Review Article

A Phytochemical and Pharmacological Review of *Sphagneticola trilobata* (L.) Pruski

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ABSTRACT

Since prehistoric times, plants have been essential to human existence. Plants were traditionally utilized as remedies in India. Phytochemicals can be found in abundance in plants. Potential phytochemicals' bioactivities and nutraceuticals / herbal formulations based on them have a big impact on how diseases are managed. A plant from the Asteraceae family is *Sphagneticola trilobata* (L.) Pruski. It is a perennial herb that forms a creeping mat in tropical and subtropical regions and originated in the Caribbean, Central America, and India's northern neighbour, South America. Other scientific names for this plant include *Thelechitonia trilobata, Silphium trilobatum, and Complaya triloba (L.), Strother* (L.) There are several popular names for it, including yellow creeping daisy, Singapore daisy, creeping ox-eye, trailing daisy, and rabbit's paw. This plant is used in traditional medicine to cure sores, ulcers, and backaches. The plant has a high number of phytochemicals, which support its various pharmacological functions. *S. trilobata* has been found to have a variety of pharmacological effects, including anti-diabetic, anti-leishmaniasis, anti-oxidant, anti-inflammatory, wound-healing, CNS depressing, cytotoxic, analgesic, anti-hypertensive, anti-proliferative, larvicidal, and anti-pyretic effects. The authors of this paper want to draw the attention of natural product researchers from all around the world to the untapped potential of *W. trilobata*, which could be useful in creating novel formulations with greater therapeutic efficacy.

Keywords: Phytochemicals, *Sphagnetiola trilobata, Wedelia trilobata*, Asteraceae, Singapore daisy.

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INTRODUCTION

The medicinal plant *Sphagneticola trilobata* (L.) Pruski belongs to the family Asteraceae (Formerly known as Compositae)[1] This plant is also known as *Wedelia trilobata* (L.) Hitch. *Sphagneticola trilobata* is a creeping mat-forming perennial herb and this has the ability to form a thick carpet and it is a soil creeper [18]

It is widely distributed around tropical and subtropical areas of the Caribbean, Central America and North of South America. Nowadays, *Sphagneticola trilobata* is used as an ornamental plant in the western world and in Southeast Asian countries [1]. Around 70 species varieties are present in this plant genus [2]. In ancient times, *Sphagneticola trilobata* is used as a medicinal plant in Ayurveda, Traditional Chinese Medicine, Unani, and Siddha [1]. In folk medicine, it is used for the treatment of backache, muscle cramps, rheumatism, stubborn wounds, sores and swellings and arthritic painful joints [3].

Leaves of this plant is used for kidney dysfunction, wounds, snakebite, purge and amenorrhea. Fruits leaves and stems are used in childbirth and in the treatment of bites and stings, fever and infection [3]. This plant contains numerous phytochemical constituents like alkaloids, saponins, Phenols, terpenoids, flavonoids [4]

In the phytochemical screening, mainly 13 constituents were screened, and ten were found in various solvent extracts. The maximum amount of constituents is present in ethanolic extract; but quinones, oxalates, and phlorotannins were absent in all extracts from different parts of the plants[2]. *Sphagneticola trilobata* the plant has extensive therapeutic potential for curing disease with minimal side effects.

Taxonomy and botanical description

Sphagneticola trilobata is a perennial herb, prostrate, diffuse, rooting at nodes; stems glabrous or pubescent. Leaves 3-10 x 3x7 cm, elliptic-obovate, usually with 3 angular lobes with toothed margins, acute at apex, basally cuneate, glabrous to sparingly pubescent; petiole short, up to 5mm. Heads radiate, 2-2.5 cm across, solitary on ebracteate 4-15 cm long peduncles. Involucre green; bracts lanceolate, 1-1.5 cm long, ciliate: inner narrower. Ray florets 5-8; corolla bright yellow, 1.5-2.0 x 0.5-0.7 cm, 3-4 denticulate; tube short. Ovary trigonous; stigma bilobed. Pappus connate into a spathiform, fimbriate cup at the apex, devoid of awns. Dis florets many; corolla

yellow; tube 5-8 mm long, 5-lobed: lobes deltoid, densely pubescent within. Anthers black, syngenecious. Style branches flattened and marginally pubescent. Figure 1 represents the *Sphagneticola trilobata* plant and its herbarium.[5]

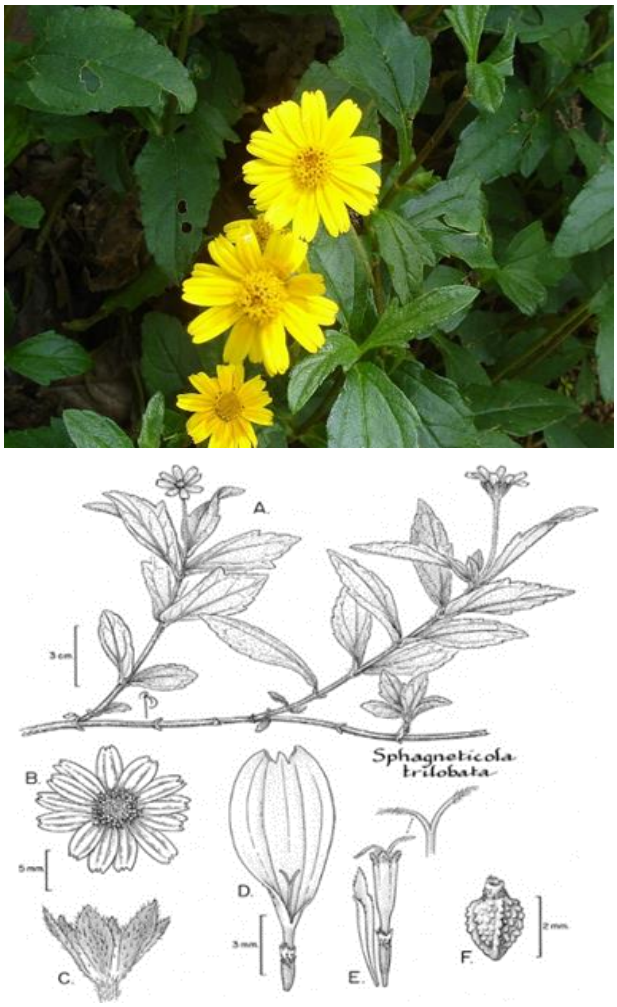

Figure 1: *Sphagneticola trilobata* plant and its Herbarium.

Table 1: Binomial Classification of *Sphagneticola trilobata* (L.) pruski.[5]

Plant name	*Sphagneticola trilobata* (L.) Pruski.
Kingdom	Plantae
Subkingdom	Tracheobionata
Family	Asteraceae
Class	Magnoliopsida
Subclass	Asteridae
Genus	*Sphagneticola*

Vernacular names

Sphagneticola trilobata is recognized as Kammal poovu in Malayalam, Marigold, Creeping daisy, Creeping Wedelia and Singapore daisy in English, Hansenfurs in Germany, America hama-guruma in Japan, Di jin hua in China, Kradum tong in Thailand, *Wedelia kuning* in Malaysia, *Singapore madeliefie* in Africa, Arnica-do-mato, pseudo-arnica and vedelia in Brazil.

Synonyms are *Complaya trilobata (*L.) *Strother, Silphium trilobatum* L., *Thelechitonia trilobata* (L.) H.Rob. & Cuatrec., *Wedelia carnosa* Rich., *Wedelia paludosa* DC., *Wedelia trilobata* (L.) A.S. Hitchc., *Wedelia triloba* (Rich.). [5]

Pharmacological potential of *Sphagneticola trilobata* (l.) Pruski.

The pharmacological potential of the *Sphagneticola trilobata* plant is widely established. Various extracts from the plant were investigated for anti-diabetic, anti-inflammatory, wound healing activity, cytotoxic activity, antiproliferative activity, larvicidal activity, anti-hypertensive activity, hepatoprotective activity, anti-oxidant, anti-leishmaniasis, CNS depressant activity, antipyretic activity. The toxicity studies for this plant have also been conducted.

Antidiabetic Activity

Kade *et al* conduct an experiment on adult male wistar rats. Diabetics was induced on mice by injecting Streptozocin diluted in 0.1 ml citrate buffer. Aqueous extract of *Sphagneticola trilobata* (50mg/kg) was infused into mice for 30 days. After the experimental period, diabetics- induced rats and control were euthanized with ether anaesthesia. For biochemical examination, tissue samples from the liver, kidney, spleen, and testes were taken, homogenised, and centrifuged. It was observed that the treatment of diabetic rats with *Sphagneticola trilobata* exerted a considerable hypoglycemic effect with concomitant improvement on the antioxidant status.[6]

Buddhakala N *et al* investigate the antidiabetic activity of ethanolic extract of *Sphagneticola trilobata* (L.) Pruski flower in rats. The rats were induced diabetics by intraperitoneal Streptozocin injection, dissolved in 20mM citrate buffer. After 8 weeks, oral administrations of *Sphagneticola trilobata* flower ethanolic extract reduced the fasting blood glucose level. The serum insulin level in ethanolic extract-treated and diabetics control rats were different.[1]

Jagger RC performed an experiment on plants to find out the hypoglycemic effect. This work concluded that *S.trilobata* possess hypoglycemic activity.[7]

Schmitz AP *et al* studied the diabetic activity of *Sphagneticola trilobata* and evaluated the cytotoxic effect of the aqueous extract of *Sphagneticola trilobata.*[8]

Wound healing Activity

Balekar N *et al* evaluated the wound-healing activity of the leaves of *Wedelia trilobata.* Ethanolic extract of *Wedelia trilobata* leaves was chosen for the column chromatography. The fractions obtained after column chromatography include hexane fraction, ethyl acetate fraction, and chloroform: methanol fraction. These were subjected to *in vitro* wound healing assays like fibroblast proliferation, *in vitro* scratch assays, oxidative stress using

hydrogen peroxide and increasing collagen content. Ethyl acetate fraction showed the fibroblast stimulation effect and chloroform: methanol fraction showed antioxidant potential by the DPPH assay method. Both of these activities indicate its potential wound-healing properties.[9]

Balekar N *et al* investigated wound healing activity on isolated ent-kaura-9(11),16-dien-19-oic acid isolated from *Wedelia trilobata* (L.) leaves. They isolated bioactive compounds from ethanolic extract of *Wedelia trilobata* (L.) leaves. The five fraction WEAI-A, B, C, D and E obtained were used for antimicrobial activity studies. The fraction WEAI-B containing ent-kaura-9(11), 16-dien-19-oic acid exhibited antibacterial activity against *S.aureus* and *S.epidermidis.* WEAI-B showed the protection of the fibroblast L929 cells against oxidative stress induced by hydrogen peroxide. WEA1-A B C D and E displayed anti-microbial activity and WEAI-B exhibited antibacterial to indicate its potential wound healing properties.[10]

Anti-Leishmaniasis Activity

Brito S *et al* investigated the isolated kaurenoic acid from *Wedelia trilobata* against *Leishmaniasis braziliensis in vivo* and *in vitro* for its anti-leishmaniasis efficacy. They carried *in vitro* studies are axenic amastigotes and promastigotes as well as infected and uninfected macrophages. The effect of the compound on cellular viability was evaluated by counting dead cells and living cells in a haemocytometer and by the calorimetric method. In *in vivo* study, the infection was induced on balb/c mice by subcutaneous injection of promastigotes L (V.) *braziliensis* and then treated with isolated compound kaurenoic acid by IP for one week. After this a 70% reduction was observed in the size of the skin lesions in balb/c mice with no evident toxic effect.[11]

Central Nervous System Depressant Activity

Tambe *et al* examined *Wedelia trilobata* leaves for their CNS depressant activity using petroleum ether, chloroform, ethyl acetate, and methanol extracts. Swiss albino mice were used for locomotor activity and phenobarbitone-induced sleeping time. The animals were given vehicle, petroleum ether extract, chloroform extract, ethyl acetate extract, and methanol extract before 30 minutes of phenobarbitone administration, and the sleeping time was then recorded. The duration of sleep induced by the extracts was recorded as, 107 minutes for petroleum ether, 89 minutes for chloroform, 84 minutes for ethyl acetate, and 70 minutes for methanol, and 42min for phenobarbitone. A photoactometer was used to measure the locomotor activity of the same species of animals. The basal reaction time was recorded before and after the treatment. The animals were treated with vehicle, diazepam, petroleum ether extract, chloroform extract, ethyl acetate, and methanol extract. The results indicated that the petroleum ether extract reduced locomotor activity compared to other extracts and the standard drug diazepam. So, it is concluded that the *Wedelia trilobata* leaves extract as efficient CNS depressant activity. The extract of *Wedelia trilobata* leaves was therefore proven to have effective CNS depressive action.[12]

Antioxidant Activity

M Govindappa *et al,* evaluated the antioxidant potential of the ethanolic extract of *Wedelia trilobata* (L.) Hitchc. The antioxidant activity was established by evaluating the DPPH radical scavenging activity and using the FRAP assay. This study revealed that the ethanolic extract of leaf and stem has strong scavenging activity in both DPPH and FRAP methods. An ethanolic leaf extract of *Wedelia trilobata* exhibited significant activity than the stem and flower. [13]

Aulya W *et al,* studied the antioxidant activity of floral extracts of *Sphagneticola trilobata* (L.) Pruski in n-hexane and ethyl acetate. The antioxidant activity of these extracts was expressed by IC50 value. The antioxidant activity was assessed by the DPPH method with a UV-VISIBLE spectrometer at a wavelength of 517 nm. The ethyl acetate extract was found to have more antioxidant activity than the n-hexane extract.[14]

Nisreen H and Kumar A studied the effectiveness of methanol and chloroform root extracts of *Sphagneticola trilobata* in reversing oxidative stress induced by H_2O_2. The activity was evaluated by using the enzymatic parameters on oxidative stress cultured lymphocytes of *Oryctolagus cuniculus* L. The antioxidant property was evaluated by enzymatic assay in, *in vitro* cultured and H_2O_2-induced lymphocytes. The result indicated that the antioxidant effectivity is restored with the pre-treatment of Methanol root extract and Chloroform root extract. It was revealed that the Chloroform root extract of Sphagneticola trilobata exhibited better efficacy in reducing oxidative stress, in comparison to Methanol root extract.[15]

Anti-Inflammatory Activity

M Govindappa *et al* studied the anti-inflammatory activity of ethanol extract of *Wedelia trilobata* (L.) Hitchc. The *in vitro* inflammatory activity was evaluated using albumin denaturation, membrane stabilization assay, and proteinase inhibitory assay. The ethanolic extract of leaf and stem showed *in vitro* inflammatory activity by inhibiting the heat-induced albumin denaturation and RBC membrane stabilization in comparison with aspirin. The leaf extract significantly inhibited the proteinase activity. [13]

Maldini M *et al* investigated the topical anti-inflammatory activity of leaves of *Sphagneticola trilobata.* The leaf extracts were prepared with chloroform and petroleum ether The anti-inflammatory effect was evaluated by inhibition of the croton oil-induced ear dermatitis in male CD-1 mice. The infection was induced by applying 80 µg/ml of croton oil dissolved in 15µg/ml of acetone to the inner surface of the right ear of the mice. It was found that croton oil-induced dermatitis in mice was greatly decreased by the chloroform extract than petroleum ether extract.[16]

Anti-proliferative Activity

Sun L *et al* investigated the anti-proliferative activity of eudesmanolides from *Sphagneticola trilobata*. They isolated and identified eight new eudesmanolides and 12 known congeners. The isolated eudesmanolides were studied for anti-proliferative activity against three human tumor cells (HeLa, HepG2, and SGC-7901) by the MTT assay method. The compounds showed significant anti-proliferative activity against the tumor cells. [18]

Anti-microbial Activity

Jaggessar RC evaluated the anti-microbial activity of various extracts of *Sphagneticola trilobata* at varying concentrations (0.025g/ml, 0.05g/ml, and 0.1 g/ml) by the disc diffusion assay method. It was concluded that the *extracts* showed AZOI of 67.17mm^2 against *E. Coli*.[7]

Indira toppo *et al* studied the anti-microbial activity of *Sphagneticola trilobata* against some human pathogenic bacteria and fungi. This activity was carried out in aqueous and methanolic extract of leaf, stem, root and flower of *Sphagneticola trilobata* against bacterias namely *Pseudomonas aeruginosa* (MTCC - 7296), *Staphylococcus aureus*, (MTCC- 7443), *Salmonella typhi* (MTCC- 733), *Mycobacterium tuberculosis* (MTCC-300) and fungal organisms namely *Microsporum canis* (MTCC –2820), *Epidermophyton floccossum* (MTCC-613), *Trichophyton rubrum* (MTCC-296) and *Aspergillus candidus* (MTCC-1989). The leaf and the root extracts exhibited significant antibacterial activity against three bacterias' *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Salmonella typhi* and fungal strains *Microsporum canis*, *Trichophyton rubrum*, and *Epidermophyton floccossum.*[19]

Leite *et al* investigated the anti-microbial activity of crude hydroalcoholic leaf extract of *Sphagneticola trilobata against* the test cultures of *Staphylococcus aureus, S. epidermidis*, *Staphylococcus spp., Escherichia coli, Serratia marcescens, Enterococcus faecalis, Pseudomonas aeruginosa, Salmonella Typhimurium,* and *Klebsiella pneumoniae* isolated from human skin and those of *Staphylococcus spp.* isolated from dog skin using the broth microdilution method. It was reported that the hydroalcoholic extract of *S.trilobata* exhibited anti-microbial activity against cultures of *Staphylococcus spp., Escherichia coli, S. marcescens,* and *Enterococcus faecalis* and *Staphylococcus spp*.[20]

Anti-Cancer Activity

Mardina V *et al* evaluated the anti-cancer activity of the methanolic and n-hexane leaf extracts of *Sphagneticola trilobata* (L.) Pruski by conducting MTT assay on MCF-7 breast cancer cell lines and Vero cell. LC 50 values were calculated using probit analysis. The study revealed that the n-hexane and methanol extracts of *Sphagneticola trilobata* were cytotoxic to breast cancer cells. [21,22]

Murali M *et al* studied the biosynthesis of ZnO-NPs from *Sphagneticola trilobata* that attenuates cell proliferation by inducing cellular-level apoptosis against colon cancer. They isolated ZnO-NPs from the aqueous leaf extract of *Sphagneticola trilobata* and evaluated its anticancer activity on HT-29 cancer cells by MTT assay. The purity of the particle (98.23%), was determined by energy-dispersive spectroscopic analysis, and the scanning electron microscopic image confirmed the particle were agglomerated. The stZnO-NPs were found to be cytotoxic towards HT-29 colon cancer cells.[23]

Larvicidal Activity

Sowmyashree *et al* evaluated the larvicidal activity of different extracts and essential oils of *Sphagneticola trilobata* using female *Anopheles stephensi* mosquitoes. Soxhlet apparatus was used for the extraction, and Clevenger apparatus for the distillation of the essential oil. Eggs and larvae of *Anopheles stephensi* were collected and treated with different concentrations of the extract and essential oil using Temephos as the positive control and acetone as the negative control. The mortality was checked after 24 hour and 48 hours of treatment. They came to the conclusion that the presence of alkaloids, terpenoids, flavonoids, and steroids might have contributed to the larvicidal and insecticidal action of the essential oil and leaf extract.[24]

Toxicity Studies

Suchantabad *et al* investigated the acute toxicity of 80% ethanolic leaf extract from *Sphagneticola trilobata* on male and female Wistar albino rats. They randomly divided the animals into 4 groups and administered various concentrations of extracts (1000, 1500, and 2000 mg/kg). The mortality was checked within 24 hours and the further lasting 14 days. Thus confirmed that the extract had no impact on body weight, relative organ weight, and haematological values including hemoglobin, hematocrit, RBC, MCV, MCH etc and thus no acute toxicity with LD50 higher than 2000 mg/kg. [3]

Suchantabad *et al* investigated the chronic toxicity of 80% ethanolic leaf extract of *Sphagneticola trilobata* (L.) Pruski using healthy Wistar albino rats. The extract was taken orally for 90 days at doses of 200 or 400 mg/kg body weight, with a weekly base recording of the body weight. It was observed that the extract had no impact on body weight, relative organ weight, hemoglobin, hematocrit, RBC, WBC, MCV, MCH, MCHC, neutrophil, lymphocyte, monocyte, platelet, alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine aminotransferase (ALT), blood urea nitrogen (BUN), creatinine, blood cell characteristics, the ultrastructure of RBC. Thus, it was proven that *Sphagneticola trilobata* leaf extract did not show any indicators of toxicity or rat mortality.[25]

Analgesic Activity

Suresh Kumar *et al evaluated* the analgesic activity of the ethanolic extract of *Wedelia trilobata* on animal models by acetic acid-induced writhing method and hot plate assay method. It was observed that the ethanolic extract had a dose-dependent inhibitory effect (500mg/kg) on the

writhing response induced on by acetic acid. The *Wedelia trilobata* extract and aspirin (500mg/kg) reduced the writhing response by 49.17% and 68.68% respectively.[26]

Mizokami *et al* experimented the analgesic activity of the *Wedelia trilobata*. From the *Wedelia trilobata* plant, kaurenoic acid (10 mg/kg) prevented overt nociception-like behaviour. caused by formalin, complete Freund's adjuvant (CFA), and phenyl-p-benzoquinone. Additionally, acute carrageenin and PGE2- and chronic CFA-induced mechanical hyperalgesia were both reduced by kaurenoic acid (1–10 mg/kg p.o.) [17]

Anti-Pyretic Activity

Madhu babu *et al* investigated the anti-pyretic activity of leaves of ethanolic extract of *Wedelia trilobata* on Wistar albino rats by inducing pyrexia by administering an intraperitoneal injection of 20% brewer's yeast (10 ml/kg body weight). Rectal temperature of rats were checked simultaneously before and after administration at 1st, 2nd and 3rd hour. It was observed that the ethanolic extract of *Wedelia trilobata* showed significant results by reducing the increased body temperature of rats with respect to the control group. Thus the ethanolic extract exhibited significant anti- pyretic activity.[27]

Reproductive Problems

Previous studies have demonstrated that Creoles and Caribbean women have historically utilized bitter herbs to regulate their menstrual cycles. Women's reproductive issues were primarily treated with plants for infertility, menstrual pain, and childbirth. Results indicated that *W. trilobata* was utilized to treat female complaints and menstrual pain. In the absence of clinical studies, the nonexperimental validation approach can be used to inform the public about which plants are safe, effective, and beneficial and which are not. This is significant because there haven't been many clinical studies on plants from the Caribbean.[28]

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