Chapter 8
Phytochemical and Pharmacological Importance of Plant Secondary Metabolites in Modern Medicine

Gnanavel Velu, Veluchamy Palanichamy, and Anand Prem Rajan

Abstract The practice of treating various disease using medicinal plants are as older as an ancient civilization. Secondary metabolites present in the plants are predominantly responsible for treating various ailments. Secondary metabolites are also called as plant constituents or natural compounds which exert significant pharmacological and toxicological effects in humankind. The chemical compounds present in the plant sources are categorized as primary and secondary metabolites based on the chemical structure and biosynthetic derivation. Secondary metabolites exhibit different series of pharmacological activity which can be further classified based on their chemical structure and functional groups present in it. The most important secondary metabolites include terpenoids, phenolics, flavonoids, alkaloids and glycosides which act as an important source for single bioactive ingredients in nutraceuticals and modern medicines. Secondary metabolites have a very good antioxidant property which can be used as an effective natural antioxidants source in nutraceuticals. Most of the secondary metabolites have a broad range of their therapeutic activity and they directly interact with the receptors, cell membranes, and nucleic acids. This review evaluates the meticulous report of secondary metabolites, their classification, phytochemistry, pharmacological activity and its application in modern medicines which may pave the way for knowledge to identify and isolate the desired pharmacologically active lead compound in the drug discovery.

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8.1 Role of Natural Products in Ancient Medicine

Ever since the primeval period, mankind has used the natural yields such as plant life, animals, microbes and aquatic organism, in medicine for the treatment of diseases. The practice of traditional medication has continued as a most reasonable and effortlessly accessible primary source of treatment for the humans since the prehistoric time in the effective management of disease and others various ailments (Hosseinzadeh et al. 2015; Manivel et al. 2009; Madhumitha et al. 2016; Roopan and Khan 2010). As per fossil documentation, the application of medicinal plants as medications accredited over 60,000 years ago (Shi et al. 2010; Fabricant and Farnsworth 2001). Sumerians have documented medication from the plant sources for the various illnesses. The primary treatment for the heart and circulatory disorders were clearly documented over 3500 years back in the papyrus. The plant-based medication accomplished by the primeval China provided a greater source of medicinal information for the treatments numerous diseases (Xiao 1988). The practice of traditional medication still exists in China. Nearly half of the total population of China indirectly depends upon the traditional medication for treating diseases predominantly in rural areas of China. There are almost five thousand different traditional medications available for the prevention and treatment of diseases throughout the China which account over one-fifth of the total pharmaceutical market of China (Li 2000). India is renowned for its greater and larger biodiversity which provided abundant valuable medicinal plants for the treatments involved in the preventive and curative medications to the mankind.

The history of Indian traditional system is as old as humankind and the extensive systematic information regarding the biochemical and pharmacological properties of important medicinal plants are clearly documented in the Rig Veda, ancient Hindu holy verses (Arash et al. 2010; Hemalatha et al. 2013; Hemalatha et al. 2015). The natural resources based medications were widely used by the ancient people around the world for the treatment and prevention of all types of diseases. These natural resources based medicines were predominantly obtained from the plant sources. The affluent diversity in plant resources supplied different kinds of natural drug materials for the curative and therapeutic effect of various kinds of infections and diseases. The other important natural resources based medicines were obtained from the marine and animal sources (Newman et al. 2000; Newman and Crag 2007). The make use of plant materials as natural medicines have resulted from the remarkable confront to earlier mankind by overcoming the difficulties in differentiating the medicinal plants from the non-edible plants (Haidan et al. 2016; Gao et al. 2007). Later the therapeutic properties of medicinal plants were classified broadly to configure definite herbal pharmacopeias which form the basis for the

indigenous remedial structure of medicinal plants based traditional medication throughout the world. The ethnobotanical study of medicinal plants provides comprehensive acquaintance of plant nature and inimitability of selective pharmacological characteristics of medicinal plant materials (Farnsworth 1990).

In current scenario, the applications of traditional knowledge on plant materials for the treatment and prevention of disease have received wide attention among the plant-based research community which resulted in the augmented exceptional attention among the drug discovery researchers towards the plant-based drug discovery research in phytochemistry and natural products (Newman and Crag 2007; Madhumitha and Saral 2009; Anupama et al. 2014). This increased wave of attention towards the plant-based natural product chemistry research in modern drug discovery accredited to numerous factors. The most important factor includes, the unchallenged therapeutic requirements, for many a dreadful diseases like Cancer, HIV, Alzheimer's diseases etc., there are no current available treatments to cure or prevent these diseases. Hence, the modern drug discoveries have turned their interest towards the plant-based drug discovery as an alternative source for the drug discovery to meet the unchallenged therapeutic requirements for this modern world. The other important factor includes the availability of wide variety of natural secondary metabolites in plant sources which act as potent curative medicines. The secondary metabolites thus obtained from these medicinal plant sources have a significant broad sequence of the inimitable chemical structure with different therapeutic activity. The novel bioactive lead compound derived from the secondary metabolites of medicinal plant sources can be easily developed as a bioactive probe into drug moiety because of the rapid advancement of modern science with wide range of modern analytical development technique availability to identify and isolate the particular desired bioactive phytocompound from the plant materials to exert the targeted pharmacological activity with minimal toxic effect (Clark 1996).

The importance of the role of traditional medicine based drug discovery was accepted by World Health Organization (WHO 1993) and documented the guiding principle for the strategic methods employed in the standardization and drug discovery development process from the medicinal plant materials (WHO 1993). The secondary metabolites rich medicinal plant materials are widely available throughout the terrestrial and aquatic world which acts as an alternative source for the novel drug discovery in the modern medicines. The large number phytocompounds were predominantly listed in the modern pharmacopoeias due to the accessibility of high efficient screening methods available to isolate the bioactive phytocompound from the medicinal plant materials and the advancement of combinatorial chemistry to modify the isolated novel bioactive phytocompound into semi-synthetic compound with improved structural activity relationship for the better efficacy of drug moiety for its targeted therapeutic pharmacological action with no or less toxic effects. So far, the very small proportional of plant materials have been systematically studied by the researchers from the total number of 500,000 existing plant species around the world. The further extensive research on the medicinal plant materials will pave the way for more isolation of novel bioactive phytocompounds that will

bring more future drug discoveries in the modern medicines (Ngo et al. 2013; Fowsiya and Madhumitha 2017).

8.2 Primary and Secondary Metabolites

Based on the biological requirements in plants, the naturally occurring phytochemicals can be broadly classified into primary metabolites and secondary metabolites. The primary metabolism process in the plants produces primary metabolites like carbohydrates, fats, amino acids and nucleic acids (Weinberg 1971). These primary metabolites are primarily important for the indispensable biological functions in plants which include the growth, development, and reproduction of plant cell (Fraenkel 1959). The secondary metabolism process in plants produces secondary metabolites which are generally important for the protective and self-defence function in plant cell caused by the ecological imbalance or harmful infections (Stamp 2003). These secondary metabolites are very specific and found great in numbers among the several groups of plants. The diverse combination of plant secondary metabolites produces unique chemical feature among the classes of plant species which plays an important tool for the taxonomical researchers to classify the taxonomy of plant species (Thrane 2001). The primary metabolites are generally produced from the plants species for the regular biological function of plant cells whereas the secondary metabolites are usually synthesized in different chemical configurations from primary metabolites by regulating the primary pathway metabolism of plant species based on the secondary metabolites requirements appropriate to the ecological influenced genetic code adaptability in plant cells (Waterman 1992).

8.3 Biosynthesis of Secondary Metabolites

The primary metabolites and secondary metabolites responsible for the biological functions of plant cells are chiefly produced through the biosynthetic pathways process (Nicolaou et al. 2011; Herbert 1989). The biosynthetic pathway process is an energy necessity process which is supplied through the energy released during citric acid cycle and glycolysis of carbohydrates (Kabera et al. 2014). Adenosine Triphosphate (ATP) is the chief energy molecule produced from the catabolic process of the primary compound and by the oxidation of amino acids, fats, and glucose. Coenzyme A is an important catalyst responsible for the hydrogen donor or hydrogen acceptor in anabolism and catabolism reaction (Michal and Schomburg 2013). Pentose pathway is responsible for the biosynthesis of glycosides and the Shikimic acid pathway is responsible for biosynthesis of phenols as mentioned in the Fig. 8.1 Similarly, Mevalonic acid and acetate malonate pathways are responsible for steroids and alkaloids biosynthesis (Dewick 2002). The acetyl coenzyme A

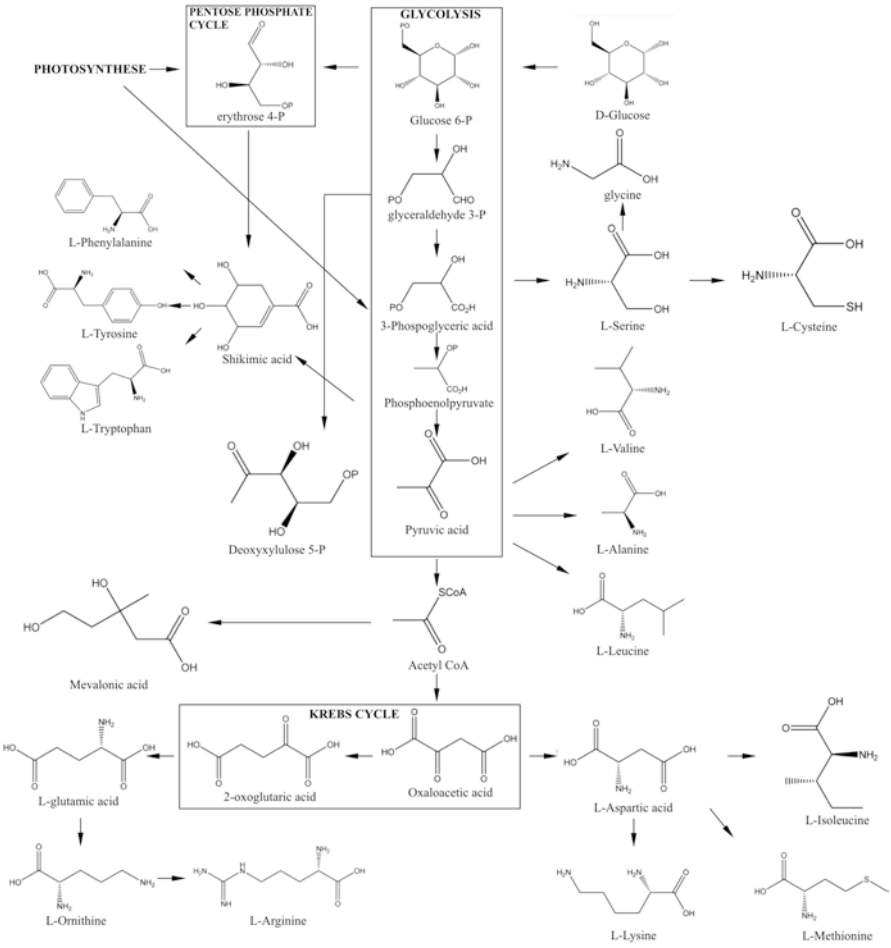

Fig. 8.1 Schematic design of plant secondary metabolites biosynthesis (Giweli et al. 2013)

is the chief important unit for the biosynthesis of secondary metabolites through the various pathways like Shikimic acid pathway, Pentose pathway, Acetate malonate pathway and Mevalonic acid pathway (Giweli et al. 2013).

8.4 Classification of Secondary Metabolites

The plant-derived phytochemicals or secondary metabolites can be further classified into different types of natural compounds based on their definite chemical structure in nature. The most important classification of secondary metabolites includes alkaloids, glycosides, flavonoids, terpenoids, phenolics, and saponins.

8.4.1 Alkaloids

Alkaloids are the most important prevalent natural group of secondary metabolites among the other chemically classified secondary metabolites. Alkaloids are made up of protein molecules containing an amino acid structural moiety which essentially holds nitrogen atom with it which are commonly occur by replacing the hydrogen atom of peptide structure with different radicals along with oxygen. Most of the alkaloid compounds are made up of carbon, oxygen, and hydrogen along with nitrogen but on the odd occurrence, further elements like phosphorus, chlorine, sulfur and bromine may also exist in the alkaloid structures (Nicolaou et al. 2011). The chemical properties of most of the alkaloids are basic in nature which turns red litmus paper into the blue. The primary, secondary and tertiary amines responsible for the basic nature present in the alkaloid groups are classified depending upon the number of nitrogen atom present in the alkaloid group. The extent of basic nature of alkaloids depends upon the variation in the chemical configuration of the molecular structure and the presence of a number of functional groups at a different location in the alkaloid molecule (Sarker and Nahar 2007). Most of the alkaloids are in solid forms but fewer alkaloids containing carbon, hydrogen, and oxygen are in liquid form also. The alkaloids produce their respective crystalline salt when treated with acids without formation of water molecule (Firn 2010). Most of the alkaloids are easily soluble in alcohol but few are sparsely soluble in water and the salt forms of alkaloids are not soluble in water. The solutions prepared from the alkaloid chemical substances are usually bitter in taste. The nitrogen atom present in the alkaloids act as a defence driving force which protects the plant cells against the bacteria, virus or microorganism infection and also from the damages caused by the other factors like herbivores attacks, ecological disturbances, and climatic modifications. These nitrogenous based alkaloids have very good pharmacological activity which can be effectively used in the modern medicinal research for the identification and drug discovery of potent drug moiety. Alkaloids are predominantly occupied in the roots and seeds of medicinal plants and found to have significant pharmacology activities like stimulation of central nervous system and anaesthesia effect (Madziga et al. 2010). Above 12,000 natural alkaloids are recognized throughout the 20% of the existing plant species around the world and most of the alkaloid compounds usually have the suffix *–line* at its end. The alkaloids from the plant origin have important medicinal application. Morphine is used as analgesics, berberine as antibiotics, vinblastine as anticancer and atropine as anti-cholinergic as discussed in the Table 8.1. The further significant alkaloids include codeine, coniine, cytisine, nicotine, quinine, solanine, strychnine and tomatine as mentioned in the Fig. 8.2. The preliminary screenings methods available for the identification of alkaloids includes the formation of cream precipitate with Meyer's reagent (Solution of Potassiomercuric iodide), formation of reddish-brown precipitate with Wagner's reagent (Potassium iodide with Iodine), formation of yellow precipitate with Hager's reagent (Picric acid solution), formation of reddish-brown or orange precipitate

Table 8.1 List of Important Alkaloids with blrPharmacological Activity

S. No.	Alkaloids	Plant Sources	Pharmacological Effect	References
1.	Atropine	Atropa belladonna, Darura stramonium, Mandragora officinarum	Muscarnic antagonist, anti-cholinergic, anti-myopia effects	McBrien et al. 2013; Gu et al. 2011
2.	Berberine	Argemone Mexicana, Xanthorhiza simplicissima, Phellodendron amurense,	Anti-inflammatory, antibacterial, antiviral, anti-cancer.	Kim et al. 2010; Zha et al. 2010; Zhang et al. 2010; Agyapong et al. 2013
3.	Codeine	Papaver somniferum	Analgesic, antitussive, anti-depressant	Simera et al. 2010; Smith et al. 2006; Vree et al. 2000; Mody et al. 1976
4.	Coniine	Conium macularum, Sarracenia flave	Neurotoxin	Panter et al. 2013; Hajek et al. 2013
5.	Cytisine	Cytisus laborinum	Acetylcholine agonist	West et al. 2011; Porreca et al. 1983
6.	Morphine	Papaver somniferum, poppy derivatives	Act on myenteric plexus, reduces shortness of breath	Rozov et al. 2014; Takita et al. 2000; Clarke et al. 1998
7.	Nicotine	Solanaceae plant family	Stimulant, insecticide, anti-inflammatory	Gandhi 2013; Melton 2006; Rhoades and Cates 1976; Achan et al. 2011
8.	Quinine	Cinchona succirubra, Cinchona calisya, Cinchona ledgeriana	Antimalarial, antipyretic, anti-inflammatory.	Adnyana 2013; El-Tawil et al. 2010; Mwita et al. 2012; Fewell and Roddick 1993
9.	Solanine	Solanum tuberosum, Solanum lycopersiam, Solanum igrum	Antifungal, sedative, anti-inflammatory, anticonvulsant	Lu et al. 2010; Kenny et al. 2013; Mohsenikia et al. 2013; Bonjoch and Sole 2000
10.	Strychnine	Loganiaceae plant family, Strychnos nux-vomica,	Anticonvulsant, pesticide	Buckingham and Nemesis 2010; Jensen et al. 2006; Umukoro et al. 2013; Dopham et al., 2014
11.	Thebaine	Papaver bracteatum	Analgesic	Fist et al. 2000; Jeong et al. 1990; Lee et al. 2011; Heal and Taylor Robinson 2010
12.	Tomatine	Solanum lycopersicum	Immune effects, anticancer, antifungal.	Morrow et al. 2004; Tomsik et al. 2013; Gao and Hu 2010.

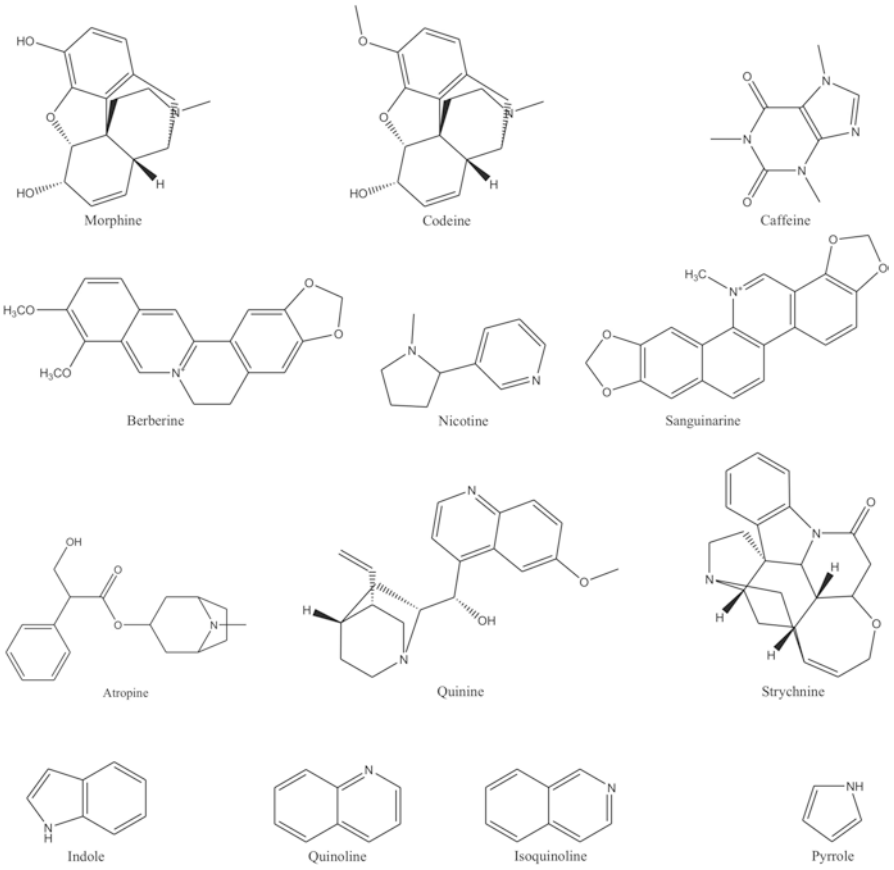

Fig. 8.2 Examples of alkaloid compounds

with Dragendorff's reagent and the formation of pink colour in Murexide test for the identification of caffeine alkaloids.

8.4.2 Glycosides

Glycosides compounds are the plant secondary metabolites compounds regularly formed by the bond attachment of condensed form of sugar moiety or glycone mostly polysaccharides with the other non-sugar moiety or aglycone (Kar 2007; Firn 2010). Glycosides are colorless alkaloid compounds with crystalline structure generally composed of carbon, hydrogen, oxygen, sulfur, and nitrogen. Most of the glycosides accumulated in the plants are inactive compounds. The enzyme hydrolysis on the inactive glycosides resulted in the formation of active glycosides which are potentially useful for the defense mechanism of plant cells (Polt 1995).

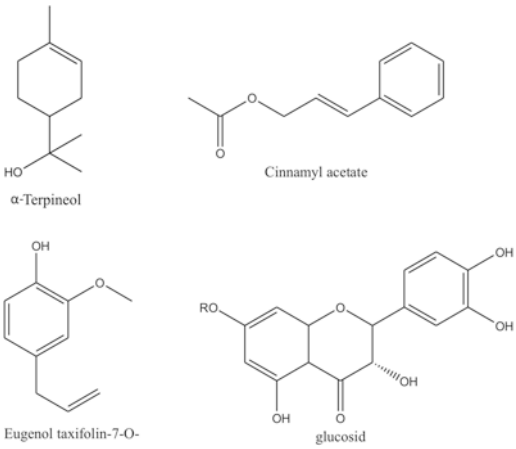

Fig. 8.3 Examples of glycoside compounds

Glycosides are also known as prodrug because the pharmacological activity of glycosides becomes active only when the aglycone part of glycosides separates from glycone part of glycosides during hydrolysis. The various hetero structure attachments of phenols, terpenes, and steroids in aglycone part of glycosides makes diverse in the classification of glycosides. The attachment of glycone and aglycone in glycosides are made up of the unique glycosidic bond which amalgamates multiple monosaccharides into different oligosaccharides and polysaccharides (Levy and Tang 1995; Newman et al. 2008). Most of the glycosides are extremely bitter in taste due to the presence of lactones group which acts on the gustatory nerves results in the excess secretion of salivary so as to increase the appetite and digestion. Cardiac glycosides are chiefly responsible for the heart disorders whereas chalcone glycosides are mainly used for anticancer activity. The important glycoside responsible for the pharmacological action includes α-Terpineol, cinnamyl acetate, eugenol taxifolin-7-O-, β-glucoside as mentioned in the Fig. 8.3. Similarly, anthracene glycosides are chiefly responsible for the management of skin infection whereas the cyanogenic glycosides are largely utilized in pharmaceutical industry as a flavour agent. The preliminary phytochemical analysis for the identification of glycosides includes addition of plant sample with hydrochloric acid and water for O-glycosides and with ferric chloride and hydrochloric acid for C-glycosides to produce violet or pink colour indicates the presence of both O-glycosides and C-glycosides.

8.4.3 Flavonoids

Flavonoids are the significant groups of polyphenols among plant secondary metabolites which are abundantly found in wide range of plants. Flavonoids are usually water-soluble compounds and are classified into flavones, flavonols and

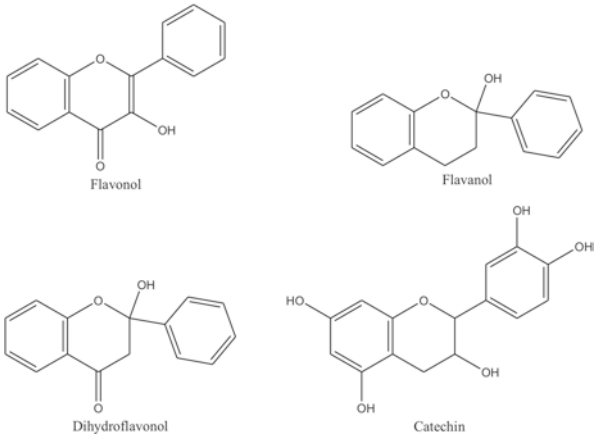

Fig. 8.4 Examples of flavonoid compounds

anthocyanins. Flavonoids play a major role in plant pollination by producing the beautiful colour over the petals of flower by filtering the ultraviolet rays which attracts the insect for pollination. Flavonoids are also act as a chemical messenger in plants which regulates the physiological function of plant cell through the inhibition of plant cell cycle. The major important flavonoids includes quercetin, quercitrin and kaempferol which are widely distributed almost over 70% of the total plant species and other class of flavonoids compounds includes flavans, flavonols, flavones, dihydroxyflavone, catechin and anthocyanidins as mentioned in the Fig. 8.4. The majority of the flavonoids have very good antioxidant property (Karr 2007) and other important therapeutic application includes anticancer, antiallergic and antiviral (Guardia et al. 2001; Hertog et al. 1995).

8.4.4 Phenols

Phenolic compounds are the most important plant secondary metabolites widely available in the all kinds of fruits, vegetables, tea leaves and other green plants. Phenolic compounds have significant pharmacology properties like antioxidant, anticancer, antimicrobial, antiseptic and anti-inflammatory activity (Pengelly 2004). Phenolic compounds are active against the oxidative stress and in the management of other diseases (Pengelly 2004). Phenolic compounds can be classified on the following basis: (1) based on the number of hydroxyl functional group, the phenolic compounds are classified as 1-, 2-, 3- and polyatomic phenols. Polyphenols are the phenolic compounds containing above one hydroxyl functional group in aromatic compounds; (2) based on the chemical configuration, the phenolic compounds are classified as mono-, di-, tri-, oligo and polyphenols; (3) based on the substitution in skeleton of carbon, the number of available carbon atom and aromatic rings in the side chain. Phenolic compounds with one aromatic ring, phenolic compounds with two aromatic rings, polymers and quinones are the four major classes of phenolic compounds. Phenolic chemical compounds with one aromatic ring are large

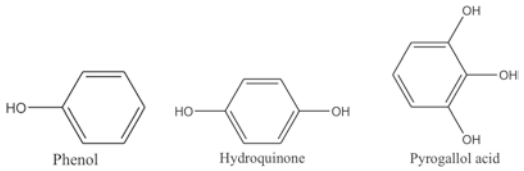

Fig. 8.5 Examples of C_6 phenolic compounds

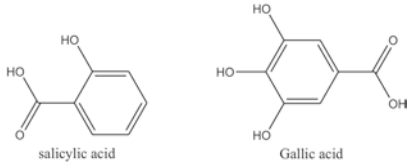

Fig. 8.6 Examples of C_6-C_1 phenolic compounds

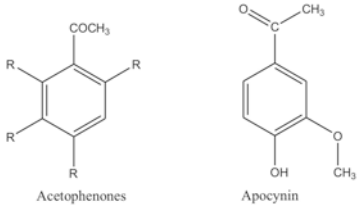

Fig. 8.7 Examples of C_6-C_2 phenolic compounds

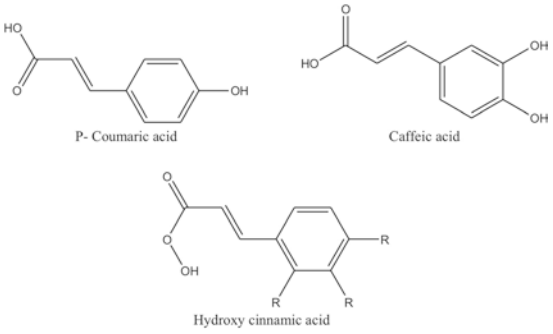

Fig. 8.8 Examples of C_6-C_3 phenolic compounds

number of phenolic compounds includes simple phenolic compounds C_6 as mentioned in the Fig. 8.5, phenolic compounds with attachment of one carbon atom C_6-C_1 as mentioned in the Fig. 8.6, phenolic compounds with two carbon atom as mentioned in the Fig. 8.7 and the phenolic compounds with attachment of three carbon atom C_6-C_2 as mentioned in the Fig. 8.8. A phenolic chemical compound with two aromatic rings includes two aromatic ring phenolic compounds linked by single carbon atom as in the case of xanthones and benzoquinones C_6-C_1-C_6 as mentioned in the Fig. 8.9. More than 8000 polyphenolic compounds are documented until now from the different plant sources and based on the characteristic features; these polyphenols are further subclassified into different groups as flavonoids along with non-flavonoids (Somasegaran and Hoben 1994).

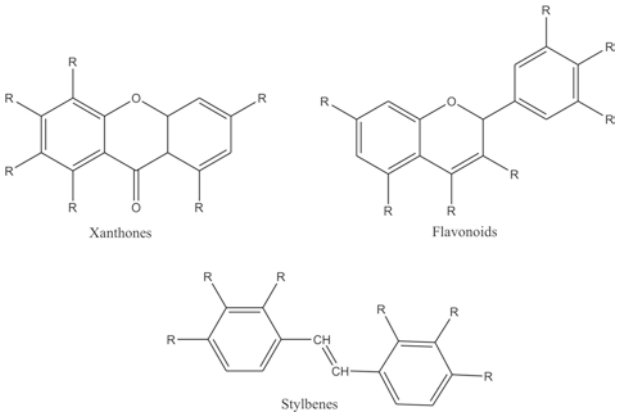

Fig. 8.9 Examples of phenolic compounds with two aromatic rings

Table 8.2 Different types of terpenoids (Kogan et al. 2006)

S. No.	Types of terpenoids	Number of carbon atoms	Number of Isoprene units	Example
1.	Hemiterpene	5	1	Isoprene, prenol
2.	Monoterpenes	10	2	Limonene, pinene
3.	Sesquiterpenes	15	3	Abscisic acid
4.	Diterpenes	20	4	Forskolin
5.	Triterpenes	30	6	Squalen, lanosterol
6.	Tetraterpenes	40	8	Carotenoids, lycopen
7.	Polyterpenes	Several	Several	Vitamin E, ubuquinones

8.4.5 Terpenoids

Terpenoids are the most important and widely available plant secondary metabolites among the major types of plant species throughout the world. Chemically, terpenoids are unsaturated hydrocarbon in liquid form mostly available in resins and essential oils (Firn 2010). Terpenoids are usually made up of isoprene units which are produced from acetate through the Mevalonic acid pathway. The different number of isoprene units unite together to form the large terpenoids which makes diverse in the structural classification of terpenoids as mentioned in the Table 8.2. All the terpenoids have a general formula $(C_5H_8)_n$ which is categorized as monoterpenoids, diterpenoids, triterpenoids and sesquiterpenoids depending on the number of carbon atom present in it. The important monoterpenoids includes menthol, eugenol and camphor reportedly having very good antioxidant property and the resins and taxol are the groups of diterpenoids having significant anticancer activity. The triterpenoids includes cardiac glycosides, ursolic acid and steroids have cytotoxic, sedative and

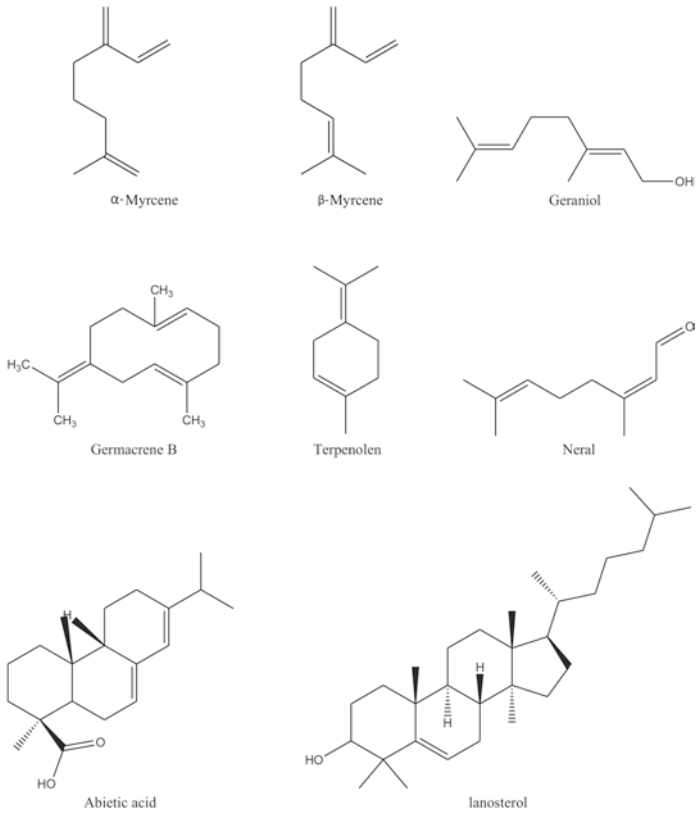

Fig. 8.10 Examples of terpenoid compounds

anti-inflammatory activity as mentioned in the Fig. 8.10. Monoterpenes are important sesquiterpenoids which forms the larger components in essential oil (Martinez et al. 2008). The recent developments in the phytochemical research on terpenoids have proved the significant pharmacological activities of terpenoids molecule for the treatment and management of disease.

8.4.6 Saponins

Saponins are the class of plant secondary metabolites which generates foam on shaking with water. The development of foam is due to the formation of colloidal solution when aglycone parts of the saponins join together with water. Sapogenin is the product formed when the aglycone of saponins hydrolysis with water. The two main types of sapogenin includes triterpenoidal and steroidal. Most of the saponins occur in glycoside form having triterpene or steroidal structure at its aglycone

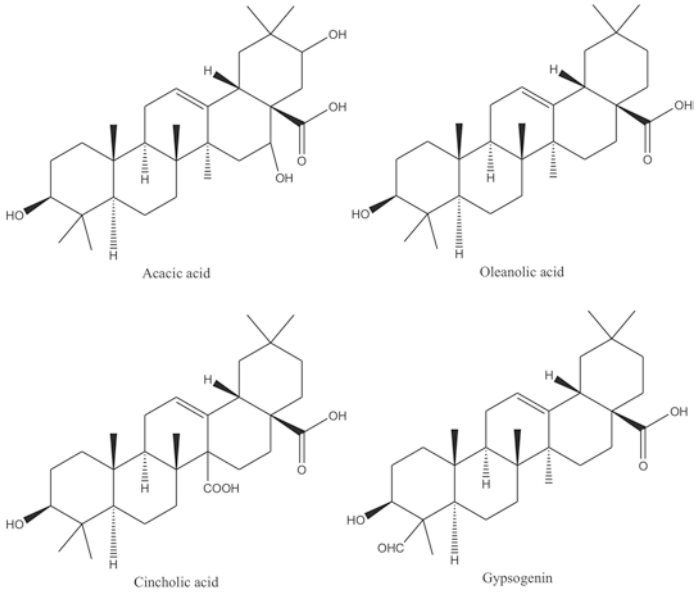

Fig. 8.11 Examples of saponin compounds

component. Diosgenin, cincholic acid, gypsogenin, oleanolic acid, acetic acid and hecogenin are the important types of saponins responsible for the hypolipidemia and anticancer activity as mentioned in the Fig. 8.11. The lowering of surface tension by the reason of grouping lipophilic sugar moiety resulted in the formation of foam over the surface (Guclu- Ustundag and Mazza 2007). Saponins are usually found in all types of plant throughout the world. Saponins have diverse physiochemical properties which makes its application significant in the preparation of pharmaceutical products. Saponins are widely used for the emulsification, altering sweetness, foam formation, increasing solubility and as surfactants by increasing critical micelle concentration.

8.5 Mechanism of Action of Plant Secondary Metabolites

There are different types of mechanism of action postulated for the plant secondary metabolites. Secondary metabolites may possibly act upon the disease-causing organism by altering the essential metabolic process and signal transduction pathway or by altering the gene expressions (Manson 2003; Surh 2003; Kris-Etherton et al. 2002).

8.5.1 Antioxidants

Antioxidants are responsible for protecting the healthy cell against the oxidative stress causing factors. These factors include the free radicals like superoxide, hydroxyl radicals and singlet oxygen which produce reactive oxygen species responsible for the destruction of the nucleus of the healthy cell (Mattson and Cheng 2006). Antioxidants obtained from the secondary metabolites play a major role in the prevention of diseases like a neurodegenerative disease, cerebral ischemia, and atherosclerosis (Uddin et al. 2008; Jayasri et al. 2009). The free radicals which are not chemically scavenged exist in metastable forms which are chemically unstable in nature and they tend to obtain the electron from the surrounding nuclear level like lipid membranes, mitochondria, DNA and another protein molecule in the cell nucleus to get the stable form leads to the disruption of cellular pathways and ultimately causing the cell death (Uddin et al. 2008). The cellular pathway disruption caused by the reactive oxygen species results in the various diseases like Alzheimer's disease, diabetes, asthma, gastrointestinal infections and meningitis (Chen et al. 2006; Uddin et al. 2008). The fewer amount of antioxidants are naturally synthesized in the human body by its own defense mechanism which is helpful in scavenging the free radicals produced in the human body (Sen 1995). The secondary metabolites obtained from the plant sources like β-carotene, vitamin E, ascorbic acid and other phytochemicals help to scavenge the remaining untreated free radicals (Diplock et al. 1998; Madsen and Bertelsen 1995; Rice-Evans et al. 1997).

8.5.2 Anti-ulcer

Plant secondary metabolites are effective against the infection of *Helicobacter pyroli* and it also inhibits the *in-vitro* anti-ulcer activity in addition to urease activity. The efficiency of anti-ulcer activity against the gastric ulcer can be improved by lowering the pH of secondary metabolites in a liquid state. It helps to reduce the Na+/K+ ATPase activity in the gastrointestinal tract and transfer of alanine in the small intestine (Jakhetia et al., 2010).

8.5.3 Anti-inflammatory

The secondary metabolites obtained from *Cinnamomum osmopholeum* have significant anti-inflammatory activity and it is also effective against the liver cell lines (HepG2). The mechanism of action of anti-inflammatory activity involves lessening the formation of inflammation causing factors like nitric oxide through the stimulation of macrophages by plant secondary metabolites like lipopolysaccharides (Jakhetia et al., 2010).

8.5.4 Anti-diabetes

The plant secondary metabolites like cinnamaldehyde play an important role in the treatment of diabetes. The phytocompound cinnamaldehyde significantly reduces the triglycerides and cholesterol level (James 2012). It also effectively increases the high-density lipoproteins cholesterol level in the streptozotocin-induced rat models. The other important plant secondary metabolites like cinnamaldehyde and polyphenols from cinnamon extracts and other plant extracts are effective in the treatment of diabetes and are widely used as oral antidiabetic and hypolipidemic agents (Jakhetia et al., 2010).

8.5.5 Anti-microbial Activity

The most important application of plant secondary metabolites is to protect its own from the fungi, insects, bacteria and other disease-causing organisms. These secondary metabolites are also effective in the prevention or treatment of various diseases in the humankind. It helps to protect the mankind from disease-causing organisms and found important application in the modern medicine (Nascimento et al. 2000; Park et al. 2001). The secondary metabolites like phenolic acids are primarily responsible for the treatment of microbial infection near the bladder, teeth and urinary tract infection. Most of the plant secondary metabolites have significant bacteriostatic and bactericidal activities. The gas phase of clove oil and cinnamon oil are used to inhibit the bacterial and fungal growth on mid-level moisture food materials with a customized atmospheric gas level of oxygen and carbon dioxide (Jakhetia et al., 2010).

8.5.6 Neuroprotective Activity

The various pharmacologically active secondary metabolites obtained from the different plant sources have significant neuroprotective activity against the neurodegenerative disorders. The neurodegenerative disorder can be described as an irreversible gradual loss of neuronal cell which is essential to perform the normal brain functions and the continuous loss of neuronal cell ultimately leads to brain death. The neurodegenerative disorder includes Alzheimer's disease, Parkinson's disease, Huntington's disease and Amyotrophic lateral sclerosis (Marcello et al. 2010). The secondary metabolites obtained from plant sources like Physostigmine, Galantamine, Huperzine A, Resveratrol, and Curcumin plays an important role in the treatment of Alzheimer's disease as mentioned in the Fig. 8.12. Physostigmine is a bioactive alkaloid compound obtained from *Physostigma venensosum* act as an important drug for the short-term treatment of Alzheimer's disease (McCaleb 1990; Sitaram et al. 1978; Julian and Pikl, 1935). The mechanism of action involved in the treatment of

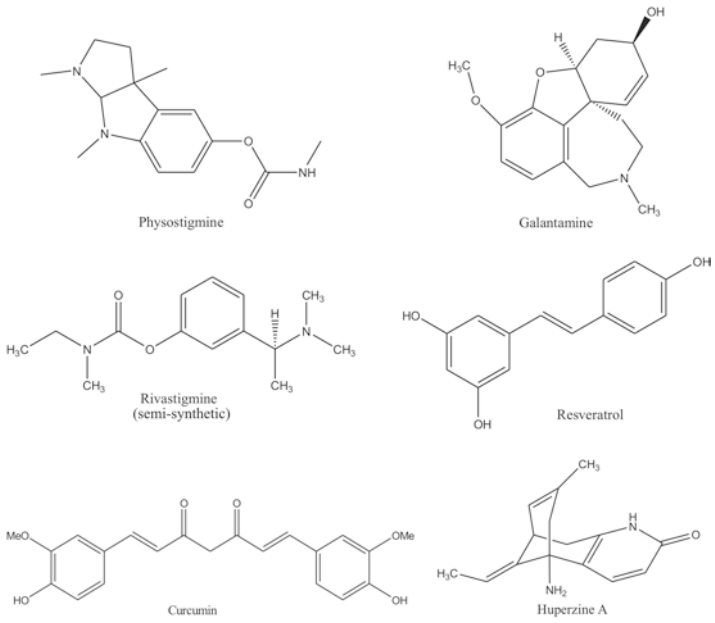

Fig. 8.12 Examples of neuroprotective compounds

Alzheimer's disease includes the reversible inhibition of cholinesterase enzymes which eventually prevents the breakdown of brain enzyme acetylcholine and also helps to restore the declined acetylcholine for the treatments involved in memory disorder (Kamal et al. 2000; Howes and Houghton 2009). Galantamine is an alkaloid type of bioactive compound obtained from *Galanthus nivalis* which is widely used in the treatment of moderate stage of Alzheimer's disease (Bores et al. 1996; Howes and Houghton 2009). Huperzine A is a bioactive alkaloid compound isolated from the *Huperzia serrata* which is widely used for the treatment of moderate stage of Alzheimer's disease by a selective inhibitor of acetylcholinesterase enzyme (Skolnick 1997; Houghton et al. 2006). Resveratrol is a bioactive polyphenol compound obtained from *Vitis vinifera* which is also widely used for the treatment of Alzheimer's disease (Marambaud et al. 2005). Curcumin is also another type of bioactive compound obtained from *Curcuma longa* is widely used for the treatment of mild stage of Alzheimer's disease by inhibiting an enzyme called cholinesterase which prevents the breakdown of brain enzymes acetylcholine (Goutam 2011; Ng et al. 2006).

8.6 Conclusion

The secondary metabolites obtained from different plant materials have diverse pharmacological activity against various diseases. This review helps to understand the classification of bioactive secondary metabolites in a systematic approach based

on the chemical nature which provides detailed information related to physiochemical and therapeutic properties of individual phytocompounds. The bioactive compounds isolated from the different plants have significant therapeutic activity in the management and treatment of many dreadful diseases with minimal side effects. Nowadays, researchers have focused more attention towards the plant-based drug discovery for the management of many diseases which are immensely challenging to the modern healthcare system. The drugs derived from the plant secondary metabolites have a wide choice of application in the management or treatment of various diseases by modifying the structural activity relationship of isolated phytocompound parent nucleus to the desired pharmacological activity with no or very minimal side effects. With more positive conclusions from the phytocompounds based drug research in recent times, the medicinal plant's based drug discovery have become a promising scope in the field of natural products drug research for the further isolation and drug development of newer bioactive phytocompounds from the secondary metabolites of medicinal plants.

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