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Review

Ethnomedicinal, pharmacological properties and chemistry of some medicinal plants of Boraginaceae in India

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Different medicinal plants and their medicinal values are widely used for various ailments throughout the world. Various chemical constituents isolated and characterized from Boraginaceous plant species are described. These included pyrrolizidine alkaloids, naphthaquinones, flavonoids, terpenoids, triterpenoids and phenols. Some important biological and pharmacological activities reported from various parts of plant species and from these plants, the isolated constituents demonstrated antimicrobial, antitumour, antiviral, anti-inflammatory, cardiotonic, contraceptive, antiplatelet, wound healing and prostaglandin inhibitory. Some experiments on transformation have been done in Boraginaceous plants. The review article will therefore, give a critical overview of different phytochemicals and various medicinal properties belonging mainly to family Boraginaceae.

Key words: Boraginaceae, pyrrolizidine alkaloids, naphthaquinones, flavonoids, terpenoids, triterpenoids, phenols.

INTRODUCTION

The study of plant medicines was first described precisely in the basic literature *Charak Samhita* of Ayurvedic medicine in India. Charak, the author of *C. Samhita* flourished in the 8th century B.C.

By the 16th century, a fundamental turning point reached in the history of medicinal plants with the advent of the Swiss-German physician Paracelsus (1439 - 1541), who gave the concept of what is now defined as 'active principles' of plants.

'Western' medicine has largely confined itself to the isolation or synthesis of single active ingredient for the treatment of specific disease (Bland, 1983). For a long time, plants have been the almost exclusive therapy available to humans. With the development of medicinal chemistry in the early 19th century, plants were also found source of substances to be developed as drugs. Nowadays, in spite of the tremendous development of synthetic pharmaceutical chemistry and microbial fermentation, 25% of the prescribed medicines in industrialized countries are of plant origin and some 120 plant derived compounds are used in modern therapy.

In spite of these rapid developments in scientific technology and the better understanding of the chemistry of natural products, it is fair to say that of the 6000 or so plants used in different traditional systems of medicine, only a few hundred have so far been examined in depth for their chemical constituents and physiological activity. The plant kingdom thus represents an enormous reservoir of pharmacologically valuable molecules to be discovered (Potterate et al., 1995; Hamburger et al., 1991; Anon, 1979, 1985). The evaluation of crude drug, which eventually notice the commercial market, is of considerable importance. Physical, sensory and biomedical characteristics of drugs formed the main features of the study in earlier age than since the latter half of the 19th century, the emphasis was laid on the crude drugs, their substitutes, fluorescence analysis, preliminary phytochemical tests and adulterants, for the reason that of the commercial practices, such compiled descriptions are given in the British Pharmacopoeia, British Pharmacopoeia Commission and other pharmacopoeias. There are also books dealing uncritically with Indian medicinal plants and suggesting miracle cures, such as in particular

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a book by Chopra et al. with the title “Glossary of Indian Medicinal Plants” (Chopra et al., 1956) . In this book, great number of Asiatic, especially the Indian plants, unknown in western countries are cited. These plants may cause intoxication by improper use. In addition, in various regions of India, different plants are marketed under the same drug name leading to confusion with fatal consequences as illustrated by several examples reported in medicinal literature (Anonymous, 1955; Kirtikar and Basu, 1967; Anonymous, 1976; Satyavati et al., 1976; Farnsworth et al., 1977; Anonymous, 1985; Jain and Defilipps, 1991; Chevallier, 1996; Trivedi, 2005). Some plants species of Boraginaceae provide the source of naphthaquinones - the red pigments. Shikonin has been known since ancient times as a dye used for silk and food products. At the same time, shikonin is recognized as a remedy showing wide range of effects. It possesses antibacterial, antifungal, anti-inflammatory and wound healing properties. The antiallergic, antipyretic and anti-neoplastic effects of shikonin and its derivatives have been demonstrated (Terada et al., 1990).

In this review, only those plants will be discussed whose phytochemical constituents have been determined unequivocally.

Chemistry of Boraginaceous

plants *Arnebia* species

1. Chemically, quinones are compounds with either a 1, 4 -diketocyclohexa 2, 5 -dienoid or 1, 2 -diketocyclohexa- 3, 5- dienoid moiety. In previous case they are named *p*-quinones and in later *o*-quinones, more naturally occurring quinones are benzo and naphthaquinones. In both cases however, the quinoid moiety consists of an alternating system of single and double bonds. This system does not occur in *m*-quinones, they are unstable (Bentley and Campbell, 1974; Leistner, 1981).

The naphthaquinones of higher plants are biosynthesized through the following routes: (a) *o*-Succinyl benzoic acid pathway (b), *p*-Hydroxybenzoic acid-mevalonic acid pathway (e.g., shikonin) (c), Homogentisic acid-mevalonic acid pathway, (d) Acetic acid - mevalonic acid pathway and (e) Mevalonic acid pathway (Ramawat and Merillon, 2003).

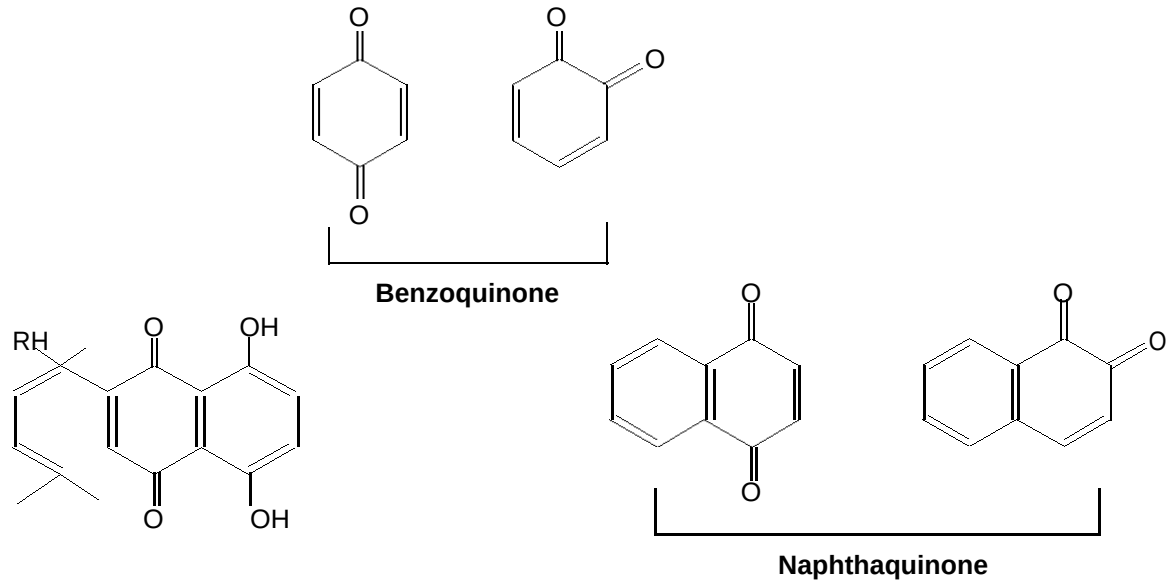
A vast majority of naphthalene derivatives found in nature are quinones and others are mainly related naphthols or naphthyl ethers. The distribution of naphthaquinones is sporadic. Nearly half of them occur in higher plants, scattered through about 20 families. They have been found in leaves, flowers, wood, root bark and fruits (Thompson, 1971). Alkannin, a naphthaquinone isolated originally from *Alkanna tinctoria* (Brockmann, 1935) and also from *Arnebia hispidissima* (Jain et al., 1999). The petroleum ether extract of roots later, yielded a red oil, mp 148 - 149°C, which after purification through copper salt yielded a pigment as glittering red solid resembling alkannin and thus identified as shikonin (Jain and Mathur, 1965), except optical rotation, it was therefore alkannin. Shikonin is reported to be extracted from *Arnebia euchroma* and *Aralia tibetana* (Fu et al., 1984; Romanova et al., 1968). The shikonin content in dried roots of *A. euchroma* was reported to be 2.47% (Zhang et al., 1989) and in *A. tibetana*, it was 4.16% (Tareeva et al., 1970).

Hexane soluble fraction of *Anthemis nobilis* roots yielded the four crystalline naphthaquinones and identified on the basis of spectral data and chemical analysis viz., arnebin- 1 [alkannin, β, β-dimethylacrylate, $C_{21}H_{22}O_6$, mp 116 - 117°C, yield 0.375%], arnebin- 2 (β ,β-dimethyl acryl ester of hydroxyalkannin, $C_{21}H_{24}O_7$, mp 92 - 94°C, yield - 0.047%), arnebin- 3 (alkannin monoace-tate, $C_{18}H_{18}O_6$, mp 104 - 105°C, yield - 0.075%) and arnebin- 4 (alkannin, $C_{16}H_{16}O_5$, mp 146°C) (Shukla et al., 1969). Shukla et al. (1969) further isolated and characterised three naphthaquinones from roots of *A. nobilis*. Arnebin- 5 [5, 8 -dihydroxy- 2 -(4´ -hydroxy- 4´ -methylpentyl) 1, 4 -naphthaquinone] $C_{16}H_{18}O_5$, mp 111 - 112°C, arnebin- 6 [5, 8 -dihydroxy- 2 -(1 - acetoxy- 4´ -hydroxy - 4 -methylpentyl)- 1, 4 -naphthaquinone] $C_{18}H_{20}O_7$, mp 88 - 90°C and arnebin- 7 [5, 8 -dihydroxy- 2 -(4´ -methylpentyl- 31 - enyl)-1, 4 -naphthaquinone], $C_{16}H_{16}O_4$, mp 95°C (Shukla et al., 1971, 1973). *A. euchroma* and *Arnebia guttata* on crude drug preparation and after chemical examination gave acetyl shikonin and four other related compounds (Lin, 1980; Lu et al., 1983). *A. euchroma* roots gave alkannin- β, β-dimethyl acrylate and β-hydroxy isovalerate (Lin et al., 1981; Khan et al., 1983). Deoxyshikonin-β, β-dimethyl acryl shikonin, acetyl shikonin, teracryl shikonin and β-hydroxy isovaleryl shikonin were isolated from roots of *A. euchroma* and *A. guttata* (Zhu et al., 1984). Figure 1 shows the naphthaquinones so far found in *Arnebia* species.

Besides shikonin and its acetate, the roots of *Ajuga decumbens* were found to contain 5, 8 -dihydroxy- 2, 1, 4 - methylpentyl- 13 -enyl- 1, 4 -naphthaquinones, shikonin isovalerate and 3,6-dihydroxy- 2 -isovaleryl- 1, 2, 4 -benzoquinones (Mohammad and Galib, 1986a, 1986b; Salim et al., 1996). Teracryl alkannin was found to be present in roots of *A. densiflora* (Kirimer et al., 1995). Cycloarnebin- 7, tiglic acid (ester of dihydroxy alkannin) and others were isolated from *A. hispidissima* (Singh et al., 2003; 2004), alkannin also produced by hairy root cultures in *A. hispidissima* (Singh et al., 2002).

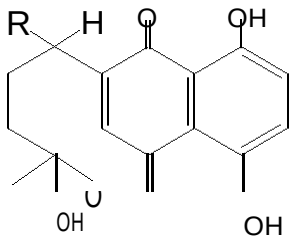
1. A novel ansa type monoterpenyl benozoid named arnebinol and a novel monoterpenyl benzoquinone named arnebinone were isolated from the roots of *A. euchroma* and *A. hispidissima* (Yao et al., 1983a, b; Eisai, 1983).

2. The *A. hispidissima* and *A. nobilis* roots ethanolic extract provided β-sitosterol (Nigam and Mitra, 1964;



-R=OH
Alkannin
- R = $OCOCH_2$ C (CH_3) = $(CH_2)_2$
Teracryl alkannin
- R = $OCOCH = (CH_3)_2$
Arnebin-1
R = $OCOCH_2CH(CH_3)_2$
Isovaleryl alkannin
- R = $OCOCH_3$
Acetyl alkannin
-R=H
Arnebin-7

----- R = OH
Shikonin
----- R = $OCOCH_2C(CH_3) = C(CH_3)_2$
Teracryl shikonin
----- R = $OCOCH = C(CH_3)_2$
β,β-dimethyl acryl shikonin
------- R = $OCOCH_2CH(CH_3)_2$
Isovaleryl shikonin
----- R = $OCOCH_2C(CH_3)_2OH$
β-hydroxy isovaleryl alkannin
----- R = $OCOCH_3$
Acetyl shikonin



R = $OCOCH=C(CH_3)_2$

Arnebin-2

R = H
Arnebin-5

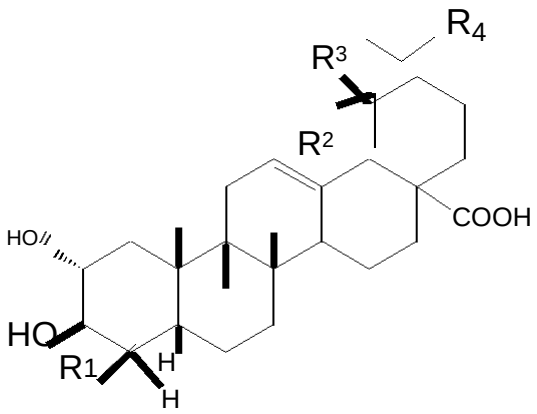
R=$OCOCH_3$
Arnebin-6

Figure 1. Structure of naphthaquinones occuring in Arnebia species.

Sharma et al., 1972), lupeol, betulin, β- amyrin acetate (Singh, 2001) . Two triterpenic acids identified as tormentic acid and 2 - -hydroxyursolic acid has been isolated from *A. euchroma* (Yang et al., 1992). Structures have been shown in Figure 2.

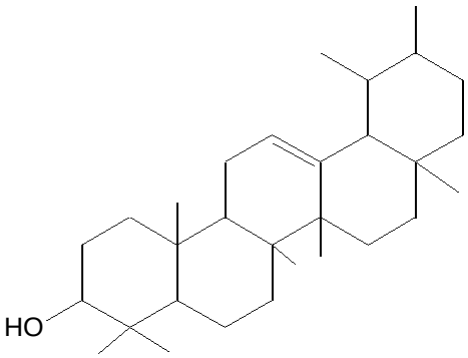
3. Several flavonoids have been isolated from fresh flowers of *A. hispidissima* [Figure 3] (Hamdard et al., 1988).

4. *A. hispidissima* gave echimidine, monocrotaline (Gamila et al., 1987), O^9-angeloyl retronecine and minor amounts of O^7 -angeloyl retronecine pyrrolizidine alkaloids were isolated from *A. euchroma* (Roeder and Rengel-Meyer, 1993; Srivastava et al., 1999). 7 and 9 - tigloyl retronecine, supinine, heliotrine, lycopsamine, europine (Figure 4) were detected by GLC, GC-MS and identified by their retention times (RT) from *A. decum-*



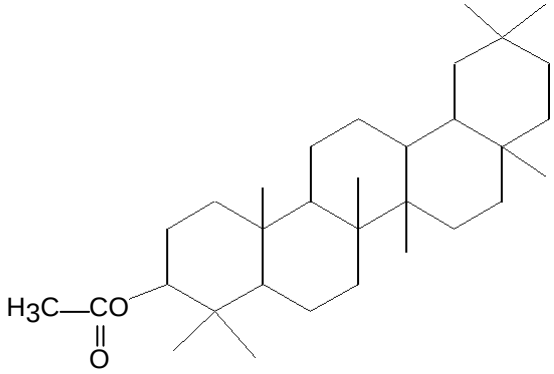
$R^1 = R^2 = Me$; $R^3 = R^4 = H$

2-α-hydroxyursolic acid

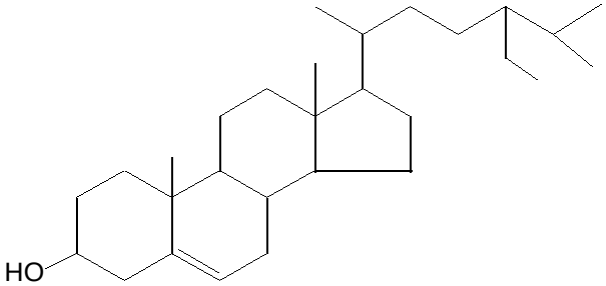


Lupeol

$R^1 = R^2 = Me$; $R^3 = OH$, $R^4 =$ H **Tormentic acid**



β-amyrin acetate



β-sitosterol

Figure 2. Examples of triterpenes isolated from Arnebia species.

bens (El-Dahmy and Ghani, 1995).

Heliotropium species

1. Pyrrolizidine alkaloids are also common in several genera of the Boraginaceae. They are generally present as ester alkaloids. More than 200 pyrrolizidine alkaloids have been isolated from plants. These alkaloids are cytotoxic and cause poisoning in livestock and people. The ester type pyrrolizidine alkaloids usually contain a necine base called necine, which is fused 5/5 ring system with a nitrogen atom as bridge head representing a tertiary base. In almost all cases, the necine has a hydroxy methyl group at C-7. These hydroxyl groups are usually esterified with a necic acid giving monoester, open chain diester and macrocyclic diester alkaloids.

In addition to hydroxyl group at C-7, they may also have a hydroxyl group at C-2 or C-6, resulting in the formation of stereoisomers. The necine can either be saturated or possess double bond in the 1, 2 -position. All known pyrrolizidine alkaloids found in the plants studied can form N-oxide derivatives except the otonecine alkaloids. The corresponding esterfication of necines containing a double bond in the 1, 2-position yields toxic alkaloids. The necic acids found in pyrrolizidine alkaloids, excluding acetic acid, possess, 5, 7, 8 and 10 carbon atoms. These can be mono-or dicarboxylic acids with branched carbon chains, bearing as substituents hydroxy, epoxy, carboxy, acetoxy, methoxy or other alkoxy groups. Thus numerous structural stereo and distereoisomers may be formed (Figure 5). The possibilities of esterfication are exemplified by several alkaloids. Necines containing one hydroxyl group can be

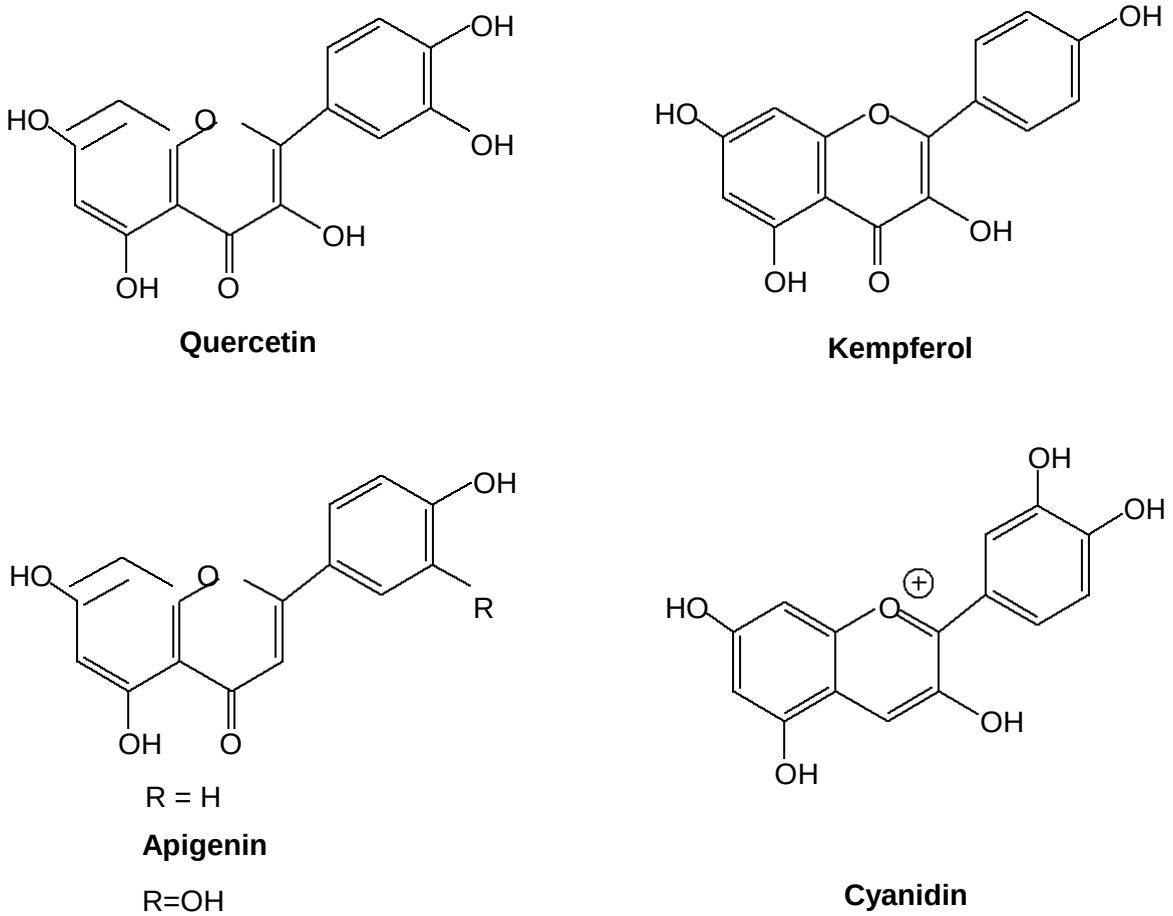
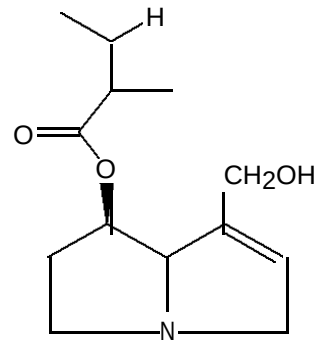
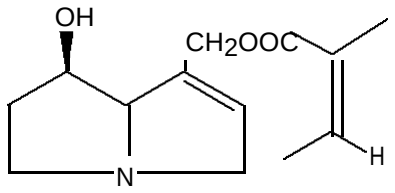


Figure 3. Structures of flavonoids.

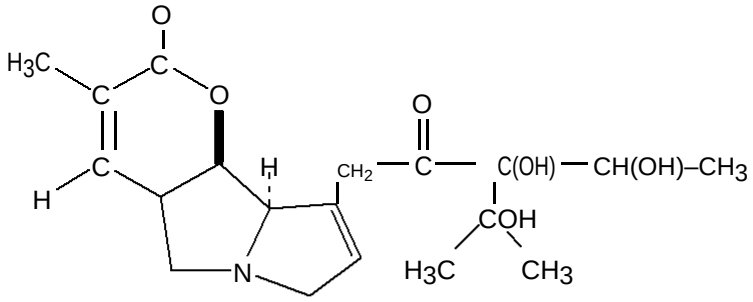
esterified with one monocarboxylic acid only as shown in Figure 6 for amabiline. Necines bearing two hydroxyl groups such as 7, 9 -necinedioles can be esterified with monocarboxylic acid either in the 7-or 9-position as demonstrated in Figure 4. Echimidine is an example of two fold esterification with dicarboxylic acids. A double esterification takes place leading exclusively to the formation of alkaloids with 11 to 14-membered ring systems. The most widely known pyrrolizidine alkaloids are the 11-membered monocrotaline, the 12-membered alkaloid is senkirkine. A large number of alkaloids may theoretically be obtained through combination of necines with necic acids. In nature more than 350 alkaloids have been found so far and their structures elucidated (Bull et al., 1968; Annon, 1983; Mattocks, 1986; Rizk, 1991; Roeder, 1995; Pelleier, 1995; Robins, 1995; Roeder, 2000; Lindell, 2002).

Heliotropium species have been widely investigated (Swain, 1963) for varied phytochemicals especially pyrrolizidine alkaloids from *Heliotropium ellipticum*, *Heliotropium subulatum* (Malik and Rehman, 1988; Jain and Singh, 1998), *Heliotropium ovalifolium* (Mohanraj and Herz, 1981), *Heliotropium ophioglossum* (Sajit et al., 1996), *Heliotropium marifolium* (Jain and Purohit, 1986), *Heliotropium spathulatum* (Roeder et al., 1991), *Heliotropium bovie* (Reina et al., 1996), *Heliotropium dygnum* (Hammanda et al., 1984), *Heliotropium curassavicum* (Davicino et al., 1988), *Heliotropium indicum* (Mattocks et al., 1961; Mattocks, 1967; Kugelman et al., 1976; Pandey et al., 1982; 1983; Alali et al., 2008), *Heliotropium burseriferum* (Marquina et al., 1988; 1989), *Heliotropium keralens* (Ravi et al., 1990), *Heliotropium arbinense* (Asibal and Zalkow, 1992), *Heliotropium scabrum* (Lakshmanan and Shanmugasunderam, 1995), *Heliotropium dasycarpum* (Rakhimore and Shakirov, 1987), *Heliotropium esfandiarii* (Yassa et al., 1996), *Heliotropium bacciferum* (Farrag et al., 1996), *Heliotropium ramossimum* (Khan and Khan, 1980), *H. stenophyllum* (Villarroel and Urzua, 1990), *H. bracteatum* (Lakshmanan and Shanmugasunderam, 1994), *Heliotropium filifolium* (Torres et al., 1994), *Heliotropium strigosum* (Mattocks, 1964), *Heliotropium hrsuitissimum* (Constitinidis, 1993), *H. suaveolens* (Guner, 1986), *Heliotropium circinatum* (Guner, 1988), *Heliotropium europium* (Hunt, 1972),

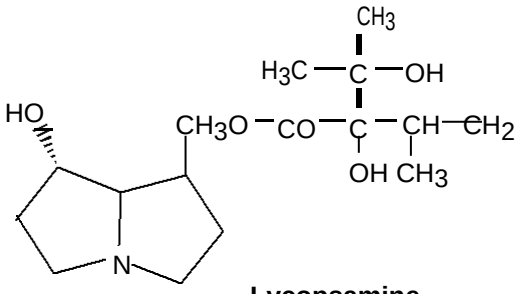




***O*^{7}-angeloyl retronecine** ***O*^{9}-angeloyl retronecine**



Echimidine



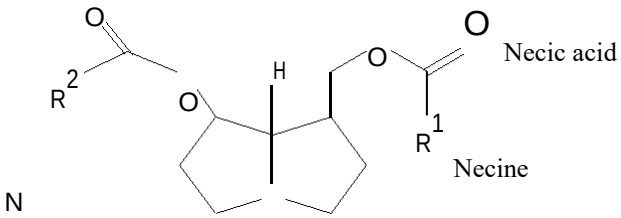
Lycopsamine

Figure 4. Structure of pyrrolizidine alkaloids reported in Arnebia species.

Heliotropium angiospermum (Birecka et al., 1984) and *Heliotropium amplexicaule* (Ketterer, 1987), has been investigated by various researchers [Figure 7].

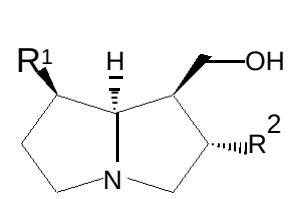
These compounds contain a characteristic base fragment, an amino alcohol, which is usually, esterified with the so called necic acids (Crout et al., *1*966; Mattocks, 1967; Suri et al., 1975; Leete and Leucast, 1976; Suri et al., 1976; Birecka et al., 1980; Huzing et al., 1980; Niwa et al., 1983; Van et al., 1994, 1995; Farsan et al., 2000; Souza et al., 2005; Frohlich et al., 2007).

Phytosterols are widely distributed in all parts of plants both in free and combined states (most frequently as esters of higher aliphatic acids and as glycosides) . Many natural sterols are unsaturated (mostly Δ^5) and rarely designated as sterols while their saturated analogues are called stanols. All the phytosterols have basic cyclopentanoperhydrophenanthrene carbon skeleton having methyl substituents at C-10, C-13 and aliphatic side chain at C-17. They occur in small amounts but have marked physiological importance. They occur invariably, where life exists and have profound importance in metabolism of organisms (Benveniste et al., 1966; Lee et



N

Necine



R^1=H;R^2=H

Isoretronecanole

R^1=OH;R^2=H

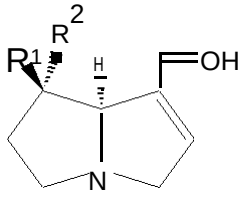
Platynecine

R^1=OH;R^2=H

Hastanecine

R^1=OH;R^2=OH

Rosmarinecine



R^1=H;R^2=H

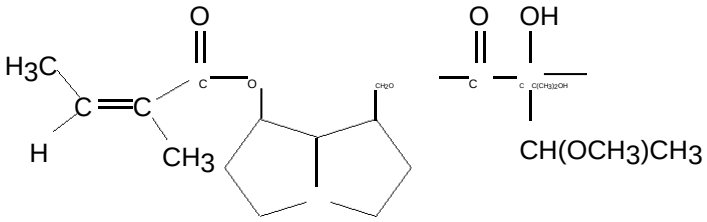
Supinidine

R^1=OH;R^2=H

Retronecine

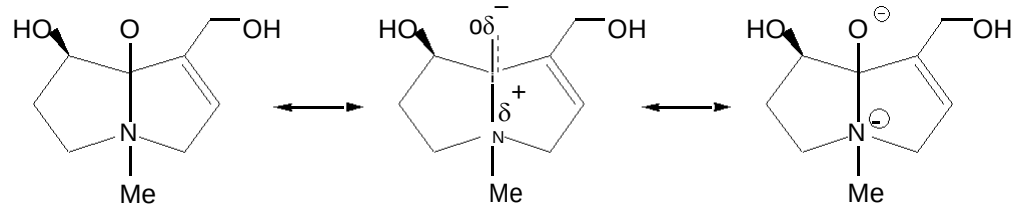
R^1=H;R^2=H

Heliotridine



N

Lasiocarpine



Otonecine

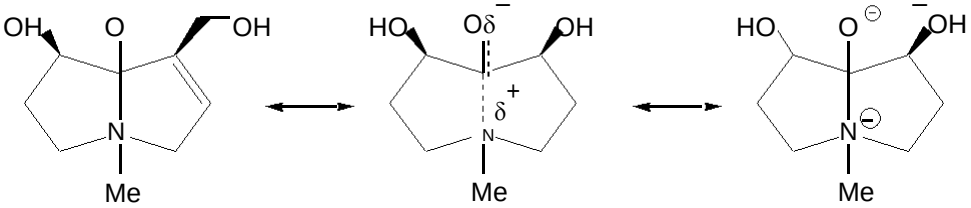
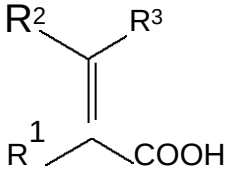


Figure 5. Structures of basic alkaloids and Dihydrootonecine from Heliotropium species.



R^1 = Me; R^2 = Me; R^3 = H

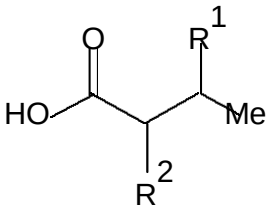
Tiglic acid

R^1 = Me; R^2 = H; R^3 =Me

Angelic acid

R^1 = CH_2OH; R^2 = H; R^3

=Me **Sarracinic acid**

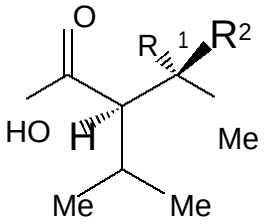


R^1 = Me; R^2 = H

2-Methyl butyric acid

R^1 = OH; R^2=H

2,3-dihydroxybutyric acid



R^1 = H; R^2= OH

(–)-viridifloric acid (vir)

R^1=OH;R^2=H **(+)-trachelanthic acid (Trc)**

R^1= OAc; R^2=H

3´-o-acetyl–(+)–trachelanthic acid (Actre)

Figure 6. Structures of necic acids.

al., 1972; Khanna and Mohan, 1973).

Triterpenoids are polycyclic, hydroaromatic, liposoluble alcohols, forming a large group of naturally occurring compounds and have been defined as a class of natural products containing C_{30} carbon atoms, assumed to be biosynthesized from six isoprene (C_5H_8) units (Kaul et al., 1967; Merinetti, 1969; Fumagalli, 1969; Knights, 1973; Heftmann, 1973, 1975; Bell and Charlwood, 1980; Rastogi and Mehrotra, 1991).

The terpenoids constitute the largest class of natural products of great structural diversity has been challenged to synthetic chemists and will continue to be more as skeleton types are found (Pfander and Stoll, 1999). These compounds are present in abundant in plants and also in cell cultures, though in low yields (Sharp et al., 1979; Staba, 1980; Harborne and Turner, 1984; Jain and Singh, 1999; Jain et al., 2001; Singh et al., 2002). Structures have been given in Figure 8.

***Trichodesma* species**

1. Pyrrolizidine alkaloids have been common in subfamilies Heliotropioideae and Boraginoideae of family Boraginaceae and widely isolated from a number of species of *Trichodesma* (Nadkarni and Nadkarni, 1954; Manske, 1960; Anonymous, 1976; Wassel et al., 1987; Hostettman and Lee, 1987; Hansch, 1990).

2. Triterpenoids and alkaloids viz., -amyrin, β-sitosterol, hexacosane, hexacosanoic acid and others (Figure 9) have been reported (Heilbron and Bunbury, 1953; Hassan et al., 1982; Hosamani, 1994; Singh and Singh, 2003; Singh et al., 2006).

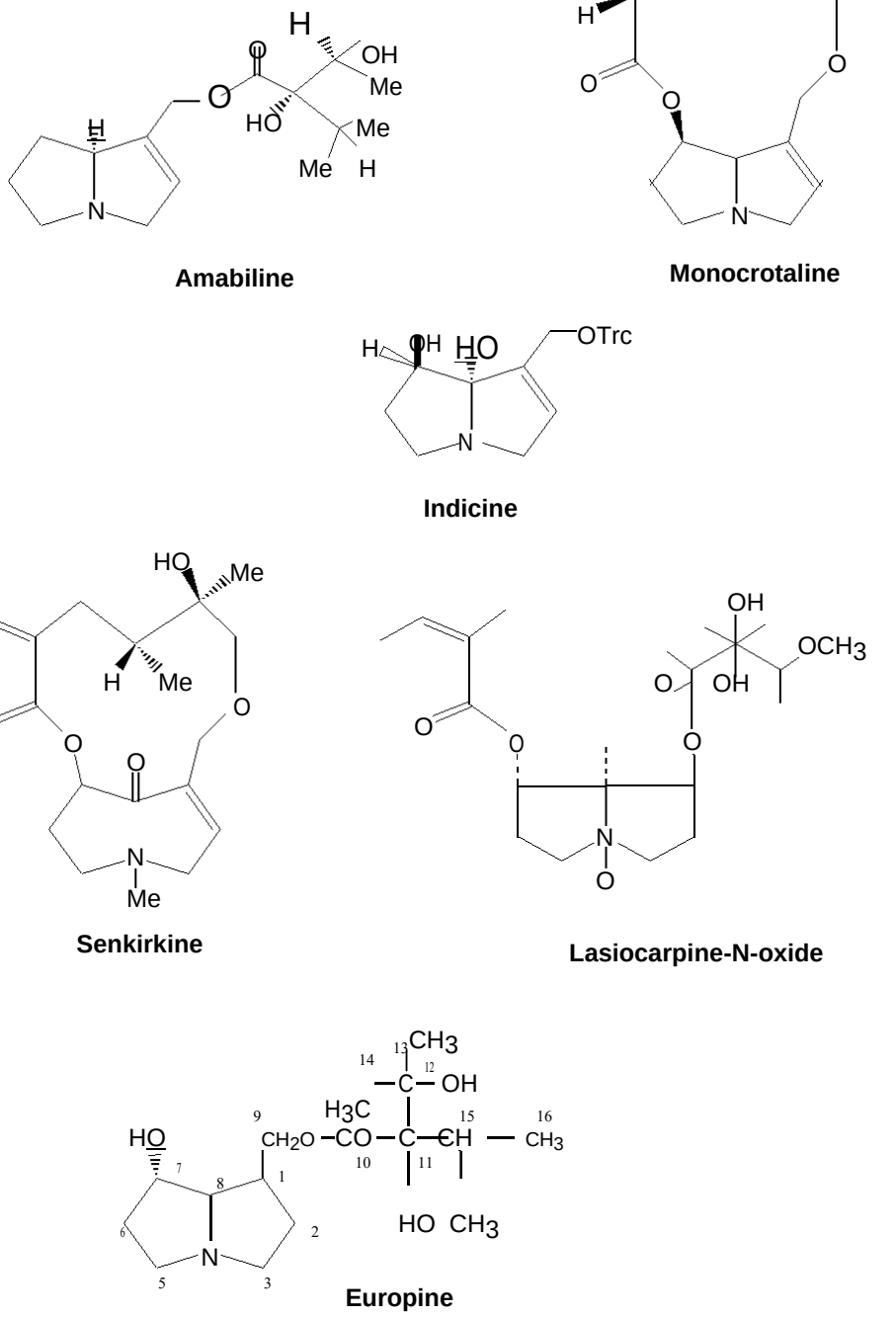


Figure 7. Examples of various pyrrolizidine alkaloids from Heliotropium species.

Cordia species

1. The *Cordia myxa* (L.) contains the nontoxic alkaloid macrophylline (Wassel et al., 1987).
2.The *Cordia* quinones have been reported by various researchers (Ishiguro and Oku, 1997; Ioset et al., 1998; Plyta et al., 1998).

Cynoglossum species

1. *Cynoglossum lanceolatum* containing the nontoxic pyrrolizidine alkaloids like as cynanstraline and slightly toxic as cynanstine (Suri et al., 1975). The *Cynoglossum* species contains the various alkaloids (Manko and Borisyuk, 1957; Manko, 1959; Pedersen, 1975; Resch

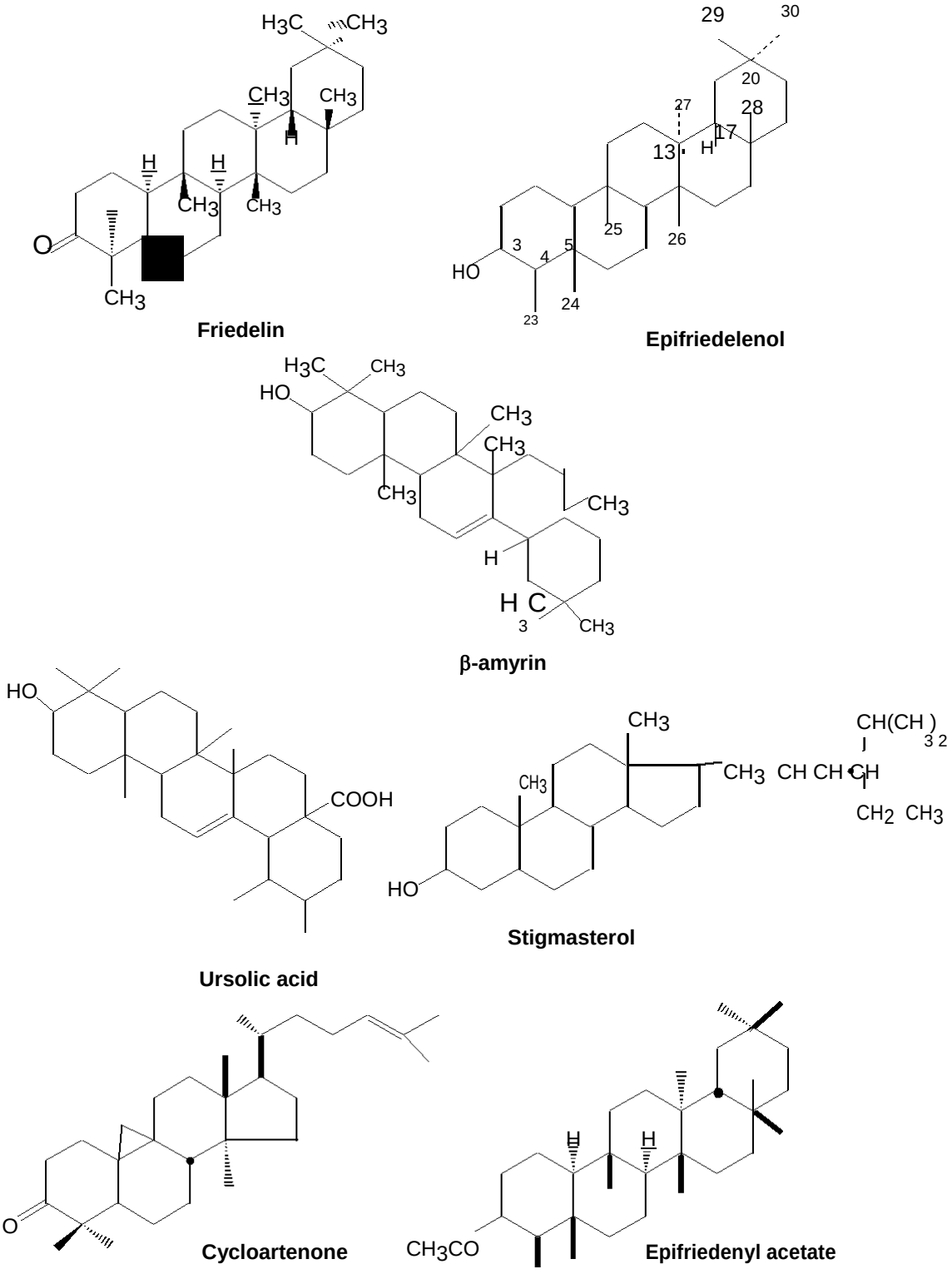


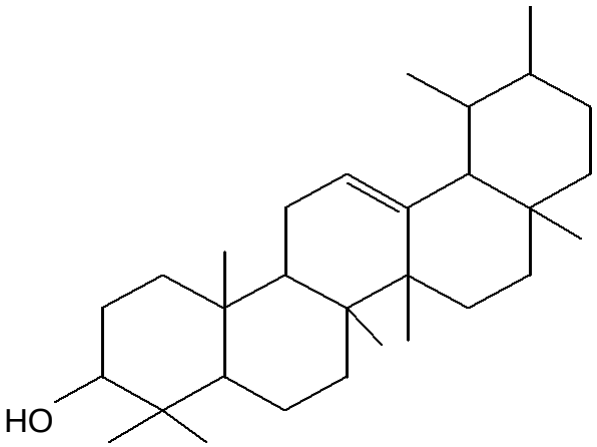
Figure 8. Structures of different triterpenoids isolated from Heliotropium species.

and Meinwald, 1982; Van Dam et al., 1994, 1995).

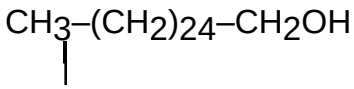
Cynoglossum amabile also contains rinderine as additional alkaloid as mentioned above (Figure 10) (Culvenor and Smith, 1967; El-Shazly et al., 1996).

Lappula intermedia

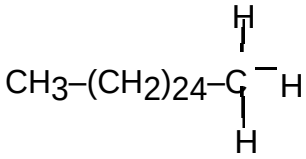
1. *Lappula* fruits contain highly toxic alkaloids lasiocarpine and their N-oxides (Figure 5) so, the plant



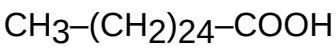
α-amyrin



Ceryl alcohol



Hexacosan e



Hexacosan oic acid

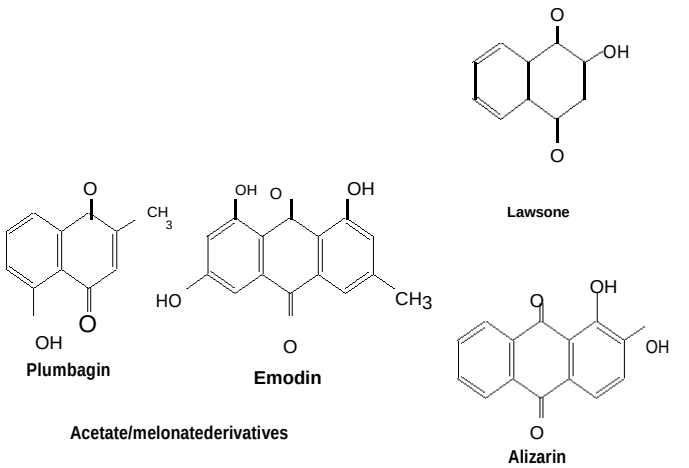
Figure 9. Structures of terpenes isolated from Trichodesma amplexicaule.

species should not be used for medicine purposes (Manko and Vasilkov, 1968).

Biosynthesis of secondary products

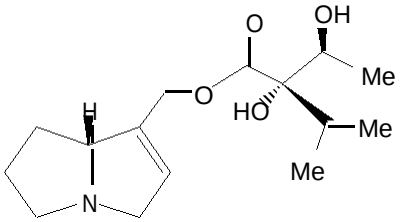
Biosynthesis of quinones

The quinones commonly occurring in nature are benzo, naphtha, anthraquinones. The polyketide pathway is found mostly in microorganisms but also exist in some higher plants e.g., Rhamnaceae, Polygonaceae. The second pathway, proceeding through succinyl benzoate, is widely distributed in higher plants. The occurrence of both pathways in plants is exemplified by the following: the naphthaquinone plumbagin from *Plumbago europaeus* (Plumbaginaceae) is formed via the polyketide pathway (acetate-melonate), but the naphthaquinone lawsone from *Impatiens balsamina* (Balsminaceae) and the anthraquinone alizarin from *Rubia tinctoria* (Rubiaceae) are derived from the succinyl benzoate pathway.

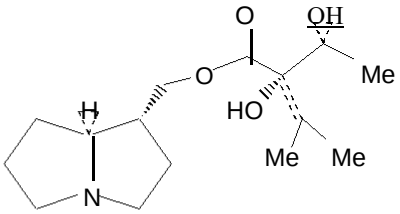


(I) Polyketide pathway

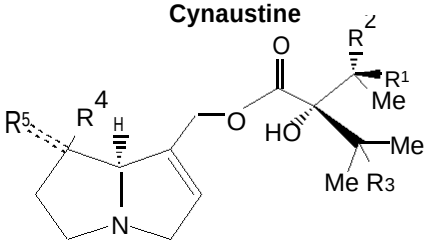
Acetyl CoA is the starting molecule for most polyketides. Linear Claisen condensation with several acetyl residues



Cynaustine



Cynaustraline



1. R^1 = OH; R^2 = H; R^3 = OH; R^4 = H; R^5 = OAng

Heliosupine

2. R^1 = OAc; R^2 = H; R^3 = OH; R^4 = H; R^5 = OAng

3´-acetylheliosupine

3. R^1=OH;R^2=H;R^3=H;R^4=H;R^5=OH

Echinatine

4. R^1 = OAc; R^2 = H; R^3 = H; R^4 = H; R^5 = OH

3´-acetylechinatine

5. R^1 = OH; R^2 = H; R^3 = H; R^4 = H; R^5 = OAng

7-angeloylechinatine

6. R^1=H;R^2=OH;R^3=H;R^4=H;R^5=H

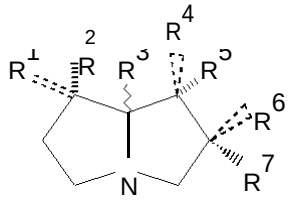
Supinine

7. R^1=OH;R^2=H;R^3=H;R^4=H;R^5=H

Amabiline

8. R^1=H;R^2=OH;R^3=H;R^4=H;R^5=OH

Rinderine

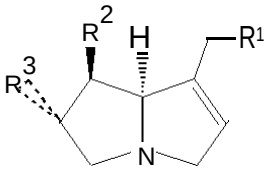


R^1=H;R^2=H;R^3=H ; R^4 = H; R^5 = CH_2OTrc; R^6=H;R^7=H

Trachelanthamine

R^1=H;R^2=H;R^3=H ; R^4 = H; R^5 = CH_2OVir R^6=H;R^7=H

Viridiflorine



R^1 =OH; R^2 = H; R^3 = OAng

7-angeloyl heliotridine

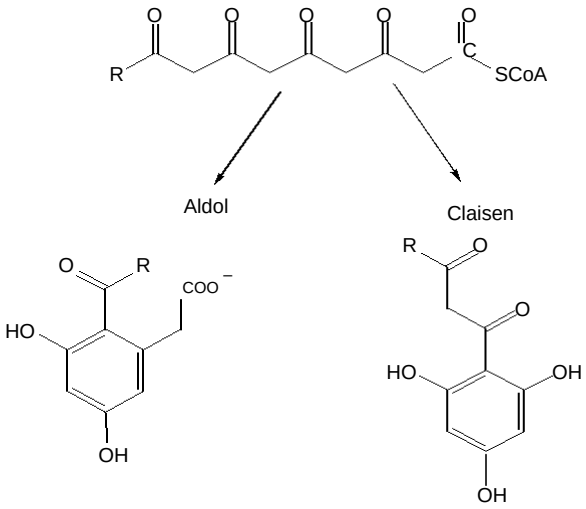
R^1 =OH; R^2 = H; R^3 = OTig

7-tigloyl heliotridine

Figure 10. Structures of Cynoglossum alkaloids.

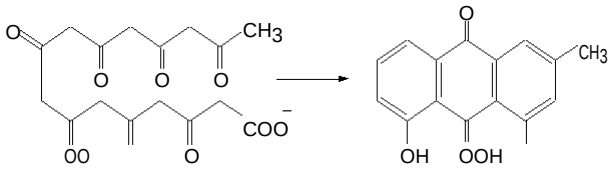
derived from melonyl-CoA leads, by concomitant loss of CO_2 to the the polyketide (acetogenin) structures [-(CH_2-CO) $_n$]. Direct condensation and cyclization gives various aromatic structures. The aromatic polyketide biosynthesis has to be distinguished from the fatty acid biosynthetic pathway, where the polyketides undergo reduction and

dehydration to form aliphatic hydrocarbons.



Aldol or claisen con den sati on

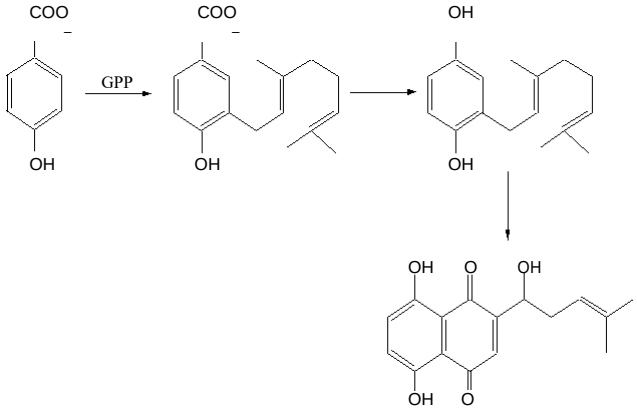
A typical folding mechanism involving aldol condensation of hypothetical polyketomethylene compound can lead to the anthraquinone chrysophanol in *Rhamnus frangula* (Rhamnaceae).



Polyketomethylene chain **Chrysophanol**

II. Succinyl benzoate pathway

Like the benzoquinones, some naphthaquinones may also be formed from 4 -hydroxybenzoate. This has been demonstrated in shikonin biosynthesis.



Shikonin

This is the pathway of mixed origin with 2 -succinyl benzoate as the key precursors. Through this pathway, several other naphthaquinones, are formed. The biosynthetic pathways leading to these products are extensions of the shikimate/ arogenate pathway, branching from chorismate, which the precursor of isochorismate. The formation of this isomer is catalyzed by the enzyme isochorismate hydroxymutase. Isochorismate in turn is converted into 2 - succinyl benzoate in the presence of 2 - oxoglutarate and thiamine pyrophosphate in a Michaelis type reaction (Figure 11).

Succinyl benzoate is subsequently activated at the succinyl residue to give a mono-CoA-ester. The activation requires ATP and yields AMP in bacteria and ADP in higher plants. Ring closure of the CoA ester to give 1, 4 - dihydroxy- 2-naphthoate in the higher plants. Most of the metabolic steps beyond the CoA-ester remain unknown in higher plants, except in juglone biosynthesis, 1, 4 - naphthaquinone is known to be an intermediate metabolite. It is, also likely that the third ring in alizarin biosynthesis is generated from dimethyl- pyrophosphate (Torsselle, 1983; Van Sumere and Lea, 1985; Williams et al., 1989; Swain et al., 1999; Dey and Harborne, 2000).

Biosynthesis of pyrrolizidine alkaloids

Several researchers have investigated the biosynthesis of pyrrolizidine alkaloids. From *in vitro* tracer experiments, it is well established that the necine base is derived from arginine or ornithine via two symmetrical intermediates, putrescine and homospermidine (Khan and Robins, 1981, 1985). The necine acid moiety is derived from isoleucine (Cahill et al., 1980; Hartmann and Toppel, 1987). The further course of the biosynthesis is the same among representatives of the genera *Heliotropium* species, *Senecio* species (Boettcher et al., 1994; Graser and Hartmann, 1997; Graser et al., 1998).

The amino acids L- isoleucine, L-leucine, L-threonine and L-valine are known to be precursors, the decarboxylation and deamination of which give e.g., C- 5 acids such as angelic acid or tiglic acid or C-10 acids such as senecic acid. Studies of Weber et al.(1999), on root cultures of *Eupatorium clemantidium* recently showed that trachelanthic acid is biosynthesized by the addition of two carbon moiety from hydroxyethyl-TPP to 2-oxoisovaleric acid followed by reduction process (Candrian et al., 1984; Bruggeman and Van der Hoeven, 1985; Mori et al ., 1985; Molteni et al., 1989; Weber et al., 1999).

Biosynthesis of triterpenoids

Before cyclization can occur in the triterpene (C_{30}) series, two molecules of FPP (C_{15}) are first joined in a head to head condensation to produce squalene. The catalyst, squalene synthase, is a prenyltransferase that catalyses a complex series of cationic rearrangement to accomplish

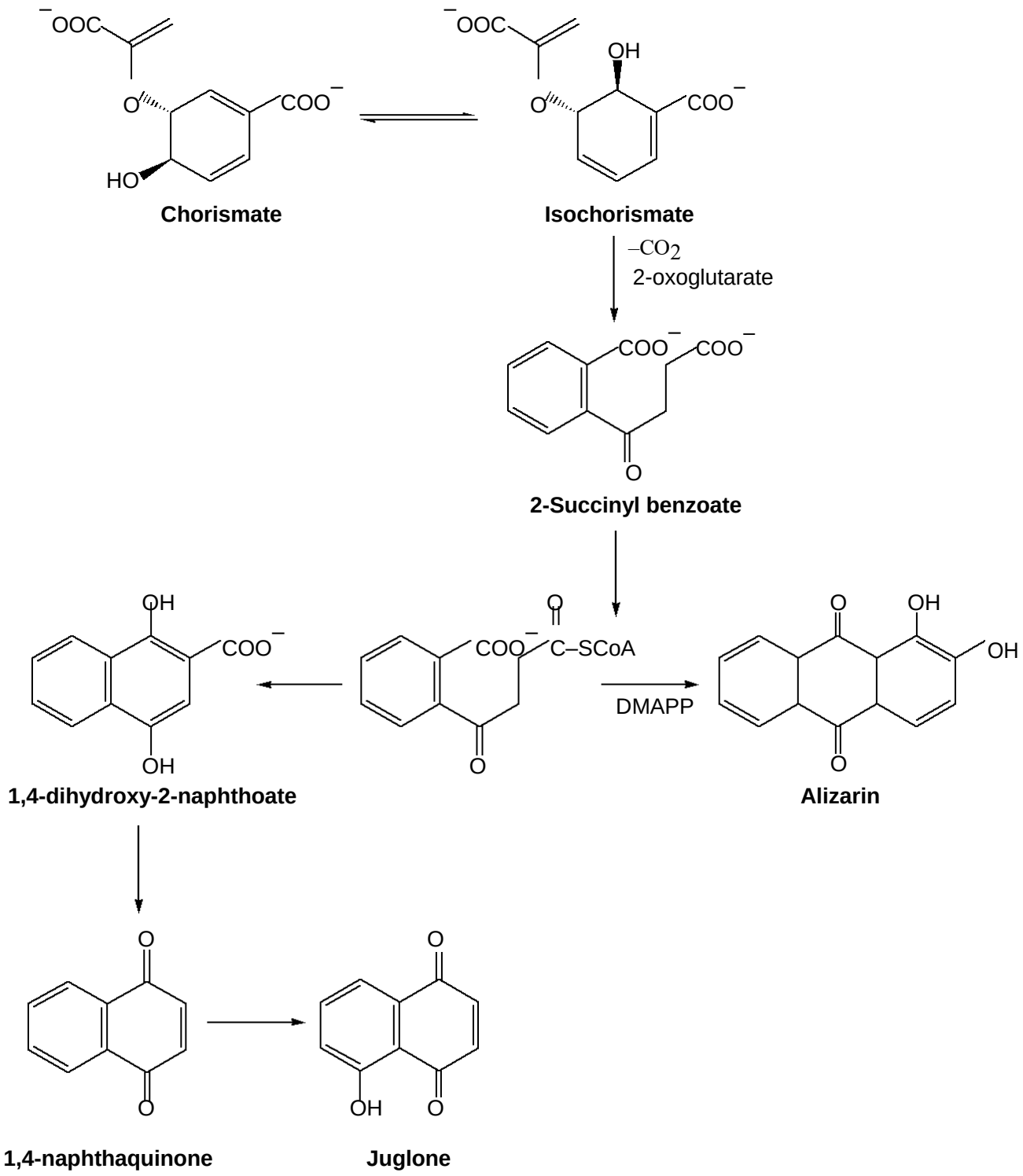


Figure 11. Postulated biosynthetic pathway of alizarin and juglone.

the chemically difficult core of joining the C-1 carbons of two farnesyl residues (Figure 12). The biosynthesis of triterpenoids has been studied by several researchers (Bell and Charlwood, 1980; Harborne et al., 1991; McGarvey and Croteau, 1995; Cane, 1999).

Biosynthesis of flavonoids

The first committed step on the flavonoid biosynthetic pathway is catalyzed by chalcone synthase. Three molecules of acetate derived melonyl CoA and one mole-

cule of *p*-coumaryl-CoA are condensed to generate a tetrahydroxy chalcone. In certain species, the coordinated action of chalcone synthase and an NADPH-dependent reductase generates a 6-deoxychalcone. The biosynthesis pathways have been investigated by several workers (Figure 13) (Harborne, 1994; Forkmann and Heller, 1999; Barton et al., 1999; Buchanan et al., 2000).

Ethnomedicinal, pharmacological and biological properties of Boraginaceous plant

Arnebia species

The plant species is a perennial grass widely distributed in India, Persia, Sudan, Arabia, China, Egypt, Nubia, Pakistan with a few species occurring in the drier parts of Rajasthan. Some common species are *Arnebia benthami*, *A. euchroma*, *A. guttata*, *A. nobilis* and *A. hispidissima* (Anonymous, 1985). Roots are used in ulcers, boils, cuts, for heart ailments, headache, fever, water extract of flowering shoot is known for tongue and throat troubles, fever and cardiac complaints; while the whole plant was used as a stimulant, tonic, diuretic and expectorant. Likewise, the roots of *A. euchroma* (Royle) Johnston are used in bruises and skin eruptions (Chopra et al., 1956; Kirtikar and Basu, 1967; Anonymous, 1976; Anon, 1990; Trivedi, 2005). *A. hispidissima* also possesses anti-inflammatory (Singh et al., 2003; Singh et al., 2004), antimicrobial (Shukla et al., 1969; Bhakuni et al., 1969; Shukla et al., 1991; Jain et al., 1999), antitumor (Sankawa et al., *1*977; Katti et al., 1979; Kashiwada et al., 1995),antiviral(Yuan-Shiun et al., 1993) and inhibition of platelet aggregation activities(Yao et al., *1*991) and prostaglandin inhibition(Wassel et al., *1*987; Yao et al., 1991).

Heliotropium species

Most of the *Heliotropium* species are distributed in India, Central Asia, China, Australia. The *H. ellipticum* whole plant is employed as an emetic and in snakebite. Leaves are used for cleaning and healing ulcers and rolled up and put into ears as a cure of headache (Chopra et al., 1956; Kirtikar and Basu, 1967). Pharmacologically, the plant species demonstrated hypotensive effect (Bhakuni et al., 1969; Gupta et al., 1972) and antimicrobial (Jain and Singh, 1998) activities.

The alkaloid heliotrine demonstrated transient hypotension *perse* in dogs and significantly reduced the nicotine induced vasopressure spasmogenic responses (Pandey et al., 1982). This species has been considered responsible for hepatic veno-occlussive disease. *H. marifolium was* used for treatment of ulcers, wounds, local inflammations, scorpion or wasp stings, bites of snakes and rabies but representatives of this group are believed to be poisonous even in many countries (Lanigan et al., 1978; Pass et al., 1979). *H. subulatum*, *H. ellipticum* and *H. marifolium* also demonstrated antimicrobial effects (Jain and Singh, 1999; Singh and Dubey, 2001; Jain et al., 2001;). *H. subulatum* also possesses antiviral and antitumor effects (Singh et al., 2002).

Trichodesma species

The plant genera has been used traditionally for antidiuretic, antirheumatism and administered as a drink of children dysentry. *T. africanum* used as emollient and diuretic, *T. amplexicaule* Roth, the whole plant used as an emollient, poultice, roots pounded and made into a paste applied to reduce swellings, given as a drink in dysentry. *T. zeylanicum* leaves are used as emollient and diuretic (Chevallier, 1996; Trivedi, 2005). *T. amplexicaule* also possesses antimicrobial (Singh and Singh, 2003), anti-inflammatory activities (Singh et al., 2006).

Cordia species

There are 13 species of the genus *Cordia* found in India (Howard, 2007). The immature fruits are used as a vegetable fodder. Fruit extract of *Cordia dichotoma* suppresses larval hatching of *Meloidogyne incognita*. Seeds of the species are anti-inflammatory, 2 compounds alpha-amyrin and 5-dirhamnoside have been isolated. The bark is medicinal and several chemicals have been identified; Allantoin, beta -sitosterol and 3', 5 -dihydroxy-4' -methoxy flavanone- 7 -O- alpha -L-rhamnopyranoside. The seed kernel has medicinal properties (Theagarajan and Prahbu, 1977; Tiwari and Srivastava, 1979; Agnihotri et al., *1*987).

Cordia myxa is a shrub which may reaches the height of 5 - 10 m and decoctions of this plant used for gastric pain. There is no objection to its use (Wassel et al., 1987).

Cynoglossum species

Cynoglossum lanceolatum used for internal indications, e.g., for nephritic oedema, acute nephritis and toothache, *Cynoglossum officinale* is a annual herb, its roots are used for the treatment of pulmonary tuberculosis, cough and hematemesis (IOSET et al., 1998; Plyta et al., 1998).

CONCLUSION

The family Boraginaceae comprises a number of medicinal plants, some important plants has been discussed in

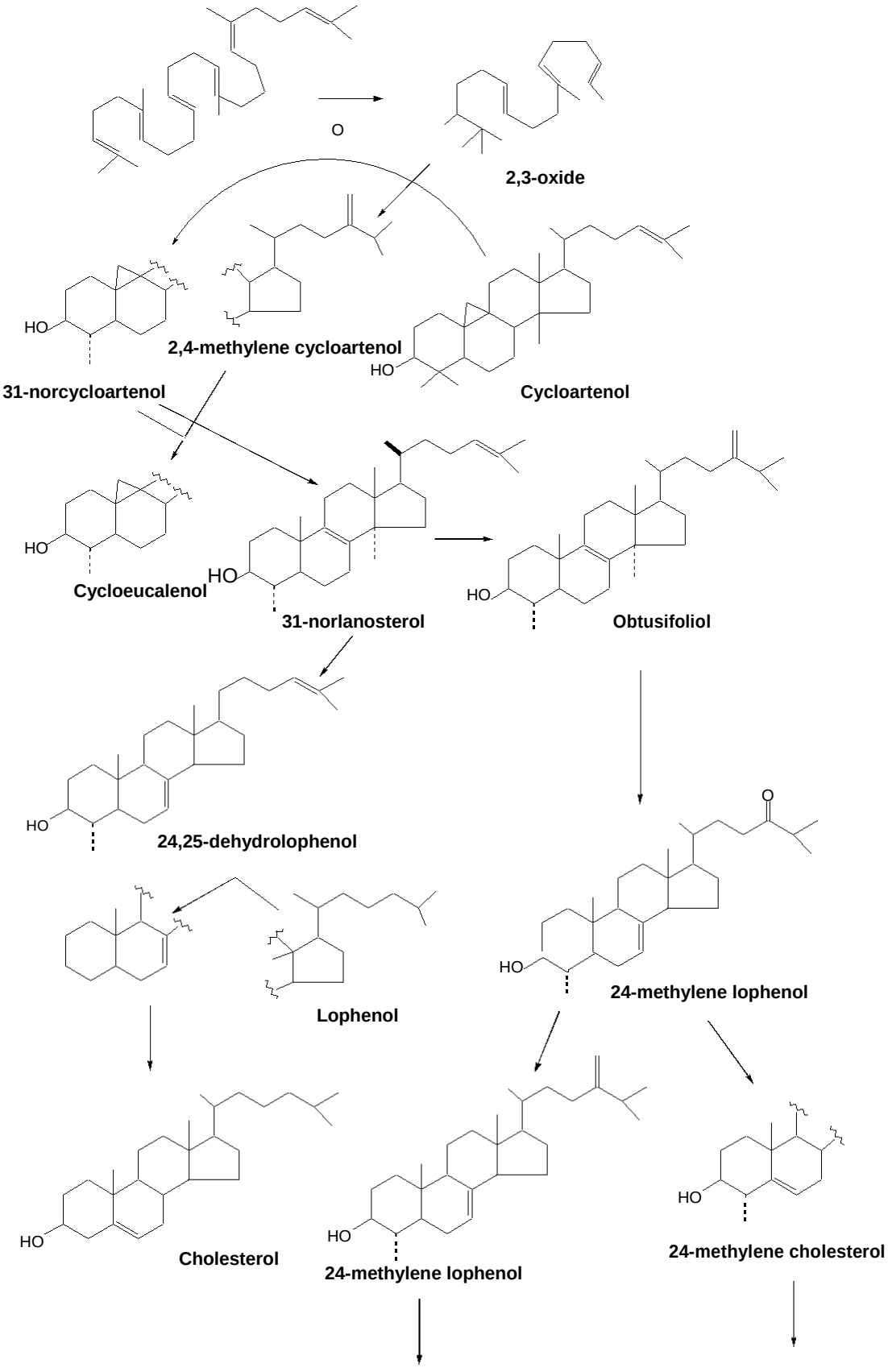


Figure 12. Schemes demonstrate the biosynthesis of triterpenes.

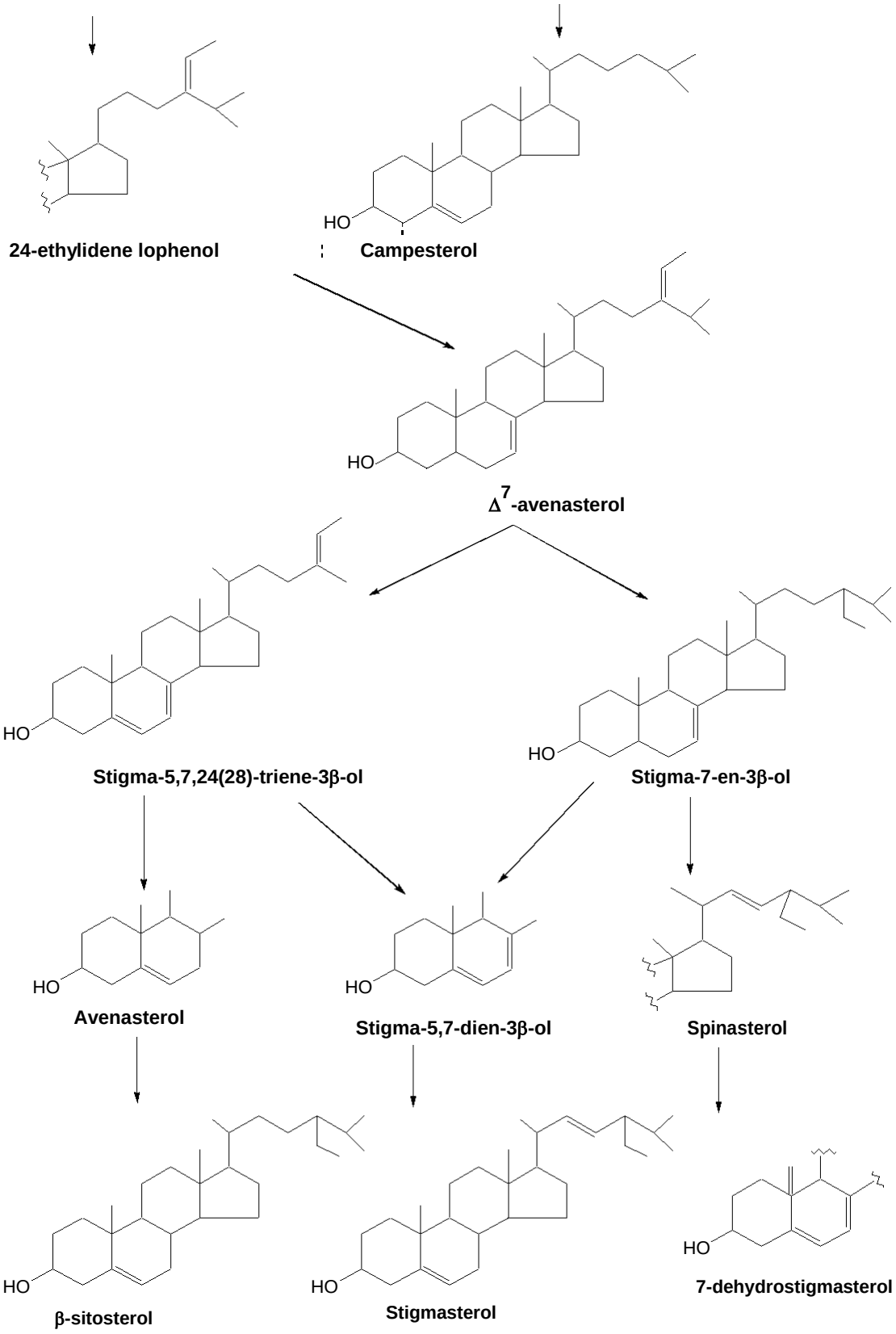


Figure 12. Schemes demonstrate the biosynthesis of triterpenes.

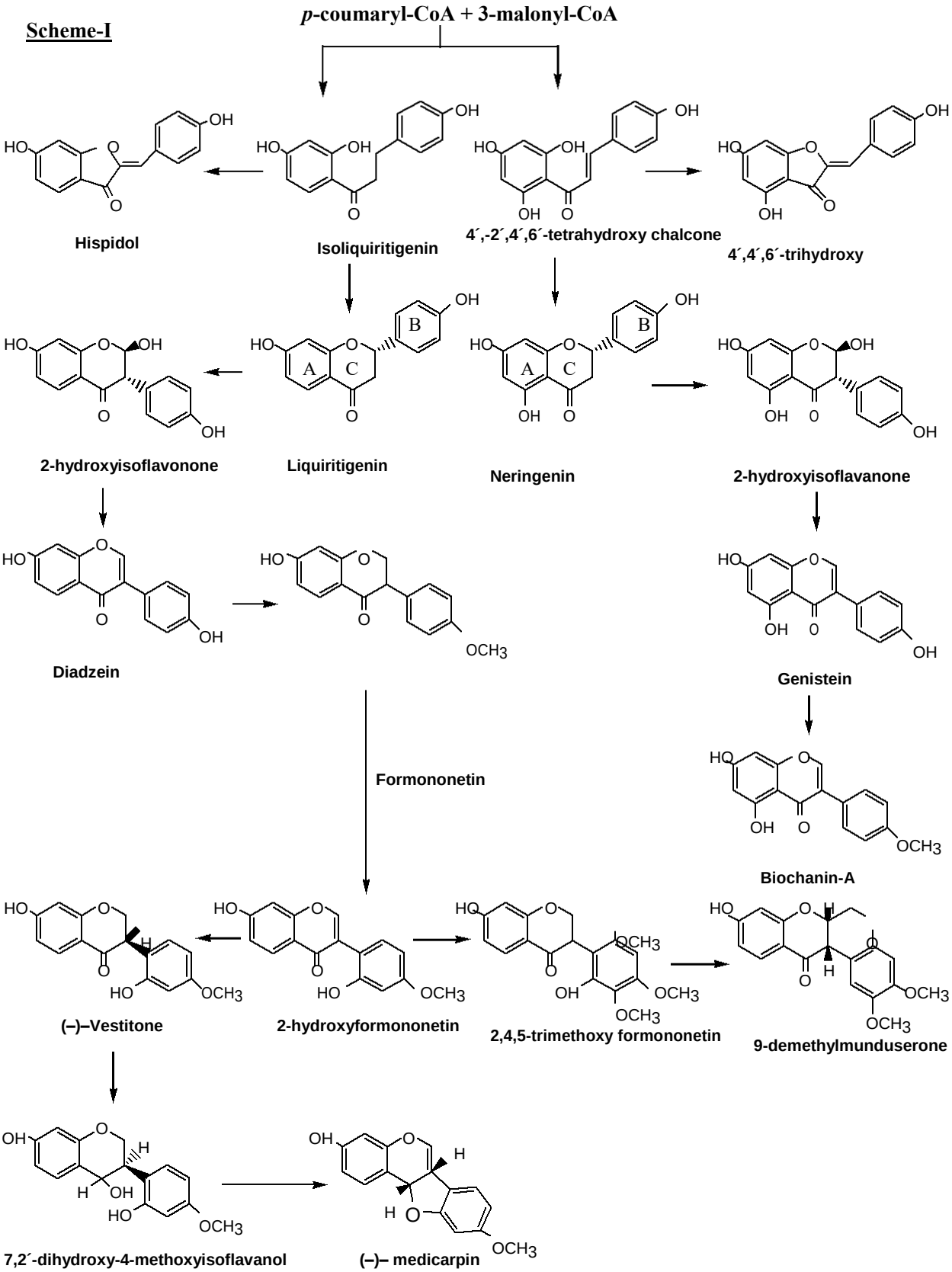


Figure 13. Steps of flavonoid biosynthesis.

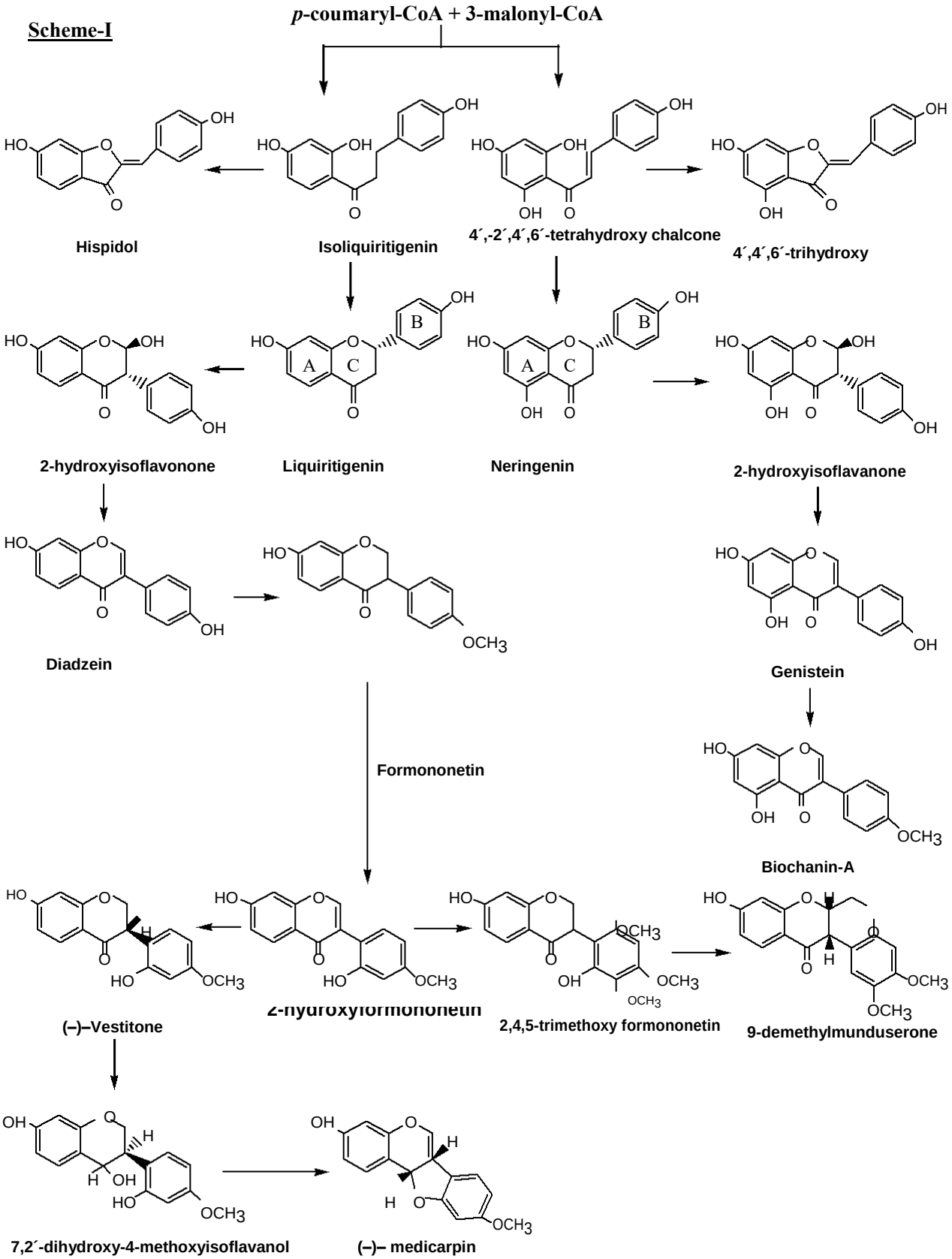


Figure 13. Steps of flavonoid biosynthesis.

the above section. A number of secondary metabolites viz.-alkaloids, flavonoids, phytosterols, terpenoids, glycol-sides, fatty acids,different types of proteins and many other metabolites are present in different plant parts. These compounds exhibits various pharmacolo-gical activities and are being used to cure various diseases and hence these plants may become a good source of indigenous medicines.

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