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Ethnomedicinal uses, phytochemical and pharmacological profiles, and toxicity of *Sida acuta* Burm. f. : A review article

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Abstract


For thousands of years, plants and herbs have been a tremendous source of food and medicine. Various parts of *Sida acuta* have been reported in many studies to be used by indigenous people from tropical countries to manage some health problems: rheumatic affections, azoospermia, oligospermia and spermatorrhea, leucorrhoea, wounds, sciatica, nervous and heart diseases, cold, cough, asthma, tuberculosis and respiratory diseases, disorders of the blood, bile and liver, elephantiasis, hemorrhoids, ulcers, gastric disorders and abdominal pain, headache, fever and malaria, skin diseases, worms, diarrhea and dysentery, venereal diseases, renal inflammation, toothache and snake bites. *Sida acuta* has been scientifically studied for its numerous pharmacological profiles such as: antioxidant, antimicrobial and antibacterial, antimalarial, cardiovascular, antiulcer, analgesic and anti-inflammatory, antipyretic, hepatoprotective, hypoglycemic, insecticidal and anticancer. Moreover, it has been proved that there was no mortality in rats administered with this plant extract up to a dose level of 2000mg/Kg body weight. Bioactive constituents such as alkaloids, saponins, coumarins, steroids, tannins, phenolic compounds, cardiac glycosides, sesquiterpene and flavonoids, significantly present in the plant extract, account for its multiple properties and uses in traditional medicine. This review study is an attempt to give a detailed survey of the literature on the ethnomedicinal uses, phytochemical and pharmacological profiles, as well as the toxicity of *Sida acuta*.

Keywords: *Sida acuta*, ethnomedicinal, phytochemical, pharmacological, toxicity

Introduction

Since the beginning of human civilization, medicinal plants have been used by mankind for their nutritional and therapeutic values. Nature has been a source of medicinal agents for thousands of years and an impressive number of modern drugs have been isolated from natural sources. Many of these isolations were based on the uses of these agents in traditional medicine. *Sida acuta* Burm.f (Malvaceae) is one of those plants currently used by indigenous people for the management of some health problems. This plant is an erect, branched small perennial herb or small shrub of about 1.5m height [1]. The bark is smooth, greenish, the root is thin, long, cylindrical and very rough; leaves are lanceolate, nearly glabrous, peduncles equal to the petioles, the flowers are yellow, solitary or in pairs; seeds are smooth and black [2, 3]. It grows abundantly on cultivated fields, waste areas and roadsides in Cameroon, where it is called "sengh" in the Western part of the country. Its common name is Sida. Once the plant becomes established, it is very competitive, holding and denying sites to other plants. The plant can be propagated both by seed and stem cuttings. All parts of this tree, including leaves, bark, root, seeds and flower are used in folkloric medicine.

Scientific classification

| | |
|-----------------------------------------------------|---------------------------------------------------------------------------------------|
| Kingdom: Plantae |  |
| Class: Dicotyledoneae | |
| Order: Malvales | |
| Family: Malvaceae | |
| Genus: Sida | |
| Specie: Sida acuta | |
| Scientific name: <i>Sida acuta</i> Burman f. | Plant image |
| Common name: Sida | |

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Traditional uses

All parts of the plant are used for therapeutic purposes, but the leaves are the most frequently request. Leaves are considered to possess demulcent, diuretic, anthelmintic and wound healing properties, and are used to treat rheumatic affections [4, 5]. The leaves decoction is used to treat abdominal pain, hemorrhoids, azoospermia and oligospermia [6]. The leaf juice is also used in India for vomiting and gastric disorders [7]. The roots of the *Sida* species are considered excellent adaptogenic and immunomodulator, general nutritive tonic and prolonged life; useful in tuberculosis and in diseases associated with injury, heart diseases, cough and respiratory diseases [8]. Root is also claimed to possess aphrodisiac, antirheumatic, stomachic, diaphoretic, diuretic, antipyretic and wound healing properties [1]. The root extract is taken in the case of leucorrhoea [9], breathing problems and cough [10]. In Papua New Guinea, the fresh root is chewed for the treatment of dysentery [11]. In Indian traditional medicine, the root of *Sida acuta* is extensively used as a stomachic, diaphoretic and antipyretic. It is regarded as cooling, astringent, tonic and useful in treating nervous and urinary diseases and also disorders of the blood, bile and liver [12], while the hot water extract of the dried entire plant is administered orally as a febrifuge, an abortifacient and a diuretic [13]. It is also used to treat gonorrhoea, elephantiasis, ulcers and is claimed to have aphrodisiac properties. The juice of the root is applied to wounds. The whole plant extract is often assumed to treat diseases such as fever, headache, skin diseases, diarrhea and dysentery [14]. It is used as diuretic in rheumatic infections and as a demulcent in gonorrhoea and chronic dysentery [8]. *Sida acuta* is an ingredient in Siddha formulation indicates in rheumatism, facial paralysis, pulmonary tuberculosis, sciatica, haemorrhage, spermatorrhoea, leucorrhoea and gonorrhoea [9]. The plant is credited with abortifacient, anthelmintic and antiemetic properties [15]. In Nicaragua, the decoction of the entire plant is taken orally for asthma, fever, aches and pains, ulcers and as an anti-worm medication; while a decoction of the dried entire plant is taken orally for venereal diseases [16, 17]. In Central America, the plant is used to treat asthma, renal inflammation, cold, fever, headache, ulcers and worms [18]. In Colombia the whole plant is known to treat snake bites and it lessened the hemorrhagic effect of *Bothrops atrox* venom [19, 20]. In Cameroon, the whole plant is claimed to possess anti-inflammatory, antirheumatic, diaphoretic and febrifuge, sedative, anti-ulcer and anthelmintic properties. A decoction of the whole plant is used for the treatment of fever and rheumatism, and to eradicate intestinal worms. The same decoction is also used to treat malaria [21]. The leaves are applied to the head as a poultice to ease headache. The root is chewed to relieve a toothache. A decoction of the leaves of plant is used to clean wounds. The plant extract is also known as an abortifacient.

Reported phytoconstituents and nutrients

Many scientific researches have been carried out in order to determine the chemical composition of *Sida acuta*. Almost all parts of the plant are concerned by these researches, but leaves and root are the most studied. The phytochemical screening of *Sida acuta* species revealed the presence of alkaloids such as vasicine, ephedrine and cryptolepine (the main alkaloid in the plant) [22, 23], saponosides, coumarins, steroids (ecdysterone, β -sistosterol, stigmaterol, ampesterol), tannins, phenolic compounds (evofolin-A, and B, scopoletin, loliolid and 4-ketopinonesinol), polyphenol, sesquiterpene and flavonoids [24]. In another study, Nwankpa *et al* evaluated the

Phytochemical and micronutrient composition of *Sida acuta* using standard analytical methods [25]. The result (mg/100g) for phytochemical composition were 91.46 \pm 0.02 tannin, 1500.36 \pm 0.36 alkaloid, 530.27 \pm 0.03 saponin, 1163.86 \pm 0.1 flavonoid, 1454.50 \pm 0.85 steroid, 115.29 \pm 0.05 terpenoids and 851.62 \pm 0.01 cardiac glycosides. The vitamin composition (mg/100g) were 0.36 \pm 0.01 thiamin, 0.19 \pm 0.02 niacin, 24.27 \pm 0.25 ascorbic acid, 1.85 \pm 0.32 tocopherol, 0.12 \pm 0.05 riboflavin, while mineral composition (mg/100mg) was 14428 \pm 0.02, 122.11 \pm 0.01, 325.12 \pm 0.02 for calcium, magnesium and zinc, respectively. Some of the general characteristics of flavonoid include potent water soluble super antioxidants and free radical scavenger; they prevent oxidative cell damage, have strong anticancer activity and protect against all stages of carcinogens [26]. Flavonoids in intestinal tract lower the risk of heart disease and inflammation [27]. Also, flavonoids have been reported to possess significant antiulcer activity in various experimental models of gastric and duodenal ulceration [28]. Isolated pure form of alkaloids and their synthetic derivatives are used as basic medicinal agents for their analgesic and bacterial effects [29], antihypertensive, antiarrhythmic, antimalarial and anti-cancer activities [30]. Tannin rich medicinal plants are used to heal a lot of illnesses; such as leucorrhoea, rhinorrhea and diarrhea. More recently, tannins have gained medical interest, because of the high prevalence of deadly ailments such as AIDS and numerous cancers [31]. In the dyestuff industry, tannins are useful as caustics for dye and ink production. Also, in the food industry, tannins have proved usefulness in the purification of wine, beer and fruit juices and also as coagulants in rubber production [32]. Saponins are responsible for antimicrobial, antifungal, anti-inflammatory, anti-yeast and antidote activates. The function of saponins in plants generally serves as anti-feedant and to protect the plant against microbes and fungi [33]. Phenols have been extensively researched as disease preventives [34]. Steroids are antioxidants *in vitro*, and have a link with reproduction in humans [35]. The results obtained from phytochemicals and micronutrients screening of *Sida acuta* gives credence to the medicinal benefits that this herb have been used for, in the past years and supports its traditional uses for the management of various health problems.

Pharmacological activities

Antimalarial activity: Karou *et al* investigated the antimalarial activity of five plants used in the traditional medicine of Burkina Faso to treat malaria, including *Sida acuta* [36]. These plants extracts were tested *in vitro* on fresh clinical isolates of *Plasmodium falciparum*. The result revealed *Sida acuta* to be the most active plant of the study (IC₅₀ value of 4, 37 μ g/mL). In another work, Marimuthu studied the larvicidal and repellent activities of crude leaf extract of *Sida acuta* against three important mosquitoes [37]. The result showed that crude extract of the plant had strong repellent action against the three species of mosquitoes investigated. The ethanolic extract and water decoction of the aerial part of *Sida acuta* from Ivory Coast was tested for their *in vitro* antiplasmodial activities on two strains of *Plasmodium falciparum*: Cameroon (chloroquine-resistant strain) and a Nigerian (chloroquine-sensitive strain). The ethanolic extract exhibited a better antiplasmodial activity than the decoction [38]. Adebayo *et al* investigated on medicinal plants used to treat malaria in Nigeria [39]. *Sida acuta* and some other plants showed intense activity against malaria parasites *in vitro* and in experimentally infected mice.

All these studies have proved that *Sida acuta* has significant antiplasmodial activity. This activity is mostly due to its alkaloid content [36]. In fact, the alkaloid cryptolepine is the antiplasmodial constituent [38].

Anti-ulcer: In a study conducted by Akilandeswari *et al*, gastric ulcers were induced in the experimental animals by Pylorus ligation, and administration of Aspirin (300mg/kg) and Ethanol (1ml/kg) [40]. Then Ethanolic extract of leaves of *Sida acuta* was administered to those animals and their effect studied. The antiulcer activity was appraised by determining and comparing the ulcer index in the test drug groups with that of the control group as well as that of Famotidine 20mg/kg (used as reference drug). This plant extract was established for its significant antiulcer activity against all the three ulcer inducing experimental models, by reducing the ulcer index in those models with a better result than famotidine group, at 200mg/kg of the extract against aspirin (300mg/kg) plus pylorus ligation model. The antiulcer activity of ethanol extract of whole plant of *Sida acuta* was also supported by Malairajan *et al* [41]. This plant extract was studied for its antiulcer activity against aspirin plus pylorus ligation gastric ulcer, HCl-ethanol induced ulcer and water immersion stress induced ulcer in rats [41]. They found that ethanol extract markedly decrease the incidence of the ulcer in the first two models. Though authors have not studied the active principles responsible for the antiulcer activity of *Sida acuta*, it is likely that flavonoids compounds, tannins, steroids and triterpenoids present in the plant may be involved in this action as flavonoids have been reported to possess significant antiulcer activity in various experimental models of gastric and duodenal ulceration [28].

Wound Healing activity: Akilandeswari *et al* investigated the effects of topical administration of methanol extract of *Sida acuta* ointment on two types of wound models in rats: (i) the excision and (ii) the incision [40]. In the excision model, the extract treated wounds were found to epithelialize faster and the rate of wound contraction was found to be greater than that of the control. In the incision wound studies, there was a significant increase in tensile strength of the 10-days old wound due to treatment with *Sida acuta* ointment and with the reference standard Nitrofurazone ointment when compared with the respective control. It was concluded that the wounds contracting ability of the methanol extract of *Sida acuta* ointment produced significantly greater response in both of the wound types tested than the control. Adetutu *et al* recorded thirty-six plant species used in the traditional wound healing preparations [42]. Most of the plant extracts, including *Sida acuta* was reported to have both antioxidant and antibacterial activities, thereby suggesting that all have some potential for wound healing. These results support the traditional use of the plants for wounds healing.

Hepatoprotective activity: Hepatoprotective effects of methanol extract of *Sida acuta* were obtained against liver damage induced by paracetamol overdose as evident from decreased serum levels of glutamate pyruvate transaminase, glutamate oxaloacetate transaminase, alkaline phosphatase and bilirubin in the *Sida acuta* treated groups compared to the intoxicated controls [43]. The hepatoprotective effect was further verified by histopathology of the liver. Pretreatment with *Sida acuta* extract significantly shortened the duration of hexobarbitone induced narcosis in mice, indicating its

hepatoprotective potential. The presence of the phenolic compound, ferulic acid in the root of *Sida acuta*, confirmed this significant hepatoprotective effect [43].

Cardiovascular activity: Kannan *et al* screened cardioactive herbs from Western Ghats of India. The heart beat rate (HBR) and blood flow during systole and diastole were tested in Zebrafish embryos [44]. The methanol extract of *Sida acuta* led to decrease in the HBR in Zebrafish embryos, which was greater than that caused by Nebivolol (used as reference drug).

Antibacterial and antimicrobial activity: Antibacterial and antifungal activity studies of leaf extracts of *Sida acuta* were carried out [40]. Two common solvents (Chloroform and Ethanol, 95% each) were used successively for extraction of active principles from the dried powdered leaves. The antimicrobial screening was done with two Gram +ve (*Staphylococcus aureus* NCIM 2079, *Bacillus subtilis* NCIM 2063) and two Gram-ve (*Escherichia coli* NCIM 2065, *Pseudomonas aeruginosa* NCIM 2036) bacteria and fungi (*Candida albicans* NCIM 3102, *Aspergillus niger* NCIM 1054) as test microorganisms. All the three microorganisms were markedly affected by both the extracts under study, with the maximum activity recorded against gram positive *Staphylococcus aureus* and gram negative *Escherichia coli* respectively. These effects were similar to that of commercially available antibiotics under the same laboratory condition. The similar result was previously obtained by Oboh *et al* [45]. In another study, antimicrobial activity of aqueous and ethanol leaves extracts of *Sida acuta* against 45 clinical isolates of *Staphylococcus aureus* isolated from nasal cavity of Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (HIV/AIDS) patients from University of Nigeria teaching hospital, Enugu, was evaluated using agar well diffusion method [46]. The minimum inhibitory concentration (MIC) of the extracts was also determined using agar well diffusion technique and the killing rate of each extract was also determined at different time intervals of 0-90 min. The results of the agar well diffusion study revealed that ethanol extracts produced the highest antimicrobial activity (86%), followed by hot water (61%) and cold water extracts (48%). The MIC obtained ranged from 0.9625-1.8125 µg/mL for ethanol extracts, 7.8125-31.25 µg/mL for hot water and 15.625-31.25 µg/mL for cold water extracts. The result of killing rate studies showed that the test organisms were killed within 0-10 min for ethanol and hot water extracts and 5-60 min for cold water extracts. The over all results indicated that *Sida acuta* extracts have appreciable antimicrobial activity against *Staphylococcus aureus* isolated from HIV/AIDS patients. In addition to authenticating the folkloric use of *Sida acuta* in the treatment of common diseases, the finding of these studies highlights the possible usefulness of this plant material in the treatment of opportunistic infections caused by *Staphylococcus aureus* in HIV/AIDS patients.

Purify water: *Sida acuta* is used to remove fluoride from water [20]. In an experiment, this plant's leaves were used in the water samples of some villages of Bhiloda taluka (with a fluoride content of about 1.55mg/L) in order to evaluate their effect on fluoride content of those samples [20]. The result showed that with the help of leaves extracts, fluoride content came down to 1.42mg/l. So it is concluded that the leaves of this plant are useful to decrease fluoride content in water. This

result is very important as it shows the use of *Sida acuta* extract to purify water. Excess content of fluoride is lethal for human being. In fact, it is responsible for so many diseases like dental fluorosis and skeletal fluorosis.

Neuropharmacological effects: In an experiment conducted by Dora *et al*, the ethanol extract from the leaves and stems of *Sida acuta*, caused significant effects on the central nervous system in experimental animals [47], and support its traditional uses as sedative.

Insecticidal properties: The ethanol leaves extracts of *Sida acuta* and three other plants in different concentrations were investigated for their insecticidal activity against *Acanthscelides obtectus*. Average mortality indicated that the extracts caused significant mortality on the target insects. The bioassay indicated that the toxic effect of the extracts was proportional to the concentration and observed overall mean mortality also increased with increase in time intervals after treatment [48].

Antioxidant activity: To determine the antioxidative potential of *Sida acuta*, twenty-four adult wistar albino rats were divided into four groups of 6 rats each [25]. Group 1 received feed and water (control) while group 2, 3 and 4 in addition to feed and water were treated with ethanol leaf extract of *Sida acuta* at 20, 40 and 60 mg/kg body weight, respectively. After one day of treatment; the rats were sacrificed and plasma obtained for oxidative stress indices assay. The result showed a significant decrease ($P < 0.05$) in mean values of plasma malondialdehyde concentration and a significant increase ($P < 0.05$) in reduced glutathione concentration at 40 and 60 mg/kg body weight compared to the control group. Plasma catalase and superoxide dismutase activity were significantly increased ($P < 0.05$) only in animals treated with 60 mg/kg body weight compared to the control group. The result showed that ethanol leaf extract of *Sida acuta* possesses an antioxidant property which, in a dose-dependent manner, reduces/ameliorates oxidative stress in rats.

Antipyretic activity: The petroleum ether, acetone, ethanol and aqueous extracts of the leaf of *Sida acuta* were evaluated for their antipyretic activity. It was observed that all the extracts lowered the temperature with passage of time but the acetone extract showed better antipyretic activity amongst other extracts. The antipyretic activity of the ethanol extract was observed to be more as compared to other extracts and its effect was seen within 1.5 hours as compared to other extracts [49].

Neutralizing activity against snake venom: Ethanolic extract of the whole plant of *Sida acuta* has a moderate neutralizing activity against the haemorrhagic effect of *Bothrops atrox* venom [50].

Hypoglycemic activity: The effect of the aqueous and methanol extracts of *Sida acuta* on blood glucose levels in both normal and diabetic rabbits was studied in glucose overloaded rabbits [51]. Extracts were also tested for anti-diabetic activity in alloxan-induced diabetic rabbits. Results showed that both extracts at 400 mg/kg significantly increased the tolerance for glucose in glucose fed normal rabbits. Blood glucose levels were reduced significantly at 5.5 hours post-

glucose load ($p < 0.05$). This reduction was consistent and persisted for 10.5 hours. The crude leaf extracts of *Sida acuta* therefore possess hypoglycemic activity.

Anticancer activity: A study aimed to screening the anticancer activity of ethanol extracts of *Sida acuta* against Nitrosodiethylamine (NDEA) and CCl₄ induced hepatocellular cancer in wistar rats was conducted by Mallikarjuna *et al* [52]. The treatment with ethanol extracts of this plant at the dose levels of 200 and 400 mg/Kg body weight for 28 days significantly restored the elevated serum levels of SGOT, SGPT, ALP, LDH and GGT with prominent increase in proteins synthesis in a dose dependent manner. The extracts showed a significant increase in activities of antioxidant enzymes that reduce the oxidative stress induced damage, hence exhibiting a potent antioxidant and anticancer activity.

Analgesic and anti-inflammatory activity: Analgesic and anti-inflammatory activity of *Sida acuta* was studied in mice and rats using the tail immersion and mouse ear oedema models [53]. The crude extracts of this plant exhibited significant ($p < 0.001$) analgesic and anti-inflammatory activities in mice. Mridha *et al* also investigated analgesic activity of leaf extract of *Sida acuta* using petroleum ether, acetone and distilled water [54]. The acetone extract of the leaf showed maximum analgesic activity amongst other extracts. This justifies the traditional use of *Sida acuta* against pain and inflammation.

Reported toxicity: A study conducted by Mallikarjuna *et al* on *Sida acuta* acute toxicity on rats demonstrated that there was no mortality in animals administered with this plant's extract, up to a dose level of 2000 mg/Kg body weight [53]. Similar result was previously mentioned by Pieme *et al* [55]. Hence, this plant's extract was found to be safe.

Conclusion

Sida acuta has been used for long time, in traditional medicine to treat numerous ailments of the human body, in many countries of the globe. All parts of the herb, including leaves, bark, root, seeds and flower are used by traditional healers. Some biological tests carried out on the plant for: antioxidant, antimicrobial and antibacterial, antimalarial, cardiovascular, antiulcer, analgesic and anti-inflammatory, antipyretic, hepatoprotective, hypoglycemic, insecticidal and anticancer activities revealed positive results without adverse side effects. Bioactive constituents such as alkaloids, saponins, coumarins, steroids, tannins, phenolic compounds, cardiac glycosides, sesquiterpene and flavonoids, significantly present in the plant extract, account for its multiple properties and uses in traditional medicine, while its rich content in minerals and vitamins validate its high nutritional value. We sincerely hope that the information provided in this review on *Sida acuta* will serve as a data base for proper evaluation of this plant extracts and for pharmaceutical applications of its bioactive components.

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