AN OVERVIEW OF THE MEDICINAL POTENTIAL OF PLANT SECONDARY METABOLITES, INCLUDING ITS ANTI-DIABETIC, ANTI-MICROBIAL, AND ANTI-CANCER PROPERTIES

Abstract

Plants are richest source of natural products. These products exhibits wide range of effects on plant, pests, animals including human beings and also on environment stresses. Plant secondary metabolites are the major natural product among all the product of plant more than 50,000 secondary metabolites were reported till now. Numerous plants are considered as medicinal herb and several modern medicines depend on secondary metabolites for their action. These compounds provide protection inside and outside to the plant through a variety of biochemical pathways. Several research and folklore medicines age shows that secondary metabolites possess various well known therapeutic applications. Recent approaches towards new /isolated /mixed/ purified secondary metabolites for the treatment and prevention of the diseases significantly augmenting for betterment of human health.

Keywords: Natural product, secondary metabolites, therapeutic and human health.

Authors

Bhagyalakshmi M
Department of Biochemistry
University College of Science
Tumkur University
Tumakuru 572103, Karnataka, India
bhagyaayanur@gmail.com

Nirmala B
Department of Studies and Research in Chemistry
University College of Science
Tumkur University
Tumakuru 572103, Karnataka, India
rmala2528@gmail.com

I. INTRODUCTION

Plants produces 80% of secondary metabolites and remaining 20% from fungi and bacteria. these secondary metabolites associated research and reviews articles showed single compound or a mixture exhibits therapeutic property. Metabolites are the intermediates or product of plant , which are involved in different function such as signaling ,stimulator molecule, fuel, structural support and inhibitory effect so on[1]. All the types of secondary metabolites are diverse variety of organic compounds, which are not involved in growth and development of plant. In the present scenario importance of these organic compounds are therapeutically and commercially increased. Hence, organic synthesis and plant tissue culture technology employed to get good amount of desired metabolites. Secondary metabolite can be extracted from root, leaves, stem, meristem, bark, flower and pods, these compounds are exclusive sources as a food additives, flavors, recreational drugs ,pharmaceuticals and industrial materials[2]. Classification of secondary metabolite classified on chemical structure, composition, solubility and biosynthesis[3].

II. CLASSIFICATION

Based on chemical structure secondary metabolites classified into terpenoids, alkaloids, Steroids and phenolics, Glycosides, tannins and saponins are the subtypes among them[4]. majority of these secondary metabolites exhibits properties such as antibacterial, antiviral , anti-cancerous, anti-inflammatory, antidiabetic , antioxidant, anti aging, cardio protective, immune modulators, neuro protective activities. Hence in this chapter we are focusing on the pharmacological effects of the metabolites ,which helpful for novel discovery and design of the drug based on the secondary metabolites .

1. **Terpenoids:** Terpenoids are polymer of isoprene derivatives and synthesized from acetate via the mevalonic acid pathway. These natural compounds are mixture of isomeric hydrocarbons as well as some oxygenated, hydrogenated, dehydrogenated derivatives. Terpenoids comprise a large family of phytoconstituents, it includes steroids, carotenoids and gibberelic acids and so on. Different molecules isolated and characterized from different plant groups, more than 23,000 structures of active compounds identified till now. Based on traditional and modern medicinal several isolated terpenoids showed pharmacological activities and used for the treatment of many diseases in both human and animals [5]. Lot of Terpene essential oils are used in the food, cosmetic, soap and drug industries as flavor/fragrant agent [6].

2. **Alkaloids:** Alkaloids are the largest diverse groups of natural chemical entities, nitrogen –containing heterocyclic compound of plants and approximately 20,000 different molecules types and subtypes of are being encompassed. The classification of alkaloids is based on nitrogen atom at any position in the molecule except amide and peptide bond [7]. Historically, from 3000 years plant alkaloids have been used by man for different purpose as a medicines, tea, narcotics, analgesics, stimulants and toxicants so on. Alkaloids acts on DNA, RNA and protein synthesis predominately stimulant central nervous system, hence, these compounds are generally used as psychoactive and stimulant drugs[8]. Several alkaloids possess strong pharmacological activity such as ion channel blockage, enzyme inhibition, interference of neurotransmission, hallucinations, loss of coordination, convulsion , vomiting and death[9].

3. **Phenolics:** Phenolic compounds are derived from pentose phosphate pathway and shikimic acid of plants through metabolization of phenylpropanoid [10]. A single phenolic ring is a parental molecule for the synthesis of its derivative substances called polyphenols, which includes tannins, flavonoids, coumarins, lignans, phenolics acids, and colored anthocyanins. Phenolics naturally distributed in plants roots, fruits, vegetables and among other parts. Many evidence showed number of hydroxyl groups of phenolics are directly connected to relative toxicity to microorganism [11]. Phenolics interfere in cell division, enzyme activities, digestion and slow growth in microorganism/animal/human.

4. **Flavonoids:** In fact these compounds are types of phenolics compounds produced by plant as a defence metabolite against the microbial infection. Approximately 10,000 types of structural diversity is observed in flavonoids , structural diversity is responsible many diversified reaction1[12]. Several research shown degree of hydroxylation and toxicity of microorganism are directly linked. Flavonoids are one carbonyl group containing flavones and flavonol also form by adding 3-OH group of phenol, these compounds are C6-C3 unit connected aromatic ring. Compounds in this group includes aurones, chalcones, isoflavonoids, flavones, , catechins, leucoanthocyanidins and anthocyanins. Lipophilic nature of the compounds causes easy penetration of the bacterial membrane and cell wall, which is toxic to infectious bacteria of the plants[13,14].

5. **Tannins:** These compounds are group of astringent and polymeric phenolics of the plant ranges from 500-3000 types. Name derived from its usage in tanning animal hides and skins to make leather[15]. Condensed tannins are quit common in plants different parts like buds, wood, leaves, stems, roots ,brak and seed[15]. Many carcinogenic incidences showed the relationship between cancer and tannins-rich food consumption like herbal tea ,betal nuts etc. Various research also documented that tannins exhibits antimicrobial activity against viruses, fungi and bacteria along with antimutagenic effect. Some tannins like tannic acid and propylgallic acid inhibits food and waterborne microbial growth, this mechanism of action is employed food industries(meat and fish) to enhance the shelf life[16]. Tannins also exhibits other pharmacological activities.

6. **Quinones:**In plants, bacteria, fungi and in few animals contains biological pigments. These compounds shows aromatic ring with ketone group and exists in several forms like polycyclic quinones, phylloquinone(Vit-K) , naphthoquinones, benzoquinones and anthraquinones[13]. Sliced some fruits and vegetables changes colour to brown due to these compounds, in some acidity and alkalinity titration quinines often used as indicator. These compound irreversibly complexs with :NH2 of amino acids of protiens during inactivation of protein , quinine also exhibits antibacterial property and other pharmacological activities[17].

7. **Glycosides:** Plant glycoside are the metabolites containing sugar moiety with non-carbohydrate. Majority of these glycosides are inactive before action during mechanism of action enzyme hydrolysis yields non-sugar moiety for particular physiological functions in animals such as reduction of blood glucose level and other medicinal properties[15].

III. PHARMACOLOGICAL ACTIVITY

1. **Antidiabetic Activity:** High blood sugar levels are the hallmark of the metabolic condition known as diabetes mellitus (DM). Increased sugar levels have a long-term impact on how proteins, carbs, and fats are metabolized, and they can also harm and disrupt many cells and tissues[]).After cancer and cardiovascular illnesses, diabetes is the third most common cause of increased morbidity and mortality(8). a number of secondary metabolites from plants that are bioactive, including glycosides, terpenoids, alkaloids, and carotenoid. Research has shown that dietary plant extract's hypoglycemic action affects both protein and enzyme activity, inhibiting the catalytic activity of -amylase and playing a role in regulating the glycemic index, or sugar content, of various food products[19]. The table.1 below provides information on the metabolites with anti diabetic activity and their likely mechanisms of action.

Table 1: List of secondary metabolite shows antidiabetic and probable Mechanism of action.

Secondary metabolite	**Mechanism of action**
Phenolics	• modulation of carbohydrate digestion and control of the glycemic index of food products[20]
Alkaloids	• Promotes glucose-stimulated insulin secretion in a dose-dependent manner in experimental animals[21]. • exhibite potential lipid lowering activity, Inhibition of α-glucosidase activity[23]
Terpenoids	• strongly enhances adipogenesis in cell lines and reported to have putative antidiabetic activity[20] • triterpenes Increase glucose uptake and enhance glycogen synthesis by activating AMPK in Hep G2 Cells[24].
flavonoids	• Several regenerated pancreatic islets and increased insulin secretion in streptozotocin (STZ)-induced diabetic rats[25,26]. • Stimulate insulin release and enhance glucose uptake from isolated islet cells[27]
Glycosides	• Glucosidase inhibitory activity in animal models[15].
Quinones	• several quinines inhibits aldolase reductase , mean while exhibits attenuation of diabetic complication[28]

2. **Antimicrobial Activity:** Human health and diseases are directly related to microorganism existence in and outside the body, Infections and disease are due to pathogenesis by Bacterial, viral and fungi . Prevention and treatment of microbial infection are done by using antibiotics, drugs and plant extracts. In the present scenario increased prevalence of antibiotic resistance, rendering more scope for plant extracts and there usages. Plant are being used for the treatment of the diseases from ancient period

and novel drugs continue to be developed through research from plant extract ,there are more than 25,000 different plant secondary metabolites are being identified with strong antimicrobial activity[27-29]. Table.2 shows some of the secondary metabolite and their potential activity.

Table 2: Antimicrobial Activity of secondary metabolite and probable Mechanism of action

Secondary metabolite	**Mechanism of action of the plant extracts**
Phenolics	• phenolics suggested to inhibits enzyme catalysed reaction through sulfhydryl groups on the proteins of gram positive and negative bacteria[30].
Alkaloids	• Polar and nonpolar extracts of different alkaloids inhibits microbial growth of species Gram-positive bacteria such as S. epidermidis, S. pyogenes, S. aureus, S. flexneri, E. coli and Enterobacter aerogenes. • Suppression of nucleic acid synthesis by inhibit the activity of dihydrofolate reductase[31].
Terpenoids	• The essential oils/terpenoids were found to exhibit antimicrobial activity against P.aeruginosa, E.coli, S.aureus and C.albicans[32].
Flavonoids	• Flavonoids crude extract exhibits MIC for food borne pathogenic bacterial strains Staphylococcus aureus (*S. aureus*), *Escherichia coli* (*E. coli*), Pseudomonas aeruginosa (*P. aeruginosa*) and *Vulgaris[33]*.
Glycosides	• Different organic solvent extract of flavoinds glycoside inhibits growth of gram+ve Bacteria growth of Shigella and Salmonella species[34].
Quinones	• Some extract like gallate shows photo catalytic activity which induces oxidative stress in microbe ex.E.coli and causing inhibition of microbial growth[35]

3. **Anti-cancer activity:** Second only to cardiovascular disorders in terms of mortality causes is cancer. Proto-oncogenes and tumor suppressor genes are the two categories of genes that often experience changes, and cancer incidence rises with age[36]. Cancer cells differ from healthy cells in that they have nuclear pleomorphisms, chromosomal abnormalities, decreased cellular gap junctions, and increased motility. Numerous medications have been developed over time and used to treat or prevent cancer. However, patients are subject to their unfavorable systemic side effects[37]. Even though improvements in the synthesis of synthetic oncogenic medications, cancer patients are becoming more and more reliant on alternative treatments because of their safety, accessibility, cost, minimal side effects, and lower likelihood of developing resistance. In the past, plants were the only source of medicine[38]. Astonishingly, due to their benefits over commercial synthetic medications, they continue to be a substantial source of medicine today, mostly in developing nations[39]. According to the World Health

Organization (WHO), around 80% of the world's population still prefers herbal remedies to traditional synthetic pharmaceuticals for treatment [40,41]. Several new cytotoxic secondary metabolites are isolated from plants each year and constitute a source of new possibilities to explore in order to fight against cancerous diseases. Research shows plant secondary metabolites are proved to be good anti-cancer agents in in-vitro condition, either independently or synergistically with other compounds through regulation of metabolic and signaling pathways, inhibition of enzymes vital for cancer progression, angiogenesis, microtubule assembly and inducing apoptosis [42,43].

Table 3: Anticancer activity of secondary metabolites and probable Mechanism of action

Secondary metabolite	**Mechanism of action**
Phenolics	• Induces mitochondrial toxicity , inhibits oxygen radical-forming enzyme or enzyme enchance DNA synthesis [45] and inhibits protein kinase involved in signal transduction of cancer cells[46]
Alkaloids	• Arrest cell cycle and target on the DNA and protein of cancerous cells[48]
Terpenoids	• Induces apoptosis and arrest cell cycle regulation in prostate cancer cell [44]
Flavonoids	• Induces cell cycle arrest, induction of apoptosis and differentiation, inhibition of angiogenesis[47]
Glycosides	• Demonstrated potent Cytotoxic effects against various cancer cell lines in initial preclinical studies[49]
Quinones	• Acts as anti-mitotic agents and tubulin polymerization inhibitor and exhibits cytotoxicity[50]

IV. CONCLUSIONS

Plant secondary metabolites and their applications have become a significant area of study in several disciplines, including genetics, pharmacology, physiology, etc. It is simpler to extract, define, and validate the findings of the usage of secondary metabolites as drug-like molecules when expertise from several domains, such as botany, chemistry, and pharmacology, is combined. Some of the significant and physiologically active substances and secondary metabolites are highlighted in this review. In addition to being advantageous for human health, these secondary metabolites also shield plants from biotic and abiotic stress.Terpenoids, alkaloids, and phenolics are just a few of the many subclasses that these secondary metabolites fall under. The pharmacological activities of each class of secondary metabolites are distinct. The therapeutic potential of secondary metabolites requires further research. To understand the precise mechanism and potential application of such bioactive

chemicals as a therapeutic molecule for humans, more and more validation studies on animal models are required.

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