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Review Article

GYMNOSPORIA MONTANA, A POTENTIAL HEPATOPROTECTIVE AND ANTICANCER DRUG – AN OVERVIEW

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ABSTRACT

Gymnosporia montana (known as Vikro), occurring throughout the arid, dry areas of India, is traditionally claimed to be useful in various ailments. In the present communication the details of the plant like taxonomic position, distribution, ecology, traditional uses, folklore claims,pharmacognosy, chemistry and pharmacology has been reviewed. It has great potential as hepatoprotective and anticancer drug.

Keywords: *Gymnosporia,* Vikro, Pharmacognosy, Chemistry, Hepatoprotective, Anticancer

INTRODUCTION

In Indian floras, the genus *Maytenus molina* (family : Celastraceae) goes under the name of *Gymnosporia* (Wt. & Arn.) Benth. & Hook. F. Two hundred species have been reported of which about 15 are available in India[1]. Flora of British India[2] mentions 16 species of Gymnosporia- *G. acuminate*, Hook. F., *G . neglecta*, Wall. Cat., *G. salicifolia*, Laws., *G. oblanceolata*, Laws., *G. puberula*, Laws., *G. fruticosa*, Thwaites Enum., *G.ovata*, Wall. Cat., *G.rothina*, W & A., *G. regulosa*, Laws., *G. heyneana*, W&A., *G. falconeri*, Laws., *G. rufa*, Wall., *G. royleana*, Wall. Cat. *G. wallichiana*, Sprenz, Syst., *G. emarginata*, Roth. Nov. and *G. montana*, Roxb.

Gymnosporia Montana (FIG.1) is a much branched, spinescent shrub or small tree, occurring throughout the arid, dry areas of India. Its systematic taxonomic position is as follows:

Kingdom	:	Plant
Division	:	Sprematophyta
Sub-division	:	Angiospermae
Class	:	Dicotyledoneae
Sub Class	:	Polypetalae
Group	:	Disciflorae
Order	:	Celastrales
Family	:	Celastraceae
Genus	:	*Gymnosporia* (Wt. & Arn.) Benth & Hook. f.
Species	:	montana
Plant's Name	:	*Gymnosporia montana* (Roth.) Benth.
Syn.	:	*Maytenus emarginata* (Willd.) D.Hou.

Regional Names[3]

Ajmere	:	Kakra.
Bengal	:	Vaichigachha
Bhil	:	Dhatti.
Bombay	:	Hurmacha, Malkangoni, Zekadi.
Canarese	:	Halumanike, Malegu, Malkanguni,Tandraja.
Central Provinces	:	Baikal, Gajachinni
Gujarati	:	Vikalo, Vikro.
Hindi	:	Baikal, Kngani, Tondarsaijhad.
Marathi	:	Bharatti, Bharuli, Vekal, Vekar, Yekkadi.
Porbandar	:	Vikaro.
Punjab	:	Dajkar, Kharai, Kingaro, Mareila, Talkar.
Sanskrit	:	Bahuphala, Brahmapadapa, Dantakashta, Gopaghantha, Granthila, Himaka, Kantakari, Kantaki, Kantapada, Kantapatra, Kinkari, Madhuparni, Mriduphala, Padarohina, Pindara, Prithubija, Putakinkani, Ravana, Sragdaru, Sruvadrum, Sruvavriksha, Sudhavriksha, Svadukanta, Vaikankata, Vikankata, Vritinkar, Vyaghrapada, Yadnavriksha, Yadniya.
Tamil	:	Kattanji
Telugu	:	Dantausi, Danti, Gajasinni, Gechangi, Peddachintu, Peddadanta, Sinni.
Uriya	:	Gourokasa.

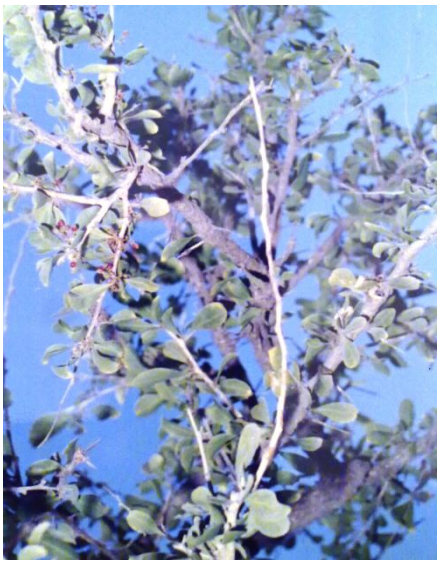

Fig 1: *Gymnosporia Montana* Plant

Distribution[3]

Throughout the arid, dry areas of India. Punjab, Sind, W.Rajputana, Gujarat, Khandesh, W.Peninsula, Deccan, C.Provinces, Afghanistan, Arabia, Mediterranean,Tropical Africa, Malaya, Australia.

Ecology and propagation[4]

The plant grows at elevations from near sea level, on the coast on sand, at forest margins, hillsides and on sea cliffs, often on limestone. Long, hot summers are needed for production of flowers and fruits.

It is an out breeding tree and shows great variability. Seeds can be sown under glass in autumn and semi-ripe cuttings of root with bottom heat in summer.

The plant grows in moderately fertile, moist but well-drained soil in full sun with midday shade.

Flowers appear in October to January, fruiting during January - February and fruit ripens in March to April; develops new leaves from June to August.

Properties and uses

In several Ayurvedic literatures like Bhavprakash[5], Nighantu Adarsh[6], Shaligram Nighantu[7], Vanaspati Shrusti[8], Aryabhishek[9], Shankar Nighantu[10], Vanaspati Chandrodaya[11], the plant has been mentioned for various uses. It is claimed to be useful in jaundice[3,6,7], inflammation and rheumatic pain[3,6-9,11,12], corneal opacity[6,9,10,12], ulcers, gastrointestinal disorders, dysentery, toothache and also as a vermifuge[3,13].

According to Shaligram Nighantu it is used in jaundice, inflammation and to cure blood disorders. Nighantu Adarsh mentions its use in kamla (jaundice). In Vanaspati Srusti the use of ripe fruit has been mentioned as blood purifier and antinflammatory. Leaf juice is used in pandu (anaemia) and used as an eye drop to cure corneal opacity. Bark is used to kill lice and in other infection on the head. The use of leaf juice in eye diseases particularly in opacity of cornea, inflammation and burning sensation has been mentioned in Aryabhishek. In Vanaspati Chandradaya the use of root pulp in rheumatic pain while gum, along with other medicines, in cholera has been advocated. Kirtikar and Basu[3] mention the fruit as appetizing and digestive and its use in jaundice and enlarged spleen. Ground seeds with turmeric are recommended to be rubbed all over the body to prevent rheumatic pain from exposure to damp winds. The external application of dry powdered leaves with a little mustered oil has shown encouraging result in rickets [14].

In Saurashtra region of Gujarat, India, the leaf juice is well known for curing jaundice[15]. Extract of leaves mixed with cow milk is taken in the morning for 3 days by the local people of Bhadra (Karnataka, India) for curing jaundice[16]. The root bark is reported to be useful in dysentery[17].

PHARMACOGNOSY

A large glabrous, woody shrub or sometimes a small tree, having young branches-reddish to purple in colour and often spinescent at the extremities, bearing leaves and flowers.

Flowers **–** Flowers are small, white, numerous, axillary. Calyx having five lobes, broadly elliptic, oblong, rounded at the apex; petals five, about 3 mm long, elliptic-oblong, white in colour; stamens five.

Fruit **–** Fruits are purple or nearly black when ripe. Two to three valved, globuse capsule as large as a small pea about 6-7 mm in diameter, 1–3 celled and 1-2 seeds are found in each cell.

Seeds are brown, arillus white, fleshy, covering the whole seed, cotyledons green and fleshy.

De et al.[18] have reported the pharmacognostic characters of *Gymnosporia montana* leaf and stem. The salient features are highlighted.

Morphology

Leaf **–** Leaves are simple, alternate or clustered, found in the axils of spines, on the spines or on small branches; sub-sessile, glabrous and exhibit a vast degree of polymorphism in their shape. Leaves are 3-8 cm long and 1-3 cm broad, apex acute, mucronate or obtuse, margin entire in the lower half and crenulate in the upper half.

Stem **–** Stems are purplish brown in colour, hard; straight, pointed and hard spines, which are modified branches with single node from which leaf originates. Bark is thin with fine longitudinal wrinkles on the outer surface and creamy white inner surface.

Microscopy

Leaf- T.S. of lamina through mid-rib shows more or less isobilateral structure; upper epidermis is double layered with round to rectangular cells, covered by a thick, striated cuticle with few stomata; lower epidermis is also biseriate with waxy cuticle and more number of stomata; two layers of palisade parenchyma in both upper and lower regions of leaf showing profuse deposits of yellowish black coloured matter and cluster crystals of calcium oxalate. In mid-rib region single layered epidermis followed by 3-4 cell layers of collenchymatous tissue on either surface and parenchymatous cells containing simple starch grains without hilum and rosettes and cluster crystals of calcium oxalate. Vascular bundle in the mid-rib is crescent shaped, conjoint, collateral and surrounded by a broken ring of sclerenchymatous pericyclic fibres. Xylem vessels are narrow and xylem fibres are small, angular, radially arranged and also contain colouring matter. Phloem, consisting of sieve tubes, companion cells and phloem parenchyma, is in the distinct curved arm of the vascular bundle. Phloem fibres are absent.

Quantitative Microscopy[15] – The average stomatal index in upper and lower leaf surface are 8.12 and 10.31 respectively and the palisade ratio is 2 to 5.

Stem

The transverse section of young stem exhibits nearly continuous, sclerenchymatous pericyclic fibres, single narrow xylem vessels, uniseriate medullary rays and big isolated, prismatic, squarish and rhomboidal calcium oxalate crystals. Dark colouring material is deposited in most of the cells.

Older stems show annular rings in which xylem vessels towards pith are much compressed, compact and narrow.

Recently Dhru et. al.[19,20] have also reported the similar pharmacognostic characters of the leaf and stem of *G. montana*.

CHEMISTRY

Several sesquiterpene pyridine alkaloids like emarginatine A, B, E, F, G and a sesquiterpene ester, celahin B, have been reported from the family Celastraceae[4,21-23]. Number of compounds, with varied chemical nature, have been reported by several workers from different parts of *Gymnosporia montana* (FIG.2).

Leaves

Several compounds viz. tingenone, 3-O-acetyloleanolic acid, hexacosane, hexacosanol, n-triacontanol, betulin, β -amyrone, β-amyrin, δ-amyrin, β –sitosterol, celacinnine and kaempferol have been isolated[24-27] from the leaves of *G. montana*. Presence of Galactose as free sugar and seven free amino acids including arginine, glutamic acid, alanine, proline, γ-aminobutyric acid have also been reported by De et al [15]. The same group has also reported [28] the presence of seven fatty acids, of which palmitic acid is the major one (72.03%), in the leaf.

Stem

Joshi et al. [24, 29] have reported isolation of iguesterin, pristimerin, tingenone, β -amyrin, β -sitosterol and maytenonic acid from the stem. It is also reported [30] to contain sesquiterpene pyridine alkaloid Emarginatine B and maytansine. Presence of β –amyrin has also been supported by Anjaneyulu and co-workers [31].

Root

Iguesterin, pristimerin, tingenone, β -amyrin, and β –sitosterol have been isolated by Joshi et. al[24,29] . Satyanarayana and his team[32] have isolated dukidol and β –amyrin whereas Akshaya Kumar et. al.[25] have reported presence of (-)epigallocatechin, Emarginatine A[33] and Emarginatine G[22], two other sesquiterpene pyridine alkaloids have also been isolated from this plant.

Several compounds have been isolated from other species of Gymnosporia (Maytenus). Presence of β -amyrin from the roots of *G. ovata* Laws[34], Maytansine from *G .diversifolia* (Gray) Maxim[35], sesquiterpenes from *M. chubutensis*[36], *M.* disticha[37] and *M.* canariensis[38], triterpenoids – maitenin, pristimerin, 22-hydroxy maitenin, rigidenol and nepetricin, as well as (-) 4'-O-methyl-epigallo catechin, proanthocyanidin-A and dulcitol from the roots of *M.*evonymoides[39] and triterpene quinone-methides, lupenone, β-amyrin, dulcitol, sitosterol from the timber, root and leaf extracts of *Gymnosporia emarginata* have been reported[40].

Data of extractive values and other preliminary phytochemical analysis of *G. Montana* leaf and stem samples are available [15, 19, 20]. The ash value of leaf and stem are 9.6 – 12.5% and 7.9% w/w respectively. The extractive values with petroleum ether, methanol / alcohol and water of leaf were 5.1-6.5%, 10.5-12.1% and 14.5% w/w respectively while that of stem were 5%, 10.3% and 9% w/w respectively. Both leaf and stem showed the presence of alkaloid, flavonoid, saponins and steroid / triterpenes. Presence of iron, calcium, magnesium, sodium, potassium has also been reported in the leaf.

Nagaraju and Karimulla[41] have studied the biogeochemical behaviour of *G. montana* leaves and reported its capability of accumulating large amounts of Ca, K, Mg, B, Ba, Cu, Mn, Sr and Zn.

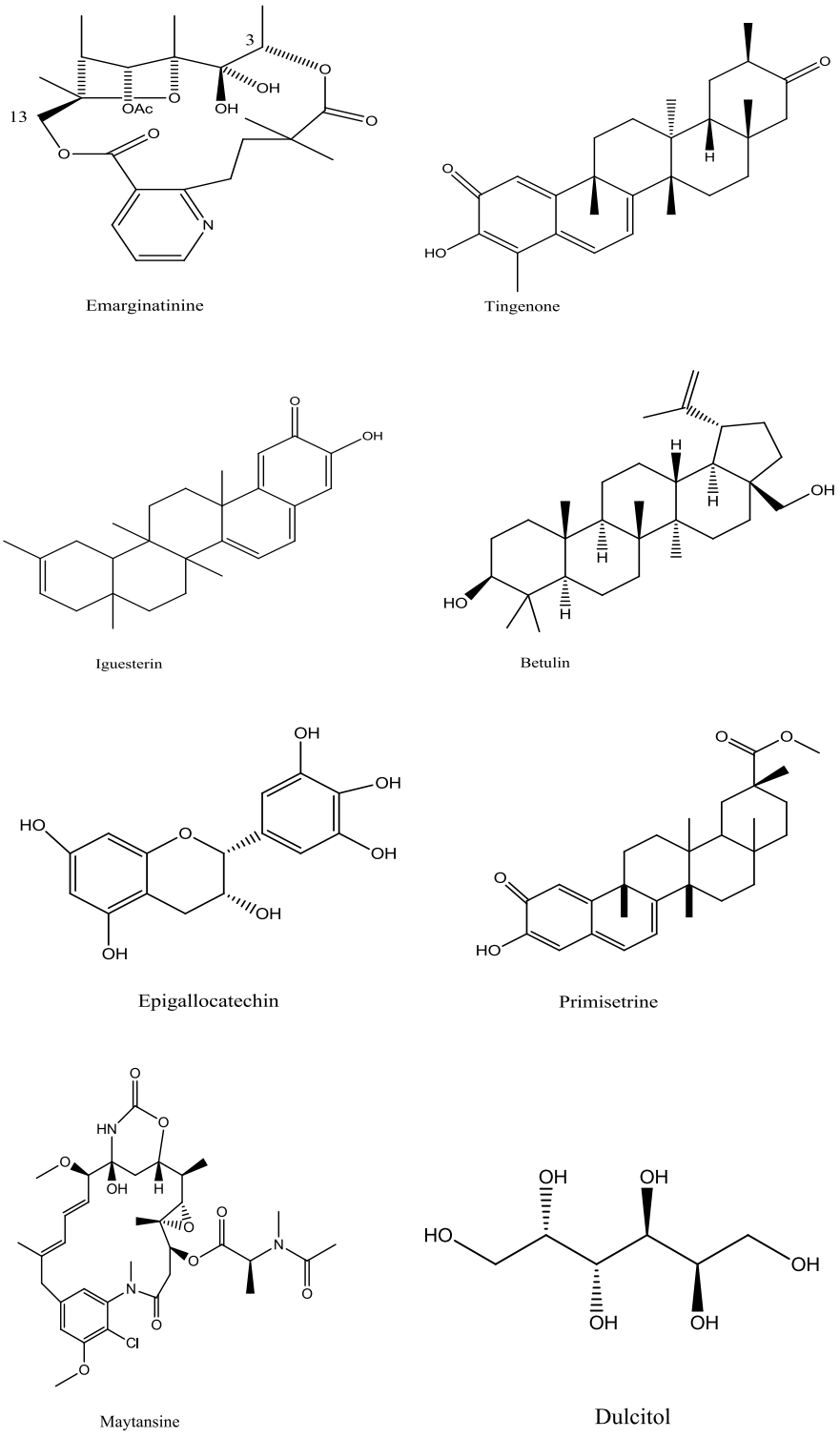

Fig 2: Structures of Some Compounds Obtained From *Gymnosporia Montana*

Pharmacology

Number of bioactive compounds with varied pharmacological activity have been reported from different species of the Celastraceae family[42], e.g. diterpene triepoxides with potent antileukemic and immunosupressive activities, triterpenoid quinonemethides (known as celastroloids) with antibiotic and cytostatic activities and sesquiterpene pyridine alkaloids with immunosuppressive or antitumor activities.

Presence of two anticancer compounds namely diterpenoid epoxide triptolide and quinine triterpene celastrol have been reported [43] from the Chinese medicinal herb *Tripterygium wilfordii* Hook (Family- Celastraceae). Methanolic extract of *Celastrus orbiculatus* has shown potent antinociceptive and sedative activities [44]. *Gymnosporia rothiana leaf* extracts have been reported to possess a dose dependent gastroprotective effect against ethanol and indomethacin induced gastric ulcer [45]. An anticancerous principle has also been isolated from this plant which, in addition to exhibiting good anticancer activities, prolongs the "S" phase of cell cycle[46, 47].

Very few reports on pharmacological activity of *Gymnosporia montana* are available. On the basis of its traditional and folk-lore claim of being useful in jaundice and inflammation, De and co-workers [48] have evaluated its leaf extracts for possible anti-inflammatory and hepatoprotective activities. Antiinflammatory activity was evaluated by noting the effect of their prior treatment on carrageenin induced rat hind paw oedema. The extracts did not affect carrageenin induced hind paw oedema – indicating lack of anti-inflammatory activity. Preliminary screening for hepatoprotective activity was carried out by noting their effect on carbon tetrachloride induced prolongation of pentobarbitone sleeping time in mice. Methanol extract of the defatted leaf was found to significantly antagonize carbon tetrachloride induced prolongation of pentobarbitone sleeping time in mice. The extract also significantly antagonized the elevation of serum transaminase activity in rats. Since the extract indicated hepatoprotection in preliminary study, it was further evaluated by the same group for its effect on CCl_4 induced alterations in different serum and liver parameters and changes in liver cytoarchitecture for confirming the hepatoprotective activity of the plant. Transaminase activity, lipid constituents of serum and liver, orosomucoid level in serum, as well as liver glycogen and phospholipids content were the main parameters studied. The extract reversed majority of the CCl_4 - induced alterations in different serum and liver biochemical parameters and also significantly antagonized the CCl_4–induced changes in the liver cytoarchitecture[49]. Later Patel et al. [50] have also reported that pre-treatment of the alcoholic extract (100mg/kg) of *G. montana* leaves in Wistar rats produces hepatoprotective activity comparable to that of silymarin (100mg/kg) against paracetamol induced hepatotoxicity. The methanolic extract of the defatted dried leaf powder, when evaluated for its antioxidant potential by estimation of lipid peroxidation (by FTC method), total antioxidant activity (by thiobarbituric acid method), DPPH radical scavenging activity and nitric oxide scavenging activity, has also shown to be a promising source of antioxidants[51]. Recently Dhuru et al. [52] have reported the anti-inflammatory, analgesic and antibacterial activity [53] of the plant. Presence of antispasmodic activity has been reported by Dhar et al.[54]. The present review reveals that *Gymnosporia montana* possess various biological activities like hepatoprotective, anticancer, antioxidant, antibacterial, analgesic, antispasmodic and it has great potential as a promising anticancerous and hepatoprotective drug.

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