Indian snakeroot, Rauvolfia Serpentina) led to mebeverine, while modifying the atropine molecule (from belladonna, Atropa Aelladonna) led to ipratropium bromide and the powerful meperidine group of analgesics. Medicinal herbs from the New World were another source of important drug substances. The leaves of the coca shrub (Erythoxylum Coca) yielded cocaine, the prototype for modern local anesthetics, while the bark of Cinchona species yielded quinine, a drug still important in the treatment of malaria as artemisinin. Resistance to this compound develops much more slowly than to synthetic antimalarial drugs. A significant portion of all currently used medications is derived, either directly or indirectly, from active principles that have been isolated from plants. Most of these substances do not occur in plants individually but in groups of compounds, such as caffeine in the group of methylxanthines, digoxin in the group of cardiac

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glycosides, and morphine in the group of opium alkaloids. These isolated compounds and groups of compounds generally produce strong, immediate effects and are in the strict sense not classified as phytomedicines (phytomedicinals) but more appropriately as plant-derived drugs. Researchers have by no means exhausted the potential of these secondary plant constituents. The sheer number of plant alkaloids that could provide the basis for the development of future remedies is estimated at more than 20,000 (*Cordell et al., 2002*).

The purpose of research on traditional herbal medicine is not only for new drug development, but also for quality control and mechanism study of herbs. Unlike screening for new drug candidates simply using one or two bioassay tests, exploration of the mechanisms of traditional herbal medicines is much more complex. The research on herbs in the past 40 years shows that they work in a way that differs from modern drugs: the effect is not from one single compound in an herb, but is a synergetic result from many components working on many targets. And researchers should not be disappointed if their results show that the most bioactive compounds screened from an herbal extract in a bioassay are popular second metabolites in plants. Examples include flavonoids, fatty acids, or amines.

Aloe Vera

Arnica montana

Plant parts used

In the context of pharmacy a botanical drug is a product that is either derived from a plant and transformed into a drug (by drying certain plant parts, or sometimes the whole plant), or obtained from a plant, but no longer retains the structure of the plant.

The following plant organs are the most important: in parentheses is the Latin name that is commonly used.

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- **Aerial parts or herb (herba):** The large majority of botanical drugs in current use are derived from leaves or aerial parts. All parts of the plant found above the ground are referred to as the aerial parts. One example is the St. John s Wort (*Hypericum Perforatum*).

- **Leaf (folia):** The leaves arise out of the stem. The leaves sometimes can be used alone or mixed with the petiole. Example of plants that are only used their leaves is the Gingko *(Gingko Biloba Common balm, Melissa officinalis L.* (*Melissae folium*).

- **Flower (flos):** Although the flowers are of great botanical importance, they are only a minor source of drugs used in phytotherapy or pharmacy. Several flowers commonly used in medicine include the Camomille flower (*Chamaemelum Nobile*), Roselle (*Hibiscus Sabdiriffa*), and the Marigold (*Calendula Officinalis*).

- **Fruit (fructus):** Fruits and seeds have yielded important phytotherapeutic products, including: Anish seeds (*Pimpinella Anisum*), the Fennel fruit (*Foeniculum Vulgare*), Serenoa repens (*Sabal fructus*) and the fruit peel of Citrus fruits (*Citrus* sp).

- **Bark (cortex**): The bark is the outer most protective layer of a tree trunk and is formed by layers of living cells just above the wood itself. There are usually high concentrations of the active ingredients in the bark e.g. Willow, Salix alba L. and Salix spp., the Quinine bark (Cinchona sp., and Cinnamon and Camphor (*Cinnamomum camphora* and *C. camphora*). Important examples of useful woods include are Rosewood, Sandalwood (*Santalum album*).

- **Root (radix):** The fleshy or woody parts of many species are used medicinally. They can be whole or sliced, peeled or unpeeled. Roots may be fibrous (Urtica Dioica nettle), solid (Glycyrrhiza Glabra of the *Leguminosae* family, Liquorice) or fleshy Devil's claw, Harpagohytum procumbens. Roots may have tuberous shape or conical, cylindrical, e.t.c.

- **Rhizome (rhizoma):** The rhizome is a woody or fleshy elongated stem that usually grows horizontally below the ground, forming leaves above the ground and roots into the ground. Medicinally important rhizomes include Kava kava (*Piper Methysticum*) and the Ginger (*Zingiber Officinalis*).

- **Bulb (bulbus):** A bulb is the fleshy structure made up of numerous layers of bulb scales, which are leaf bases. Bulbs popular for medicinal use include the Onion and Garlic (*Allium Cepa* and *A. Sativum*, respectively).

- **Seeds:** Seeds are contained in the fruit e.g. White mustard, Sinapis alba L. (*Sinapi semen*), and the seeds of the Fennel (*Foeniculum Vulgare, Apiaceae*).

- **Gums-Resins:** Gums are solids consisting of mixtures of polysaccharides. Gums flow from a damaged stem as a defense mechanism or sometimes as a protective system against the invasion of bacterial and fungal rots e.g. Gum Arabic (*Acacia Senegal*), Benjoin (*Terminalia bentzoe*) and Aloe gel (Aloe Vera gum of the *Liliaceae*). Resins are excreted from

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specialized cells or ducts in plants. E.g. *Pistachia Lentiscus* (mastiha medicinalis of Chios), and the well-known since Biblical times Frankincense (*Boswellia Sacra*) and Myrrh (*Commiphora Myrrha*) both of the *Burseraceae* family.

- **Fatty oils:** These derive from the seeds or from the fruits of plants e.g. Almond oil is used in cosmetics, and Olive oil is a useful example as is used for its own therapeutic potential but also used in liquid formulations and ointments.
- **Essential oil:** These are volatile oils extracted from plants through a process of either steam distillation or extraction. They are of considerable importance as active ingredients of medicinal plants e.g. Rosemary oi (*Rosmarinus officinalis*), Peppermint oil (*Mentha Piperita*), origanum oil (*Origanum Vulgare*), Ylang Ylang oil (*Cananga Odorata*) amongst others.

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Unit 4 Herbal preparations - Phytomedicines - Dosage & mode of administration

Plant drugs, also known as phytomedicines or phytopharmaceuticals, are plant-derived medicines that contain a chemical compound or more usually mixtures of chemical compounds that act individually or in combination on the human body to prevent disorders and to restore or maintain health. Phytomedicines are medicinal products whose pharmacologically active components contain only preparations that are made from medicinal herbs. (Gaedcke F, Steinhoff B. 2000)

The traditional ways of using medicinal plants are the forms of herbal teas, decoction, and alcoholic extracts etc. Very often these plant materials are used in a non-standardized manner. However, nowadays more and more emphasis is being put on the use of standardized materials.

Mixtures are products with medicinal properties and which contain 2 or more plants or herbs that can act individually, additively or even synergistically to restore or maintain health. In

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Traditional medicines, medicinal plants are typically used in mixtures. (The National Formulary)

Extracts are concentrated preparations of liquid, powdered or viscous forms that are ordinarily made from dried plant parts (the crude drug) by maceration or percolation. The extract ratio for herbs is typically 5:1 and the chemical compounds can then be extracted from plant material using water or organic solvents, such as alcohol (ethanol). The fluidextracts are liquid preparations that usually contain a 1:1 ratio of fluidextract to dried herb [w/w] or volume-to-weight [v/w]. Ethanol, water, or mixtures of ethanol and water are used as solvents. Solid or powdered extracts are preparations made by evaporation of the solvent used in the production process (raw extract). Essentials oils are extracted by steam distillation or by solvent extraction. (European Pharmacopeia (2002)

Medicinal teas or infusions prepared by steeping herbs in boiling water. They are called Teas because of the similarity in preparations. A typical medicinal tea consists of several herbs. In European phytotherapy, the general rule considered as sound pharmaceutical practice, is to have no more than 4-7 herbs in a blended tea (Wichtl, 1989). In some cases the efficacy of a medicinal tea is obvious. Anthranoid-containing herbs have a definite laxative action, teas with aromatic bitters stimulate the appetite, and nothing is usually better for an upset stomach than fasting and Dictamus tea or Sideritis tea. There are basically three ways to prepare tea: Decoction, Infusion and Cold maceration. (Schilcher H (1982)

a) Decoction: are preparations of hard woody parts of plants such as bark, roots, seeds and nuts. They are quite similar to the infusions and require more heat in preparing and transmitting their chemical compounds in the water. They are usually prepared by boiling 1 to 2 coffee teaspoons of the hard part of the plant for 1-10 minutes. For the preparation of the beverage, is better not to put hot water on the herb, but instead to add cold water and heat the mixture to boil. After boiling the liquid should be left for 15 minutes to rest and then can be drained (except for plants containing astringents which drain immediately after boiling). The beverage is better to be drunk in a single dose, as in this way its active elements will be kept unchanged. For the procedure, is better not to use stainless steel utensils, but to use clay, enamel, glass or similar. Also, decoctions are prepared in proportion (part of the plant in gr/gr of water) 1:10 or 1:20 for internal use and 1:5 for external use.

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b) Infusion (hot tea or beverage): The infusion is prepared by using boiling water but without boiling the herb. This means that boiling water is pour in a cup with the pharmaceutical preparation and the mixture is left covered for 15-20 minutes to rest. In this way, the active substances from delicate medicinal plant parts (usually flowers, leaves) will not evaporate or neutralize with extensive boiling. The ratio of herbal preparation and boiling water is usually 1:10 or 1:20, but for formulations with a strong effect it can arise up to 40. Usually 1 - 2 coffee teaspoons of crumbled herb are used for a glass or a cup of boiling water. More specifically 1 ounce or 25 grams of dried herbs, or 2 ounces or 50 grams of fresh aromatic herbs, should be added to 1 pint or 600 ml of boiled water. The hot beverage should be drunk immediately, but also can be stored in the refrigerator for up to 24 hours. In a chronic disease, a cup of medicinal tea should be consumed three times a day, since in an acute phase the herbal tea can be consumed 6 times a day. (Leimbeck R (1987)

c) Maceration: refers to a preparation made by adding cold water to the required amount of the drug, which is allowed to soak at room temperature for 6–8 h before it is strained.

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The meaning of the term tea gradually broadened in the English language, first referring to the dried tea leaf, then to the beverage brewed from it, and soon it was applied to all herbs from which potable infusions can be made.

A basic distinction is drawn between:

- Non-medicinal teas that are consumed for pleasure, such as black tea and its blends.
- Medicinal teas that are used either as single teas or, more commonly, as tea mixtures.

Dosage of teas

Prepared tea (irrespectively to the way of preparation) should be consumed within 24 hours of preparation; otherwise the solution could be a suitable environment for the growth of various microorganisms that will poison the tea with their toxins. Tea with unpleasant odor, blur and color change should not be drunk. The infusion after preparation should be stored in glass or enamel containers and not metallic, because the tea can react with the metal releasing harmful substances. As a rule, the infusion is stored in dark and fresh places, at room temperature or in the refrigerator. (Hiller K (1995).

The teas of medicinal plants are drained and sweetened preferably with honey, it is advised to be used warm, usually 3 glasses a day, morning fasting (before eating), noon after eating and the evening before sleep, but the following exceptions should be noted:

- Diuretic tea is taken at breakfast time; 1 liter should be consumed in one sitting if possible.
- Appetite-stimulant teas are taken about 30 min before meals.
- Teas that are used as a laxative or for sleep aid should be taken at night.

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- Peppermint and chamomile teas for an upset stomach should be taken at the patient's usual meal times or as needed.
- Diaphoretic teas such as Linden blossom tea and elderflower tea has no effect in the morning, but when taken in the afternoon as the body temperature is rising, it promptly induces profuse sweating. (Wichtl M (Hrsg) (1989)

Tincture: Tinctures are obtained by immersing an herb in an alcoholic solution for a period of 3 weeks. During this time, the active ingredients of the herb are dissolved in the alcoholic solution resulting in the tincture being formed, as alcohols are able to extract mainly the alkaloid and falconoid components of the herbs. For the preparation the most commonly used alcohol is ethanol solution (40 - 70%) such as vodka, jean or white rum. The crushed plant is placed in a glass container and covered with alcohol (1:5, 1:10 or 1:20), and left in a warm place for 21 days. Then the liquid is pressed, drained and stored in firmly closed glass containers, in dark places, as are designed for longer shelf life and storage. The tinctures of poisonous plants and those with strong action are kept separate from other formulations. Tinctures are used internally as drops diluted in water.

Also, tincture can be pouring directly into the mouth for immediate absorption, or can be drunk with a small amount of water or juice. If the alcohol, smell is not preferable the appropriate dose of the tincture can be dissolved in about half a glass of warm water and the alcohol will evaporate in just a little while. Generally tinctures are much more effective than infusions and infusions.

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Syrups: is a viscous solution of 66% pure sugar in water (e.g. plain syrup) or other liquids (such as wine, etc.). It is offered as a beverage or as a medicine depending on other flavoring or therapeutic substances that contains. Medicinal syrups contain extracts or infusions of the medicinal plants, which are added to the basic syrup prepared with raw sugar or honey, as it has softening properties. The unpleasant taste of some herbs is covered by the sweet taste, making the use easier for children and persons who mind the bitter and intense flavors. Furthermore the sugar content of syrups is essential for extending their shelf life. Microorganisms cannot proliferate in saturated sugar solutions, because highly concentrated solutions deprive the microbes of the water necessary for their development. (Hartling Ch. (1983)

Juice: Fresh juice is prepared by freshly harvested plant parts, which are macerated in water and pressed. For this purpose, fresh plants and fresh fruit are compressed in a mixer machine and then squeezed to juice. The juice is stored in dark glass containers in the refrigerator for one day to settle down and then should be filtered. The product can be pasteurized to extend their shelf life. Some common sources of plant juices are birch leaves, nettle, watercress, St. John's worth, garlic, dandelion, lemon balm, radish, and horsetail. Juices are taken at a fixed dose.

Powder: The powder is prepared by grinding thoroughly the dried plant matter or the combination of medicinal plants. For this purpose, the dried plants are crushed and then pulverized by using a mortar, or chopping machine. The final product sold in sachets, is used for the preparation of beverages and there is no need for filtering. It is also possible the powder to be taken directly on the tongue or to be mixed with food such as soup or yogurt.

Poultice-Compass (compress). It's a moist mixture that is applied directly to the body, where is necessary. For the preparation, fresh or dried herbs are used as a poultice. When fresh leaves, stems or roots, are used should be breached or crushed before. If dried herbs are used, a little hot water can be added to the herbs, which are either finely chopped or powdered. For the therapeutic procedure first on the crushed plants powder, are added a few drops of boiling water and then stir until pasta is formed. Then, the mixture is spread on gauze and placed externally on

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the painful part wrapped with fine net gauze. The pouch is hold in place with a bandage and kept warm.

Ointment: Ointments are semi-solid preparations aimed at external application. They usually contain medicinal substances in a suitable carrier substance (watery or oily solvents). Ointment is a viscous substance that often spreads to a surface. Ointments are mixtures that are used for therapeutic purposes, for massage to relieve muscle pain, to stimulate the muscles and body joints. They are prepared by warming or simply mixing vegetable oils with herbs and alcohol tinctures. The easiest way to make an ointment is to use petroleum jelly or natural beeswax and mix it with appropriate herbs or herbal tinctures or essential oils. Ointments can be easily absorbed by the skin and transferred to the affected area of the body, the therapeutic ingredients they contain. They are used externally and kept in a fresh and dark place.

Medicinal Oils (Pharmaceutical Plant Infusions in Oil): are fatty oils or liquid waxes containing solutions or extracts of medicinal plants. They are prepared when the herb is left with oil (usually olive or sunflower oil), for a few days in the sun. Then the active ingredients of medicinal plants are extracted in the oil. Medicinal oils are used both internally and externally usually as massage oils, especially in aromatherapy. Examples of medicinal oils prepared by extraction of plant material are St. John's worth oil and garlic oil maceration. (Bauer KH, Fromming KH, Fiihrer C (1989)

Medicinal essences: is a solution of a volatile substance in alcohol or in mixture of water and alcohol. They are prepared either by dissolving the volatile oil in alcohol, or by distillation. Medicinal spirits are produced by mixing aromatic herbs with alcohols, and allowed to stand until

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the volatile components of the plant have dissolved out of the herbal tissue. Finally, the active ingredients are recovered by distillation. A known medicinal essence for example is peppermint Spirit made by peppermint oil.

Capsules: are usually small soft or hard drug containers normally made from gelatin. They can contain medicinal products or extracts in a predetermined dose, protected from air, light and moisture. Hard gelatin capsules consist of a two cylindrical shells, which are fitted together when the drug is inserted. Soft gelatin capsules present a gelatin shell, spherical, oval, or oblong, in shape, enclosing semisolid or liquid contents that must be free of water (e. g., oily herbal extracts). Enteric-coated capsules or tablets that release the drug substance after entering the bowel protect the drug substance from deactivation or decomposition by gastric juices. They should never be taken during or after meals, but approximately 1 hour before meals.

Tablets: are made by compression of powdered active material and suitable inert excipient, and other additives, improving color, or flavor. There are two types or tablets—uncoated and coated tablets. The uncoated ones can contain disintegrators to ensure that the tablet rapidly dissolves when placed in water. Coated tablets are compressed tablets covered with a coating of sugar, dyes, fat, wax, and/or protein, protecting the medicinal core, against external influences such as light, moisture, and mechanical stresses. When used the medication release can be controlled or delayed (enteric-coated tablets, controlled-release tablets). (Hefendehl FW (1984)

Lozenges: (pastilles) are designed to release the active ingredients slowly into the oral cavity while sucked or chewed. For the purpose the medicament is absorbed on a base, which is composed of sucrose (usually more than 90 %), acacia (about 7 %), gelatin, and water (e.g. *Echinacea lozenges*). They can have the appearance of a tablet (round, oblong, etc.) but differ from tablets in that they are not made by compression but are cut from pliable mass of varying composition.

Suppositories: are tablet-like products usually oblong to oval in shape that is designated to insert into the rectum, vagina or urethra and melt there. Herbal products are rarely used in this form but aromatherapy suppositories, are produces from essential oils.

Modes of administration

- **Oral:** decoctions, infusions, tinctures, syrups and tablets are taken orally and sometimes sublingually.
- **Nasal (Smoking, snuffing or steaming):** Essential oils suspended in hot liquids or powdered materials may be snuffed so that the active compounds are absorbed through the mucosa.
- **Skin:** Lotions, oils, ointments or creams containing extracts of medicinal plants are applied directly to the skin, where the active compound is absorbed.

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- **Rectal:** The liquid preparations can be administered as enemas and the solid as suppositories. The active compounds are absorbed by the mucous membrane of the rectum.
- **Bathing:** Herbs or herbal extracts may be added to bath water.
- **Sub-cutaneous or intramuscular injections:** Some phytomedicines (often pure chemical entities derived from medicinal plants) are injected into the bloodstream.

DOSOMETRIC GUIDE FOR THE PREPARATION OF PHYTOMEDICINES

For the preparation of phytomedicines in domestic conditions the following ratios are given:

- One pinch (as much as the three fingers get dust) contains 0.5 - 1 g crushed preparation.
- One teaspoon full, filled with crushed preparation contains 1.5-2g of medicinal plants.
- A spoon full, filled with crushed preparation contains about 5 g of combination of medicinal plants.
- A spoon full filled, contains about 4 g of flowers or leaves.
- A spoon full filled contains about 8g of roots or wood.
- A spoon full filled contains about 7,5 g of seeds or stalks.

- **Dosage proportions for liquid tea are:**
  - One teaspoon full contains 5 g of tea (liquid).
  - A spoon full filled contains 15 g of tea (liquid).
  - A cup of coffee full contains 50 g of tea (liquid).
  - A cup of tea full contains 100 g of tea (liquid).
  - A full glass of water contains 150-200 g of tea (liquid).

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- **Dosage proportions for the preparation of infusions and beverages:**

  The most common ratios are:

  JJJ. 1-3 teaspoons or 1 spoon full filled with a medicinal preparation for a glass of water, or

  KKK. 6 teaspoons full filled with crushed preparation in 1 lit of water.

Typical doses of liquid tea therapy are:

- Adults take about 3 glasses of tea per day (morning before eating, lunch after eating and evening before bedtime).
- Children aged 6-14 take ½ of the adult dose.
- Children aged 2 to 6 take 1/4 of the adult dose.
- Children aged 0-2 years receive 1/8 of the adult doses.

Duration of the treatment with herbal medicinal products.

Usually the therapeutic effect of medicinal plants is slow, so treatment should be continued for 2 to 4 weeks. When prolonged use is required, then it is recommended after 1.5-2 months, the treatment to be stopped for 1-2 weeks, and restarted. The action of medicinal plants is always effective and without any side effects, which is mainly due to the synergy of the medicinal substances they contain. Often the failure of herbal therapy is due to the omission of the above rule.

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Unit 5: Limitations in medicinal use, Efficacy & Safety

Contraindications, Side effect, toxicity and interactions with other drugs.

Clinical efficacy of phytomedicines

Through ages many traditional herbs have been used by humans to treat or prevent diseases. Recently, there is an increasing interest in alternative or herbal medicine use, and this leads to an also increasing concern about the safety of medicinal plants application. Many people mistakenly believe that herbal products are safe. Although most herbal medicines are relatively safe in comparison with modern drugs, results from toxicological studies show that this is not always true. (Claude, J.R. and Claude, N. 2004)

Patient Expectations

A well-known German institute of demographic research conducts regular opinion surveys to explore the attitudes of the German public toward natural remedies (IFD Survey 7016, 2002). In 2002 the institute surveyed a representative cross section of 2172 people ranging from 16 to 90 years of age. Thirty-five percent of the responders considered the prescription of natural remedies to be “very important,” 41% rated it as “important,” and 13% rated it as “not very important”. This survey demonstrates the generally high regard in which phytomedicines are held by the German public. When asked whether these products were effective, 4% said no, 38% had no opinion, and 54% were convinced that herbal remedies are effective. Most of the responders believed, however, that natural remedies worked differently from synthetic drugs.

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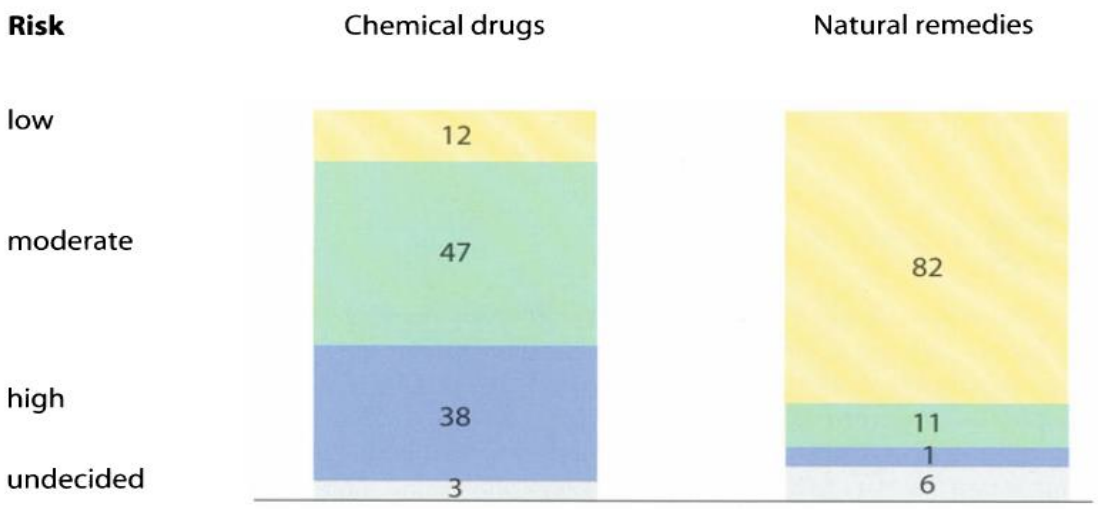

Figure 1. Results of a representative survey of 2172 German citizens on the risks of synthetic drugs versus natural remedies. The latter are believed to have a very large therapeutic range and a high safety margin (IFD Survey 7016, 2002).

Opinions on product safety were even more revealing: 82% of those surveyed rated the risk of treatment with natural remedies as ‘‘low,” while 84% rated the risks of synthetic drugs as “moderate to high” (Fig. 1). Devotees and opponents of natural remedies held about this opinion equally. Thus, the demand of many patients, especially the elderly, for herbal remedies is rooted partly in the emotional perception, that natural products are gentler and safer than chemical products. Beyond some very concrete evidence for certain active plant constituents, even a consultation with their doctor would be unlikely to shake patients from this preconceived notion. A more reasonable approach is to base the prescription and recommendation of herbal remedies, on the way in which patients actually use these products, which presupposes that the products generally have a broad, safe therapeutic range. (Ernst E, Pittler MH, Stevinson C, White A 2001).

Potent plant-based medicines, such as preparations made from cardiac glycoside-containing plant parts like the foxglove (*Digitalis spp*.), tropane alkaloids from belladonna (*Atropa belladonna*), or colchicine from the autumn crocus (*Colchicum autumnale*) do not meet these safety criteria, and so it is best not to use the term “herbal” or “botanical” when referring to these products. For these indications it is better to prescribe pure “chemical” compounds such as digitalis glycoside, atropine, colchicine, etc. (Anderson, H. and Spliid, H. (2000)

At the same time, confidence on a remedy is the best foundation for its successful use in selected therapeutic applications. Once the treatment decision has been made, it is better to encourage patients’ confidence and their self-healing powers by educating them about the selected medication (and any associated risks!) in positive terms. The basic background information about a synthetic drug mainly involves its chemical structure, which is of little interest to most patients.

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But with an herbal medication, the patient can be shown a picture of the medicinal plant and told its history, providing an excellent context for the treatment interview.

Doctors, who recommend plant-derived medicines, should become familiar with the plants from which they are derived. They should know about their botanical characteristics, the plant parts that are used medicinally, and their traditional therapeutic uses.

SAFETY PHARMACOLOGY

The criteria of safety for herbal medicine should be the same as for chemical drugs. Therefore, it is necessary to give a brief introduction about the guidance and regulation of the safety of drugs. Unfortunately, many countries have no official regulations for quality control on the manufacturing or labeling claims of herbal remedies and dietary supplements.

When performing safety pharmacological studies on herbal materials, two issues must be considered:

a) The concentration of active or toxic compounds and other chemicals varies in different parts of the plant, for different harvest seasons, and when extracted with different methods.

b) The geography, soil composition and its contaminants, and year-to-year variations in soil acidity, water, weather conditions, and other growth factors all have significant effects on the therapeutic properties and safety of the medicinal plants.

The guideline ICH S7A has been adopted by the regulatory authorities of Europe, the United States, and Japan, and referenced by the relevant departments of many other countries. A number of important issues relating to safety pharmacology as it is currently defined by regulatory agencies are described in this section. According to this guideline, pharmacological studies can be divided into three categories: primary pharmacodynamic studies, secondary pharmacodynamic studies, and safety pharmacology studies. The specific objectives of safety pharmacology studies include:

- to identify undesirable pharmacodynamic properties of a substance that may have relevance to human safety.
- to evaluate adverse pharmacodynamic and/or pathophysiological effects of a substance observed in toxicology and/or clinical studies.
- to investigate the mechanism of the adverse pharmacodynamic effects observed and/or suspected.

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A successful clinical trial depends on accurate scientific design. The trial of an herbal product is more complicated due to the complex composition and difficult quality control of the components in comparison to the trial for a single chemical drug.

Similar to conventional drugs, clinical evidence on herbal medicine comes primarily from case reports, uncontrolled clinical trials and randomized controlled trials (RCTs). Randomized controlled trials, especially if double blind, are considered as the most rigorous system for evaluating the efficacy of drugs. Unfortunately, many of the reported results of clinical studies on herbal medicine so far are not reliable due to more or less unscientific design. Quite often, the results of clinical trial for one herbal medicine obtained by different research groups vary significantly. However, it may happen that diverse, even rigorous, clinical trials do not always yield the same conclusion. Hence, only the totality of the available data, which can be collected in a systematic review, offers the most reliable evidence of efficacy. Systematic reviews and meta-analyses are at the top of the pyramid of the clinical evidence. (Valentin, J.P. and Hammond, T.J. 2008)

Terminology of: Contraindications, Side effect, Toxicity and Interactions with other drugs.

TERM	MEANING
Contraindications	A remedy's contraindications inform you when it is unsuitable to be used. Contraindication makes a particular treatment or procedure inadvisable. A contraindication is a condition or factor that serves as a reason to withhold a certain medical treatment due to the harm that it would cause the patient.
Cautions	A caution means that it is possible the remedy may not be recommended in some circumstances, but it is not as strong as a contraindication. Cautions include the fact that some herbs may irritate the stomach. It is up to the individual to decide if they mind the possibility of this side effect.
Side Effects	Side effects of a medicine are effects, which may occur to the body due to taking the medicine, in addition to the desired effect. Side effects may include effects that are seen in most people taking that medicine, or side effects that may have occurred only once!
Interactions	An interaction occurs when the administration of one medication (whether herbal or not) affects the action of another medication. These interactions can occur either by one medication directly acting on the other, or through their effects on the human body.

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Up to now, only the most popularly used herbs, very few have been well known with respect to pharmacological effects on animals. In the past 3 years, a discrete number of systematic reviews/meta-analyses concerning the clinical efficacy of herbal extracts used mainly in western countries have been published. Furthermore, other recently published systematic reviews provided evidence of efficacy for black cohosh (*Cimicifuga racemosa*) in menopausal women, Dang Shen (*Codonopsis pilosula*) for chronic obstructive pulmonary disease and some botanical preparations for dermatological conditions but failed to show clear beneficial effects for pomegranate (*Punica granatum*) in the prevention and treatment of cardiovascular diseases, for Hibiscus sabdariffa in lowering serum lipids and for saw palmetto (Serenoa repens) in patients with benign prostatic hyperplasia. (Saad, B., et al. 2006)

Adverse effects of the use of herbal medicines

There are general and herb-specific concerns regarding herbs and their potential to produce adverse effects. The assumption that 'natural' equals to 'safe' is obviously deceptive. Natural products contain pharmacologically active molecules potentially able to cause danger to human health. Classical examples of toxicity associated with herbal use include the hepatotoxicity due to pyrrolizidine alkaloids-containing plants, Aconitum poisoning due to Aconitum alkaloids, which are highly toxic cardiotoxins and neurotoxins and the severe – in some cases lethal – cardiovascular side effects associated with Ephedra sinica, whose sales have been prohibited by the Food and Drug Administration since 2004. (Dunnick, J.K., et al. 2007)

Not many people realize that when herbs are extracted and purified, the toxicity might be increased along with the increase in therapeutic efficacy. Here, take the rhizome of Angelica Pubescens f. biserrata, a Chinese herb used for arthritis with anti-inflammatory activity. When this herb was extracted and then fractionated with petroleum benzene, chloroform, ethyl acetate and, n-butenol, respectively, into several fractions and given to a mouse with ear swelling, induced by mixed inflammatory solution for pharmacological study in our lab, the petroleum benzene fraction showed not only the highest potential inhibition on ear swelling, but also the highest toxicity. Three out of 10 mice died after administration.

Accidental herbal adverse effects may occur as a result of collecting wrong raw materials and inappropriate preparation due to a lack of knowledge on active and toxic components in the materials and pharmaceutical quality control, or overdosed or over-lasting administration due to the mistaken belief that herbal remedies are harmless. Unfortunately, many countries have no official regulations for quality control on the manufacturing or labeling claims of herbal remedies and dietary supplements. (Colson, C.R. and De Broe, M.E. 2005)

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materials and inappropriate preparation due to a lack of knowledge on active and toxic components in the materials and pharmaceutical quality control, or overdosed or over-lasting administration due to the mistaken belief that herbal remedies are harmless. Any conventional medication can have side effects. These side effects are described and reported after drug trials and research studies have been conducted. Side effects are further reported and evaluated after the marketing of the medication.

Herb drugs interactions

In the last 20 years, multiple case reports, case series and pharmacokinetic trials have clearly highlighted that herbal medicines can interact with prescribed medicines.

The drug interactions that have reported are from:

I. human studies – published research done on healthy individuals human clinical studies – published research from therapeutic trials on patients being treated for a condition

II. empirical – traditional knowledge or consensus based on experience from extensive use human case reports – published individual responses to using herbal products human case series – published responses from several patients using a preparation of the same herb

III. in animals (types listed) – laboratory tests using live animals (*in vivo*) and various modes of administering the herb or herbal component(s)

   a. *ex vivo* –laboratory interaction finding on cells, tissue, or organs from animals or humans who were administered the herbal agent (as contrasted to *in vivo* when studies are done on the living organisms themselves)

   b. *in vitro* –laboratory interaction finding with cell or tissue samples from animals or humans speculative – using pharmacological evidence from *in vitro* research, animal studies, or human studies to infer probable or potential interactions or effects in humans

IV. [dubious interactions], as shown in brackets with the drugs underlined rather than in bold type, are based on preliminary findings, speculation, inaccurate information, and/or false assumptions that have been contradicted by established evidence.

From a mechanistic viewpoint, interactions can have either a pharmacokinetic and pharmacodynamic basis or both, and herbal medicines may interact with prescribed drugs at the intestine, liver, kidneys and targets of action. Most of herbal remedies involved in drug interactions have been shown to up-regulate or down-regulate cytochrome P450s and/or P-glycoprotein, but the roles of drug transporters including the organic anion and cation transporters and the nuclear pregnane-X receptor are now becoming increasingly apparent.

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(Claude J. and Claude, N. (2004). For example the herb St John's Wort (*Hypericum Perforatum*) causes one of the processes in the liver (the P450 enzyme system) to be more efficient. While this is not normally considered as an issue in a healthy person not taking any medication, it does cause some drugs that are metabolized by the liver to be removed from the body more quickly - meaning that they would no longer be as effective. This includes the contraceptive pill!

The use also of *Hypericum perforatum* with immunosuppressive (e.g. cyclosporine), antiretroviral (e.g. indinavir and nevirapine), cardiac (e.g. digoxin) or antineoplastic (e.g. irinotecan and imatinib) drugs may result in reduced plasma concentration of the pre- scribed drug and, hence, reduced efficacy, and patients with cardiovascular conditions are therefore greatly at risk, as are those taking immunosuppressant drugs. The anticoagulant warfarin is the most common drug involved in all kinds of drug interactions, including herbal, and St John's wort the most common herb involved in all herb–drug interactions, so caution should be used whenever these are used in combination with other drugs. (Shayne, C. 2003)

Use of herbal remedies during pregnancy and by breastfeeding women

Complementary and alternative therapies, including herbal medicines, are widely used during the third trimester of pregnancy, and pregnant women tend to believe that such treatments are safer than prescribed drugs. According to a British survey, 57.8% of pregnant women used one or more herbal remedies, the most common being ginger (*Zingiber officinale*), cranberry (*Vaccinium macrocarpon*), raspberry (*Rubus ideaus*) leaf, chamomile (*Matricaria recutita*), peppermint (*Mentha piperita*) and echinacea (*Echinacea* spp.). Herbal medicines are also used by breastfeeding women. According to recent systematic reviews, herbal medicines have been evaluated in survey studies, safety studies and efficacy studies. However, because of the poor methodological quality of the clinical data, there is little evidence supporting their efficacy and safety among the lactating women.

Use of herbal remedies in the paediatric and adolescent population

Herbal remedies are popular in paediatric and adolescent populations. For example, in 2014, an estimated 5.8% of German children and adolescents between the ages of 0 and 17 years and 3.9% among children 0–17 years old in the USA used herbal remedies (CDC National Health Statistics Report, 2007). It is therefore crucial to define their efficacy and possible risks in children. Main adverse events reported include neurological (35% seizures, central nervous system depression and lethargy), cardiovascular (10% hypertension and blood concerns) and gastrointestinal (14% nausea, vomiting and diarrhoea) systems as well as liver toxicity and jaundice (11%). Also many of the case reports were poorly documented. Among the best-documented case reports, fleeceflower (*Polygonum multiflorum*) root and kava (*Piper methysticum*) were associated with acute hepatitis, blue cohosh (*Caulophyllum thalictroides*) with

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neonatal congestive heart failure and Siberian ginseng (*Eleutherococcus senticosus*) with neonatal hirsutism. The accidental ingestion of tea tree (*Melaleuca alternifolia*) oil was associated with ataxia and unresponsiveness. **(**Colson, C.R. and De Broe, M.E. 2005)

Use of herbal remedies in the geriatric population

Many elderly subjects use herbal products for the relief of symptoms or medical diseases that are believed to be not easily treated by conventional prescribed remedies. The majority of the studies were performed in the USA. The most commonly used herbs were gingko (*Ginkgo biloba*) and garlic (*Allium sativum*), and both of them have the potential to interact with prescribed drugs, especially in patients under anticoagulants. Other herbal remedies frequently used by elderly subjects include ginseng (*Panax ginseng*), Aloe vera, chamomile (*Matricaria recutita*), ginger (*Zingiber officinale*) and spearmint (*Mentha spicata*).

General Considerations

Assessing the safety and efficacy of herbal medicines remains problematic, with inadequate or inconsistent methods being used, and the issues have been discussed here using examples of recent systematic reviews and meta-analyses. It is apparent that generalizations about the efficacy and safety of herbal remedies are not advisable, even though many have been effectively used for diseases and as functional foods, especially in Asian countries. Certain herbal medicines have been shown to be efficacious (e.g. ginger for preventing and treating nausea and vomiting), whereas others have been shown to be effective for a specific indication but not others (e.g. ginseng for improving glucose metabolism, but not for Alzheimer's disease). Several herbs have been associated with serious adverse events, including herb–drug interactions (St John's wort in particular). However, many clinical studies have been performed without sufficient rigor and recorded detail; therefore, the findings must be interpreted cautiously. (Porsolt, R.D., et al. 2002)

Clearly, more high quality research in this field is needed to firmly establish the efficacy and/or safety of many herbal products. Most importantly, herbal research should be conducted with the same meticulous care as any other medical research, and as part of this, all herbal products administered to patients should ideally be chemically characterized, standardized if possible, and of known quality. For many herbs, mono- graphs of pharmacopoeial standards are available and contain validated general methods for testing for microbiological and other forms of contamination. Furthermore, all clinical studies should conform to the standards reported in the Consolidated Standards of Reporting Trials and Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines. (Sullivan, A.T. and Kinter, L.B. 1995)

Information about drug components: interactions, usage in pregnancy or while breastfeeding for pediatric patients, and dosing limits, are outlined and made available in standard references for doctors treating patients. Furthermore, the formulations of the drugs must satisfy strict quality

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control standards to ensure conformity. In contrast to conventional medications, unconventional treatments (such as herbs) have little or no actual scientific basis, so doctors to be able to guide their patients regarding proper usage or potential toxicity. There are no standardized references and most of the herbal formulations have not been analyzed, are not uniform, and have not been quality controlled. One batch can be very different from the next one. Moreover, even if a given herb has a known toxicity, the manufacturer may or may not warn consumers. Manufacturers are not required to alert consumers to known dangers. Doctors, who recommend plant-derived medicines, should become familiar with the plants from which they are derived. They should know about their botanical characteristics, the plant parts that are used medicinally, and their traditional therapeutic uses.

In general, the key thing to consider is that if you are deciding to use herbal medication by yourself, then you are responsible for your own healthcare. The following list indicates when you should be especially careful when using herbal remedies.

- Where the patient is young (i.e. from infant to approximately 11 years old).
- If you are taking any prescription medicines.
- If you are treating a significant health complaint.
- If you are normally sensitive or allergic to substances.
- If you do not have a diagnosis from a medical professional.
- Pregnancy: During pregnancy and breastfeeding professional advice is essential.

Examples of Cautions and Contraindications of Some Herbs

(Specific information on each plant is given in TBP project's online encyclopedia)

St John's Wort (*Hypericum perforatum*)

Contraindications: Pregnancy due to its ability to stimulate the uterus, and if breastfeeding. If you are taking conventional anti-depressants or you are suffering from severe depression.

Cautions: It is recommended that foods containing tyramine, such as cheese, wine, yeast and beer, are avoided whilst taking St. John's Wort. If you are HIV positive and receiving treatment it is recommended that you consult a qualified medical practitioner before taking St. John's Wort.

Side-effects: Some individuals with fair skin have experienced an increased sensitivity to the sun whilst taking St. John's Wort. It is therefore recommended that you avoid excessive amounts of

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sun exposure and wear a good quality sunscreen (as you should do anyway!) if you anticipate being exposed to the sun for long periods of time.

Interactions: St John's Wort affects the function of a group of liver enzymes termed the Cytochrome P450 enzymes, and can therefore affect the metabolism of a variety of drugs by either clearing them more quickly or slowly from the body. This is of particular importance if you are taking the contraceptive pill, anti-coagulants (such as warfarin), digoxin, cyclosporine, theophylline tablets for asthma or chronic bronchitis, statin drugs, protease inhibitors, e.g. Indinavir, or medication for epilepsy or migraines as the herb may stop them from acting properly.

Raspberry Leaf (*Rubus idaeus*)

Contraindications: Raspberry leaf is contraindicated in pregnancy, if the pregnant lady has a history of early labour.

Cautions: Raspberry leaf tea should be taken as a tea only during the last trimester of pregnancy (Week 28-36 and onwards).

Gingko Biloba

Contraindications: Ginko Biloba is contraindicated if you are undergoing surgery. You should stop taking the herb at least 7 days prior to any surgery.

Chamomile drug interactions

Allergic reactions can occur, particularly in persons allergic to ragweed. Reported reactions include abdominal cramps, tongue thickness, tightness in the throat, and swelling of the lips, throat and eyes, itching all over the body, inflammation, and blockage of the breathing passages. Close monitoring is recommended for patients who are taking medications to prevent blood clotting (anticoagulants).

Echinacea drug interactions

The most common side effect is an unpleasant taste. Echinacea can cause liver toxicity. It should be avoided in combination with other medications that can affect the liver.

Garlic Drug interactions

Allergic reactions, skin inflammation, and stomach upset have been reported. Bad breath is a notorious accompaniment. Studies in rats have shown decreases in male rats' ability to make sperm cells. Garlic may decrease normal blood clotting and should be used with caution in patients taking medications to prevent blood clotting (anticoagulants).

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Unit 6 Improvement of everyday life and general health status: Alternative pharmaceutical products, and best practice for a better life.

In the contemporary world, living habits can drive to body toxication. External body toxication is caused by food and water, through lungs, skin, and other way, as parenteral, ocular, etc. Internal toxication is caused by disturbed cell metabolism. Detoxication or drainage is the process through which, one or more organs of the body are mobilized or stimulated for the elimination of toxins. According to the Russian academic Levin, toxin is any substance found in the body at the wrong

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place, time or quantity. It may be a derivative component of the organism's biochemical laboratory or an external substance originating from the external environment.

Symptoms of toxicosis are bowel dysfunction, metallic or bitter taste, fatigue, poor mood, headache, hair loss, obesity, cellulitis, edema, skin problems. It is understandable that all diseases are burdened when there is toxicosis.

Plants can help us improve our daily life. Before we talk about it, we need to deal with the meaning of detoxication.

The main causes of the poisoning.

1. Bad eating habits.

Our diet needs to be balanced in order to get all essential nutritional elements. Any excess in diet can lead to toxicosis. This means that even nutrients, such as vitamins, can be converted into toxins if we take them in bigger dose or for a very long time. A typical example of vitamin A hypervitaminosis was first described in explorers of the Poles. They ate large quantities of pollen and suffered acute vitamin A poisoning. Even excessive amounts of water can cause toxicity that occurs with low sodium content in the blood, having very unpleasant health consequences. Water poisoning is very common in endurance sports and power sports, lasting longer than 4 hours.

Another important factor is the way food is grown. It is understandable that when someone consumes organically cultivated food, takes fewer chemicals than those eating foods that have been cultivated by using fertilizers, pesticides, etc.

2. Intense stress.

It is well known that in order for the body to function properly, the functioning of the sympathetic and parasympathetic system must be balanced. In chronic stress, there is an increased chronic prevalence of the sympathetic and which results in metabolic dysfunction and toxicosis.

3. Environmental contamination.

A great risk for our body is the substances that have no biological role, such as arsenic, lead, other heavy metals, dioxins, etc. They are imported from the external environment into the body either through inhalation, via food and water consumption, or by using detergents, for household applications, etc. One category of such substances is heavy metals. Some heavy metals (such as copper, selenium, zinc) biologically active are used as catalysts of human body metabolic reactions. But at higher concentrations they are also toxic to the organism (Karamperopoulos D., 2011).

4. Chemical substances imported into the body, such as strong chemotherapy, vaccines, etc.

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It is well known that during many medical therapies large amounts of chemicals are introduced into the body that can cause various side effects.

5. Lack of physical activity.

Physical exercise has positive effect on balancing the function of nervous system, both sympathetic and parasympathetic, and this result in better functioning of the excretory organs of human body and the improvement of overall metabolic function.

6. Disorders of mind and emotion.

Disturbances in intellect and emotion can cause disorder on the function of the nervous system, resulting in chronic sympathetic dysfunction and its side effects.

KEY INFORMATION FOR DETOXIFICATION

Metabolism and Excretion of Toxins.

Once a substance enters the body, it will undergo the natural processes of metabolism and excretion-elimination. For this case, various systems of the organism work together as part of human's body excretory system.

During metabolism, a chemical substance is converted into one that is less toxic, so to be eliminated easily or faster from the body (Parsons M.E, Ganellin C.R, 2006). Under certain conditions toxins and heavy metals are very difficult to metabolize and then they rise up to toxic concentrations. However, in the human body there are mechanisms for the elimination of substances that threaten the health of the body.

Liver is the primary organ of metabolism. As part of the excretory system, it serves to degrade several substances. This is performed by its enzymes that metabolize the substances found in the blood (Lesch J.E, 2007). It is important because these mechanisms cannot act on toxins and heavy metals stored in tissues. These toxins and heavy metals must first leave the tissues and reach the blood. After toxins and heavy metals metabolize into less toxic or more easily eliminated forms, they are excreted. The human excretory system consists of five major organs. These are the lymphatic system, the kidneys, the intestine, the lungs and the skin. There are other functions involved in the elimination of toxins such as saliva, cerebrospinal fluid, period in women, semen in men and breast milk. If any of the five major organ systems are under-functioning, all the rest are burdened and the disposal of waste products of the metabolism becomes more difficult. (Dai, N., et al. 2007)

The *lymphatic* system: The lymph collects intracellular waste and brings it to the blood. Then, they are processed by the liver and filtered by the kidneys. Lymph circulation is dependent on the

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movement of the limbs and the action of the muscles. Consequently, exercise greatly benefits the lymph. Studies on the function of the lymphatic system shows, the lymph system to be the basic system for detoxification because if it does not function, all other relevant systems are not functioning properly (Aldrich T.B., 1905).

The main burden of excretion is taken by the kidneys and the intestine (along with the toxins that are excreted from the bile). The *kidneys* are the most sophisticated excretory organs and offer an extra capacity for blood filtration and the elimination of toxic substances and unnecessary fluids. They are the so-called urinary system, which includes in addition the two ureters, the urinary bladder and the urethra. The main function of the kidneys is to filter the blood and for this reason each kidney is directly connected to a pair of blood vessels. The main metabolic products excreted by the kidneys are water, salts and urea. (Debelle , F.D. , et al. 2008)

The function of the *intestines* is directly related to the elimination of food residues. Apart from the elimination of the waste materials created by the digestion function, it functions as an excretory organ of substances that are excreted in the gut as well, from bile through bile vessels. Proper bowel function is associated with body toxicosis also for another reason. When intestinal function is problematic, toxins enter through the intestinal wall into the blood and the lymph, and are deposited in the tissues. In this case its own toxic waste detoxifies the body. Proper bowel function is directly related to the immune system, this is why the intestine is considered as the "governor" of the immune.

The function of the *lungs* is related to the removal of carbon dioxide (CO2) produced during cellular respiration. Carbon dioxide diffuses from the cells to the bloodstream and reaches the lungs, where it expels on exhale with a small amount of water vapor. Obviously when a person does not breathe right for years, this will have consequences on a cellular level (Ward J.W., 2007). The lungs are important in eliminating toxins produced in the organism as breathing gases, such as alcohol and some chemicals from cigarette smoke. This is why the breath of smokers has a smell.

The *skin* is involved in the elimination of toxins mainly by sweating. Sweat is a mixture of three metabolic by-products: water, salts and urea, but at concentrations different from those found in the urine. Elimination of toxins can also be done through hair. When toxicosis is intense and the body cannot cope, eruptions appear on the skin. All skin rashes are excretion of body toxins and that is why we need to be very careful in dealing with them (Wermut C.G., 2008).

Summarizing: The main responsibility of toxin collection and cell purification belongs to the lymphatic system. The kidneys and the intestine, along with the toxins excreted from the bile, undertake the main burden of excretion. The lungs contribute significantly when breathing, like

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alcohol and some chemicals from cigarette smoke, can excrete the toxin. The skin is mainly involved through sweat, and if all the mechanisms are not enough, a rash occurs.

The excretory system plays the most important role in maintaining homeostasis. If the body could not dispose of metabolic waste products, they would soon reach high concentrations that can be life threatening. It is important to be able to recognize which of the symptoms are due to excretory function, so that we do not apply methods of suppression, because in this case there will be established a general disorder inside the organism.

When the body does not detoxify properly, there is a tendency for oxidation, acidity and inflammation.

As oxidation, we can define cell damage by the increased concentration of free radicals, which can be devastating, with varying degrees of severity. The disorders caused may vary from premature aging to cancer.

Acidification is the process that tends to lower the pH of the cell, resulting in super acidity in the body. Acidosis of the extracellular fluid is a predisposing factor for the appearance of many functional disorders and if is not treated properly can cause tissue damage.

Inflammation is the body's reaction to any harmful cause. Inflammation is a defensive function of the organism against microorganisms (viruses, bacteria, fungi, parasites, etc.) or mechanical-chemical agents (e.g. injuries, burns, poisoning). When inflammation occurs, chemicals from the white blood cells of the body are released into the blood or tissues affected to protect the body from foreign substances. This chemical's release increases the flow of blood to the area of injury or infection and can lead to redness and increased local heat. Some of the substances that reach the tissues cause swelling of the tissues locally. This protective process can stimulate the nerves and bring pain.

In immune disorders (allergies, autoimmune procedures), chronic inflammation may occur. Chronic inflammation has been recognized as the substrate of almost every chronic disease.

Plants can benefit us if we put them in our lives in the following ways:

1. We can reduce stress and improve our mood.

2. We can detoxify the body by acting proactively, preventing the development of any pathology.

3. We can help reduce and eliminate symptoms from various organ-state dysfunctions. In such cases, it is essential that the medical practitioner be informed and consulted.

Examples of plants used for improving certain health conditions

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Plants with anti-inflammatory action: ALOE VERA, ACHILLEA MILLEFOLIUM, ALLIUM SATIVUM, ANGELICA ARCHANGELICA, CALENDULA OFFICINALIS, CARDUUS MARIANUM, CHAMOMILLA RECUTITA, GENTIANA LUTEA, ECHINACEA, HYPERICUM PERFORATUM, SAMBUCUS NIGRA, TANACETUM PARTHENIUM, TARAXACUM OFFICINALE, URTICA DIOICA, VACCINIUM MYRTILLUS

Plants with an antioxidant effect: CHAMOMILLA RECUTITA, MENTA PIPERITA, TILIA EUROPEA, ALLIUM SATIVUM, PISTACIA LENTISCUS, VITIS VINIFERA

Plants to reduce stress symptoms and improve mood: ALLIUM SATIVUM, CHAMOMILLA RECUTITA, CRATAEGUS MONOGYNA, HYPERICUM PERFORATUM, HUMULUS LUPULUS, LAVENDULA OFFICINALIS, MELISSA OFFICINALIS, PASSIFLORA INCARNATA, VALERIANA OFFICINALIS,

Plants used for detoxification: ALOE VERA, ALLIUM SATIVUM, ARCTIUM LAPPA, CARDUS MARIANUM, CHELIDONIUM MAJUS, CISTUS CRETICUS, CYNARA SCOLYMUS, URTICA DIOICA,

Plants for improving circulation: ALLIUM SATIVUM, CRATAEGUS MONOGYNA, HAMAMELIS VIRGINIANA, VACCINIUM MYRTILLUS, VITIS VINIFERA,

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