4.1 Introduction and definition

Active components are substances which are found in different parts and organs of plants, and which change or modify the functions of human and animal organs and systems. Scientific research has allowed us to discover a wide range of active components, of which the most important—as far as health is concerned—are essential oils, alkaloids, glycosides or heterosides, mucilage and gums, and tannins. Other relevant active constituents in plants, such as vitamins, minerals, amino acids, carbohydrates and fibres, some sugars, organic acids, lipids, and antibiotics, are called essential nutrients.

Active components are classified in groups according to their chemical structure:

- **Products resulting from primary metabolism** (chemical processes which are directly linked to survival, growth and reproduction): glucides, lipids, amino acid derivations.
- **Products derived from secondary metabolism** (these are not essential for the metabolism, but are synthesised as defences, adaptation, etc…). These are the most important active components, which will be introduced through this course.

**Heterosides.** Anthraquinones, cardiac glycosides, cyanogenics, coumarins, phenols, flavonics, ranunculosides, saponosides, sulphurides

**Polyphenoles.** Phenolic acids, cumarins, flavonoids, lignans, tannins, quinones

**Terpenoids.** Essential oils, iridoids, lactones, diterpones, saponins.

**Alkaloids.**

For each of these groups we shall look at basic chemical structure, distribution in the plant world, and industrial uses.

Although heterosides belong to several groups, we shall group them in their own, separate category. Given their importance, we shall study essential oils as a separate topic.

4.2. Heterosides

Glycosides or heterosides are compounds which are made up of two parts: one is a sugar moiety (e.g. glucose) and the other a non-sugar moiety or aglycone. The bond between the two
parts (moieties) involve a hydroxyl group, which can form an O-glycoside, (C-glycosides), (N-glycoside) or (S-glycoside).

Glycosides are broken down upon hydrolyses with enzymes or acids, releasing the aglycone, the truly active constituent. This break is catalysed by ferments contained in the plant itself. They are classified according to the nature of the non-sugar or aglycone as we can see in the table below. The names end in –oside, although some prefer to use the traditional names ending –ine (e.g. digoxin).

They make up the active components of many plants, and their pharmacological activity is basically due to the non-sugar part.

<table>
<thead>
<tr>
<th>Type</th>
<th>Properties</th>
<th>Species</th>
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<tbody>
<tr>
<td>Anthraquinones</td>
<td>Purgatives</td>
<td>Holy peel, Sen</td>
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<tr>
<td>Cardiac glycoside</td>
<td>Diuretic, Heart tonic</td>
<td>Digital</td>
</tr>
<tr>
<td>Cyanogenics</td>
<td>Anaesthetics, Anti-</td>
<td>Cherry tree. Almond tree.</td>
</tr>
<tr>
<td>Coumarine</td>
<td>Antibacterial, Anti-coagulant. Protection from the sun.</td>
<td>Oats.</td>
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<tr>
<td>Phenol</td>
<td>Anti-pyretic and febrifugues.</td>
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<tr>
<td>Flavonoids</td>
<td>Weak capillaries. Vitamin C.</td>
<td>Sunflower, rude.</td>
</tr>
<tr>
<td>Ranunculosides</td>
<td>Irritation of the skin.</td>
<td>Berry plants.</td>
</tr>
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</table>

The most important groups are the Anthraquinonics, Cyanogenics, cardiotonics, and cumarins, but also including the phenolics, because in this group we find salicin, the forerunner of salicylic acetyl acid or aspirin.

c. Anthraquinonic Heterosides.

Anthraquinones are yellow-brown pigments, most commonly occurring as O-glycosides or C-glycosides. Their aglycone portions consist of two or more phenols linked by a quinine ring (anthracene derivative). They are used as laxatives and purgatives. They can be found in the following plants:

_Aloes (aloe juice, especially liliacs)._ 

_Rhubarb (rhizomes from Rheum especially F. Polygonaceae)._ 

_Senna (leaves and pods of Cassia, especially F. Caesalpinaceae leguminous plants)._ 

_Buckthorns (bark of the Rhamnus catharticus and R.frangula. F. Rhamnaceae)._ 

_Cascara sagrada (bark of the Rhamnus pursiana. F. Rhamnaceae)._ 

b. Cardiac glycosides /Heterosides

This group contains a number of active constituents which act directly on the cardiac muscle, and thus exert therapeutic influence on congestive cardiac insufficiency, or on cardiac arrhythmia. However, given the gravity of this affliction, and also the special characteristics of these active components, whose therapeutic margin is extremely narrow, many of the drugs which contain them are not now used directly as phyto therapeutic products, even though their active constituents in isolation are still indispensable for therapy.
Some of the plants which contain this type of substance are:

*Digitalis purpurea* and *D. lanata* (F. Scrophulariaceae) whose pharmacological effects were described by Whiting in the 18th Century. Cardiac heterosides are also known as digoxin, which is actually a derivative of lantoside C, one of the glycoside in Digitalis.

*Adonis vernalis* (F. Ranunculaceae).

*Urginea maritima* also known as escila (F. Liliaceae).

*Nerium oleander* (F. Apocynaceae).

*Strophanthus* (F. Apocynaceae). Its active principle, ouabaine, is used as a tool for pharmacological research.

They share a common characteristic by acting specifically on the heart; no synthetic substitute has been currently found for some of them. Cardiotoxic based on drugs are highly toxic (10 g of dried leaf or 40 g of fresh leaf are lethal). Strophans were used as poison for both hunting and warfare.

*Digital:* dried leaf of *Digitalis purpurea*

*Strophanth:* seeds of two different types of the species, *Strophantus gratus* and *Strophantus kombe* (Apocynaceae).

*Escila:* dried scales of bulbs of *Urginea maritima* or *Scilla maritime* (Liliaceae).

c. Cyanogenic Heterosides

Some plants give off hydrocyanic acid (a process known as cyanogenesis). A number of amino acids are known precursors of these glycosides (amygdalin and prunasin). They have caused lethal poisoning.

Properties. The only drug which is used for fitotherapy because it contains these substances is the wild cherry laurel (*Prunus serotina*), which contains prunasin. It is used as distilled water, as an anti-spasmodic, to stimulate breathing, and as an aromatic.

They are found mainly in

*Rosaceae.*

*Fabaceae* (leguminous plants)

*Euforbiaceae.*

*Poaceae less common gramineae.*

Organs include:

*Roots:* manioc (*Manihot utilissimo,*) belonging to *Euforbiaceae, gives starch and tapioca.*

*Bark:* the wild cherry laurel.

*Leaves:* elder (*Sambucus nigra).*
Seeds: bitter almonds (Prunus dulcis) and the kernel of apricot, peaches and plums. The sweet variety is edible, the bitter variety contains amygdalin, a cyanogenic heteroside. The bitter variety also differ in taste and because when crumbled and mixed with water, they give off a smell like benzaldehyde. If eaten they are toxic because they contain cyanide ions. 20-50 almonds are enough to kill an adult. They are used to make oil for use in cosmetics.

d. Coumarinic Heterosides

Coumarin is an aromatic. These plants contain vitamins, diminish capillary permeability, and increase the resistance of capillary walls (they protect us from capillary weakness and act as a tonic for the veins). Some have sedative properties, such as angelican. They may have hypnotic properties.

Gentian contains amarogentin. Because they are bitter, they stimulate appetite and digestion, and excite the taste-buds of the tongue. As a reflex reaction, they act on the stomach, increasing motility and helping to increase secretion. They should not be used when lactating as the active components pass into mother’s milk.

The bark of the Indian chestnut also contains them. Both the bark and the seeds act similarly, but the active components are different. Only the bark contains coumarins.

Ash leaves, Fraxinus excelsior (fraxina). They have diuretic, anti-rheumatic, and anti-arthritic properties. They are used to treat the kidneys and the bladder, or in cases of urine retention.

4.3. Polyphenoles

These are substances with a benzene nucleus supporting a hydroxile group. They usually bond with sugars to form heterosides, but they may be found separate. They range from very simple substances to very complex ones such as lignines and tannins. The main groups in this category are phenolic acids or phenols, cumarines, flavonoids, lignanes, tannins, and quinines.

a. Phenolic acids.

These are aril-carboxilics, and contain one or more OH groups in the aril. They have various pharmacological properties and uses: anti-oxidant, analgesics, choleretic... Eugenol, for example, is an antiseptic and also a local anaesthetic used in dentistry. Unbonded phenols provide important constituents of essences, such as timol and its isomer, carvacrol (essence of thyme). Many phenols are found in an oxidized ether state in essences. These include estragol, miristicine, apiol, and atenol.
b. Flavonoids

Flavonoids are yellow pigments derived from phenil-benzoγ pirona or phenil cromome. They are frequently found in the vegetable kingdom, usually in the form of heterosides. Their molecular structure is of the type C6-C3-C6. They are a very varied family of compounds, although all the final products are typically polyphenolic and soluble in water. There are 6 main classes, chalcones, flavones, flavonols, anthocyanins, and condensed tannins, as well as two others, xantones, and aurones. The figure shows the basic structure of flavonoids.

These compounds are important for plants, because they are responsible for the colouration of many flowers, fruits and leaves, thus helping pollination by attracting insects. They also take an active part in the plant’s life, acting to protect it from the harmful effects of UV radiation, and acting as an efficient anti-oxidant.

Of all these, the most interesting in terms of pharmacology fall within the group of flavonoids: flavones, flavonols, and flavones, and their correspondent heterosides and anthocyanosides. Many of them act on the vascular system, for example rutoside or citroflavanoids, which are thus named because they have been isolated in species belonging to the citrus family.

They act on the vascular system by dilating blood vessels. Furthermore, they are able to trap free radicals. Among the medicinal plants whose activity is related to flavonoid content are the passion flower (Passiflora incarnate) with approximately 2% of flavonoids; roman camomile (Chamaemelum glabra) and aquilea (Achillea millefolium); liquorice (Glycyrrhiza glabra) and gingko (Ginkgo biloba); the Marian thistle (Sylilum marianum) and the white thorn (Crateagus). Isoflavones have fitoestrogenic properties so they are used treat menopausal symptoms (e.g. soya).

We must make special mention within the flavonoid group, of the antocyanoside group, the red and blue pigments in flowers, which have special characteristics and are highly soluble in water. For example, the cranberry Vaccinium mirtyllus (Ericaceas), and the blackcurrant Ribes nigrum (Saxifragaceas).

c. Coumarins

These are benzo-α pyrones. The name cumarines refers to large group of phenolic active components found in medicinal plants, which share a chemical structure 2H-1-benzopiran-2-ona known as cumarin. Substitutes of different chemical nature follow this structure which gives us different types of cumarins: simple and complex.

Practically all cumarins, with the exception of cumarin itself, have a hydroxilic substitute (OH) at number 7, be it free, as in umbelipherone or in combination (methyle, sugars, etc...).
As a group, it’s not particularly interesting in pharmacological terms. Nevertheless, we must mention its effects on the vascular system (both on arteries and veins) and its use as a treatment for certain ailments of the skin such as psoriasis, due to its photosensitizing properties. Some of them are:

*Cumarin*, found in extracts of the melilotus (*Melilotus officinalis*), which is used to treat veno-lymphatic insufficiency.

*Esculoside*, found in Indian chestnuts (*Aesculus hippocastanum*). It is both a tonic for the veins and a protector of the cell wall.

*Visnadine* is a dilator of the blood vessels found in the fruit of the visnaga, *Amni visnaga*.

*Dicumarol* is an anti-coagulant which forms in melilotuses when conditions for conservation are bad.

Furanocumarins are photosensitizing and are used to treat psoriasis. Sometimes they are used in sun creams as they enhance melanin production (photodynamic), for example, essence of bergamot (*Citrus bergamia*).

d. **Lignanes**

These are molecules whose structure is the union of two units of phenile propane (C6-C3). They are very common in the plant world. Podophiliotoxin, for example, is found in the podophylle rizome (*Podofilum peltatum*) and is the fore-runner of two substances (etoposide and teniposide) used for anti-tumor therapy. Silimar in too, a protector of the liver obtained from the marian thistle (*Sylilbum marianum*).

e. **Tannins**

These are complex substances which we cannot classify under one single chemical structure. They are non nitrogenised polyphenolic hydro-soluble substances of vegetable origin, having a molecular weight between 500-3000. Apart from reacting in the classic phenol way, they precipitate gelatine, alkaloid salts, and heavy metals. They can be both hydrolizable and condensed.

Tannin is found mainly in the roots, bark, and sometimes in the leaves of plants. These compounds have antibacterial, astringent, and antiseptic properties. They are found especially in the Ericaciae, Legume, Rosaceae, and Salicaceae families.

Historically, they are substances used for tanning leather as they form hydrogen bridges with the fibres of collagen in the skin. External pharmacological properties are astringent, constriction of blood vessels (for treating haemorrhages), and cicatricizing (burns). Internal properties: anti diarrhea, and, as they precipitate alkaloids, antidote to intoxication.

f. **Quinones**

These are aromatic dicetones which come from the oxidising of phenols. There are several types:


Naphthoquinones: naphthalene derivates. Anti-bacterial and antifungal. Junglone, from the walnut tree (*Juglans regia*). Lawsona, from henna (*Lawsonia inermis*) used as a dye and as shampoo. Plumbagona, from the drosera (*Drosera rotundifolia*), which is anti-expectorant. Vitamin K1 is found in alfalfa (*Medicago sativa*).
Anthracicflaxnes: naphtacene derivates. They are the nucleus of important antibiotics such as daunomicine and doxorubicine, as well as tetraciclines.

Anthraquinones and fenanthraquinones: anthracene and fenantrene derivates, they act as laxatives and purgatives, when in heteroside form (see anthraquinonic heterosides).

4.4. Terpenoids

Terpenoids are made up of a whole number of isoprene (C5) units. Depending on this number, they are classified as:

- Monoterpenes (2 units of isoprene = C10)
- Sesquiterpenes (3 units of isoprene = C15)
- Diterpenes (C20)
- Triterpenes (C30)
- Carotenes (C40)
- Polyterpenes (Cn)

They include essential oils as we shall see in the next lesson (lesson 7), iridoids, lactones, sesquiterpenics, saponins, and cardiotonic heterosides (see above).

a. Iridoids

These are monoterpenic compounds and the name comes from a type of Australian ant (Iridomirmex) whence iridodial, the simplest compound in this group, was first isolated. They are usually found in plants in the form of heterosides, in the Gencianacae and Valerianacae families. They are part of the active principle of some plants, such as the valsepotriates of the valerian root (Valeriana officinalis), harpagosides of the harpagophite (Harpagophytum procumbens), oleuropeoside in olive leafs (Olea europea), and genciopicroside in the roots of the genciana (Gentiana lutea).

b. Sesquiterpenic lactones

These are found in abundance in the Composite, Lauraceae and Magnoliaceae families, and are responsible for the bitter taste of many drugs; the holy thistle (Cnicus benedictus), absinthe (Artemisia absinthium), or dandelions (Taraxacum officinale). They are antibacterial and antifungal. Some produce dermatitis as they cause the formation of allergens.

c. Saponins

Or saponosides, from the Latin sapo = soap. They are substances which produce foam in water solutions, and are naturally tenso-active. Many have haemolytic properties (disintegration of erithrocites), and are highly toxic when injected into the blood. Their toxicity is less when taken orally. They are toxic to cold-blooded animals.

There are triterpenic and steroidal types. The former are found in the seed of the Indian chestnut, in liquorice (Glycyrrhiza glabra), the Asian centella (Centella asiatica), and in ginseng (Panax ginseng). The latter in Ruscus (Ruscus aculeatus), agave (Agave sisalana), and in dioscorea (Dioscorea).
4.5. Alkaloids

a. General characteristics

This is a group of natural products of particular interest to pharmacology. Within this group we can find substances which are toxic even in small doses. The first alkaloid to be isolated was morphine (Sertüner 1805). The name ‘alkaloids’ was hit upon in 1819, because of their basic nature. Although they were first isolated in the 19th century, their complexity meant that their structure was not established until later.

This was the case with strychnine (vomic nut seed). It was isolated in 1819. In 1870 its structure was established approximately. In 1889 it was produced synthetically. In 1946 its structure was finally determined.

Our knowledge of natural alkaloids has progressed thanks to the development of new techniques of separation and identification. In 1930, more than 300 were isolated and the structure of 200 was established. In 1950 more than 1,000 were isolated, in 1973, between 5 and 6,000.

They are sensitive to light and to heat and can be stabilized with inorganic acids. In nature, they are found in the form of salts, although they can also be found free. In plants, they were thought to be products obtained by extraction and not particularly soluble in typical extraction solvents because of their polarity. They undergo isomerisation (lysergic and isolysergic acid) and racemization (hiosciamin and atropine).

There are several types, depending on the molecule from which they derive (tropane, quinoleine or isoquinoleine).

b. Alkaloid drugs derived from tropane:

These are parasympathemimetic substances or antagonists of acetyl coline (synaptic transmitters). They have the following effects on the central nervous system:

*In large doses, vertigo, delirium, hallucinations*

*In very large doses, death by respiratory paralysis*

*The drugs potency is Hiosciamine>Atopine>Escopolamine*

Some examples of these drugs are:

Cocaine. A powerful local anaesthetic. Sympaticomimetic (it lengthens the effects of anaesthesia by constricting blood vessels). It excites the central nervous system. In extreme doses, it causes death by respiratory paralysis. Leaves of the *Erythroxyllum coca* (Eritroxilaceae).

Lysergic acid. This drug is obtained from a fungus, *Claviceps purpurea*, which grows around the ovary of rye.

Caffeine. This drug is the almond or grain of the Caffea seed. The Coffee tree originated in Africa.

Teine. The drug is the young leaves of the *Camelia thea*. They are typical of Southeast Asia. Nowadays it comes from plants grown in India, China and Sri Lanka.

Atropine. In leaves and flowers of *Atropa belladonna* (Solanaceae)
Daturin. In stramonium leaves *Datura stramonium* (Solanaceae)

Hiosciamin. In belenium leaves. *Hyoscyamus niger* (Solanaceae). It is used to treat Parkinson’s disease.

c. **Drugs with alkaloids derived from quinoline (Quine).**

The drug is the dried bark of the trunk, branches and roots of the *Cinchona* (Rubiaceae). The most important species are:

*Cinchona succiruba* (red quine)

*Cinchona leogeriana* (leogerine quine)

*Cinchona Calisaya* (yellow quine)

*Cinchona Hybrida*

*Cinchona robusta*

Their main effect is anti-malarial due to the quinine, which is toxic to the protozoa and paramecia especially for the plasmodium genre which produce malaria (*Plasmodium vivax, Plasmodium malariae*). It acts against asexual or schizontic forms.

d. **Drugs with alkaloids derived from isoquinoline:**

Opium. This is dried latex obtained from incising unripe pods of the different varieties of *Papaver somniferum* (paveracea). We obtain morphine from it. Even in low doses it is analgesic, and decreases the perception of pain; particularly useful against persistent, acute pains. Its properties are:

- Sedative to the central nervous system, leading to an unpleasant drowsiness.
- It produces a sense of wellbeing and euphoria. Repeated administration causes addiction, tolerance, and physical and psychological dependence.
- It causes respiratory depression and bradicardia.
- In the intestines it is an emetic and diminishes peristalsis.
- Overdoses cause death by cardiac and respiratory arrest.

4.6. Other active Constituents

**Mucilage and gums**

These are heterogeneous polysaccharides, formed by different sugars. In general, they contain uronic acids. They are characterised by the formation of viscous colloidal dissolutions, in water, jellies. The difference between mucilage and gums is difficult to ascertain and normally, everything is treated as gum. Nowadays, the difference is thought to be in the fact that mucilage are normal components of plants, whereas gums are products which only appear under certain circumstances, via the destruction of cellular membranes and exudation. The most important are in the leguminous plant family.

Properties

- They swell and form gels in water
- They dissolve forming viscous solutions
- They easily lose some monosaccharides in hydrolysis, but a more resistant nucleus which needs more energetic enzymes always remains.
Uses

Emollients and demulcents: anti-inflammatory. They can be used externally (haematomas), as cataplasms (respiratory). Internal uses: anti-inflammatory treatment of the respiratory system, mechanical laxatives. Laxative effects are due to their capacity for water retention, which makes them lubricants, thus aiding passage through the intestine. Because they retain water, they swell and press against the intestine wall, thus increasing peristalsis. They protect gastric mucus and act against diarrhea, especially those caused by bacterial toxins.

4.7. References

