Bioactive Compounds in Medicinal Plants: A Condensed Review

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- Bioactive compounds
- Medicinal plants
- Pharmacological significance
- Phenolics
- Terpenoids

1. Abstract

Herbal drugs form the basis of all ancient medicines and majority of modern-day medicines. They are derived, the world over, from medicinal plants. The pharmacological properties of herbal drugs derived from these plants are rooted in the plants’ secondary metabolites. The plant secondary metabolites with known pharmacological significance are more appropriately called as bioactive compounds. The present review summarizes their emerging importance, classification, and pharmacological significance. The classification terminology presented here is based on that given by M. Daniel in his book, Medicinal Plants- Chemistry and Properties, since it is one of the most comprehensive classifications available in published literature. As the need and demand for plant-based medicines increase, so will the exploitation of their resources. Hence, the present review also explores the plausible futuristic perspectives pertaining to their efficient utilization and conservation.

2. Medicinal plants and their emerging importance

For centuries, Phyto-medicines have dominated the health scenario in India. Plants have been a source of natural medicines and drugs in traditional systems such as Unani and Ayurveda from ancient times. Since plant-based medicines have very few side-effects compared to the synthetically produced ones, people are more inclined towards the usage of the former. Also, Phyto-medicines are more affordable, especially in poor and developing countries [84,87]. The research in the area of secondary metabolite production by plants has gained importance in view of their being recognized as natural sources of herbal drugs, pharmaceuticals and Phyto-medicines. These compounds have also gained importance in the area of Nutraceuticals, which have chronic positive health effects and may prove to be advantageous in the treatment of diseases like cancer, cardiovascular diseases and diabetes [40]. Plant-based medicinal compounds serve as the prototype for the preparation of their synthetic analogues [157]. According to the National Medicinal Plant Board, the revenue from the Indian herbal drug industry is likely to increase up to Rs. 80 to 90 billion [154].

3. Bioactive compounds in Medicinal plants

Bioactive compounds in plants have been defined as “secondary plant metabolites eliciting pharmacological or toxicological effects in man and animals” [15]. These are present in comparatively higher concentrations in medicinal plants and are produced from primary metabolites through methylation, hydroxylation, and glycosylation biochemical pathways [97]. During severe and/or chronic stress, the plant
may shift its metabolism more towards the secondary, making more resources available for defense, hence compromising on growth [168]. Bioactive compounds have a wide range of biological activities like serving as antibiotics and counteracting oxidative stress. When herbal medicines are ingested, these compounds are expected to play the same role in the human body [75, 81]. However, their functions cannot be established with conviction. For instance, a compound may not have the same function in the plant as when it is extracted, purified, and used ex-planta. Azadiractin, a commercially important pesticide, but the neem tree, its source, is attacked by insects probably because the latter overcome the feeding barrier induced by this compound and also because this toxin is concentrated in the neem seeds and not the leaves which are under insect attack [72]. Also, some bioactives have multiple functions. For example, salicylic acid serves as a signal molecule during the plant pathogen attack, pollination (e.g. Arum lily), herbivory (e.g. Salix spp.), and allelopathy (e.g. Quercus falcate) [134]. Thirdly, some compounds function as both primary and secondary metabolites. For example, canavanine protects *Canavalia ensiformis* from bruchid beetle attack; it also metabolizes during seed germination, serving as a carbon source [53]. Lastly, secondary metabolites are complex molecules, with a plethora of structures.Synthesized via innumerable intertwined pathways, the end product of interest is synthesized along with a multitude of other secondary compounds. Consequently, it becomes difficult to assign a unique function to any particular compound [72]. Bioactive compounds can be divided broadly into alkaloids, terpenoids/terpenes, and phenolics. A detailed classification [46], is outlined here. Though the compounds have been classified, there is no watertight compartmentalized classification. For instance, many of the alkaloids have phenolic groups attached to them and can be categorized as both alkaloids and phenolics. Also, alkaloids can be categorised into monoterpenoid, diterpenoid, sesquiterpenoid, steroidal, etc.

### 3.1. Alkaloids

Alkaloids are plant secondary metabolites containing carbon, hydrogen, nitrogen, and occasionally oxygen. Their alkaline nature is due to nitrogen. Their biosynthesis pathways are complex, involving 20 or more enzymatic steps. A majority of alkaloids are derived from amino acids (such as ornithine, leucine, phenylalanine, tyrosine, and tryptophan, amongst others), while others have their structural basis in compounds like purine, nicotine, acetate, and isoprenoids [54, 78]. They may be distributed throughout the plant or restricted to storage tissues, like fruits, roots, and seeds. They protect the plants against herbivory and microbial attack, attract insects for pollination, and are important from nutritional as well as pharmacological perspective [46]. As per [46], alkaloids have been categorized into 17 categories. A brief description of these is given here. Their medicinally active components and their pharmacological importance are summarized in Table (1).

#### Table 1: Classification, plant sources, medicinal/pharmacological compounds, and medicinal properties of some major categories of alkaloids.

<table>
<thead>
<tr>
<th>Alkaloids</th>
<th>Some Source(s)</th>
<th>Active Ingredients</th>
<th>Medicinal Properties</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkaloidal amines</td>
<td><em>Sida cordifolia</em>, <em>Ephedra sinica</em>, <em>Catha edulis</em>, <em>Urtica dioica</em></td>
<td>Ephedrine, pseudoephedrine, cathinone</td>
<td>Cardiac stimulants, anti-inflammatory, sympathomimetic, adaptogenic, immune-stimulant, treatment of paralysis, arthritis, haemorrhages, as hypoglycemic, diuretic, expectorant, blood purifier</td>
<td>Daniel 2006, Mallikarjuna <em>et al.</em>, 2013</td>
</tr>
<tr>
<td>Diterpenoid alkaloids</td>
<td><em>Aconitum napellus</em>, <em>A. ferox</em>, <em>A. heterophyllum</em></td>
<td>Aconitine, artisine, ajacine</td>
<td>Analgesic, diaphoretic, diuretic, anti-diabetic, antimicrobial, anti-diarrhoeal, hypotensive, sedative, febrifuge, tonic, useful in</td>
<td>Daniel 2006, Srivastava <em>et al.</em>, 2010</td>
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</tbody>
</table>

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<thead>
<tr>
<th>Alkaloids Type</th>
<th>Species</th>
<th>Active Compounds</th>
<th>Uses</th>
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</thead>
<tbody>
<tr>
<td>Imidazole alkaloids</td>
<td><em>Lepidium meyenii</em>, <em>Pilocarpus jaborandi</em>, <em>P. microphyllus</em>, <em>P. pinnatifolius</em></td>
<td>Pilocarpine, pilosine, lepidiline A and B</td>
<td>Contraction of eye-pupil, stimulate saliva secretion</td>
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<td></td>
<td></td>
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<td>Daniel 2006, Santos and Moreno 2013</td>
</tr>
<tr>
<td>Indole alkaloids</td>
<td><em>Catharanthus roseus</em>, <em>Uncaria guianensis</em>, <em>U. tomentosa</em>, <em>Strychnos nux-vomica</em>, <em>Physostigma venenosum</em>, <em>Ipomoea nil</em>, <em>I. mauritiana</em>, <em>Rauwolfia serpentina</em>, <em>Passiflora incarnate</em>, <em>Alstonia scholaris</em></td>
<td>Ergolines, vincristine, brucine, vinblastine, leurosidine, leurosine, vincolidine reserpine, ergometrine, ergotamine, physostigmine, serpentine, strychnine</td>
<td>Treat arthritis, inflammation, tumours, diabetes, gastric ulcers, chronic dysentery, cholera, rheumatism, delirium, impotence, leucorrhoea, insomnia, skin diseases, used as anthelmintic, aphrodisiac, sedative, diuretic, anti-depressant, respiratory stimulant, brain stimulant, anti-hypertensive, tranquilizer, improve mental function, reduce stress, effective in fevers, treatment of insanity, epilepsy, nervous delibility, gastric and duodenal ulcers, leukoderma, conjunctivitis, paralysis, high blood pressure, insanity, schizophrenia, snake bites, chronic diarrhoea, bowel complaints, as blood purifier, anthelmintic, cardiac depressant, diuretic, laxative, nerve tonic, for insomnia, liver congestion, dropsy, ulcers, sores, cardiac disorders, ulcers, nausea, biliousness, dyspepsia</td>
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<td></td>
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<td>Szantay 1990, Daniel 2006</td>
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<tr>
<th>Isoquinoline alkaloids</th>
<th>Papaver somniferum, Lophophora williamsii, Tiliacora racemosa, Argemone mexicana, Berberis aristata, Chelidonium majus, Alangium salvifolium, Mahonia aquifolium, Sanguinaria Canadensis</th>
<th>Ipecac, berberine, sanguinarine, papaverine, sanguinarine, dihydrosanguinarine, coptisine, protoverine, protopine, chelidonine chelerythrine allocryptopine cissampeline, pareirubines A and B</th>
<th>Antimicrobial, antimalarial, astringent, anthelmintic, purgative, emetic, hypoglycaemic, antispasmodic, expectorant, cholagogue, laxative, diaphoretic, immunosuppressive, anti-inflammatory, analgesic, anti-hepatotoxic, diuretic, antipyretic, antileukemic, emmanagogue, treatment of pain, cancer, bacterial infections, amoebic dysentery, skin diseases, eye infections, ulcers, haemorrhoid, haemorrhages, jaundice, piles, conjunctivitis, rheumatism, diabetes, fever, dysentery, piles, dropsy, urinogenital troubles, tuberculosis, asthma, HIV, stimulation of bone-marrow leucocytes and myocardial contractility, exhibit anticholinesterase activity, as rejuvenating agent, and for improving intellect</th>
<th>Cui et al., 2006; Daniel 2006</th>
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<tr>
<td>Monoterpenoid alkaloids</td>
<td>Valeriana officinalis, Enicostemma hyssopifolium, Alstonia rostrata</td>
<td>Valerian, gentianine, actinidine, β-skytanthine, boschniakine</td>
<td>Carminative, antispasmodic, sedative, restorative, anti-diabetic, in fevers and snakebites</td>
<td>Bao et al., 2012, Ishikura et al., 2013</td>
</tr>
<tr>
<td>Class</td>
<td>Plant Species</td>
<td>Alkaloids</td>
<td>Actions</td>
<td>References</td>
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<td></td>
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<td>tyloindicines A–J, tylocrebrine, O-methyl tylophorinidine</td>
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<tr>
<td>Pyridine-piperidine alkaloids</td>
<td><em>Areca catechu</em>, <em>Piper nigrum</em>, <em>P. longum</em>, <em>Punica granatum</em>, <em>Conium maculatum</em>, <em>Lobelia inflata</em></td>
<td>Caffeine, theobromine, theacrine, triacanthine, theophylline, 7-methylxanthosine</td>
<td></td>
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<tr>
<td>Quinoline alkaloids</td>
<td>Cinchona spp., Toddalia asiatica, Glycosmis pentaphylla, Camptotheca acuminata, Ruta chapelensis, Zanthoxylum heitzii, Pilocarpus grandiflorus</td>
<td>Camptothecin, skimmianine, kokusaginine, evoxine, quinine, choisyine, cinchonine, quinidine, cinchonidine, sonminine, dictamine, isodictamine, haplopine, robustine, isopteleine, 5-methoxydictamine</td>
<td>Diaphoretic, stomachic, anti-pyretic, carminative, mutagenic, possess stimulatory ganglionic-blocking, curare-like, spasmodic activities, treatment of malaria, diarrhoea, cough, gonorrhoea, rheumatism, anaemia, jaundice, fever, liver complaints, eczema, skin diseases</td>
<td>Daniel 2006, Pi et al., 2010</td>
</tr>
<tr>
<td>Quinolizidines/Lupinane alkaloids</td>
<td>Cytisus scoparius, Boerhavia diffusa, Lupinus varius orientalis, L. albus albus, L. hartwegii, L. densiflorus</td>
<td>Sparteine, lupanine, cytisine, lupanine, laburnine, 13-hydroxylupanine</td>
<td>Diuretic, anti-inflammatory, cardioprotective, anticancer, block ganglionic transmission, decrease cardiac contractility, and contract uterine smooth muscles</td>
<td>Daniel 2006, Bunsupa et al., 2012</td>
</tr>
<tr>
<td>Alkaloid Class</td>
<td>Plant Specie</td>
<td>Compounds</td>
<td>Uses</td>
<td>References</td>
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<tr>
<td>Sesquiterpene alkaloids</td>
<td>Celastrus paniculatus, Euonymus japonica</td>
<td>otosenine, platyphylline, senecionine, integerrimine, retrorsine, usaramine, supinine</td>
<td>Sedative, emetic, diaphoretic, emmenagogue, anti-dysentric, anti-pyretic, analgesic, tranquilizer, anti-tumour, treatment of hysteria, pneumonia, blood pressure, cancer, rheumatism, lupus, depression, sharpen memory</td>
<td>Han et al., 1990, Daniel 2006</td>
</tr>
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</table>
3.1. Alkaloidal Amines: This is a group of about 50 members also called protoalkaloids. Derived from the aromatic amino acids (phenylalanine, tyrosine, and tryptophan), these compounds are not heterocyclic, and are also referred to as pseudo-alkaloids. They are found in families like Cactaceae, Chenopodiaceae, Ephedraceae, Fabaceae, Celastraceae, Malvaceae, and Urticaceae [31,46].

3.1.2. Monoterpenoid alkaloids: The alkaloids are about 20 and present in families like Valerianaceae, and Gentianaceae. Most of them are derived from iridoid monoterpenes. Iridoids are a class of bicyclic monoterpenes and often serve as intermediates in the synthesis of alkaloids. They are typically found in plants as glycosides, most often bound to glucose. Iridoids are found in many medicinal plants and may be responsible for some of their pharmaceutical activities. They are produced by plants as defence against herbivores and/or microorganisms [46,153].

3.1.3. Sesquiterpene alkaloids: Families in which these alkaloids are found include Celastraceae, Orchidaceae, Ranunculaceae, Garryaceae, Ericaceae, Asteraceae, Rosaceae, and Fabaceae. Majority of these compounds are confined to two major groups: the dendrobines and guaipyrirdines, the latter being relatively structurally simpler than the former [28]. The dengobine sesquiterpenoid alkaloids possess a highly condensed tricyclic skeleton with a nitrogen atom, a bridged lactone, and a cyclohexane ring, the latter being surrounded by six stereogenic centers. The guaipyrirdine alkaloids are bi- or tri-cyclic compounds with a 7-membered carboxylic ring and only two stereogenic centers [28,153].

3.1.4. Diterpenoid alkaloids: Consisting of about 90 compounds, a majority of them are isolated from Ranunculaceae (Aconitum and Delphinium). Garryaceae, Asteraceae, and Rosaceae are the other families in which these compounds are present [46]. Majority of these compounds are derived from complex polyhydric alcohols possessing a diterpenoid skeleton. These are further categorized into C18-, C19-, and C-20 diterpenoid alkaloids [176].

3.1.5. Imidazole alkaloids: These alkaloids are found mainly in the families of Rutaceae, Euphorbaceae, and Fabaceae [46]. These are biosynthesized from the precursors derived from histidine. Pilocarpine is the only alkaloid which is economically and pharmaceutically important [46]. Other alkaloids with an imidazole nucleus are histamine, histidine, and pilosine [5].

3.1.6. Indole alkaloids: This is the largest class of alkaloids with about 600 members. They are practically confined to families Apocyanaceae, Asclepiadaceae, Rubiaceae, Loganiaceae, Convolvulaceae, Clavicipitaceae, Passifloraceae, Fabaceae, Zygophyllaceae, and Rutaceae [46]. A majority are derived from tryptophan and in many cases contain a part derived from mavalonate via geraniol. They provide protection against UV-B radiation [17].

3.1.7. Quinoline alkaloids: Comprising of about 100 members, these alkaloids are primarily reported from...
Rubia and Rutaceae [46]. 4-methylquinoline nucleus combines with quinuclidine nucleus forming ruban, which, in its alcoholic form of 9'-rubanol is the basic skeleton for various quinolone alkaloids such as quinine and quinidine [5].

3.1.8. Isoquinoline alkaloids: These are about 400 in number and possess an isoquinoline nucleus. These are found in the families of Cactaceae, Papaveraceae, Menispermaceae, Ranunculaceae, Rubiaceae, Berberidaceae, Alangiaceae, Aristolochiaceae, Araliaceae, and Nymphaceae. These can be further sub-divided into simple isoquinolines, benzylisoquinolines, and phenanthrenes [46]. These alkaloids are derived from tyrosine [153].

3.1.9. Quinolizidines/ Lupinane alkaloids: These are distributed in Ranunculaceae, Magnoliaceae, Lythraceae, Asteraceae, Leguminoseae, and Nyctaginaceae. These are generally toxic. The only medicinally important alkaloid is sparteine [46]. These alkaloids are derived from lysine and structurally consist of two fused 6-membered rings sharing a nitrogen atom. Higher concentrations of these alkaloids are found in young photosynthetic tissues. Lupine alkaloids (from the genus Lupinus) are the simplest alkaloids of this group [5,153].

3.1.10. Quinazoline alkaloids: These are found in families like Acanthaceae, Polygonaceae, Cruciferae, Malvaceae, Fabaceae, Araliaceae, Rubiaceae, Scrophulariaceae, Asteraceae, Poaceae, and Rutaceae [44]. Vasicine and related alkaloids form the important members of this group. Some example of quinazoline alkaloids are vasicine, ferbifugine, glomerin, and homoglomerin. Their primary biosynthetic precursor is anthranilic acid, but phenyalanine can also be a candidate in some cases [5].

3.1.11. Phenanthro-indolizidine alkaloids: Only 5 alkaloids possessing both phenanthrene and indolizidine nuclei are known at present. They are present in members of Asclepiadaceae, Apocynaceae and Moraceae [46]. These alkaloids are derived from ornithine, phenylalanine, and tyrosine. The most commonly known compound of this group is tylophorine [153].

3.1.12. Purine alkaloids: They are found in the families like Rubiaceae, Malvaceae, Fabaceae, and Theaceae [46]. These are implicated in protection against UV-B radiation. They are biosynthesized via N-methyltransferases. The basic roles of these purine alkaloids in plants are restricted to providing defence against herbivores and pathogens and allelopathy [7].

3.1.13. Pyridine-piperidine alkaloids: About 125 alkaloids in this group are known. The important alkaloids of this group include arecoline, lobeline, pelletierine, conine, piperine, nicotine, and anabasine found primarily in Arecaceae, Piperaceae, Puniceae, Apiaceae, Lobeliaceae, Solanaceae, Palmae, and Campanulaceae [46,125].

3.1.14. Pyrrolizidine alkaloids: About 360 pyrrolizidine alkaloids are found in plants. These are primarily restricted to the Boraginaceae, Asteraceae, Fabaceae, Orchidaceae, Apocynaceae, Ranunculaceae and Scrophulariaceae [46]. These are derived from ornithine and sometimes from arginine. Structurally they have two 5-membered rings fused together with a nitrogen atom at a common junction of both rings. They are biosynthesized in the roots and from there are transported to other parts of the plant. Most alkaloids of this group are potential poisons [5,153].

3.1.15. Steroidal alkaloids: It is a large group of about 250 alkaloids, most of them occur as glycosides and resemble saponins. They are practically confined to families Liliaceae, Ranunculaceae, Buxaceae, Apocynaceae, and Solanaceae. Their synthesis is presumed to start from cholesterol and likely occurs in the cytosol [83]. These alkaloids have a 21-, 24-, or 27-carbon heterocyclic skeleton and are structurally divided into solanidanes, spirophanes, and jervanes [86].

3.1.16. Tropane alkaloids: Tropane alkaloids form a small family of about 40 members belonging to families Solanaceae, Erythroxylaceae, Euphorbiaceae, Convolvulaceae, Lentibulariaceae, Brassicaceae, Astereaceae, and Proteaceae [46]. Tropane alkaloids are derived from arginine or ornithine via condensation with three acetate or malate units. Roots are the biosynthetic organs for these alkaloids from whence they are transported to the aerial plant parts. (S)-tropane, derived from phenylalanine, upon esterification, also synthesizes many tropane alkaloids [46,153].

3.1.17. Tropolone alkaloids: About 25 alkaloids in this group are known which are confined to Liliaceae, Verbenaceae, and Capparaceae [46]. Colchicine is an important compound possessing significant medicinal importance (Table 1). Benzocycloheptanotropolone is the main structural ring in colchicine. These compounds are sensitive to light and when exposed, convert to their luminal derivatives [171].

The structures of the one of the representative compounds from the above-mentioned group are given in Figure (1).

3.2. Terpenoids

Terpenes include more than 30,000 lipid-soluble compounds. A majority of them are volatile and are responsible for the plants’ fragrance. The term ‘terpene’ was initially used to describe a mixture of hydrocarbons with a molecular formula C10H16 occurring in the essential oils obtained from plant tissues. ‘Terpenoids’ is a more general term to describe the hydrocarbons with the general formula (C5H8)n as well as their oxygenated, hydrogenated, and dehydrogenated derivatives. The 5-carbon building blocks of terpenes in plants are the interconvertible isomers isopentenyl pyrophosphate (IPP) and dimethylallylpyrophosphate (DMAPP). They are condensed by prenyltransferases to give rise to a number of products like
geranyl, farnesyl, geranylgeranyl, pyrophosphates, squalene, and phytoene, which are the precursors of terpenes. Their subsequent modifications (like oxidation, cyclization, and skeletal rearrangement) give rise to various isoprenoids [27]. The terpenoids range from monoterpenes (C\textsubscript{10}) to tetraterpenes (C\textsubscript{40}) depending upon the number of C5 units present in their structure. They are found prominently in leaf glandular trichomes, bud exudates, and bark resins. In plants they function as electron carriers (quinones), plant hormones (side chain of cytokinins, abscisic acid, gibberellins, and brassinosteroids), photosynthetic pigments (chlorophyll, phytol, and carotenoids), and essential oils [80]. They act as feeding deterrents, pollination attractants, defence compounds photoprotectants, free-radical scavengers, and signalling molecules [100,129]. They are exploited for their aromatic qualities and pharmacological properties such as antibacterial, anti-inflammatory, inhibition of cholesterol synthesis, sedatives, etc. [127,179]. [46] has classified the terpenoids into the following detailed categories as given below. The medicinal properties of this class of compounds are outlined in Table (2).

Figure 1: Structures of one of the representative compounds of various categories of alkaloids
3.2.1. Monoterpenes: These are a group of C\textsubscript{10} isoprenoids constituting about 1000 metabolites formed by head-to-tail, head-to-head, or tail-to-tail condensation of two isoprene units. Most of them are colourless volatile oils [110] containing volatile open chain and cyclic compounds like menthol, limonene, geraniol, linalool, and pinene. They act as pollinator attractants, and antioxidants [110].

3.2.2. Sesquiterpenes: More than 1200 sesquiterpenes are known today. They comprise three isoprene units and occur as volatile oils and bitter principles of many plants. Sesquiterpene lactones occur primarily in Compositae, Asteraceae, Apiaceae, and Magnoliaceae and act as feeding deterrents, phytoalexins and antibiotics [46].

3.2.3. Diterpenes: These comprise of more than 3000 different compounds occurring in almost all plant families. Biosynthesised in the plastids, they arise from the metabolism of geranylgeranyl pyrophosphate (GGPP). They act as growth hormones, defence compounds, and occur as phytol side chain of chlorophylls, tocopherols and phylloquinone [27]. The above three categories of compounds, i.e. mono-, sesqui-, and diterpenes together form the majority of essential oils and are distributed in more than 2000 plant species belonging to some 60 families (e.g. Rutaceae, Myrtaceae, Umbelliferae, Labiatae, Compositeae, Pinaceae, to name a few). They have several important functions in plants like protection against predators (microorganisms, fungi, insects, and herbivores), attraction of pollinators and dispersal of spores, inhibitors of germination and growth, and ameliorating the effects of abiotic stress on plants, amongst others [36].

3.2.4. Triterpenoids:

3.2.4.1. Triterpenoids and steroids: These are C\textsubscript{30} carbon chains derived from the head-to-head condensation of two molecules of FPP (farnesyl pyrophosphate) to form squalene which is the precursor for steroids, important membrane constituents, via squalene synthase [18]. Triterpene derivatives such as glycosides or fatty acid esters are also accumulated by plant cells, for example, saponins [163] which can be exploited as sources of drugs (like liquorice and ginseng) as these possess medicinal and cytoprotective activities (Table 2) [71].

3.2.4.2. Limonoids and Quassinoids: These C\textsubscript{30} members may be alipathic, tetracyclic, or pentacyclic. Tetracyclic members include limonoids primarily confined to order Rutales. The families producing these compounds include Meliaceae, Rutaceae, Cneoraceae, and Simaroubaceae. They protect the plants against herbivory and have pharmacological importance [19]. Quassinoids are highly oxygenated triterpenes from Simaroubaceae family. C20 quassinoids are especially prominent in pharmacological investigations and are divided into tetracyclic and pentacyclic categories [66].

4.2.4.3. Glycosides: These compounds are usually found bonded to mono- or oligosaccharide or to uronic acid. They are further categorized into five major types:

3.2.4.3.1. Cardiac glycosides: They occur in plant families such as Apocynaceae, Asclepiadaceae, Fabaceae, Celastraceae, Scrophulariaceae, Solanaceae, Hyacinthaceae, Asclepiadaceae, Asteraceae, Moraceae, Apocynaceae, Asparagaceae and Leguminoseae, Ranunculaceae, Sterculiaceae, Cruciferae, Tiliaceae and Brassicaceae, Liliaceae [92]. The core structure consists of a steroid nucleus with a five membered lactone ring (cardenolides) or a six membered lactone ring (bufadienolides) and sugar moieties [119]. As the name indicates, the majority of the compounds of this group have cardioprotective properties (Table 2).

3.2.4.3.2. Cyanogenic glycosides: They are common in families like Rosaceae, Sapindaceae, Fabaceae, Linaceae Euphorbiaceae, Papaveraeaceae, and Asteraceae, but rare in others. They protect the plants against herbivores due to their bitter taste and release of toxic hydrogen cyanide (HCN) on wounding/tissue disruption [183]. Most of these compounds are derived from tyrosine, phenylalanine, valine, leucine, and isoleucine and have also been described as nitrogen storage compounds [32].

3.2.4.3.3. Glucosinolates: Families containing glucosinolates include Bataeae, Brassicaceae, Bretschneideraceae, Cruciferae, Capparidaceae, Caricaceae, Euphorbiaceae, Gyrostemonaceae, Limnanthaceae, Moringaceae, Pentadiplandraeae, Phytolaccaceae, Pittosporaceae, Resedaceae, Salvadoraceae, Tovaricaeae, and Tropaeolaceae [16]. They are sulphur containing compounds and depending upon their precursor amino acids. These can be divided into three groups: aliphatic (from alanine, leucine, isoleucine, valine, and methionine), benzenic (from phenylalanine or tyrosine), and indolic (from tryptophan). They provide defence against herbivores [47].

3.2.4.3.4. Saponins: These C\textsubscript{30} constituents are abundant in nature. They get their name from soapwort plant (Saponaria), the root of which was used historically as a soap. Depending upon the structure of aglycone, they are categorised into steroidal and the pentacyclic triterpenoid types. They occur in the families like Liliaceae, Caryophyllaceae, Sapindaceae, Polygalaceae, Sapotaceae, Phytolaccaceae, Ranunculaceae, Papaveraceae, Linaceae, Rutaceae, Myrtaceae, Cucurbitaceae, Araliaceae, Oleaceae, Rubiaceae, and Compositeae [46]. They protect the plants from pathogens and ruminants [48].

3.2.5. Carotenoids: These are a group of about 700 lipophilic pigments. They are tetraterpenoids (containing 40 C atoms) with eight C5 isoprene units linked in a regular head-to-tail manner except in the centre of the molecule where the order is tail-to-head so that the molecule is symmetrical. Carotenoids can be classified into carotenes and xanthophyll depending
upon the absence or presence of additional O-containing groups. GGPP is also the biosynthetic precursor of the carotenoids, which carry out essential functions in the life cycle of green plants [57]. They act as accessory pigments in the light-harvesting steps of photosynthesis and provide colouration to flowers and fruits. Carotenoid concentrations have been known to increase under UV-B radiation [85]. Due to the presence of the conjugated double bond system, they are capable of absorbing light in the range of 350-500nm [13]. Xanthophylls are functional in the light harvesting complex of the chloroplasts. They quench triplet excited states in chlorophyll by dissipating excess excitation energy via non-photochemical quenching. Carotenoids in plants are also precursors for the synthesis of the hormone abscisic acid [74].

3.2.6. Polyterpenes: Comprising of many isoprene units, these have a molecular weight of over 1,00,000 and are the constituents of rubber (Z-isomer of poly-isoprene) and gutta percha (E-isomer of poly-isoprene). The rubber-like substances of many other plants have similar composition. Their biosynthesis occurs in the latex vessels or lacticifers.

3.2.7. Resins: These are lipid-soluble complexes comprising of volatile fraction (di- and triterpenoid compounds) as well as non-volatile fraction (mono- and sesquiterpenoids). They harden on exposure to air [15]. Oleoresin terpenes are synthesised from isopentenyl diphosphate. These do not attenuate UV-B radiation, but resin droplets may cause scattering or reflection of UV-B radiation from the stem surface. Families of plants producing resins include Pinaceae, Apocynaceae, Cupressaceae, Arecaceae, Platanaceae, Plumbaginaceae, Rutaceae, Guttiferae, Cannabaceae, Moraceae, Dipterocarpaceae, Anacardiaceae, Araucariaceae, Sapindaceae, etc. [175]. They protect the plants against insect/pathogen attack, attract insects for pollination, as well as prevent herbivory [186,21]. Some of the representative compounds from the above-mentioned groups are given in Figure (2).

### Table 2: Classification, plant sources, medicinal/pharmacological compounds, and medicinal properties of some major categories of terpenoids.

<table>
<thead>
<tr>
<th>TERPENOIDS / TERPENES</th>
<th>Some Source(s)</th>
<th>Active Ingredients</th>
<th>Medicinal Properties</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monoterpenes</td>
<td>Valeriana officinalis, Tanacetum parthenium, Thuja occidentalis, Quercus ilex, Salvia leucophylla</td>
<td>Valerian, borneol, camphor, limonene, pinene, carene, linalool, sabinene, camphene, thujene, geraniol, carvone, nerol, ocimene, α-phenandrene, menthol, citral</td>
<td>Tranquilizers, sedative, antimicrobial, anti-leukemic, laxative, hypotensive, analgesic, anaesthetic, expectorant, anti-puritic, antiseptic, diuretic, sedative, spasmylytic, anti-inflammatory</td>
<td>Heinrich et al., 2004, Gurib-Fakim 2006, Kashani et al., 2012</td>
</tr>
<tr>
<td>Compounds</td>
<td>Plants/Species</td>
<td>Bioactive Properties</td>
<td>References</td>
<td></td>
</tr>
<tr>
<td>------------------------------------------------</td>
<td>-------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Limonoids and Quassinoids</td>
<td>Picrasma excelsa, Ailanthus excelsa, Azadirachta indica, Brucea javanica</td>
<td>Anti-cancer, anti-neoplastic, anti-tumour, antimalarial, antiviral, anti-inflammatory, anti-leukemic, anti-feedant, insecticidal, amoebicidal, antiulcer, herbicidal, potent inhibitors of induced inflammation and arthritis</td>
<td>Manners and Hasegawa 1999, George <em>et al.</em>, 2000, Boeke <em>et al.</em>, 2004</td>
<td></td>
</tr>
</tbody>
</table>

### Glycosides:

| Cardiac glycosides | Digitalis purpurea, Calotropis gigantea, C. procera, Nerium oleander, Thevetia peruviana, Helleborus niger | Ouabain, digoxin, digitoxin, digitalis, oleandrin | Cardioprotective, treatment of cancer | Newman et al., 2008, Bernhoft, 2010 |
| Cyanogenic glycosides | Manihot esculenta, Passiflora edulis, Macadamia ternifolia, Prunus persica, Holocalix balansea, Nectandra megapotamica | Linamarin, amygdalin, linustatin, dhurrin, prunasin, vicianin | Hypothyroidism, supress and soothe dry coughs | Vetter 2000, Ganjewala et al., 2010 |
| Saponins | Smilax spp., Polygala senega, P. tenuifolia, Platycodon grandiflorum, Agave americana, Asparagus racemosus, Glycyrrhiza glabra, Bacopa | Bacopasaponin, Giganteoside D and E, Frondoside A, Lotoidosides, Macranthoside B | Anti-inflammatory, anti-neoplastic, antibacterial, antifungal, anti-cholesterolemic, anticancer, regulate body immunity | Rajput et al., 2007, Podolak et al., 2010 |
### 3.3. Phenolics

Phenolics are ubiquitous across the plant kingdom with about 10,000 structures identified to date. Structurally, they have at least one hydrocarbon ring with one or more hydroxyl groups attached. They range from simple low molecular weight compounds (coumarins, benzoic acids and their derivatives) to more complex structures (flavonoids, stilbenes, and tannins). Flavonoids are the largest and the most diverse group, with about 6,000 members. They share a common structure of two 6-carbon rings, with a 3-carbon bridge, which usually forms the third ring. The modification of this basic structure gives rise to chalcones, flavanones, isoflavones, flavan-3-ols, and anthocyanins [25].

Phenolics play several important functions in plants. They protect cellular membranes and tissues from lipid peroxidation, act as pollinator attractants and UV-B absorbers, repair DNA by electron transfer reactions, are involved in plant growth and reproduction, and provide resistance against pathogens and predators [151]. Phenolics are mainly derived from phenylalanine and tyrosine via the phenylpropanoid pathway. Table 3 gives an overview of this class of compounds [46], including their sources, medicinal components, and pharmacological properties. Phenolics have been categorised into the following classes:

**3.3.1. Flavonoids:** Flavonoid biosynthetic pathway is conserved in plants. Enzymes such as isomerases, reductases, hydroxylases, and several Fe2+/2-oxoglutarate-dependent dioxygenases modify the basic flavonoid skeleton leading to the different flavonoid subclasses [115] and transferases modify the backbone so formed with sugars, methyl groups, and/or acyl groups. This leads to the different classes having different solubility, reactivity, and physiological activities [25, 56]. Variations in the heterocyclic ring, position and number of substituents (hydroxyl groups, methyl groups, for instance) cause flavonoids to be divided into flavones, flavonols, flavanones, catechins, anthocyanidins, and isoflavones. These are induced in response to UV-B radiation and provide organ protection by absorbing in the wavelength range of 280-350 nm. They also stimulate root nodule formation, and offer disease resistance [134].

**Flavonoids have been classified into following categories:**

<table>
<thead>
<tr>
<th>Phenolics</th>
<th>Plant Source</th>
<th>Antioxidant, anticancer, cardioprotective, modulating gene expression and immune response</th>
<th>Antimicrobial agents, for healing wounds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyterpenes</td>
<td><em>Hevea brasiliensis, Achras sapota</em></td>
<td>rubber, gutta-percha</td>
<td>Bernhoft 2010</td>
</tr>
<tr>
<td>Resins</td>
<td><em>Pistacia lentiscus var. Chia, P. terebinthus var. Chia, Betula pendula, Pinus contorta, P. banksiana</em></td>
<td></td>
<td>Bernhoft 2010</td>
</tr>
</tbody>
</table>
3.3.1.1. Anthocyanins: Anthocyanins are an important group of colouring pigments in plants. They are responsible for attraction of pollinators and seed dispersal by animals eating fruits. They may from conjugates with hydroxycinnamic or other organic acids. They are structurally related to flavones and are derived from them by addition or substitution of hydroxyl groups or by methylation or glycosylation [46,162].

3.3.1.2. Anthocyanidins: These are anthocyanins without sugar moiety. They provide colours to flowers and fruits and hence attract insects for pollination. They also provide plant protection against excessive light. Anthocyanins and anthocyanidins (e.g. cyanidin, delphinidin, malvidin, peonidin, and pelargonidin) and their glycosides are widely distributed in the medicinal herbs such as inflorescences of Prunella vulgaris and flowers of Rosa chinensis [33]. Camellia sinensis and Areca catechu contained proanthocyanidins and leucoanthocyanidins respectively [33,166].

3.3.1.3. Aurones: Aurones, (Z)-2-benzylidenebenzofuran-3-(2H)-ones, are a rare subclass of flavonoids occuring in nature. They provide bright yellow colour of some important ornamental flowers, such as snapdragon (Antirrhinum majus, Scrophulariaceae) and plants belonging to the Asteraceae family (e.g. Coreopsis sp., Comos sp., and Dahlia sp.) in their glycosylated forms. They are biosynthesized from chalcones by the key enzyme aureusidin synthase [126]. Aurones primarily occur in the epidermal cells of the flowers, however they may also be found in bark, wood, leaves, seedlings, and nectar. Aurones have been shown to be derived from chalcone [123].

3.3.1.4. Flavan-3-ols and Flavan-3,4-diols: Flavan-3-ols are flavonoids which generally polymerise to give rise to proanthocyanidins (PAs) which are stored in the vacuole. They are highly potent antioxidant compounds [138]. Flavan-3,4-diols (such as leucocyanidin), are precursors for anthocyanin synthesis [20].

3.3.1.5. Chalcones: These are biosynthesised through a combination of acetate-malonate and shikimate pathways. They are the precursors of open chain flavonoids and isoflavonoids. Chalcones are α,β unsaturated ketones consisting of two aromatic rings (ring A and B) having diverse substituents. In plants they act as pollinator attractants, and provide defence against pathogens, and contribute to the plants’ medicinal properties (Table 3). They are found in families like Astereaeae, Solanaceae, Anacardiaceae, Caesalpiniaeae, Piperaceae, and Apiaceae [34].

Dihydrochalcones, 1,3-diphenylpropan-1-ones, natural phenolics related to chalcones, are restricted to about 30 plant families like Rosaceae, Rutaceae, Lauraceae, and Leguminosae. Both chalcones and dihydrochalcones are synthesised via common pathway involving chalcone synthase [62].

3.3.1.6. Flavonols: These are flavonoids occurring as O-glycosides and are widely distributed in plants. Examples include myricetin, quercetin, and kaempferol (Table 3). They absorb UV-B light in the 280-320 nm region and they are thought to act as UV-B filters [1]. They also function as reactive oxygen species (ROS) scavengers [2], regulate auxin transport and cell growth processes [95]. Families possessing these compounds include Ranunculaceae, and Apiaceae amongst others.

### Table 3: Classification, plant sources, medicinal/pharmacological compounds, and medicinal properties of some major categories of phenolic compounds.

<table>
<thead>
<tr>
<th>PHENOLICS</th>
<th>Some Source(s)</th>
<th>Active Ingredients</th>
<th>Medicinal Properties</th>
<th>References</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Plant Sources</th>
<th>Activities</th>
<th>Additional Information</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>Anticancer, antimicrobial, antioxidant, anti-hormonal, anti-inflammatory, anti-leishmanial, enzyme inducing/inhibitory activities, potential for treating malaria, diabetes, viral infections, skin diseases, Alzheimer’s disease</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chalcones</td>
<td><em>Artocarpus nobilis</em>, <em>Angelica Keiskei</em>, <em>Dalbergia odorifera</em>, <em>Alpinia rafflesiana</em>, <em>Nymphaea caerulea</em>, <em>Piper methysticum</em>, <em>Glycyrrhiza uralensis</em>, <em>Artemisia</em></td>
<td>Antioxidant, cytotoxic, anticancer, antimicrobial, antiprotozoal, antiulcer, antihistaminic, anti-inflammatory, cytotoxic, chemopreventive, anti-angiogenic, anti-infective, antimalarial, aldose reductase inhibitory, anti-protozoal, antibacterial, anti-filarial, anti-fungal, anti-convulsant, anti-</td>
<td></td>
</tr>
<tr>
<td>Bioactive Compounds</td>
<td>Medicinal Plants</td>
<td>Pharmacological Activities</td>
<td>Source</td>
</tr>
<tr>
<td>---------------------</td>
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<td>-----------------------------</td>
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</tr>
<tr>
<td>absinthium</td>
<td>Absinthium</td>
<td>Anti-mutagenic, antioxidant, antimicrobial, anti-carcinogenic, anti-hypertensive, anti-allergic, anti-depressant, anti-diabetic, enzyme-inhibitors, cardioprotective, chemopreventive,</td>
<td>Bruneton 1999, Cai et al., 2004, Goutam and Delip 2006</td>
</tr>
<tr>
<td>Flavonols</td>
<td>Aconitum tanguticum, Sutherlandia frutescens, Acacia nilotica, Terminalia arjuna, Aloe barbedensis, Moringa oleifera, Ficus religiosa</td>
<td>Quercetin, kaempferol, myricetin, morin, galangin, and their glycosides</td>
<td>Anti-tuberculosis, antimicrobial, anti-tumour, antioxidant, anti-inflammatory, anti-proliferative, anti-angiogenic, anti-estrogenic, improvement of blood circulation</td>
</tr>
<tr>
<td>Flavones</td>
<td>Scutellaria baicalensis, Biophytum umbraculum, Gentiana triflora, Torenia hybrida</td>
<td>Luteolin, apigenin, baicalein, chrysin, diosmin, rutin, sibelin and their glycosides</td>
<td>Anti-tuberculosis, antimicrobial, anti-tumour, antioxidant, anti-inflammatory, anti-proliferative, anti-angiogenic, anti-estrogenic, improvement of blood circulation</td>
</tr>
<tr>
<td>Flavanones and flavanones</td>
<td>Harungana madagascariensis, Arachis hypogaea, Hemizonia increscens, Eriodictyon glutinosum, Thymus vulgaris, Sophora flavescens</td>
<td>Naringenin, hesperetin, eriodictyol, fisetin, taxifolin, and their glycosides (e.g. naringin, hesperidin, and liquiritin)</td>
<td>Antioxidant, antiproliferative, estrogenic, radio-protective, anti-inflammatory, analgesic, anti-hypercholesterolemic, anti-carcinogenic, antimicrobial, hepatoprotective, CNS depressants</td>
</tr>
<tr>
<td>Isoflavones</td>
<td>Psoralea corylifolia, Trifolium pratense,</td>
<td>Genistean, daidzein, glycitein,</td>
<td>Anticancer, neuroprotective, cardioprotective</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Phenolic Compounds</th>
<th>Bioactive Compounds</th>
<th>Pharmacological Actions</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythrina variegata, Pueraria lobata</td>
<td>fromononetin, and their glycosides</td>
<td>Anticancer, cardioprotective</td>
<td>Manach et al., 2004, Cheynier 2005, Kashani et al., 2012</td>
</tr>
<tr>
<td>Neoflavonoids</td>
<td>Vaccinium myrtillus, Sambucus nigra, Hibiscus rosa-sinensis, Fagopyrum esculentum, Camellia sinensis</td>
<td>Melanin, daidzein, genistein, glycine</td>
<td></td>
</tr>
<tr>
<td>Simple phenolics</td>
<td>Clematis chinensis, Paeonia suffruticosa, Matteuccia struthiopteris, Agrimonia pilosa, Angelica sinensis, Tripterygium wilfordii</td>
<td>Catechol, resorcinol, eugenol, phloroglucinol, pyrogallol</td>
<td>Antiseptic, antibacterial, antifungal, local anaesthetic, antioxidant</td>
</tr>
<tr>
<td>Phenolic acids</td>
<td>Barringtonia racemosa, Cornus officinalis, Cassia auriculata, Polygonum aviculare, Punica granatum, Rheum officinale, Sanguisorba officinalis, Terminalia chebula, Cinnamomum cassia, Lawsonia</td>
<td>Gallic acid, p-hydroxybenzoic acid, protocatechuic acid, vanillic acid, syringic acid, ferulic acid, caffeic acid, p-coumaric acid, chlorogenic acid, sinapic acid, salicylic acid</td>
<td>Anticancer, cardio-protective, anti-ulcer, cytotoxic, antioxidant, antiseptic, antimicrobial, anti-inflammatory, anti-tumour, anti-spasmodic, antidepressant, treatment of dyspepsia</td>
</tr>
<tr>
<td>Bioactive Compounds</td>
<td>Plants</td>
<td>Activities</td>
<td>References</td>
</tr>
<tr>
<td>---------------------</td>
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<td>------------</td>
</tr>
<tr>
<td>Protocatechuic acid, vanillic acid, syringic acid</td>
<td><em>inermis, Foeniculum vulgare, Ipomoea turpethum, Lavandula officinalis, Rosmarinus officinalis</em></td>
<td>Anti-asthmatic, anti-inflammatory, antioxidant</td>
<td>Müller et al., 1999, Kedar et al., 2010</td>
</tr>
<tr>
<td>Dextropropoxypine, phenylpropanolamine</td>
<td><em>Gnetum ula, Artemisia anua, Tannacetum polypecephalum, Cynanchum bungei</em></td>
<td>Anticancer, antibacterial, antiviral, anti-parasitic, antioxidant, anti-inflammatory, cytotoxic, anti-HIV, estrogenic</td>
<td>Ma et al., 2003, Seidlova-Wuttke et al., 2004</td>
</tr>
<tr>
<td>Benzophenones 1-12</td>
<td><em>Humulus lupulus, Curcuma longa, Capsicum annum, Piper methysticum, Securidaca diversifolia, Hypericum elegans</em></td>
<td>Antioxidant, anti-tumour, anti-inflammatory, anti-allergy, anti-bacterial, anti-fungal, anti-viral, anti-allergic, anti-malarial</td>
<td>Akao et al., 2008, Yang et al., 2009, Shan et al., 2011</td>
</tr>
<tr>
<td>Gentisin, mangiferin</td>
<td><em>Gentiana lutea, Mangifera indica, Madhuca indica</em></td>
<td>Antioxidant, anti-tumour, anti-inflammatory, anti-allergy, anti-bacterial, anti-fungal, anti-viral, anti-allergic, anti-malarial</td>
<td>Daniel 2006, Kontogiorgis et al., 2007, Borges et al., 2009</td>
</tr>
<tr>
<td>Umbelliferone, daphnatin, warfarin, scopoletin, fraxetin, 4-methylcyclothinate, dicoumarol, marmelosin</td>
<td><em>Aegle marmelos, Feronia limonia, Eclipta alba, Mammea americana, Torresea cearensis, Justicia pectoralis, Eclipta alba, Pterodon polygaliflorus</em></td>
<td>Antihelminthic, anti-asthmatic, anti-coagulant, anti-tumour, antiviral, anti-inflammatory, anti-oxidant, anti-microbial and enzyme-inhibitory, anti-obesity, anti-mutagenic, digestive, astringent, stomachic, heart tonic, hypoglycaemic, spasmylytic, vasodilators</td>
<td>Daniel 2006, Kontogiorgis et al., 2007, Borges et al., 2009</td>
</tr>
<tr>
<td>Phytochemicals</td>
<td>Plants</td>
<td>Compounds/Chemical Structures</td>
<td>Pharmacological Properties</td>
</tr>
<tr>
<td>----------------</td>
<td>--------</td>
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<td>---------------------------</td>
</tr>
<tr>
<td>Chromones</td>
<td>Hybanthus ipecacuanha, Bergenia ciliata, Ammi visnaga, Eranthis hyemalis, Baeckea frutescens</td>
<td>Eucryphin, cromolyn, 6,7-dimethoxy-2,3-dihydrochromone</td>
<td>Anti-inflammatory anti-viral, anti-microbial, anti-cancer, antioxidant, biocidal, anti-spasmodic, anti-diabetic, anti-ulcer, anti-HIV, wound healing, immune stimulatory activities</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stilbenes</td>
<td>Reynoutria japonica, Polygonum cuspidatum, Rhodomyrtus tomentosa, Passiflora edulis</td>
<td>Resveratrol, oxyresveratrol, piceatannol, petrostilbene, pinsylvin</td>
<td>Chemoprotective, anticancer, antioxidant, anti-ageing, anti-angiogenesic, neuroprotective, anti-fungal, immune modulation</td>
</tr>
<tr>
<td>Quinones:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Naphthoquinones</td>
<td>Plumbago zeylanica, Rhinacanthus nasutus, Tabebuia avellanedae</td>
<td>Plumbagin, ubiquinone, plastoquinone K vitamins, juglone</td>
<td>Antibiotic, anti-viral, anti-inflammatory, anti-pyretic, anti-proliferative, cytotoxic, anti-allergic, anti-asthmatic</td>
</tr>
<tr>
<td>-------------------------</td>
<td>-----------------------------------------------------------------</td>
<td>--------------------------------------------------------</td>
<td>-------------------------------------------------------------</td>
</tr>
<tr>
<td>Anthraquinones</td>
<td>Embelia ribes, Plumbago indica, Cassia tora, C. fistula, C. augustifolia, Hypericum perforatum, Rumex crispus</td>
<td>Hypericin, emodin, rhein</td>
<td>Anti-inflammatory, anti-depressant, antimicrobial, anti-dermatics, anthelmintic, purgative, tonic, treatment of gout, rheumatism, leukaemia, responsible for peristaltic colon movement and water and electrolyte secretion</td>
</tr>
<tr>
<td>Tannins</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Condensed tannins</td>
<td>Rhus javanica, Quercus lusitanica, Geranium thunbergii, Tellima grandiflora, Mimosa tenuiflora, Caesalpinia pyramidalis, Agrimonia pilosa</td>
<td>Procyanidin, prodelphinidins</td>
<td>Antioxidant, anti-cancer, anti-HIV, anti-diarrhoea, anti-inflammatory, antibacterial</td>
</tr>
<tr>
<td>Hydrolysable tannins</td>
<td>Neoregelia laevis, Diospyros crassiflora, Embelia schimperi, Polygonatum falcatum</td>
<td>Gallotannins, ellagittannins</td>
<td>Anti-diarrhoea, antidote in poisoning by heavy metals</td>
</tr>
</tbody>
</table>
3.3.1.7. Flavones: These compounds bear very close resemblance to flavonols. Most of them occur as 7-O-glycosides though various substitutions are also possible including methylation, hydroxylation, O- and C- alkylation and glycosylation [40]. They differ from flavonols in lacking a 3-hydroxyl substitution; this affects their UV absorption properties. Flavones normally occur in herbaceous plants. They act as UV filters and prevent light penetration to internal tissues. They are mainly distributed in Labiatae, Apiaceae, Asteraceae, and so forth such as the roots of Scutellaria baicalensis, inflorescences of Chrysanthemum morifolium, and aerial parts of Artemisia annua. Examples include luteolin, apigenin, baicalein, chrysin, and their glycosides (Table 3) [77].

3.3.1.8. Flavanones and flavanonols: Flavanones (also termed dihydroflavonones) are a minor subclass of plant flavonoids. The basic chemical structure involves two benzene rings (A and B) linked by a third heterocyclic, saturated ring. Flavanones occur in several plant families including Labiatae, Annonaceae, Acanthaceae, Compositae, Leguminosae, Rosaceae and also Rutaceae [26]. They are synthesised from chalcones via chalcone-flavanone isomerase. Examples include naringenin, hesperetin, eriodictyol, and their glycosides (e.g. naringin, hesperidin, and liquiritin) [77]. Flavanonols may act as precursors to anthocyanins involving enzymes like dihydroflavonol 4-reductase (DFR), anthocyanidin synthase (ANS), and anthocyanidin 3-glycosyl transferase (3GT) [178].

3.3.1.9. Isoflavones: These compounds comprise the largest group of isoflavonoids. They differ from flavones in the location of the phenyl group which is attached to the third position of the heterocyclic ring rather than the second. They are present in families such as Leguminoseae, Chenopodiaceae, Polygalaceae, and Iridaceae [51]. They play...
a role in nitrogen-fixation and act as defence compounds. Some important isoflavones are genistein, daidzein, glycitein, fromononetin, and their glycosides (Table 3) [77].

### 3.3.1.10. Neoflavonoids:
Neoflavonoids are derived from isoflavonoids and depending upon their structural variations are further categorised into 4-phenyl coumarins, dalbergiones, and aryl chromans. Neoflavonoids are concentrated in many plant families: Gentianaceae, Leguminoseae, Rubiaceae, Passifloraceae, Polyodiaceae, and Compositae [46].

### 3.3.2. Simple Phenolics:
These are C₆ compounds. Simple phenolics are substituted phenols with one of the functional groups being the hydroxyl group. These consist of a singly substituted phenolic ring with either alcoholic, aldehydic, or carboxylic acid groups. These are toxic to microorganisms but their occurrence is rare in plants [149].

### 3.3.3. Phenolic Acids:
Phenolic acids comprise two parent structures: hydroxycinnamic and hydroxybenzoic acids. The former include ferulic acid, caffeic acid, p-coumaric acid, chlorogenic acid, and sinapic acid while the latter includes gallic acid, p-hydroxybenzoic acid, protocatechuc acid, vanilnic acid, and syringic acid [34]. Phenolic acids occur in either free or conjugated forms, usually as esters or amides. These are widely distributed in the plant kingdom. They play a role in plant growth and reproduction, in rhizospheric plant-microbe interactions, and act as defence compounds against stresses [172]. They are also involved in plant nutrient uptake, protein synthesis, photosynthesis, as structural components and in allelopathy. A majority of them occur in bound form to the structural components of the plants (cellulose, protein, lignin) or to larger polyphenols (flavonoids) or smaller organic molecules (e.g. glucose, quinic, maleic or tartaric acids) or other natural products (e.g. terpenes) [144]. They are synthesised via phenylpropanoid pathway, as by-products of the monolignol pathway and as breakdown products of lignin and cell wall polymers in vascular plants [113].

### 3.3.4. Acetophenones:
These are derived from phenylalanine [50]. They are aromatic ketones and some occur as glycosides. Families possessing these compounds include Loranthaceae, Gnetaceae and Urticaceae. Their usage as drugs is limited to raw material in the synthesis of several pharmaceuticals (Table 3) [90].

### 3.3.5. Benzophenones:
Benzophenones are the precursors of xanthones. They are low molecular weight compounds containing two phenol rings and various hydroxy groups. These are prominent in the families Hypericaceae, Olacaceae, Clusiaceae, Gentianaceae Polygalacaeae, Moraceae and Guttiferae. These are capable of absorbing UV-A (315-400nm) and UV-B (280-315 nm) radiation and this property and are in the production of sunscreens and skin lotions [165].

### 3.3.6. Xanthones:
Xanthones (dibenzo-γ-pyron) have nearly one thousand known naturally occurring derivatives. They are biosynthesised via mixed shikimate-acetate pathway [131]. Simple xanthones contain simple substituents such as hydroxy, methoxy or methyl [116]. These compounds are found in families such as Gentianaceae, Guttiferae, Logoniacaeae, Podostemaceae, Hypericaceae, Moracea, Polygonaceae and Clusiaceae [46].

### 3.3.7. Coumarins:
These are aromatic constituents of plants (C₆-C₃ derivatives), numbering more than 1300 and almost all are O-substituted. They are found in families such as Apiaceae, Asteraceae, Fabaceae, Moraceae, Rosaceae, Rubiaceae and Solanaceae Thymelaeaceae, Rutaceae, Umbelliferae, and Euphorbiaceae [46]. Their pharmacological and biochemical properties depend upon their pattern of substitution. The simple coumarins occur as hydroxylated, alkoxyated, alkylated and glycosylated derivatives of the parent compound [98].

### 3.3.8. Chromones:
These compounds are synthesized via the acetic acid pathway involving the condensation of five acetate molecules. They are similar to coumarins in structure and properties. They are usually characterized by a methyl group at C₂ and oxygen at C₄ and C₇. Families possessing chromone alkaloids include Melliaceae, Rubiaceae, and Fabaceae. They play antioxidative and defensive roles in plants [46,170].

### 3.3.9. Stilbenes:
They are derived from malonyl CoA and 4-Coumaroyl CoA via enzyme stilbene synthase from the phenylpropanoid pathway. Examples include picetannol and resveratrol which accumulate under UV-B [185]. They occur in plants as monomers and oligomers. They function as defence compounds, phytoalexins, allelopathic agents, and respond to oxidative stress generated by UV irradiation [38,68]. These are produced by a number of unrelated plant families like Pinaceae, Cyperaceae, Vitaceae, Polygonaceae, Betulaceae, Fabaceae, and Poaceae [38].

### 3.3.10. Lignans and Lignin:
They are formed via general phenylpropanoid and the monolignol pathway [177], and are composed of two phenylpropanoid units forming a C₁₈ skeleton with various functional groups. Lignans are widespread in the plant kingdom, p-coumaroyl alcohol, coniferyl alcohol, and sinapyl alcohol are the main precursors of all lignins and lignans. Lignins in gymnosperms are primarily derived from coniferyl alcohol, and to a lesser extent, p-coumaryl alcohol, whereas angiosperm lignins contain coniferyl and sinapyl alcohols in roughly equal proportions. These lignin constituents are synthesised from phenylalanine via various cinnamic acid derivatives [63]. The main function of lignin in plants includes cell wall strengthening, facilitating water and minerals to be conducted through the xylem. The presence of lignin reduces cell wall digestibility and blocks the growth of pathogens [177].
3.3.11. Quinones: Quinones are aromatic rings with two ketone substitutions, ubiquitous in nature and occur in free state as well as in the form of glycosides. More than 500 compounds of the group are known about half of which are found in higher plants. These are primarily confined to the bark and roots [46]. Quinones have been known to act as plant growth regulators [153]. Depending upon the number of rings in their structure, quinones are usually divided into benzoquinones, naphthoquinones, and anthraquinones.

3.3.11.1. Benzoquinones: Benzoquinones are a class of small molecules that contain two carbonyl groups on a benzene ring. In plants, these are found in families such as Myrsinaceae, Connaraceae, Geraniaceae, Liliaceae, Leguminosae Umbelliferae, Labiatae, Ranunculaceae, Compositae, Cupressaceae, Pyrolaceae, Primulaceae, and Apocynaceae. In this category, plastoquinones and ubiquinones are physiologically significant as being important for the processes of photosynthesis and respiration, respectively [153,46].

3.3.11.2. Naphthoquinones: These are derived from naphthalene, and occur as 1,4-naphthoquinones, and rarely 1,2-naphthoquinones. The families comprising these compounds include Bignoniaceae, Droseraceae, Plumbaginaceae, Boraginaceae, Juglandaceae, Dioncophyllaceae, Avicenniaceae, Acanthaceae, Boraginaceae, Ebenaceae, Drosoraceae, Balsaminaceae, Steraliciaceae, Nepenthaceae, and Ulmaceae. They are synthesised via the shikimate/ succinyl CoA combined pathway and the shikimate/mevalonate pathway [9]. They prevent plants from pathogen attacks. They have also been known to possess phytotoxic properties [153].

3.3.11.3. Anthraquinones: Anthraquinones comprise the largest group of natural quinones usually found in the form of glycosides or in carboxylated state. They function as protective plant compounds against insects and pathogens [153]. They occur in families such as Rubiaceae, Rhamnaceae, Leguminosae, Polygonaceae, Bignoniaceae, Verbenaceae, Scrophulariaceae, and Liliaceae, amongst others [46]. Anthraquinone is an aromatic organic compound and sometimes contribute to their colouring pigments [109].

3.3.12. Tannins: These are basically found in families like Leguminosae, Anacardiaceae, Combretaceae, Rhizophoraceae, Myrtaceae, and Polinaceae but are distributed widely throughout the plant kingdom. These are synthesised via phenylpropanoid pathway and are commonly found combined with alkaloids, polysaccharides, and proteins [70]. Structurally, they possess 12 to 16 phenolic groups and 5 to 7 aromatic rings per 1,000 units of relative molecular mass [99]. With the exception of some high molecular weight compounds, these are soluble in water. Their molecular weight usually ranges from 500 to 20,000. Plant tannins also serve as defences against microorganisms and herbivores. These usually classified into two classes: hydrolysable tannins (gallo- and ellagi-tannins) and condensed tannins (proanthocyanidins) [33].

3.3.12.1. Condensed tannins: These are also termed proanthocyanidins and are synthesised via polymerization of flavan-3-ol units. They are frequent constituents of woody plants and amongst the most abundant polyphenols in the plant kingdom. The most common members of the PAs are the procyanidins (PCs), composed of the monomeric flavan-3-ols (+)-catechin and/or (-)-epicatechin [79]. They play protective roles in plants acting against pathogens, herbivores, and UV-B radiation [33].

3.3.12.2. Hydrolysable tannins: These comprise of a monosaccharide core associated with several catechin derivatives [99]. They are comparatively less stable than condensed tannins and are readily degraded into smaller molecules [15]. Gallic acid is the principle phenolic unit of hydrolysable tannins [58]. They also contribute to astringent quality of tannin-containing beverages [46].

Figure 3A and Figure 3B shows the structures of the one of the representative compounds from the above-mentioned groups.

4. Summary and Future Perspectives

With the demand for herbal medicines on the rise, it is only obvious that the sources of these medicines, the medicinal plants, will also be consumed in much higher quantities. This scenario, however, raises concerns about the exploitation of these resources and their unsustainable use. To counter the overexploitation of these natural resources, following measures needs to be brought into action:

4.1. Conservation of medicinal plants and their sustainable and judicious use: Medicinal plants, not only in India, but the world over, have been facing increased risk of extinction due to habitat destruction, bioprospecting or biopiracy, and overharvesting. According to A Native Plant Conservation Campaign Report, about 15,000 plants face extinction as a result of habitat loss and overharvesting. Also, the current extinction rates are likely to result in the loss of a potential major drug every two years [145]. To counter overexploitation of natural resources, and consequent threat to biodiversity, sustainable practices have been recommended and several worldwide organisations have established guidelines for collection and sustainable cultivation of medicinal plants [91].
4.2. Enhancement of the compound of interest in the plant(s)/ plant part(s) via the following:

4.2.1. Biotic/ abiotic elicitors: Various biotic (such as bacterial and fungal infestation and herbivory) and abiotic (such as temperature, UV-B exposure, and water deficit) elicitors have been reviewed by [128] which influence the levels of secondary metabolites in plants. It has been observed that under duress, the secondary metabolites in plants, along with the bioactive compound(s) of interest, usually increase. Thus, it can be safely reasoned that if more amount of the desired bioactive component can be harvested from a unit amount of plant tissue, the resulting number of plants required to obtain the same amount of the bioactive component would reduce. This may prove to be effective in easing the pressure on the harvest rates of medicinal plants in the long run.

4.2.2. Genetic and metabolic engineering: Genetic engineering holds vast potential for the transformation of plants suited for particular needs. This may include manipulating the existing pathways, overcoming the rate-limiting steps, and/or over-inducing the desired genes and pathways to enhance the production of the required pharmaceutical compound from the plant. Another approach can be the synthesis of a novel compound in a plant by introduction of appropriate heterologous genes. Genetic manipulations in some medicinal and aromatic plants have been reviewed by [61]. They have also touched upon the concept of ‘metabolons’ or metabolic channelling. The targeted genetic interventions might be advantageous if the mechanisms and principles underlying the formation of metabolons are more thoroughly understood. These may facilitate the accumulation of medicinal compounds of commercial importance at the cost of less or non-commercial ones and in turn might accelerate the evolutionary processes in plants besides being expedient for health purposes.

4.2.3. Cell and tissue culture: Via cell and/or tissue culture many of the secondary metabolites, for instance anthocyanins, alkaloids such as vincristine and vinblastine etc. have been produced. Since these systems are free from the interfering compounds such as pectins, excess polysaccharides, and enzymes, they allow easy, rapid, and efficient isolation of the desired compound(s). These cultures also provide the advantages of faster growth, proliferation, and metabolism compared to the field-grown plants [143]. For instance, Raman and Jayabaskaran (2008) observed the enhanced production of catharanthine and vindoline from *C. roseus* cell cultures, when irradiated with UV-B for 5 min.

The majority of the vast wealth of herbal natural compounds and their sources is yet to be discovered, and the compounds already in place are yet to be utilized to their full potential. To achieve this objective, and to prevent the loss of biodiversity, medicinal plants and their bioactive compounds need to be revered and conserved.
Figure 3A: Structures of one of the representative compounds of various categories of phenolic compounds.
Figure 3B: Structures of one of the representative compounds of various categories of phenolic compounds

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