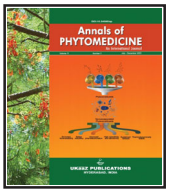
Annals of Phytomedicine 11(2): 245-254, 2022

DOI: http://dx.doi.org/10.54085/ap.2022.11.2.27

Annals of Phytomedicine: An International Journal
http://www.ukaazpublications.com/publications/index.php

Print ISSN : 2278-9839 Online ISSN : 2393-9885



Review Article : Open Access

An overview of the traditional importance, phytochemistry, and pharmacological properties of *Sida acuta* Burm.f.

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Article Info

Article history
Received 5 October 2022
Revised 29 November 2022
Accepted 30 November 2022
Published Online 30 December-2022

Keywords
Sida acuta Burm. f.
Indian traditional system of medicines
Phytochemistry
Pharmacological activity
Antimalarial activity
Antioxidant activity

Abstract

Sida acuta Burm.f., (SA) a member of the Malvaceae family, has traditionally been prescribed for a variety of ailments. The plant is traditionally used to treat skin problems, fevers, ulcers, and liver problems. The plant is rich in wide variety of phytochemicals, and several laboratory studies have been undertaken to support the scientific basis behind these uses, resulting in the isolation of many components from the plant. A range of research platforms have been used to acquire traditional medical knowledge, pharmacological significance, and phytochemical information of SA. Recent scientific studies have shown that SA can be a promising agent for treating a variety of diseases, including antioxidants, ulcers, malarial infections, diabetes, cancer and liver disorders. This review summarizes this recent information in order to provide the necessary information for developing new molecules from the medicinal plant and directing additional scientific investigations.

1. Introduction

The pharmacological properties of plants have been recognized for a long time. Herbal remedies have been used for centuries by indigenous cultures around the world to treat a variety of ailments. The pharmaceutical industry has grown significantly over the last century as a result of the identification and exploitation of chemicals with defined mechanisms of action (Zeouk and Bekhti, 2020). Plant-based products and their analogues are now widely used in clinical application due to the development of extremely effective medications (Máthé and Khan, 2022). Despite the many benefits of utilizing plant-based products to treat a wide range of diseases, some complex illnesses cannot be effectively treated. In the early nineteenth century, research into medicinal plant-derived agents laid the foundation for today's pharmaceutical industry. Although, a limited number of these molecular entities have been approved by the US Food and Drug Administration for the treatment of diseases, many have not been widely used over an extended period of time (Parveen *et al*., 2020; Patridge *et al*., 2016). Herbal remedies typically contain a combination of several ingredients mixed in a specific ratio. It is hypothesized that the therapeutic effects seen in holistic formulations are due to the synergistic interaction of individual ingredients. The combinatorial effect is a phenomenon that can be responsible for the pharmacological efficacy of chemicals. In the treatment of chronic diseases, traditional herbal remedies have had limited success (Ansari and Ahmad, 2019). A greater understanding of the underlying mechanisms behind traditional holistic prescriptions could help to inform complex disease biology, paving the way for the development of novel therapeutics. *Sida* is a genus of flowering plants with approximately 200 species, most of which are found in warm climates around the world. Seventeen species have been reported to occur in India. The majority of the *Sida* species found in India are known by the general name "Bala" and are referred to as *Balachatustaya* in the Ayurvedic system. *Sida acuta* Burm.f. (Figure 1) is a plant used in many traditional medical systems to manage health issues (Ajitha Bai *et al*., 2012). *Kapacurak kutinir*, a part of the Siddha system of medicine, contains SA root as one of its ingredients and is referred to as *Vattatiruppi* (Kumar *et al*., 2021). The synonym of SA is *S. carpinifolia* Auct. Non - Linn. f. In Tamil language, it known as *Pillavalatthi chedi* (Ignacimuthu *et al*., 2006). This plant is commonly seen in tropical areas or hotter part of India and Nepal. In folk medicine, it is known as *Jangali Methi* and Ayurveda refers to it as *Balaa*. Bark surfaces are smooth and greenish in colour. A thin, long, cylindrical root is characteristic of the plant. The leaves have a lanceolate shape. Yellow coloured flowers, solitary or in pairs, and their seeds are black (Khare *et al*., 2002). Different plant part of SA consists of complex phytochemicals, which are responsible for biological activity. The roots and seeds of this plant revealed the presence of pharmacologically active alkaloids, with a concentration of 0.066% and 0.26%, respectively (Khare, 2008). In this study, we provide an in-depth critical overview of *Sida acuta's* traditional importance, pharmacological properties, and chemical constituents.

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Figure 1: *Sida acuta* Burm.f.

2. Methodology

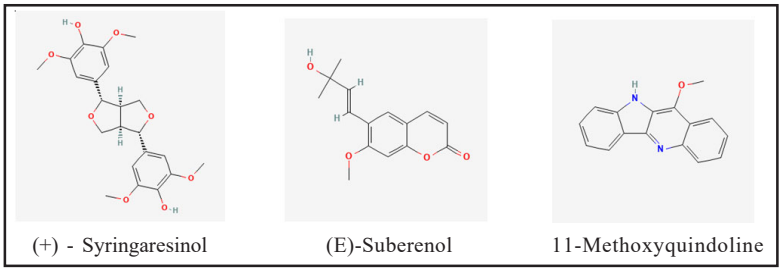
To conduct the literature review, the following search terms were used: "traditional uses," "phytochemistry or phytochemicals," and "pharmacological or biological importance." These terms are usually prefixed with *S. acuta* . The above keywords were used to search in electronic databases, books, and printed journals for information about *S. acuta*. Several databases were searched for relevant articles. These included PubMed, Google Scholar, Research Gate, Web of Science, and NOPR. Our review focused on *in vivo* and *in vitro* studies published in English between January 2000 and March 2022. Among the 108 publications that were initially screened, 65 studies were included in the study. In this review, only primary literature was included. The review process excluded duplicate articles, non-relevant articles, and articles written in languages other than English. The scientific literature that has been peer-reviewed is generally considered to be more reliable than other types of research. The review of literature was limited to peer-reviewed publications related to *Sida acuta*.

3. Traditional importance of SA

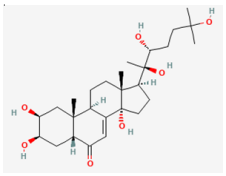
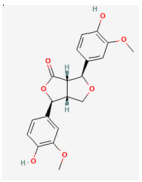
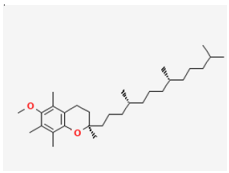
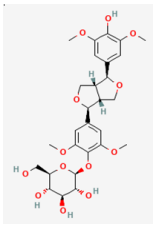
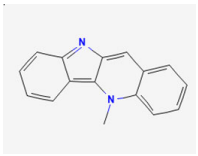
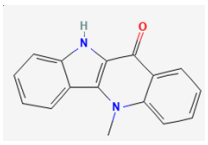
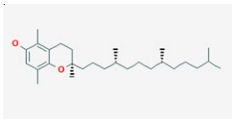
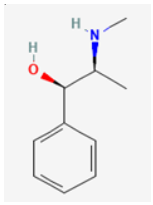
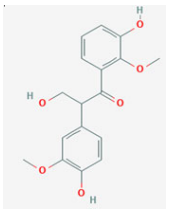
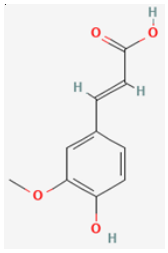
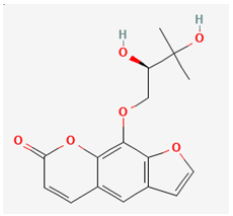
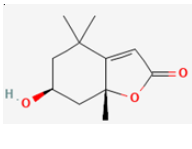
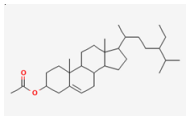
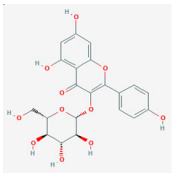
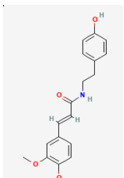
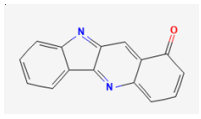
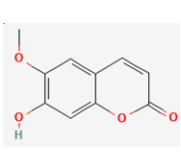
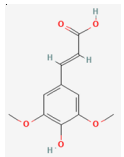
Traditional medicine offers a reliable and effective method of delivering health care to the public. Several medicines have been developed from the knowledge of tropical forest people, and it is likely that there will be more in the future. In the Indian traditional system, SA is an important medical treatment for a wide variety of ailments. SA bark and roots are among the most effective parts of the SA for treating a variety of diseases. The root of SA is used extensively as an astringent, cooling agent, stomach problems, diaphoretic and antipyretic. The plant can also be used to treat nervous and urinary troubles, as well as disorders of the blood, bile, and liver (Khare, 2008). It is used to treat sexually transmitted diseases such as gonorrhoea, parasitic disease lymphatic filariasis, and certain types of ulcers. Treatment often involves applying a root juice to the wound. The entire plant is used in traditional medicine to reduce the haemorrhagic effects of the venom of *Bothropsatrox* (Gupta, 2003). Combined with coconut oil, leaves of a SA are used to kill dandruff and improve hair health (Ignacimuthu *et al*., 2006).

4. Phytochemistry of SA

Phytochemicals are naturally occurring compounds found in plants with a variety of functions, including providing defences against diseases and environmental stressors. Some phytochemicals can also promote human health, and they are being studied for their potential to prevent or treat various diseases. The medicinal plant SA consists of a variety of phytocompounds and the chemical structures are shown in Figure 2. An analysis of ethanol extracts from SA leaves revealed the presence of alkaloids, flavonoids, steroids, tannins, terpenoids, and cardiac glycosides (Adeniyi *et al*., 2010). Vitamins and minerals present in SA leaves include ascorbic acid, niacin, thiamine, riboflavin, and β-carotene, as well as calcium, iron, phosphorus, sodium, and magnesium (Raimi *et al*., 2014). The methanolic seed extracts of SA contained a significant amount of 20-hydroxyecdysone (Dinan *et al*., 2001). Also reported in SA are heraclenol, beta-sitosterol, acanthoside B, and daucoglycoside (Pieme *et al*., 2010). Biologically active chemicals were detected in an activity-guided fractionation of the ethyl acetate-soluble extract of SA whole plant, including quindolinone, cryptolepinone, 11-methoxyquindoline, N-trans-feruloyltyramine, vomifoliol, Ioliolide, 4-ketopinoresinol, scopoletin, evofolin-A and evofolin-B. In addition, the entire plant extract contains five compounds, namely ferulic acid, sinapic acid, syringic acid, (+)-syringaresinol, and vanillic acid (Jang *et al*., 2003). The ethanolic extract of the whole SA plant contains ephedrine and also it contains cryptolepine (Banzouzi *et al*., 2004). Quantification by HPLC-PAD method, aerial part of the strong base extract of SA contains the highest amount of cryptolepine (168.01 g/g) when compared with extract of MeOH (12.54 g/g), 2% HCl - MeOH (4.93 g/g) and water (1.73 g/g) (Chatterjee *et al*., 2013). The methanolic extract of the whole plant contains a tocopherol derivative, 7a-methoxy-α-tocopherol, and a taraxastane triterpene, taraxast-1, 20(30)-dien-3-one. Additionally, the plant contains known compounds such as α and β-tocopherol, and α-tocospiro-B (Chen *et al*., 2007). The bioassay-guided separation of SA whole plants led to the isolation of an alkaloid along with two kaempferol glycosides, namely kampferol-3-O-α-L-rhamnopyranosyl-α-d-glucopyranoside and kampferol-3-O-β-d-glucopyranoside (Ahmed *et al*., 2011). A hydroalcoholic extract of the whole plant of SA, followed by column chromatography, revealed the presence of xylitol dimer, an unknown phytocompound, as well as cryptolepine, 20-hydroxyecdysone, (E)-suberenol, thamnosmonin, and xanthyletin (Kamdoum *et al*., 2021).



(+) - Syringaresinol (E)-Suberenol 11-Methoxyquindoline

		
20-hydroxyecdysone	4-ketopinoresinol	7a-methoxy-α-tocopherol
		
Acanthoside-B	Cryptolepine	Cryptolepinone
		
β-tocopherol	Ephedrine	Evofolin-B.
		
Ferulic acid	Heraclenol	Ioliolide
		
β-Sitosterol	Kampferol-3-O-β-d-glucopyranoside	N-trans-feruloyltyramine
		
Quindolinone	Scopoletin	Sinapic acid

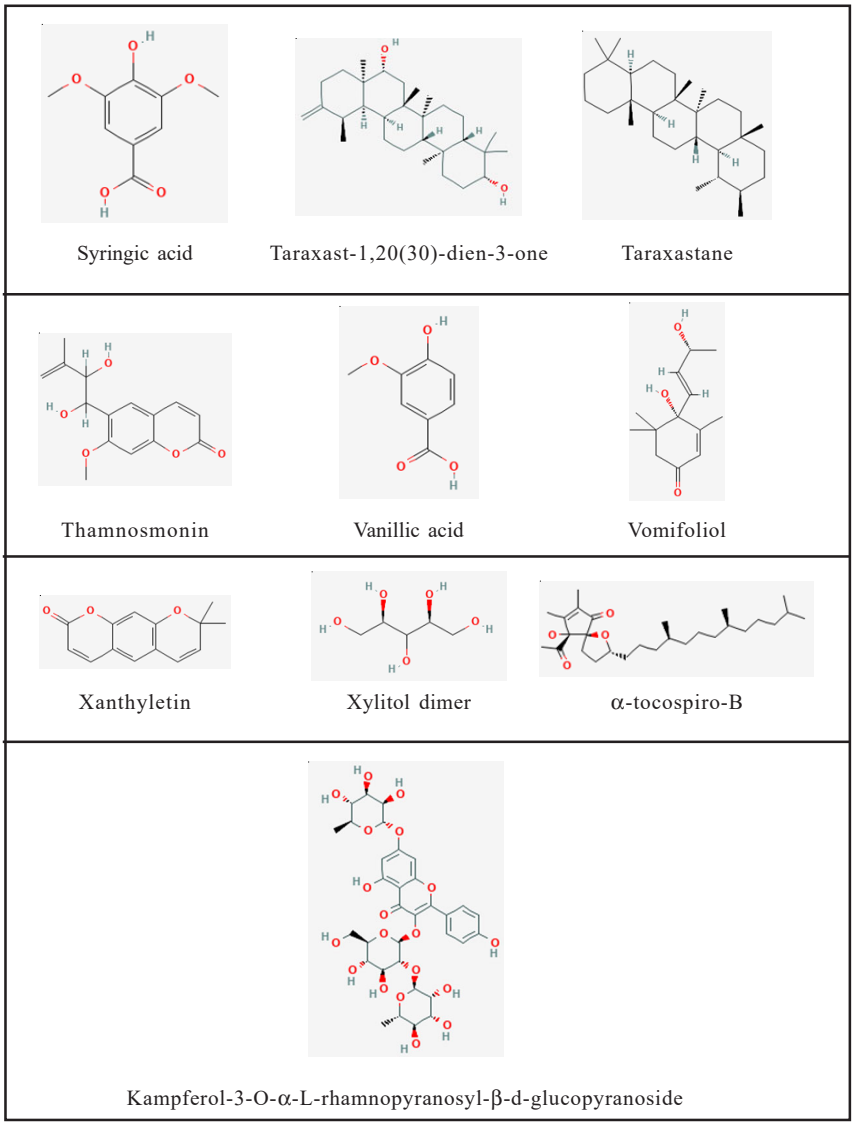


Figure 2: Chemical structures of the phytoconstituents isolated from *Sida acuta* Burm.f.

5. Pharmacological activity of SA

5.1. Antimicrobial activity

Phytochemicals and plant extracts possess antimicrobial properties and have been used for centuries as antibacterial agents prior to the discovery of antibacterial agents. A collaboration of scientists from diverse fields has led to the discovery of phytochemicals as a lead compound to treat infectious as well as non-infectious diseases. The recent research outcomes revealed that overuse of antibiotics has been linked to unforeseen health effects, such as the emergence of antibiotic-resistant strains. An excessive use of antibiotics has been associated with adverse health effects, including the development of antibiotic-resistant strains. As the incidence of drug-resistant pathogens has increased, there has been an increased interest in the antimicrobial properties of plant and metabolite compounds (Das *et al*., 2010; Sethumathi *et al*., 2021). The alkaloid-rich powder is prepared from the aerial part of SA. Agar-well diffusion assays demonstrate promising antimicrobial properties against gram-positive bacteria. Results from the broth microdilution assay revealed a MIC range of 16 to 400 g/ml, and a MBC range of 80 to 400 g/ml. A gas chromatography-mass spectrometry (GC-MS) analysis of the SA extract showed that cryptolepine and quindoline are the primary active components present, which may be responsible for its antimicrobial efficacy (Karou *et al*., 2006). In another study, both ethanolic and aqueous extracts of SA possess potent antimicrobial properties, particularly against skin infections caused by microorganisms. The phytochemical screening of these two extracts indicates that a higher proportion of alkaloids, saponins, anthraquinones, cardiac glycosides, and flavonoids are present in moderate quantities. The ethanolic extract showed better inhibition against *S. aureus* and *B. subtilis* (zone of inhibition ranging from 6 to 43 mm) than the aqueous extract. The antimicrobial activity was compared with gentamicin. The efficacy of antimicrobial activity has been found to be largely dependent on the quantity of the dose administered. There is no evidence that the extracts are beneficial in combating fungal organisms (Ekpo and Etim, 2009). Moreover,

chloroform and ethanol extracts of SA leaves have been shown to be effective against both fungi (*C. albicans* NCIM 3102 and *A. niger* NCIM 1054) and bacterial (*S. aureus* NCIM 2079, *B. subtilis* NCIM 2063, *E.coli* NCIM 2065 *P. aeruginosa* NCIM 2036) stains (Akilandeswari *et al*., 2010). The aqueous leaf extracts of SA and *Artemisia annua* were used to synthesise AgNPs. Both nanoparticles inhibited *E. coli, S. aureus,* and *C. albicans*, significantly (Johnson *et al*., 2014). Human infections caused by *E. coli* that produces extended-spectrum beta-lactamases are a major concern, particularly in nosocomial infections. Aqueous and acetone extracts of SA leaf are active against ESBL-producing *E. coli* from urinary tract infections (Prabhu, 2016). There was a study that identified leaf extracts to contain more alkaloids than stem and root extracts (2.31 ± 0.03 mg/ 100 g). A leaf extract was found to be more successful at inhibiting the growth of *P. aeruginosa, M. varians,* and *C. albicans.* Conversely, a root extract was determined to be more effective against *E. coli, S. typhi,* and *A. flavus* (Ezeabara and Egenti, 2018). In a study comparing the antimicrobial effects of four species of *Sida*, a methanolic extract of SA was found to be effective against *S. aureus*. The extract showed an inhibition zone of 20.5 mm due to the presence extract contains active ingredients (Asha *et al*., 2018). Similarly, copper nanoparticles (Cu-NPs) from SA have been shown to possess antimicrobial activity against *E. coli, P. vulgaris,* and *S. Aureus* (Sathiyavimal *et al*., 2018). The green synthesis method is utilized to fabricate cerium oxide nanoparticles (CeO_2 NPs) through the reduction and capping of the particles with phytochemicals derived from SA leaf extracts. The obtained CeO_2 NPs have a cubic fluorite structure in a spherical shape. A field emission scanning electron microscopy image of *E. coli* treated with CeO_2 nanoparticles indicates significant morphological changes and damage to the cell membrane (Senthilkumar *et al*., 2019). Globally, urinary tract infections pose a serious health threat. *Phyllanthus amarus, Phyllanthus muellerianus*, and SA leaf extracts have been found to be more active against microorganisms involved in UTI. According to the antioxidant assay, SA had the highest levels of total flavonoids and phenols. These compounds were found in 339.86 mgQUE/g and 27.63 mgGAE/g, respectively. SA crude extract had inhibition zones ranging from 14.7 ± 1.53 mm to 27 ± 2.00 mm, as well as MICs and MBCs limiting from 12.5 mg/ml to 50 mg/ml. According to the toxicology analysis, SA had a lethal dose concentration of 130.11 mg/ml. The extract from SA showed strong antimicrobial properties against all organisms tested, with *C. albicans* being the most sensitive (Obuotor *et al*., 2021).

5.2 Wound healing properties

Indian traditional medicine, known as Ayurveda, utilizes natural resources to derive medications for a variety of conditions. *Vranaropaka* (wound healers) is a classification used for medications derived from plants, minerals, and animals that are used to promote wound healing. Physical disabilities are often a result of wounds that cause functional impairments. There are several potential causes of these wounds, including physical, chemical, microbial, or immunological factors. The plant, SA, has been screened for its wound healing properties in multiple pharmacological models. Decoctions of SA leaves are traditionally used to treat wounds in Nigeria (Adetutu *et al*., 2011). A methanolic extract of SA ointment is effective in healing wounds. In comparison to control wounds, both excision and incision wound models epithelised faster and wound contraction is more rapidly, facilitating the healing process. SA extract's wound healing properties are mainly due to its presence of phytoconstituents (Akilandeswari *et al*., 2010_a; Oduwegwu *et al*., 2017).

5.3 Antimalarial activity

Traditional medicine has been an essential component of public health care in most rural communities around the world, particularly in developing countries. Malaria continues to be a serious worldwide health issue in many underdeveloped countries. A variety of medicinal plants and herbal combinations have been explored as possible antimalarial medicines. Currently, there is no vaccine available to prevent malarial infection. Moreover, due to resistance to chemotherapy and other factors, there are various challenges associated with the treatment of malaria with synthetic antimalarial drugs. Secondly, more effective antimalarial medicines must be developed on a routine basis to combat drug resistance. Some medicinal plants have mechanisms that are similar to synthetic antimalarial medications, and scientific research has revealed this. Traditionally, SA was used to treat malaria and other febrile illnesses (Adebayo and Krettli, 2011; Banzouzi *et al*., 2004). The ethanolic extract of the SA whole plant demonstrated a strong antimalarial effect against *Plasmodium falciparum* out of the four different plants. The IC_{50} values of SA against *Plasmodium falciparum* 3D7, chloroquine-sensitive strains, ranged from 0.05 to 57.04 µg/ml, while the IC_{50} values for chloroquine phosphate were found to be less than 0.042 µg/ml on average, with a median of 0.0097 µg/ml. The ethanolic extract of SA contains a high level of alkaloid content, which could be responsible for its antimalarial properties (Karou *et al*., 2003). In another study, cryptolepine is an alkaloid derived from the active fraction of the SA aerial part that exhibits antimalarial activity against two different resistant strains of *Plasmodium falciparum* (Banzouzi *et al*., 2004). *In vivo* studies have revealed that a phenolic-rich extract obtained from SA leaves effectively suppresses the plasmodium parasites. In comparison to alkaloid and flavonoid rich extracts, phenolic rich extract (600 mg/kg body weight) exhibited the highest plasmodial suppression (64.64%) and was very close to the positive control (chloroquine) in terms of plasmodial suppression (76.79%) (Adesina *et al*., 2020). In *Plasmodium berghei*-infected mice, treatment with ethanol extracts of SA leaves reduces parasite density. Additionally, ethanolic extracts of SA leaves improved the haematological and biochemical state of infected mice. The existence of secondary metabolites is principally responsible for the antimalarial action of SA ethanolic extract, but their specific composition is unknown (Enechi *et al*., 2021).

5.4 Antioxidant activity

Across the globe, there is a growing interest in finding antioxidants that are pharmacologically effective and have minimal side effects. There are a number of medicinal plants that possess remarkable antioxidant properties. The levels of reactive oxygen species (ROS) in the body are increased when under stress, exceeding those produced by enzymatic and non-enzymatic antioxidants. As a result of exposure to harmful ROS, oxidative stress can occur. It is possible to prevent disease development by quenching ROS with antioxidants. A plethora of studies have illustrated that antioxidants can be used as an effective or supportive treatment option for various human diseases, such as cancer, cardiovascular disease, and inflammatory conditions. Currently, synthetic antioxidants such as BHT and BHA are used as food additives. Many medicinal plants are rich in antioxidants, and SA is one of them. Tocopherols and triterpenoids

are isolated from methanolic extracts of SA's whole plant. Among the six isolated compounds three tocopherols are showing promising antioxidant activity. As measured by DPPH radical scavenging activity, 7a-methoxy-α-tocopherol, β-tocopherol, and α-tocopherol demonstrated significant antioxidant activity. The EC_{50} values of isolated compounds are 86.9, 68.2, and 70.9 µM, respectively (Chen *et al*., 2007). The silver nanoparticles (AgNPs) from aqueous leaf extracts of SA and *Artemisia annua* demonstrated strong antioxidant activity even at low concentration when assessed using the DPPH method, with ascorbic acid employed as a control (Johnson *et al*., 2014). Another study found that albino rats fed with an ethanolic extract of SA had lower plasma malondialdehyde levels and increased reduced glutathione levels than the control group. Animals given 60 mg/kg body weight had significantly higher plasma catalase and superoxide dismutase activity. An ethanolic leaf extract of SA exhibits dose-dependent antioxidant activity (Nwankpa *et al*., 2015). The entire SA plant is extracted using organic solvents with increasing polarity. SA's chloroform extract displays modest antioxidant activity when compared with ascorbic acid due to the existence of a considerable amount of phytochemicals (Muneeswari *et al*., 2016). The total phenolic content of aerial parts of SA ranged from 26.07 to 34.89 mg gallic acid/g, with higher concentrations found in dichloromethane and ethyl acetate extracts. SA methanolic extract exhibited a high total flavonoid content (43.09 mg rutin/g), and dichloromethane extract was highly flavonoid-rich. Contrary to its antioxidant properties, the aqueous extract exhibited the most potent scavenging abilities. (DPPH - IC_{50}: 1.05 mg/ml and ABTS IC_{50} - 1.02 mg/ml) (Uysal *et al*., 2021).

5.5 Antidiabetic activity

Diabetes mellitus is the result of an insufficient production of insulin or a lack of effectiveness of the insulin produced by the body. In the Indian traditional system of medicine, a variety of medicinal plants have been used to treat diabetes and its complications. These plants might offer potential sources of novel drugs or new leads to new drugs. In India, the traditional system of medicine, Ayurveda, has found several medicinal plants that can help to lower blood sugar levels. Indian medicinal plants are known for their therapeutic impact on various types of diabetes (Divya Singh and Sanjeev Singh, 2021). The hypoglycaemic effects of aqueous and methanol leaf extracts of SA were evaluated in rabbits with alloxan-induced diabetes, with both extracts exhibiting beneficial effects on the animals' blood glucose levels. It was observed that both extracts significantly increased glucose tolerance in normal rabbits fed glucose at a dose level of 400 mg/kg. At 5.5 h after a glucose load, the crude leaf extracts of SA showed hypoglycaemic activity that was stable and lasted for 10.5 h (Okwuosa *et al*., 2011). Another finding revealed that administering methanolic leaf extract of SA ingestion led to a modest drop in blood glucose levels after two and four hours (Arya *et al*., 2012). Methanolic, hexanoic, and ethyl acetate extracts of SA and *S. rhombifolia* exhibited antihyperglycemic action against yeast and mammalian α-glucosidase enzymes. The acetone extracts inhibited yeast enzymes the most, but no substantial inhibition was detected in mammals (Arciniegas *et al*., 2017).

5.6 Antiulcerogenic activity

Many people suffer from ulcers, a common gastrointestinal disorder. The cause of ulcers may be attributed to the regular use of drugs, irregular eating habits, stress, *etc.* A targeted treatment approach is required in order to treat peptic ulcer disease effectively and avoid complications such as mucosal bleeding and infection. Antiulcer drugs are expensive and have a high rate of reversal, side effects, and drug interactions associated with synthetic drugs. Many herbs are prescribed to cure ulcers and reduce their recurrence. The alcoholic extract of the SA plant shows promising antiulcer effectiveness in rats against three different ulcer models. The oral administration of alcoholic extract of SA has significantly reduced the incidence of ulcers caused by aspirin plus pylorus ligation and HCL-ethanol. This extract also effectively reduced stomach volume, free acidity, and ulcer index by 53.69%, when compared to the effectiveness of sucralfate. The total acidity was not greatly reduced, and the pH was not significantly reduced. It also demonstrated 55.14% gastroprotective activity, compared to 94.85% for sucralfate. A water immersion stress ulcer had a 24.4% protection index, whereas omeprazole, a standard drug, had a 100% protection index (Malairajan *et al*., 2006). Studies have shown that *Helicobacter pylori* can cause gastrointestinal ulcers, gastritis, and even cancer in humans. The aqueous and alcoholic extracts of SA leaf were found to be beneficial in treating *H. pylori*-induced ulcers in mice. The extract treatment significantly reduced the bacterial load of stomach tissue, the severity of ulcers, and the gastric volume. The histological results confirmed the effect of SA on ulcer healing (Ekwealor *et al*., 2020).

5.7 Hepatoprotective effect

The liver is a major organ in our body. There are few treatments available for liver diseases, and side effects are often more common than the underlying disease. Medicinal plants may be a viable option for the treatment of these conditions, as they have been shown to be effective and have a low incidence of side effects. A recent study has revealed that a root methanolic extract from SA plants can reduce the liver toxicity risks associated with paracetamol consumption in rats. The methanolic root extract of SA helps to alleviate the toxicity by reducing serum levels of SGPT, SGOT, ALP, and bilirubin. Among the three different doses of methanolic extract of SA, the 100 mg/kg dose showed greater activity. As a result of pre-treatment with SA extract, hexobarbitone-induced narcosis was significantly reduced in mice. The root of SA contains a phenolic compound known as ferulic acid, which is responsible for its hepatoprotective properties (Sreedevi *et al*., 2009). In another study, both n-hexane and ethyl acetate fractions of SA leaves were found to reduce the toxic effects of thioacetamide on rats. A decrease in the serum liver parameters, which were elevated due to toxin exposure, as well as an increase in albumin levels (Mgbemena *et al*., 2015). A dose-dependent protective effect was observed for ethanolic extracts of SA leaves in treating drug-induced hepatotoxicity and nephrotoxicity. A treatment involving SA alcoholic extract led to normalized levels of lipid profile, serum parameters, urea, uric acid, and bilirubin. Additionally, malondialdehyde (MDA) levels in tissue homogenates were reduced. Superoxide dismutase and catalase activity were notably increased while glutathione (GSH) levels were augmented. This protective effect was compared with that of silymarin (Ogunmoyole *et al*., 2022).

5.8 Neurodegenerative diseases

Natural products can help prevent and treat neurodegenerative disorders and neuronal dysfunction. Protein aggregation, oxidative damage, and inflammation have been linked to a number of neurodegenerative illnesses. The use of natural products has been shown to be effective in mitigating the symptoms of a variety of

diseases, improving the longevity and overall health of those affected. Phytocompounds, including polyphenols and alkaloids, have been demonstrated in some studies to forestall neurodegeneration and increase cognitive function and memory. These benefits are most likely related to the plant's anti-inflammatory and antioxidant characteristics. SA's antioxidant and anti-inflammatory properties make it effective in the treatment of neurological illnesses. In experimental rats, an ethanolic extract of SA leaves led to dose-dependent hyperplasia and hypertrophy of neuronal cells in the cerebral cortex. It has been suggested that prolonged or high doses of SA may result in the development of neurological disorders when used for medicinal purposes (Eluwa *et al*., 2013). A recent study conducted on mice has revealed that ethanolic extracts of SA leaves and stems have potential beneficial effects on the central nervous system. Treatment with the extract has a sedative effect and also protects against pentylenetetrazole-induced seizures, as well as anxiolytic effects (Benjumea *et al*., 2016). SA ethanol extracts have been demonstrated to have neuroprotective potential against cisplatin-induced toxicity in the brains of adult male albino rats. Cisplatin treatment causes severe brain deterioration and anatomical alterations. SA ethanol extract has been proven to have antioxidant characteristics that may contribute to its neuroprotective action, in addition to shielding these neurons from the toxicity of cisplatin (Owoeye, 2017). In female rats, treatment with ethanolic leaf extract of SA suppresses monosodium glutamate (MSG)-induced toxicity. MSG (4 g/kg BW) and ethanolic leaf extracts of SA (400 mg/kg BW) were co-administered and significantly reduced MDA and elevated GSH levels, improved the SOD and CAT activities, improved the levels of PCV and neutrophil count. SA treatment reversed the effect of MSG on the microanatomy of cerebellar purkinje cells and CA3 pyramidal neurons (Owoeye and Salami, 2017a). Nicotine administration leads to oxidative stress, which is manifested in disruption of the cytoarchitecture of the cerebellum. Concomitant administration of an aqueous extract of SA (1 mg of nicotine and 500 mg of SA per kg BW) tends to reduce nicotine-caused cerebellar impairment in rats (Oyeleke and Faniyan, 2018). A recent study reveals that SA at a dose of 200 mg/kg BW increased Purkinje cell degeneration when compared to a control. The ethanolic leaf extract of SA has the risk of causing neurological damage (Okon *et al*., 2021).

5.9 Antiproliferative activity

Cancer is the world's second greatest cause of mortality, trailing only cardiovascular disease. In recent years, medical science has made advances in the treatment and management of cancer, though there remain opportunities for further improvement. Treatments for cancer, including chemotherapy, can have a number of undesirable side effects. The metabolites derived from natural sources may prove to be a viable treatment for numerous types of cancer. A total of fifteen compounds are isolated from the whole SA plant's ethyl acetate fraction. An organ culture study of mouse mammary glands revealed that six compounds had a statistically significant influence on pre-neoplastic lesions induced by 7, 12-dimethyl benz [a] anthracene. A dose of 10 µg/ml of cryptolepinone (83.3%), N-trans-feruloyl tyramine (75%), and a derivative of quindolinone, 5,10-dimethylquindolin-11-one (66.7%) showed significant chemopreventive effects (Jang *et al*., 2003). In a recent study, it was found that an alkaloid cryptolepine isolated from SA, had a dose-dependent effect on sensitizing gastric adenocarcinoma cells to tumour necrosis factor-induced apoptosis (Ahmed *et al*., 2011). The chloroform extracts of whole plant SA possess anticancer properties against A-431 human epidermoid carcinoma and HeLa-human cervical cancer cells (Lakshmi kanta kanthal *et al.,* 2017). A recent *in vitro* study revealed the promising anticancer effects of a methanol extract of SA on MDA-MB-231 human breast cancer cells, with an IC_{50} value of 102.4 µg/ml (Uysal *et al*., 2021).

5.10 Toxicity

Despite the perception of medicinal plants and their products as generally safe, there have been several reported cases of adverse events associated with them. In comparison to synthetic pharmaceuticals, limited data exists on the relative safety of herbal remedies. Clinical and experimental data are lacking for the majority of medicinal plants and their products. Consequently, there is a lack of data regarding the long-term toxic effects of medicinal plants. According to the acute toxicity test, the LD_{50} value for aqueous acetone extracts of SA is 3.2 g/kg. The low toxicity, as evidenced by the LD_{50} values, suggests that therapeutic doses have a significant margin of safety. The extracts have no noticeable impact on biochemical parameters (Konaté *et al*., 2012). In another study, treatment with alcoholic extracts of the roots and leaves of SA alters kidney parameters, potentially resulting in glomerular dysfunction and tubular dysfunction. It is suspected that SA root and leaf extracts are harmful to the kidney, resulting in renal failure (Nwankpa *et al*., 2018).There is also evidence that ethanolic leaf extracts of SA may have a detrimental effect on nerve cells, particularly when administered in high doses (Okon *et al*., 2021; Eluwa *et al*., 2013).

5.11 Miscellaneous

Urolithiasis, urinary tract infections, and prostatic disorders are among the most common issues related to the urinary tract. Many people around the world suffer from urinary stone problems. If untreated, they can cause significant pain and hinder normal urine flow. Synthetic drugs prescribed to treat kidney stones can come with potential side effects. In recent years, medicinal plant have become a popular option for treating kidney stones. In most urinary calculi, calcium oxalate dominates, followed by struvite, cystine, and uric acid. Aqueous and methanol extracts of the root of SA inhibit calcium oxalate crystal growth. The crystal morphology of calcium oxalates crystals will be altered effectively by treatment with methanol extract rather than aqueous extract. Changes in crystal column lengths, shape, size, and transparency indicated SA's inhibitory effect on calcium oxalate crystal growth (Vimala and Gopalakrishnan, 2012). *Proteus mirabilis* is a gram (-) bacterium that is commonly associated with urinary tract infections, leading to the formation of struvite stones. Ethanol extract from SA leaves is an effective treatment for struvite stones caused by these bacteria. The ethanolic extract of SA produced dose-dependent inhibition of the average weight of struvite crystals at various concentrations. The existence of polyphenolic compounds may account for SA's anti-proteus action (Smanthong *et al*., 2022). Residents of tropical and developing countries are particularly at risk of helminthic infections, which are a serious public health concern. Although the prevalence of these infections is high in these areas, much more needs to be done to reduce the associated risks. In the Indian system of medicine, there are a variety of medicinal plants with potential to treat helminthic infections. At varying doses, SA ethanolic and chloroform leaf extracts have considerable anthelmintic activity against *Pherithemapostuma*. When compared to the standard drug, piperazine

citrate, both extracts exhibited vermifuge and vermicide activity (Ravishankar, 2012). The analgesic effects of SA aqueous acetone extracts were demonstrated in an acetic acid-induced writhing test in mice, showing a dose-dependent inhibition of writhing (Konaté *et al*., 2012). The SA ethyl acetate leaf extract has better insecticidal property than methanol extract against *Dysdercuscingulatus* fab (Gadewad and Pardeshi, 2018).

6. Conclusion

This review summarizes the traditional importance, phytochemical presence, and pharmacological importance of SA that we conducted since 2001 to current date. A phytochemical profile of SA has revealed that the medicinal plant is comprised of various novel and known natural compounds, each conferring its own unique biological activity. Such compounds are often used in traditional medicine. The most common phytochemicals found in SA include alkaloids, flavonoids, steroids, terpenoids, tannins, and phenolic compounds. The phytocompounds quindolinone, cryptolepine, cryptolepinone, *etc*., are encouraging. A number of pharmacological studies conducted both *in vitro* and *in vivo* have demonstrated a correlation between traditional uses of the plant SA. It has been reported in many research articles that there are a number of constituents in SA plants that have significant pharmacological activity. *In vitro* and *in vivo* experiments have revealed a host of therapeutic benefits associated with SA, including antimicrobial, wound healing, antioxidant, antimalarial, antidiabetic, antiulcer, hepatoprotective, neuroprotective, and anticancer effects. However, it is reported that at higher doses, they may be toxic to human use. While SA may provide a variety of exciting opportunities, one should also be aware of its limitations. It is important to do a detailed examination of biochemical and physiological processes, bioavailability, pharmacokinetics, and pharmacodynamics in order to understand the effects of the drug. There is a need for controlled clinical trials in the treatment of various illnesses in order to support claims made for SA. Because of their physical resemblance, several species are quite likely to be substituted for distinct medicinal purposes. Quality control measures are necessary to prevent misidentification and accidental adulteration of the SA. A comprehensive and integrated approach is necessary to harness the potential of SA.

Acknowledgments

The authors would like to express their gratitude to the Department of Pharmacy at Annamalai University in Annamalai Nagar, Chidambaram for their support in conducting this literature survey.

Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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Citation **N. Srinivasan and R. Murali (2022). An overview of the traditional importance, phytochemistry, and pharmacological properties of *Sida acuta* Burm.f.. Ann. Phytomed., 11(2):245-254. http://dx.doi.org/10.54085/ap.2022.11.2.27.**