Review Article

An Overview on Therapeutic Potential and Phytochemistry of *Sida rhombifolia* Linn.

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ABSTRACT

The current review puts an attempt to introspect the medicinal plant, *Sida rhombifolia* Linn., which is found throughout the tropical and subtropical parts of India. It belongs to family Malvaceae and is restricted to moist and waste places as weed. This review article provides detailed informations on the morphology, traditional uses, phytochemistry and various pharmacological activities reported previously for the plant *Sida rhombifolia.* It also makes a brief account on therapeutic potential of the whole and different parts of plant and its various extracts, fractions and isolated compounds against different diseases. The pharmacological activities reported includes anti-bacterial, anti-inflammatory, antipyretic, antiasthmatic, hypotensive, free radical scavenging, anti-cancer, antimalarial and hypoglycaemic activities. Thus, the present review may be able to give a point of information to the researchers to carry out their research work smoothly and may play an essential role in human health care system.

Keywords: *Sida rhombifolia,* therapeutic potential, phytochemistry

INTRODUCTION

The plants have been utilizing to control various health problems and to prevent diseases in different countries since the earliest day of mankind. They are now considered as important natural wealth, which provide healthcare services to people from all sorts of life.[1]

The knowledge of their medicinal properties has been transferred from one generation to the next generation of the human communities over the centuries. According to World Health Organization, medicinal plants may be the best source of variety of potential drugs and about 80 % population of the world depend on traditional herbal medicine for their primary health care.[2]

Now-a-days, the search for new active compounds from the plants depends on ethnic and folk informations obtained from traditional healers and is still considered as an important source for new drug discovery. In view of the worldwide interest on using medicinal plants, the present review on *Sida rhombifolia* Linn. provides current information on botanical, ethnopharmacological, phytochemical and pharmacological studies reported earlier in various literatures. *Sida rhombifolia* Linn. belongs to the family Malvaceae is commonly known as Barela and Paddy's lucerne. It is a perennial shrub with rough branches and stellate hairs, leaves of rhomboid-lanceolate to lanceolate.

Botanical Description

Sida rhombifolia Linn. is a small erect woody, very variable annual or perennial undershrub about 1.5 meters high with rough branches and stellate hairs. Leaves are very variable in shape up to 5mm by 18mm, short petioled, rhomboid-lanceolate to lanceolate, serrated towards the top, entire towards the base. The flowering and fruiting in the plant start from September to December. Flowers are yellow or white, axillary, solitary or in pairs.

The leaves are reduced on the flowering branches. The fruits are depressed, globose, schizocarpic, enclosed within the calyx, separating into one-seeded indehiscent unit. Seeds are black and smooth.[3,4]

Vernacular Names[3]

Sanskrit

Pitapuspi, Ahikhanda, Atibala, Bala, Barela, Brihadagala, Devaarha, Devabala, Devasaha, Gandhavallari, Gandhavalli, Jyeshthabala, Karambhara, Kesarika, Keshawardhini, Keshruha, Lalbarila, Mahabala, Mahagalarthaprasadini, Mahagandha, Mriga, Mrigadini, Mrigarasa, Pitapushpa, Pitapushpi, Prasadini, Sahadeva, Sahadevi, Samanga, Sarini, Varshapushpa, Varshpushpi, Vataglini, Vatya, Vatyayan.

Hindi

Pitabala, Pitabariyar, Bariara, Bhiunli, Kharenti Pitabala, Sahadebi, Sahadeva, Swetharela.

English

Arrow-leaf sida

Kannad

Binnegangagida, Bolamgadale, Kisangihettuttigida.

Bengali

Pitabedala, Kheriti, Pitabala, Pithala, Svetbarela.

Gujarati

Mahabala, Baladana

Marathi

Mahbala

Punjabi

Khurunti

Tamil

Kuruntotti, Anaikurundotti, Kurundotti, Tenacham

Telugu

Pulagamu, Athobalacettu. Gubatada, Pedda Mutheera Pulagum, Atibala, Gubatada, Mayilumanikyau, Muttavapulagamu.

Malayalam

Anakkuruntotti, Totti, Valankuruntotti, Vatturam

Odia

Dholabadianla

Scientific Classification

Kingdom - Plantae

Division – Angiospermae

Class - Eudicots

Order - Malvales

Family - Malvaceae

Genus - Sida

Species - *Sida rhombifolia*

Occurrence and Distribution

The plants are distributed throughout India, as a weed of waste places, open scrub forests and along roadsides and in other countries like Sri Lanka, Pakistan, Nepal, etc.[5]

Parts Used

The root, stem and leaf are used for the treatment of various diseases.

Traditional Uses[6,7]

The roots and leaves are sweetish, aphrodisiac, tonic, remove "tridosha", good in urinary complaints, discharges and strangury. These are also useful in fever, heart diseases, burning sensations, piles and all kind of inflammations (Ayurveda). The plant in combination with other drugs is prescribed as an antidote to snake venom (Charaka) and scorpion venom (Charaka, Sushrata). The root is held in great repute in the treatment of rheumatism. The Mundas apply the pounded leaves on swellings. In Assam the roots are taken internally to help child birth. The herb is also tied round the abdomen for the same purpose.

The stems are abound in mucilage and are employed as demulcent and emollients both for external and internal use. In Europe, the plant has been regarded as a valuable remedy in pulmonary tuberculosis and rheumatism. In Madagascar the plant is mostly used as an emollient and the infusion of the root is given in dysentery. The leaves are pounded and applied to tumors or chewed and applied to boils.

Ethnomedicinal Information on *Sida rhombifolia* Linn.

The hot aqueous extract of dried aerial parts of *Sida rhombifolia* is used for snake bite in East Africa[6]. The hot aqueous extract of entire plant of *S. rhombifolia* in Borneo is used as an abortifacient when it is taken orally by pregnant women.[7] The hot aqueous extract of entire plant is used as an abortifacient on oral administration in pregnant women in Central Africa.[8] In India, the decoction of entire plant of *S. rhombifolia* when given orally to human adults reduces rheumatic pain. The decoction is also mixed with equal proportion of cow's milk and taken every morning for about a week for the same purpose.[9] The hot aqueous extract of the plant in Malaysia is used for irregular menses when taken orally by adult females.[10]

The decoction prepared from entire plant of *S. rhombifolia* in Mexico is used to treat head cold when applied externally.[11] The hot aqueous extract of the entire plant in Mozambique is used for cough when given orally to both sexes of human adults.[12] The roots and leaves in Honduras are used as poultice when applied externally on boils.[13] The hot aqueous extracts of the entire plant in India is used as an aphrodisiac and in treatment of fever and urinary diseases when given orally to adult humans.[14,15] The infusion of dried leaf of *S. rhombifolia* in Central Africa is used for diabetes, chest pain and diarrhoea on oral administration. The infusion of this plant is applied locally for the treatment of skin diseases and infected wounds.[16]

The leaf juice of the plant in India has been in use for the treatment of spermatorrhea on oral administration.[17] The leaf juice of this plant in Madagascar is applied externally in abscesses and the leaf is useful in treating menstrual pain in Argentina.[18,19] The leaf and root infusions of the plant in Cameron are given orally in dysentery and diarrhoea whereas in Mozambique, these are applied externally as emollient.[20,7] The decoction of leaf and root of this plant are given orally to facilitate child birth.[21] The hot aqueous extracts of dried leaf and root of the plant in India are used to treat nervous diseases, heart diseases, burning sensation of the body and as aphrodisiac and tonic.[22] The decoction of leaf and stem of *S. rhombifolia* in Guatemala is taken orally in urinary inflammation.[23] In India the leaf juice mixed with sesame oil for the treatment of snake bite and the fresh leaf juice is given orally in spermatorrhoea. The fresh leaf juice in New Guinea has been in use for the treatment of diarrhoea in children.[24,25] The fresh plant juice in India, is taken orally to dissolve stones in urinary tract,[22] while in Nepal, the plant juice is applied externally for boils.[26]

The plant is eaten by pregnant women during third or fourth month of pregnancy in Borneo for abortion, while

the aqueous extract of the root in Central Africa is taken orally to induce abortion.[27,28] The dried root in Australia is used by traditional people for abdominal upset and in Buka Island it is taken for the treatment of diarrhoea.[29] The decoction of root in India is used orally for the treatment of pulmonary tuberculosis and the aqueous extract to treat malaria.[30,31] The dried root of the plant, in combination with *Casuarina equisetifolia,* is chewed for 2 days by the local people to treat dysentery in Papua-New Guinea.[29] The decoction of the dried root of the plant along with *Cissampelos pareira* var. *orbiculata* in Tanzania is used to treat habitual abortion.[6]

The twig of the plant is used by local people in India as toothbrush to strengthen gums. The leaf paste is applied topically for boil and taken orally with milk in dysentery.[32,33] The stem of the plant in Rotuma is chewed for dental hygiene and the infusion is used for prevention of miscarriage.[34] The infusion of flower, fruit and leaf are used by adult human externally for loss of hair in Mexico. The decoction of flower is used for cleansing open sores, while the infusion is used as an emollient and for dysentery in Madeira.[35,36]

The *S. rhombifolia* infusion is taken orally in Guatemela for the treatment of gonorrhoea and the leaf juice in Guina is applied by traditional healer in vagina as an antiseptic.[37,38] The leaf paste of the plant is applied externally for cuts and boils by the Tharus of Nainital district in India.[39] In Nicaragua, the decoction of leaf of the leaf is taken orally by adult human in the treatment of fever, cough, aches, infections, cold, diarrhoea and childbirth.[40]

The leaf of *S. rhombifolia* in Peru is used traditionally in gonorrhoea, tuberculosis, tumors, snake bite, alopecia, lupus, urinary bladder ailments, urethritis and as analgesic, sedative, emenogogue, lactogogue and diuretic.[41] The hot aqueous extract of the dried leaf is used externally in Guatemela for abscesses, furuncles, erysipelas, scrofula, skin eruption, dermatitis, inflammation and conjunctivitis.[42] The decoction of the leaf is taken orally by Garifuna of eastern Nicargua in fever, aches, pain, infections, venereal diseases, respiratory and pulmonary disorder.[43]

Biological Activity of *Sida rhombifolia* Linn.

Antimicrobial Activity

Mishra and Chaturvedi reported that the alkaloid fraction of aerial parts of *Sida rhombifolia* possesses antiyeast activity (1 mg/ml) against *Cryptococcus neoformans*, antibacterial activity (1 mg/ml) against *Bacillus anthracis, Staphylococcus aureus, Bacillus subtilis, Pseudomonas aeruginosa, Escherichia coli, Cryptococcus neoformans*, antifungal activity against plant pathogens and weak antibacterial activity (2 mg/ml) against *Salmonella typhosa, Proteus vulgaris, Corynebacterium pyrogens* using agar plate medium.[44]

Goyal and Rani reported that the sterol fraction of the entire plant of *S. rhombifolia* showed antibacterial activity against *Escherichia coli, Klebsiella species, Staphylococcus aureus, Staphylococcus albus and Pseudomonas pyocyanae* at concentrations of 0.5, 1, 0.5, 0.5, 1 mg/ml respectively and weak antibacterial activity against *Shigella dysentrica, Bacillus subtilis and Proteus vulgaris* at the concentration of 1 mg/ml using agar plate medium.[45] The methanolic extract of the entire plant of *S. rhombifolia* was reported to exhibit antifungal activity against *Candida albicans* and *Cladosporium cucumerinum* using agar plate medium and poor antioxidant activity at the concentration of 100 µg/ml. However, the dichloromethane extract was found to exhibit antioxidant activity at the same concentration.[46]

The decoction of leaf extract of *S. rhombifolia* was reported to have antibacterial activity against *Staphylococcus aureus, Schigella flexneri* (MIC; 250 µg/ml), *Pseudomonas aeruginosa* (MIC; 62.5 µg/ml), *Salmonella enteritidis* (MIC 125 µg/ml) and *Citrobacter diversus* and *Klebsiella pneumonae* (MIC; 125 and 250 µg/ml) using agar plate.[47]

Caceres reported that the tincture (10 gm of plant in 100 ml methanol) of *S. rhombifolia* leaf in Guatemala exhibited weak antiyeast activity against *Candida albicans* and antibacterial activity against *Escherichia coli*, *Pseudomonas aeroginosa* and *Staphylococcus aureus* at the concentration of 30 µl /disc.[42] The fatty acid mixture of leaf of *S. rhombifolia* was reported for its antibacterial activity against *Staphylococcus aures* and *Escherichia coli*.[48]

Islam reported that petroleum ether, chloroform, ethyl acetate and aqueous extracts of the leaf of *S. rhombifolia* showed weak antibacterial activity against several bacterial strains at 200 µg/disc.[49] Muanza reported that the methanolic extracts of leaf of *S. rhombifolia* exhibited poor antibacterial activity (10 mg/ml) against *Escherichia coli, Pseudomonas aureginosa, Salmonella typhimurium* and promising activity (12.5 and 250 mg/ml) against *Klebsiella pneumonia, Staphylococcus aureus* and *Streptococcus mutans*.[50] It also exhibited antifungal activity (MIC; 250 µg/ml) against *Aspergillus niger*, *Microsporium gypseum*. The essential oil of the leaf of *S. rhombifolia* was reported for its antifungal activity against plant pathogen, *Fusarium oxysporum*.[51]

Anti-inflammatory Activity

Bork reported that the ethanol extract (95 %) of aerial parts of *S. rhombifolia* possesses anti-inflammatory activity in Het-Cam assay and inhibit NF-Kappa B activation (100 µg/ml) using cell culture of CA-Hela.[52]

The ethanol extract of leaf of *S. rhombifolia* was found to have anti-inflammatory activity on EPP-induced rat oedema at the dose of 0.8/ear while the same extract at 100 µg/ml do not inhibit prostaglandin synthesis.[53] Various extracts of *S. rhombifolia* leaves were studied for antinociceptive and anti-inflammatory activities at a dose

of 200 mg/kg. Ethyl acetate extract has shown significant (P<0.01) antinociceptive activity.[54]

Antispasmodic Activity

Dhar found that the ethanol-water (1:1) extract of the plant subjected to cell culture of CA-9KB antispasmodic activity.[55] Mishra and Verma reported that the alkaloidal fraction of this plant, when administered intravenously showed antispasmodic activity (80 µg/ml) against acetylcholine-induced and KCl-induced contractions.[56,57]

Hypotensive Activity

Weak hypotensive activity was also exhibited by the methyl chloride and ethanol (60 %) extracts of this plant.[58] Mishra and Verma reported that the alkaloidal fraction of this plant, when administered intravenously at the dose of 2-4 mg/kg body weight to the dog, it exhibited biphasic blood pressure effect, cardiac depressant activity.[56]

Uterine Stimulant Effect

Satthawongsakul reported that ethanol (95%) and aqueous extracts of the entire plant of *S. rhombifolia* showed uterine stimulant activity against oxytocin induced contractions on female rat.[59] The ethanol (95%) and aqueous extracts of this plant also exhibited antiplantation effect on pregnant rat at the dose of 1-2 gm/kg for 5 days of treatment. Mishra and Verma reported that the alkaloidal fraction of this plant, when administered intravenously at the dose of 2-4 mg/animal, exhibited uterine stimulant effect (100 µg) on the uterus of rabbit.[56]

CNS Effect

The fresh leaf aqueous extract of *S. rhombifolia* when administered intragastrically and intraperitonially at the dose of 1 gm/kg was reported to have CNS effect (Hippocratic screen) in mice and spasmolytic activity at the concentration of 2 mg/ml in guinea pig against electrical stimulation.[60]

Antimalarial Activity

The methanol-water extract (1:1) of dried fruit of the plant was reported to have antimalarial activity against *Plasmodium berghei* at100 µg/ml, while the ethanol-water extract (50%) showed weak antimalarial activity against the same strain at 1 gm/kg for 4 days treatment.[61] Valsaraj found that the ethanol-water extract (1:1) exhibited antimalarial activity against *Plasmodium berghei* at the dose of 10µg/ml and poor antimalarial activity at the dose of 1 gm/kg.[62]

Antioxidant Activity

Munasinghe reported that water soluble fraction of dried root of *S. rhombifolia* showed weak radical scavenging effect against DPPH radical and deoxyribose degradation inhibition.[63] Ethanolic extract of *S. rhombifolia* were found to be good scavengers of the 1,1-diphenyl-2-picrylhydrazyl radical in the order root > leaves > whole plant > stem with 50% inhibitory concentrations of 546.1, 852.8, 983.8, and 1,222.5 µg/mL respectively. The root extract inhibited lipid peroxidation in rat liver and brain homogenate and highest antioxidant activity was observed in case of root extract.[64]

Cytotoxic Activity

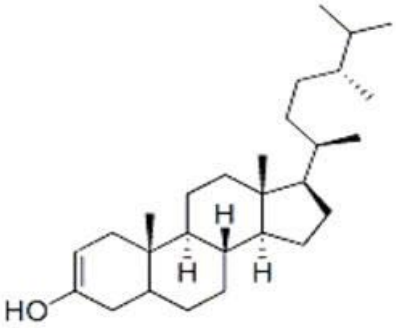
The cytotoxicity of crude extracts from the leaves of *S. rhombifolia* has been investigated against cell culture of CA-HS-578-T, CA-Mammary-MCF-7, MCF-7/ADR, human breast cancer cell line-MDA-MB-231, MDA-Mb-435, MDA-N, T47-D, human leukaemia cell line CCRFCEM, HL-60-TB, MOLT-4, Cells-RPMI-8226, Leuk-SR, Leuk-K562, human non-small cell lung cancer cell line -A549(ATCC), EKVX, HOP-62, HOP-92, human colon cancer cell line- HCC-2998, Ca-human-colon-HCT 116, CA-HCT-15, human CNS cancer cell line SF-539, SNB-19, SNB-75, melanoma-M14, human melanoma cell line-MAIME- 3M,human ovarian adenocarcinoma-IGROV-1, CA-human ovarian-OVCAR-3, human renal cancer cell line-CAKI-1 and SN-12C. The ethyl acetate extract showed potent cytotoxicity with LC_{50} values (5.41 ppm) comparable to the reference standard, gallic acid.[65] Dhar found that the ethanol-water (1:1) extract of the plant subjected to cell culture of CA-9KB, exhibited poor cytotoxic activity.

Islam[49] reported that petroleum ether, chloroform, ethyl acetate and aqueous extracts of the leaf of *S. rhombifolia* showed weak antibacterial activity against several bacterial strains at 200 µg/disc, while chloroform (IC_{50}; 13.87 ppm), ethyl acetate (IC_{50}; 5.41 ppm), aqueous (IC_{50}; 25.95 ppm), and petroleum ether extracts (IC_{50}; 21.52 ppm) of the same plant showed anticrustacian activity against *Artemia salina*, which was intended to predict for the antitumor activity of the plant. Nakanishi[66] reported that the methanol-water extract (1:1) of the plant was administered intraperitonially to mouse at maximum tolerable dose (LD_{50}>1 gm/kg) for toxicity assessment and exhibited antitumor activity on rat at the dose of 1 gm/kg.[43]

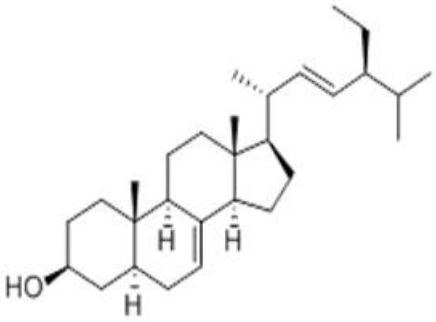
The ethanol extract showed lethality against the brine shrimp nauplii.[67] It showed different mortality rate at different concentrations, where LC_{50} and LC_{90} were deduced (LC_{50} = 40 mg/ml; LC_{90} = 80 mg/ml).

Phytochemical Studies of *Sida rhombifolia* Linn.

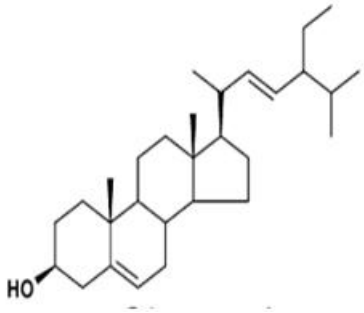
The defatted leaf of *Sida rhombifolia* was reported to contain various amino acids *viz*., alanine, phenyl alanine, asparagine, arginine, aspartic acid, glutamic acid, glutamine, glycine, histidine, leucine, lysine, serine, threonine, tyrosin, valine and fatty acids like myristic acid, oleic acid, stearic acid and palmitic acid.[48] The entire plant was reported to contain aurantiamide benzoate, betain, campesterol, 22-diydro-campesterol, cholesterol, 24-methylene-cholesterol, β-sitosterol, spinasterol, 22-dihydro-spinasterol, stigmasterol and stigmast-8(14)-en-3-beta-ol[45]. The dried root and aerial part were found to contain betain, miscellaneous alkaloids *viz*., choline, ephedrine and pseudoephedrine[68].



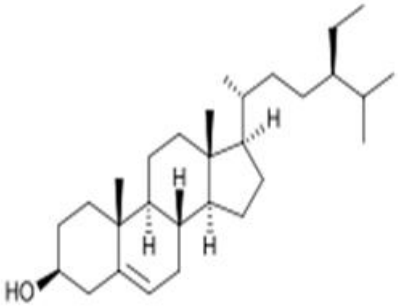
Campesterol



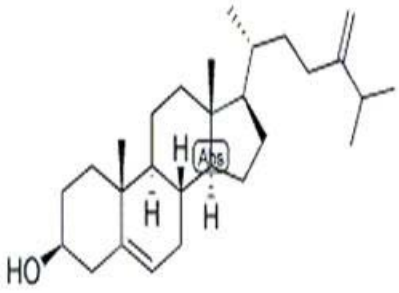
Spinasterol



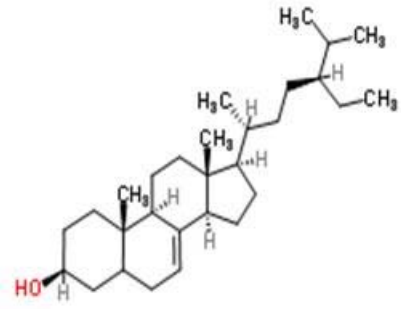
Stigmasterol



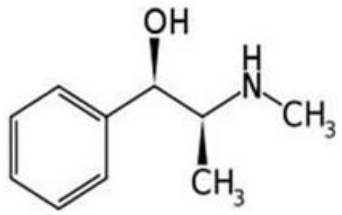
β-Sitosterol



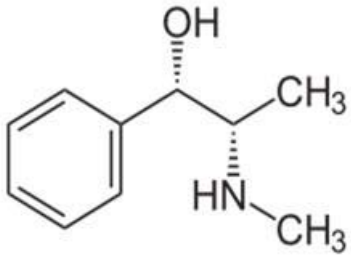
24-methylene-cholesterol



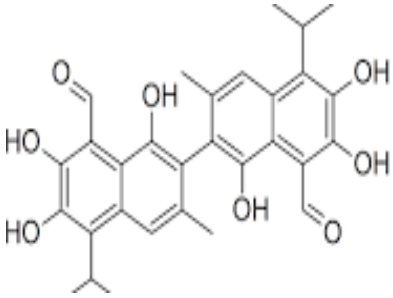
Stigmast-8(14)-en-3-beta-o



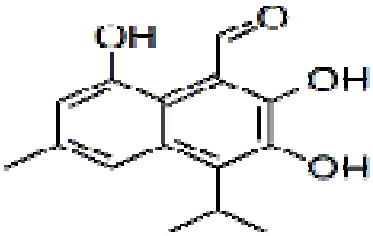
Ephedrine



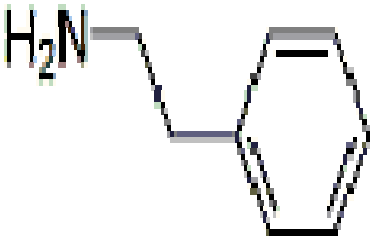
Pseudoephedrine



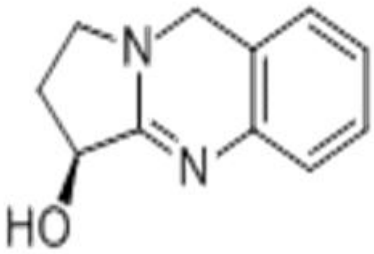
Gossypol



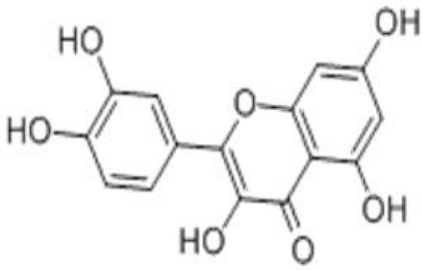
Hemi-gossypol



Vasicine



Phenethylamine



Quercetin

Schmidt and Wells found that the dried seed of *S. rhombifolia* contains sesquiterpenes like gossypol and hemi-gossypol.[69]

The dried leaf of the plant was reported to have alkaloids, while the fresh shoot contains alkaloids, flavonoids and saponins.[70]

The fresh leaf found to contain alkaloids, sterols and triterpenes.[71]

Prakash reported that the dried aerial parts and dried root of *S. rhombifolia* contain isoquinoline alkaloids *viz*., β-phenylethylamine, vasicine, vasicinol, vasicinone, vasinone, (DL)-vasinone and tryptophan and N-(B)-methyl.[68] The leaf of the plant also contains quercetin.[72]

The dried aerial part of the plant was reported to have alkanes (C15-C35), 22- dehydro-cholesterol, cholesterol, 24-methylene-cholesterol, β-sitosterol, spinasterol, 22-dihydro-stigmast, stigmast-8(14)-ene-3-beta-ol and stigmasterol.[73]

The preliminary phytochemical screening of the plant extracts indicated the presence of alkaloids, steroids and/or triterpenoids and their glycosides, tannins, flavonoids, carbohydrates and absence of cardiac glycoside.[54]

CONCLUSION

S. rhombifolia Linn is a widely accepted medicinal plant in the world due to its large number of beneficial therapeutic effects.

In Ayrurvedic system of medicine, it is used in fever, heart diseases, burning sensations, piles, scorpion bite, snake bite and all kind of inflammations.

The wide number of active compounds and pharmacological activities of this plant may lead to innovative research in the field of pharmaceutical industry.

This review study is aimed at encouraging and attracting attention of researchers to develop new drug molecules for treatment of various ailments.

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