

Ethnobotanical, Pharmacological Benefits and Phytochemistry of *Sida cordifolia* (Linn.): A Review

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ABSTRACT

The inclusive information is provided in this review on traditional uses, antimicrobial activity, phytochemistry and pharmacology of *S. cordifolia*. In ayurveda it is commonly known as bala. According to Ayurveda, the plant is tonic, astringent, emollient, aphrodisiac and useful in treatment of respiratory system related troubles. *S. cordifolia* is alternative tonic, astringent, emollient, aphrodisiac etc. Bark is considered as cooling. Seeds are considered as aphrodisiac. Roots are regarded as cooling, astringent, stomachic and tonic, aromatic, bitter, diuretic. It has a depressant rather than a stimulant effect on the central nervous system. Many pharmacological investigations have been carried out based on its chemical constituents. Extensive literature survey revealed many pharmacological properties includes antibacterial, antifungal, anticancer, anticonvulsant, antidiabetic, antimutagenic, anticlastogenic, antiulcer, antioxidant, antiviral and wound healing activities.

Keywords: *Sida cordifolia* Linn., pharmacology, folk medicine, antimicrobial potential and phytochemistry.

INTRODUCTION

Plants have unlimited ability to synthesize secondary metabolites such as tannins, terpenoids, alkaloids, glycosides and phenols which have been found to have antimicrobial properties. It has been estimated that 14-28% of higher plant species are used in medicinal purposes and that 74% of pharmacologically active plant derived components were discovered after following upon ethnobotanical uses of the plants¹⁻³.

Sida cordifolia (Linn.) belongs to the family malvaceae. It is widely distributed along with other species throughout the tropical and sub tropical plains all over India and Sri Lanka up to an altitude of 1050 m. It is also known as the "Bala" in Hindi and Sanskrit⁴.

S. cordifolia, with its ephedrine and pseudoephedrine has gained a lot of interest and is now sold by many companies⁵.

Momin *et al.*, (2014)⁶ investigated phytochemical screening of ethanolic extract of *S. cordifolia* roots and reported antioxidant, antimicrobial and analgesic activity.

Botanical description

S. cordifolia grows well through the plains of India, especially, in damp climates. The shrub grows up to 0.75-1.5 meters in height. The root and the stem are stout and strong. The leaves are 2.5-7 cm long and 2.5-5 cm broad, with 7-9 veins. They are heart shaped, serrate and truncate. The flowers are small, yellow or white in colour, solitary and axillaries. The fruits are moong-sized, 6-8 mm in diameter. The seeds are called as Bijabanda in Ayurveda, are greyish black in colour and smooth. The flowering is occurs from August to December⁷. *S. cordifolia* is a small, erect, downy shrub. The leaves of the plant are chordate-oblong or ovate-oblong and fruits with a pair of awns on

each carpel. Roots are 5-15 cm long with few lateral roots of smaller size. The tap roots are generally branched at the tip. The outer surface of the root is greyish yellow. It is almost odourless with slightly bitter taste⁸.

Vernacular names

Hindi - Kungyi
English - Country mallow
Sanskrit - Bala
Tamil - Mayir-manikham
Bengali - Brela
Gujarati - Junglimethi
Malayalam - Velluram
Punjab - Simak
Maharashtra - Chikana

Taxonomy

Kingdom - Plantae
Division - Angiospermae
Class - Eudicots
Order - Malvales
Family - Malvaceae
Genus - *Sida*
Species - *cordifolia*

Occurrence and Distribution

S. cordifolia is widely distributed along with other species are common throughout the tropical and sub tropical plains all over India and Sri Lanka up to an altitude of 1050 m., growing wild along the roadside.

Traditional uses

It has a long history of use by Ayurveda and rural area particularly for medicinal properties. It is in use as folk medicine in India since time immemorial. According to Ayurveda, the plant is tonic, astringent, emollient,

aphrodisiac and useful in treatment of respiratory system related troubles⁹.

S. cordifolia is alternative tonic, astringent, emollient, aphrodisiac etc. Bark is considered as cooling. Seeds are considered as aphrodisiac. Roots are regarded as cooling, astringent, stomachic and tonic, aromatic, bitter, diuretic. It has a depressant rather than a stimulant effect on the central nervous system. It decreases both blood pressure and heart rate. It also has a hypoglycaemic activity. Its extract is used to reduce body weight. It used to reduce blood pressure and improves the cardiac irregularity. *S. cordifolia* is also useful in ophthalmic, rheumatism, colic and nervous disorders. *S. cordifolia* has also been reported to improve sexual strength. *S. cordifolia* oils are used topically to the sore muscles and sore joints in rheumatism and arthritis. The crushed leaves can be carried out a cataplasm to alleviate local pains. The bronchodilator value of the vasicinone, vasicine and vasicinol are used to elaborate preparations for the treatment of the bronchial affections, especially in what refers to the cough, asthma, bronchitis, nasal congestion, flu, pain in the chest, etc. Decoction of the root of bala and ginger is given in intermittent fever attended with cold shivering fits. Root juice is also used to promote healing of wounds. Oil prepared from the decoction of root bark mixed with milk and sesame oil used in diseases of the nervous system and is very efficacious in curing facial paralysis and sciatica¹⁰. According to Ayurveda 'Bala' balance all the doshas-vata, pitta, kapha. It has more effect on vata dosha. Leaves are cooked and eaten in cases of bleeding piles. Juice of the whole plant, pounded with a little water is given in doses of ¼ seers for spermatorrhea, rheumatism, and gonorrhoea.

Pharmacological activity

Central nervous system activity

Franco *et al.*, (2005) reported that rather than being a stimulant, *S. cordifolia* actually acts as a depressant and decreases CNS activity. Hydro alcoholic extract of *S. cordifolia* at a dose of 1000 mg/kg (i.p. and p.o.) produced sedation, decrease of the ambulation, reduction of answer to the touch, analgesia and decrease of urination same dose caused significant reduction ($p < 0.001$) of the spontaneous locomotors activity in comparison with the control group at 30 and 60 min as well as did not cause a significant difference in the motor coordination of the treated animals in comparison with the control group¹¹.

Analgesic activity

Kant and Diwan, (1999) reported acetic acid induced writhing test method on analgesic activities. The number of writhing episodes of eight groups of six animals was compared with those of aspirin. At a 600 mg/kg dose both *S. cordifolia* root and aerial extract exhibited significantly ($p < 0.001$) better activity than that elicited by aspirin¹².

Anti-inflammatory activity

Kanth and Diwan (1999) demonstrated that *S. cordifolia* can increase pain tolerance and appears to have anti-inflammatory properties. When rats were exposed to heat, rats that consumed *S. cordifolia* had a greater heat tolerance¹². It may be effective as an antioxidant¹³. Diwan and Kulkarni (1983) studied anti-inflammatory activity of

ethyl acetate and alcohol extracts of *S. cordifolia* was studied in rats. The percent inhibition of oedema was calculated with reference to the control group. The aerial part exhibited significant anti-inflammatory activity only at a dose level of 600 mg/kg. Both *S. cordifolia* aerial and root extract showed dose dependent activity¹⁴.

Franzotti *et al.*, (2000) studied the anti-inflammatory, analgesic activity and acute toxicity of an aqueous extract of *S. cordifolia* in animal models. The aqueous extract showed a significant inhibition of carrageenin-induced rat paw edema after oral administration. It also increased the latency period for mice in the hot plate test and inhibited the number of writhes produced by acetic acid. The aqueous extract of *S. cordifolia* showed low acute toxicity in mice¹⁵.

Sutradhar *et al.*, (2007) reported anti-inflammatory activities of a new bioactive alkaloid (5'-Hydroxymethyl-1'-(1,2,3,9-tetrahydro-pyrrolo[2,1-b]quinazolin-1-yl)-heptan-1-one) (compound 1), isolated from *S. cordifolia* were evaluated. The analgesic activity was investigated in the acetic acid induced writhing and the radiant heat tail-flick model in mice and the carrageenan-induced rat paw edema model was used for the anti-inflammatory study¹⁶. Sutradhar *et al.*, (2007) investigated two new bioactive flavones of 5,7-dihydroxy-3-isoprenyl flavone and 5-hydroxy-3-isoprenyl flavone, along with two known compounds β -sitosterol and stigmasterol from the chloroform extract of *S. cordifolia*. Flavones were tested and shown significant analgesic and anti-inflammatory activity¹⁷.

Momin *et al.*, (2014) phytochemical screening of the crude extract indicated the presence of reducing sugar, alkaloids, steroids, and saponins. In diphenylpicrylhydrazyl scavenging assay, the half maximal inhibitory concentration (IC₅₀) value was found to be 50 μ g/ml which was not comparable to the standard ascorbic acid. The crude extract produced 44.30% inhibition of writhing at the dose of 500 mg/kg body weight which is statistically significant. The *in vitro* antimicrobial activity of extract showed no activity against five types of microorganisms⁶.

Hypotensive activity

Medeiros *et al.*, (2005)¹⁸ performed the aqueous fraction of hydro alcoholic extract of *S. cordifolia* induced hypotension and bradycardia on mean arterial pressure and heart rate in non anaesthetized rat. Administration of atropine completely abolish the Aqueous fraction of hydro alcoholic extract of *S. cordifolia* induced hypotensive and bradycardic responses. Administration of hexamethonium potentiates significantly the hypotensive response and significantly attenuate bradycardic response. The administration of hexamethonium+1-NAME significantly attenuates the same extraction induced hypotensive response¹⁹.

Silveira *et al.*, (2003) evaluated the cardiovascular effects of vasicine, an alkaloid isolated from the leaves of *S. cordifolia*. The results of the study showed that vasicine produced hypotension and bradycardia which appeared to be due to the stimulation of cardiac muscarinic receptors (directly and/or indirectly), and by a decrease of the peripheral resistances²⁰.

Santos *et al.*, (2005) investigated the cardiovascular effects on unanesthetized normotensive rats induced by the total alkaloid fraction of *S. cordifolia* and observed induction of hypotension and bradycardia, which appear to be mediated by direct and indirect activation of muscarinic receptors. Nitric oxide also appears to be involved in the hypotensive response²¹.

Hepatoprotective activity

Fumaric acid isolated from *S. cordifolia* was reported to be hepatoprotective²². Recent works has reported hepatoprotective effect of aqueous extract of *S. cordifolia* after partial hepatectomy. It was investigated that *S. cordifolia* stimulates insulin release by pancreatic β cells, acting like sulphonylureas. Knowing that insulin acts as an important co-mitogen it can be raised the hypothesis that the augmented release of this hormone, stimulated by *S. cordifolia*, can exert a permissive role in the hepatocellular synthesis of DNA and, consequently, in liver regeneration process²³.

Rao and Mishra (1998) carried out hepatoprotective activity of the powder with different extracts of the whole plant of *S. cordifolia* against CCl₄ (carbon tetrachloride) induced model. The methanolic, aqueous and total aqueous extracts showed significant hepatotoxic activity comparable to that of Silymarin in galactosamine and thioacetamide induced toxicities in rat isolated hepatocytes²⁴.

Kotoky and Das (2000-2001) studied the anti-hepatotoxic activities of various extracts of the roots of *S. cordifolia* against carbon tetrachloride intoxicated rats. The methanolic extract exhibited marked protection evidenced by serum biochemical parameters and histological examination²⁵.

Antibacterial activity

Mahesh and Satish, (2008) reported that *S. cordifolia* methanolic leaf extract showed highest antibacterial activity against *F. verticillioides*²⁶.

Kalaiarasan and John (2010) reported antibacterial activity of ethanolic and methanol extracts of *S. cordifolia* against *Escherichia fecalis* and *Pseudomonas aeruginosa*²⁷. The methanol extract was found to be an effective against all phytopathogens with low MIC of 6 μ m/mm and the methanol extract exhibited a higher inhibition activity against *E. coli*, *Enterobacter aerogenes*, *Mycobacterium* sp., and *Micrococcus variance*, *Pseudomonas aeruginosa* and *B. subtilis*²⁸.

Reddy *et al.*, (2012) evaluated antimicrobial activity using different extracts of *S. cordifolia* against bacteria and fungi by disc diffusion method. Solvent control dimethyl sulphoxide (DMSO) showed no effect against the tested bacteria and fungi. Aqueous extract showed highest inhibitory activity compared to other extracts²⁹.

Antifungal activities

Reddy *et al.*, (2012) reported antifungal potential of *S. cordifolia* leaf extract aqueous against *Candida albicans* and *Cryptococcus neoformans* at a concentration of 2mg/disc²⁸.

Adaptogenic activity

Plant adaptogen are smooth prostressors which reduce the reactivity of host defense system. The mode of action of

adaptogens is basically associated with stress system. Adaptogen increase the capacity of stress to respond to the external signals of activating and deactivating mediators of stress response subsequently. The stress induced increase in total WBC count is decreased by SCE, indicating adaptogenic activity³⁰.

Anti Parkinson's disease

Parkinson's disease Ayurveda treatment aims at balancing disturbed vata. Massage therapy, enema, medication methods are applied. In addition to *Mucuna pruriens* (known by names violet bean, cowhage, naikkurana and kaunch beej), Ashwaganda (*Withania somnifera*), *S. cordifolia* are the prime herbs usable in Parkinson's disease Ayurvedic treatment³¹.

Wound healing activity

S. cordifolia used in wound healing activity. Tissue healing is an important process which is the basis of various surgical manipulations it can be enhanced by several herbal medicines. Plants and their extracts have immense potential for the management of different types of wounds. The phytomedicines for wound healing are not only cheap and affordable but are also purportedly safe. However, there is a need for scientific validation, standardization and safety evaluation of plant of the traditional medicine before these could be recommended for healing of the wounds. Pharmacological screening of botanicals is necessary for viewing new chemical entities in normal subjects, which is designed to search for novel drug actions at an early stage of drug development³².

Anti-hypertriglyceridemic activity

The antihypertriglyceridemic potential of *S. rhomboidea* leaf extract mediated via decreased intestinal absorption. Pharmacological evidence for use of sida leaf extract as a folklore medicine for controlling obesity amongst north-eastern population of Indian subcontinent³².

Hypoglycemic activity

S. cordifolia use as a weight loss product is through its hypoglycaemic activity. Research studies have shown that it possesses a significant blood-sugar lowering activity and therefore may help to reduce the storage of fat with fat cells³³.

Antioxidant activity

S. cordifolia possesses effective reducing power and free-radical scavenging activity. Only the root extract exhibited superoxide-scavenging activity and inhibited lipid peroxidation in rat liver homogenate. All these antioxidant properties were concentration dependent. The highest antioxidant activity was observed in the root extract. The antioxidant property of ethanolic extract of *S. cordifolia* was assessed by DPPH (1, 1-diphenyl-2-picryl hydrazyl) free radical scavenging activity. It was shown that the percentage (%) scavenging of DPPH radical was increased significantly with increasing dose (P<0.001). IC₅₀ value of the extract was found to be significant when compared to the IC₅₀ value of the reference compounds ascorbic acid and BHA respectively. The potentiality of the extract of *S. cordifolia* as antioxidant may be due to the presence of tannins, phenolics might be responsible for its activity³².

In gynaecological practices

S. cordifolia has been used in threatened abortion and strengthens placental retention in expectant mothers. As per ayurvedic concept, leukorrhoea in females develops due to weakness in the body. One teaspoonful of fine *S. cordifolia* powder prescribed twice daily provides the desired strength. In the case of inflammation of the ovary, a compound preparation of *S. cordifolia* along with *Balaydighrit* is given to the mother and to the newborn infant³⁴.

As a blood coagulant

In bleeding piles, where blood is passed with feces and the problem is aggravated by indigestion and constipation, 10 g of *S. cordifolia* powder, boiled with 80 ml of water until reduced to 20 ml is strained. One cup of milk is added to the filtrate. This mixture is taken in the morning. It not only helps with hemorrhoids but also coagulates blood in the other parts of the body, such as nose and mouth³⁴.

In sexual inadequacies

5-6 g of root powder of *S. cordifolia* in the morning on an empty stomach increases the viscosity of semen and prevents its involuntary discharge in males. In swollen testes, a decoction of *S. cordifolia*, 4 teaspoons along with 2 teaspoons of castor oil, is prescribed³⁴.

Anti-fertility activity

Pokale and Kulkarni (2012) reported the anti-fertility potential of aqueous extract of *S. cordifolia* in Swiss albino mice. The treatment caused decrease in weight of ovaries and uterus, which supports its antifertility activity³⁵.

Anti-helminthic activity

Pawa et al., (2011) reported the *in vitro* studies on ethanol and aqueous extract of whole plant *S. cordifolia* for anthelmintic using *Pheretima posthuma* properties³⁶.

Hypolipidemic activity

Asdaq et al., (2008) reported the effect of hydroalcoholic extracts of *S. cordifolia* leaves on lipid profile in rats and reported that the chronic administration of the extract in high dose has definite cardioprotective potential, which was determined by serum levels of total cholesterol, triglyceride, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, aspartate aminotransferase, and alanine aminotransferase³⁷.

Anti-pyretic activity

Philip et al., (2008) reported the anti-pyretic properties of methanolic extract of *S. cordifolia* aerial parts in rats and showed that the extract significantly reduced pyrexia induced by TAB vaccine³⁸.

Anti-rheumatism

Sutradhar et al., (2007) reported leaves of *S. cordifolia* in anti-rheumatism reported in rats¹⁶. Amritpaul (2006) reported that decoction of root bark has ability to treat sciatica and rheumatism. Traditionally oils prepared from this herb are very useful in arthritis and diseases that affect the joints³⁹. Yusuf and Kabir (1999) reported that aqueous extract of whole plant of *S. cordifolia* was used in anti-rheumatism⁴⁰.

Anti-ulcerogenic activity

Akilandeswari et al., (2013) reported the gastric anti-ulcer activity with the ethanol extract of leaf of *S. cordifolia*. The ulcers were induced in 36 hrs fasted albino rats by pylorus ligation model, ethanol (1ml/kg) and aspirin (300 mg/kg)

induced gastric lesions and comparison made with reference drug famotidine at dose level (20 mg/kg). The plant extract of *S. cordifolia* (100 and 200 mg/kg, b.wt) exhibited potent anti-secretory volume, acidity and ulceration, thus, establishing significant antiulcer activity against different ulcer induced models⁴¹. Philip et al., (2008) evaluated for anti-ulcerogenic activity of methanolic extract of *S. cordifolia* at a dose level 500mg/kg against ethanol and aspirin induced gastric ulcers³⁸.

Anti-diabetic activity

Kanth and Diwan et al., (1999) reported hypoglycemic, analgesic and anti-inflammatory activities with aerial and roots of *S. cordifolia* extracts and found to have anti-diabetic properties¹². Mahrukh et al., (2014) reported hypoglycemic, and anti-hyperlipidemic of alcoholic extract of *S. cordifolia* at a dose of (200 and 400 mg/kg) in streptozotocin-induced diabetes rats at the dose of 55 mg/kg. At a dose of 400 mg/kg *S. cordifolia* extracts showed significant reduction of the blood glucose level in diabetic rats and there was a decrease in total cholesterol, triglycerides, low-density lipid, plasma creatine, plasma-urea nitrogen⁴².

Nephroprotective activity

Bhatia et al., (2012) reported that the ethanolic and aqueous extracts of *S. cordifolia* showed nephron protective activity when compared to gentamicin⁴³. Mehul et al., (2012) studied effect of *S. cordifolia*, as nephron protective agent, using aqueous extract at a dose level of 200 mg/kg and 400 mg/kg concentrations against gentamycin (100 mg/kg) and cisplatin (7 mg/kg) as inducing agents⁴⁴.

Anti-stress activity

Sumanth and Mustafa (2009) reported about the adaptogenic activity in *S. cordifolia* Linn. The extracts were prepared and administered orally in rats. Ashwagandha which was in water-soluble powder form was used as reference standard. The result showed that *S. cordifolia* extracts reduced plasma cortisol level as well as blood glucose³⁰.

Anticancer and cytotoxic activity

Matsui et al., (2007) previously established a bioassay method to screen for compounds that activate the promoter activity of p21WAF1/CIP1, a potent inhibitor of cyclin-dependent kinases, in a p53-independent manner. As an activator of p21WAF1/CIP1 promoter activity, authors isolated cryptolepine (CLP: 5-methyl indolo (2,3b)-quinine), an indoloquinoline alkaloid, from *S. cordifolia*. They showed here that CLP-induced the expression of p21WAF1/CIP1 with growth arrest in p53-mutated osteosarcoma human osteosarcoma cell line (MG63 cells)⁴⁵.

Joseph et al., (2011) reported the bioactive compounds from the *S. cordifolia* and observe its cytotoxic effect on Hela cell lines. The results from gas chromatography-mass spectrometry analysis showed mainly four different compounds such as vasicinol, ephedrine, vasicinone, and hypaphorine based on retention time and peak observation. The results of cytotoxic activity on Hela cells treated with *S. cordifolia* extracts showed that cells with uncontrolled

growth have been arrested and there is decline level of cancerous cells²⁸.

Anti-nociceptive property

Hemayet *et al.*, (2012) evaluated for the anti-nociceptive property of the ethanolic extract of *S. cordifolia* root against acetic acid induced writhing model in mice. Acetic acid-induced writhing model represents pain sensation by triggering localized inflammatory response. The ethanolic roots extract of *S. cordifolia* exhibited significant ($p > 0.001$) writhing inhibition in acetic acid induced writhing model⁴⁶.

Phytochemistry

S. cordifolia leaves contain small quantities of both ephedrine and pseudoephedrine. However, the quantities are low, with less than 2% of ephedrine and pseudoephedrine found in the leaves of *S. cordifolia*. Ephedrine is known to stimulate the central nervous system (CNS), and as such can enhance weight loss. Traditionally nutrition companies used plants such as *Ma-Huang* (Ephedra plant), because it contained relatively large amounts of ephedrine, in their weight loss products. Ephedrine, a 2-aminophenylpropane alkaloid was first isolated from *Ephedra sinica*. *Ephedra gerardiana* is widely used in Ayurvedic system of medicine. Ephedrine is a potent bronchodilator. Another alkaloid reported from *Ephedra* sp. is pseudoephedrine which seems to be present in lower concentrations in *S. cordifolia*. Ephedrine and nor ephedrine suppresses the appetite resulting in weight loss. Other alkaloids like norpseudoephedrine are less potent as compared to ephedrine and norephedrine (phenylpropanolamine) and can cause serious ill effects. Therapy with nor ephedrine has been linked with stroke in young age group⁵.

Major chemical constituents

Ephedrine

Pseudoephedrine

Sterculic, malvalic and coronaric acid

Fatty acids

Saponine

Betaphenethylamine

Hypaphorine

Ecdysterone

Indole alkaloides

Palmitic, stearic and β – sitosterol

CONCLUSION

The extracts of different parts might be added value in the scientific evaluation of medicinal application of *S. cordifolia*. Many pharmacological investigations have been carried out based on its chemical constituents. Extensive literature survey revealed many pharmacological properties includes antibacterial, antifungal, anticancer, anticaries, anticonvulsant, antidiabetic, antimutagenic, anticlastogenic, antiulcer, antioxidant, antiviral and wound healing activities.

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