

PHCOG REV.: Plant Review

The Genus *Berberis* Linn.: A Review

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ABSTRACT

Berberis Linn. (Family: Berberidaceae), a genus of shrubs or small trees, distributed in the temperate and sub-tropical parts of Asia, Europe and America. The genus consists of species which are commonly used in many traditional systems of medicines. About seventy seven species are reported from India. The crude extracts of various parts and pure isolates of *Berberis* species were reported to possess hypoglycemic, anticancer, gastro irritant, antifatigue, anticoagulant, antipyretic, local anesthetic, antiprotozoal, antibacterial, hypotensive, anti-inflammatory and CNS-depressant activities. *Berberis* species have been found to possess tonic, stomachic, astringent, antiperiodic, diaphoretic properties and are also useful in the treatment of jaundice, enlargement of spleen etc. The widespread uses of *Berberis* species in traditional systems of medicine have resulted in their extensive chemical analysis for their bio-active principles. The comprehensive compilation of the chemical constituents isolated from *Berberis* species covering the literature up to 2007 is presented in this paper. This article briefly reviews the botany, chemistry and pharmacology of *Berberis* species.

KEYWORDS: Berberidaceae, *Berberis aristata*, berberine, pharmacology, chemical constituents

INTRODUCTION

The *Berberis* (Ber-be-ris, barberry, Pepperidge bush) (Family: Berberidaceae), a genus of about 450-500 species of deciduous and evergreen shrubs, are very commonly used in traditional system of medicines. The genus is distributed in temperate and subtropical parts of Asia, Europe and America (1). Almost all parts of the plant viz., whole plant, root, root-bark, stem, leaves and fruits have been investigated chemically and biologically. This review provides an update and comprehensive compilation of different classes of compounds isolated from various species of *Berberis* genus along with their biological properties. Our endeavor will help the researchers to know more about *Berberis* species.

Botanical Description

Berberis, a genus of shrubs and small trees. In India nearly seventy seven species are reported and they are commonly known as Barberry (Venn.- Kashmal, Kinjosa) (2). Several species are grown in gardens for their ornamental leaves and bunches of succulent, acidic and edible berries. The berries are edible and rich in vitamin C (3). The genus is characterized by dimorphic shoots, with long shoots which form the structure of the plant and short shoot only 1-2mm long.

American Barberry, *B. canadensis* P. Mill., is a perennial small shrub, 10-25 inch tall with brown to purplish branches and found in open woodlands. The alternate arranged leaves are spatula-shaped with a grayish white underside without prominent veins. The leaf edges have 2-12 teeth. The notched yellow flower petals appear in May on racemes containing 5 to 10 flowers each. The fruit is an oblong red berry (4-5).

In some evergreen species from China (e.g.- *B. candidula*, *B. verruculosa*) the leaves are brilliant white. The flowers are produced singly or in racemes of upto 20 on a single flower head. They are yellow or orange, 3-6mm long, with six sepals and six petals in alternating whorls of three. The sepals

usually coloured like the petals. The fruit is a small berry and 5-15mm long. Common Barberry, *B. vulgaris* L is an introduced species from Europe (6) that reaches height of 9 feet and has grayish branches with 3 parted spines. It can be found growing in the northern regions of USA and Canada, near woodland edges and old fields. The leaves are similar to *B. canadensis* but are serrated (12-21 teeth) with prominent veins underneath. The yellow flowers are not notched and may contain 10-20 flowers per raceme. The bark of the root of *B. vulgaris* L. was formerly included in the secondary list of the U.S. Pharmacopeia under the name of *Berberis*. The root and inner bark have been used for yellow dyeing (4).

B. thunbergii, Japanese barberry, is an introduced species that reaches height of 3-4 feet. The leaves are entire with simple (one part) spines, flowers are solitaire or on a small umbel. The fruit is a red oblong berry. The wood and inner bark in all the three species is yellow, signifying berberine content and out of these species, *B. vulgaris* is the most widely used (4-5).

In India mainly *B. angulosa*, *B. aristata* DC, *B. asiatica* Roxb. ex. DC, *B. coriaria* Royle ex Lindl, *B. Chitria* Lindl, *B. tinctoria* Lesch, *B. umbellata*, *B. virescens*, *B. coriaria* Royle, *B. lycium* Royle, *B. floribunda* are found and are being planted as hedges due to their straggling habit. Barberry bushes generally bloom from February to June and attract bees for the pollen and nectar. The honey obtained is dark and has a strong flavour similar to molasses. The wood of various species cannot be distinguished with certainty. It is bright yellow, hard to very hard, moderately heavy to very heavy (wt 620-960 kg/mt³), usually straight grained and very fine in textures (7-8). *B. aristata* DC is an erect glabrous, spinescent shrub, 3-6 m in height with obovate to elliptic, subacute to acute, toothed leaves, yellow flowers in corymbose racemes and oblong-ovoid, bright red berries (8-

10). *B. asiatica* Roxb. ex DC is a pretty shrub, 1.8-2.4 m in height, armed with trifid spines, oblong-ovate, acute, mucronate, long petioled leaves with aritadentate margin, yellow flowers in umbellate racemes and oblong-ovoid edible berries. It commonly grows in Himachal Pradesh at an altitude of 600-2700 m eastwards to Bhutan and to Assam at 1500-1800 m and on Parasnath hills in Bihar, Panchmari in Madhya Pradesh and Mount Abu in Rajasthan (11). *B. chitria* Lindl. syn. *B. aristata* is an erect spiny shrub, 3.6 m in height with obovate or elliptic-acute, spinose-serrate leaves, deep yellow flowers in loose corymbose panicles and dark red brown oblong-ellipsoid berries, occurring in Himalaya from Kashmir to Nepal at an altitude of 1500-2400 m. (12).

B. lycium Royle is a suberect rigid, spiny shrub, 2.7-3.6 m in height with oblanceolate, acute or subacuminate leaves, small pale yellow flowers in 20 flowered racemes and ovoid black berries. It occurs abundantly from Kashmir to Kumaon at an altitude of 900-2700 m (13-14). *B. tinctoria* Lesch is 1.8 to 2.4m tall shrub, occurring in Nilgiri and Palni Hills at an altitude of 1,800 m and in Shevaroy Hills of South India. The roots of this plant contain four alkaloid out of which berberine is 2.3% and fruits are used for making jams. *B. Umbellata* Wall. Ex. G. Don is a shrub and 1.8 to 2.4m in height, occur in Himalays from Garhwal and Kumaon to Sikkim and Bhutan. The stem bark contains umbellatine (0.68%) alkaloid (15). *B. virescens* is a spreading shrub, 1.8 to 3.0 m in height with oblong- obovate leaves, pale yellowish green flowers. It occurs in Nepal, Sikkim and Bhutan at 3,000m (16). *B. coriaria* Royle, a tall shrub found in Kumaon hills upto 3,000m. *B. floribunda* in part is endemic to Nepal (17-18).

Ethnopharmacology

Traditional uses

Rasanjana or Rasaut or Rasavanti, a thick extract is being made from the root-barks, roots and lower stem-wood of *B. aristata* by boiling them with water. It is one of the traditional preparations. The drug is regarded as bitter tonic and is reported to be used as cholagogue, stomachic, laxative, diaphoretic, antipyretic and antiseptic. It is useful in eye diseases particularly in conjunctivitis, indolent ulcers and in hemorrhoids (19). The crude drug alone or in combination with other ingredients shows efficacy against allergic conjunctivitis, acne vulgaris, rheumatic pain, premature ejaculation, fungal infection and viral hepatitis. *B. aristata* possesses stomachic, astringent, antiperiodic and diaphoretic properties. Crude extract of the leaves exhibited hepatoprotective activity against paracetamol-induced liver damage in rats. The fruits either fresh or in dried form exhibited hypocholesterolemic activity (20). The whole plant extract forms one of the constituents of a herbal cream, DERMOCEPT used against sarcoptic mange lesions. It also forms one of the constituents of a crude Ayurvedic drug formulation exhibiting inhibitory effect against *Salmonella typhi* *in vitro*. The plant extract with another crude drug exhibited antiamebic activity against *Entamoeba histolytica*. The extract also showed inhibitory effect against enzyme activity of DNase, RNase, aldolase, alkaline phosphatase, acid phosphatase, α -amylase and protease (21).

B. asiatica constitutes a composite drug which minimizes the lesions of hepatotoxicity of paracetamol poisoning. In Nepal, boiled leaf bud extract is used to treat eye inflammation and in toothache (22). Bhutia tribals eat ripe fruits of *B. insignis* (23). *B. lycium* Royle roots are used for the treatment of intestinal colic and pharyngitis. The root-bark is astringent and used for healing internal wounds, cracked bones and urine burning and also as a tonic in pregnancy (24). Various parts of *B. vulgaris* have been used for the treatment of diarrhea, gall bladder and liver dysinfections, leishmaniasis, malaria, stomach problems and urinary tract diseases (25). A berry tea is used for poor appetite, also as a diuretic, expectorant and laxative, used for jaundice, hepatitis, hemorrhages and diarrhea. It is also considered as an astringent, diaphoretic and antiseptic. A tincture of root bark was used for arthritis, rheumatism and sciatica. In Chinese medicine, barberry is used to increase white blood cell and platelets after chemo or radiation cancer therapy. The ripe fruit is also considered a wild food source and can be used as a cooked fruit (5).

Phytoconstituents

The widespread uses of *Berberis* genus in traditional systems of medicine have resulted in considerable chemical analysis of the plant and their active principles. The phytochemical investigation of genus *Berberis* as carried out so far has afforded more than 105 compounds with varying structural patterns. Among these constituents, we present alkaloids, flavanoids, anthocyanins, phenolic compounds, carotenoids and vitamins from the major classes together with other compounds according to the following classification.

Alkaloids: Berberine is found to be the chief active alkaloid of *Berberis* species. Berbamine, Jatrorrhizine and Palmatine were the other principle alkaloids present in various *Berberis* species (Table 1 and chemical formulae 1-71).

Flavanoids: Some flavanoids (compounds 72-76) based on the 2, 3-dihydro-2-phenyl-4n-1-benzopyran-4-one (flavone) nucleus from different *Berberis* species were reported. (Table 2).

Anthocyanins: Nearly 18 anthocyanins with basic cyanidin frameworks (compounds 77-94) have been isolated from different *Berberis* species and are presented in Table 3.

Carotenoids and Vitamins: Only few (compounds 95-106) of this class have been reported from *Berberis* (Table 4).

Phenolic Compounds: Three phenolic compounds (107-109) were isolated from *B. vulgaris* (Table 5).

Pharmacological reports

Berberis species are major source of berberine and other alkaloids also namely berbamine, palmatine, isotetrandrine and jatrorrhizine. Palmatine was shown to have anticholinesterase activity. Isotetrandrine antagonizes ileal contraction induced by histamine or acetylcholine. Jatrorrhizine reduces spontaneous activity of mice and prolongs the animal sleep elicited by pentobarbital. It also induces sleep in mice given subthreshold doses of pentobarbital (85).

Berberine, an isoquinoline alkaloid present in numerous species of genera *Berberis*. It has a wide range of pharmacological and biological activities, including anti-

Table 1: Alkaloids from various *Berberis* species

| Phytoconstituents | Species |
|----------------------------------|---|
| Berberine[1] | <i>B. asiatica</i> (12) , <i>B. aristata</i> (10,26-27), <i>B. Lycium</i> (10,26-27), <i>B. Vulgaris</i> (29), <i>B. coriaria</i> (30), <i>B. iliensis</i> (30), <i>B. Koreana</i> (31), <i>B. chitria</i> (32), <i>B. Floribunda</i> (32), <i>B. himalacia</i> (32), <i>B. Jaeschkeana</i> (33), <i>B. Lambertii</i> (33), <i>B. petiolaris</i> (34), <i>B. tinctoria</i> (32), <i>B. mingetsensis</i> (35), <i>B. morrisonensis</i> (36), <i>B. guimpeli</i> (36) |
| Palmatine[2] | <i>B. asiatica</i> (12), <i>B. aristata</i> (10,26-27), <i>B. lycium</i> (13, 28), <i>B. vulgaris</i> (29), <i>B. koreana</i> (31), <i>B. Chitria</i> (32), <i>B. floribunda</i> (32), <i>B. jaeschkeana</i> (33), <i>B. lambertii</i> (33), <i>B. petiolaris</i> (34), <i>B. tinctoria</i> (32), <i>B. guimpeli</i> (36) |
| Columbamine[3] | <i>B. asiatica</i> (12), <i>B. vulgaris</i> (29), <i>B. floribunda</i> (32), <i>B. lambertii</i> (33) |
| Jatrorrhizine[4] | <i>B. asiatica</i> (12), <i>B. aristata</i> (10,26-27), <i>B. vulgaris</i> (29), <i>B. iliensis</i> (30), <i>B. chitria</i> (32), <i>B. Poiratii</i> (37-38), <i>B. floribunda</i> (32), <i>B. Himalaica</i> (32), <i>B. Lambertii</i> (33), <i>B. Tinctoria</i> (32), <i>B. Morrisonensis</i> (36) |
| Oxyacanthine[5] | <i>B. asiatica</i> (12), <i>B. aristata</i> (10,26-27), <i>B. Coriaria</i> (30), <i>B. Iliensis</i> (30), <i>B. koreana</i> (31), <i>B. Chitria</i> (32), <i>B. Floribunda</i> (32), <i>B. Lambertii</i> (33), <i>B. virescens</i> (33) |
| Berbamine[6] | <i>B. asiatica</i> [12], <i>B. aristata</i> [(10, 26-27)], <i>B. Vulgaris</i> (29), <i>B. Coriaria</i> (30), <i>B. Iliensis</i> (30), <i>B. Koreana</i> (31), <i>B. Poiratii</i> (37-38), <i>B. Floribunda</i> (33), <i>B. Jaeschkeana</i> (33), <i>B. lambertii</i> [28], <i>B. Petiolaris</i> (34), <i>B. Tinctoria</i> (32), <i>B. Mingetsensis</i> (35), <i>B. Morrisonensis</i> (36) |
| Baluchitine[7] | <i>B. lycium</i> (13, 28) |
| Aromoline[8] | <i>B. aristata</i> (10, 26-27), <i>B. Heteropoda</i> (131) |
| Oxyberberine[9] | <i>B. asiatica</i> (12), <i>B. aristata</i> |
| Tetrahydropalmatine[10] | <i>B. asiatica</i> (12) |
| Karachine[11] | <i>B. aristata</i> (39) |
| Taxilamine[12] | <i>B. aristata</i> (40) |
| Chenabine[13] | <i>B. lyceum</i> (40) |
| Punjabine[14] | <i>B. lycium</i> (13, 28) |
| Jhelumine[15] | <i>B. lyceum</i> (40) |
| Penduline[16] | <i>B. lycium</i> (13, 28), <i>B. coriaria</i> (30) |
| O-methylcorydine-N-Oxide[17] | <i>B. chitria</i> (32) |
| Gilgitine[18] | <i>B. lycium</i> (13, 28) |
| Baluchistanamine[19] | <i>B. lycium</i> (13, 28) |
| Sindamine[20] | <i>B. lyceum</i> (13, 28) |
| O-methylisothaliceberine[21] | <i>B. chilensis</i> (41), <i>B. laurina</i> (42) |
| 7-O-demethylisothaliceberine[22] | <i>B. chilensis</i> (40) |
| Oblongamine[23] | <i>B. oblonga</i> (51) |
| Espinine[24] | <i>B. laurina</i> (42) |
| Espinidine[25] | <i>B. laurina</i> (42) |
| Lauberine[26] | <i>B. laurina</i> (42) |
| Berberilaurine[27] | <i>B. laurina</i> (43) |
| Pakistanine[28] | <i>B. baluchistanica</i> (44) |
| (-)-O-methylarmepaine[29] | <i>B. laurina</i> (42) |
| (+)-N-methylisococlaurine[30] | <i>B. laurina</i> (42) |
| Pakistanamine[31] | <i>B. baluchistanica</i> (44), <i>B. julianae</i> (45) |
| Baluchistamine[32] | <i>B. baluchistanica</i> (46,47) |
| Quettamine[33] | <i>B. baluchistanica</i> (48) |
| Gandharamine[34] | <i>B. baluchistanica</i> (49) |
| Oblongine[35] | <i>B. oblonga</i> (50) |

| | |
|--------------------------------|--------------------------------|
| Calafatine[36] | <i>B. buxifolia</i> (52) |
| Calafatimine[37] | <i>B. buxifolia</i> (53) |
| Kalashine[38] | <i>B. orthobotrys</i> (54, 55) |
| Chitraline[39] | <i>B. orthobotrys</i> (54, 55) |
| Khyberine[40] | <i>B. calliobotrys</i> (56) |
| Puntarenine[41] | <i>B. empetrifolia</i> (57) |
| Coyhaiquine[42] | <i>B. empetrifolia</i> (58) |
| Natalinine[43] | <i>B. empetrifolia</i> (59) |
| Santiagonamine[44] | <i>B. darwinii</i> (60) |
| Aconcaguine[45] | <i>B. actinacantha</i> (61) |
| (+)-Epiberbaldine[46] | <i>B. actinacantha</i> (62) |
| (+)-Rupancamine[47] | <i>B. actinacantha</i> (62) |
| Dehydropuntarenine[48] | <i>B. actinacantha</i> (63) |
| Dehydrosaulatine[49] | <i>B. actinacantha</i> (63) |
| Hediamine[50] | <i>B. actinacantha</i> (63) |
| Waziristanine[51] | <i>B. waziristanica</i> (64) |
| Bernumidine[52] | <i>B. nummularia</i> (65) |
| Bernumicine[53] | <i>B. nummularia</i> (65, 66) |
| Intebrinine[54] | <i>B. integerrima</i> (67) |
| Intebrimine[55] | <i>B. integerrima</i> (67) |
| Berpodine[56] | <i>B. heteropoda</i> (67) |
| Turconidine[57] | <i>B. turcomanica</i> (69) |
| Ilicifoline[58] | <i>B. ilicifolia</i> (70) |
| Densinine[59] | <i>B. densiflora</i> (71) |
| Densiberine[60] | <i>B. densiflor</i> (71) |
| Epiberberine[61] | <i>B. floribunda</i> (32) |
| Lambertine[62] | <i>B. lambertii</i> (33) |
| Tetrandrine[63] | <i>B. petiolaris</i> (34) |
| Isotetrandrine[64] | <i>B. morrisonensis</i> (36) |
| Obaberine[65] | <i>B. tschonokiana</i> (72) |
| Magnoflorine[66] | <i>B. morrisonensis</i> (36) |
| N-methyl-dihydro berberine[67] | <i>B. heteropoda</i> (68) |
| 8-oxoberberubine[68] | <i>B. heteropoda</i> (68) |
| 1-O-methylpakistanine[69] | <i>B. aristata</i> (122) |
| Pseudopalmitine chloride[70] | <i>B. aristata</i> (122) |
| Pseudoberberine chloride[71] | <i>B. aristata</i> (122) |

Table 2: Flavanoids from various *Berberis* species

| Phytoconstituents | Species |
|--------------------------------|---------------------------|
| Luteolin[72] | <i>B. gagnepaini</i> (73) |
| 3-isorhamnetin galactoside[73] | <i>B. gagnepaini</i> (73) |
| Hyperoside[74] | <i>B. gagnepaini</i> (73) |
| Rutin[75] | <i>B. gagnepaini</i> (73) |
| Quercitinside[76] | <i>B. gagnepaini</i> (73) |

Table 3 : Anthocyanins from *Berberis* species

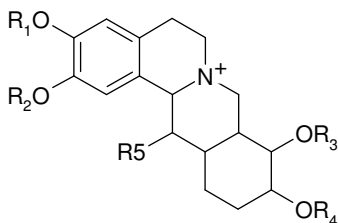
| Phytoconstituents | Species |
|---|---|
| Peonodin[77] | <i>B. vulgaris</i> (74) |
| Cyanidin[78] | <i>B. vulgaris</i> (74) |
| Delphinidin[79] | <i>B. vulgaris</i> (74) |
| Leonidin-3-glucoside[80] | <i>B. Buxifolia</i> (75) |
| Leonidin-3-rutinoside-5-glucoside[81] | <i>B. buxifolia</i> (75) |
| Malvidin-3-rutinoside[82] | <i>B. buxifolia</i> (75) |
| Malvidin-3-glucoside[83] | <i>B. buxifolia</i> (75), <i>B. darwinii</i> (77) |
| Petunidin-3-rutinoside[84] | <i>B. buxifolia</i> (75), <i>B. darwinii</i> (77) |
| Petunidin-3-glucoside[85] | <i>B. buxifolia</i> (75), <i>B. Darwinii</i> (77), <i>B. Oblonga</i> (78) |
| Petunidin-3-gentibioside[86] | <i>B. buxifolia</i> (75), <i>B. darwinii</i> (77) |
| Petunidin-3-rutinoside-5-glucoside [87] | <i>B. buxifolia</i> (75) |
| Delphinidin-3-rutinoside[88] | <i>B. buxifolia</i> (75), <i>B. darwinii</i> (77) |
| Delphinidin-3- glucoside[89] | <i>B. buxifolia</i> (75), <i>B. oblonga</i> (78) |
| Pelargonidin-3-glucoside[90] | <i>B. thunbergii</i> (76), <i>B. oblonga</i> (78) |
| Cyanidin-3- glucoside[91] | <i>B. thunbergii</i> (76), <i>B. oblonga</i> (78) |
| Peonodin-3-glucoside[92] | <i>B. darwinii</i> (77) |
| Delphinidin-3- diglucoside[93] | <i>B. oblonga</i> (78) |
| Cyanidin-3- diglucoside [94] | <i>B. oblonga</i> (78) |

Table 4 : Carotenoids and vitamins from *Berberis* species

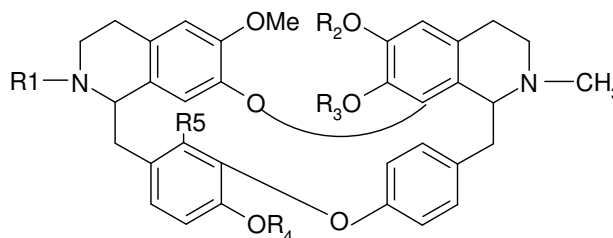
| Phytoconstituents | Species |
|------------------------|--|
| α -Carotene[95] | <i>B. vulgaris</i> (79), <i>B. spp.</i> Fruits(80) |
| β -Carotene[96] | <i>B. vulgaris</i> (79), <i>B. spp.</i> Fruits(80) |
| Lutein[97] | <i>B. vulgaris</i> (79), <i>B. spp.</i> Fruits(80) |
| Zeaxanthin[98] | <i>B. vulgaris</i> (79), <i>B. spp.</i> Fruits(80) |
| Chryanthaxanthin[99] | <i>B. vulgaris</i> (79) |
| Flavoxanthin[100] | <i>B. vulgaris</i> (79), <i>B. spp.</i> Fruits(80) |
| Auroxanthin[101] | <i>B. vulgaris</i> (79) |
| Capsanthin[102] | <i>B. vulgaris</i> (79), <i>B. spp.</i> Fruits(80) |
| Phytofluene[103] | <i>B. spp.</i> Fruits(80) |
| Antheraxanthin[104] | <i>B. spp.</i> Fruits(80) |
| cis-Mutatoxanthin[105] | <i>B. spp.</i> Fruits(80) |
| Ascorbic acid[106] | <i>B. nummularia</i> (81), <i>B. Oblonga</i> (81), <i>B. Heteropoda</i> (81), <i>B. Vulgaris</i> (81), <i>B. Dasystachya</i> (82), <i>B. Craetiegina</i> (84), <i>B. Dielsiana</i> (83), <i>B. Integerrima</i> (81), <i>B. Sibirica</i> (81) |

Table 5 : Phenolic compounds from *Berberis vulgaris*

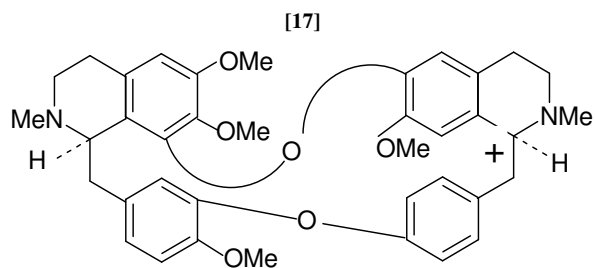
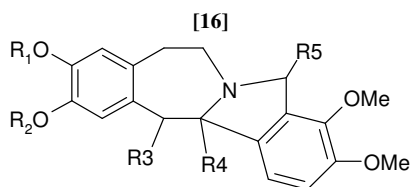
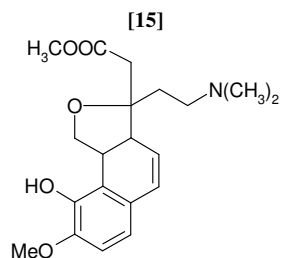
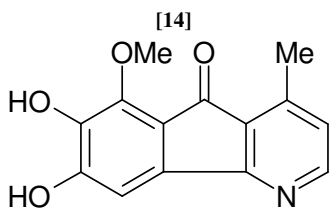
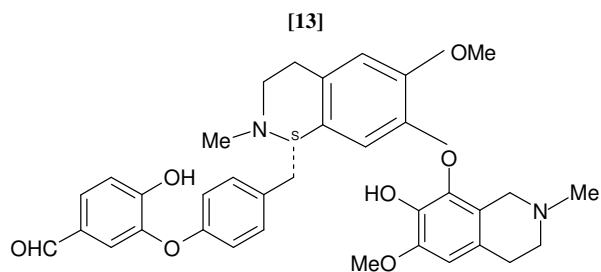
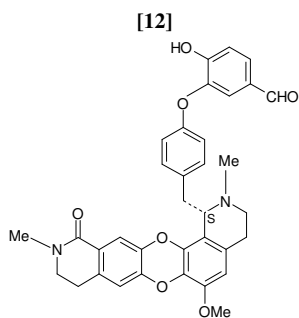
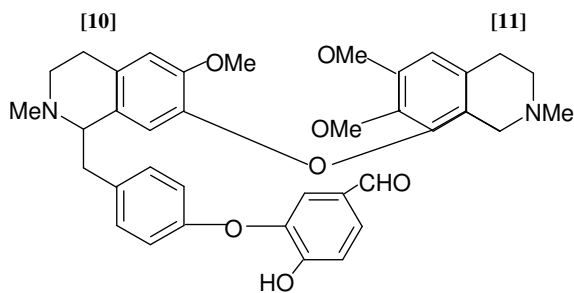
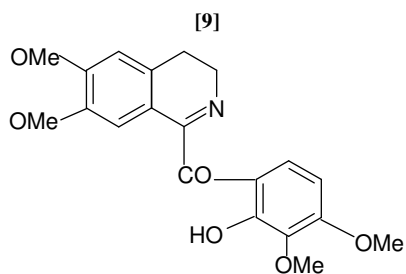
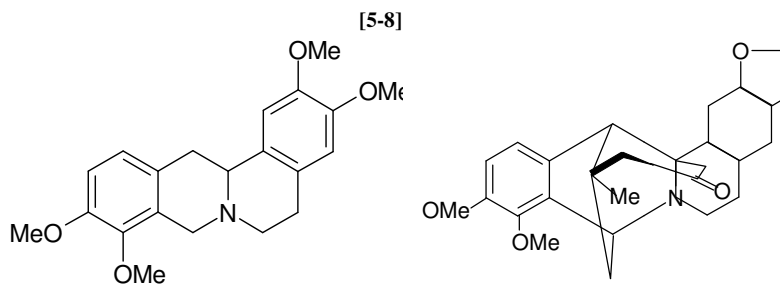
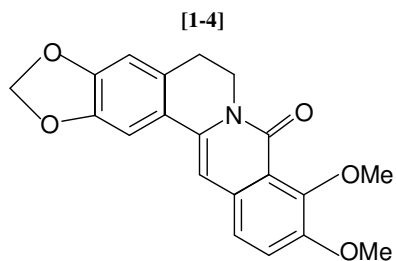
| Phytoconstituents | Species |
|-------------------------------------|--------------------------|
| N-(p-trans-Coumaroyl) tyramine[107] | <i>B. vulgaris</i> (121) |
| Cannabisin G[108] | <i>B. vulgaris</i> (121) |
| (\pm) - Lyonirosinol[109] | <i>B. vulgaris</i> (121) |



1. $R_1+R_2=CH_2$; $R_3=R_4=CH_3$; $R_5=H$
2. $R_1=R_5=H$; $R_2=R_3=R_4=CH_3$
3. $R_1=R_3=R_4=CH_3$; $R_2=R_5=H$
4. $R_1=R_2=R_3=R_4=CH_3$; $R_5=H$



5. $R_1=R_2=R_3=R_4=CH_3$; $R_5=H$
6. $R_1=R_2=CH_3$; $R_3=R_4=R_5=H$
7. $R_1=R_2=R_3=CH_3$; $R_4=R_5=H$
8. $R_1=R_2=CH_3$; $R_3=R_4=R_5=H$

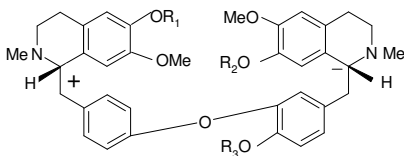
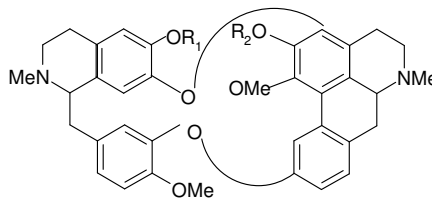


[18] $R_1+R_2=CH_3$; $R_3=R_5=O$; $R_4=OH$

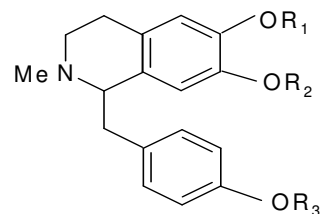
[19] $R_1=R_2=CH_3$; $R_3=R_5=O$; $R_4=OH$

[20] $R_1=R_2=CH_3$; $R_3=R_5=O$; $R_4=H$

[21]

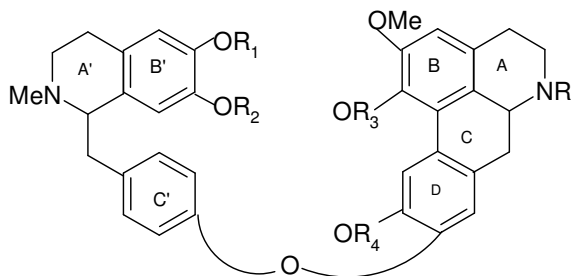


- la - R₁=R₂=R₃= H
- lb - R₁=R₂=R₃= Me
- lc - R₁=R₂=R₃= Et
- ld - R₁=R₂= H, R₃= Et
- le - R₁=R₂= Et, R₃= Me

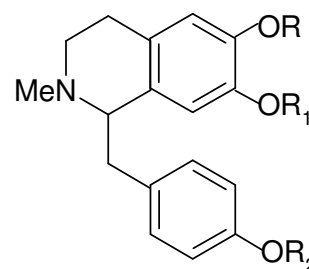


- IIa R₁= Et, R₂= Me, R₃= H
- IIb R₁= Me, R₂=R₃= Et
- IIc R₁= Me, R₂= Et, R₃= Me

- [22] R₁=R₂=R₃=CH₃
- [23] R₁=R₂=CH₃ ; R₃=H

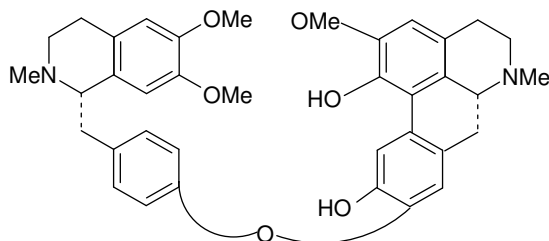


- [26] R₁=R₂=R₃=R= CH₃ ; R₄= H
- [27] R₁=R₂=CH₃ ; R₃=R₄=R=H
- [28] R₂=R₃=R₄=H ; R=CH₃

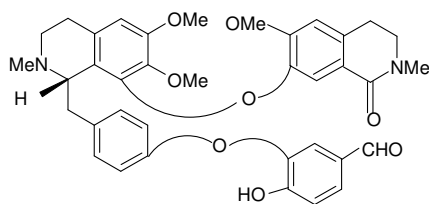


- [29] R=R₁=R₂=Me
- [30] R=R₂= H, R₁= Me
- [29-30]

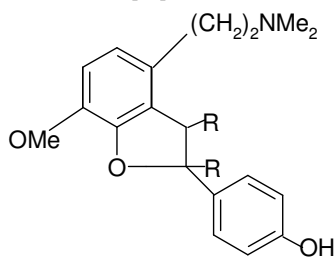
[26-28]



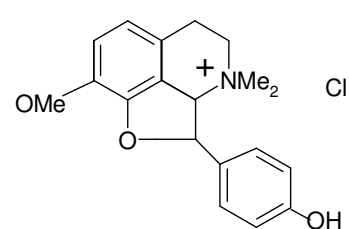
[31]



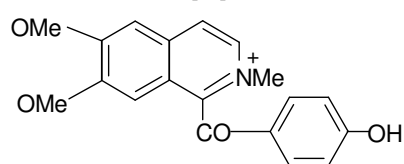
[32]



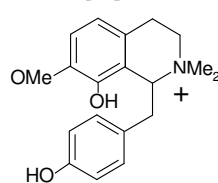
[33] - I



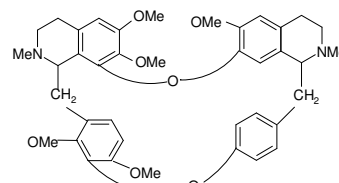
II



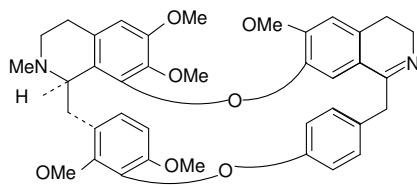
[34]



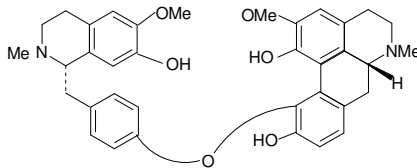
[35]



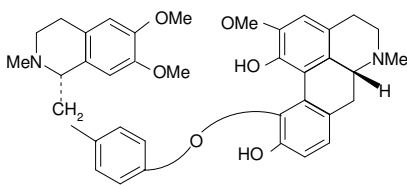
[36]



[37]

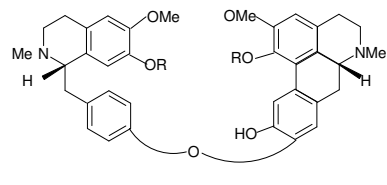


[38]

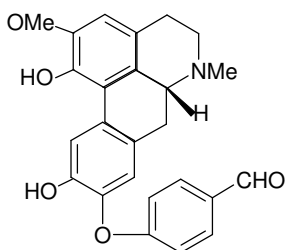


R=H

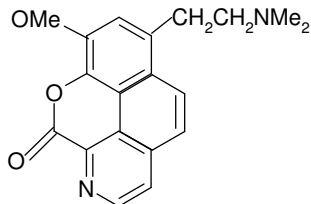
[39]



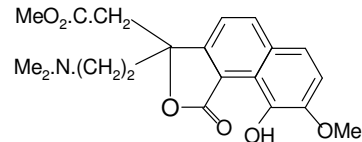
[40]



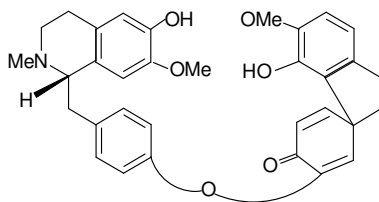
[41]



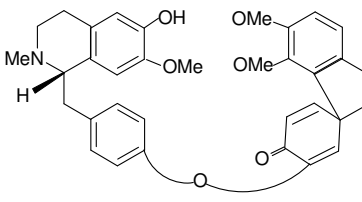
[42]



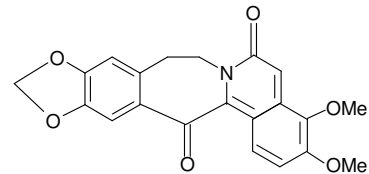
[43]



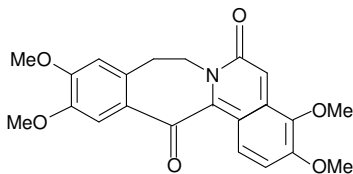
[44]



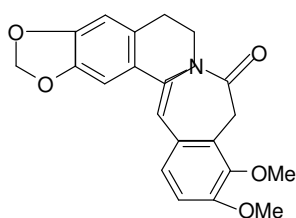
[45]



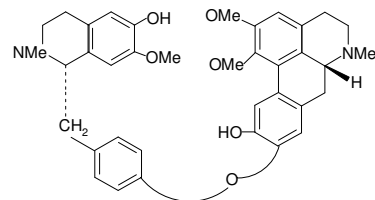
[46]



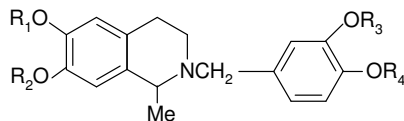
[47]



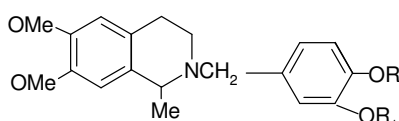
[48]



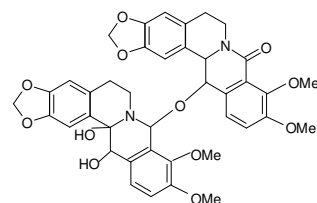
[49]



[50]



[51]



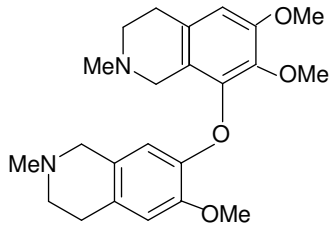
[52] ($R_1 = R_2 = \text{Me}, R_3, R_4 = \text{CH}_3$)

[53] ($R_1 = \text{H}, R_2 = R_3 = R_4 = \text{CH}_3$)

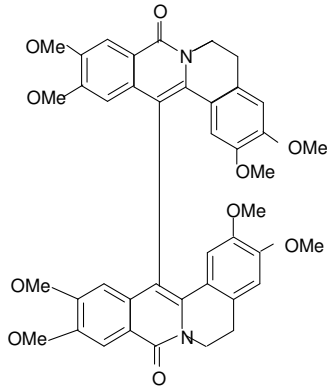
[54] $RR_1 = \text{CH}_2$

[55] $R = R_1 = \text{CH}_3$

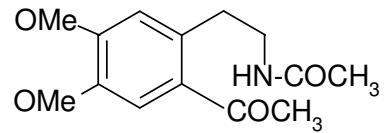
[56]



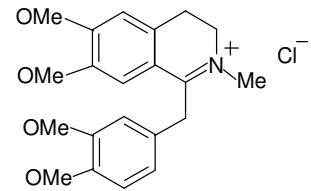
[57]



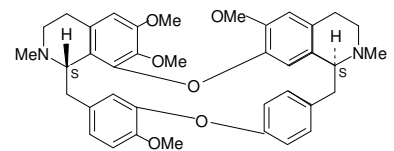
[58]



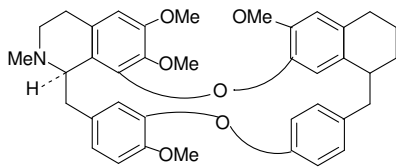
[59]



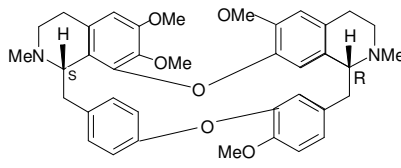
[60]



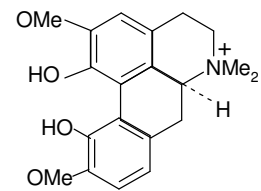
[61]



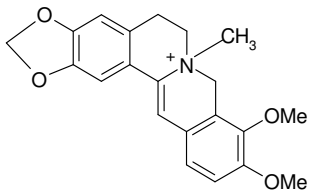
[62]



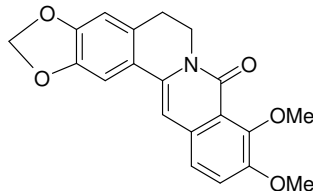
[63]



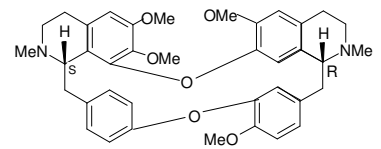
[64]



[65]



[66]

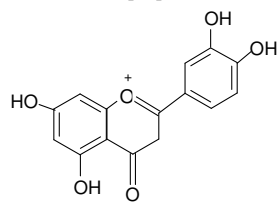


[67]

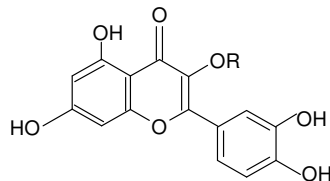
[70] Pseudopalmatine chloride

[71] Pseudoberberine chloride

[68]



[72]



R=Rhamnose

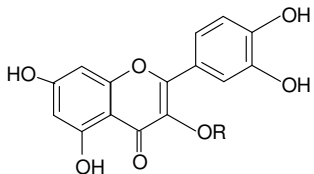
[76]

[69]

[73] 3-isorhamnetin galactoside

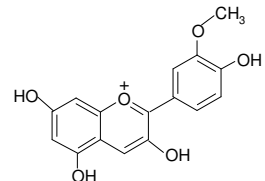
[69]

[73] 3-isorhamnetin galactoside

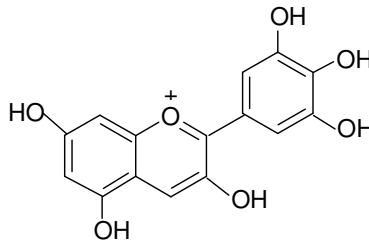
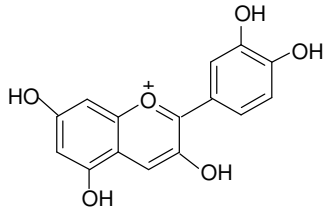


[74] R= Galactose

[75] R = Glucose⁶-Rhamnose

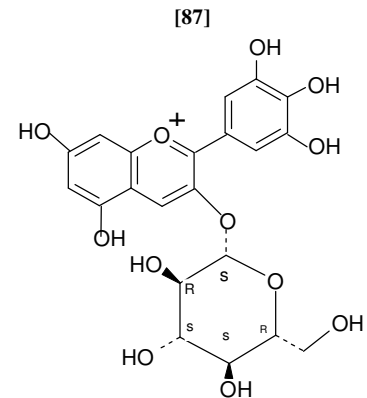
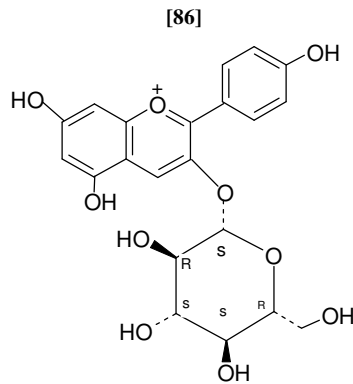
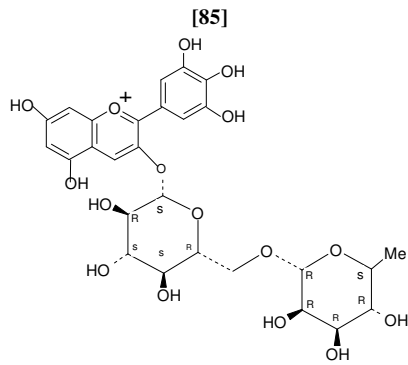
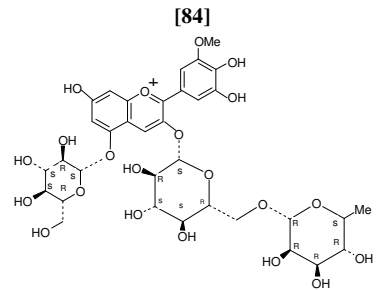
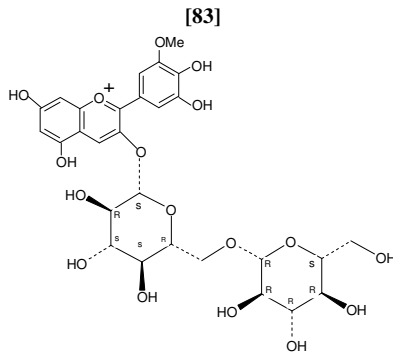
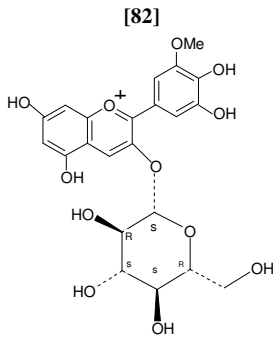
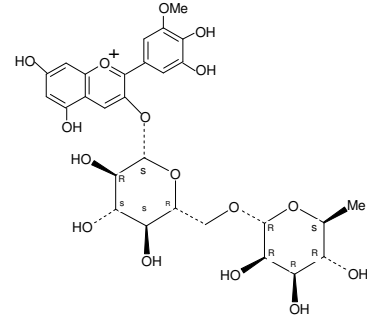
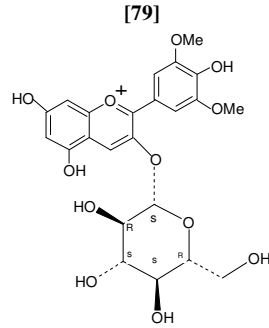
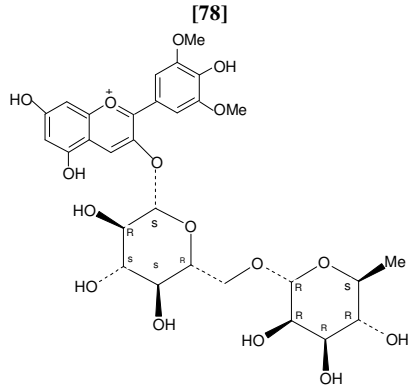


[77]



[80] Leonidin-3-glucoside

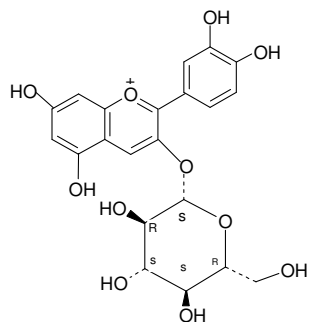
[81] Leonidin-3-rutinoside-5-glucoside



[88]

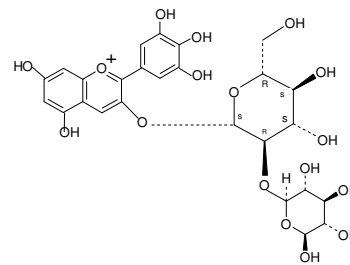
[89]

[90]



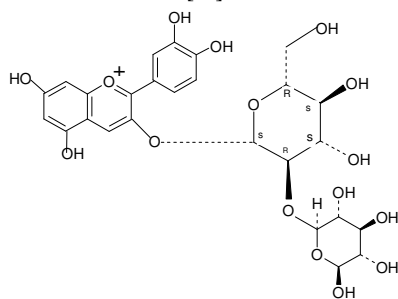
[91]

[92] Peonodin -3-glucoside

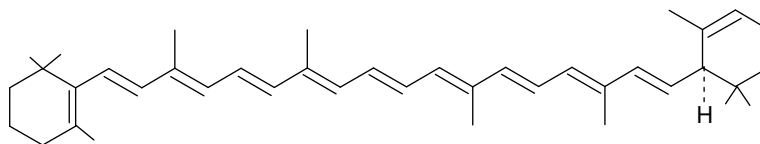


[92]

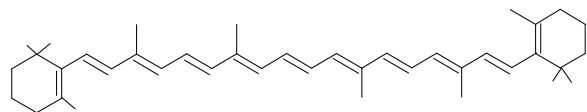
[93]



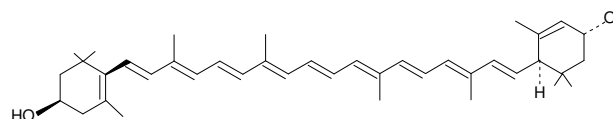
[94]



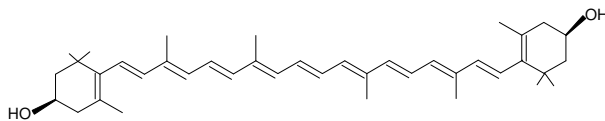
[95]



[96]

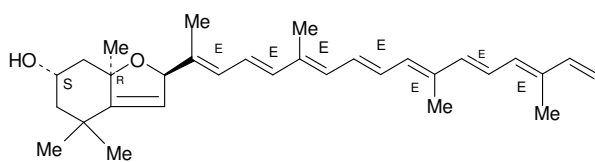


[97]

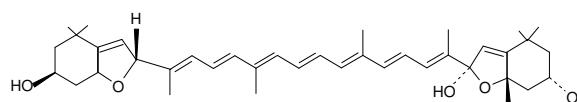


[98]

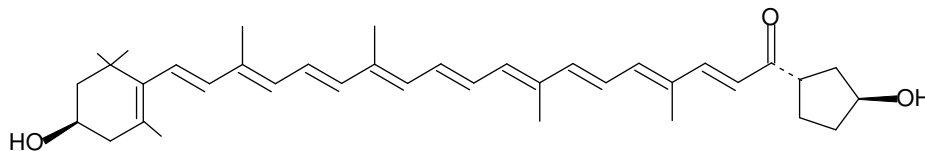
[99] Chrysantheraxanthin



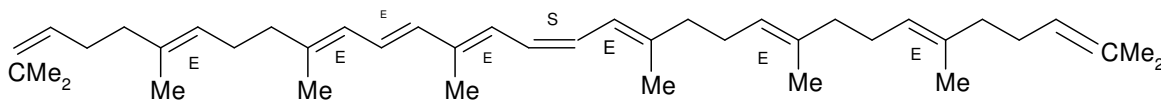
[100]



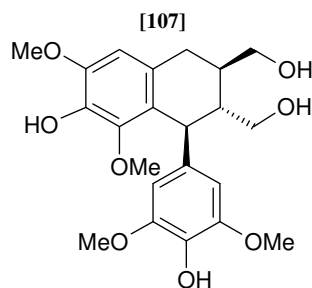
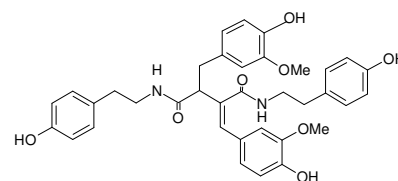
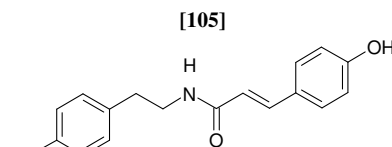
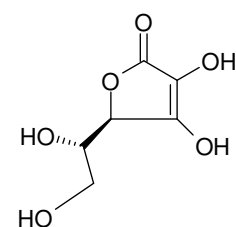
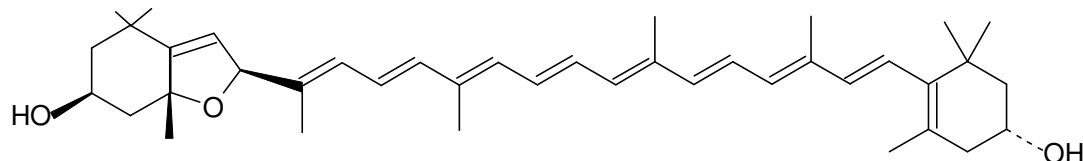
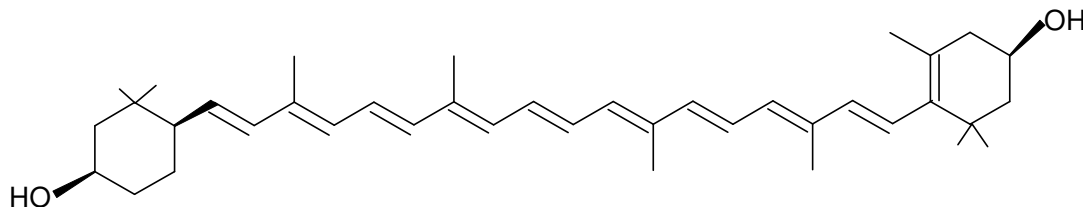
[101]



[102]



[103]



inflammatory, antimicrobial and anti-tumour (86-91). It has been used in traditional eastern medicine for more than 2 millennia in the treatment of bacterial or secretory diarrhea and gastroenteritis (92-93). Its therapeutic benefits have been attributed in part to antimicrobial (94) and antisecretory actions (95-96). In addition, the inhibitory action of berberine on cyclooxygenase-2 has been demonstrated (97-98). Its synthetic derivative dihydroberberine is used in brain tumour (2). Berberine displays beneficial effects in the treatment of diabetes and obesity at least in part via stimulation of AMPK activity (99).

Miura *et al.*, 1997 (100) reported the inhibitory action of berberine on apoptosis and Ckless *et al.*, 1995 (101) reported the inhibition of *in vitro* lymphocyte transformation by berberine. The lipoxygenase inhibition and antioxidant properties of berberine have also been reported by Misik *et al.*, 1995 (102). The administration of berberine markedly reduced the inflammation in rats with TNB-induced colitis, as verified by effects on macroscopic and histological damage and MPO activity (103). It also showed depressant action on the isolated rabbit heart and auricles which is not opposed by

atropine. Intra-veinal administration of 5mg/ kg and 10mg/ kg doses of berberine to dogs produce an acute fall in blood pressure followed immediately by a gradual recovery to initial level of blood pressure. The blood pressure fall is accompanied by cardiac depression (104). The lethal dose [LD₅₀] of berberine isolates in humans is thought to be 27.5mg/kg. It is absorbed slowly orally and achieves peak concentration in 4hrs. and take 8hrs. to clear (105). Berberine is excreted in urine and human studies of berberine shows that it can be absorbed through skin. In humans it can cause blocking of receptors in smooth muscles, blocking potassium channels in the heart and reducing ventricular tachycardia, inhibiting intestinal secretion and toxin formation in the gut and increasing bile secretion (106). Inhibition of MDR efflux causes a substantial increase in berberine antimicrobial activity, suggesting that berberine and potentially many other compounds could be more efficacious if an effective MDR pump inhibitor could be identified (107). Effect of some of the alkaloid in the root and bark of the stem of *B. aristata* was studied. The crude extract (1% solution) was administered to dogs in the concentration of 1, 5, 10 and 20

mg /kg and was examined before and after 30 minutes application. Treatment with 20 mg/ kg produced 100% mortality. The preparation increased the time of coagulation and tolerance of plasma to heparin, prothrombin and thrombin times and slightly influenced the contents of fibrinogen, prothrombin and factor V (108-109). Berberine shows positive inotropic action on amphibian heart and has a stimulant action on the peripheral circulation. O-methyl-isothalic berine (OMI) is a bisbenzyl isoquinoline alkaloid isolated from *B. chilensis* caused a significant reduction of mean arterial pressure (MAP) in normotensive anaesthetized rats (110). The total alkaloids from *B. integerrima* leaves had weak hypotensive and peripheral adrenolytic effects in cats, stimulated rats and guinea pig uterine muscle tonus. The specific alkaloids berbamine and obaberine did not have adrenolytic effects. Berbamine had a spasmolytic effect on rabbit intestinal musculature while obaberine has a much weaker spasmolytic effect and anti-inflammatory activity in rats (111). Many bisbenzylisoquinolines are isolated from *Berberis* as their major constituents. The anti-inflammatory and immunosuppressive activity of the bisbenzylisoquinolines berbamine, tetrandrine and chondocurine is well established (91).

Berbamine has been isolated from several *Berberis* species and was tested *in vitro* against both a chloroquine-resistant and a chloroquine-sensitive strain of *P. falciparum* and its effect when used in combination with chloroquine and artemisinin. It was found active against both the resistant and sensitive strains of *P. falciparum*. Pharmacological studies demonstrated that berbamine possess significant leukogenic effects in rats and dogs injured by an anticancer agent and clinical observation demonstrated a therapeutic effect on patients with leukopenia. Berbamine also potentiated the antitumour action of cyclophosphamide in rats (112). *B. aristata* leaves seems to preserve the structural integrity of the hepato-cellular membranes which is evident by a significant reduction in acetaminophene induced rise in serum alkaline phosphatase, GOT and GPT levels (113). The stem/root is one of the constituents of a polyherbomineral formulation, D-400 with known antidiabetic action, which shows a significant reduction in blood urea, nitrogen, serum creatinine and serum uric acid levels in streptozotocin-induced diabetic rats and considerable lowering of AUC in oral glucose tolerance test (OGTT). The D-400 treated group also showed significant lowering of triglycerides and HDL cholesterol (114). Berberine chloride and tincture of berberine were tested by the agar diffusion and liquid-dilution methods against a number of microbial species. There was a marked inhibitory activity against *Candida* species (115).

Berberine isoquinoline alkaloid is composed of a planar aromatic cationic centre that is thought to be the primary pharmacophore responsible for both antibacterial activity and recognition by efflux proteins in microbial cells, rendering them ineffective against efflux-resistant pathogens. Stermitz *et al.* identified a potent efflux proteins inhibitor from the extract of the leaves of *B. ferromontii* as 5'-methoxyhydnocarpin (5'-MHC), a flavonoid derivative which

potentiates the activity of compounds that were typical NorA efflux substrates, berberine, ethiotiumbromide, tetraphenyl phosphonium ion, pentamidine, benzaalkonium chloride and palamate (116). Kazunori Fukuda *et al.*, 1999 also found that berberine effectively inhibits COX-2 transcriptional activity in colon cancer cells in a dose and time dependent manner at concentrations higher than 0.3µm (117). Multiple bacteria and fungi along with selected protozoa and Chlamydia are susceptible to berberine *in vitro* (118). The alcoholic and water extract of *B. chitria* roots were screened for their antimicrobial properties against five micro-organisms (*E. coli*, *S. aureus*, *B. proteus*, *S. typhii* and *P. pyocyanase*). The alcoholic extract was found to be a better microbial agent than the water extract and effectiveness of which was compared with standard antibiotics (119). Berberine sulfate obtained from the rhizome cortex of *B. vulgaris* showed bactericidal activity and at 50-600 µg /ml of culture medium inhibited the growth of 70 % of 196 strains of *Staphylococcus aureus*. Strains resistant to berberine sulfate were usually more active biochemically and belong mainly to bacteriophage group IV. Cross-resistance between berberine sulfate and antibiotics used in therapy was not observed except with streptomycin (120). Two phenolic compounds Cannabisin G and (l)-Lyoniresinol isolated from *B. vulgaris* showed antioxidant activity. Further it was found that Cannabisin G showed cytoprotective activity in cultured MCF-7 cells modulated by hydrogen peroxide (122).

CONCLUSION

The present review describes the usefulness of *Berberis* genus which has a great impact with regard to multidirectional pharmacological applications in indigenous system of medicine. Moreover, species of *Berberis* genus are rich sources of a variety of organic compounds of varying structural patterns and due to their natural distribution are thus highly relevant not only for medicinal but also for chemotaxonomic studies.

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