

Study on Plant Secondary Metabolites and their Pharmaceutical Properties with Emphasis on Depression Treatment

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Abstract—Plants are important source for the discovery of new products of medicinal value for drug development. In fact, the medicinal properties of plants are due to the presence of some plant compounds called secondary metabolites which include three large molecule families: Phenolics, Terpenes - Steroids and Alkaloids-Flavonoids. On the other hand, plants secondary metabolites are the best sources for pharmaceuticals food additives, flavors and other industrial values. Nowadays, utilization of chemical medicines has been replaced by the consumption of herbal drugs due to the lack of side effects, availability and cheaper price. In this article, some of the pharmacological properties of secondary metabolites and effectiveness of alkaloids on depression treatment will be investigated.

Keywords: Secondary metabolites, Phenolics, Terpenes and Steroids, and Alkaloids, Flavonoids, Depression.

Introduction

Plants are important source for the discovery of new products of medicinal value for drug development. In fact, the medicinal properties of plants are due to the presence of some plant compounds called secondary metabolites. Hence, investigation on these type of plant compounds is considered by researchers and medicinal organizations. Kossel was the first to define these metabolites as opposed to primary ones. It has been clearly demonstrated that secondary products play a major role in the adaptation of plants to their environment. Due to antiviral, antibiotic, and antifungal activities have been recorded to ability to protect plants from pathogens[13].

Primary metabolism in a plant involved all metabolic pathways which are necessary to the plant's survival whereas secondary metabolites are compounds constructed in other metabolic pathways and are not required for plant survival[6].

Secondary metabolites are organic components produced by fungi, or plants and bacteria which are not directly involved in the normal growth, development, or reproduction of the organism while primary metabolism in a plant included all metabolic pathways which are necessary to the plant's survival. Primary metabolites are components which are directly included in the growth and development of a plant [6]. Humans use secondary metabolites as medicines, pigments, flavours [17] insecticides, scents, rubber, and other industrial materials like resins, gums for human welfare[7]. Particular secondary metabolites are often restricted to a narrow set of species within a phylogenetic group[17].

Discussion

Secondary metabolites are organic components produced by fungi, or plants and bacteria. Secondary metabolism produces a large number of specialized components (guesstimated 200, 000) that do not aid in development and the growth of plants but are essential for the plant to survive in its environment. Secondary metabolism is connected to primary metabolism by applying biosynthetic and building blocks enzymes derived from primary metabolism [6]. Well known secondary metabolites compounds involve alkaloids, flavonoids, polyphenols and terpenoids. Humans use quite a lot of these compounds, for culinary, medicinal and nutraceutical purposes. [4]. There is no fixed, commonly agreed system for classifying secondary metabolites. Based on their biosynthetic origins, plant secondary metabolites can be divided into three major groups: Terpenoids, Flavonoids and allied phenolic and polyphenolic compounds, and Nitrogen-containing alkaloids and sulphur-containing compounds[2].

Alkaloids: Alkaloids are originally specified as pharmacologically active, nitrogen-containing basic compounds of plant origin. And they can inhibit enzymes, block ion channels or interfere with neurotransmission, producing hallucinations, loss of coordination, convulsions, vomiting, and death.

Phenolics: Phenolics interfere with digestion, block enzyme activity, slow growth and cell division, or just taste awful [1].

Terpenes: Terpenes are a unique group of hydrocarbon based natural products whose structures may be derived from isoprene. Terpenes are the most widespread chemically diverse groups of natural products. The function of terpenes in plants is generally considered to be both ecological and physiological: Allelopathy, Insecticidal, Insect pollinators, Plant hormone (gibberellin, Abscisic acid).

Flavonoids: Flavonoids constitute an enormous class of phenolic natural products with more than 4500 different representatives known thus far. Present in most plant tissues, often in vacuoles and perform a wide range of functions. Specific flavonoids can also function to protect plants against UV-B irradiation. The flavonoids consist of various groups of plant metabolites which include flavanones, isoflavonoids, chalcones, anthocyanins, leucoanthocyanidins, catechins, flavones, flavonols and aurones.

Coumarins and Stilbenes: Coumarins belong to a widespread family of plant metabolites called the benzopyranones, with more than 1500 representative in more than 800 species. In plants these compounds can occur in seed coats, fruits, flowers, roots, leaves, stems, although in general the greatest concentration are found in fruits and flowers. Their roles in plants appear to be mainly defense-related, given their germination inhibitor, antimicrobial and UV-screening properties.

Due to their large biological activities, plant secondary metabolites have been used for centuries in traditional medicine. Some alkaloids compounds include Ephedrine, Quinine Cocaine, Psilocin, Caffeine, Nicotine, Morphine. Atropine is a type of secondary metabolite called a tropane alkaloid. Flavonoids are also known as Vitamin P or citrin. These metabolites are mostly used in plants to produce yellow and other pigments which play a big role in coloring the plants [4].

Nowadays, they correspond to valuable compounds such as pharmaceuticals, cosmetics, fine chemicals. Recent surveys have established that in western countries, where chemistry is the backbone of the pharmaceutical industry, 25% of the molecules used are of natural plant origin [14].

Application of secondary metabolites:

Some products which successfully produced in plant cell cultures include drugs to control cardiovascular disorders (digoxin), hypotensives (reserpine), perfumes (jasmine), insecticides (pyrethrin), muscle relaxants (atropine),

analgesics (codeine) antimalarial (quinine), anticancer agents (vincristine) and food sweeteners (stevioside)[8].

Secondary metabolites have well-known medical uses, which include antitumor, antimicrobials, cholesterol-lowering, antiprotozoal, antihelminth, antiviral, anti-ageing and immunosuppressant activities. Polyene antibiotics, such as amphotericin B, are of use as antiprion agents, antitumor drugs and against leishmaniasis. Pigments like prodigiosin and shikonin have antitumor activity, while violacein has anti-ulcer and antitumor activity and also acts as an antiprotozoal agent [15].

Some medicinal properties of plant secondary metabolites

Phyto-compounds are known to play a major role in the adaptation of plants to their environment, but also represent an important source of pharmaceuticals [16]. There for, several plant species are being screened for these herbal compounds and are also isolated from the plants. Plants produce a vast variety of secondary compounds as natural protection against microbial and insect attack [11]. Here some of the medicinal benefits of secondary metabolites have been considered.

Antitumor activity:

The inhibitory effects of 151 natural products, representing most of the frequently occurring types, on the cytotoxicity to MM2 tumor cells of polymorphonuclear leucocytes (PMN) induced by TAK, a polysaccharide immunomodulator, were examined. Forty-two compounds inhibited the TAK-induced activation of PMN. Among them, some naturally occurring quinones and various alkaloids (nicotine, Cinchona alkaloids, isoquinoline alkaloids such as cepharanthine, and indole alkaloids such as ajmaline) exhibited potent inhibitory effects [12].

Anti-diabetic Activity

DM (Diabetes mellitus) is a metabolic disorder characterized by chronic hyperglycemia or increased blood glucose level with the disturbance in carbohydrate metabolism resulting from absolute or relative lack of insulin secretion. The frequency of this disorder is on the rise globally and is likely to hit 300 million by 2025.- Aloe vera L.: Percent inhibition activity of alpha-amylase by different extracts of leaves of *Aloe vera* L. were evaluated and both flavonoids and alkaloids were found to show alpha-amylase inhibitory activity by showing 55.83 ± 0.12 to 57.70 ± 0.09 with IC_{50} value of 0.0002 mg/ml [10].- *Melothriamaderaspatana*: Percent inhibition activity of alpha-amylase by steroids and Alkaloids sample of the leaf of *Melothriamaderaspatana* was evaluated. The IC_{50} value was calculated in the studies to be 65.10 μ g/ml and 74.12 μ g/ml. Steroids extracted shows significant anti diabetic potential from stem and flavonoids extracted from the fruit and leaf showed the highest inhibitory activity IC_{50} value was reported to be 61.42 μ g/ml [3].

- *T. cucumerina*: Alpha-amylase inhibitory activity of different extracts of the fruit of *T. cucumerina* showed $25.23 \pm 0.38\%$ to $36.74 \pm .59\%$, $40.47 \pm 0.66\%$ to $63.74 \pm 1.14\%$, $43.49 \pm .72\%$ to $52.22 \pm 0.48\%$ inhibition at the concentration of 0.3 to 1.5 mg/ml in methanol, flavonoids, steroids and alkaloids respectively. IC₅₀ values of methanol, flavonoid, steroids and alkaloids extract were 209.36 µg/ml, 40.77 µg/ml, 74.61 µg/ml and 135.77 µg/ml respectively.

The fruit and leaf part of the plant are a good source of flavonoids so these parts have significant α-amylase activity showing their anti-diabetic potential[3].

Antioxidant Activity

Antioxidants have been reported to prevent oxidative damage caused by free radicals. All organisms are protected from free radical attack by defense mechanisms that scavenge and stabilize free radicals but when the production rate of free radicals exceeds oxidative stress generates, a deleterious process that can damage cell structures, including lipids, proteins, and DNA. For the prevention and treatment of disease of disease, whose mechanisms involves the process of oxidative stress, many antioxidant based drug formulation is used. Secondary metabolites from following plants have been found to possess antioxidant activity.

- *Limoniaacidissima*: The preliminary studies of the *Limonia* shows the presence of Flavonoids.. A compound similar to flavonoids 2, 3-dihydro-3, 5-dihydroxy-6-methyl-4H-pyran-4-one is revealed in the GC-MS study. Leaf of *Limoniaacidissima* shows that it has the highest antioxidant potential as compared to other plant parts. The IC₅₀ value is reported to be 50.03µg /ml by DPPH assay[21].

- *Sisymbriumirio*: The stem of *Sisymbriumirio* is rich in antioxidant activity. *Durantaerecta*: The GC MS study of *Durantaerecta* shows the presence of 14 compounds which are common in all parts such as Benzene 1, 4- diol, Trans-cinnamic acid 1, 2-Benzene-dicarboxylic acid many compounds similar to flavonoids are also found such as 2H-1-Benzopyran-2-one, 6, 7-dimethoxy-, 2(4H)-Benzofuranone, etc[20]. - *Murrayakoenigii*: By TLC examination three compounds were found to be present namely Kaempferol, quercetin, and luteolin. The leaf of it shows the maximum antioxidant capacity by the DPPH and Lipid peroxidation assay. The IC₅₀ value is reported to be 49.86 µg/ml by DPPH assay[21].

Antimicrobial Activity:

Antibiotics are used to cure the microbial infections and also as chemotherapeutic agents with the belief that it eventually would eradicate all the infectious diseases. The use of plant extracts and phytochemicals, both with known antimicrobial properties, are of great significance to treatment. Antimicrobial activity of various herbs and spices in plant leaves, flowers, stem, roots, and fruits has been carried out by various investigators in different solvent extracts.-

Rumexvesicarius: the acetone, pet ether and benzene extracts were most effective against fungi and acetone against bacterial strains while methanolic and aqueous extracts were least effective. Flower fraction shows maximum antimicrobial activity against *P. funiculosum* (DIZ30 mm, MIC 25 mg/ml), the petroleum ether extract of leaf exhibited maximum antimicrobial activity against *P. funiculosum* (DIZ 30 mm, MIC 12.5 mg/ml) and bacteria *E. coli* (DIZ 20 mm, MIC 25 mg/ml). Crude alkaloid extract shows the highest fungal activity against *P. funiculosum* and *E. coli*[18].-

Durantaerecta: The antimicrobial activity of extracts in different solvents of the selected plant was carried out by disc diffusion, well diffusion and broth dilution. The results showed that methanolic extract of the stem has a potent activity against *A. flavus*, *P. chrysogenum*, and *Rhizopus spp.* The root extract of the plant shows activity against *P. chrysogenum*[20].-*Petreavolubilis*: Root shows antimicrobial capacity among all part parts it has activity against fungus *P. funiculosum* DIZ 16 mm MIC 12.5 mg/ml while the leaf and root against bacteria *D. subtilis* DIZ 25 mm MIC 3.13 mg/ml and against *S. aureus* DIZ 16 mm [19]

Anti-depression activity

Using herbal medicine is an alternative therapy of depression. Currently there are variety of different plants containing indole alkaloids among which *Passifloraincornata L.* (Passion flower) and *Mitragyna speciose* (korth) are two of the well-known plants having enough efficacy on depression treatment. Therefore, these plants and their containing alkaloids boost brain serotonin which leads to happiness and prevention of depression[5][9].

Conclusion

This study focuses on a small part of plant secondary-metabolites and their roles in defence mechanisms and some of their medicinal efficacies. There are many other secondary metabolites and plants which pass very effective medicinal. Plants, microorganisms including bacteria, action bacteria, and fungi are the most important sources of secondary metabolites. Since many researchers in all over the world are studding on pharmaceutical properties of herbal plants which can cure cancers, cardiac disorders, pests, cytotoxic, mosquitoes, depression disorders, infectious diseases, and autoimmune disorders. Secondary metabolites with noteworthy biological activity are considered as an alternative to most of the synthetic drugs and other commercially valuable compounds.

References:

- [1] Bourgaud F., A. Gravot, S. Milesi, E. Gontier —Production of plant secondary metabolites: a historical perspective. 2001. Volume161, Issue 5, Pages 839–851.
- [2]"Chapter 1. Phenols, Polyphenols and Tannins: An Overview". *Plant Secondary Metabolites: Occurrence, Structure and Role in the Human Diet.*, 2007.

- [3] Chaudhary S: Isolation and characterization of bioactive compounds of *Melothriamaderasptarnia* and *Trichosanthes cucumerina* Linn. Ph.D. thesis, Department of Botany, University of Rajasthan, Jaipur 2016.
- [4] Demain AL, Fang A. The natural functions of secondary metabolites. *Advances in Biochemical Engineering/Biotechnology*. 2000;69:1-39
- [5] Fred R. West, Jr. and Edward S. Mika. "Synthesis of Atropine by Isolated Roots and Root-Callus Cultures of Belladonna." *Botanical Gazette*: 1957. Vol. 119, No. 1 . pp. 50–54 .
- [6] Gold P., Goodwin F. K., Chrousos G. P. (1988). Clinical and biochemical manifestations of depression. Relation to the neurobiology of stress (2). *New Engl. J. Med.* 319, 413–420. 10.1056/NEJM198808183190706 [PubMed] [Cross Ref] [Google Scholar]
- [7] https://en.wikipedia.org/wiki/Plant_secondary_metabolism
- [8] <http://www.biologydiscussion.com/biomolecules/secondary-metabolites-biomolecules/secondary-metabolites-meaning-role-and-types/44935>.
- [9] <http://www.biologydiscussion.com/biotechnology/plant-biotechnology/secondary-metabolites-in-plant-cultures-applications-and-production/10646>.
- [10] Han J., Ji C.-J., He W.-J., Shen Y., Leng Y., Xu W.-Y., et al. . (2011). Cyclopeptide alkaloids from *Ziziphus petala*. *J. Nat. Prod.* 74, 2571–2575. 10.1021/np200755t [PubMed] [CrossRef] [Google Scholar].
- [11] Jain C, Kumar P and Singh A: Hypoglycemic activity of flavonoids and alkaloids extracted from *Aloe vera* in two districts of Rajasthan: A comparative study. *Elixir International Journal* 2013; 62: 17877-17879.
- [12] John Wallace R. —Antimicrobial properties of plant secondary metabolites *Proceedings of the Nutrition Society*, (2004).63, 621–629.
- [13] Kinoshita K, Morikawa K, Fujita M, Natori S. Inhibitory effects of plant secondary metabolites on cytotoxic activity of polymorphonuclear leucocytes. *Planta Med.* 1992 .58(2):137-45.
- [14] Kossel A. —Über die chemische Zusammensetzung der Zelle *Archiv für Physiologie*(1891) 181-186.
- [15] Payne G.F., V. Bringi, C. Prince, M.L. Shuler —The quest for commercial production of chemicals from plant cell culture in: G.F. Payne, V. Bringi, C. Prince, M.L. Shuler (Eds.), *Plant cell and Tissue Culture in Liquid Systems* | Hanser, 1991. pp. 1-10.
- [16] Preeti Vaishnav and Arnold L. Demain. Unexpected applications of secondary metabolites. *Biotechnology Advances*. 2011. Volume 29, Issue 2, Pages 3-229.
- [17] Rao RS and Ravishankar GA: Plant cell cultures: Chemical factories of secondary metabolites. *Biotechnol Adv* 2002; 20: 101-153.
- [18] "Secondary metabolites - Knowledge Encyclopedia". *www.biologyreference.com*. Retrieved 2016-05-10.
- [19] Shah A, Singh T and Vijayvergia R: *In-vitro* antioxidant properties and total phenolic and flavonoid contents of *Rumex vesicuis* *International Journal of Pharmacy and Pharmaceutical Sciences* 2015; 7(7) 81-84.
- [20] Sharma P: Isolation and identification of bioactive compounds from some medicinal plants of Verbenaceae. D. thesis; Department of Botany, University of Rajasthan, Jaipur 2015.
- [21] Sharma N and Vijayvergia R: Study of primary metabolites and antimicrobial activities of *Gomphrenacelosoides* *International Journal of Pharma and Bio Sciences* 2011; 2(4). IP-5.121.