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Plants Secondary Metabolites: The Key Drivers of the Pharmacological Actions of Medicinal Plants

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Abstract

The vast and versatile pharmacological effects of medicinal plants are basically dependent on their phytochemical constituents. Generally, the phytochemical constituents of plants fall into two categories based on their role in basic metabolic processes, namely primary and secondary metabolites. Primary plant metabolites are involved in basic life functions; therefore, they are more or less similar in all living cells. On the other hand, secondary plant metabolites are products of subsidiary pathways as the shikimic acid pathway. In the course of studying, the medicinal effect of herbals is oriented towards the secondary plant metabolites. Secondary plant metabolites played an important role in alleviating several ailments in the traditional medicine and folk uses. In modern medicine, they provided lead compounds for the production of medications for treating various diseases from migraine up to cancer. Secondary plant metabolites are classified according to their chemical structures into various classes. In this chapter, we will be presenting various classes of secondary plant metabolites, their distribution in different plant families and their important medicinal uses.

Keywords: secondary plant metabolites, phenolics, alkaloids, saponins, terpenes

1. Introduction

Plant chemistry is the basis of the therapeutic uses of herbs. A good knowledge of the chemical composition of plants leads to a better understanding of its possible medicinal value. Modern chemistry has described the role of primary plant metabolites in basic life functions such as cell division and growth, respiration, storage and reproduction. They include the components of processes such as glycolysis, the Krebs or citric acid cycle, photosynthesis

and associated pathways. Primary metabolites include small molecules such as sugars, amino acids, tricarboxylic acids, or Krebs cycle intermediates, proteins, nucleic acids and polysaccharides. Eventually, the primary metabolites are similar in all living cells [1].

Secondary plant metabolites are numerous chemical compounds produced by the plant cell through metabolic pathways derived from the primary metabolic pathways. The concept of secondary metabolite was first defined by Albrecht Kossel, Nobel Prize winner for physiology or medicine in 1910 [2]. Thirty years later, Czapek described them as end-products [3]. According to him, these products are derived from nitrogen metabolism by what he called 'secondary modifications' such as deamination. In the middle of the twentieth century, advances of analytical techniques such as chromatography allowed the recovery of more and more of these molecules, and this was the basis for the establishment of the discipline of phytochemistry.

Secondary metabolites have shown to possess various biological effects, which provide the scientific base for the use of herbs in the traditional medicine in many ancient communities. They have been described as antibiotic, antifungal and antiviral and therefore are able to protect plants from pathogens. Besides, they constitute important UV absorbing compounds, thus preventing serious leaf damage from the light. It was noticed that some herbs as forage grasses such as clover or alfalfa can express estrogenic properties and interact with fertility of animals [4].

Secondary plant metabolites are classified according to their chemical structures into several classes. In this chapter, the nature of secondary plant metabolites will be discussed as a foundation for a review of the main categories of constituents considered to be of therapeutic importance. Each section includes an overview of a class of the secondary plant metabolites regarding structure, botanical distribution and generalizations about pharmacology, followed by examples of representative molecules. The classes of secondary plant metabolites include:

- Phenolics
- Alkaloids
- Saponins
- Terpenes
- Lipids
- Carbohydrates

2. Phenolics

Phenolics probably constitute the largest group of plant secondary metabolites. They share the presence of one or more phenol groups (**Figure 1**) as a common characteristic and range from simple structures with one aromatic ring to highly complex polymeric substances. They are widespread in plants where they contribute significantly to the color, taste and flavor of many herbs, foods and drinks. Some phenolics are valued pharmacologically for their

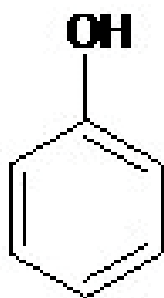


Figure 1. Phenol.

anti-inflammatory activities such as quercetin or antihepatotoxic properties such as silybin. Others exert phytoestrogenic activity as genistein and daidzein, while others are insecticidal as naringenin [5]. Many of the phenolic molecules are also effective antioxidants and free radical scavengers, especially flavonoids. Phenolics can be classified according to their structure or biosynthetic origin. According to their structures, phenolics can be classified into:

- Simple phenolics
- Tannins
- Coumarins
- Flavonoids
- Chromones and xanthenes
- Stilbenes
- Lignans

2.1. Simple phenolics

Phenolic acids are ubiquitous among plants; although free phenols are rare, gallic acid is relatively widespread and is the parent compound of the gallotannins (**Figure 2**). Gallic acid is well known for its astringent properties but has demonstrated many other activities in vitro, including antibacterial, antiviral, antifungal, anti-inflammatory, antitumor, antianaphylactic, antimutagenic, choleric and bronchodilatory actions. It also inhibits insulin degradation and promotes smooth muscle relaxation [6]. The phenolic compounds in this group vary according to their functional group, which may be hydroxyl, aldehydic, or carboxylic group; these include eugenol (a phenolic phenylpropane), vanillin (a phenolic aldehyde) and salicylic, ferulic and caffeic acids (phenolic acids). Hydroquinone is also among the most widely distributed of the simple phenols, occurring in a number of plants as the glycoside arbutin. Glycoside formation is common, and the widely distributed glycoside coniferin and other derivatives of phenolic cinnamic alcohols are precursors of lignin [7, 8].

The pharmacological properties of these widely found constituents are probably best demonstrated by the urinary tract antimicrobial arbutin [9] and the anti-inflammatory salicylates [10]. A property shared by all phenols is antimicrobial activity. In fact, phenol itself was the first antiseptic used in surgery [11].

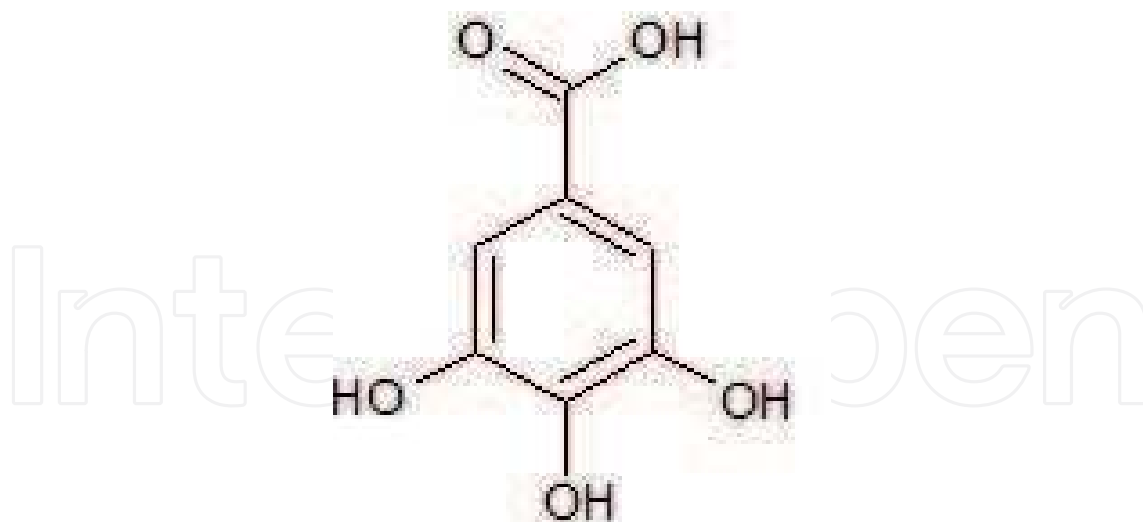


Figure 2. Gallic acid.

The pharmacological activities of many plants are attributed to simple phenolics among which the antimicrobial and diuretic activities of *Arctostaphylos uva-ursi* were attributed to its phenolic content [12]. *Capsicum* spp. showed circulatory stimulant, rubefacient and analgesic activities due to the presence of capsaicinoids, which are simple phenolic compounds [13]. Moreover, the cholagogue activity of *Cynara scolymus*, the anthelmintic activity of *Dryopteris filix-mas*, the anti-inflammatory analgesic activity of *Filipendula ulmaria* as well as the antitarrhal and diuretic activities of *Solidago virgaurea* are all attributed to the action of simple phenolics [8]. **Figure 3** illustrates some examples of simple phenolics.

2.2. Tannins

Tannins are polyphenols which have the ability to precipitate protein. These compounds have been used for decades to convert raw animal hides into leather. In this process, tannin molecules crosslink the protein and make it more resistant to bacterial and fungal attack. Today, however, many substances considered to be tannins by virtue of their structure and biosynthetic origin have limited, if any, ability to make leather [14]. There are two major types of tannins: hydrolyzable tannins and condensed tannins. Hydrolyzable tannins are formed from several molecules of phenolic acids such as gallic and hexahydroxydiphenic acids, which are united by ester linkages to a central glucose molecule. Two principal types of hydrolysable tannins are gallotannins and ellagitannins, which are, respectively, composed of gallic acid and ellagic acid units. Ellagitannins found in plants of medicinal interest and for which structures have been elucidated include geraniin (isolated from *Geranium robertianum* (Herb Robert) and *Geranium maculatum* (American cranesbill) [15]) and tellimagrandins 1 and 2 [16] (isolated from *Quercus alba* (Oak bark), *Punica granatum* (pomegranate) and *Filipendula ulmaria* (Meadowsweet)) [7].

Condensed tannins, or proanthocyanidins, are compounds whose structures are based on oligomeric flavonoid precursors and vary in the type of linkages between flavonoid units; hydroxylation patterns; stereochemistry of carbons 2, 3 and 4 of the pyran ring and the

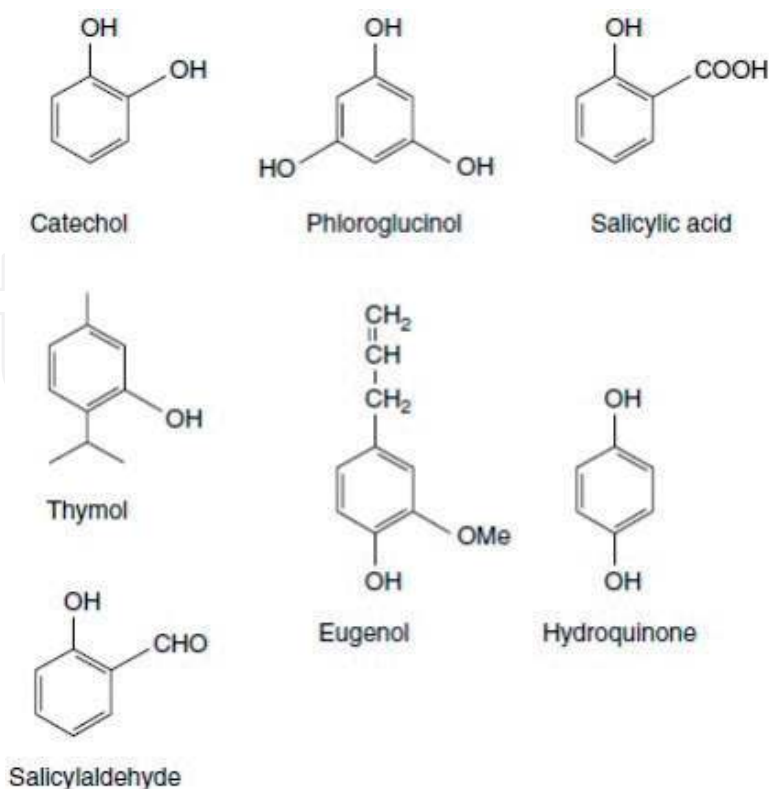


Figure 3. Examples of simple phenolics.

presence of additional substituents. Some drugs (e.g., *Camellia sinensis* (tea), *Hamamelis virginiana* leaves and bark) contain both hydrolyzable and condensed tannins [17].

Tannin-containing drugs act as antidiarrhoeals and have been employed as antidotes in poisoning by heavy metals and alkaloids. Epigallocatechin-3-gallate, the active principal in tea, has been shown to be antiangiogenic in mice. *Vaccinium oxycoccos* (cranberry) juice has long been used as urinary antiseptic [18], which was scientifically proven in a randomized, double-blind, placebo-controlled trial that has been carried out on 153 elderly women [19]. **Figure 4** illustrates some examples of hydrolysable tannins.

2.3. Coumarins

Coumarins are derivatives of benzo- α -pyrone, the lactone of *O*-hydroxycinnamic acid, coumarin. Some 1000 natural coumarins have been isolated. Coumarin itself has been found in about 150 species belonging to over 30 different families. The richest sources of coumarin are sweet clover or melilot (*Melilotus* spp.), *Dipteryx odorata* (tonka bean) and *Galium odoratum* (sweet woodruff) [8]. Aesculetin, umbelliferone and scopoletin are common coumarins present in plants both in the free state and as glycosides. Plants rich in coumarins include *Atropa belladonna*, *Datura stramonium* (Solanaceae), *Daphne mezereum* (Thymeliaceae), *Ruta graveolens* (Umbelliferae) and certain *Aesculus hippocastanum* (Horse-chestnut) (Hippocastanaceae) and certain Rosaceae [7]. Anti-inflammatory, anticoagulant, anticancer and anti-Alzheimer's activities are the most important biological activities reported for coumarins [20]. Examples of coumarins are shown in **Figure 5**.

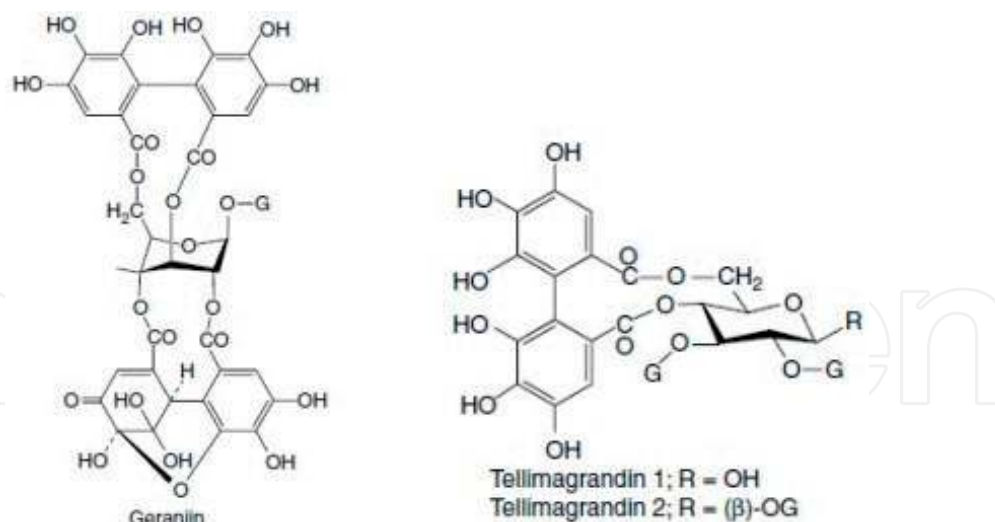


Figure 4. Examples of hydrolysable tannins.

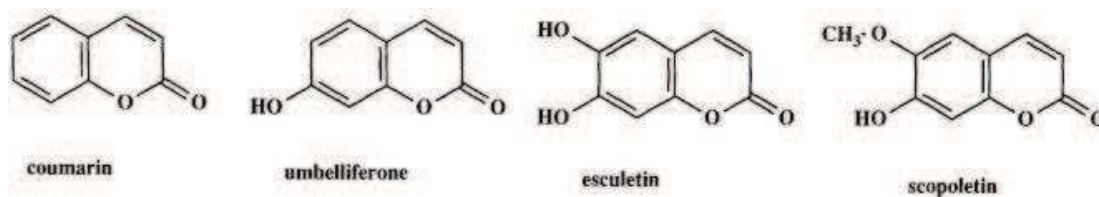


Figure 5. Examples of coumarins.

2.4. Flavonoids

Flavonoids are the largest group of naturally occurring phenols. More than 2000 of these compounds are now known, with nearly 500 occurring in the free state [7]. The structural skeleton of flavonoids includes a chroman ring bearing an aromatic ring in position 2, 3 or 4. Flavonoids may be divided into various classes according to the oxidation level of the central ring (ring C). The most common of these are anthocyanins, flavones and flavonols. The flavones and their close relations are often yellow (Latin *flavus*, yellow). They are widely distributed in nature but are more common in the higher plants and in young tissues, where they occur in the cell sap. They are abundant in the Polygonaceae, Rutaceae, Leguminosae, Umbelliferae and Compositae. Recent researches have demonstrated the medicinal action of drugs containing flavonoids such as *Glycyrrhiza glabra* (licorice root), *Chamaemelum nobile* (Roman chamomile) and *Ginkgo biloba* (gingko). A number of flavonoid-containing herbs have now been included in the *British Pharmacopeia*, examples are *Betula pendula* (Birch Leaf), *Calendula officinalis* Flower, *Sambucus nigra* (Elder Flower), *Equisetum ramosissimum* (Horsetail), *Tilia cordata* (Lime Flower), *Leonurus cardiaca* (Motherwort) and *Passiflora edulis* (passion flower). The group is known for its anti-inflammatory and anti-allergic effects, for antithrombotic and vasoprotective properties, for inhibition of tumor promotion and as a protective for the gastric mucosa [21, 22]. Examples of flavonoids are shown in **Figure 6**.

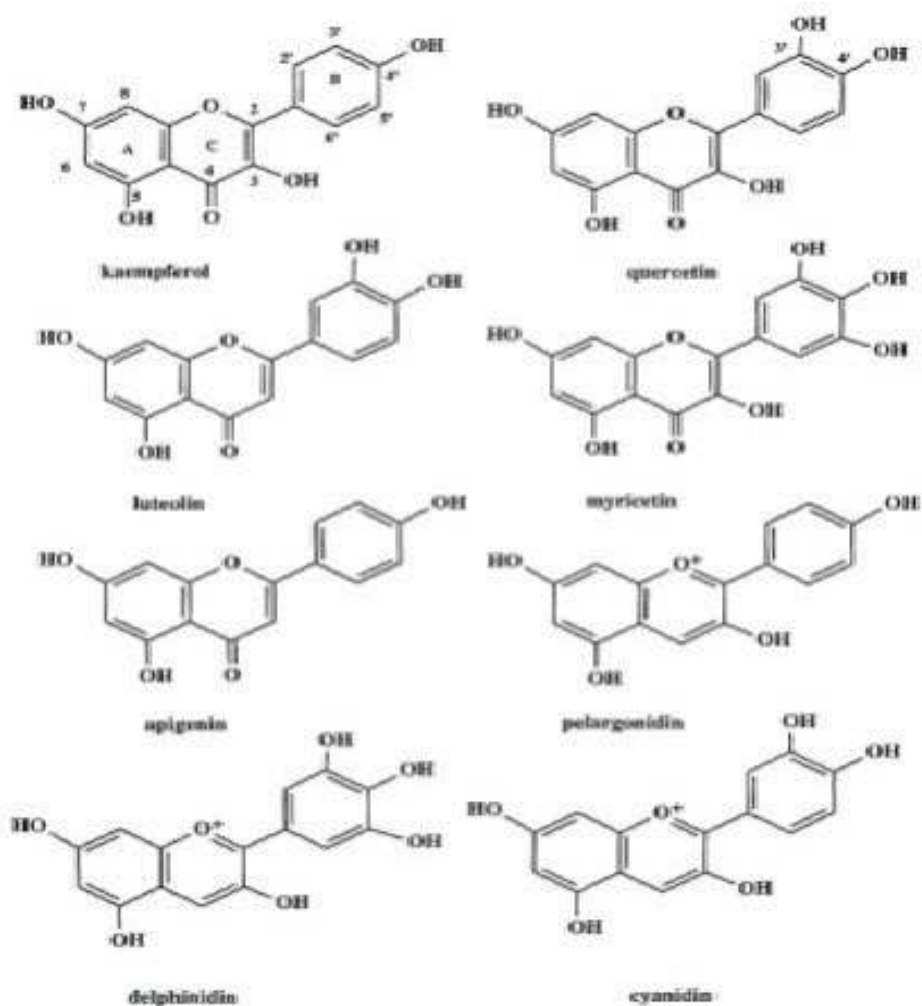


Figure 6. Examples of flavonoids.

2.5. Chromones and xanthenes

These compounds are structural derivatives of benzo- γ -pyrone, and although not of great pharmaceutical importance, a few compounds are worthy of mention; eugenin is found in the clove plant and khellin from mustard seeds [7]. More complex are the furanochromones, the active constituents of the fruits of *Ammi visnaga*. Xanthenes are found mainly in the Gentianaceae and Guttiferae, otherwise scattered sporadically throughout the plant kingdom as in the Moraceae and Polygalaceae. *Polygala nyikensis* is used by the highlanders of Malawi and bordering countries to treat various skin problems of fungal origin. The root of the plant was recently shown to exert its antifungal activity owing to the presence of xanthenes [23].

2.6. Stilbenes

Stilbenes are a relatively small, but widely distributed, group of plant secondary metabolites found mostly as heartwood constituents in a heterogeneous assembly of plant species. They are especially important in the heartwood of trees of the genera *Pinus* (Pinaceae), *Eucalyptus*

(Myrtaceae) and *Madura* (Moraceae) [1]. The *para-hydroxylated* compound, resveratrol, is the most widespread stilbene in nature. Resveratrol possesses estrogen-like activity and occurs in *Picea*, *Pinus*, the Fabaceae, Myrtaceae and the Vitaceae [24].

2.7. Lignans

Lignans are dimeric compounds formed essentially by the union of two molecules of a phenylpropene derivative reported from the members of Asteraceae (e.g., *Achillea lingulata* [25]), Pinaceae (e.g., *Cedrus deodara* [26]) and Rutaceae (e.g., *Fagara heitzii*) [27]. Four major subtypes occur: dibenzylbutane derivatives, dibenzylbutyrolactones (lignanoides or derivatives of butanolide), monoepoxy lignans or derivatives of tetrahydrofuran and bisepoxylignans or derivatives of 3,7-dioxabicyclo(3.3.0)-octane. Many of these compounds showed antimicrobial and antifungal activities [1], while others showed cytotoxic activities such as wikstromal, matairesinol and dibenzyl butyrolactol from *Cedrus deodara* [26].

3. Alkaloids

Alkaloids are organic compounds with at least one nitrogen atom in a heterocyclic ring. Their definition is problematic, as they do not represent a homogeneous group of compounds from any standpoint, whether chemical, biochemical, or physiological. Except for the fact that they are all nitrogen-containing compounds, no general definition fits all alkaloids. Alkaloids can be divided according to their basic chemical structure into different types. The following are basic types of alkaloids: acridones, aromatics, carbolines, ephedras, ergots, imidazoles, indoles, bisindoles, indolizidines, manzamines, oxindoles, quinolines, quinozolines, phenylisoquinolines, phenylethylamines, piperidines, purines, pyrrolidines, pyrrolizidines, pyrroloindoles, pyridines and simple tetrahydroisoquinolines [28].

Although plants containing alkaloids have been used by man for at least 3000 years as medicines, teas and potions, the compounds responsible for activity were not isolated and characterized until the nineteenth century [1]. Alkaloids are not common in lower plants. Lysergic acid derivatives and sulfur-containing alkaloids, e.g., the gliotoxins, are detected in fungi. Concerning the pteridophytes and gymnosperms alkaloids reported for their medicinal uses include the lycopodium, ephedra and *Taxus* alkaloids. Alkaloids are unevenly distributed among the angiosperms. The following are the orders reported to be rich in alkaloids: Centrospermae (Chenopodiaceae), Magnoliales (Lauraceae, Magnoliaceae), Ranunculales (Berberidaceae, Menispermaceae, Ranunculaceae), Papaverales (Papaveraceae, Fumariaceae), Rosales (Leguminosae, subfamily Papilionaceae), Rutales (Rutaceae), Gentiales (Apocynaceae, Loganiaceae, Rubiaceae), Tubiflorae (Boraginaceae, Convolvulaceae, Solanaceae) and Campanulales (Campanulaceae, sub-family Lobelioideae; Compositae, subfamily Senecioneae). However, there is no report for the presence of alkaloids in Salicales, Fagales, Cucurbitales and Oleales dicot orders till the present time [7].

Alkaloids demonstrate a diverse array of pharmacological actions including analgesia, local anesthesia, cardiac stimulation, respiratory stimulation and relaxation, vasoconstriction,

muscle relaxation and toxicity, as well as antineoplastic, hypertensive and hypotensive properties. The activity of alkaloids against herbivores, toxicity in vertebrates, cytotoxic activity, the molecular targets of alkaloids, mutagenic or carcinogenic activity, antibacterial, antifungal, antiviral and allelopathic properties have been reported in literature. Many alkaloids are sufficiently toxic to animals to cause death if eaten. Several (e.g., nicotine and anabasine) are used as insecticides [1, 8].

Examples of some alkaloids:

3.1. Nicotine

Nicotine is found in the tobacco plant (*Nicotiana tabacum*) and other *Nicotiana* species; it has tranquilizing properties and is the addictive component of tobacco. It is also extremely toxic, causing respiratory paralysis at high doses (Figure 7). Nicotine is a ganglion cholinergic-receptor agonist with complex pharmacological actions, including effects mediated by binding to receptors in the autonomic ganglia, the adrenal medulla, the neuromuscular junction and the brain [29].

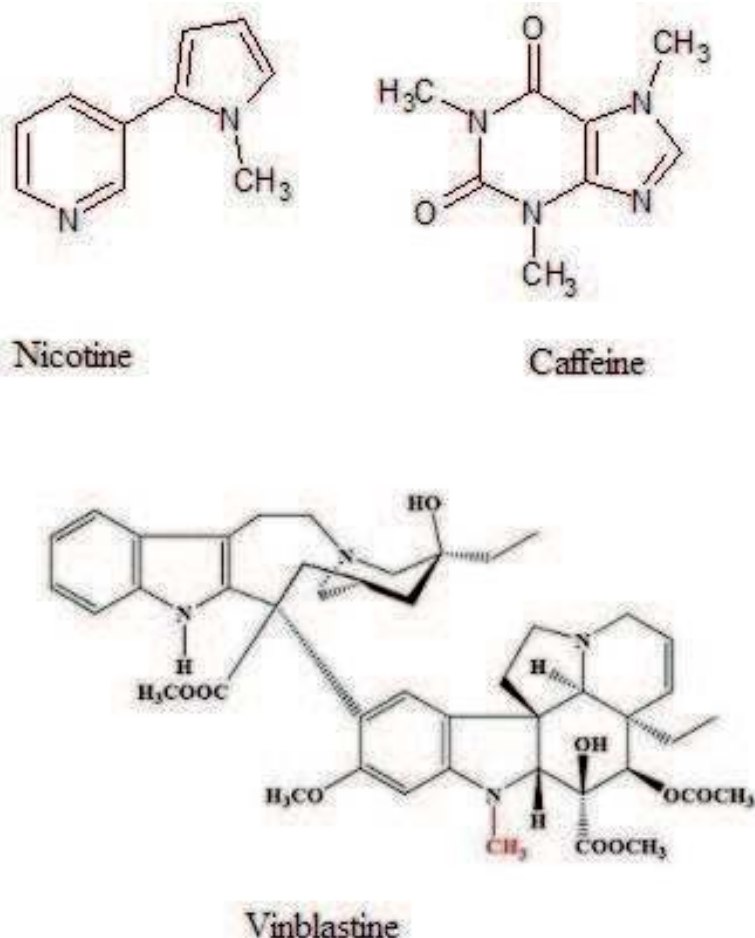


Figure 7. Examples of alkaloids.

3.2. Caffeine

Caffeine occurs in a number of botanically unrelated species, including coffee (*Coffea* spp.), tea (*Camellia sinensis*), mate (*Ilex paraguariensis*), guarana (*Paullinia cupana*) and kola (*Cola acuminata*) (Figure 7). Caffeine is bound to chlorogenic acid in raw coffee beans. The roasting process liberates the caffeine and other compounds that contribute to the aroma of coffee. Caffeine is a diuretic and has stimulant effects on the respiratory, cardiovascular and central nervous systems [30].

3.3. Vinblastine

Vinblastine is isolated from *Catharanthus roseus* G. (Figure 7) and has been used to treat diabetes and high blood pressure and as disinfectant. Nevertheless, Vinblastine is so important for being cancer fighters. It is used along with the other vinca alkaloids vinorelbine, vincristine and vindesine, which are in clinical use in the United States and Europe [31].

4. Saponins

Saponins are compounds that possess a polycyclic aglycone moiety with either a steroid (steroidal saponins) or triterpenoid (triterpenoidal saponins) attached to a carbohydrate unit (a monosaccharide or oligosaccharide chain) (examples illustrated in Figures 8 and 9). These sugar units are composed variously of pentoses, hexoses, or uronic acids. This hydrophobic-hydrophilic asymmetry means that these compounds have the ability to lower surface tension and are soap-like. They form foam in aqueous solutions and cause hemolysis of blood erythrocytes in vitro. The aglycone portion of the saponin molecule is called the *genin* or *sapogenin*. Saponins are widespread among plants, having been reported from more than 500 plants from at least 90 different families; these substances have been isolated from all parts of

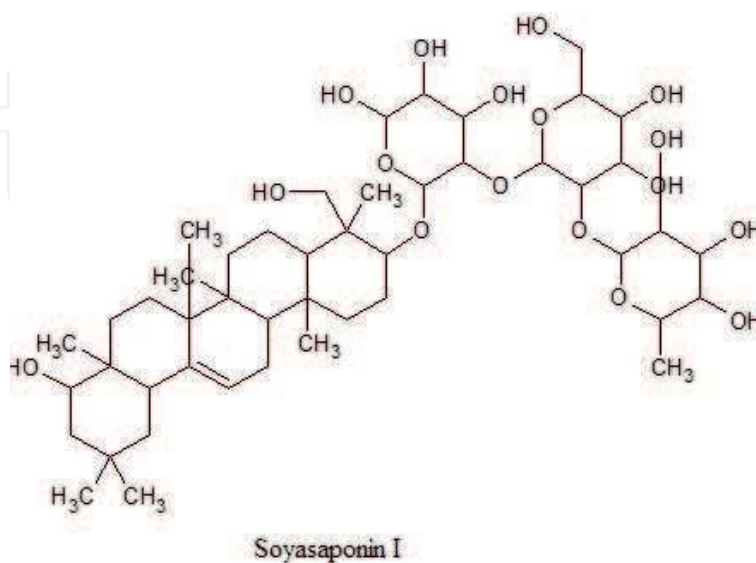


Figure 8. Example of triterpenoidal saponin.

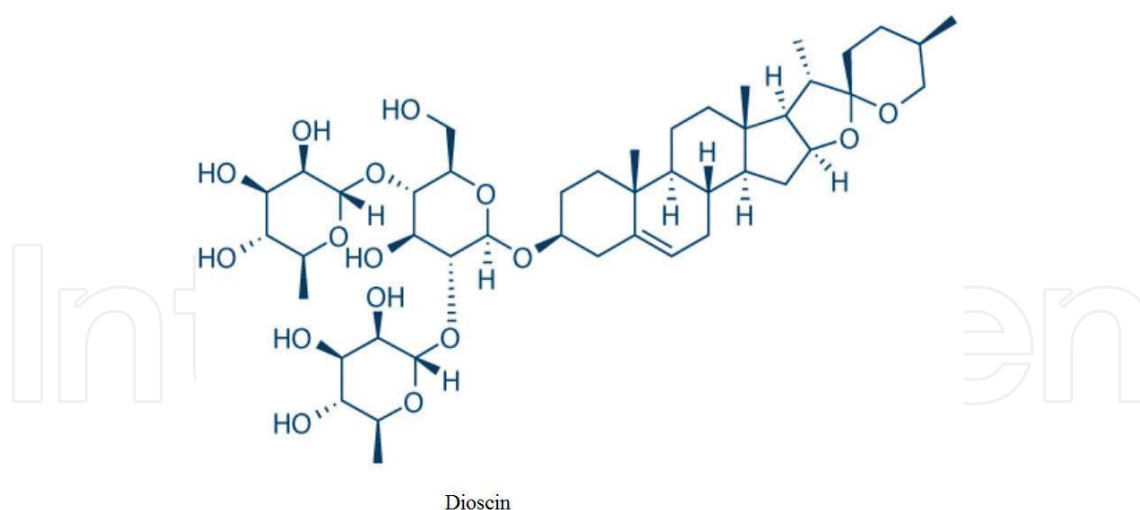


Figure 9. Example of steroidal saponin.

plants: leaves, stems, roots bulbs, flowers and fruits, although they tend to be concentrated in the roots of many species such as *Digitalis purpurea* (foxglove), *Dioscorea villosa* (wild yam), *Eleutherococcus senticosus* (Siberian ginseng), *Gentiana lutea* (gentian), *Glycyrrhiza* spp. (licorice) and *Panax ginseng* (Korean ginseng) [32].

Saponins have demonstrated numerous pharmacological properties. Some saponins have antitumor, piscicidal, molluscicidal, spermicidal, sedative, expectorant and analgesic properties. Glycyrrhizin from *glycyrrhizae radix* (from *Glycyrrhiza glabra*, Fabaceae) is useful as expectorant and antitussive agent. It is also used to treat chronic hepatitis and cirrhosis. Some saponins have anti-inflammatory properties as the saponins from *Bupleurum falcatum* (Apiaceae). *Phytolacca americana* roots are reputed to possess anti-inflammatory properties in Korean medicine. Similar properties have been demonstrated for a number of other saponins, for example aescin, from horse chestnut (*Aesculus hippocastanum*), has been shown to be 600 times more effective than rutin in reducing rat paw edema [33].

5. Terpenes

Terpenes are the largest and most diverse group of plant secondary compounds. The name “terpene” is derived from the word “turpentine,” which in turn comes from the old French *ter(e)binth*, meaning “resin.” They are all derived chemically from 5-carbon isoprene units assembled in different ways [8]. Terpenes are classified according to the number of isoprene units in the molecule; a prefix in the name indicates the number of terpene units as follows.

5.1. Hemiterpenes

They consist of a single isoprene unit. Isoprene itself is considered the only hemiterpene, but oxygen-containing derivatives such as angelic acid isolated from *Angelica archangelica* and isovaleric acid from *Vaccinium myrtillus* are hemiterpenoids [1].

5.2. Monoterpenes

They consist of *two isoprene* units and have the molecular formula $C_{10}H_{16}$ (see **Figure 10**). They are important components of plant essential oils or volatile oils. Monoterpenes tend to occur in members of certain plant families, such as Lamiaceae, Pinaceae, Rutaceae and Apiaceae, from which many essential oils are commercially produced. Some of these compounds, such as geraniol, are almost ubiquitous and can be found in small amounts in the volatile secretions of most plants. Monoterpenes are further classified into unsaturated hydrocarbons (e.g., limonene), alcohols (e.g., linalool), alcohol esters (e.g., linalyl acetate), aldehydes (e.g., citronellal) and ketones (e.g., Carvone). Monoterpenes and other volatile terpenes have a number of widespread medicinal uses. Compounds such as camphor and menthol are used as counterirritants analgesics and anti-itching agents. Many monoterpenes have been used as anthelmintics. A series of monoterpene glycosides appear to have vasodilation effect on coronary vessels and the femoral vascular bed [16].

5.3. Sesquiterpenes

They consist of *three isoprene* units and have the molecular formula $C_{15}H_{24}$ (see **Figure 11**). Based on biogenetic origin, there are more than 200 different structural types of sesquiterpenes, and several thousand such compounds are known. These compounds can be conveniently classified into three main groups according to structure: acyclic (e.g., farnesol), monocyclic (e.g., bisabolol) and bicyclic (e.g., caryophyllene). A number of sesquiterpene lactones show antibacterial, antifungal and antiprotozoan activities. Sesquiterpenes from *Vernonia colorata* inhibit *Entamoeba histolytica* at concentrations comparable to metronidazole, an antiamebic drug. Helenalin and a series of related compounds are responsible for the cardiotoxic properties of *Arnica montana* flowers. *Atractylodis rhizoma*, from *Atractylodis macrocephala* (Asteraceae), is clinically used as diuretic, analgesic and anti-inflammatory. The activity is related to the presence of active compounds including eudesma-4(14)-7(11)-dien-8-one and atractylenolide I. Several related medicinal plants are also used for the same purposes due to the presence of sesquiterpenes [1, 34].

5.4. Diterpenes

They are composed of *four isoprene* units and have the molecular formula $C_{20}H_{32}$ (see **Figure 12**). Diterpenes are classified into acyclic and macrocyclic compounds. Moreover, macrocyclic

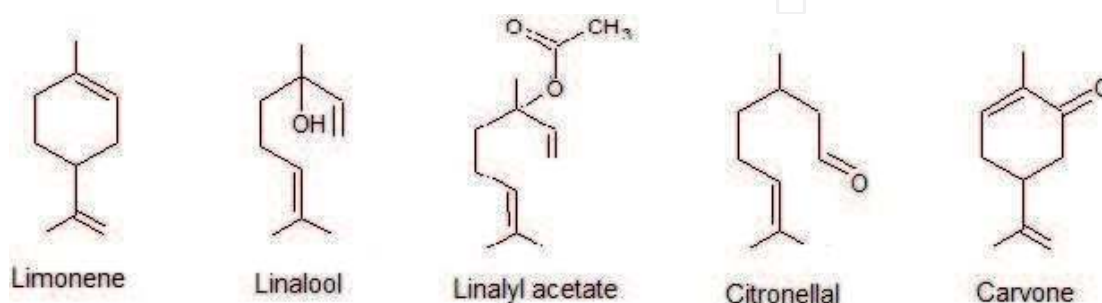


Figure 10. Examples of monoterpenes.

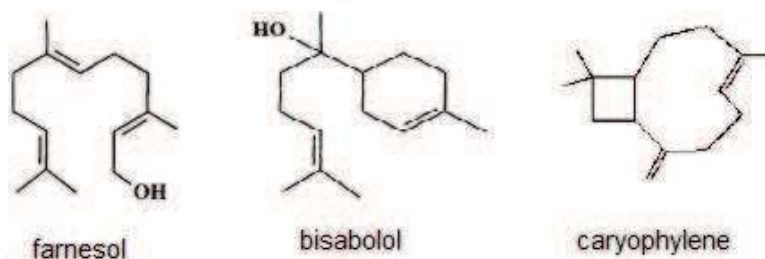
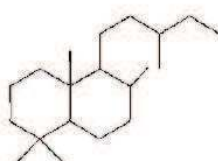


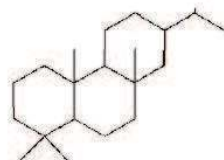
Figure 11. Examples of sesquiterpenes.



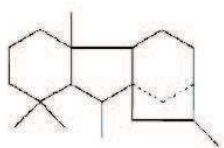
Phytane



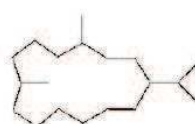
Labdane



Abiatane



Gibberellane



Cembrane

Figure 12. Examples of diterpenes.

diterpenes are classified according to the number of ring systems present. Diterpenes may be 6-membered ringed structures or they may have fused 5- and 7-membered ringed structures. In addition, many diterpenes have additional ring systems. These occur as side substituents as esters or epoxides [8]. Diterpenoids constitute the active constituents of a number of medicinal plants. Vitamin K1, an antihemorrhagic compound, first discovered in plants in 1929, is a diterpene. Vitamin A, a diterpenoid, is referred to, together with the related compounds, as "carotenes." The bitter principles of *Jateorhiza palmata* (calumba root) belong to furanoditerpenes. *Teucrium chamaedrys* (wall germander) and *T. scorodonia* (wood sage) family

Labiatae, both produce diterpenes of the neoclerodane type. They are used in herbal medicine as diaphoretics and antirheumatics [35]. Like all groups of terpenes, diterpenes have demonstrated a range of pharmacological properties including: analgesic, antibacterial, antifungal, anti-inflammatory, antineoplastic and antiprotozoal activities [8]. Some diterpenes from *Kalmia latifolia* (Ericaceae) have antifeedant properties with respect to the gypsy moth. The gibberellins, first obtained from fungi of the genus *Gibberella* but also found in higher plants, are diterpenoid acids, which have a marked effect on growth of seedlings [7].

5.5. Sesterterpenes

Terpenes having 25 carbons and *five isoprene* units are rare relative to the other sizes (the *ses-* prefix means half to three, i.e. two and a half). An example of a sesterterpenoid is geranyl farnesol isolated from seed oils of *Camellia sasanqua* (sasanqua) and *Camellia japonica* (camellia), family Theaceae [36]. Geranyl farnesol showed cytotoxic activity in mouse leukemic M1 cells [37].

5.6. Triterpenes

They consist of *six isoprene* units and have the molecular formula $C_{30}H_{48}$ (see **Figure 13**). The linear triterpene squalene, the major constituent of shark liver oil, is derived from the reductive coupling of two molecules of farnesyl pyrophosphate. Triterpenes constitute a significant portion of the lipid substances of all plants; more than 4000 triterpenoids have been isolated. These compounds are precursors to steroids in both plants and animals. Both triterpenes and steroids occur free, as glycosides or in other combined forms. The structures of triterpenes and steroids may be subdivided into about 40 major types [1]. β -Boswellic acids (ursane-type triterpene) and α -boswellic acids (oleanane-type triterpene) that are isolated from the oleo-gum-resin of *Boswellia carterii* are known for their anti-inflammatory and anti-rheumatic activities [38].

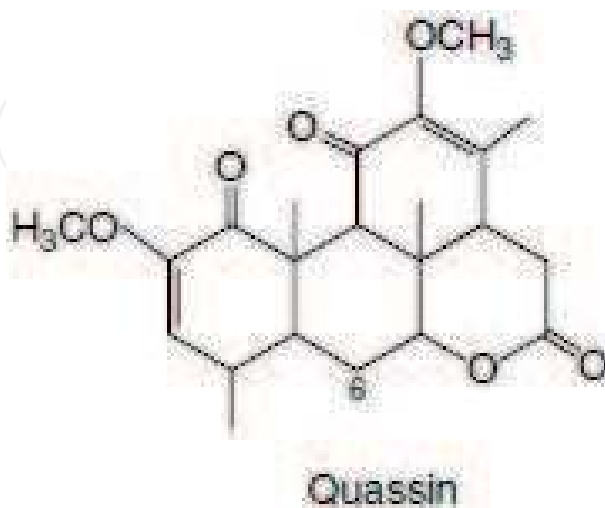


Figure 13. Example of triterpene.

One group of compounds showing a range of interesting biological activity is the quassinoids isolated from *Quassia amara*. These are degradation and rearrangement products of triterpenes. *Quassia* is used as a bitter tonic, as an insecticide and as an enema for the expulsion of thread worms.

Terpenes also include sesquiterpenes (*seven isoprene units*, $C_{35}H_{56}$), tetraterpenes (*eight isoprene units*, $C_{40}H_{64}$) as well as polyterpenes and norisoprenoids (long chains of *many isoprene units*).

6. Lipids

Lipids comprise a group of naturally occurring molecules that include fixed oils, waxes, essential oils, sterols, fat-soluble vitamins (such as vitamins A, D, E and K), phospholipids and others. Lipids serve various biological actions as major structural components of all biological membranes and as energy reservoirs and fuel for cellular activities in addition to being vitamins and hormones [39, 40]. Although lipids are considered primary plant metabolites, recent studies revealed pharmacological activities to members of this class of phytochemicals.

6.1. Fixed oils

Fixed oils constitute of high molecular aliphatic long-chain fatty acids, such as palmitic, stearic and oleic acids, esterified with glycerol. Fixed oils contain a relatively higher percentage of liquid glycerides (polyunsaturated) such as glycerin oleate, while fats are rich in solid glycerides such as glycerin stearate. [39]. Flax and linseed and its oil are obtained from *Linum usitatissimum*, family Linaceae. Polyunsaturated fatty acids in some fixed oils cause reduced excretion of lipid peroxidation products and hence are potent antioxidants and anti-inflammatory. They are used as prophylactic to decrease the risk of atherosclerosis and cardiovascular disease [41].

6.2. Waxes

Waxes are lipoidal matter constituting mainly from long aliphatic chains that may contain one or more functional groups. They may contain hydroxyl groups as in the case of primary and secondary long-chain alcohols that are frequently present in the form of esters. Others contain unsaturated bonds, aromatic systems, amide, ketonic, aldehydic or carboxylic functional groups. On the other hand, synthetic waxes constitute of long-chain hydrocarbons (alkanes or paraffins) that lack functional groups. They are similar to the fixed oils and fats since they are esters of fatty acids, but with the difference that the alcohol is not glycerin. The seeds of *Simmondsia chinensis* yield the liquid wax, jojoba wax, which consists of straight chain esters of fatty acids and alcohols [42]. Jojoba wax has anti-inflammatory, anti-aging and wound healing activities, and hence it can be utilized in several skin conditions. Jojoba wax has also been used in topical medications to enhance drug absorption. In addition, it is used in skin care products and in cosmetics such as sunscreens and moisturizers [43].

6.3. Essential oils

Essential oils are volatile aromatic complex mixtures of relatively low molecular weight compounds. Although they may contain up to 60 components, yet they are characterized by the presence of two or three major components at fairly high concentrations (20–70%) compared to other components present in trace amounts. For example, *Origanum compactum* essential oil contains carvacrol (30%) and thymol (27%) as major components. Linalol is the major component of *Coriandrum sativum* essential oil reaching up to 68%. Other examples are *Artemisia herba-alba* essential oil which contains α - and β -thuyone (57%) and camphor (24%) as major constituent, *Cinnamomum camphora* essential oil with 1,8-cineole (50%) as major constituent and finally *Mentha piperita* essential oil with menthol (59%) and menthone (19%) being the major constituent. Generally, these major components determine the biological properties of the essential oils [44]. They have many and important medical uses such as antiseptic, antimicrobial, analgesic, sedative, anti-inflammatory, spasmolytic and locally anesthetic remedies. They are also used as fragrances in embalmment and in food preservation [45].

7. Carbohydrates

Carbohydrates are universally present in living beings on our planet. As the first product of photosynthesis, carbohydrates are the starting point for all phytochemicals and also, by extension, for all animal biochemicals. More carbohydrates occur in nature than any other type of natural compound. The most abundant single organic substance on Earth is cellulose, a polymer of glucose, which is the main structural material of plants. Although carbohydrates are primary metabolites, they are incorporated in plenty of secondary metabolites through glycosidation linkages. Polymers of simple sugars and uronic acids produce mucilages and gums [46].

Carbohydrates consist of carbon, hydrogen and oxygen with the last two elements usually present in the same proportions as in water. They are classified into four chemical groups: monosaccharides, disaccharides, oligosaccharides and polysaccharides. Monosaccharides contain from three to nine carbon atoms, although those with five and six carbon atoms (pentoses, $C_5H_{10}O_5$, and hexoses, $C_6H_{12}O_6$) are accumulated in plants in greatest quantity. Condensation of monosaccharides results in the other types according to the number of saccharide units involved. In addition to the important biological and structural function of carbohydrates in plants, some members show medicinal effects such as mucilage. Mucilage, viscous sticky material produced by almost all plants and some microorganisms, plays a protective role in thickening membranes in plants. It also serves in storage of water and food and in seed germination. Chemically it constitutes of a polar glycoprotein and an exopolysaccharide. Mucilage is used medicinally as demulcent. Cactus (and other succulents) and *Linum usitatissimum* (flax seeds) are the major sources of mucilage. The extract of the mucilaginous root of the marshmallow plant (*Althaea officinalis*); used traditionally to make marshmallows, were used as cough suppressant due to its demulcent effect. *Ulmus rubra* (the slippery elm) inner bark, is also used as a demulcent due to its mucilaginous content. Mucilage acts primarily as a local demulcent or emollient when it comes in direct contact with mucous membrane

surfaces or skin. Here, they produce a coating of “slime” that soothes and protects exposed or irritated surfaces of the gastrointestinal tract. They are used extensively in the management of inflammatory digestive disorders, especially when there is ulceration. Their relative indigestibility and hydrophilic properties have important influences on bowel behavior [47].

8. Conclusion

According to the abovementioned data, there are several classes of secondary plant metabolites that are responsible for the biological activities of herbal medicines. Eventually, secondary plant metabolites exert their action on molecular targets that differ from one case to the other. These targets may be enzymes, mediators, transcription factors or even nucleic acids. The use of herbal medicines should be based on comprehensive phytochemical studies for the determination of the chemical constituents of the herbs involved. Hence the knowledge of the resultant pharmacological and toxicological effects can be deduced, as well as the possible synergistic or antagonistic effects due to the use of multiple component herbal formulae. For this reason, the isolation and structural elucidation of secondary plant metabolites, though ancient, is still a huge and fast growing approach, and the techniques used for separation and analysis are advancing continuously.

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