Journal of Pharmaceutical Research International

33(33A): 100-114, 2021; Article no.JPRI.69304
ISSN: 2456-9119
(Past name: British Journal of Pharmaceutical Research, Past ISSN: 2231-2919, NLM ID: 101631759)

An Overview on the Biosynthetic Pathways and Medicinal Values of Secondary Metabolites

Ashwini V. Armarkar[1*], Divyani S. Mahure[1], Anita R. Pounikar[1], Rani T. Bhagat[1] and Dhanashri N. Nagare[1]

[1]Datta Meghe College of Pharmacy, Datta Meghe Institute of Medical Sciences (Deemed to be University) Salod, Sawangi, Wardha-442107, India.

Authors' contributions

This work was carried out in collaboration among all authors. Author AVArmarkar wrote the final draft of the manuscript. Authors DSM and ARP wrote the first draft of the paper. Author RTB managed the literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JPRI/2021/v33i33A31777
Editor(s):
(1) Dr. Jongwha Chang, University of Texas, College of Pharmacy, USA.
Reviewers:
(1) Adaora Stellamaris Ogbuagu , Nnamdi Azikiwe University, Nigeria.
(2) Rajarajan, Bengaluru North University, India.
Complete Peer review History: http://www.sdiarticle4.com/review-history/69304

Review Article

Received 08 April 2021
Accepted 12 June 2021
Published 24 June 2021

ABSTRACT

Nature is a treasure hunt of novel molecules which are extensively used by humans for their medicinal values for millennia. Herbal medicines have emerged as life savers all over the world due to their multifunctional and diverse array of activities on the human body. Plants supply numerous bioactive molecules which are capable of treating disease conditions. Plants produce varieties of phytochemicals which are commonly recognized as primary and secondary metabolites. Secondary metabolites are inimitable resources for exploitation for pharmaceuticals, food additives e.t.c. They are often involved in the control of abiotic or biotic stress. They play distinctive roles in the defense mechanism of plants, act as insect repellant, regulate signaling pathways, and also exhibit varied range of pharmacological actions such as antibacterial, antioxidant, anticancer anti-diabetic and others. Secondary metabolites are derived from one or mixed pathways that give rise to formation of various compounds i.e., alkaloids, volatile oils, tannins, glycosides and resins etc. which have great importance in modern medicine. Isopentenyl diphosphate and Shikimic acid pathway serve as primary precursors for the synthesis some of types of secondary metabolites. The present review deals with the brief introduction, significance of secondary metabolites in the plants, biosynthetic pathways, and therapeutic importance of some commonly known secondary metabolites.

**Corresponding author: E-mail: ashwini20armarkar@gmail.com.;*

Keywords: Secondary metabolites; alkaloids; flavonoids; biosynthetic pathway; metabolism.

1. INTRODUCTION

Nature is widespread and vast in its diversity with the evolution of several billion years ago. The total number of reported plant species is 25,000, 30,000 million species of insects, and millions of prokaryotes are still in existence [1]. Plants have been vital and stunning source of medicines to mankind since ancient periods and they have provided humanity with numerous bioactive compounds. These structurally diverse bio-active compounds are capable of treating pathological conditions. With the efficiency in recent extraction methods, it has made possible for man to extract and isolate various secondary metabolites which are found in both plants and microbes. Herbal medicines have received much more attention in the recent past and are used as medicine all over the globe [2]. Half of the total populations in all the developing countries are still reliant upon herbal drugs for the cure or treatment of several diseases. The massive utilization of herbal products described in ancient books such as Vedas and by the tribal community are mainly obtained from medicinal plants and traditional herbs that are traced for their biogenetic origin [3].

2. SECONDARY METABOLITES AND THEIR ROLE IN PLANTS

Secondary metabolites are considered as the by-products of plant metabolism. Plants synthesize a diverse chemical compounds or phytochemicals known as primary or secondary metabolites. The primary metabolites are involved mainly in growth, reproduction, and photosynthesis [3]. Unlike primary metabolites, secondary metabolites are not involved in growth but found to plays major roles in plant defense mechanisms and are also utilized by a human for their medicinal value. Evidences shows that the production of secondary metabolites increases when a plant is attacked by herbivores or pathogens [4]. Numerous types of secondary metabolites are produced by plants, which have been subsequently utilized by humans for their valuable roles in diverse array of applications i.e., used as colorants, medicine and flavoring agents [5]. These secondary metabolites have been found to play major roles in plant defense mechanisms, many of them act as insect repellents and also serve as attractants for pollinators, specific odors, tastes, and impart color to plants, Fig.1. Some are involved in the control of biotic and abiotic stress, signaling, and regulation of primary metabolites [6].

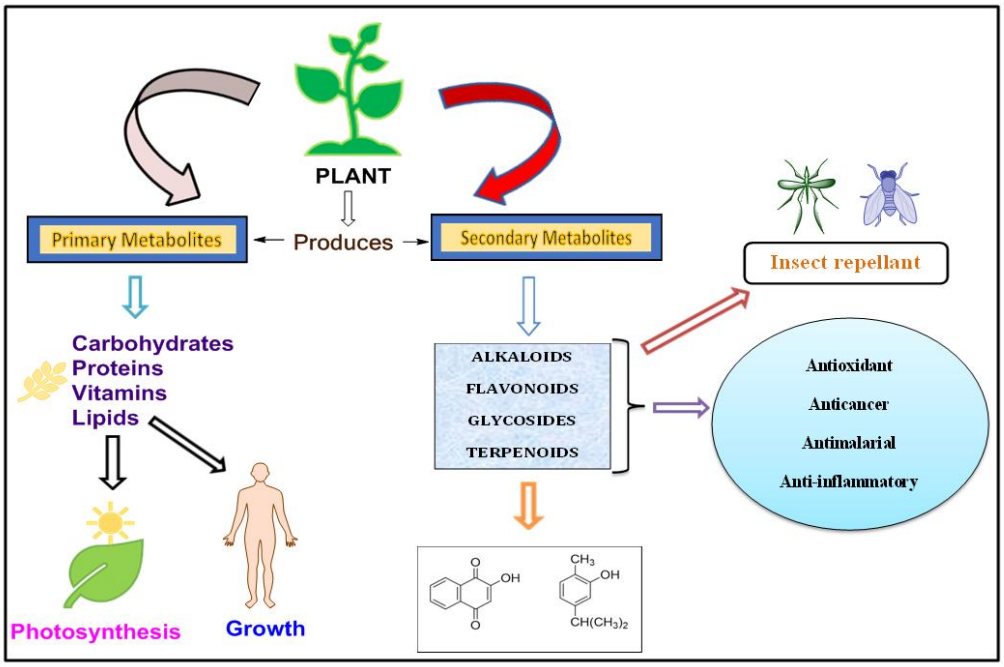


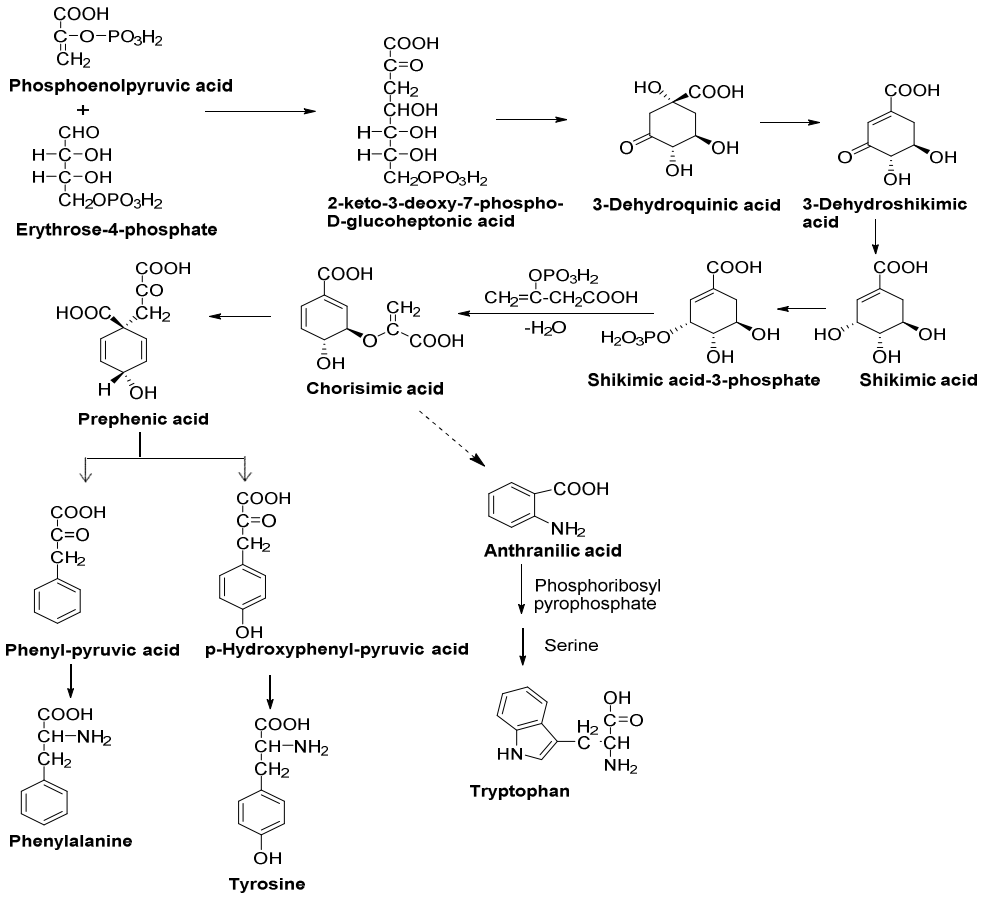
Fig. 1. Schematic representation of plant synthesizing primary and secondary metabolites and their significant role

2.1 Classification of Secondary Metabolites and their Biosynthetic Pathways

Secondary metabolites can be categorized based on their chemical nature and the biosynthetic pathway involved in their synthesis. Most of the secondary metabolites are formed from just a few building blocks; the phenylalanine/tyrosine-derived C9-unit (phenylpropanoids), the acetate C2-unit (polyketides) and the isopentenyl diphosphate C5-unit. The Shikimic acid pathway is the key precursor for the biosynthesis of various amino acids and also serves as an intermediate in the formation of flavones, coumarins, and tannins Scheme.1 [7].

2.1.1 Alkaloids

A German scientist “Meissner” coined the term alkaloids for the first time in 1819. The term “alkaloids” represents alkali-like substances which are basic compounds containing nitrogen incorporated in their heterocyclic ring. The alkaloids are widespread in various families like Liliaceae, Solanaceae, Apocynaceae, etc. In plants, alkaloids act as a reservoir of nitrogen supply [8]. They are mostly colorless except berberine which is yellow coloured and are crystalline solids except for nicotine and coniine which are liquid and volatile. Alkaloids are soluble in organic solvents but insoluble in water [9]. The first-ever isolated alkaloid was Narcotine in 1803 by a French scientist followed by isolation of Morphine from opium in the same year by Serturner which was then marketed by Merck in 1827.Alkaloids have broad spectrum of therapeutic activities like antimalarial, anticancer, stimulant and analgesic. Based on their biosynthetic pathway and heterocyclic ring system; the compounds have been classified into different classes including purine, imidazole, pyrrolizidine, pyrrolidine, indole, tropane, piperidine, quinolizidine, and isoquinoline alkaloids [8].



Scheme 1. Production of amino acids via Shikimic acid pathway

Alkaloids are classified into the following types:

a) **True alkaloids:** They originate from amino acids and contain nitrogen in their heterocyclic ring and exert physiological activity. Their examples include opium and atropine
b) **Proto alkaloids:** They are simple amines in which nitrogen is not part of their heterocyclic ring, examples include colchicine and ephedrine among others.
c) Pseudoalkaloids: They are not derived from amino acids but respond to standard qualitative tests of alkaloids, examples are conessine and caffeine.

Based on the above classification, the structures of some isolated alkaloids are shown in Fig. 2.

Table 1 summarizes various alkaloid containing crude drugs obtained from various parts of plant and their therapeutic activity.

2.1.1.1 Biosynthetic pathway of Alkaloids

The biosynthesis of different groups of alkaloids have been studied to some extent using radioactively labeled precursors. Most alkaloids are derived from decarboxylation of amino-acid precursors (i.e. tyrosine, tryptophan, ornithine, lysine, and histidine) to yield their respective amines, or from anthranilic acid or nicotinic acid [10]. The plausible biosynthetic pathways involved in the production of some important classes of the alkaloid are discussed below.

2.1.1.2 Biosynthetic pathway of Papaverine

Benzylisoquinoline alkaloid, "Papaverine" is isolated from the latex of opium poppy and used for its vasodilatory and spasmolytic activity. 3,4-dihydroxy phenyl pyruvic acid serve as starting precursor for the biosynthesis of papaverine, which is followed by the formation of Norlaudanosoline carboxylic acid that yields Norlaudanosoline (tetrahydro papaverine). The Norlaudanosoline is a key intermediate in the biosynthesis of papaverine, Scheme. 2. In the final step of the synthesis, tetrahydro papaverine is aromatized to papaverine [11].

2.1.1.3 Biosynthetic pathway of Tropane alkaloids

Ornithine acts as a primary precursor in the synthesis of tropine, a class of tropane alkaloids that are chiefly distributed in plants like Datura, belladonna acting on the central nervous system. In the first step of atropine synthesis, ornithine undergoes methylation to form N-methyl ornithine its further decarboxylation yields N-methylputrescine compound that on oxidation results into formation of 4-(methyl-1-amino) butanal, which under normal physiological conditions is thought to spontaneously rearrange into *N*-methyl-Δ^1-pyrrolinium the five-membered-ring compound shown in Scheme. 3 [12].

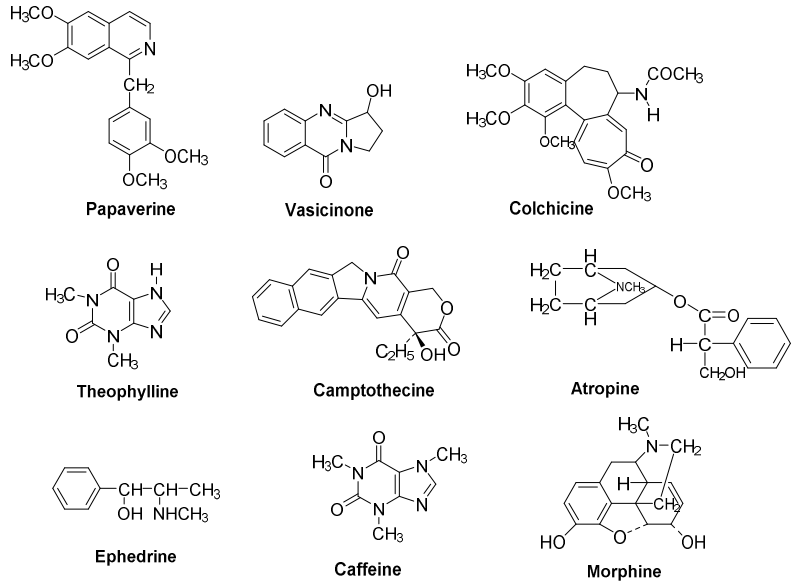


Fig. 2. Structures of isolated alkaloids

Table1. Medicinal Properties of some well- known alkaloids [7-9]

Sr. No	Crude Drug	Part of plant used	Chemical constituents isolated	Therapeutic activity Reported
1.	Rauwolfia	Roots	Reserpine, Rescinnamine	Hypotensive, tranquilizers
2.	Belladonna	Leaves	Atropine, *l*-hyoscyamine	Antispasmodic
3.	Nux-vomica	Seeds	Strychnine, brucine	CNS stimulant
4.	Opium	Latex	Morphine, codeine, papaverine	Narcotic analgesic
5.	Vinca	Entire plant	Vincristine, vinblastine	Anticancer
6.	Cinchona	Root or stem bark	Quinine, quinidine	Antimalarial, Bitter tonic
7.	Kurchi	Bark	Conessine, isoconessien	Antiamoebic
8.	Datura	Leaves	Scopolamine,hyoscyamine	Anticholinergic
9.	Vasaka	Leaves	Vasicine and vasicinone	Antitussives and expectorant
10.	Coffee	Ripe seeds	Caffeine	Stimulant
11.	Ashwangdha	Roots	Withanolides, withaferine	Sedative
12.	Ephedra	Stems	Ephedrine, pseudoephedrine	Antiasthmatic
13.	Berberis	Roots and rhizomes	Berberine	Astringent
14.	Hyoscyamus	Flowering top and dried leaves	Hyoscine	Antispasmodic
15.	Lobelia	Dried leaves and tops	Lobelanidine, lobeline	Respiratory stimulant
16.	Colchicum	Corm and seeds	Colchicine	Induction of polyploidy and antirheumatic
17.	Ipecacuanha	Roots and rhizomes	Emetine, cephalin	Antiamoebic, emetic
18.	Aconite	Roots	Aconitine	Antirheumatic
19.	Duboisia	Leavs	Scopolamine	Anticholinergic
20.	Pilocarpus	Leaves	Pilocarpine	Anticholinergic
21.	Tea	Leaves	Theophylline, theobromine	Diuretic, CNS stimulant
22.	Phyostigma	Seeds	Physostigmine	Hypotensive, In glaucoma
23.	Coca	Leaves	Cocaine	Local anesthetic

2.1.1.4 Biosynthetic pathway of l-hyoscyamine

L-hyoscyamine belongs to a class of tropane alkaloids which exerts anticholinergic and diuretic effect. The plausible biosynthetic pathway involved in the synthesis of l-hyoscyamine uses phenylalanine as starting precursor that converts phenyl pyruvic acid into tropic acid followed by the addition of tropine which is biosynthesized from ornithine, that leads to the formation of l-hyoscyamine as shown in Scheme. 4 [7].

2.1.2 Flavonoids

The word flavonoid was derived from Latin word 'flavus' which means yellow. Flavonoids are a class of low molecular weight polyphenolic compounds having 15 carbon atoms present in the form of a C6-C3-C6 skeleton. Flavonoids exist in a free-state or glycoside form in plants [13]. They are mostly yellow-colored substances except anthocyanins which are blue, red or purple in color. They are widely distributed in seeds, vegetable fruits, herbs, spices, stems, and flowers. Flavone, flavone, flavan-3-ols, isoflavones, anthocyanidins and flavanones, naringin are some of the commonly known flavonoids which are produced by plants and are abundant in families of Umbelliferae, Rutaceae, Leguminosae, and Compositae [14]. Flavonoids are associated with a broad spectrum of health-promoting effects and play crucial roles in

nutraceutical, pharmaceutical, medicinal and cosmetic applications [15]. They show a wide range of biological activities like antioxidant, antimicrobial, anticancer, etc. The natural sources of flavonoids include fruits, vegetables, legumes, etc. In plants, flavonoids play major roles in protection against different abiotic and biotic stresses. They are also involved in the pigment or aroma of flowers and attract pollinators. The structures of some important classes of flavonoids can be seen below Fig. 3.

The flavonoids can be classified according to their dietary sources, from which they are obtained; chemical constituents isolated and therapeutic activity reported which is illustrated in Table 2.

2.1.2.1 Biosynthetic pathway of Flavonoids

Flavonoids are produced in the plant by the shikimic acid pathway and acetate pathway. The first step in the biosynthesis of flavonoids involves condensation of two molecules of acetate phenyl propanoid precursor along with 3 malonyl coenzyme-A units to derive polyketide as an intermediate which results in the formation of chalcone,Scheme.5 The chalcone acts as a key intermediate in the synthesis of the majority of flavonoids like flavones, flavanones, Isoflavone, etc. in the plant kingdom [13].

Table 2. Flavonoids, chemical constituents, therapeutic potential and their dietary sources

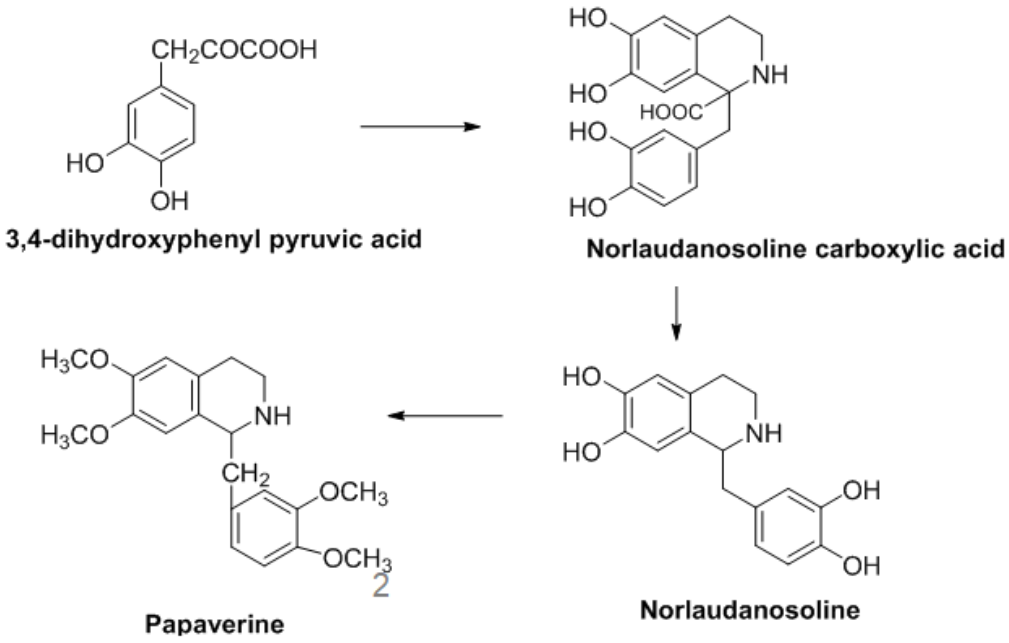
Sr. No	Class	Chemical Constituents	Dietary sources	Pharmacological activity	References
1.	Flavones	Luteolin	Broccoli, olive oil green pepper, rosemary, thyme, dandelion, perilla, chamomile tea, carrots, peppermint,	Anticancer and antioxidant	[16]
2.	Flavonols	Rutin	Apple, citrus fruits, Green tea, grape seeds	Antioxidant and anti-inflammatory	[17]
3.	Chalcone	Catharine	Safflower		[15]
4.	Flavones	Apigenin	Milk, chocolate, commercial, reduced fat	Anticancer, antibacterial and antioxidant	[18]
5.	Flavanones	Hesperedin, Naringenin	Oranges, grapes, lemons	Anti-inflammatory and analgesic	[19]
6.	Isoflavone	Genistein	Psoralea, beans, fats, oils, beef, red clover, soybeans, kudzu	Antidiabetic and anticancer	[20]
7.	Coumarin	Scopoletin	Coffee, Vinegar	Antidepressant and	[21]
8.	Flavan-3-ols	Epicatechin	Chocolate, commercial reduced fat, milk	Antioxidant, antidiabetic	[22]
9.	Anthocyanidin	Pelargonidin, Cyanidin,	Grapes, Blueberry	Antioxidant, neuroprotective and anticancer	[23,24]
10.	Isoflavone	Daidzein	Soybeans, tofu	Anticancer, cardioprotective	[25]
11.	Flavonols	Kaempferol	Grapes,apples, potatoes, onions, tomatoes, green tea, cucumbers, blackberries, raspberries, spinach	Antioxidant, antimicrobial, anticancer, cardioprotective,	[26]

2.1.3 Terpenoids

Terpenoids comprises of a large class of natural products with around 64000 known compounds. The term “terpene” originated from the German word turpentine. They are usually hydrocarbon molecules and their basic building block is the isoprene unit. Terpenoids are formed by oxidation or rearrangement of their carbon skeleton. Terpenoids are a prominent class of secondary metabolites produced by plants, fungi, and animals and are mostly volatile in nature, responsible for aroma of various compounds. They are chiefly distributed in Umbelliferae, Rutaceae, Zingiberaceae, and Labiatae families. They display various pharmacological actions including carminative, antiallergic, antihyperglycemic, anti-inflammatory, etc. They also play a diverseroles in plants like phytol and carotenoids function as photosynthetic pigments [27] Fig. 4 represents the structures of some commonly isolated terpenoids from natural sources [7].

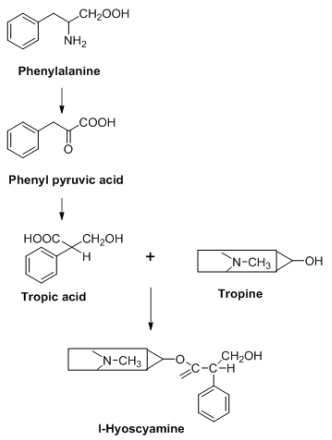
Terpenoids can be classified on the basis of isoprene unit and number of carbon atoms present in their structure as shown Table 3.

The list of terpenoid obtained from natural drugs, their chemical constituents and uses are briefly summarized in Table 4.



Scheme 2. Biosynthesis of Papaverine

Scheme 3. Biosynthetic pathway of Tropine



Scheme 4. Biosynthetic pathway of l-hyoscyamine

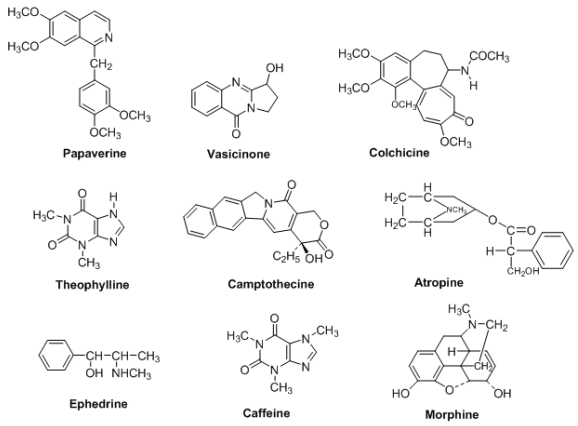
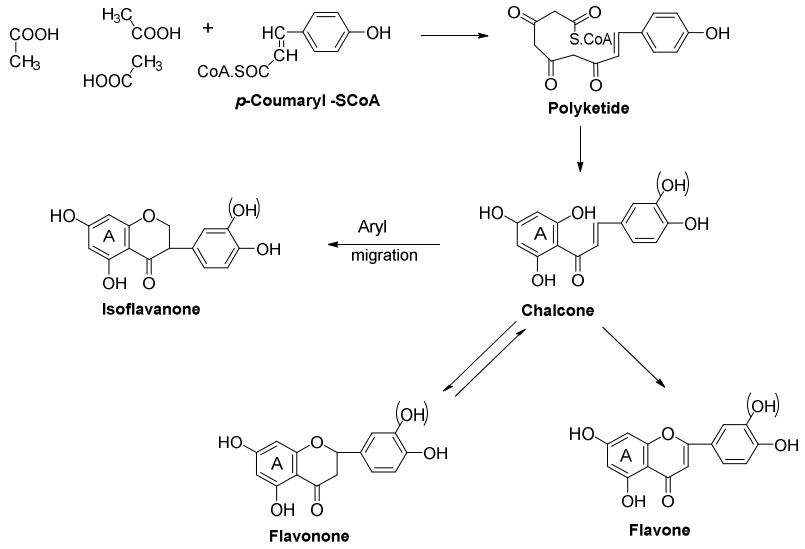


Fig. 3. Structures of the different class of flavonoids



Scheme. 5. Biosynthetic pathway of Flavonoids

Table 3. Classification of terpenoids based on isoprene unit [9]

Sr.No	Class of terpenoid	No. of carbon atoms	No. of isoprene unit	General formula
1	Homoterpenoids	5	1	C_5H_8
2	Monoterpenoids	10	2	$C_{10}H_{16}$
3	Sesqueterpenoids	15	3	$C_{15}H_{24}$
4	Diterpenes	20	4	$C_{20}H_{32}$
5	Sesterpenes	25	5	$C_{25}H_{40}$
6	Triterpenoids	30	6	$C_{30}H_{48}$
7	Tetraterpenoids	40	8	$C_{40}H_{64}$
8	Polyterpenoids	>40	>8	$(C_5H_8)n$

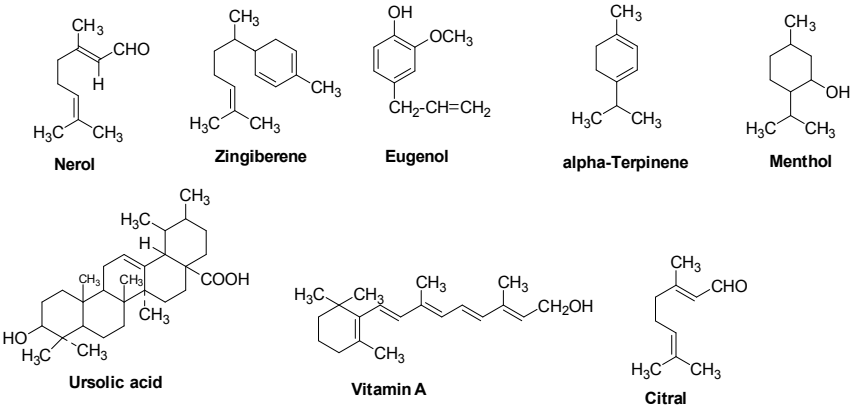
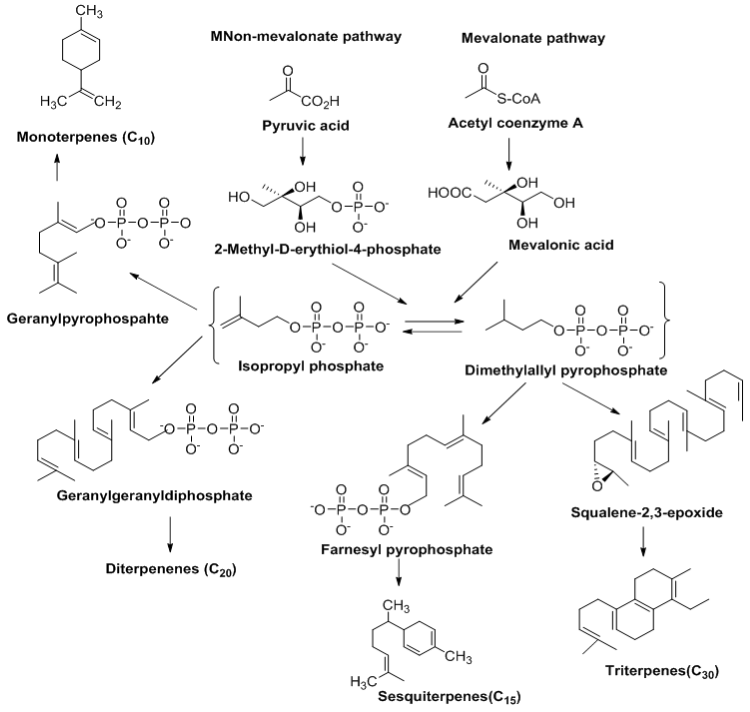


Fig. 4. Structures of some commonly known terpenoids



Scheme 6. Biosynthesis of Terpenoids

Table 4. Crude drugs containing terpenoids and their application in medicine [28,29]

Sr.No	Natural product	Class of terpene	Chemical constituent	Application in medicine
1.	Camphor oil	Monoterpenes	Camphor, d-pinene, saffrole	Rubefacient, counter-irritant
2.	Lemongrass oil	Monoterpenes	Citral, citronella	In perfumery, a flavoring agent
3.	Cumin	Monoterpenoids	Cuminaldehyde, phellandrene	Carminative, dyspepsia
4.	Orange peel	Monoterpenes	Hesperidin, Vit. C, citral	Stomachic, flavoring, and carminative
5.	Caraway	Monoterpenes	Carvone, carvacrol	Stimulant, flavoring agent
6.	Fennel	Monoterpenes	Fenchone, anethole	Stimulant, flavor & expectorant
7.	Coriander	Monoterpenes	Coriandrol	Carminative, stimulant
8.	Garlic	Monoterpenes	Allin, Allicin	Disinfectant, condiment, expectorant, rubefacient
9.	Cinnamon	Monoterpenes	Eugenol, cumin aldehyde	Antiseptic, carminative
10.	Musk	Monoterpenes	Musckone, cholestrin	Perfumery
11.	Black pepper	Monoterpenes	Piperine, piperidine	Aromatic, bioenhancer, carminative
12.	Taxus	Diterpenes	Taxol, deacetyl baccatin	Antitumour
13.	Coleus	Diterpenes	Forskolin	Cardiostimulant, Vasodilator
14.	Annatto	Tetraterpenes	Bixin	Hepatoprotective, coloring agent
15.	Saffron	Polyterpenes	Crocin, picrococin	Flavour, antispasmodic
16.	Feverfew	Sesquiterpenes	Chrysanthemin A & B, patholide	In the treatment of migraine, fever, and arthritis
17.	Artemisia	Sesqueterpenes	Artemisin, cineole	Anthelminitic
18.	Clove	Sesqueterpenes	Eugenol, Eugenia	Dental analgesic, carminative
19.	Acorus	Sesqueterpenes	Acorine, asarone	Vermifuge, carminative
20.	Sandalwood oil	Sesqueterpenes	α,β-santalol, santene	In dysuria, perfumery
21.	Valerian	Sesqueterpenes	Valerine, borneol	In cough, antispasmodic, carminative
22.	Saussurea	Sesqueterpenes	Resinoids, inulin	In asthma, disinfectant
23.	Davana oil	Sesqueterpenes	Davanone,non-davanone	Perfume, flavour
24.	Ambergis	Triterpenes	Amberin. Coprostemone	Perfumery

2.1.3.1 Biosynthetic pathway of Terpenoids

Terpenoids are biosynthesized from the precursors isopentenyl pyrophosphate (IPP) and dimethylallyl pyrophosphate (DMAPP).They undergo multiple steps of rearrangement, and cyclization reactions [29]. Two main and distinct biosynthetic pathways involved in the production of these universal precursors have been reported, the classical mevalonate (MVA) pathway and the most recently characterized 1-deoxy-D-xylulose- 5-phosphate (DXP) pathway also known as 2C-methyl-D-erythritol-4-phosphate (MEP) pathway. The MEV pathway occurs in eukaryotes, cyanobacteria whereas the MVP pathway is associated with the cytosol and mitochondria of plants. The MEP pathway converts pyruvate (precursor) and glyceraldehyde-3-phosphate, to IPP and DMAPP through eight enzymatic reactions, while the

MVA pathway undergoes seven enzymatic reactions to convert the precursor acetyl-CoA to IPP and DMAPP, Scheme. 6. In the biosynthetic pathway of terpenoids, there is head-to-tail addition of active isoprene unit C-5 i.e., isopentenyl diphosphate (IPP) to its isomer dimethylallyl diphosphate (DMAPP) resulting in the synthesis of geranyl diphosphate (GPP, C10). Further, condensation of enzyme-bound geranyl diphosphate with additional IPP units forms sequentially larger prenyl diphosphates e.g. farnesyl diphosphate (FPP, C15), Geranylgeranyl pyrophosphate synthase (GGPPS) and farnesyl geranyl pyrophosphate synthase (FGPPS) are responsible for the formation of GGPP (C20) and FGPP (C25). The starting material of GPP, FPP, GGPP, and FGPP might undergo cyclization and/or rearranged by different terpene synthase enzymes to produce the different classes of terpenoids [30].

2.1.4 Glycosides

Glycosides are the most abundant secondary metabolites found in plants. They are derived from the plant through post modification of secondary metabolites which is accelerated by plant enzymes, glycosyltransferases followed by oxidation, acylation, and degradation. These are organic compounds that on acid or enzymatic hydrolysis yield sugar moiety (glycone) and aglycone (non-sugar moiety) also called genin [31]. They are widely distributed in families of the plants including Liliaceae, Leguminosae, and Polygonaceae. They exert wide range of therapeutic actions, and are used as a laxative, cardiotonic, bitter tonic, and antidiabetics.The glycone part of a glycoside is water-soluble whereas the genin or aglycone part is water-insoluble. The pharmacological actions of glycosides are attributed to aglycone moiety while saccharide influences water solubility, pharmacokinetics, and pharmacodynamics properties. Glycosides play prominent action in plants converting toxic material to non-toxic, also act as a source of energy, regulation of growth [32].

2.1.4.1 Classification of Glycosides

Glycosides are categorized based on the types of linkage present across glycone and aglycone part such as O-glycosides, C-glycosides, N-glycosides, and S-glycosides. The C-glycoside linkage is found in anthraquinone glycosides such as aloe, cascara whereas O-glycoside linkage is predominately present in plants like Senna, rhubarb, etc. The other two types of linkages present in plants is S-glycoside which is present in black mustard.

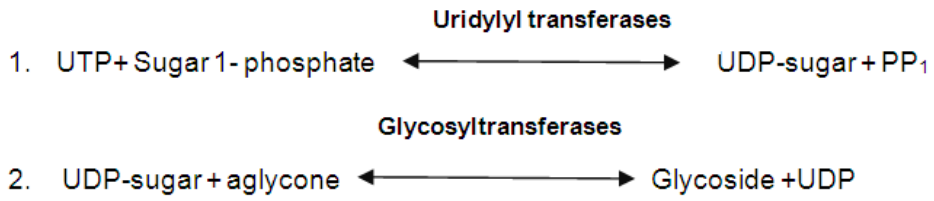
Glycosides are also classified on the basis of sugar part attached to glycone moiety. The sugars present are mostly rhamnose, fructose, and glucose and are termed as rhamnoside, fructoside, and glucoside.

Another approach for the classification of glycosides is based upon the chemical nature of genin or aglycone moiety which is depicted in the Table 5.

2.1.4.2 Biosynthetic pathway of Glycosides

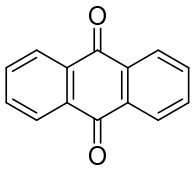
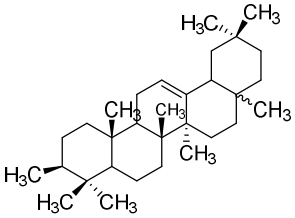
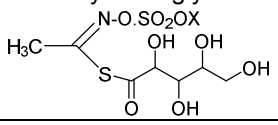
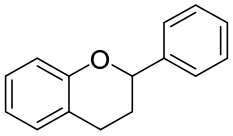
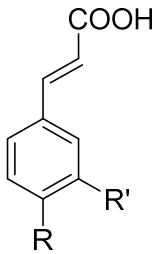
The principal route of glycoside formation in plants occurs via two steps. In the first step of glycoside synthesis uridylyl group is transferred from uridine triphosphate to sugar-1-phosphate under the presence of enzyme uridylyl transferases followed by subsequent reaction of UDP i.e uridine triphosphate with aglycone moiety and the enzyme catalyzing reaction is known as glycosyltransferases which finally results in the formation of glycosides, Scheme. 7 [28].

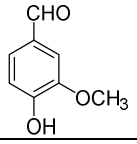
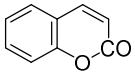
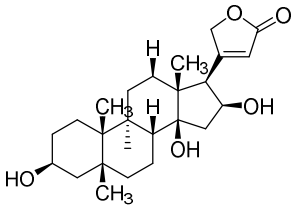
The sugar attached in glycosides is mainly fructose, rhamnose or fucose, and digitoxose in cardiac glycosides. Phenylalanine an amino acid acts as key precursor in synthesis or formation of different class of glycosides i.e., (Coumarin, Phenolic, and aldehyde glycosides) Scheme.8 [8].

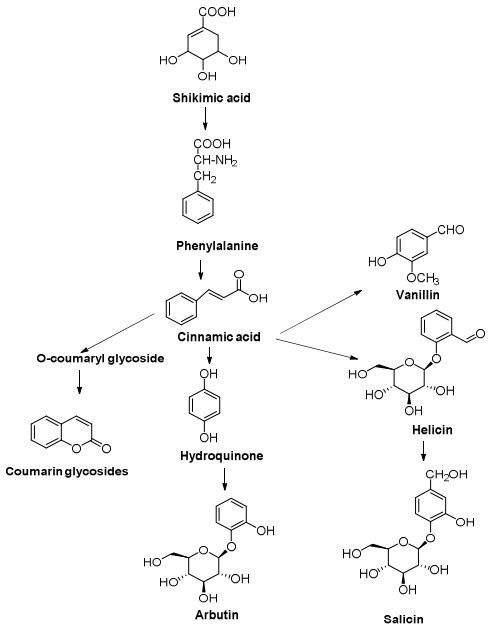


Scheme 7. Reaction steps for the formation of glycoside

Table 5. Classification of glycosides based on the chemical nature and therapeutic uses of aglycone moiety [8,33]

Sr. No	Nature of aglycone moiety present	Example of crude drugs	Chemical constituents	Therapeutic uses
1.	Anthraquinone glycosides 	Aloe	Alo-emodin, barbaloin	Purgative, antibacterial
		Rhubarb	Rhein, aloe-emodin	Purgative
		Cascara	Cascarosides A,B,C ,D, E & F	Purgative
		Senna	Sennosides A & B	Laxative
		Hypericum	Hyperforin, hypercin	Anti-depressant
		Cochineal	Carminic acid	Colouring agent
2.	Saponin glycosides 	Liquorice	Glycyrrhizin	Expectorant
		Ginseng	Ginsenosides,panaxosides	Adaptogen
		Gokhru	Gitogen,diosgenin	Diuretic
		Momordica	Charantin,Momordicin	Hypoglycemic
		Brahmi	Bacosides A & B	Nervine tonic
		Centella asiatica	Asiaticoside, Asiaticoside A	Adaptogen, antidepressive
		Milk vetch	Isoastragalosides I and II, cycloartanes	Antiviral hepatoprotective & adaptogenic
		Senega	Senegin, polygallic acid	Stimulant expectorant
		Dioscorea	Diosgenin,smilagenin	Synthesis of corticosteroids, rheumatic arthritis
3.	Isothiocyanate glycosides 	Black mustard	Sinigrin	Emetic, counter-irritant
4.	Flavonoid glycosides 	Gingko	Gingkolide A,B, C & ginkgetin	In asthma, vascular disorders
		Buck wheat	Rutin	Retinal hemorrhages
		Milk thistle	Silymarin	Hepatoprotective
		Knotweed herb	Quercetin, hyperoside	Diuretic, anti-rheumatic
		Citrus fruits	Hesperidin	In capillary fragility
5.	Phenol glycosides 	Melissa Leaf	Chlorogenic and rosmarinic acid.	Antispasmodic, anti-inflammatory
		Bearberry	Arbutin, ursone	Diuretic and in cystitis
		Meadowsweet	Monotropitin	Anti-inflammatory Anti-microbial Anti-rheumatic
		Populi folium	Salicin, populin	Anti-microbial Anti-rheumatic Antipyretic
		Willow Bark	Salicortin, tremulacin,	Antipyretic effect Anti-rheumatic
6.	Aldehyde glycosides	Vanilla	Vanillin, glucovanillic acid	Perfumery and flavoring agent

Sr. No	Nature of aglycone moiety present	Example of crude drugs	Chemical constituents	Therapeutic uses
				
7.	Coumarin glycosides 	Angelica Root	Angelicin, bergapten	Used in dyspeptic, spasms
		Horse-Chestnut Bark	Esculin, scopoletin	Antioxidant
		Tonka bean	Coumarin	Flavoring agent
		Ammi	Xanthotoxin	In the treatment of vertigo
		Cantharides	Cantharidin	Counter-irritant, rubefacient
		Psoralea	Psoralen, corylifolin	In the treatment of leucoderma
		Visnaga	Khellin, visnagin	Coronary vasodilator
8.	Cardiac glycosides 	Digitalis	Digitoxin, Purpurea glycoside	Cardiotonic
		Indian squill	Scillaren A & B	Cardiotonic
		Ouabain	Ouabagenin	Carditonic
		Thevetia	Theventin, Thevenerin	Cathartic, Emetic
		Strophanthus	K-strophanthoside,	Cardiotonic
10.	Steroidal-Glycoalkaloids	Solanum	Solasodine	Synthesis of steroidal Drugs



Scheme. 8. Biosynthetic route for the formation of Coumarin, aldehyde, and phenolic glycosides

3. CONCLUSION

Nature is a remarkable source of wonderful complex molecules which has been exploited by humans to alleviate disease or aliments. Plants are a proven source for producing medicinally active compounds known as primary and secondary metabolites. Secondary plant metabolites are 'bioactive compounds showing pharmacological or toxicological effects in man and animals. Secondary metabolites synthesize numerous phyto compounds which have diverse range of therapeutic activities. Several life-saving drugs manufactured and supplied by pharmaceutical companies are semi-synthetic derivatives of natural products which serve as valuable drug entities. They are considered as products of 'biochemical sidetracks' in the plant cells that help in the growth and development of plants, with no essential role in the maintenance of life processes. Several of them are found to play role in protection, attraction, or signaling. Numerous crude drugs such as cinchona, taxol, and many more have received high market value since the last decade for their ability to treat several infectious and non-infectious diseases like malaria, cancer, diabetes and leprosy, etc. Researchers need to focus more on recent extraction techniques which will aid in the faster extraction, isolation and genetic bioengineering methods to improve yield of these vital secondary metabolites. More herbal plants need to be explored to discover their hidden therapeutic potentialities. The cure to the ingress of new and several deadly diseases in the human population could also be found in plants- we never know. Therefore, the fundamental biogenetic pathway for the formation of various secondary metabolites using radioactive labeled isotope tracer studies should be investigated.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

ACKNOWLEDGEMENT

The author wish to thank the Management of Datta Meghe College of Pharmacy, Salod (Hirapur), Wardha (MH) - 442107, India for providing opportunity for review work.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Verpoorte R. Exploration of nature's chemodiversity: the role of secondary metabolites as leads in drug development. Drug Discov Today. 1998;3(5):232–8.
2. Ahmed E, Arshad M, Khan MZ, Amjad MS, Sadaf HM, Riaz I, et al. Secondary metabolites and their multidimensional prospective in plant life. J Pharmacogn Phytochem. 2017;6:205–14.
3. Jain C, Khatana S, Vijayvergia R. Bioactivity of secondary metabolites of various plants: a review. Int J Pharm Sci Res. 2019;10(2):494–8.
4. Bennett RN, Wallsgrove RM. Secondary metabolites in plant defence mechanisms. New Phytol. 1994;127(4):617–33.
5. Pagare S, Bhatia M, Tripathi N, Pagare S, Bansal YK. Secondary metabolites of plants and their role: Overview. Curr Trends Biotechnol Pharm. 2015;9(3):293–304.
6. Devika R, Koilpillai J. An overview on plant secondary metabolites: Its medicinal importance. J Pharm Res. 2012;5(2):984–6.
7. Kokate CK, Purohit AP, Gokhale SB. Pharmacognosy book. 41st ed. Pune Nirali Publ; 2008;5.19-5.21.
8. Shah BN. Textbook of pharmacognosy and phytochemistry.Ist ed. Elsevier India;New Delhi;2009:145-149 & 258.
9. Kaur R, Arora S. Alkaloids-important therapeutic secondary metabolites of plant origin. J Crit Rev. 2015;2(3):1–8.
10. De Luca V, Laflamme P. The expanding universe of alkaloid biosynthesis. Curr Opin Plant Biol. 2001;4(3):225–33.
11. Han X, Lamshöft M, Grobe N, Ren X, Fist AJ, Kutchan TM, Spiteller M, Zenk MH, et al. The biosynthesis of papaverine proceeds via (S)-reticuline. Phytochemistry. 2010;71(11-12):1305-12.
12. Kohnen-Johannsen KL, Kayser O. Tropane alkaloids: chemistry, pharmacology, biosynthesis and production. Molecules.2019;24(4):796.
13. Romano B, Pagano E, Montanaro V, Fortunato AL, Milic N, Borrelli F. Novel insights into the pharmacology of

flavonoids. Phyther Res. 2013;27(11):1588–96.
14. Tapas AR, Sakarkar DM, Kakde RB. Flavonoids as nutraceuticals: a review. Trop J Pharm Res. 2008;7(3):1089–99.
15. Kesarkar S, Bhandage A, Deshmukh S, Shevkar K, Abhyankar M. Flavonoids: an overview. J Pharm Res. 2009;2(6):1148–54.
16. Shimoi K, Okada H, Furugori M, Goda T, Takase S, Suzuki M, et al. Intestinal absorption of luteolin and luteolin 7-O-β-glucoside in rats and humans. FEBS Lett. 1998;438(3):220–4.
17. Atanassova M, Bagdassarian V. Rutin content in plant products. J Univ Chem Technol Metall. 2009;44(2):201–3.
18. Shukla S, Gupta S. Apigenin: a promising molecule for cancer prevention. Pharm Res. 2010;27(6):962–78.
19. Khan MT, Orhan I, Şenol FS, Kartal MU, Şener B, Dvorská M, Šmejkal K, Šlapetová T, et al. Cholinesterase inhibitory activities of some flavonoid derivatives and chosen xanthone and their molecular docking studies. Chemico-Biological Interactions. 2009;181(3):383-9.
20. Thompson LU, Boucher BA, Liu Z, Cotterchio M, Kreiger N. Phytoestrogen content of foods consumed in Canada, including isoflavones, lignans, and coumestan. Nutr Cancer. 2006;54(2):184–201.
21. Gálvez MC, Barroso CG, Pérez-Bustamante JA. Analysis of polyphenolic compounds of different vinegar samples. Zeitschrift für Leb und Forsch. 1994;199(1):29–31.
22. Arts ICW, van de Putte B, Hollman PCH. Catechin contents of foods commonly consumed in The Netherlands. 1. Fruits, vegetables, staple foods, and processed foods. J Agric Food Chem. 2000;48(5):1746–51.
23. Truong V-D, Deighton N, Thompson RT, McFeeters RF, Dean LO, Pecota K V, et al. Characterization of anthocyanins and anthocyanidins in purple-fleshed sweetpotatoes by HPLC-DAD/ESI-MS/MS. J Agric Food Chem. 2010;58(1):404–10.
24. Jaiswal YS, Guan Y, Moon KH, Williams LL. Anthocyanins: Natural Sources and Traditional Therapeutic Uses. InFlavonoids-A Coloring Model for Cheering up Life. Intech Open; 2019.
25. Zhang Y, Wang G-J, Song TT, Murphy PA, Hendrich S. Urinary disposition of the soybean isoflavones daidzein, genistein and glycitein differs among humans with moderate fecal isoflavone degradation activity. J Nutr. 1999;129(5):957–62.
26. M Calderon-Montano J, Burgos-Morón E, Pérez-Guerrero C, López-Lázaro,et al. M. A review on the dietary flavonoid kaempferol. Mini Rev Med Chem. 2011;11(4):298-344.
27. Abdallah II, Quax WJ. A Glimpse into the Biosynthesis of Terpenoids. KnE Life Sci. 2017;81–98.
28. Ali M. Textbook of pharmacognosy. CBS Publishers & Distributors; Delhi. 2007;1:255.
29. Jaeger R, Cuny E. Terpenoids with special pharmacological significance: a review. Nat Prod Commun. 2016;11(9):1934578X1601100946.
30. Eisenreich W, Rohdich F, Bacher A. Deoxyxylulose phosphate pathway to terpenoids. Trends Plant Sci. 2001;6(2):78–84.
31. Bartnik M, Facey PC. Glycosides. In: Pharmacognosy. Elsevier; 2017. p. 101–61.
32. Croteau R, Kutchan TM, Lewis NG. Natural products (secondary metabolites). Biochem Mol Biol plants. 2000;24:1250–319.
33. Rangari VD. Pharmacognosy & phytochemistry. 4th ed;Career publications;Nashik. 2019:221-222.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/69304