جَـامعة
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PHARMACOGNOSY 1

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1. MEANING OF PHARMACOGNOSY

Pharmacognosy, known initially as *materia medica*, may be defined as the study of crude drugs obtained from plants, animals and mineral kingdom and their constituents.

There is a historical misinformation about who created the term pharmacognosy. According to some sources, it was C. A. Seydler, a medical student at Halle, Germany, in 1815; he wrote his doctoral thesis titled *Analectica Pharmacognostica*. However, recent historical research has found an earlier usage of this term. The physician J. A. Schmidt (Vienna) used that one in his *Lehrbuch der materia medica* in 1811, to describe the study of medicinal plants and their properties. The word pharmacognosy is derived from two Latin words pharmakon, 'a drug,' and gignoso, 'to acquire knowledge of'. It means 'knowledge or science of drugs.

Crude drugs are plants or animals, or their parts which after collection are subjected only to drying or making them into transverse or longitudinal slices or peeling them in some cases.

Most of the crude drugs used in medicine are obtained from plants, and only a small number comes from animal and mineral kingdoms. Drugs obtained from plants consist of entire plants, whereas senna leaves and pods, nux vomica seeds, ginger rhizome and cinchona bark are parts of plants. Though in a few cases, as in lemon and

orange peels and in colchicum corm, drugs are used in fresh condition, and most of the drugs are dried after collections.

Crude drugs may also be obtained by simple physical processes like drying or extraction with water. Therefore, aloe is the dried juice of leaves of Aloe species, opium is the dried latex from poppy capsules and black catechu is the dried aqueous extract from the wood of Acacia catechu. Plant exudates such as gums, resins and balsams, volatile oils and fixed oils are also considered as crude drugs.

Drugs obtained from animals are entire animals, as cantharides; glandular products, like thyroid organ or extracts like liver extracts. Similarly, fish liver oils, musk, bees wax, certain hormones, enzymes and antitoxins are products obtained from animal sources.

Drugs are organized or unorganized. Organized drugs are direct parts of plants and consist of cellular tissues. Unorganized drugs, even though prepared from plants are not the direct parts of plants and are prepared by some intermediary physical processes, such as incision, drying or extraction with water and do not contain cellular tissue. Thus aloe, opium, catechu, gums, resins and other plant exudates are unorganized drugs. Drugs from mineral sources are kaolin, chalk, diatomite and other bhasmas of Ayurveda.

2. HISTORY OF PHARMACOGNOSY

In the early period, primitive man went in search of food and ate at random, plants or their parts like tubers, fruits, leaves, etc.

As no harmful effects were observed he considered them as edible materials and used them as food. If he observed other effects by their eating they were considered inedible, and according to the actions he used them in treating symptoms or diseases.

If it caused diarrhea it was used as purgative, if vomiting it was used as memtic and if it was found poisonous and death was caused, he used it as arrow poison.

The knowledge was empirical and was obtained by trial and error. He used drugs as such or as their infusions and decoctions. The results were passed on from one generation to the other, and new knowledge was added in the same way.

2.1. Empirical Period

2.1.1. Ancient China

Chinese pharmacy, according to legend, stems from Shen Nung (about 2700 B.C.), emperor who investigated the medicinal value of several hundred herbs. He was reputed to have tested many of them on himself, and to have written the first Pen T-Sao, or Native Herbal, recording 365 drugs. Shen Nung conceivably examined many herbs, barks and roots brought in from the fields, swamps and woods that are still

recognized in pharmacy (podophyllum, rhubarb, ginseng, stramonium, cinnamon bark and ephedra).

Inscriptions on oracle bones from the Shang Dynasty (1766–1122 B.C.), have provided a record of illness, medicines and medical treatment. Furthermore, a number of medical treatises on silk banners and bamboo slips were excavated from tombs which were copied from books dating from the period between (300 B.C.–A.D. 3) and constitute the earliest medical treatises existing in China.

With the interest in alchemy came the development of pharmaceutical science and the creation of a number of books In which we can find a description of hundreds of herbs classified in six categories: (1) stone (minerals), (2) grasses and trees, (3) insects and animals, (4) fruits and vegetables, (5) grains and (6) named but unused.

From the Sung Dynasty (960–1276) the establishment of pharmaceutical system has been a standard practice throughout the country. Before the ingredients of Chinese medicine can be used to produce pharmaceuticals, they must undergo a preparation process, e.g. baking, simmering or roasting. The preparation differs according to the needs for the treatment of the disease. Preparation methods, production methods and technology have constantly been improved over time.

In 1552, Li Shi Zhen (1518–1593) began work on the monumental Pen T'sao Kan Mu (Herbal with Commentary). After 27 years and three revisions, the Pen T'sao Kan Mu

was completed in 1578. The book lists 1892 drugs, 376 described for the first time with 1160 drawings. It also lists more than 11,000 prescriptions.

2.1.2. Ancient Egypt

The most complete medical documents existing are the Ebers Papyrus (1550 B.C.), a collection of 800 prescriptions, mentioning 700 drugs and the Edwin Smith Papyrus (1600 B.C.), which contains surgical instructions and formulas for cosmetics. The Kahun Medical Papyrus is the oldest, it comes from 1900 B.C. and deals with the health of women, including birthing instructions.

However, it is believed that the Smith Papyrus was copied by a scribe from an older document that may have dated back as far as 3000 B.C. Commonly used herbs included: senna, honey, thyme, cumin, (all for digestion); pomegranate root (for worms) as well as pine-tar, aloe, caraway, cedar, coriander, fennel, garlic, wild lettuce, onion, peppermint, poppy-plant and saffron. turpentine and acacia gum were also used.

2.1.3. Ancient India

In India knowledge of medicinal plants is very old, and medicinal properties of plants are described in Rigveda and in Atharvaveda (3500–1500 B.C.) from which Ayurveda has developed.

Ayurveda is the term for the traditional medicine of ancient India. Ayur means life and veda means the study of which is the origin of the term. The oldest writing—Charaka Samhita—is believed to date back six to seven centuries before Christ. It is assumed to be the most important ancient authoritative writing on Ayurveda. Most of mentioned medicines origin from plants and animals, e.g. ricinus, pepper, lilly, valerian, etc

2.1.4. Ancient Greece and Rome

Greek scientists contributed much to the knowledge of natural history. Hippocrates (460–370 B.C.) is referred to as father of medicine and is remembered for his famous oath which is even now administered to doctors.

Aristotle (384–322 B.C.), a student of Plato was a philosopher and is known for his writing on animal kingdom which is considered authoritative even in twentieth century.

Dioscorides, a physician who lived in the first century A.D., described medicinal plants, some of which like belladonna, ergot, opium, colchicum are used even today.

Pliny wrote 37 volumes of natural history and Galen (131–A.D. 200) devised methods of preparations of plant and animal drugs, known as 'galenicals' in his honour.

The Doctrine of Signatures: dating from the time of Dioscorides and Galen, states that herbs resembling various parts of the body can be used by herbalists to treat

ailments of those body parts. A theological justification, as stated by botanists such as William Coles, was that God would have wanted to show men what plants would be useful for.

Pulmonaria officinalis: Its large elongated leaves, of a beautiful dark green, are frequently covered with white spots. These spots represented the pulmonary alveoli (vesicles). the plant is very rich in mucilage, which gives it some softening and expectorant virtues.

Ranunculus ficaria: Its roots are swollen in the form of elongated tubercles and strangely recall hemorrhoids. It was proved later its efficiency as an analgesic and anti-inflammatory drug.

Filipendula ulmaria & *Salix alba* : Both of them grow near water, and so they were used to treat diseases that are caught in the water, or at least in cold. Salicylate derivatives (anti-inflammatory agent) were isolated from both plants.

2.1.5. Ancient Arabic world

After the collapse of the Greco-Roman civilization, the vast Arabic speaking world of the Middle Ages performed a great service to mankind by acting as a link between ancient and modern medical science. For them the Middle Ages were not an era of darkness but an era enlightened by a renaissance of scientific study which not only preserved for the world much of the medical knowledge of the Greeks and ancient Semites but also contributed, much that had been unknown in medical science.

It was the Christian Syrians who first translated Greek medical literature. The works of such early scientists as Galen, Aristotle, Plato, Dioscorides....

Hunain ibnIshaq, known as Johannitius (809-873 A.D.) who was a scholar of the Greek language and adapted many of the Greek terms to his development of scientific Arabic terminology. He is credited with writing the first textbook on ophthalmology. Johannitius and his predecessor, Ibn Masawayh, are representatives of the transition period in Arabic medicine when physicians no longer limited themselves to translations of Greek medical literature but also began to develop originality in their medical studies and practices.

Al-Razi " Rhazes" is considered as the greatest of all the Arabic medical men lived from 850- 923 A.D. Over 200 books were written by Rhazes and of this number several have been of great importance in the development of medical science, "Al-Judari w-al-Hasbah" & " al-Hawi"; The last one was an encyclopaedic work of the medical information known in his day. It was translated into Latin in 1280 A.D. and was one of the total of nine books that composed the library of the Faculty of Medicine of Paris in 1395.

Ibn Sina (Avicenna, 980-1037 A.D.) had the most brilliant mind in Arabic medicine, who wrote the *Canon* of Medicine which was translated into Latin and Hebrew and was widely used as a textbook until as late as the middle of the 17th century.

2.2. Scientific period

Pharmacy separated from medicine and *materia medica*, the science of material medicines, describing collection, preparation and compounding, emerged.

Even upto the beginning of twentieth century, pharmacognosy was more of a descriptive subject close mainly to botanical science, and it consisted of identification of drugs both in entire and powdered conditions and concerned with their history, commerce, collection, preparation and storage.

The development of modern pharmacognosy took place later during the period 1934–1960 by simultaneous application of disciplines like organic chemistry, biochemistry, biosynthesis, pharmacology and modern methods and techniques of analytic chemistry, including paper, thin layer, and gas chromatography and spectophotometry.

The substances from the plants were isolated, their structures elucidated and pharmacological active constituents studied.

The development was mainly due to the following four events:

1- Isolation of penicillin in 1928 by Fleming and large-scale production in 1941 by Florey and Chain.
2- Isolation of resperpine from *rauwolfia* roots and confirming its hypotensive and tranquilizing properties.

3- Isolation of vinca alkaloids, especially vincristine and vinblastine. Vincristine was found useful in the treatment of leukaemia. These alkaloids also have anticancer properties.

4- Steroid hormones like progesterone were isolated by partial synthesis from diosgenin and other steroid saponins by Marker's method. Cortisone and hydro- cortisone are obtained from progesterone by chemical and microbial reaction.

Pharmacognosy is no longer a descriptive study of plants used in traditional medicine, but it is a substantial science based on a combination of multiple expertise in various fields like organic & Analytic chemistry and Pharmacology.

Nowadays, pharmacognosy is a multidisciplinary science which could be defined after the American society of pharmacognosy, as the study of the physical, chemical, biochemical and biological properties of drugs, drug substances or potential drugs or drug substances of natural origin as well as the search for new drugs from natural sources"

3. CURRENT USE OF MEDICINAL PLANTS

The current use of medicinal plant can be summarized as follows:

1- Natural form

Powders for herbal teas by infusion, decoction, digestion. The plants are delivered in bulk or in tea-bag, are alone "simple" or in mixtures or even powders in capsule.

2- Galenic forms: containing the majority of the active constituents in a reduced volume. Alcoholic tinctures, extracts (by water, ether, alcohol, ...) dried (powders), Soft extracts, Fluid extracts.

3- Sources of bioactive molecules: When these molecules are difficult or very expensive to synthesize

4- Source of raw materials for hemisynthesis:

To facilitate the synthesis of molecules of interest, reducing the steps and the cost of the manipulation (Cost-effective synthesis !!!)

5- Other uses: food and cosmetics industry (preservatives, antioxidants, thickening agents, etc...).

4. PHARMACOGNOSTICAL SCHEME

To describe drugs in a systematic manner is known as pharmacognostical scheme, which includes the following headings:

4.1. Biological Source

This includes the biological names of plants or animals yielding the drug and family to which it belongs. Botanical name includes genus and species. Often some abbreviations are written after the botanical names, of the biologist responsible for the classification, for example, *Acacia arabica* Willd. Here Willd indicates the botanist responsible for the classification or nomenclature (Carl Ludwig Willdenow a German botanist, pharmacist).

According to the biennial theory, the botanical name of any plant or animal is always written in italic form, and the first letter of a genus always appears in a capital later. Biological source also includes the family and the part of the drug used. For example, biological source of senna is, *Senna* consists of dried leaflets of *Cassia angustifolia* Delite, belonging to family Leguminosae.

4.2. Geographical Source

It includes the areas of cultivation, collection and route of transport of a drug.

4.3. Cultivation, Collection and Preparation

These are important to mention as these are responsible for quality of a drug.

4.4. **Morphological Characters**

In case of organized drugs, the length, breadth, thickness, surface, colour, odour, taste, shape, etc. are covered under the heading morphological characters, whereas organoleptic properties (colour, odour, taste and surface) should be mentioned, if the drug is unorganized.

4.5. **Microscopical Characters**

This is one of the important aspects of pharmacognosy as it helps in establishing the correct identity of a drug. Under this heading all the detailed microscopic characters of a drug is described.

4.6. **Chemical Constituents & Chemical Tests**

The most important aspect which determines the intrinsic value of a drug to which it is used is generally described under this heading. It includes the chemical constituents present in the drug. These kinds of drugs are physiologically active.

The knowledge of chemical tests becomes more important in case of unorganized drugs whose morphology is not well defined. The drug may be correct but something happened during the harvest, drying, storage and transport, would affect the quantity and the quality of the chemical constituents.

4.7. **Uses**

It includes the pharmaceutical, pharmacological and biological activity of drugs or the diseases in which it is effective.

4.8. **Substituents**

The drug which is used during non-availability of original drug is known as substituent. It has the same type of physiological active constituents; however, the percentage quantity of the drug available may be different.

4.9. **Adulterants**

With the knowledge of the diagnostic characters of drugs, the adulterants can be detected. One should have the critical knowledge of substances known to be potential adulterants.

Most of the times the adulterants are completely devoid of physiologically active constituents, which leads in the deterioration of the quality, sometimes it would induce undesirable side effects or even toxicity.

CULTIVATION, COLLECTION & PRODUCTION OF HERBAL DRUGs

The crude drugs which reach the market and pharmaceutical industries will have passed through different stages that have some effect in the nature and amount of active constituents responsible for therapeutic activity. Those stages are to be concerned more in order to make a drug useful to the mankind by all means.

1. CULTIVATION

Wild sources could be a good choice as it presents plants identical to that used in traditional medicine, without any additives or fertilizers, but the wild plants are insufficient to meet the demand or because, owing to spare distribution or inaccessibility, collection is difficult. it can't ensure a regular supply of a crude drug because of unstable weather conditions or orver-harvesting..etc.

Cultivation is essential in the case of drugs such as Indian hemp or opium, which are subject to government control, and recently for those in danger of over-exploitation. In many cases cultivation is advisable because of the improved quality of drug.

The advantages of cultivation may be briefly summarized as follows:

1. It ensures quality and purity of medicinal plants. Due to the controlled environmental growth better plant product is obtained and makes the collection and processing steps easier when compared to wild sources.

Crude drugs derive their utility from chemical contents in them. If uniformity is maintained in all operations during the process of cultivation, drugs of highest quality can be obtained.

For example Cultivation of rhizomes demands an adequate quantity of fertilizers and proper irrigation. Systematic cultivation results in raising a crop with maximum content of volatile oil and other constituents. The examples of ginger, turmeric and liquorice can be cited to illustrate this point. If the cultivated plants are kept free of weeds, the contamination of crude drugs can be conveniently avoided.

2. Collection of crude drugs from cultivated plants gives a better yield and therapeutic quality. However, it is a skilled operation and requires some professional excellence, if the collection of crude drugs for market is done from cultivated plants by skilled and well-experienced personnel, the high yield and therapeutic quality of drugs can be maintained. For example, collection of latex from poppy capsules and oleo-resins from *Pinus* species, if done by experienced persons, can result in better yield of crude drugs. Preservation of green color of senna leaves and minimizing the deterioration of cardiac glycosides in freshly collected leaves of digitalis can be achieved only by skilled labour.

3. Cultivation ensures regular supply of a crude drug. In other words, cultivation is a method of crop-planning. Planning a crop cultivation regularizes its supply and as a result the industries depending upon crude drugs do not face problem of shortage of raw material.

4. The cultivation of medicinal and aromatic plants also leads to industrialization to a greater extent. The cultivation of coffee and cocoa in Kerala has given rise to several cottage and small scale industries.

5. Cultivation permits application of modern technological aspects such as mutation, polyploidy and hybridization. Thus it produces improved quality of plants and helps in selecting the species, varieties or hybrids that have the desired phyto-constituents.

2. COLLECTION OF CRUDE DRUGS

Collection is the most important step which comes after cultivation. Drugs are collected from wild or cultivated plants and the tasks for collection depends upon the collector, whether he is a skilled or unskilled labour.

Drugs should be collected when they contain maximum amount of constituents in a highly scientific manner.

The season at which each drug is collected is so important, as the amount, and sometimes the nature, of the active constituents could be changed throughout the year. For example, Rhubarb is collected only in summer seasons because no anthraquinone derivatives would be present in winter season but anthranols are converted to anthraquinones during summer.

The age of the plant should be taken in to great consideration since it governs not only the total amount of active constituents produced in the plants but also the proportions of the constituents of the active mixture. High proportion of pulegone in

young plants of peppermint will be replaced by menthone and menthol and reduction in the percentage of alkaloids in datura as the plant ages are examples of the effect of aging in plants.

Moreover the composition of a number of secondary plant metabolites varies throughout the day and night, and it is believed that some inter-conversion would happen during day and night.

Generally the leaves are collected just before the flowering season, e.g. digitalis, at this time it is assumed that the whole plant has come to a healthy state and contain an optimum amount of metabolites, flowers are collected before they expand fully, e.g. clove, saffron, etc., and underground organs as the aerial parts of plant cells die, e.g. liquorice, rauwolfia, etc.

Some fruits are collected after their full maturity while the others are collected after the fruits are ripe. Barks are usually collected in spring season, as they are easy to separate from the wood during this season.

Underground parts should be collected and shaken, dusted in order to remove the adhered soil; water washing could be done if the adhered particles are too sticky with plant parts. The unorganized drugs should be collected from plants as soon as they oozes out, e.g. resins, latex, gums, etc. Discoloured drugs or drugs which were affected by insects should be rejected.

3. DRYING OF CRUDE DRUGS

Drying consists of removal of sufficient moisture content of crude drug, so as to improve its quality and make it resistant to the growth of microorganisms. Drying inhibits partially enzymatic reactions, it also facilitates pulverizing or grinding of a crude drug. Slow drying at moderate temperature is necessary when enzymatic action is to be encouraged (Orris rhizomes, Coca seeds and Gentian root)

In certain drugs, some special methods are required to be followed to attain specific standards, e.g. fermentation in case of *Cinnamomum zeylanicum* bark. The slicing and cutting into smaller pieces is done to enhance drying, as in case of *glycyrrhiza, and squill*. The flowers are dried in shade so as to retain their colour and volatile oil content. Depending upon the type of chemical constituents, a method of drying can be used for a crude drug. Drying can be of two types:

3.1. NATURAL DRYING (SUN-DRYING)

In case of natural drying, it may be either direct sun-drying or in the shed. If the natural colour of the drug (digitalis, clove, senna) and the volatile principles of the drug (peppermint) are to be retained, drying in shed is preferred. If the contents of the drugs are quite stable to the temperature and sunlight, the drugs can be dried directly in sunshine (gum acacia, seeds and fruits).

3.2. ARTIFICIAL DRYING

Drying by artificial means includes drying the drugs in (a) an oven; i.e. tray-dryers; (b) vacuum dryers and (c) spray dryers.

(a) Tray dryers: The drugs which do not contain volatile oils and are quite stable to heat or which need deactivation of enzymes are dried in tray dryers. In this process, hot air of the desired temperature is circulated through the dryers and this facilitates the removal of water content of the drugs (belladonna roots, cinchona bark, tea and raspberry leaves and gums are dried by this method).

(b) Vacuum dryers: The drugs which are sensitive to higher temperature are dried by this process, e.g. Tannic acid and digitalis leaves. The pressure maintained in vacuum drying is generally 0.0296 –0.059 atm and the boiling point of water is 25-30 °C. The vacuum drying process is a batch operation which is performed at reduced pressures and lower relative humidity compared to ambient pressure. That is why the drying occurs faster under these conditions.

(c) Spray dryers: Few drugs which are highly sensitive to atmospheric conditions and also to temperature of vacuum-drying are dried by spray-drying method. The technique is followed for quick drying of economically important plant or animal constituents, rather than the crude drugs. Examples of spray drying are papaya latex, pectin, tannins, etc.

4. STORAGE OF CRUDE DRUGS

Preservation of crude drugs needs sound knowledge of their physical and chemical properties. A good quality of the drugs can be maintained, if they are preserved properly. All the drugs should be preserved in well closed and, possibly in the filled containers. They should be stored in the premises which are water-proof, fire proof and rodent- proof. Long storage is not to be recommended, except in a few cases such as cascara bark

- Moisture A number of drugs absorb moisture during their storage and become susceptible to the microbial growth. Some drugs absorb moisture to the extent of 25% of their weight. The moisture, not only increases the bulk of the drug, but also causes impairment in the quality of crude drug. The excessive moisture facilitates enzymatic reactions resulting in decomposition of active constituents e.g. digitalis leaves and wild cherry bark. Gentian and ergot receive mould infestation due to excessive moisture.
- Radiation due to direct sun-light also causes destruction of chemical constituents.
- Atmospheric oxygen is also destructive to several drugs and hence, they are filled completely in well closed containers, or the air in the container is replaced by an inert gas like nitrogen; e.g. shark liver oil, papain, etc.
- Insect or mould attacks Apart from protection against adverse physical and chemical changes, the preservation against insect or mould attacks is also important. Different types of insects, nematodes, worms, moulds and mites infest

the crude drugs during storage. They can be prevented by drying the drug thoroughly before storage and also by giving treatment of fumigants. The common fumigants used for storage of crude drugs are methyl bromide, carbon disulphide and hydrocyanic acid.

- Temperature is also very important factor in preservation of the drugs, as it accelerates several chemical reactions leading to decomposition of the constituents.

OTHER SOURCES OF DRUGS

1. MARINE ORGANISMS AS POTENTIAL SOURCE OF DRUGS

Knowledge of biological activities and/or chemical constituents of marine organisms is important not only for the discovery of new therapeutic agents but such information may also be of immense value in exploring, new sources of economic materials, precursors for the synthesis of complex chemical substances and compounds of novel chemical structure, thereby prompting the chemist for the synthesis of a series of modified compounds of therapeutically importance.

The invention of the aqualung and the advent of new technology in the past few decades led to the awareness that the oceans may be a new frontier of biomedical research, as it has vast resources for the discovery of marine-derived medicine.

Extracts from marine organisms had been evaluated for various biological activities. This has led to the isolation of substances possessing antimicrobial, antibiotic, antiviral, anticancer, cardioactive, anti-inflammatory, anthelmintic, anticoagulant, neurophysiological and insecticidal activities.

Although, numerous compounds have been isolated from marine organisms and the biological activities attributed too many of them; but still very few of them have been marketed or are under development. Few drugs have been approved by Food and Drug Administration (FDA) or European Medicines Agency (EMEA), and several compounds in different phases of the clinical trials. Some of the currently marketed

compounds, like (Prialt®, Yondelis® and Carragelose®), became drugs without any modification of the original natural molecule, while the rest of them suffered lead optimization, in different steps of their development.

1.1. Cytarabine, Cytosar-U®(Bedford Laboratories, USA) and Vira-A®(King Pharmaceuticals, NJ, USA): the election drug for the treatment of myeloid leukaemia, non-Hodgkin's lymphoma and meningeal leukemia. Activity occurs as the result of inhibition of DNA polymerase.

Crucially, more than 40 years after its approval, cytarabine a synthesized drug inspired from a marine natural product (isolated from the gorgonian *Eunicella cavolinii*), is still in the forefront of cancer drug treatment.

1.2. Ziconotide Prialt® by Elan Corporation (Dublin, Ireland): first intrathecal analgesic drug to be approved after morphine, it was granted FDA and EMEA approval in 2004 and 2005 respectively, for the management of severe chronic pain associated with cancer, AIDS and neuropathies. Ziconotide was synthesized in 1987 after its equivalent, a naturally occurring peptide, isolated from the venom of the cone snail *Conus magus* (molluscs with fatal stings). The ziconotide-induced blockade in the spinal cord inhibits release of pain-relevant neurotransmitters from central terminals of primary afferent neurons.

1.3. Lovaza® by GlaxoSmithKline (Brentford, UK): is the brand name for an anti-hypertriglyceridemia drug, composed by ethyl esters of several omega-3 fatty acids sourced from fish oils. The approach to this drug discovery was the

statistical observation that certain ethnic populations, such as the native Alaskans, had much lower mortality rates from cardiovascular diseases, a fact that was later correlated with their high polyunsaturated fatty acids diets content.

1.4. Trabectedin Yondelis® by PharmaMar (Madrid, Spain): is a novel marine antineoplastic alkaloid. The active substance is a natural product, originally isolated from the Caribbean sea squirt *Ecteinascidia turbinata* with a 0.0001% yield; It takes 1 t of animals to isolate 1 g of trabectedin, The problem was finally solved with the development of a semi-synthetic industrial viable route to produce trabectedin.

1.5. Carrageenans® Marinomed (Vienna, Austria): are polysaccharides that are extracted from red edible seaweeds, mainly *Rhodophyceae*. They are widely used in the food and pharmaceutical industry, for their gelling, thickening, and stabilizing properties.

1.6. Tetrodotoxins: is a potent neurotoxin produced by the pufferfish (Tetraodontidae) and marine bacteria. This dangerous toxin shows the cardiovascular and neurophysiological activity in experimental animals, responsible for human intoxications (coma) and fatalities.

2. PLANT TISSUE CULTURE

Definition: Tissue culture is *in vitro* cultivation of plant cell or tissue under aseptic and controlled environmental conditions, in liquid or on semisolid well-defined

nutrient medium for the production of primary and secondary metabolites or to regenerate plant.

This technique affords alternative solution to problems arising due to current rate of extinction and decimation of flora and ecosystem.

Requirements: The whole process requires a well-equipped culture laboratory and nutrient medium. This process involves various steps, viz. preparation of nutrient medium containing inorganic and organic salts, supplemented with vitamins, plant growth hormone(s) and amino acids as well as sterilization of explant (source of plant tissue), glassware and other accessories inoculation and incubation.

Explant can be defined as a portion of plant body, which has been taken from the plant to establish a culture. It may be taken from any part of a plant (root, stem, leaf, floral parts like anthers & stamens, meristematic tissue...etc).

Advantages of Tissue Culture Technique over the Conventional Cultivation Techniques

1- Availability of raw material:

Some plants are difficult to cultivate and are also not available in abundance. Unlimited cutting of plants also leads to deforestation, natural imbalance and sometimes may lead to extinction of a particular species. In addition to variation in quality of drug due to changes in climate, crop diseases and seasons.

Tissue culture is considered a better source for regular and uniform supply of raw material, manageable under regulated and reproducible conditions in the medicinal plants industry for the production of phytopharmaceuticals.

2- Easy purification of the compound

The natural products from plant tissue culture may be easily purified because of the absence of significant amounts of pigments and other unwanted impurities.

3- Political reasons

If a natural drug is successfully marketed in a particular country of its origin, the government may prohibit its export to up-value its own exports by supplying its phytochemical product, e.g. *Rauwolfia serpentina* and *Dioscorea* spp. from India.

4- Crop improvement

Plant tissue culture is advantageous over the conventional cultivation technique in crop improvement by somatic hybridization or by production of hybrids.

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CLASSIFICATION OF CRUDE DRUGS

In order to pursue (or to follow) the study of the individual drugs, one must adopt some particular sequence of arrangement, and this is referred to a system of classification of drugs. A method of classification should be simple, easy to use, and free from confusion and ambiguities.

Because of their wide distribution, each arrangement of classification has its own merits and demerits, but for the purpose of study the drugs are classified in the following different ways:

- Alphabetical classification
- Morphological classification
- Pharmacological classification
- Chemical classification
- Taxonomical classification
- Chemotaxonomical classification

1- Alphabetical Classification

Crude drugs are arranged in alphabetical order of their Latin (European Pharmacopoeia) or English names (United States Pharmacopoeia U.S.P.) or sometimes local language names (vernacular names). This method is adopted by the pharmacopoeias, dictionaries and some reference books.

It is easy to use with no repetition of entries and is devoid of confusion, but There is no relationship between previous and successive drug entries.

2- Morphological Classification

In this system, the drugs are arranged according to the morphological or external characters of the plant parts or animal parts, i.e. which part of the plant is used as a drug, e.g. leaves, roots, stem, etc.

It can be helpful to identify and detect adulteration. There is no correlation of chemical constituents with the therapeutic actions. Repetition of drugs or plants occurs.

3- Pharmacological Classification (Therapeutic)

Grouping of drug according to their pharmacological action or of most important constituent or their therapeutic use is termed as pharmacological or therapeutic classification of drug.

Drugs like digitalis, squill and strophanthus having cardiotonic action are grouped irrespective of their parts used or phylogenetic relationship or the nature of phytoconstituents they contain.

Drugs having different action on the body get classified separately in more than one group that causes ambiguity and confusion. Cinchona is antimalarial drug because of presence of quinine but can be put under the group of drug affecting heart because of antiarrhythmic action of quinidine.

4- Chemical Classification

Depending upon the active constituents, the crude drugs are classified. The plants contain various constituents in them like alkaloids, glycosides, tannins, carbohydrates, saponins, etc. Irrespective of the morphological or taxonomical characters, the drugs with similar chemical constituents are grouped into the same group.

It is a popular approach for phytochemical studies, but ambiguities arise when particular drugs possess a number of compounds belonging to different groups.

5- Taxonomical Classification

All the plants possess different characters of morphological, microscopic, chemical, embryological, serological and genetics. In this classification the crude drugs are classified according to kingdom, subkingdom, division, class, order, family, genus and species.

Taxonomical classification is helpful for studying evolutionary developments, but it does not correlate in between the chemical constituents and biological activity of the drugs.

6- Chemo-taxonomical Classification

This system of classification relies on the chemical similarity of a taxon, i.e. it is based on the existence of relationship between constituents in various plants. There are certain types of chemical constituents that characterize certain classes of plants.

This gives birth to entirely a new concept of chemotaxonomy that utilizes chemical facts/characters for understanding the taxonomical status, relationships and the evolution of the plants.

For example, tropane alkaloids generally occur among the members of Solanaceae, thereby, serving as a chemotaxonomic marker. It is the latest system of classification that gives more scope for understanding the relationship between chemical constituents, their biosynthesis and their possible action.

PRIMARY AND SECONDARY METABOLITES

All organisms need to transform and interconvert a vast number of organic compounds to enable them to live, grow, and reproduce. An integrated network of enzyme-mediated and carefully regulated chemical reactions is used for this purpose.

Despite the extremely varied characteristics of living organisms, the pathways for generally modifying and synthesizing carbohydrates, proteins, fats, and nucleic acids are found to be essentially the same in all organisms, apart from minor variations. These processes demonstrate the fundamental unity of all living matter, and are collectively described as primary metabolism, with the compounds involved in the pathways being termed primary metabolites.

In contrast to these primary metabolic pathways, there also exists an area of metabolism concerned with compounds, called secondary metabolites. They are found in only specific organisms, and are an expression of the individuality of species.

Secondary metabolites are not necessarily produced under all conditions, and in the vast majority of cases the function of these compounds are not yet known.

Some are undoubtedly produced for easily appreciated reasons, un example: for survival purposes, e.g. as toxic materials providing defense against predators, as volatile attractants towards the same or other species, or as colouring agents to attract or warn other species, but it is logical to assume that all do play some vital role

for the well-being of the producer. It is this area of secondary metabolism which provides most of the pharmacologically active natural products.

These secondary metabolites can be summarized as follows:

1- Carbohydrate and derived products;

2- Lipids;

3- Phenols (Phenolic acids, coumarines, Flavonoides, anthocyanes, tanins…);

4- Terpens (monoterpens, diterpens, triterpens…….);

5- Alkaloids;

6- Cardio-active Glycosides;

7- Volatile oils and resins.

Taxonomical Classification

Taxonomy is concerned with the laws governing the classification of plants. The term taxonomy includes two Greek words taxis – arrangement and nomos– laws. Plant taxonomy is otherwise known as systematic botany. Classification, identification, description and naming the plants are the bases of plant taxonomy.

The taxonomical classification aims to:

- arrange plants in an orderly sequence based upon their similarities,
- establish phylogenetic relationships among the different groups of plants.

The earliest systems of classification were simple and based on one or few characters. They gave importance to vegetative characters. The later systems of classification gave more importance to floral characters because floral characters are more stable and permanent.

For classification purposes the plant is divided into a number of phyla and in addition to the phyla. the classification includes groupings of gradually diminishing size:

Class:

- Angiospermae (Angiosperms) are plants that produce flowers.
- Gymnospermae (Gymnosperms) which don't produce flowers.

Subclass:

- Dicotyledonae (Dicotyledons, Dicots) are plants with two seed leaves

- Monocotyledonae (Monocotyledons, Monocots) with one seed leaf.

Superorder: A group of related plant families. The names of the superorders end in –idae.

Order: Each superorder is further divided into several orders. The names of the orders end in –ales.

Family: Each order is divided into families. These are plants with many botanical features in common, and are the highest classification normally used. At this level, the similarity between plants is often easily recognizable by the layman.

Modern botanical classification assigns a type plant to each family, which has the particular characteristics that separate this group of plants from others, and names the family after this plant. The names of the families end in –aceae.

Subfamily: group of plants within the family that have some significant botanical differences. The names of the subfamilies end in –oideae.

Tribe: A further division of plants within a family. The names of the tribes end in –eae.

Genus: This is the part of the plant name that is most familiar; the normal name that you give a plant—Papaver (Poppy), and so on. The plants in a genus are often easily recognizable as belonging to the same group.

Species: This is the level that defines an individual plant. Often, the name will describe some aspect of the plant— the colour of the flowers, size or shape of the leaves, or it may be named after the place where it was found.

Together, the genus and species name refer to only one plant, and they are used to identify that particular plant. The name, of the species should be written after the genus name, in small letters, with no capital letter.

Variety: A variety is a plant that is only slightly different from the species plant, but the differences are not so insignificant as the differences in a form. The name follows the genus and species name, with var. before the individual variety name.

Form: A form is a plant within a species that has minor botanical differences, such as the colour of flower or shape of the leaves. The name follows the genus and species name, with form (or f.) before the individual variety name.

In this chapter the principal plant families of pharmaceutical interest are arranged according to the botanical scheme of Engler (German botanist 1844-1930):

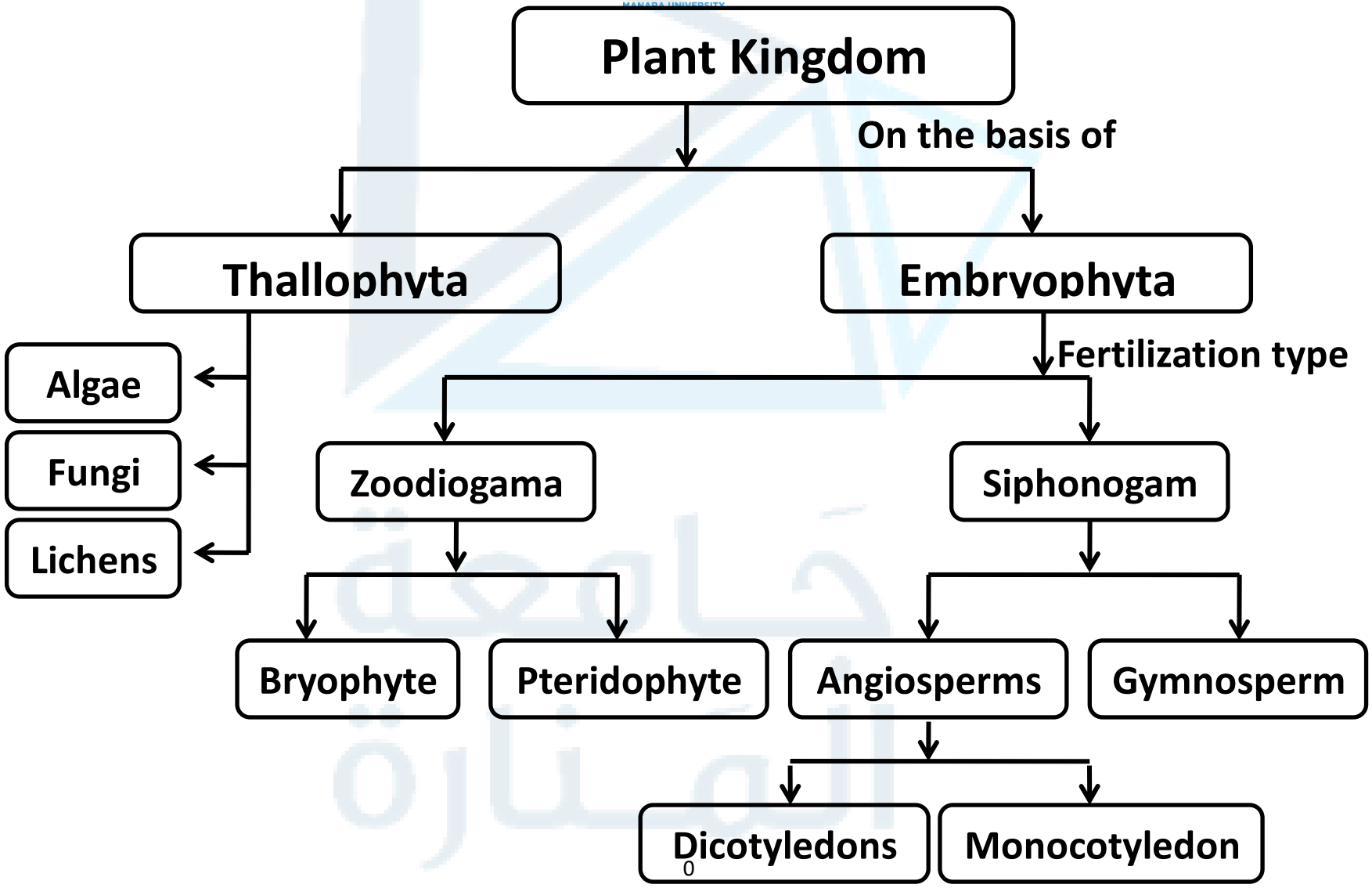
- Thallophytes
- Bryophytes & Pteridophytes
- Gymnosperms
- Angiosperrns: Dicotyledons and Monocotyledons

Engler and Prantl (two German botanists) classified all the plants from algae to angiosperms, they gave the phylogenetic classification of plant kingdom. This classification based on embryogenesis and fertilization type.

Plants can be divided into two groups, the thallophyta (no embryo) and the embryophyta including higher plant with embryo.

Embryophyta was later subdivided in two divisions, *Embryophyta* Zoodiogama (bryophytes, pteridophytes) and *Embryophyta Siphonogama* (Spermatophytes: gymnosperms, angiosperms).

For Zoodiogama members the fertilization is made by motile male gametes reaching the female gametes by swimming; while the male gametes of Siphonogama are non-motile and reach the female gametes through pollen tube.


Plant Kingdom
On the basis of
Thallophyta
Embryophyta
Fertilization type
Algae
Fungi
Lichens
Zoodiogama
Siphonogam
Bryophyte
Pteridophyte
Angiosperms
Gymnosperm
Dicotyledons
Monocotyledon

1. THALLOPHYTES

The old term thallophyte includes those plants which are not differentiated into root, stem and leaves. There are no vascular tissue in the plant body.

Asexual reproduction by mitotic spores is common, thus sexual reproduction may occur. there is no embryo formation after gametic union. most of plants are aquatic.

Engler divides them into 13 phyla. They include bacteria algae, fungi and lichens. The positions of the main families of pharmaceutical interest are indicated below.

1.1. BACTERIA AND ALGAE

The bacteria are unicellular organisms, the great majority of which range in size from 0.75 to 8 µm. They reproduce by binary fission. Most species of bacteria contain no chlorophyll, although there is one group whose members contain a chlorophyll-like pigment and photosynthesize.

Phyla	*Orders*	*Families*
Bacteriophyta	Eubacteriales	Rhizobiaceae
		Micrococcaceae
Chrysophyta (Diatomeae)	Discales	Actinodiscaceae
	Pennatales	Fragilariaceae
		Navicullariaceae
Phaeophyta (Brown Algae)	Laminariales	Laminariaceae
	Fucales	Fucaceae
		Sargassaceae
Rhodophyta (Red Algae)	Gelidiales	Gelidiaceae
	Gigartinales	Gracilariaceae
		Gigartinaceae

Bacteria are most important in medicine and pharmacy in the following respects:

- as disease-producing organisms (about l0% of bacteria are probably pathogenic);
- for producing antibiotics (Actinomycetes);
- for effecting biochemical conversions
- in genetic engineering involving recombinant DNA (production of human insulin);
- Bacteria also play a vital role in nature for example, in the nitrogen cycle atmospheric nitrogen is fixed by *Azotobacter*.
- Bacteria are important in sewage purification;
- in the retting of fibers such as jute and flax, and in the ripening of cheese.

1.1.1. PHAEOPHYTA (Brown Algae)

1.1.1.1. LAMINARIALES: Laminariaceae

The brown algae are mainly marine and vary from microscopic branched filaments to leathery frond-like forms up to 60 m in length. They owe their brown colour to the carotenoid pigment fucoxanthin. which masks the other pigments.

Many of the 30 species of *Laminaria* are used in coastal districts for agricultural purposes. They are used for the manufacture of alginic acid (polysaccharide), mannitol and iodine.

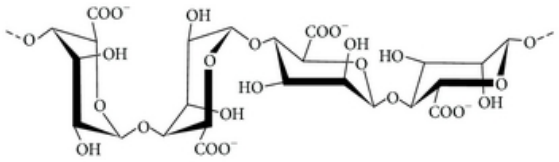
1.1.1.1.1. *Laminaria angustata* have been used as a hypotensive agent in Japanese folk medicine. The constituents of *Laminaria* include iodine, potassium, magnesium, calcium, iron and amino acids (e.g. L-lysine, L-arginine, and choline). Laminine was found to have a transitory hypotensive effect; it depressed the contraction of excited smooth muscles.

1.1.1.1.2. *Laminaria saccharina* (or *Saccharina latissima*)

Description: Yellow brown, to 3m in length with a claw-like holdfast, a small, smooth, flexible stipe and an undivided laminate blade to 3m long with parallel, ruffled sides and elongated, tongue-like appearance.

Usage: source of sodium alginate

a



b

Figure (2): (a) *Laminaria saccharina* (or *Saccharina latissima*) – (b)Alginic acid structure.

1.1.1.2. FUCALES: Fucaceae & Sagassaceae

Examples of the Fucaceae and *Fucus* (about 30 spp.) and of the Sargassaceae about 250 species of *Sargassum*. these are collected on a large scale in many parts of the world for the production of alginic acid and its derivatives. The species have been much investigated for biologically active properties.

1.1.1.2.1. *Fucus Vesiculosus:*

Description: Mild-shore wrack easily recognized by its paired bladders occurring on either side. It is attached by a small, strongly attached disc which give rise to a short stipe. the reproductive receptacles are swollen area at the tips of the fronds. The eggs and sperm are liberated onto the surface of the receptacles and a pheromone (sex-attracting substance) is released by the eggs that attracts the sperm. Fertilization results in a zygote that forms a new Fucus adult.

Distribution: This species is common in the North Atlantic south to the Canary Islands.

Usage: :*Fucus vesiculosus* is used in cosmetic preparations and in thalassotherapy, for the production of alginic acid and its derivatives, and as a bulk laxative.

Figure (3): *Fucus vesiculosus*

Application of Alginic acid derivatives:

Sodium alginate finds many applications as a stabilizing and thickening agent in a variety of industries, particularly food manufacture, and also the pharmaceutical industry, where it is of value in the formulation of creams, ointments, and tablets.

Calcium alginate is the basis of many absorbable haemostatic surgical dressings. Alginic acid or alginates are incorporated into many aluminium- and magnesium-containing antacid preparations to protect against gastro-oesophageal reflux. Alginic acid released by the action of gastric acid helps to form a barrier over the gastric contents.

1.1.2. RHODOPHYTA (red algae)

1.1.2.1. GELIDIALES: Gelidiaceae

The red algae are divided into 11 orders. The 3000 species are mainly marine and are particularly abundant in the tropics and subtropics. Most are relatively small. Their plastids contain chlorophyll, the red pigment phycoerythrin (usually in sufficient quantity to mask the other pigments. and sometimes the blue pigment phycocyanin. Many of these are used in the preparation of agars.

1.1.2.1.1. *Gelidium spinosum* (Gelidiaceae)

Description: Cartilaginous, crimson to purplish red, 20-60 mm long. Main axes distinctly flattened, often narrower at base, ultimate branches short, often opposite, spine-like or spathulate

Usage: a source of agar production

Figure (4): *Gelidium spinosum*

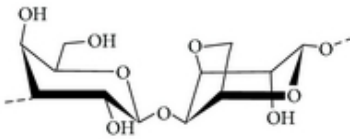
1.1.2.2. GIGARTINALES: Gigartinaceae & Gracilariaceae

1.1.2.2.1. *Gracilaria gracilis* (Gracilariaceae) (100 spp) source of agar.

Description: Cartilaginous, cylindrical, dull purple-red fronds, to 500 mm long, one or several arising from small, fleshy, perennial discoid holdfast. Branching very irregular.

Usage: A species of importance for agar production in other parts of the world.

a



b

Figure (5): (A) *Gracilaria gracilis* – (B) Agar structure

Agar is a carbohydrate extracted using hot dilute acid from various species of red algae (seaweeds), including *Gelidium* (Gelidiaceae) and *Gracilaria* (Gracilariaceae). Agar's main application is in bacterial culture media, where its gelling properties are exploited. It is also used to some extent as a suspending agent and a bulk laxative.

1.1.2.2.2. *Chondrus crispus* (Gigartinaceae, chondrus, or Irish moss)

Common names: Irish Moss, Carragheen, Carrageen, Carrageen Moss (Eng.), Mousse d'Irlande (French).

Description: Cartilaginous, dark purplish-red fronds, up to 150 mm high. Stipe compressed, narrow, expanding gradually onto a flat branched blade, in tufts from a discoid holdfast. frond thicker in centre than margins.

Distribution: the red alga collected from Irish and other Atlantic coasts in Europe.

Usage: A source of carrageenan (a sulphated polysaccharide), widely used in the food and pharmaceutical industries as thickening agents, and in Ireland as a remedy for respiratory disorders (colds, influenza and tuberculosis).

a b c

Figure (6): (a & b) *Chondrus crispus*, Irish Moss –(c): kappa carrageen structure.

1.2. FUNGI

The fungi are saprophytic or parasitic members of the Thallophyta. entirely devoid of chlorophyll. Called saprophytes, they act as recyclers of dead organic matter,

obtaining food from this material. Hyphal tips release enzymes that eventually decompose and release organic materials into the surrounding environment.

The plant body is made up of filaments or hyphae, which together constitute the mycelium.

Sexual and asexual reproduction occur, when environmental conditions are favorable, asexual reproduction occurs rapidly. When unfavorable conditions stress the organism, sexual reproduction occurs and the offspring have an increased likehood that they will be better suited for the environment.

The characteristic spores of the sporophyte generation are known as oospores (produced endogenously) or basidiospores (produced exogenously).

Class	*Orders*	*Families*
Phycomycetes	Mucorales	Mucolaceae
Ascomycetes	Protoscales	Saccharomycetaceae
	Plectascles	Aspergillaceae
	Sphaeriales	Hypocreaceae
	Clavicipitates	Clavicipetaceae
Basidiomyctes	Polypolinales	Polyporaceae
	Agaricales	Tricholometaceae
		Amantiaceae
		Agaricaceae
	Phallinales	Phallinaceae
Fungi Imperfect	moniliales	Dematiaceae

1.2.1. PHYCOMYCETES

1.2.1.1. MUCORALES: Mucolaceae

These fungi have an aseptate mycelium: members include *Phytophthora infestans* which causes potato blight. In the Mucoraceae we have *Mucor* (40 spp.) and *Rhizopus* (8 spp.), which are among the moulds associated with badly stored food products. Some *Rhizopus* species are used industrially for the saccharification of starchy material and for producing of lactic acid from glucose; they are important in the microbiological conversions of steroids.

1.2.2. ASCOMYCETES:

1.2.2.1. PROTOASCALES: Saccharomycetaceae

Saccharomycetaceae This group includes the yeasts. some 30 species of Saccharomyces. Dried yeast is prepared from a strain of *S. cerevisiae*, used in brewing beer and baking, a rich source of proteins and vitamins B.

Saccharomyces cerevisiae is a versatile microorganism that can be exploited as a cell factory for biotechnological and pharmaceutical uses.

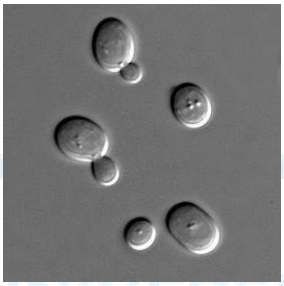


Figure (7): *Saccharomyces cerevisiae*

1.2.2.2. PLECTASCALES: Aspergillaceae

Penicillium **(over' 100s pp.) yields important antibiotics. such as penicillin; the immunosuppressant: mycophenolic acid, antihypercholesteremia: mevastatin and also antifungal agents like griseofulvin...**

A*spergillus*.(60 species); Cause number of disease called aspergillosis, in human ear cause otomycosis.

A. oruzae **may be noted, used in the manufacture of soya sauce and fermentation of alcholo.**

A. flavus **producing aflatoxin in poorly stored feeding material (maize, rice and pistachio nuts).**

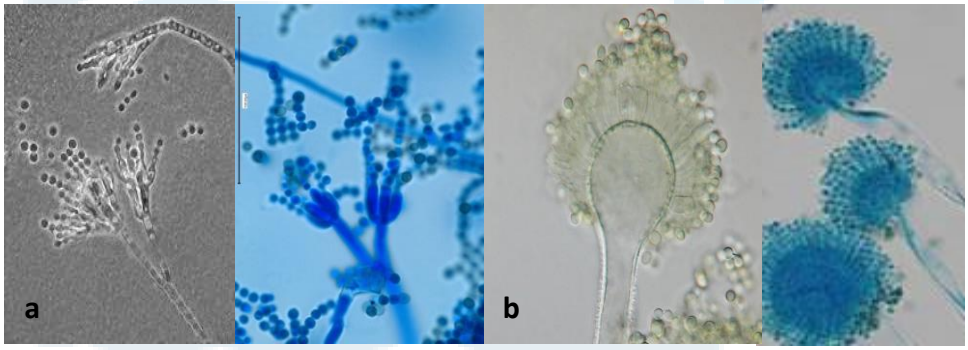


Figure (8): (a) *Penicillium sp.* – (b) *Aspergillus flavus*.

Aflatoxins, (mycotoxins) a group of highly toxic metabolites produced by *Aspergillus flavus* and *Aspergillus parasiticus*, and probably responsible for the high incidence of liver cancer in some parts of Africa. These compounds were first detected following the deaths of young turkeys fed on mould-contaminated peanuts (*Arachis hypogaea*; Leguminosae/Fabaceae).

The aflatoxins primarily affect the liver, causing enlargement, fat deposition, and necrosis, at the same time causing cells of the bile duct to proliferate, with death resulting from irreversible loss of liver function. In the case of aflatoxin B1, is most acutely toxic and carcinogenic example, it is metabolized in the body to an epoxide. The epoxide intercalates with DNA, this leads to inhibition of DNA replication and of RNA synthesis, and initiates mutagenic activity.

1.2.2.3. CLAVICIPITATES: Clavicipitaceae

Like other Ascomycetes. the ascospores are produced in a sac or ascus. Genera of the Clavicipitaceae include *Claviceps* (10 spp.).

Claviceps purpurea: a medicinal ergot is the dried sclerotium of the fungus (Clavicipitaceae) developed on the ovary of rye, Secale cereal (Graminae/Poaceae). Ergot is a fungal disease of wild and cultivated grasses, and initially affects the flowers. In due course, a dark sclerotium, the resting stage of the fungus, is developed instead of the normal seed.

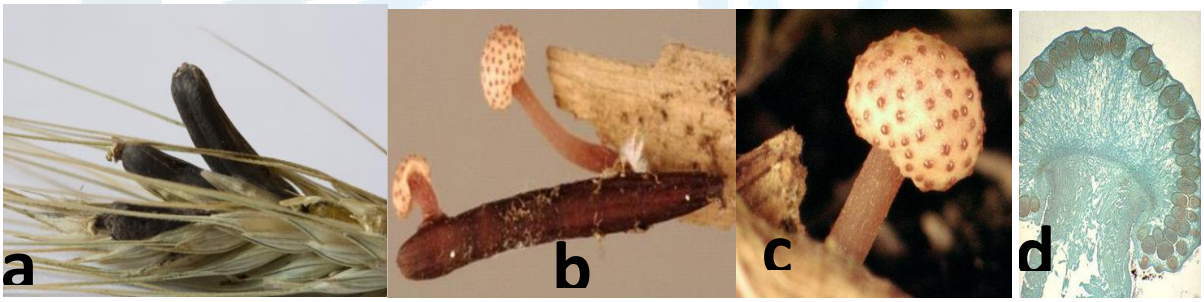


Figure (9): *C. purpurea*, (a: Grain head with sclerotia, b: Germinating sclerotium, c+d: stroma).

The vasoconstrictor effect leads to restricted blood flow in small terminal arteries, death of the tissue, the development of gangrene, and even the shedding of hands, feet, or limbs. Gangrenous ergotism was known as St Anthony's Fire; Despite these unpleasant effects, whole ergot preparations have been used since the 16th century to induce uterine contractions but this use turned to be dangerous and has led to fatalities.

The ergot sclerotia contain from 0.15–0.5% alkaloids:

Ergometrine is used as an oxytocic and is injected during the final stages of labour and immediately following childbirth, especially if haemorrhage occurs. Bleeding is reduced because of its vasoconstrictor effects, and it is valuable after Caesarian operations.

Ergotamine is used in the treatment of acute attacks of migraine, where it reverses the dilatation of cranial blood vessels.

Lysergic Acid Diethylamide or LSD; (synthesized derivative) This widely abused hallucinogen, known as 'acid', is probably the most active and specific psychotomimetic known. An effective oral dose is from 30 to 50 µg, even the trace amounts absorbed during its handling were sufficient to give its dramatic hallucinations.

1.2.3. BASIDIOMYCETES:

The Basidiomycete produce basidiospores, borne externally on the spore mothercell or basidium. They have septate mycelia which produce elaborate fruiting bodies (e.g. mushrooms).

1.2.3.1. POLYPORINALES: polyporaceae

The polyporaceae includes many genus like *polyporus, Ganoderma* and *Boletus*.

Polyporus officinalis (white agaric) was formerly used in medicine.

Boletus edulis is an edible mushroom.

Ganoderma lucida, originated from Asia, has long been used in Chinese medicine and its biologically active triterpenoids have attracted recent attention.

Figure (10): *Ganoderma lucida*

Ganoderma is highly regarded in Oriental medicine, research is conducted worldwide. From PubMed database, around 500 papers were published since the early 1970s, Most of these papers are on *Ganoderma*'s effect on the immune system and antioxidant activity.

Recent claims were made about its anti-tumor properties. Studies are currently conducted to study Ganoderma 's effect on cancer cells.

However, there are significant data supporting Ganoderma's effects on:

- Lowering blood pressure;
- Increase production of immune cells;
- Enhance immune cells activity;
- Antioxidant activity.

AGARICALES: agaricaceae and amanitaceae

Some members are edible like common mushroom or *Agaricus campestris* (from agaricaceae). others are poisonous like fly agaric, *Amanita muscaria* (from amanitaceae), producing muscarine a potent toxic alkaloid .

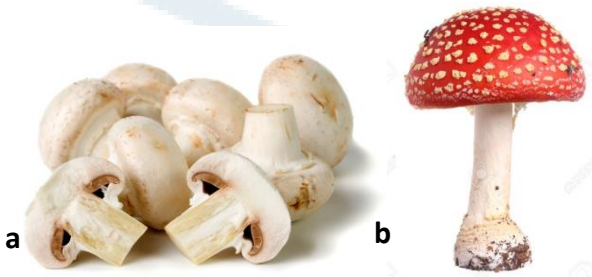


Figure (11): (a) *Agaricus sp.* – (b) *Amanita muscaria*.

1.3. LICHENS

A lichen is a symbiotic association of an algae and a fungal partner. With this mutualism both, fungi and algae, gain benefits. The algae, representing the food supplier, produces the carbohydrate while the fungi holds the structure and provides mineral elements.

Most lichenized fungi are from Ascomycetes, while 90% of the lichens consist of *Trebouxia sp.* as an algae.

Even though lichens are very resistant to natural environment extremes, they are extremely sensitive to air pollution particularly SO_2, thus they are considered as indicators of air pollution. Some, particularly in arctic regions, are used as food. Lichen dyes were formerly much used in the textile industry.

- ***Evernia prunastri*** **The 'oak moss' used as a fixative in perfumery is the lichen.**
- ***Iceland moss, Cetraria islandica*****, has been used for disguising the taste of nauseous medicines and with other species (e.g.** ***Cladonia*** **spp.) for the treatment of cough. Containing Polysaccharides (25-50%), it is used as a demulcent for the symptomatic treatment of oral or pharyngeal irritation and associated dry cough.**

  Cetraria islandica **grows in arctic and subarctic areas, in northern and eastern Europe, Siberia and North America and alpine mountains.**

Figure (12): ***Cetraria islandica*****, Iceland moss.**

2. BRYOPHYTA AND PTERIDOPHYTA

These two phyla are of relatively small pharmaceutical importance, but have some phytochemical interest.

2.1. BRYOPHYTA

They are the simplest and most primitive land plants, may be aquatic. They do not have roots, but have rhizoids, which are relatively simple, sometimes multicellular filaments of thin-walled cells that extend from the photosynthetic tissue into the soil.

They do not have true vascular tissue and are therefore non-vascular plants. They are composed of haploid cells, containing only one set of chromosomes, have a two-stage life cycle: gametophyte and sporophyte.

The gametophyte generation is a leaf-like thallus in the liverworts and a leafy plant with a stem in the mosses.

There are about 2,000 species of bryophytes, the phylum is divided in to two classes, Hepaticae (liverworts) and Musci (mosses). Both show alternation of generations.

Class	*Orders*	*Genera*
Hepaticae	*Jungermaniinales*	*Bazzania*
		Solenostoma
		Gymnomitrion
		Diplophyllum
	jubulineales	*Lunularia*
Musci	Sphagnales	*Sphagnum* (336 spp.)
	Dicranales	*Dicranum* (52 spp.)
	Funariales	*Funaria* (117 spp.)

Lunularia cruciata (liverworts): **it was believed that it could cure diseases of the liver (Doctrine of Signatures!!!), reduces erosion along stream banks.**

Asexual reproduction occurs by Gemma Cup (1n) Figure (13-a).

Sexual production: The female gametophyte Figure (13-b).bears the archegonial head containing the egg and the male gametophyte hold the antheridial head giving the swimming sperms. the sperm swims into the archegonium and fertilizes the egg; the embryo (2n) grows and produce spores by meiosis; then the spore grows into a thalus with rhizoids.

Figure (13): *Lunularia cruciata* (liverworts)(a), The female gametophytes (b)

2.2. PTERIDOPHYTA

The Pteridophyta includes the Filices (ferns), Articulatae (horsetails) and Lycopsida (club mosses).mostly terrestrial, may be aquatic. The plant body differentiates into root, stem and leaves. These plants present vascular tissues. A few are of medical importance.

Class	*Orders*	*Families*	*genus*
Filices	Filicales	*Polypodiaceae*	*Polypodium* (about 50 *spp.*)
			Dryopteris (about 150 *spp.*)
			Preridium (1 sp.)
Articulatae	Equisetales	*Equisetaceae*	*Equisetum* (32 *spp*)
Lycopsida	Lycopodiales	*Lycopodiaceae*	*Lycopodium* (about100 *spp.*)

Pteridium aquilinum: Common bracken is a herbaceous perennial plant, deciduous in winter. The large, roughly triangular fronds are produced singly, arising upwards from an underground rhizome, and grow to 1–3 m tall; the main stem, or stipe, is up to 1 cm diameter at the base.

It has been a recent cause of concern owing to its carcinogenic properties and known bovine poisoning. The use of the young shoots for culinary purposes is discouraged and avoidance of bracken spores in the atmosphere suggested. The toxic constituent is ptaquiloside, an unstable glycoside of sesquiterpene.

Figure (14): *Pteridium aquilinum*, Common bracken

Dryopteris filix-mas (Polypocliaceae): Male fern, The semi-evergreen leaves have an upright habit and reach a maximum length of 150 cm, with a single crown on each rootstock. The bipinnate leaves consist of 20-35 pinnae (leaflet) on each side of the rachis. The leaves taper at both ends, with the basal pinnae (leaflet) about half the length of the middle pinnae.

It is one of many ferns containing phloroglucinol derivatives. The pterosins (terpenes derivatives) are widely distributed in ferns and attracted considerable research.

Male fern crude drug consists of the dried rhizome, it is collected late in the fall, divested of its roots, leaves, and dead portions, and sometimes sliced longitudinally to facilitate drying; The dried rhizome was used as anthelmintics (taeniafuge and a vermifuge) to expel tapeworm, in very large doses it is a violent irritant, giving rise to acute gastro-enteritis.

Figure (15): *Dryopteris filix-mas*, Male fern.

Equisetum arvense (Equisetaceae): The sterile stems are 10–90 cm tall and 3–5 mm diameter, with jointed segments around 2–5 cm long with whorls of side shoots at the segment joints; the side shoots have a diameter of about 1 mm. Some stems can have as many as 20 segments. The fertile stems are of a succulent texture, off-white, 10–25 cm tall and 3–5 mm diameter, with 4–8 whorls of brown scale leaves and an apical brown spore cone 10–40 mm long and 4–9 mm broad.

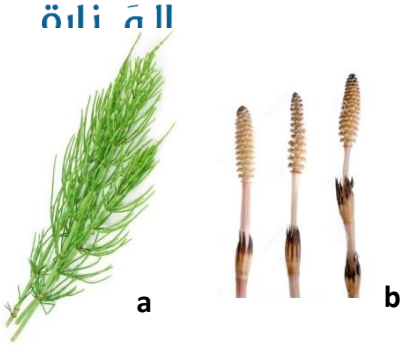


Figure (16): *Equisetum arvense*, horsetail, sterile stems (a), fertile stems(b) .

The dried sterile stems of the horsetail are used in herbal medicine and ale listed in the BHP. Preparations are used internally as a diuretic and anti-inflammatory agent to treat inflammation and mild infections of the genitourinary tract and externally for wound healing, fractures.....etc. . Horsetails give a high mineral ash containing considerable amounts of silica, thus it promotes strong bones and healthy skin, hair and nails..

There are apparently two chemotypes of the species with different flavonoids compositions. Correct identification of the herb is important, cause the related species *E. palustre* is poisonous (especially in cattle), It may cause vitamin B (Thiamin) deficiency.

Lycopodium clavatum (Lycopodiaceae): is a perennial evergreen plant that grows in pastures, woodlands of Northern Europe, and North America, it has a slender stem that trails along the ground and vertical branches that grow to 7.5-10 cm. The plant belongs to the Lycopodiaceae family and is related to mosses and ferns. It is often called club moss. Other names include wolf's claw and vegetable sulfur.

Lycopodium spores (crude drug) were the combination of hemisphere and tetrahedron in their shape, pale yellow, odorless, water resistant, and highly flammable. For this reason, it used to be a component of fireworks. It was also used for coating pills.

The spores of lycopodium are used:

- in quantitative microscopy (evaluation of crude drugs by microscope), Lycopodium spores are very characterized in shape and appearance and uniform in size (25µm) on average 94000 spores present/mg of lycopodium powder.
- to a limited extent in medicated snuffs
- as dusting powders and lubricants. As a dusting powder for rubber gloves. It has been known to give rise to dermatitis and mild caution has been expressed regarding its use as a lubricant non-stick agent for condoms relative to a possible cause of granulomas.

Figure (15): *Lycopodium clavatum*, lycopodium spores (b,c).

3. GYMNOSPERMS

The division Gymnospermae contains many fossil members of the 11 orders in the Engler classification, it is only necessary to mention five orders and 10 families:

The gymnosperms are one of the two great divisions of the seed-bearing plants or spermaphyta. They differ from the angiosperms in having ovules which are not enclosed in an ovary. A perianth is absent except in the Gnetales. The seeds usually contain one mature embryo with from two to 15 cotyledons embedded in endosperm. The wood is composed largely of tracheids, vessels being absent.

The word "gymnosperm" comes from the Greek word *gymnospermos*, meaning "naked seeds". Gymnosperm seeds develop either on the surface of scale or leaf-like appendages of cones, or at the end of short stalks.

The largest group of living *gymnosperms* are the conifers (pines, cypresses and relatives) and the smallest is ginkgo, a single living plant species found in China.

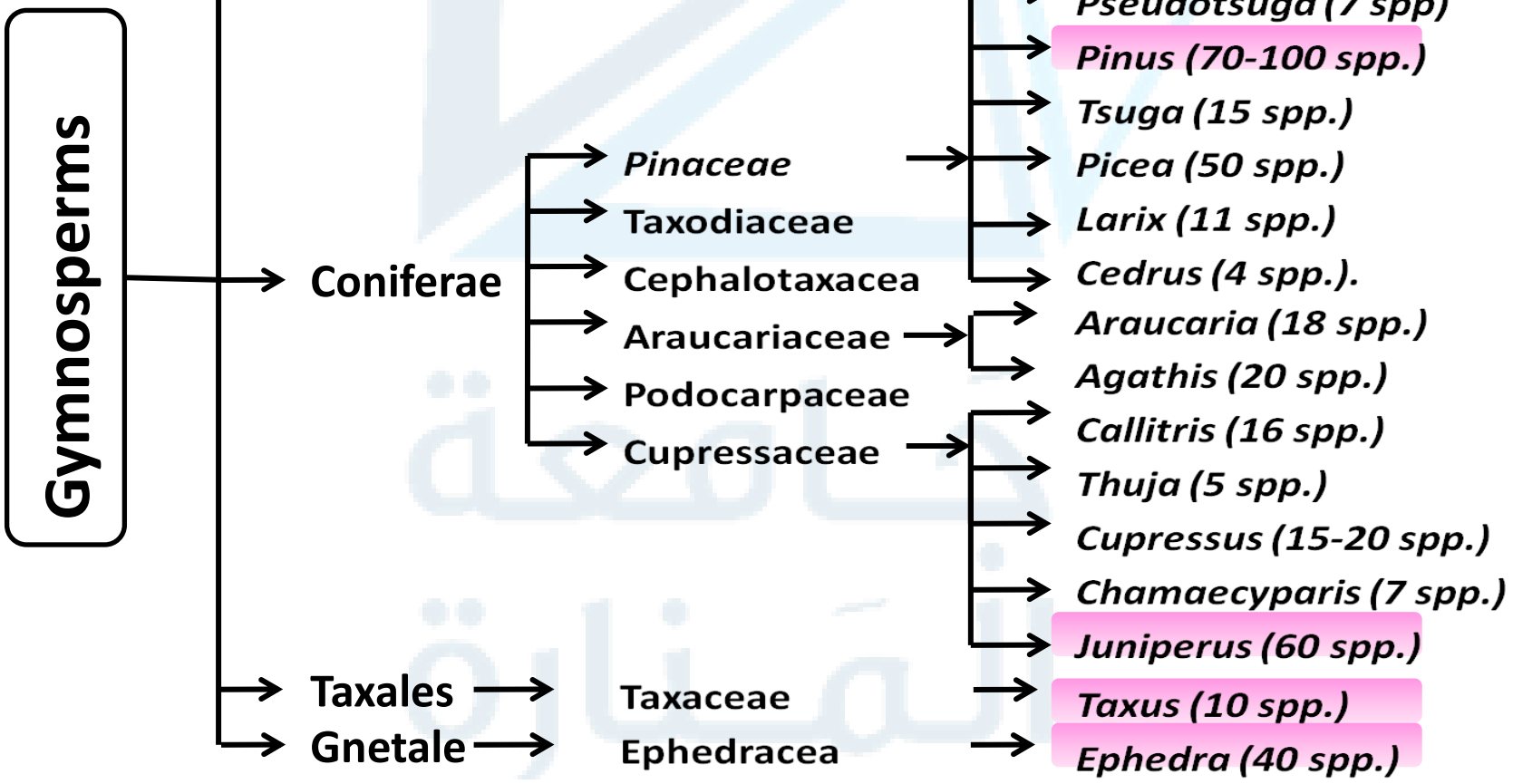


Figure (16): Classification of gymnosperms.

3.1. CYCADALES: CYCADACEAE

The order contains only 10 genera and about 100 species. The family Cycadaceae contains the single genus *Cycas* with 20 species. A sago, un edible starchy product from Southeast Asia, is obtained from the trunk pith of *Cycas circinalis* and *C. revoluta*.

3.2. GINKGOALES: GINKGOACEAE

With the exception of *Ginkgo biloba*, the maidenhair-tree, the plants of this order are found only as fossils. In recent years, owing to their increasing use for the treatment of various disease associated with the ageing process, the leaves of the ginkgo tree have been extensively investigated.

3.2.1. Ginkgo biloba L. (Ginkgoaceae)

Ginkgo is a primitive member of the gymnosperms and the only survivor of the Ginkgoaceae, also called the living fossil.

- Botanical characteristics

Ginkgo is a medium-large tree, a dioecious specie; The bark is pale grey and roughly rutted. The leaves are presented either alternately on long annual shoots, or in bunches on shorter shoots. They have a characteristic fan-shape and generally bilobed *(biloba*). The venation of the ginkgo tree runs parallel, a reminder that it was once related to the conifer at a much earlier stage in its development. In the fall the leaves turn a golden yellow color and fall to the ground.

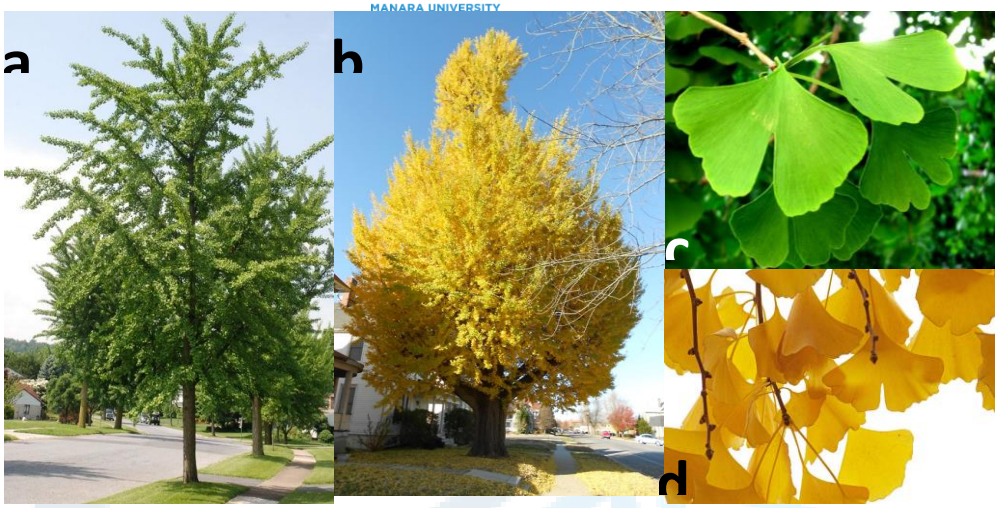


Figure (17): *Ginkgo biloba* tree (a; b: tree in the fall) & leaves (c; d: leaves in the fall).

Reproductive structures: Male ginkgo trees produce pollen in clusters of pollen sacs that resemble catkins 3-6 cm long. Pairs of green ovules are borne on female trees on stalks 4-5 cm long: Each ovule has a drop of fluid, the pollination drop, that traps pollen to enable fertilization, usually only one ovule develops into a seed.

Unlike the others gymnosperms members, ginkgo seed resembles a fruit because the seed coat has a fleshy outer layer. The seed hangs on a slender stalk, only 1 seed per stalk; Mature seeds are shed in the fall. The hard inner layer of the seed coat is light-colored, round to egg-shaped, and encircled by a small ridge.

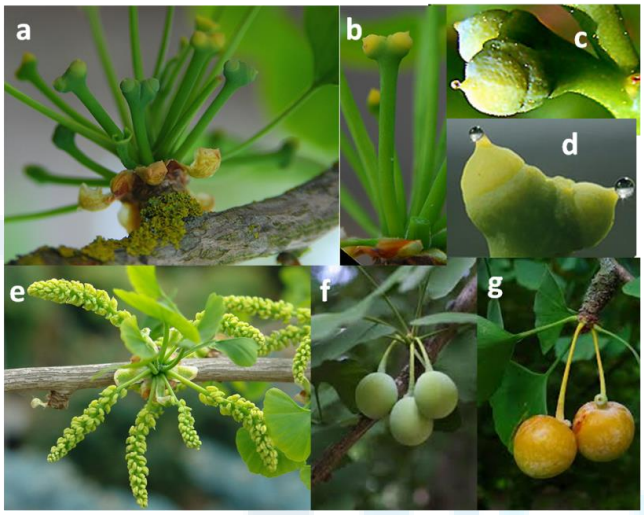


Figure (18): *Ginkgo*, ovules in clusters(a-b),enlarged ovules (c-d) pollen catkin (e), fruit (f-g).

- Habitat:

It is a tree native to China, but widely planted as an ornamental especially mal trees because the female trees produce an undesirable odor (foul smelling) as the seed coat starts to decompose. It is also cultivated for drug use in Japan, Korea, France and the United States.

- Chemical composition:

The active constituents have been characterized as mixtures of terpenoids and flavonoids.

- Uses:

Standardized extracts of the leaves are marketed against cerebral vascular disease and memory disorders. Extracts have been shown to improve peripheral and cerebro-vascular circulation.

The decline in cognitive function and memory processes in old age can be due to disturbances in brain blood circulation, and thus ginkgo may exert beneficial effects by improving this circulation, and assist with other symptoms such as vertigo, and hearing loss. Virtually all clinical studies report positive results regarding cerebral insufficiency.

3.3. CONIFERAE (or CONIFERALES):

3.3.1. PINACEAE

All members of the older are trees or shrubs: mostly evergreen with needle-like leaves: monoecious or dioecious. Sporophylls usually in cones. Resin ducts occur in all parts.

The Pinaceae are trees, rarely shrubs. Important genera are: *Abies* (50 *spp.*). *Pseudotsuga* (7 spp.), *Tsuga* (15 *spp.*), *Picea* (50 *spp.*). *Larix* (11 *spp.*), *Cedrus* (1 *spp.*). and *Pinus* (70-100 *spp.*).

They are abundant in the northern hemisphere and extend southwards to Indonesia and Central America.

Commercial use:

- They are of great value as timber (used to produce furniture) and paper-making material;
- Many species (e.g. *Pinus pinaster* or *P. maritima*) yield oleoresin "turpentine"; Other species are *Abies* balsamea. yielding Canada balsam used as an adhesive in optical devices;
- Source of essential oil (*Pinus sylvestris* L.) extracted by distillation from the leaves or the turpentine;

- The barks of larch (*Larix europaeus*) and hemlock spruce are tanning materials;
- *Pinus pinea* (the umbrella pine) produces large edible seeds (pignons);
- Some are used for ornamental purposes.

3.3.1.1. *Pinus sylvestris* L. (Pinaceae)

- Botanical characteristics:

pine is a large conifer, up to 30 m. It often has a crooked trunk, sparse branching and an irregular crown. Leaves are evergreen needles growing in bundles of two. Needles are stiff and twisted, 4 - 8 cm long, with sharp tips.

Pollen cones are small, 3-6 mm long, yellow to orange, borne in spring in clusters below new developing shoots.

Seed cones are borne in spring at the tips of new branches, emerging as tiny pink cones. After being pollinated, it takes 2 to 3 years for them to reach maturity and release their seeds. During the second season, the seed cones become brown and woody, about 2.5-5 cm long. When fully ripe, their scales open to release the seeds.

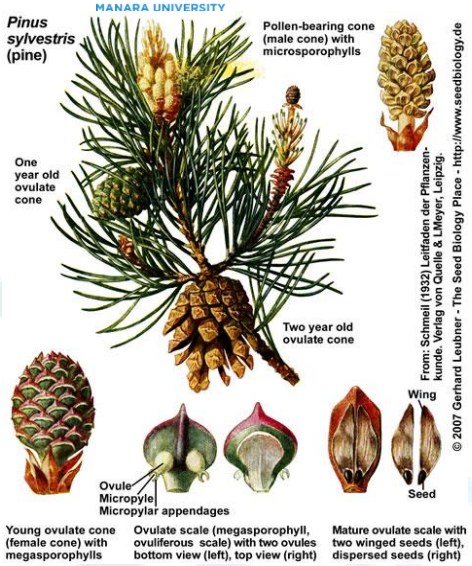


Figure (19): *Pinus sylvestris*

- **Habitat: Originated from Europe and Asia; It is widely distributed and many countries have considerable reserves of pine forest.**
- **Chemical composition:**

The active constituents have been characterized as mixtures of terpenoids (α-pinene, β-pinene and camphene).

- **Uses:**

the buds are traditionally used in the oral symptomatic treatment of cough and acute bronchial infections; Externally in the case of a stuffy nose of colds as well as analgesic in the oral and pharynx infection.

3.3.1.2. Colophony resin (rosin) and turpentine:

The pharmaceutical products colophony and oil of turpentine are regarded as being derived from oleoresin collected from some trees mainly pines.

The Turpentine oil (essential oil) is prepared by hydro-distillation of the crude oleoresin of pines, and the exhausted residue called colophony. the latter (colophonhy or rosin) contains resin acids (about 90%), neutral inert substance formerly known as resins and esters of fatty acid.

Collection of the crude oleoresin

Three methods of collection have been employed:

- Cup and gutter method (gum naval stores): the traditional way of collecting by peeling the bark and then incise the trunk of the living pine trees; The crude oleoresin flows is directed by means of gutters and then collected in suitable receiver. Trees can be tapped by this method for about 40 years, starting when the tree is about 20-30 years old.

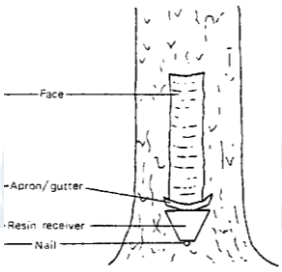


Figure (20): Cup and gutter method (gum naval stores)

The flow of oleoresin can be increased by the application of 50% sulphuric acid, as it has the effect of collapsing the thin-walled cells lining the ducts, thus enlarging the channels.

- Wood naval stores: in this case, pine stumps, usually over'40 years old, are used for the preparation of rosin (Colophony) and wood turpentine by extraction and distillation of the chipped wood (waste of wood industry).
- Sulphate naval stores: which are derived as by-products of the sulphate Kraft process for the pulping of softwoods during the production of paper, thus the sulphate turpentine and tall oil rosin is obtained.

Preparation of resin (rosin): The crude oleoresin arrives at the distillery in barrels. It is mixed in a heated stainless steel vessel with water about 20% weight of turpentine and after filtration is allowed to stand to separate water and other impurities. The diluted oleoresin is then transferred to copper or stainless steel stills and the turpentine is removed by steam distillation. When distillation is complete (1-2 h for 2.5 tones of oleoresin) the molten resin is run through strainers in to barrels. in which it cools and is exported.

Uses:

the use of turpentine is very limited in pharmacy; It was formerly used as oral expectorant, it is still used ,externally, as rubefacient. The main consumption is by the fragrance and aroma industry, in addition to the production of detergent and glue.

The amount of colophony used in pharmacy for the preparation of zinc oxide and other adhesive plasters, ointments. etc.. is relatively small. Much rosin is artificially

modified by hydrogenation or polymerization; products involving its use include paper, adhesives, printing inks, rubber, linoleum, thermoplastic for tiles and surface coatings.

3.3.2. CUPRESSACEAE

A family of 19 genera and 130 species of trees and shrubs.

Cupressaceae is another family of arborescent to shrubby conifers. The leaves are persistent, small, scale-like, opposite or in whorls. Male strobili (*pl.* strobilus, cones) are small; microsporophylls are somewhat peltate bearing 2 to 6 microsporangia. Female cones are on short branches bearing few scales; ovuliferous scales are flattened or peltate bearing 1 to 12 ovules.

Female cones are dry in *Thuja*, *Cupressus*, etc., but fused fleshy, berrylike in *Juniperus.*

The genera include *Callitris* (16 spp., Australasia), *Thuja* (5 *spp*. China, Japan and North America). *Cupressus* (15-20 *spp.*), *Chamaecyparis* (7 spp.), *Juniperus* (60 spp., northern hemisphere).

Commercial use:

- *Juniperus communis* yields juniper berries and volatile oil.
- *J. Virginiana* the red cedar wood used for pencils.
- *J. sabina*, volatile oil of savin; *J. oxycedrus*, by destructive distillation, yields oil of cade which was formerly much used in veterinary work. This tar-like oil contains cadinene and phenols.

3.3.2.1. *Juniperus communis* (Cupressaceae).

- Botanical characteristics:

Juniper berries are the dried ripe fruits of *Juniperus communis* (Cupressaceae). an evergreen dioecious shrub or small tree. It has needle-like leaves in whorls of three.

The female cones consist of scales arranged in whorls of three. The berry-like fruit takes 2 years to ripen, eventually becoming a deep purple colour and having a bluish-grey bloom.

On drying, the berries become somewhat darker and shrivel slightly. They are about 3-10 mm in diameter.

The seeds lie close together in the centre of the fruit and are hard and woody. Large oleoresin glands are partly embedded in the hard coat of each seed. The drug has a pleasant, somewhat terebinthinate odour. and a sweetish taste.

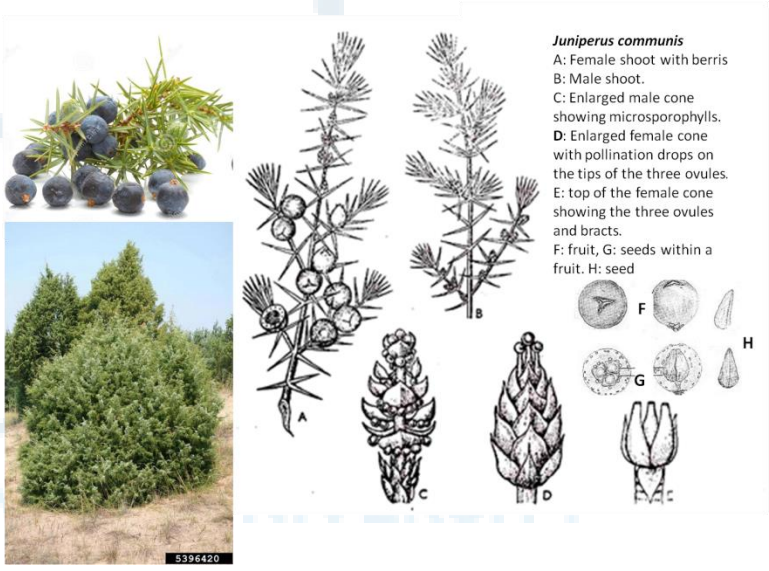


Figure (21): *Juniperus communis*

- Habitat: Europe; Western and Northren Asia; Africa and North America.

- Chemical constituents:

The main constituent are volatile oil (about 0.5-1.57%) and resin. Oil of juniper contains over 60 compounds, of which the terpenes, α-pinene and camphene. The oil from the leaves appears to contain a similar profile of compounds. Juniper berries are used for the preparation of oil of juniper and in making certain varieties of gin.

- Uses:

The oil has diuretic and antiseptic properties used in urinary infection, in addition to its benefits in solving urinary stones (α-pinene and camphene). It has been reported that commercial oils vary in composition and prolonged intake of some may cause kidney damage. these side-effects are correlated with a high terpene hydrocarbon content and a low proportion of terpinen-4-ol.

3.3.3. ARAUCARIACEAE

A family of beautiful trees with branches in whorls. Leaves needle-like with single vein or broad with parallel veins, spiral or distichous. Male cones large, catkinlike. Female cones are woody and very large.

Figure (22): *A. heterophylla*

Two genera and 38 species of trees. which sometimes have pungent leaves.

Araucaria (18 *spp.*), ornamental tree, provides useful timbers; and *Agathis* (20 spp.), the resins known as copals or animes, which are used for varnish. Manila copal is obtained from the Malaysian *Agathis alba*; and kauri copal from *A. australis*, the kauri pine, In Austlalia and New Zealand. The best copals are usually those found in the ground long after the trees are dead (sub-fossils).

Figure (23): fossil copal

3.4. TAXALES

An order of only one family Taxaceae, which includes the genera *Taxus* (10 spp.), *Amentotaxus*, *Austrotaxus*, *Pseudotaxus* and *Torreya*.

- Botanical characteristics:

Taxaceae also is a family of trees with small needle-like to falcate or scaly leaves borne spirally. Cones are small with spiral members. Bracts and ovuliferous scales are almost completely fused. There may be 2 to 9 ovules on an ovuliferous scale. Pollens are wingless. In addition to alkaloids a cyanogenetic glycoside and antitumor agent (taxol) have been reported in the genus.

3.4.1. *Taxus brevifolia* L. (the Pacific yew)

The Pacific yew, (Taxaceae) is a slow-growing shrub/tree found in the forests of North-West Canada (British Columbia) and the USA (Washington, Oregon, Montana, Idaho and N. Columbia).

Although the plant is not rare. it does not form thick populations. and needs to be mature (about 100 years old) to be large enough for exploitation of its bark. At this age, the tree will be some 6-9 m high, and have a trunk of about 25cm in diameter. The bark is removed from mature trees during the period May-August.

The wood of *Taxus brevifolia* not suitable for timber. and in some areas, plants have been systematically destroyed to allow cultivation of faster growing commercially exploitable conifers.

It is realized that this cannot be expected to provide a satisfactory long-term supply of the drug. It requires the bark from about three mature 100 year-old tree to provide one gram of taxol, and a course of treatment may need 2 grams of taxol. Current demand for taxol is in the region of 100-200kg per annum.

3.4.2. *Taxus baccata* Nutt.

The common yew (European yew / English yew) , produces valuable wood. The fruit has a fleshy red aril. All parts of the plant are very poisonous. Cattle and horses can die very rapidly after eating the leaves and stems (cyanogenetic glycoside).

Figure (24): *Taxus baccata* Nutt

- Habitat: The yew tree is distributed throughout the northern hemisphere, and occurs in eight distinct geographical regions.
- Chemical constituents:

The potent anticancer drug taxol, a nitrogenous diterpene, was first reported in the bark of *Taxus brevifolia*. Low yields from the bark and the lack of raw material leading to damage to forests by, often illegal, over-collection hampered the development of the drug.

The investigation of alternative sources has now led to:

1- Tissue culture procedures for the production of taxol but the yields are still low.

2- Semi-synthesis: A promising development involving a renewable source has been the isolation of 10-deacetylbaccatin III from the fresh needles of *Taxus baccata* in up to 0.1% yield, and its chemical conversion to taxol.

- Uses:

Taxol® (paclitaxel) is being used clinically in the treatment of ovarian cancers, breast cancers and non-small cell lung cancer. It may also have potential value against other

cancers. Taxotere® (docetaxel) is a side-chain analogue of taxol. which has also been produced by semi-synthesis from 10-deacetylbaccatin III. It has improved water-solubility and is used in treatment of breast cancers.

3.5. GNETALES

The order consists of three families (Gnetaceae, Ephedraceae and Welwitchiaceae), three genera and about 70-75 species. The Ephedraceae contains the single genus Ephedra, about 10 species of shrubs.

They occur in arid regions of the subtropics and tropics. their seed with two cotyledons is enclosed in a perianth, which becomes woody. Various species yield the drug ephedra and the alkaloide ephedrine.

3.5.1. Ephedra

Various species of *Ephedra* (Ma-huang) (Ephedraceae) are used as a source of the alkaloids ephedrine and pseudoephedrine, which may also be prepared by synthesis. Among these are the Chinese species *Ephedra sinica* and *E. equisetina* and the Indian and Pakistani *E. gerardiana, E. intermedia* and *E. major*, Although ma-huang was known to the Chinese over 5000 years ago and ephedrine isolated in 1887, it only came into extensive use during the last century.

3.5.1.1. *Ephedra sinica* Stapf.

- Botanical characteristics:

The plants are small bushes with slender aerial stems and minute leaves, giving the appearance of being effectively leafless. The stems are about 30 cm long, ashy greyish-green in colour, and slightly rough.

Figure (25): *Ephedra sinica* Stapf

- Habitat: native to Mongolia, Russia and northeastern China.
- Chemical constituents: The ephedras contain about 0.5-2.0% of alkaloids. Of the total, ephedrine (and its isomers) forms from 30 to 90%, according to the species. Pseudoephedrine (BPC 1979) is also present.
- Uses:

Ephedrine: It has bronchodilator activity, giving relief in asthma and hay fever, plus a vasoconstrictor action on mucous membranes, making it an effective nasal decongestant. Pseudoephedrine: is also widely used in compound cough and cold preparations and as a decongestant.

Pseudoephedrine is preferred because it has less side-effect than ephedrine. The ephedrine and pseudoephedrine used medicinally are usually synthetic.

The herbal drug ephedra is currently being traded as 'herbal ecstasy'. Consumption gives central nervous system stimulation, but in high amounts it can lead to hallucinations, paranoia, and psychosis. Dietary supplements containing Ephedra are sold as an appetite suppressant for weight loss and endurance enhancement; but, because of misuse and abuse, these have been regulated or even banned in some countries.

Ephedrine has repeatedly been implicated in adverse and sometimes fatal outcomes despite compliance with recommended dosages. The FDA cited significant cardiovascular risk of ephedrine like elevated blood pressure and tachycardia, in addition to psychosis and hallucinations.

The FDA bans over-the-counter sales of cold medicines that contain the ephedrine and the pseudoephedrine, so they are only available with a prescription.

4. ANGIOSPERMS

The angiosperms or flowering plants include more than 250 000 species of herbs, shrubs and trees. The sporophylls (stamens and carpels) are usually arranged with other leaves (the perianth) to form a 'flower'. The ovules are enclosed in a chamber (the ovary) formed from the carpels, and a stigma is provided for the reception and germination of the pollen. The emrbryo plant contained in the seed has one or two seed leaves or cotyledons. The wood almost invariably contains true vessels. The phylum is divided into monocotyledons and dicotyledons.

The division of angiosperms into these two large classes is based on the following factors:

1- In dicotyledons, the embryo bears two cotyledons, and only one in monocotyledons.

2- In dicotyledons, the primary root persists and gives rise to the tap root, while in monocotyledons, the primary root soon perishes and is replaced by a cluster of fibrous roots.

3- As a rule, leaf venation is reticulate in dicotyledons and parallel in monocotyledons (with but few exceptions). Further, in dicotyledons, the veinlets end freely in the mesophyll of the leaf, whereas in monocotyledons, veins or veinlets do not end freely.

4- The dicotyledonous flower usually has a pentamerous symmetry (petals in multiples of five), sometimes tetramerous (as in Cruciferae and Rubiaceae), while the monocotyledonous flower has a trimerous symmetry.

5- In the dicotyledonous stem, the vascular bundles are arranged in a ring and are collateral and open, while in the monocotyledonous stem, however, the bundles are scattered in the ground tissue and are collateral and closed. Hence, there is no secondary growth (with but few exceptions).

6- In the dicotyledonous root, the number of xylem bundles varies generally from 2 to 6, but in the monocotyledonous root there are many, seldom (5–8). The dicotyledonous root has the cambium, as a secondary meristem, and gives rise to secondary growth, but Secondary growth in monocots is not observed as cambium is absent.

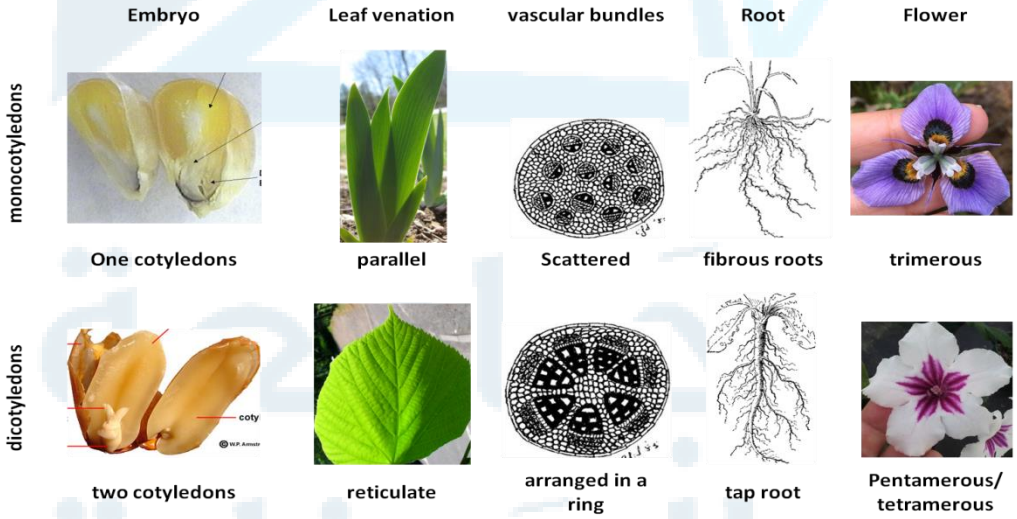


Figure (26): Monocot *vs.* Dicot

- Angiosperm Phylogeny Group (*)

The Angiosperm Phylogeny Group, or APG, refers to two international groups of systematic botanists who came together to try to establish a consensus view of the

taxonomy of flowering plants that would reflect new knowledge in angiosperm relationships based upon molecular systematic studies.

In 1998, the first Angiosperm Phylogeny Group (APG) classification of the orders and families of flowering plants (which we will term APG I; APG, 1998) was published, and this classification initiated a new approach to this long tradition. APG I was not written by one or two authoritative individuals; rather the APG process tried to produce a consensus classification that reflected results and opinions of experts in many groups of flowering plants.

Several important studies have been published since 1998, which resulted in successive publications of classification APG II in 2003, and APG III in 2009.

Higher-level classification of angiosperms has received continuing attention since APG III (2009) and enough progress has been made that an update to the APG classification is warranted, thus the latest classification APG IV was published in 2016, with some changes from APG III as a result of placements of some genera that required erection of new families, and we recognize several new orders.

(*) An update of the Angiosperm Phylogeny Group classification for the orders and families of flowering plants: APG IV. THE ANGIOSPERM PHYLOGENY GROUP; *The Linnean Society of London, Botanical Journal of the Linnean Society*, 2016, 181, 1–20.

4.1. MONOCOTYLEDONS:

As the name indicates, monocotyledons have an embryo with one cotyledon. Many members are herbs, usually with parallel-veined leaves. The stem has scattered, closed vascular bundles; the flowers are usually trimerous. Secondary growth in monocots is not observed as cambium is absent. As with the dicotyledons a much abbreviated form of Engler's classification indicating the main orders and families of pharmaceutical and phytochemical interest is given below.

Orders	Families	Orders (APG IV), 2016
Liliiflorae	Liliaceae	Liliales
	Colchicaceae	
	Smilacaceae	
	Dioscoreaceae	Dioscoreales
	Hypoxidaceae	Aspargales
	Agavaceae (Aspargaceae APG IV)	
	Iridaceae	
	Amaryllidaceae (Alliaceae)	
Microspermae	Orchidaceae	
Bromeliales	Bromeliaceae	Poales
Graminales	Gramineae (Poaceae)	
Cyperales	Cyperaceae	
Principes	Palmae (arecaceae)	Arecales
Spathiflorae	Aracea	Alismatales
	Lemnacea (Aracea)	
Scitamineae	Musacea	Zingiberales
	Zingiberaceae	
	Cannaceae	
	Marantacea	

4.1.1. Liliaceae

A widely distributed family of about 250 genera and 3700 species; mostly perennial herbs and climbers, and rarely shrubs or trees with a bulb or rhizome, or with fibrous roots.

Liliaceae may be recognised by their rather large flowers with six free and often spotted tepals three of which have nectaries, six stamens, and a superior ovary.

Many members of the family are cultivated for their flowers, ornamentals, like *Tulipa spp.* and *Lilium spp.*

Figure (27): *Tulipa* (a) and *Lilium* (b) (*Lys)* flowers.

4.1.2. Colchicacea:

4.1.2.1. *Colchicum autumnales* L.: (Eng. autumn crocus, meadow saffron)

- Botanical characteristics

It is a perennial herb with conduplicate, blade with midrib leaves up to 25 cm long.

The flowers are solitary (4–7)cm, with six tepals (undifferentiated sepal and petal)

and six stamens. The ovary is below ground at the level of the bulb, if it gets fertilized and seeds develop, they (seeds) will emerge the following year in the center of the foliage.

Colchicum is characterized by a particular vegetative cycle; In October a group of (2–6) trimerous flowers appears with perianth colored in purplish pink . After Hibernation (winter sleep), April to June, appear linear leaves with the fruit in the middle.

Figure (28): *Colchicum autumnales*

- Habitat: Europe and eastern shores of the Black Sea.
- Crude drug: seeds (very toxic) and bulbs.
- Chemical constituents: 0,3-1,2% Alkaloids, the major compound is colchicine.
- Uses: (Colchicine)
  - Colchicine is the classical drug for the treatment of acute attack of gout. It may act by reducing the inflammatory response caused by deposits of urate crystals in the joint.

- The colchicine is considered as a mitotic poison, as it binds to tubulin in the mitotic spindle, yet it can't be used as anticancer agent because it is very toxic, and this restricts its general use.
- Application in plants breeding (mutation led to new varieties of plant):

  Polyploidy can be artificially induced in many plants by colchicine, chromosomes will continue to divide without the formation of a mitotic spindle.

4.1.3. Dioscoreaceae:

Plant rhizomatous, lianes or vines classified in four genera according to the latest classification APG IV : *Dioscorea*, *Stenomeris*, *Tacca* and *Trichopus*.

4.1.3.1. *Dioscorea spp.* L.: Yam

- Botanical characteristics

About 600 species of *Dioscorea* are more or less herbaceous dioecious vines, with small and not very brightly coloured flowers borne along often branched inflorescences; The ovary is inferior and often ridged in fruit.

They are climbers recognized by their quite long-petiolate leaves with broad blades. The blade has several strong longitudinal veins and reticulate fine venation (dicotyledonous features).

Figure (29): *Dioscorea bulbifera* (a), inflorescence (b) and tubers (c)

- Habitat: Many species in the genus *Dioscorea* forms edible tubers (5-50 kg). They are cultivated for the consumption of their starchy tubers in Africa (*Dioscorea bulbifera*), Asia (India and China), and Latin America (Mexico).
- Chemical constituents: Steroidal saponins, like diosgenin, present in high levels in their tubers
- Uses:

In addition to being important sources of starch *(Dioscorea alata*), tubers of *Dioscorea spp.*(*D. composite* and *D. mexicana*) can contain very large amounts (4-8%) of steroidal saponins that provide the precursors of drugs like testosterone, progesterone, estrone, cortisone, and the like that are now synthesized by semi-synthesis.

Powdered *Dioscorea* (wild yam) root or extract is also marketed to treat the symptoms of menopause as an alternative to hormone replacement therapy, as there is little definitive evidence that diosgenin is metabolized in the human body to progesterone.

4.1.4. Aspargaceae APG IV (ex. Agavaceae)

4.1.4.1. *Drimia maritima (Urginea maritima)* (ex. Liliaceae)

- Botanical characteristics

The squill is a perennial mediterranean plant, with a large bulb (2-4 kg) formed by nested scales.

The leaves are tall and lanceolate (1m), They die away by fall, when the bulb produces a tall (1-2m) narrow raceme of trimerous flowers.

Figure (30): *Drimia maritima*

- Habitat: It is native to southern Europe, western Asia, and northern Africa.
- Chemical constituents: the bulb of squill contains cardiac glycosides (4%), called the bufadienolides.

- Uses:

The crude drug consists of the dried sliced bulbs; It is not usually used for its cardiac properties, as the glycosides have a short duration of action.

- white squill, white variety of *D. maritima,* it is employed as expectorant in preparations such as Gee's linctus. Large doses cause vomiting and a digitalis-like action on the heart.
- Red squill ,red variety of *D. maritima,* has mainly been employed as a rodenticide. Rodents lack a vomiting reflex and are poisoned by the cardiac effects.

4.1.5. Iridaceae

4.1.5.1. *Crocus sativus* L. Saffron

- Botanical characteristics

The plant is a small, perennial herb, 6–10 cm high.

The corms are planted in July–August. It gives long, linear green leaves forming tufts. In the following year flowering takes place in October–December. Each corm is replaced by daughter corms. The flower has 6 purple petals, 3 golden yellow stamens and one red pistil which shows as 3 stigmas (filaments).

The flowers are collected early in the morning. The style of each flower is separated just below the stigma and dried by artificial heat for 30–45 min. The drug is coated and stored in dry place.

About 1 kg of dried drug is collected from nearly 100,000 flowers.

- Habitat: The plant is native of south Europe and is found in Spain, France, Macedonia, Italy, Austria, China, Germany, Switzerland, and Iran. In India, the plant is cultivated in Kashmir.

Figure (31): *Crocus sativus* (c), (a) the stigmas and (b) the flower.

- Chemical constituents

The crude drug the (stigmas) has a reddish-brown colour, this is mainly due to the presence of carotenoid compounds, it contains volatile oil and aromatic compound which give a strong odour and aromatic taste.

- Uses:

Saffron is used as spice, a coloring and flavoring agent, and in cosmetic pharmaceutical preparations. Saffron has spasmolytic properties.

- Adulterant:

Saffron is frequently adulterated with styles, anthers and parts of corolla of Saffron. Exhausted Saffron, flowers, and floral parts of some Compositae like *Calendula* species, *Carthamus tinctorius* and dyed corn silk.

4.1.6. Amaryllidaceae

Most of this family members are subdivided into two subfamilies: Amaryllidoideae and Allioideae, formerly known as two distinctive families Amaryllidaceae and Alliaceae, respectively.

4.1.6.1. Allioideae

Allioideae can be recognized by their smell, their often rather fleshy and soft leaves, and their scapose umbellate inflorescence with medium-sized flowers that have superior ovaries.

Allium cepa (onion), *Allium sativum* (garlic) and many ornamental species

4.1.6.1.1. *Allium sativum* (garlic):

It is a perennial herb having bulbs with several cloves, enclosed in a silky white or pink membraneous envelope.

In Germany, garlic is consumed as a complement in the diet of hyperlipidemic patients. Garlic or its constituents exhibit various biological activities, such as antibacterial, antifungal, antiviral, and ant-diabetic effects.

4.1.6.2. Amaryllidoideae

Amaryllidoideae are usually bulbous herbs that can be recognized by their rather fleshy and two-ranked leaves and their scapose, umbellate inflorescence of generally large flowers with six stamens and an inferior ovary.

The bulbs of this subfamily are well-known for their toxic Alkaloids, at least one fatality in the UK being recorded in 1999 as a result of mistaken consumption of daffodil bulbs for onions.

Well-known genera of Amaryllidoideae: *Leucojum spp. Narcissus spp. Galanthus spp* and *Amaryllis spp.*

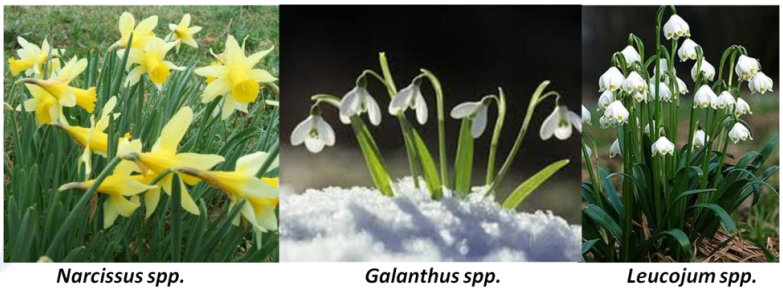
4.1.6.2.1. *Narcissus spp.* daffodil

The botanic name Narcissus stands for a genus of mainly hardy plants growing from bulbs, that all belong to the Amaryllidaceae family.

- Botanical characteristics:

Most of their species are spring flowering. A common feature of all species is the central corona that may have a trumpet-, bowl- or disc-like shape and is surrounded by six floral leaves, three sepals and three petals. The coloration of floral leaves and corona may be the same (e.g. yellow) or different and extends from white for the former to orange for the latter.

- Habitat: native to Europe, North Africa and Asia.



Narcissus spp. *Galanthus spp.* *Leucojum spp.*

Figure (32): Genera of Amaryllidoideae

- Chemical constituent:

The active secondary metabolites are alkaloids especially the Galanthamine, as it is shown to be a metabolite of many species of different genera of the family, like *Leucojum spp.*(snowflakes) and *Galanthus spp.*(snowdrop). Galanthamine originally isolated, in 1950s, from a species of *Galanthus* (snow-drop) found in the Eastern Europe used by the local people for muscle weakness.

- Uses

After large-scale production of galanthamine by extraction of daffodil bulbs (*Narcissus spp.*), successful clinical studies have led to the licensing of this compound in Europe as a symptomatic treatment for the early stages of Alzheimer's disease. The Drug, as Reminyl ®, was granted European marketing approval in July 2000.

4.1.7. Bromeliaceae

The Bromeliaceae contains about 44 genera and 1400 species, mainly tropical and subtropical plants. These interesting plants vary very much in size and habitat; many are grown as house-plants or in greenhouses. Genera include *Bromelia* (40 spp.) and *Ananas* (5 spp.). *Ananas comosus* (syn. *A. sativus*) is the pineapple, the juice of which contains bromelain, a protein-splitting enzyme which can be used in the treatment of trauma and oedema.

4.1.8. Poaceae (ex- Graminae)

The Gramineae contains about 707 genera and 11337 species. Mostly herbs with fibrous roots, rarely shrubs or trees. Annuals, biennials and perennials almost universally distributed and many of great economic importance. they have been the most important human food crops: rice from *Oryza sativa*, wheat from *Triticum*, barley from *Hordeum*, maize from *Zea mays* and sugar cane from *Saccharum officinarum*.

4.2. DICOTYLEDONS (EUDICOTS) (APG IV)::

The dicotyledons are herbs,. shrubs or trees, the seeds of which have two cotyledons. The leaves are usually reticulately veined and the typical stems structure is a ring of open vascular bundle. Dicotyledons flowers are usually pentamerous or tetramerous flowers. They may be unisexual (e.g. Salicaceae). but are more usually bisexual. The perianth may or may not be differentiated into sepals and petals. and the latter may be free from one another or fused.

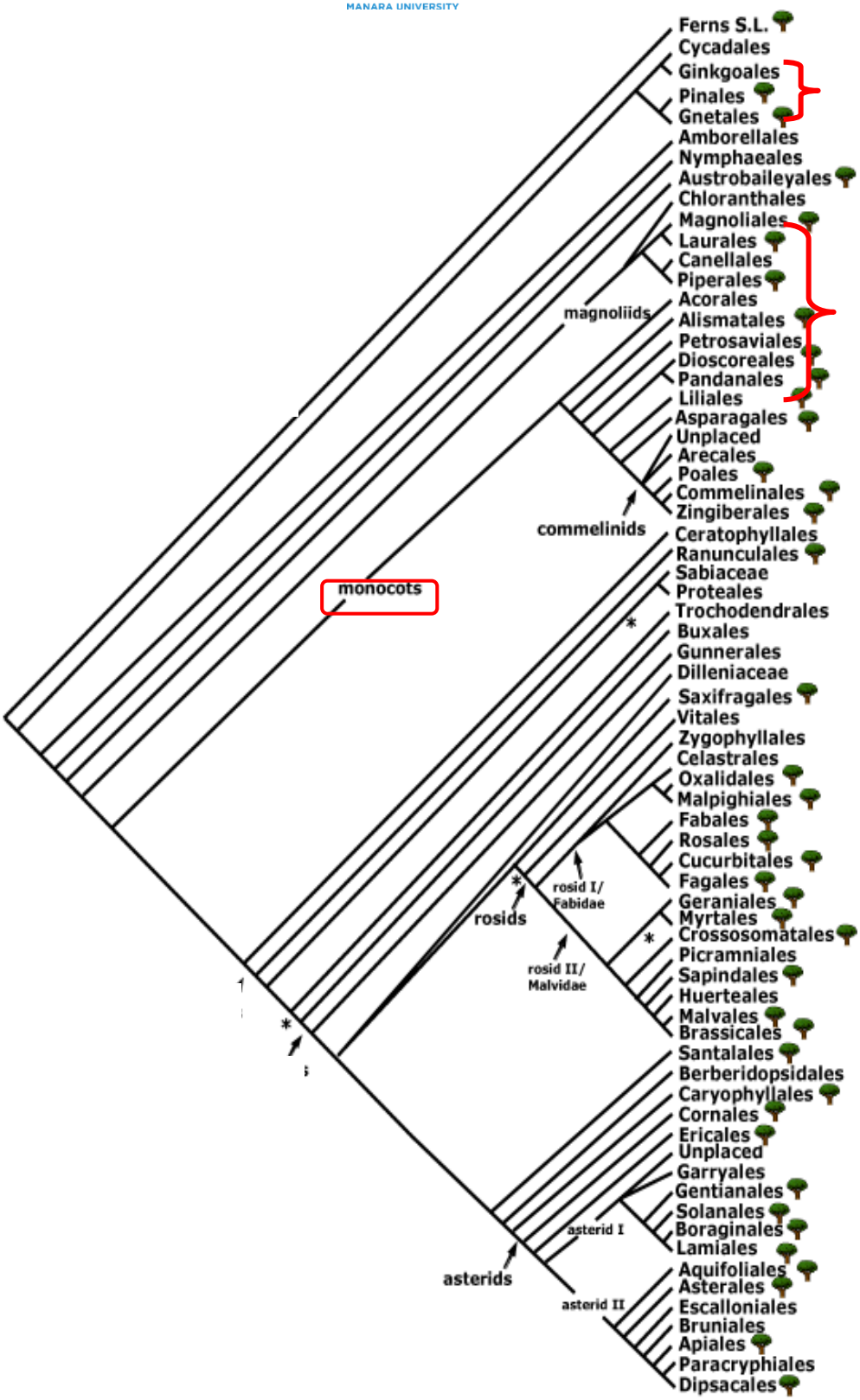


Figure (33): Phylogenetic tree (APGIV)

4.2.1. RANUNCULALES (APG IV)::

An order of seven families

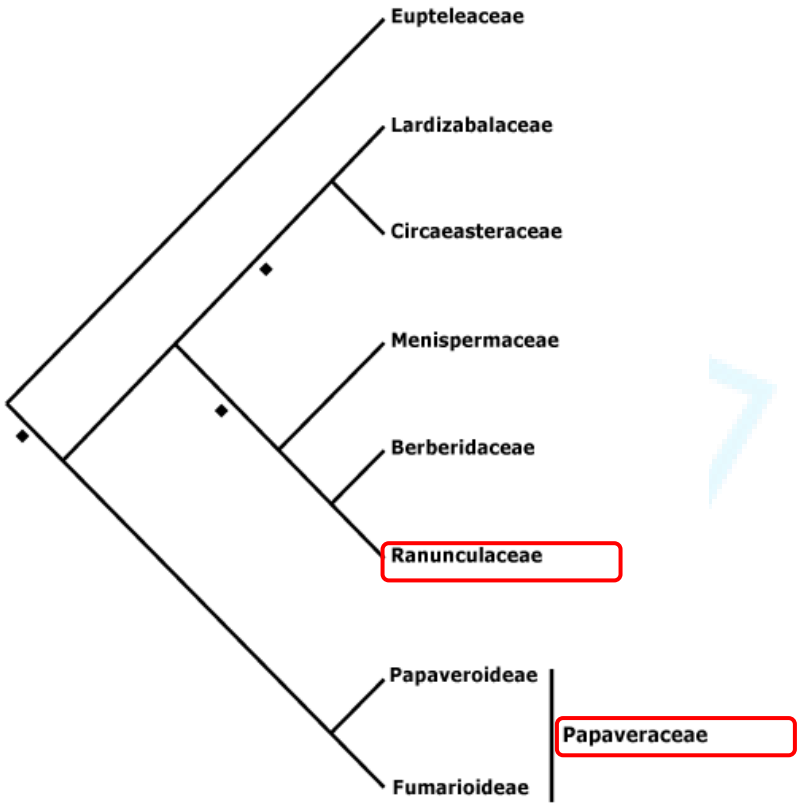


Figure (34): Phylogenetic tree of Ranunculales (AP website)

4.2.1.1. Ranunculaceae:

The family Ranunculaceae is in the major group Angiosperms. Nearly 2,525 species of *Ranunculaceae* belong to 62 plant genera. Many well-known wild and cultivated flowers *(Anemone spp.*)in the temperate zones, some used as a spice like *Nigella sativa.*

Distribution: Worldwide but mostly in temperate and boreal regions of the Northern Hemisphere.

Remarkable features: Mostly herbs, some are aquatic, and a few are low shrubs or vine, leaves with sheathing base, blade often divided, flowers bisexual, petals with nectary, stamens and carpels numerous, free and spirally arranged, ovary superior, fruit a follicle or achene.

Major genera: *Ranunculus* (400 species), *Clematis* (200), *Delphinium* (250), *Aconitum* (245), *Anemone* (150) and *Thalictrum* (100).

4.2.1.1.1. *Ranunculus ficaria* L.*:* pilewort

perennial herbs, fruit achene, distinct calyx and corolla, 6 bright yellow petals with nectary at base.

The fleshy tubers (tuberous roots) resemble hemorrhoids (piles), and according to the doctrine of signatures this resemblance suggests that pilewort could be used to cure hemorrhoids (traditionally).

- Chemical constituents: the tuberous roots are very rich in saponines.

Figure (35): *Ranunculus ficaria* L.*:* pilewort

4.2.1.1.2. *Aconitum napellus L.:* wolfsbane or aconite

perennial herb with tuberous root, palmately divided leaves. The flowers are dark purple to bluish-purple, narrow oblong raceme appears showy in early-midsummer.

- Habitat: native and endemic to western and central Europe.
- Chemical constituents: the tubers contains alkaloids of which the most important is aconitine.
- Uses: Aconite is a very potent and quick-acting poison which is now rarely used internally. The Aconitum spp. was formerly used as arrow poisons in China, India and other parts of Asia.

Figure (36): *Aconitum napellus L.* botanical illustration.

4.2.1.2. Papaveraceae:

Papaveraceae are usually herbs with an exudate of some kind whose fleshy leaves have broad bases. The flowers are 2-merous, and the calyx and corolla are clearly distinguishable; the gynoecium has two (or more) carpels, parietal placentation, and usually a short style.

4.2.1.2.1. Papaveroideae:

Papaveroideae are usually herbs that may be recognized by their often soft or rather rough-hairy leaves, copious latex, and flowers with two, large, fugacious sepals enclosing the bud, crumpled petals, usually numerous stamens, and syncarpous gynoecium with at most a short style and parietal placentation. The fruit is generally a capsule, with numerous seeds.

All members contain latex tissue. The latex is sometimes in vessels which accompany the vascular system. The subfamily is rich in alkaloids. Some, such as the opium alkaloids are of great medical and economic importance.

4.2.1.2.1.1. *Papaver somniferum* L.: opium poppy

- Botanical characteristics:

The opium poppy, is an annual herb about 50-150 cm in height. The leaves are about 10 cm in length, entire and sessile. The margin is dentate but varies somewhat in the different varieties.

The flowers, which are borne on a slightly hairy peduncle, are solitary, nodding in the bud, They are large flowers of white, pink, or dull red–purple colour.

The ovary contains numerous ovules attached to parietal placentas. It bears at its apex a flat disc formed by the union of the radiating stigmas. The capsule opens by means of small valves, which are equal in number to the carpels and situated immediately below

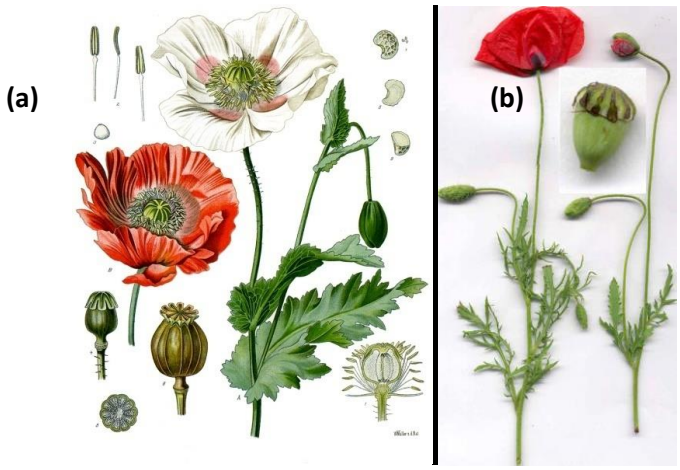


Figure (37): *Papaver somniferum* botanical illustration (a), *Papaver* rhoes (b)

The crude drug is called the opium; it is the air-dried milky exudate, or latex, obtained by incising the capsules of the opium poppy.

- Opium production: the capsules are carefully incised with a knife to open the latex tubes. Cuts are made transversely or longitudinally according to custom. The initially white milky latex quickly oozes out, but rapidly turns brown and coagulates.

The main producer of medicinal opium for the world market is India, with China producing supplies for its own domestic use. Poppy straw is cultivated in Australia, France, Hungary, Spain, and Turkey, and more recently in the United Kingdom. Almost all (more than 90%) of the opium destined for the black market now originates from Afghanistan; other sources include Southeast Asia, (mainly in Myanmar (Burma) and Laos) and Latin America (principally Mexico and Colombia).

- Chemical constituent: Opium contains some 30 alkaloids. according to the British pharmacopeae the opium is required to contain not less than 10% of morphine and not less than 2% of codeine.
- Uses:

Opium has been known and used for 4000 years or more. Crude opium has been used since antiquity as an analgesic, sleep-inducer (narcotic), and for the treatment of coughs.

In modern medicine, only the purified opium alkaloids and their derivatives are commonly employed, like morphine, a powerful analgesic and narcotic, and codeine as an analgesic and antitussive.

4.2.1.2.1.2. *Papaver rhoes*: red poppy

red poppy is known as an agricultural weed, the petals are used to make a sedative syrup as they contain alkaloids with mild sedative action

4.2.1.2.2. Fumarioideae:

Fumarioideae are often fleshy herbs with watery sap and distinctive 2-merous mono- or disymmetric flowers that are usually spurred; the calyx is usually very small or almost invisible, certainly not green and enveloping the flower bud, and there are usually six stamens.: they contain a watery, not milky, juice. Isoquinoline alkaloids are a feature of the family.

4.2.1.2.2.1. *Fumaria officinalis*: fumitory

F. officinalis or fumitory The whole herb, which features in a number of commercial Indian preparations, is used for liver disorders; It contains isoquinoline alkaloids.

Figure (38): *Fumaria officinalis*, fumitory

4.2.2. MALPIGHIALES (APG IV)::

Sieve tubes, extra-floral nectarines with leaf margin toothed. An order of 36 families, 716 genera, 16,065 species.

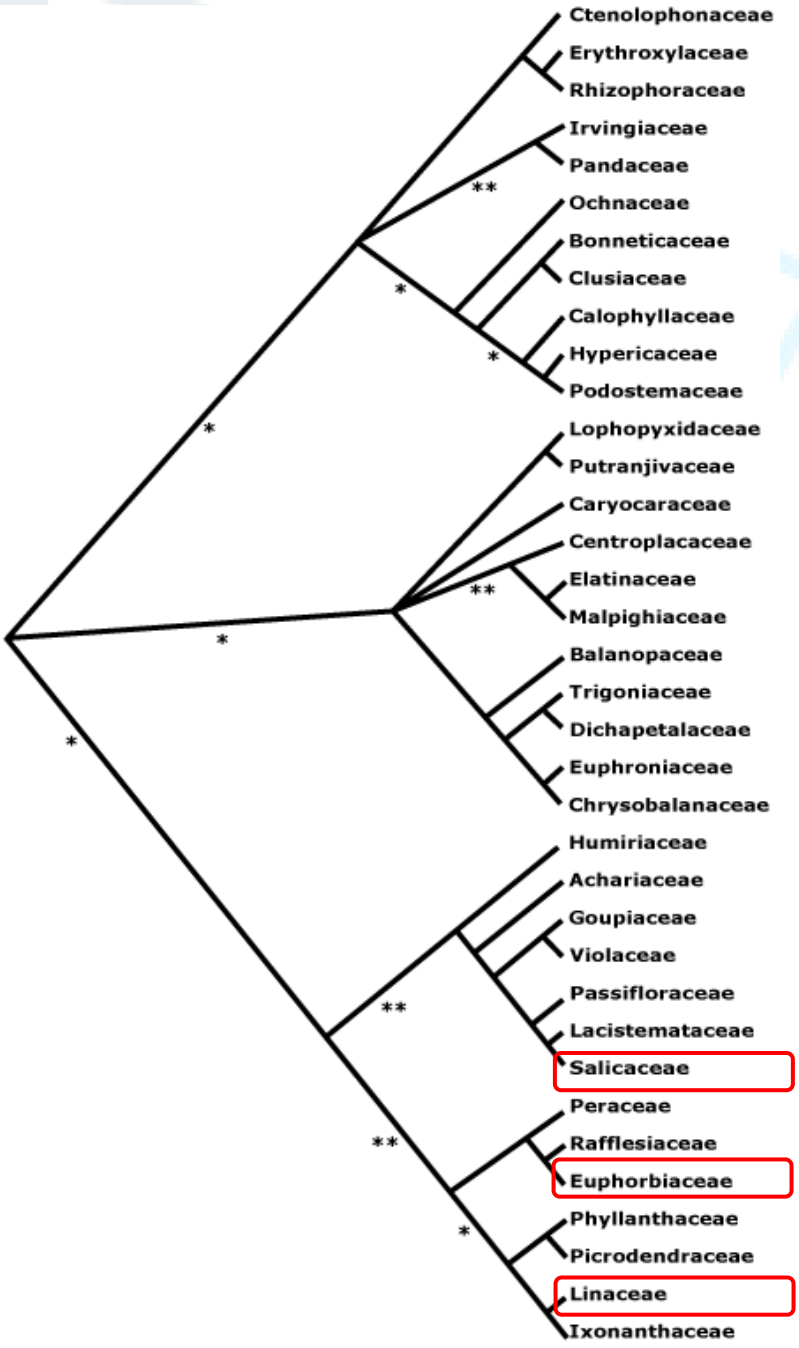


Figure (39): Phylogenetic tree of Malpighiales (AP website)

4.2.2.1. Euphorbiaceae :

A family of 218 genera and 6,745 species.

- Remarkable features: Plants usually with milky latex, leaves alternate, flowers unisexual, carpels 3, 3 chambered ovary superior.
- Distribution: Distributed widely in tropical and subtropical regions, with few species in temperate regions.
- Major genera: Euphorbia (2420 species), Croton (1300), Acalypha (430), Manihot (100) and Jatropha (180).
- Economic importance: The family includes a number of valuable plants:
  1. *Hevea brasiliensis* (rubber tree) is the source of natural rubber. Rubber is also obtained from *Manihot glaziovii* (ceara rubber).
  2. Thick roots of *Manihot esculentus* (cassava or tapioca) are important source of starch in tropical regions.
  3. Castor oil obtained from *Ricinus communis* is used as purgative.

4.2.2.1.1. *Ricinus communis* L.:

perennial herb, palmately lobed leaves (5-12 lobes); terminal inflorescence in cluster. The fruit is a spiny, greenish to reddish-purple capsule containing large, oval seeds.

- Chemical constituent: seeds oil or Castor oil contains triglycerides & fatty acids.
- Habitat: endemic to southeastern Mediterranean Basin, Eastern Africa, and India, today it is widespread throughout tropical regions.

- Toxicity: The shiny, bean-like seeds are highly poisonous for containing the Ricin, a toxic protein.
- Uses: Castor oil is used as laxative and purgative after a detoxification process.

Figure (40): *Ricinus communis* L.

4.2.2.2. Salicaceae:

- Remarkable features: Deciduous trees and shrubs, leaves with salicoid teeth, flowers unisexual, inflorescence a catkin, naked flowers (apetalous), 2 carpels with many ovules and hairy seeds.
- Distribution: Distributed widely, mainly in north temperate to arctic regions, in moist open habitats.
- Major genera: *Salix* (450 species) and *Populus* (35).
- Economic importance: The family is important for several species grown for ornamentals and wood production like willow (*Salix spp.*); The bark of Salix contains salicylic acid, which is constituent of aspirin.

4.2.2.2.1. *Salix* alba, *Salix purpurea* and *Salix fragilis*: Willow

The crude drug, Willow bark, is an ancient remedy, much esteemed for its analgesic, anti-inflammatory and febrifuge (anti-fever) properties.

Figure (41): *Salix* alba botanical illustration.

4.2.3. FABALES (APG IV)::

An order of 4 families, 754 genera, 20140 species.

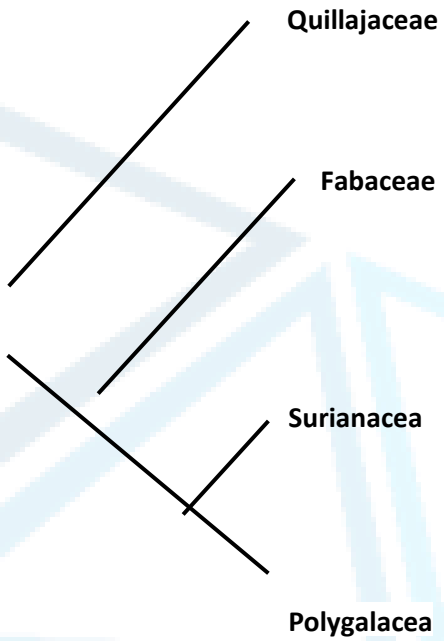


Figure (42): Phylogenetic tree of Fabales (AP website)

4.2.3.1. Fabaceae: ex-Leguminosae

A family of 766 genera /19,580 species

- Remarkable features: Fabaceae may be recognized by their compound, stipulate leaves whose leaflets are entire, and papilionoid flowers with a single carpel, free petals (or two may be connate). The fruit is usually dry and elongated called a pod. The often flattened seeds are borne in a single series.
- Distribution: Cosmopolitan in distribution, primarily in warm temperate regions.

- Economic importance: ranking second to Poaceae. It is the source of several pulse crops such as kidney bean (*Phaseolus vulgaris*), lentil (*Lens esculenta*), chick pea (*Cicer arietinum*) and pea (*Pisum sativum*). Soybean (*Glycine max*) and peanut (*Arachis hypogaea*) yield oil and high-protein food.

4.2.3.1.1. *Cassia angustifolia*: Senna

Senna leaf and fruit are obtained from *Cassia angustifolia* (India and Pakistan), or less commonly from *Cassia senna* (*syn Cassia acutifolia*), which is described as Alexandrian senna (Sudan).

Early harvests provide leaf material, whilst both leaf and fruit (senna pods) are obtained later on.

- Chemical constituent:

The active constituents are anthraquinone glycosides, principally sennosides A and B.

There are no significant differences in the chemical constituents of the two sennas, or between leaf and fruit drug,

However, amounts of the active constituents do vary, and this appears to be a consequence of cultivation conditions and the time of harvesting of the plant material.

- **Uses: Senna (leaves and fruits) is a stimulant laxative and acts on the wall of the large intestine to increase peristaltic movement.**

Figure (43): *Cassia spp.* Senna

4.2.4. ROSALES (APG IV):

An order of 9 families, 261 genera and 7725 species.

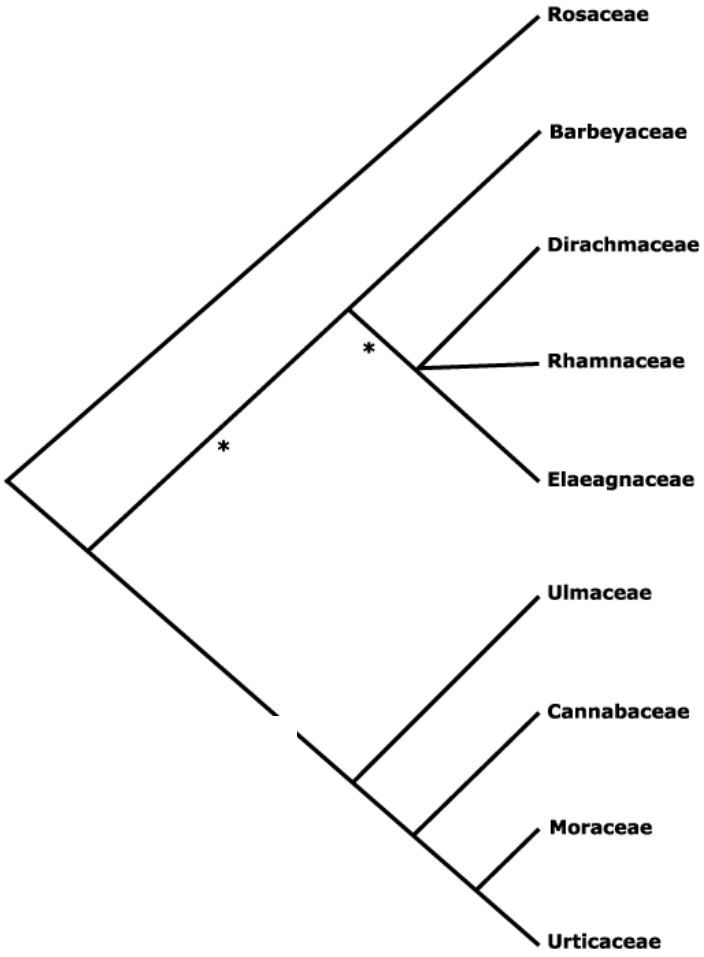


Figure (44): Phylogenetic tree of Rosales (AP website)

4.2.4.1. Rosaceae :

A family of 90 genera and nearly 3,000 species

Widespread but best represented in the Northern Hemisphere, mainly in the temperate and arctic climate.

- Remarkable features: Herbs shrubs or trees, leaves usually serrate, stipules conspicuous, flowers actinomorphic (star-shaped), usually perigynous and

with hypanthium, sepals and petals 5 each, petals usually well-developed nectary on hypanthium or base of stamens, stamen numerous, carpel single or numerous and free, rarely united, fruit usually fleshy.

- Major genera: *Rubus, Prunus , Crataegus , Rosa , Alchemilla, Pyrus, Malus, Geum and Fragaria.*
- Economic importance: The family is largely known for its temperate fruits: apple (*Malus domestica*), pear (*Pyrus*), cherries (*Prunus avium, P. cerasus*) peaches (*Prunus persica*), almonds (*Prunus dulcis*), apricots (*Prunus armeniaca*), strawberry (*Fragaria vesca*), raspberries (Rubus), quince (Cydonia), etc.

Popular ornamentals include species of *Rosa*, (rose) *Rubus* (raspberry) and *Crataegus* (hawthorn). Flowers of *Rosa damascena* are used for extracting attar of roses. Several species are also valuable sources of timber.

4.2.4.1.1. *Crataegus monogyna* Jacq.: common hawthorn

C. monogyna is a shrub or small tree of (4-14m) with a thick crown. The younger stems bear sharp thorns. Leaves, deeply lobed (3-5), are arranged alternately on the branch.

Flowers are borne in compact clusters (5-25) together; each flower is about 10mm diameter, and has five white petals, numerous red stamens, and a single style; they are moderately fragrant.

Fruits are round dark-red berry, up to 6 mm, structurally a pome (false fruit) containing a single seed (*monogyna*)

Chemical constituents: The leaves and the flowers contain 1-2% of flavonoides and 2-3% proanthocyanidols.

Habitat: native to Europe, northern Africa and western Asia.

Uses: It was shown that the extracts of the leaves and the flowers of hawthorn have positive effect in cardiac insufficiency and hypertension.

Figure (45): *Crataegus monogyna* common hawthorn.

4.2.4.2. Rhamnaceae

A family of 52 genera and 1055 species

- Distribution: worldwide, more common in tropical and subtropical regions.

- Remarkable features: Trees and shrubs, leaves toothed with strong secondary veins, flowers perigynous, petals strongly concave, stamens opposite the petals, hypanthium with nectary inside, ovules on basal placentas.

- Major genera: *Rhamnus*, *Ziziphus, Ceanothus* and *Gouania*.

4.2.4.2.1. *Ziziphus jujuba* Mill.: produces edible fruits, known as French jujubes and are used in traditional Chinese medicine as a mild sedative.

4.2.4.2.2. *Rhamnus spp.*: the bark of two *Rhamnus* species are well known as purgative drugs:

- *Rhamnus purshiana* DC. (*Frangula purshiana* Cooper): cascara bark.
- *Rhamnus frangula* L. (*Frangula alnus* Mill.) Alder buckthorn

The active constituents of these plants are purgative quinones (anthraquinones. anthranols and their glycosides).

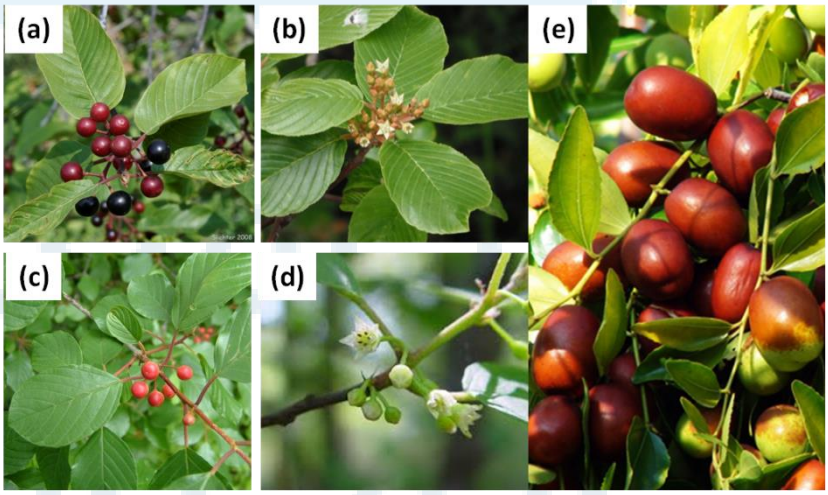


Figure (46): *Rhamnus purshiana* (a-b), *Rhamnus frangula* (c-d) and *Ziziphus jujuba* (e)

DC: de Candolle, Augustin Pyramus - France , Switzerland. Mill. Miller, Philip (1691-1771)- United Kingdom.

4.2.5. MALVALES (APG IV):

An order of 10 families, 338 genera and 6005 species.

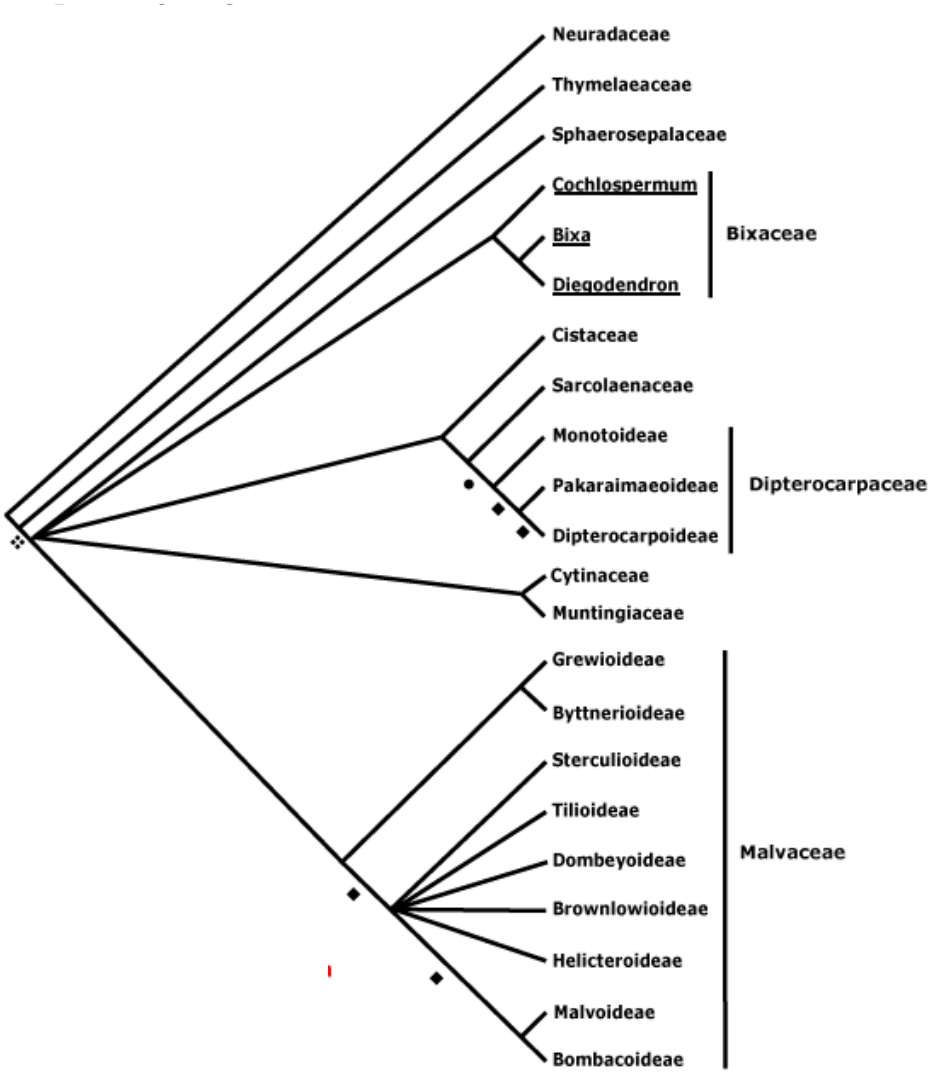


Figure (47): Phylogenetic tree of Malvales (AP website).

4.2.5.1. Malvaceae (APG IV):

A family of 9 subfamilies with 243 genera and 4,225 species.

- Distribution: in tropical and temperate climates, mainly in the South American tropics.
- Remarkable features: Herbs and shrubs with stellate pubescence, often mucilaginous, leaves palmately veined, stipules prominent, flowers usually with epicalyx, stamens numerous with united filaments, anthers monothecous, carpels five or more, ovary superior, placentation axile.
- Economic importance:

The family is represented by several ornamentals *Hibiscus spp*. and hollyhock (*Althaea rosea*); Young fruits of okra (*Hibiscus esculentus*) are used as vegetable; *Malva sylvestris* and *Corchorus olitorius*, both are consumed as local potherb.

Cotton is obtained from the seed hair (protective fiber of the capsule) of *Gossypium sp*.

Cocoa (chocolate source) is obtained from seeds of *Theobroma cacao*, *Cola nitida* (both formerly under Sterculiaceae and recently Sterculioideae APG IV) yields cola.

4.2.5.1.1. *Malva sylvestris* L.: common mallows

- Botanical description: This perennial herb of the MALVACEAE family is a velvety plant. The leaves are short-petioled, shallow-lobed (3-7) with dentate margins.

The flowers, bright pinkish-purple with dark stripes, appear on an axillary clusters with 5 petals and triangular sepals.

- **Chemical constituents: Leaves and flowers contain mucilage (polysaccharid), phenols and flavonoids.**
- **Medicinal Use: Due to its high mucilage content, mallows make excellent soothing demulcent herbs, especially for cases of inflammation and irritation, either for the urinary, digestive or respiratory systems.**

It is also used in the symptomatic treatment of constipation, and digestive disorders.

Figure (48): *Malva sylvestris* L.: common mallows

4.2.6. SOLANALES (APG IV):

An order of 5 families, 165 genera and 4,125 species.

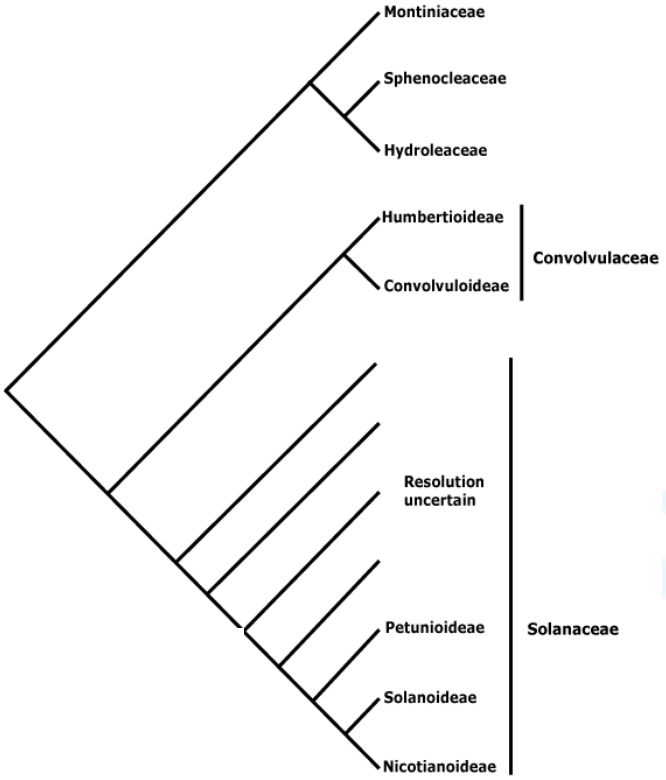


Figure (49): Phylogenetic tree of SOLANALES (AP website).

4.2.6.1. Solanaceae

A family of 102 genera and 2,460 species.

- Remarkable features: Leaves alternate, stipules absent, flowers actinomorphic, carpels 2, ovary superior, 2-chambered, placenta swollen, ovules numerous, fruit a berry or capsule.
- Major genera: *Solanum* (≈1300 species), *Lycianthus*, *Cestrum*, *Nicotiana*, *Physalis, Lycium, Capsicum, Hyoscyamus & Datura.*
- Economic importance: The family includes a number of food plants such as tomato (*Lycopersicon esculentum*), potato (*Solanum tuberosum*), egg plant

(*S. melongena*), ground cherry (*Physalis peruviana*). Peppers (*Capsicum annuum*) are used both as a food source (young) and spices (ripe). Many poisonous species are important drug plants such as *Atropa belladona* (atropine), *Hyoscyamus niger* (hypnotic drug), *Datura stramonium* (stramonium).

Tobacco (*Nicotiana tabacum* and *N. rustica*) contains toxic alkaloid nicotine and is grown for chewing, smoking and snuff. and many ornamental genera include *Cestrum* (night blooming jessamine) and *Petunia*.

4.2.6.1.1. *Nicotiana tabacum* L.: Tabbaco

annual herb indigenous to tropical America, but cultivated widely for smoking.

- Botanical description approx 1–3 m high. The stem is erect with few branches. Leaves are ovate, elliptic, or lanceolate, up to 100 cm or more in length, usually sessile or sometimes petiolate with frilled wing or auricle. The inflorescence is a panicle with several compounds branches. The tubular flowers are light red, light pink, or white.
- Chemical constituents: Tobacco leaves may contain from 0.6 to 9% of nicotine which is considered the major alkaloid.
- Uses: Nicotine in small doses can act as a respiratory stimulant, though in larger doses it causes respiratory depression. Nicotine is used by smokers who wish to stop the habit. It is available in the form of

chewing gum, patches or nasal spray. Powdered tobacco leaves have long been used as an insecticide.

- Toxicity: Tobacco smoke contains over 4000 compounds, including more than 60 known carcinogens, but NOT nicotine, formed by incomplete combustion of these aromatic hydrocarbons.

Figure (50): *Nicotiana tabacum* L.

4.2.7. SAPINDALES (APG IV):

An order of 9 families, 479 genera and 6,550 species.

Figure (51): Phylogenetic tree of SAPINDALES (AP website).

4.2.7.1. Rutaceae:

A family of 161 genera and 2070 species.

Distributed in warm temperate and tropical regions with the greatest diversity in Australia and South Africa.

- Remarkable features: Trees or shrubs, sometimes armed with thorns or spines, rarely herbs, often aromatic, leaves usually compound sometimes unifoliate due to reduction of lower two leaflets (Citrus),.and gland dotted, ovary superior, seated on a nectary disc, fruit a berry or hesperidium (*Citrus spp.*).
- Major Genera: *Zanthoxylum*, *Agathosma*, *Citrus*, *Ruta* and *Murraya*.
- Economic importance: The family is important for its citrus fruits such as lemon (*Citrus limon*), lime (*C. aurantifolia*), sweet orange (*C. sinensis*), orange, tangerine (*C. reticulata*) and grapefruit (*C. paradisi*).

4.2.7.1.1. *Citrus sinensis:*

This fruit is a hybrid obtained from the pomelo (*Citrus maxima*) and the tangerine (*Citrus reticulata*), a mandarin orange. In a number of languages oranges are called China's apples according to their geographic origin China, e.g. in Dutch as sinaasappel.

The sweet orange was brought from India to Europe in the 16th century by Portuguese traders. Already during his second voyage to the New World, Columbus brought citrus seeds to the Carribean. The mandarin oranges came much later in the 19th century from China to Europe, and were first grown in Palermo, Sicily.

- Botanical description:

These plants are large shrubs or small to moderate-sized trees, with spiny shoots and alternately arranged evergreen leaves with an entire margin. The flowers are solitary or in small cluster, with five (rarely four) white petals and numerous stamens; they are often very strongly scented.

The fruit is a *hesperidium*, a specialised berry, globose to elongated, with a leathery rind or "peel" called a pericarp. The outermost layer of the pericarp is an "exocarp" called the flavedo, commonly referred to as the zest with oil glands. The middle layer of the pericarp is the mesocarp, which in citrus fruits consists of the white, spongy "albedo". The innermost layer of the pericarp is the endocarp consists of many segments filled with juice vesicles.

- Chemical constituents:

Flowers, leaves and fruits are rich in terpenoid essential oil. the fruits, rich in vitamin C, considered as a major source of flavonoids (citroflavonoids).

- Uses:

Almost every part of oranges is used for different applications: they are not only a source of orange juice, but also of sweet orange oil, made by pressing the peel, which is used as a flavouring for beverages and a fragrance constituent of perfumes.

Important source of polysaccharide pectin, which is extracted from the white part of the peel (albedo). Pectin, as a thickening agent, is used on an industrial scale.

The flavanone glycoside hesperidin, from Citrus peels, have been included in dietary supplements as vitamin P used in venous insufficiency and in hemorrhoidal disease.

It is claimed to be of benefit in treating conditions characterized by capillary bleeding by increasing the capillary resistance. Useful antioxidants and anti-inflammatory properties have been also demonstrated.

However, similar structures like Neohesperidin from bitter orange (*Citrus aurantium*) and naringin from grapefruit peel (*Citrus paradisi*) are also used for the same therapeutic effect.

Figure (52): *Citrus sinensis*

4.2.8. GENTIANALES (APG IV):

An order of 5 families, 1,118 genera and 19,840 species.

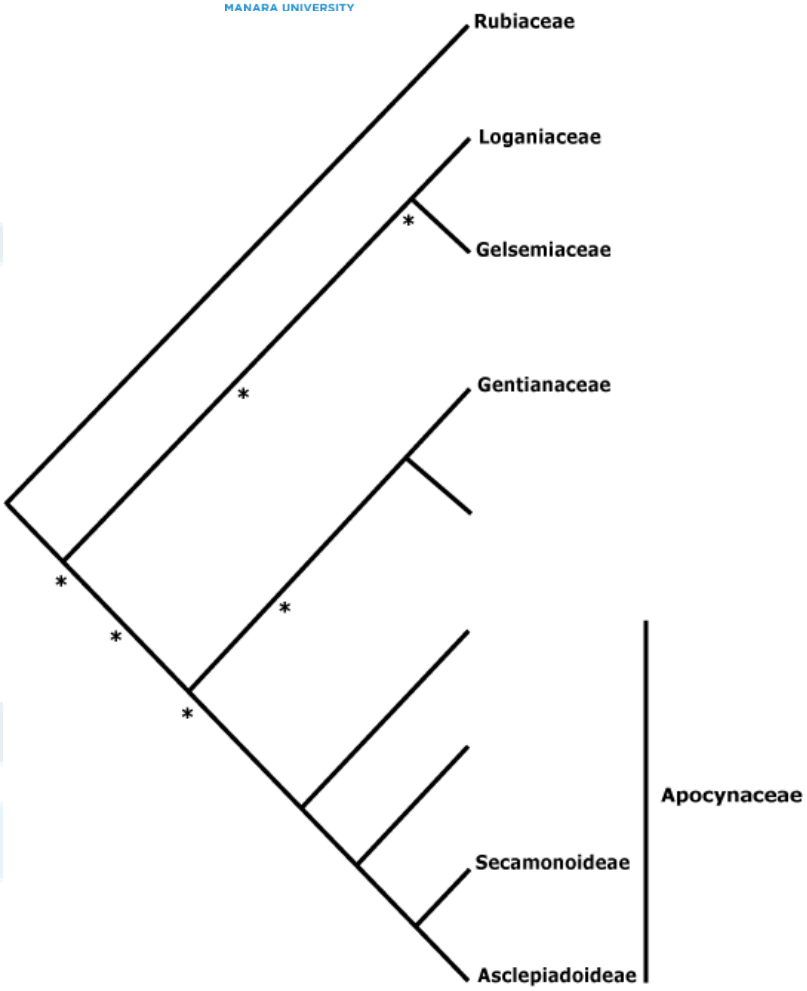


Figure (53): Phylogenetic tree of GENTIANALES (AP website).

4.2.8.1. Rubiaceae (APG IV):

A family of 611 genera and 13,150 species.

Worldwide in distribution, but mainly distributed in the tropics and subtropics, especially the woody members.

- Remarkable features:

Members of the family can be recognized in the vegetative state by their opposite, sometimes whorled, and entire leaves that often dry blackish and interpetiolar

stipules that have axillary colleters. The ovary is inferior, the flowers are polysymmetric, often with a narrow corolla tube and spreading lobes, and are quite often rather small and aggregated into heads.

- Major Genera: *Psychotria, Galium, Ixora* and *Gardenia*.
- Economic importance:

The family is economically important for being the source of coffee, quinine and a large number of ornamentals. Coffee is obtained from roasted seeds of *Coffea arabica* and *Coffea canephora* (robusta). Quinine, a remedy for malaria is derived from several species of *Cinchona.* Madder (*Rubia tinctoria*) was formerly cultivated for its red dye alizarin. Important ornamentals include *Gardenia, Ixora, Hamelia.*

4.2.8.1.1. *Cinchona succirubra*:

Large trees indigenous to Colombia, Ecuador, Peru and Bolivia. The name 'Cinchona' is said to be derived from a Countess (comtesse) of Chinchon, wife of a viceroy of Pero who it was long believed was cured in 1638 from a fever by the use of the bark, she introduced the bark to treat fevers in the area where she lived near Madrid. Whether Amerindians used the bark as an indigenous remedy for fevers has been the subject of much academic discussion. Jesuit missionaries worked in Peru in the early sixteenth century and so perhaps it was the missionaries who first took the cure back to Europe rather than the Countess. One of its common names, Jesuits' bark, reflects this belief. However, it was some time before this 'miraculous cure' of powdered bark was accepted by European doctors as they had their own 'cures' for malaria from which

they gained financially. By the late seventeenth century quinine bark was widely used as a malarial remedy.

- Botanical description:

These trees, with their glossy, evergreen leaves and terminal panicles of red, pink or white flowers, can reach around 12 metres in height.

- Chemical constituents

It is the bark that represent a very good source of medicinal alkaloids

- Uses:

The bark has been instrumental in curing malaria due to the presence of antimalaria alkaloids as quinine. Other alkaloids ,quinidin, in the bark are extracted for the treatment of ailments such as cardiac arrhythmia.

Figure (54): *Cinchona succirubra* botanical illustration.

4.2.8.2. Apocynaceae (APG IV):

A family of 400 genera and 4.555 species.

Mostly tropical and subtropical with a few species in temperate regions.

- Remarkable features:

Herbs shrubs or climbers, latex milky, leaves opposite or whorled, throat of corolla tube with scales, ovary superior, fruit a follicle, seed with a tuft of hairs.

- Major Genera: *Asclepias, Tabernaemontana, Cynanchum, Rauvolfia and Catharanthus.*
- Economic importance:

Nerium (oleander), *Catharanthus* (Madagascar periwinkle), *Hoya* (wax plant) and *Plumeria* (frangipani) are grown as ornamentals. *Nerium* and *Thevetia* are poisonous (can be fatal). Roots of *Rauwolfia serpentina* yield reserpine used as tranquillizer for patients suffering from schizophrenia and hypertension. *Catharanthus* provides antileukaemic drugs.

4.2.8.2.1. *Nerium oleander* (APG IV):

Oleander or Nerium is one of the most poisonous commonly grown garden plants.

- Botanical description:

Oleander is latex usually milky shrub. The thick leathery leaves are narrow lanceolate in whorls of three. Inflorescence grow in clusters at the end of each branch; They are white, pink to red. Flowers are deeply 5-lobed corolla round the central corolla tube. The fruit is long narrow pair of follicles.

- Chemical constituents

The leaves of oleander are very toxic because they contain cardiac glycosides.

Figure (55): *Nerium Oleander*.

4.2.9. LAMIALES:

An order of 24 families, 1,059 genera and 23,810 species.

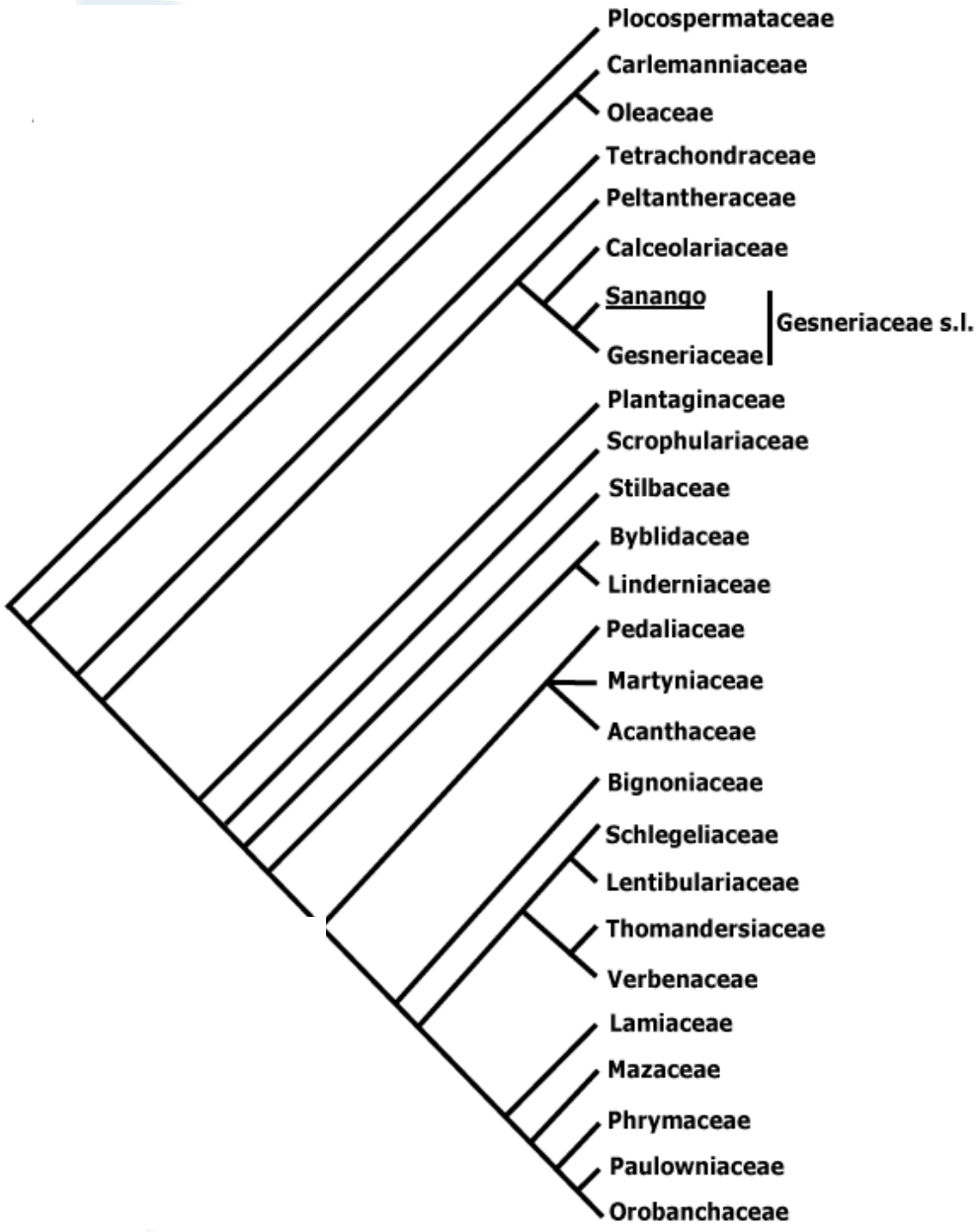


Figure (56): Phylogenetic tree of LAMIALES (AP website).

4.2.9.1. Lamiaceae Martynov/ Labiatae Jussieu:

A family of 236 genera and 7,203 species.

Worldwide in distribution, largely concentrated in the Mediterranean Region.

- Remarkable features:

Lamiaceae are herbs, also shrubs, lianes and rarely trees, that may be recognized by their opposite, usually serrate leaves, more or less square (4- angled) stems, and monosymmetric (zygomorphic) flowers usually borne in clearly cymose clusters. The plants are often aromatic. The calyx is an integral part of the dispersal mechanism.

- Major Genera: *Salvia, Clerodendrum, Thymus, Plectranthus, Ocimum, Lamium, Marrubium, Mentha and Lavandula.*

- Economic importance:

The family includes several plants used in cooking and flavoring such as spearmint (*Mentha spicata*), peppermint (*M. piperita*), thyme (*Thymus vulgaris*), sweet basil (*Ocimum basilicum*), pot marjoram (*Origanum vulgare*) and sage (*Salvia officinalis*). The family is also source of popular perfumes such as lavender (*Lavandula angustifolia*) and rosemary (*Rosmarinus officinalis*). Many are ornamentals (*ex. Salvia*).

List of most used Lamiaceae species as a medicinal herbs:

Salvia officinalis L.

leaves and flowers

gastroprotective, antispasmatic, and bactericidal

Ocimum basilicum L.

leaves, flowers, and seeds

Antibacterial and antispasmodic

Mentha piperita L.

Leaves

antimicrobial, sedative and antispasmodic

Melissa officinalis L.

aerial part

digestive, tranquiliser, antimicrobial and antioxidant

Origanum vulgare L.

Leaves

antioxidant, antibacterial, for digestive & respiratory problems

Rosmarinus officinalis L.

aerial part

antiseptic, antispasmodic and hepatoprotective

Thymus vulgaris L.

flowered aerial part

antioxidant and antibacterial

4.2.10. APIALES:

An order of 7 families, 494 genera and 5489 species.

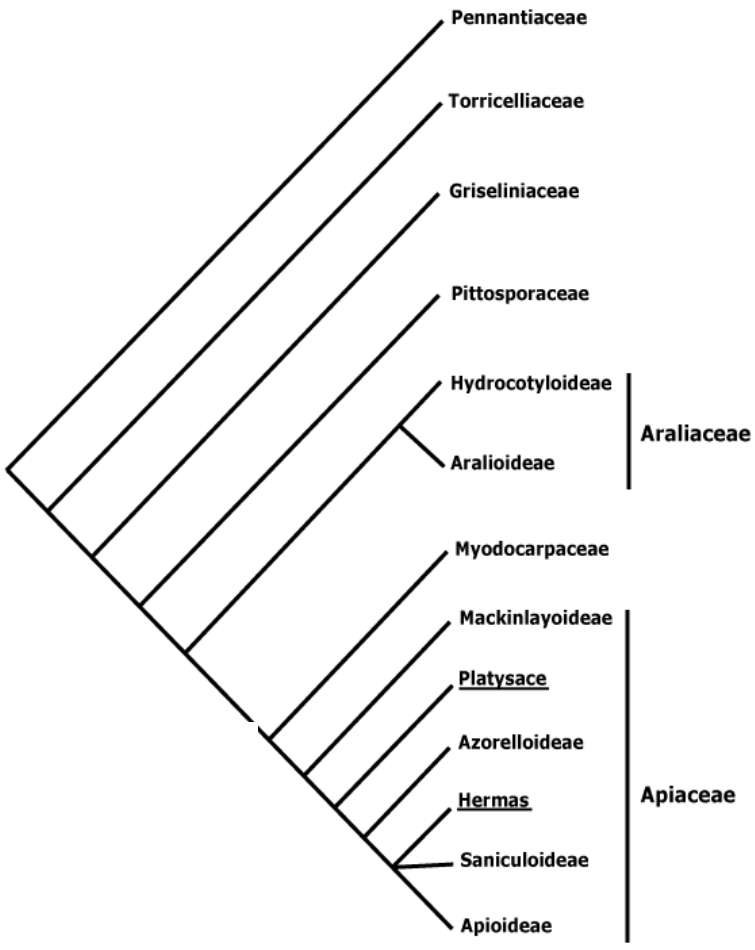


Figure (57): Phylogenetic tree of APIALES (AP website).

4.2.10.1. Apiaceae Lindley or Umbelliferae Jussieu:

Worldwide, mainly distributed in north temperate regions.

- Remarkable features:

Apiaceae are usually Aromatic herbs with compound leaves that have broad, sheathing bases. Their inflorescences are usually umbels of umbels (compound umbels), rarely heads; and their polypetalous flowers usually have a minute calyx, clawed petals with incurved apices, and two carpels; the fruits are dry and separate into two 1-seeded portions.

Apioideae: usually have more or less finely-divided leaves, compound umbels, and the usually the fruit consists of two fused carpels that separate at maturity into two mericarps, each containing a single seed.

- Economic importance:

The family is the source of food plants, spices and condiments. Carrot (*Daucus carota*) and parsnip (*Pastinaca sativa*) are important root crops. Important flavouring plants include fennel (*Foeniculum vulgare*), coriander (*Coriandrum sativum*), caraway (*Carum carvi*), anise (*Pimpinella anisum*) and celery (*Apium graveolens*).

- Medicinal uses:

Most reported medicinal uses were for treatment of gastro-intestinal, respiratory system, urinary system, gynecological and skin disorders, and also they were used as

antiseptic, anthelmintic, calmative, carminative (relieving flatulence), galactogogue and appetizer agents.

4.2.10.1.1. *Ammi visnaga*: Khella

The dried ripe fruits of *Ammi visnaga* (Apiaceae/Umbelliferae) have a long history of use in the Middle East as an antispasmodic and for the treatment of angina pectoris.

The drug contains small amounts of coumarin derivatives, e. g. khellin.

Khellin, as coronary vasodilator and spasmolytic agent, has been used in the treatment of bronchial asthma and urinary disorder (smooth muscle relaxant in renal colics).

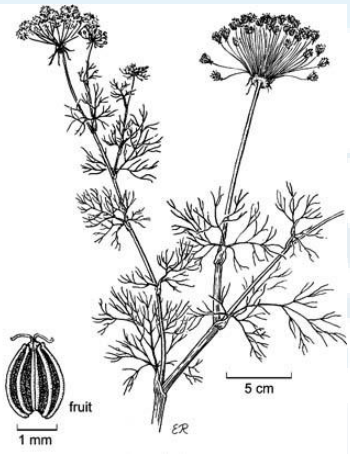


Figure (59): *Ammi visnaga* Khella

4.2.11. ASTERALES

An order of 11 families, 1743 genera and 26,870 species.

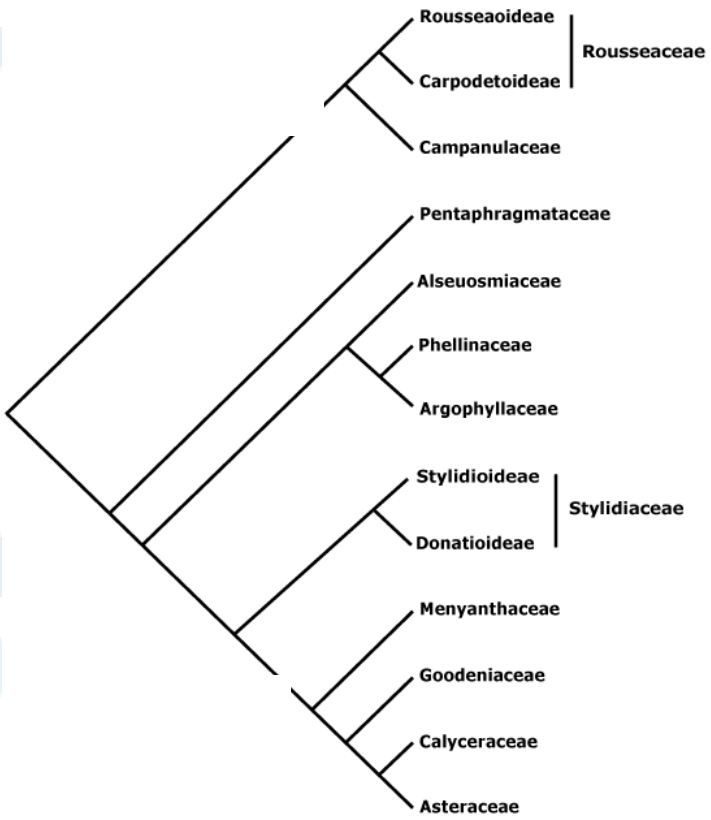


Figure (60): Phylogenetic tree of ASTERALES (AP website).

4.2.11.1. Asteraceae (Martinov)/ Compositae (Giseke)

Asteraceae considered being one of the largest family of flowering plants (angiosperms), with 1,620 genera and 25,040 species.

- Remarkable features:

Usually herbs, leaves usually alternate, stipules absent, inflorescence a capitulum with ray florets and disc florets (one type or both in a head), surrounded by bracts, anthers united forming a cylinder around style, style

with two branches. The rather small, single-seeded fruits often have a plumose pappus and are then dispersed by wind.

- Economic importance:

Common valuable ornamentals include species of *Aster*, *Dahlia*, *Chrysanthemum*, *Gerbera* and *Helichrysum*. A few food plants include *Lactuca* (lettuce), *Cynara* (artichoke), *Helianthus* (sunflower oil), and *Cichorium* (chicory, added to coffee). Safflower a red dye is obtained from *Carthamus tinctorius*. Latter is now more commonly cultivated for its seeds yielding safflower oil, used in cooking.

4.2.11.1.1. *Matricaria chamomilla* or (*M. recutica*).German chamomile

Two types of chamomile are commonly employed in herbal medicine: Roman chamomile *Chamaemelum nobile* and German chamomile

German chamomile, an annual plant, is the more important commercially and is often called matricaria to distinguish it from the perennial Roman chamomile. It grows to a height of 15-60 cm and can be found naturally all over Europe and the temperate areas of Asia. In the true *M. recutita* chamomile species, the receptacle is hollow and lacks scales.

- Chemical constituents:

Both plants are cultivated to produce the flower-heads which are then dried for drug use. Volatile oils obtained by steam distillation or solvent extraction.

- Uses:

Matricaria is used as a digestive aid, but is mainly employed for its anti-inflammatory and spasmolytic properties.

Extracts or the volatile oil find use in creams and ointments to treat inflammatory skin conditions, and as an antibacterial and antifungal agent.

Taken internally, matricaria may help in the control of gastric ulcers and as carminative.

Figure (61): *Matricaria chamomilla*