

# Those Responsible for the Pharmacological Actions of Plants are the Active Secondary Metabolites

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**Abstract: Objectives:** To relate the presence of the active secondary metabolites in the pharmacological actions and the therapeutic effects of the plants. **Methods:** Search about the topic in the last 5 years and present some active secondary metabolites that explain the pharmacological actions and therapeutic effects of medicinal plants. **Conclusions:** It was based on the search of articles in the Virtual Library in Health (Spanish: BVS) and using the key words: secondary metabolites, phytotherapy, medicinal plants.

**Key words:** Metabolites, primary metabolites, secondary metabolites, phytotherapy, natural medicine, medicinal plants.

## 1. Introduction

Man's interest to know the different vegetables has always been and continues being an indispensable necessity, because sustainability of life depends of plants and then subsistence of the rest of alive beings, because they are the only ones that transform the inorganic material into organic, that is to say, in food.

To study these important and indispensable organisms, human knowledge has created the science of Botany that is in charge of studying vegetables in all their aspects and importance [1]. Then Botany studies vegetable organisms. At first sight, a vegetable is distinguished basically of an animal by the nature of its tissues [2].

Macroscopic or morphologic characters of a drug are determined in each organ, they are known examining their typical characteristics as, for example, form and size, external marks and its color, or the fracture and internal color. Identification of a vegetable is indispensable in all chemical work in this respect.

Even at present hundreds of plants are used in medicine, but modern science, analyzing and studying

the therapeutic effects of plants, wants to specify, compare and classify the diverse properties, not with the purpose of diminishing this trust in nature, but to group the plants of similar effects, to know the responsible active principles of cutting, to alleviate or to cure illnesses, to separate them of the plants that contain it, to determine their chemical structures, to offer their synthesis, to propose modifications to the principle of the secondary metabolism (secondary metabolites) that are considered as not essential for life, although they can be fundamental so that they can operate a certain biological function. They are, without any doubt some, the compounds of more pharmacological interest, those that will constitute what are called active principles of the drug [3]. An analysis of this nature should be carried out as a multidisciplinary action with the intervention of botanical, chemical, pharmacologists and pharmacognosists, among others [4].

## 2. Characteristic of Phytotherapy

Contrary to the synthetic or conventional medicine, phytotherapy uses complex vegetable wombs. These wombs are constituted by whole plants or parts of them (leaves, roots, etc.), and also products of them, results of direct treatments with some solvent or mean

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that concentrates the related compounds and facilitate their administration, they are the ones called extracts. Anyway in this complex world we meet with a without number of compounds of different chemical nature, this mixture is called fitocomplex [5] which is the mixture of active substances and other companions that act as a whole to achieve a therapeutic end, that would not be the same one if they were administered separately, that is to say as monosubstances [6]. These active substances are called secondary metabolites technically they refer to substances that are the secondary product of the photosynthesis and that intervene in vegetable processes as defense from pathogenic elements, and protection to rays UV, among others [7]. Mixtures of secondary metabolites are unique for each species, since their biosynthesis is governed mainly by the vegetable genetics, but they are also influenced by the physiology, stress, geographical origin and conditions of gathering the vegetable, among other factors [8].

### 3. Terminology and Definitions

**Drug:** It is defined as all product of natural origin that gathered or separated from its means has a composition and such properties inside its complexity that constitutes the gross form of a medication.

**Crude drug:** The term raw (in pharmacognosy) is applied to some natural product whose value has not been improved or sophisticated chemically for: drying, crumbling, mill, trituration or some other treatment that doesn't exceed the primordial thing for a correct packaging and preservation until the precise moment of its elaboration. The term improved, when it is applied in connection with the natural products, means all product whose value or condition has been improved with regard to its raw state by means of any mechanical or physical process that exceeds the essential thing for its correct packaging and preservation until the moment of its elaboration, but it doesn't include any product that has been blended artificially with other substances or whose molecular

structure has been altered.

**Raw material:** It is all drug or product of natural origin dedicated to the extraction of active principles or the elaboration of complex preparations or not, agreeably prepared for its application. Often raw drugs are used as therapeutic agents, but in their majority they are used for obtaining their active principles. These principles are generally known as extractive or derived, without damage that it is a single substance or mixture substance.

**Medication:** It is all active principle that any source is (natural or synthetic) can be used for the elaboration of a medication [9].

A chemical substance is responsible for the pharmacological activity and of therapeutic use of a drug. A drug can contain several active principles. It can also contain antagonistic active principles (with contrary effects) or with synergic principles [10].

### 4. Primary and Secondary Metabolites

The most important inorganic components are water and minerals.

Water, is in variable quantity according to the species and to the part of the plant, in this way, leaves and shafts contain more quantity of water, until 80% in some cases, while seeds contain less quantity.

Minerals can be presented in diverse forms like solubilized salts (chlorides, nitrates, phosphates, etc.), crystallized salts (calcic carbonate, calcic oxalate, etc.). They are also oligoelements (magnesium, iron, manganese, fluorine, etc.). Minerals are combined with organic substances inside the vegetal species [11].

Inside the organic components we can mention so much to the basic or primary metabolites related with the cellular essential metabolism and the secondary metabolites that are not necessarily related with the essential metabolism but they are in their majority responsible for the therapeutic activity of vegetable drugs, the most important are summarized as follow (Table 1).

**Table 1 Primary and Secondary components of the metabolism of Plants.**

Compound coming from the Primary Metabolism	Compound coming from the Secondary metabolism
Glauuids • Lipids and Fatty • Amino acids • Proteins • Nucleic acids • Nitrogenous Compounds (Ciano genetic glycosides, enzymes)	• Isoprenoids: terpenes, essential oils, saponines, cardio tonics • Derived Phenolics: simple phenols, Phenolic acids, tannins, coumarin, lignans, quinones, flavonoids: anthocyanins • Alkaloids

## 5. Secondary Metabolites

Basic metabolic routes constitute origins of the secondary metabolism of plants, resulting a varied series of compound, some of them are responsible for scents and colors of vegetables, others are responsible for culinary, medicinal or poisonous virtues.

Secondary metabolites are accumulated in big quantities in the vegetable cells or they can be expelled outside of them.

The most important secondary metabolites are:

### 1. Isoprenoids

They are formed through the route of the mevalonic acid starting from the Acetyl-coA where units of C5 are incorporated, they present diverse structures and they can be as such or being part of more complex compounds.

Isoprenoids can be classified in the following way:

#### A) Terpenes

The basic structural elements of the terpenes are known as isoprene units, because the terpenes can break down to high temperatures giving as a result an isoprene.

#### B) Essential Oils

The essential oils are volatile substances of complex nature; frequently they are associated to rubbers and to resins. These essences are exclusively in superior vegetables. Many essential oils are of terpenoid origin, only a small number of them contains aromatic derived (benzenics) blended with terpenes.

#### C) Saponins

They are structures formed by a glusidic part and a non glusidic one (aglicon) and their name is due to

their soapy properties.

#### D) Cardiotoxic Heterosides

They are formed by a glusidic part which is constituted by one or several units of sugar and an aglicon that has a steroidal nucleus (C27 tetracyclic) joined to an unsaturated lactonic ring [11].

### 2. Alkaloids

Typical alkaloids are of vegetable origin, they contain one or more atoms of Nitrogen (generally in a heterocyclic ring).

#### A) Phenolic derivatives

Plants produce a great variety of secondary products that contain a hydroxyl group in an aromatic ring that confers them a phenolic structure.

There are two basic routes implied in their biosynthesis: The route of the acetate that leads to the formation of polycyclic chains which result in polycyclic aromatic compounds by means of cyclation and the route of the shikimic acid that is precursory of a series of benzoic acids, hydroxylated and amino acid. In most of the cases aromatic compounds come from this route and they are usually formed by deamination of aromatic amino acids [12].

Among the most important phenolic compounds we have: simple phenols, phenolic acids, tannins, coumarin, and lignans.

They are not very frequent and they are in the plants in form of heteroside.

#### B) Simple Phenols

They can be free or together to sugars (heteroside), they can form esters when uniting with the quinic acid as much as with another phenolic acid.

C) Phenolic acids, quinones, flavonoids: anthocyanins, etc.

3. Tannins

Tannins possess a wide group of hydro soluble compounds with polyphenol structure.

4. Coumarin

Coumarin are derived of the benzo -  $\alpha$  - pyron, many of them are Phenolics, for that reason they are included inside the phenolic derivatives.

5. Lignans

Lignans are compounds that possess a structure constituted by two phenyl propane units.

6. Quinonas

They are aromatic compounds with two ketone groups; they are unsaturated diketones that become polyphenols by reduction.

7. Flavonoids

Flavonoids constitute a wide group of natural phenols, they can be finding as free aglicon or in heteroside form. At present more than 2000 of these compounds are known, of which about 500 are in free state [13].

## **6. Considerations about Secondary Metabolites (MS)**

Plants, contrary to other organisms, dedicate a significant quantity of assimilated carbon and energy to the synthesis of a wide variety of organic molecules that don't seem to have a direct function in the primary metabolic processes as photosynthesis, breathing, assimilation of nutritious, solutes transport or synthesis of proteins, carbohydrates or lipids which are denominated secondary metabolites [14].

In a smaller measure Secondary metabolites also act into the reproduction as attractive of pollinators and animals that feed from fruits, as pigments of flowers and/or fruits, as well as they participate in the communication of plants with other organisms [14].

It is considered that there are around 1200 of secondary compounds which have a variable distribution inside the vegetable Kingdom. Each type of MS is generally found in a single species or group of plants taxonomically related [15, 16].

The mixture of secondary metabolites is unique for each species [15], having variations along the year [17], since diverse factors, as solar radiation, age, phenolic state of the plant, nutrition, hydric stress, geographical origin, precipitation, interaction with herbivores, conditions of gathering of the vegetable biotical interactions among others, influence so that they generate mechanisms of adaptation among them that determine the production of secondary metabolites [18].

Secondary metabolites have diverse functions that are related with the ecological interactions between plant and environment, mainly in defense of the plant against depredators and pathogens, acting as attractive or repellent of animals, propitiating them bitter flavor to plants, to reduce their digestibility and palatability in the herbivore ones and even converting in toxic for them, inhibiting in this way the development of insects, nematodes, mushrooms, bacteria, improving the growth and the consistency of plants [16-19].

They also protect plants from the abiotic stress, as the ultraviolet radiations [20].

It is known that these compounds are more common in the tropical vegetation than in the temperate ecosystems and the humid atmospheres in comparison to the dry ones [21].

On the other hand, besides the seasonal variation, the MS are not distributed equally even among all their structural components, there is bigger concentration, reactivity and diversity of secondary metabolites in the yolks in growth, young leaves, reproductive organs, dispersion, and in general all the parts in annual growth [22].

Nevertheless, we should keep in mind that certain medicinal plants have not shown the properties that attribute them the popular experience, and even some of them have been dangerous. Then a scientific studies of these plants to be used as alternative medicine is needed, and it is also necessary the negative of doctors to the disordered employment of remedies and methods of popular medicine as self-medication.

## 7. Alternative or Complementary Medicine?

If Phytotherapy is a therapy that uses mixtures of substances of medium to low activity, it will be useful in affections of medium to low graveness, sporadic, light, reversible or to attenuate light symptoms of chronic affections or to limit its evolution. In this last case it will constitute only a complement, likewise like in the prevention of degenerative events [1].

A soft therapy can only constitute an alternative in episodes of the same nature, therefore, the term alternative will be relative, because if the kindness of the medicinal plants are used to mitigate nuisances and symptoms of chronic illnesses or burden that are treated by a derived potent medication of the conventional medicine, including the phyto-pharmacy, we will refer to the phytotherapy as complementary therapy and this term can lead to serious therapeutic errors. When we speak about an alternative we are choosing one option by another. When this election contemplates a soft therapy in a sharp or serious illness it is not certainly the correct alternative. Therefore, which suffering it would be, what is responsible is to consider, when referring to phytotherapy, of a complementary therapy, because it doesn't deny the option of a conventional treatment or, other complementary ones [6].

The great accessibility of medicinal plants and their elaborated products, the concept that the entire natural is good, the lack of inspection with regard to their production, how it is expended, the publicity or the idea of miraculous plants that cure serious illnesses, favor self-medication and the problems of public health previously mentioned.

A classic and worrying example is constituted by the ingestion of natural products and medicinal plants by pregnant. If pregnant women should avoid the use of any drug during the first months of pregnancy, why will an exception be the use of medicinal plants? If who suffer of some renal affection or liverwort that have a special likeness for these organs should avoid the use of drugs, why an exception will be the use of

medicinal plants? These cases put in evidence the lack of education and popularization of the information.

Another aspect that foments the question regarding with the effectiveness and security of medicinal plants and its products is the insurance of quality. Insurance of quality is a process that consists of controls according to international protocols that include from the cultivation and crop of the vegetable species until controls in the finished product being the plant in its natural state or a product of it.

It is also fundamental to assure the wanted pharmacological effect and the uniform content of the active substances in the case of products like phyto-medications. The above-mentioned is achieved through a process called standardization. In a standardized preparation it is easier to establish the therapeutic doses and to minimize the appearance of non-wish able effects since they make sure the content uniformity and of active substances, what is achieved through the use of chemical or biological markers [23-25].

## 8. Pharmacological Actions of Some Secondary Metabolites

### 8.1 Terpens

Pharmacological actions: The activity of an essential oil cannot be confused with that of the plant of which this oil proceeds. This overlapping is very far from being possible of all the cases; for example the choleric action attributed to the rosemary can be related with the presence of phenolic acids, while the essential oil is antiseptic.

Antiseptic power: the antiseptic power (no antibiotic) is manifested in front of varied pathogens bacteria and includes certain anti bio resistant stumps. Some essential oils are also active in front of inferior mushrooms responsible for mycosis, and even in front of yeasts. The most antiseptic species are: cinnamons, thyme, nail, lavender and eucalyptus. Compounds as: carvone, Mentone, citronellol, menthol, linalool, citral, geranial and thymol are 1.5; 2.25; 3.8; 4.0; 5.0; 5.2;

7.1 and 20.0, respectively more antiseptic than the phenol.

It is remarkable the activity anthelmintic of several constituent essences (apasote)

Irritating properties: (expectorants and diuretics): products like the turpentine, when they are used by the external road, they cause an increase of the microcirculation, important rube faction, sensation of heat and, in certain cases, slight local anesthetic action.

Administered by internal via, the essential oils unchain irritation phenomena at different levels. Those of eucalyptus, niaouli and pine stimulate cells of the mucus and it increases the movements from the ciliate epithelium to level of the bronchial tree; in a similar way some essential oils, at renal level can produce vasodilatation, causing diuretic effect, as the case of the juniper.

Many ointments, creams or gels based on essential oils exist, designed to treat sprains, hurts, twists and other muscular pains or of the articulations for their irritating properties.

Spasmolytic and sedative properties: the essential oils with anethole, those of many Umbelliferous, those of the mints, that of the verbena, they are shown effective to diminish or to suppress the gastrointestinal spasms; frequently they intensify the gastric secretion, for what you/they have been classified as digestive and "stomachic" with all the consequences that can derive of this "eupepsia". Some improve certain insomnias, of diverse psychosomatic dysfunctions, what can explain the employment of the same ones.

Some essential oils show neurovegetative tropism and they exercise neurosedative action (lavender and Melisa). Other activities (choleric, colagoga, anti-inflammatory, healing, etc.) they have been demonstrated in some plants.

They act in a diverse way on the SNC. The camphor, borneol, fenchone, carvone and their respective essences can cause excitement of the Central Nervous System (SNC); others as the

chamomile possess sedative and narcotic action. In continuous or high dose it can produce convulsive phenomena and other dangerous reactions (Rosemary).

### *8.2 Saponins*

They are mucolytic and expectorants, because they clarify the dense mucus facilitating their expulsion and get that the new mucus that is formed flows easily. Also, their irritative action produces an increase of the secretion of all the glands, what is also reflected in the bronchuses. They possess diuretic and depurative properties, very useful in the event of edemas.

In phytotherapy, they are used because of their power of producing an increase in the liberation of red globules (this makes of them dangerous substances, because they can end up being toxic). In medicine, they are used as diuretics, expectorants, disinfectant of the apparatus genitourinary. Plants rich in saponines are the mullein, ginseng, birch, gauna, spring, licorice and saponaria, among others.

They are biologically very active substances in small dose. Therefore, if their posology is not controlled they can produce toxicity. The alkaloids have always been used, although in the antiquity only with ends magic-religious because they exist alkaloids that can end up producing hallucinations, alterations of the organic perception, etc. Not in vain some of the most potent narcotics owe their activity to the alkaloids.

### *8.3 Cuban Tannins*

Most of the biological properties of the tannins are associated to their capacity to form complex with the macromolecules, in particular with the proteins (digestive enzymes and other funguses and viral proteins). In the traditional medicine their more grateful properties are: They precipitate the proteins of the superficial cells of the mucous ones and fabrics to the overdraft, forming protective linings of the skin and mucous and of the underlying layers. Therefore, they limit the loss of fluids, waterproofing, diminishing the volume of the secretions, they

attenuate the sensibility, the absorption of irritating or toxic substances is annulled, external aggressions are prevented and the development of infectious agents is avoided, reinforcing the regeneration of fabrics in the event of superficial wounds or burns.

Acting as antiseptic, because the one mentioned lining impedes the development of microorganisms, besides the own disinfectant action that confers them their enolic character (antibacterial and antifungal). They are good for the treatment of the dermatitis.

Antidiarrheal, due to their astringent properties at intestinal level, their astringent action also causes a decrease of the mucous secretions.

They have effect vasoconstrictor on the small superficial glasses. They are hemostatic, because they precipitate the proteins of the blood, originating clots. They stop capillary hemorrhages.

They are antidotes, because they reduce the capacity of intestinal absorption and they unite to alkaloids, toxic metals, etc., resulting insoluble precipitates.

To the condensed tannins has been attributed near properties to the flavonoids: they diminish the fragility and capillary permeability, they increase the vascular tone and the stabilization of the collagen.

In natural medicine they are used to combat the cough, bronchitis, burns, chilblains, wounded (clotting), hemorrhoids, diarrheas and excessive sweating. Some authors attribute an effect that counteracts the poisoning with alkaloids of vegetable origin. Many plants possess tannins, besides those previously enunciated, they are: the walnut tree, raspberry, common alder, pimperl, red Mangrove, etc.

A possible secondary effect is the hepatotoxicity that can end up taking place with high dose of tannins. Also interact with the alkaloids that precipitate in presence of tannins.

#### 8.4 Flavonoids

Their structural diversity is as big as their biological activities:

The principal property attributed to flavonoids is that they diminish the fragility and capillary permeability.

Simple phenols, generally more than flavonoids are kidnappers of free radicals formed under different circumstances, preventing the associated degradations to their intense activity on the phospholipids of membranes.

As general rule flavonoids are inhibitors *in vitro* of enzymes that carry out important functions in the organism.

These properties can explain, in many cases, the anti-inflammatory and antiallergic properties attributed to several drugs with flavonoids.

Flavonoids can also be hepatoprotectors, antispasmodics, diuretics, antibacterial, antivirals, they can diminish the sanguine cholesterol and some others are cytostatics *in vitro*.

## 9. Conclusions

The principles of primary metabolism (primary metabolites) are in all plants and they carry out vital functions for the development of vegetables, as the obtaining of the energy, the morphogenesis or the reproduction. Here they include nitrogenized bases, fatty acids, amino acids and you dare, as well as their respective final derived products; nucleic acids, lipids, proteins and holosides [3]. Basic metabolic routes constitute the origins of the secondary metabolism of plants, giving place to a varied series of compound, some of them are responsible for scents and colors of vegetables, others are responsible for culinary, medicinal or poisonous virtues. The mixture of secondary metabolites is unique for each species [15], presenting variations along the year [17].

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