A DETAILED REVIEW ON SIEGESBECKIA ORIENTALIS

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Abstract
Medicinal plants have a vital part in the health of both humans and animals. Siegesbeckia orientalis L. commonly known as St. Paul's Wort is a natural herb cultivated annually. It is a member of the Asteraceae family, which has been used for centuries to treat a variety of diseases. It can be found in Africa and Asia, as well as tropical, subtropical and temperate zones. Leprosy, syphilis, sores and gangrenous ulcers are all treated with it topically. This herb has a variety of biologically active and beneficial phytoconstituent elements that are thought to be accountable for the plant's health promoting properties. Sesquiterpene lactone, orientin, and diterpenes are bioactive chemical substances discovered in the aerial portions of S. orientalis. The presence of 3, 7-dimethyl quercetin in the whole plant has been documented. Analgesic, anti-inflammatory, antimalarial, antirheumatic, antihypertensive, anti-snake venom, immunosuppressive and antiproliferative properties have been observed. The whole plant has traditionally been used as a hypoglycemic agent. Phytochemical studies of the leaves of Siegesbeckia orientalisL revealed the presence of Siegesbeckia orientalis L. The present review highlights the medicinal uses, chemical constituents and pharmacological studies carried out with this plant.

Keywords:*Siegesbeckia orientalis,* MedicinalHerb, Pharmacological activity, Phytoconstituents.

Introduction

Traditional medicine is "the knowledge, skills and practices based on the theories, beliefs and experiences indigenous to different cultures, used in the maintenance of health and in the prevention, diagnosis, improvement or treatment of physical and mental illness". For thousands of years, plants have been used for health and medical purposes. Various plant parts such as leaves, flowers, stem barks, roots, seeds and fruits have all been used as constituents of herbal medicine. Medicinal plants serve an important part in human health care. Knowledge of medicinal plants opens up new possibilities for current drug development [1]. Herbal medications are in high demand in primary health care in the developed world due to their safety, efficacy, and lack of adverse effects. Over 4,000 plants have real therapeutic benefit that is either little known or unknown to the general public [2]. Herbal medications became more sensitive to side effects than synthetic medicines, increasing the availability for herbal resources and awareness of the importance of maintaining raw material quality and purity [3]. Herbal medicines are widely used as treatments for ailments by the great majority of people on the planet [4]. Various ancient

cultures recognised the therapeutic qualities of many botanical medicines. In this article, detailed review of this plant *Siegesbeckia orientalis* has been discussed.

Scientific Classification [5]

- Kingdom: Plantae
- Sub-Kingdom: Tracheophytes
- Super division: Angiosperms
- Division: Eudicots
- Class: Asterids
- Order: Asterales
- Family: Asteraceae
- Genus: Sigesbeckia
- Species: S. orientalis

Common name [5]: St. Paul's Wort, Eastern St. Paul's-wor, holy herb, Indian weed, sticky weed

Synonyms [6]: *Siegesbeckia orientalis, Minyranthes Heterophylla*

Vernacular names [6, 7, 8]:

Kannada: antu huvinagida
Tamil: kadambu katampam
Telugu: kadambu, katampam
Guajarati: pilibadkadi
Garhwali: Lichkura
Bihar: Latlatia, marangkalmegh
Assam: Gawal bahalgani, soh-barthud-lib
Biological type: Annual

Botanicaldescription [8, 9]

Siegesbeckia orientalis is an Asteraceae medicinal plant. It's also known as "St Paul's wort."The plant is a huge annual herb that grows to a height of 0.6 - 1.2 metres.Stem is tall and stiff, with horizontal and dichotomously branching branches below and above; stem and branches are purple-tinged, terete, and pubescent. Leaves are opposite, about 2.5–11 cm length and 1.5–7cm width, acute or acuminate, triangular ovate intensely & irregularly toothed (uppermost leaves much smaller and nearly entire) finely pubescent on both surfaces, cuneate base, 3 nerved, leaf stalk winged. Flowers are yellow, those of the ray red beneath. Involucre bracts in the two rows, very dissimilar; the outer exceeding 1.3 cm long, linear spathulate or clavate, horizontally spreading with recurved margins, the upper surface covered with large viscous glandular hairs; the 5 inner bracts short, boat shaped, obtuse, glandular-hairy on the back, each bract enclosing one of the ray-flowers.Ray flowers are generally five, ligulate, with recurved ligules and a three-toothed tip. Achenes are glabrous, slightly rough, and black, and are contained in a boat-shaped bract.

Microscopy [8, 9]

The stem with many narrow ridges and furrows has more or less circular shape. Pericyclic sclerenchymatous cells in clusters are found below the collenchyma in the ridge portion.

Under the ridges, secondary xylem grows at a faster rate. Pith is a hollow.Pith is absent from the root, which has a broad secondary xylem and 2-3 seriate medullary rays.Simple conical trichomes with gland cells on both epidermises, leaf with protuberated midrib and smooth lamina, anomocytic stomata on lower epidermis. In the centre region of the lamina, there are conjoint, collateral vascular bundles at regular intervals. Petiole has one large central vascular bundle and two smaller lateral vascular bundles.

Cultivation [8]

Siegesbeckia orientalis is found wild from the warm temperate to the tropical zone, growing best where the temperature is within the range 10-27°C during the growing season. It is not usually found in drier areas.It can be cultivated on both heavy and sandy soils, preferring moist, fertile but well drained conditions and a sunny position. The plant has spread as a weed and is considered to be invasive in several areas, including several of the pacific islands. The plant has an unpleasant aroma. The plant is said to smell like a pig and have an acrid, bitter taste. Under favourable growing conditions two life cycles of *Siegesbeckia orientalis* can be grown in the same year. The plant can flower throughout the year in warm climates, but has its peak during the rainy season. Proliferation of the flowers can occur under humid conditions [6].

Traditional Medicinal Use

The whole plant is febrifuge, cardiac, anodyne, salve, and stimulates blood circulation [10]. The juice and tincture of the plant is used externally in the treatment of ringworm, other parasitic infections and as a protective cover for wounds. It is also used topically for the treatment of syphilis, leprosy, gangrenous ulcers and sores [11, 12].
In Europe, a mixture of equal parts of the tincture and glycerin is used externally, as antifungal agent. A paste of the plant is applied to wounds between the toes that have been caused by prolonged walking barefoot in muddy water [13].
A decoction of the plant is also used in the treatment of rheumatoid arthritis, pains and aches in the legs and sides, hemiplegia, sciatica, weeping dermatitis and mastitis, traumatic bleeding [14]. A paste of the root is used in the treatment of indigestion. The juice of the root is applied to wounds. The aerial parts of *Siegesbeckia* have been used as the traditional Chinese medicine in the treatment of rheumatic arthritis, hypertension, malaria, neurasthenia, and snakebite [15].
In Philippines the decocted leaves are used as an alternative and, applied in the form of a lotion, as a vulnerary. In Tahiti the plant enters into the preparation of every cure for wounds, sprains, dislocations, and contusions. It is also used to induce menstruation [16].
Anti-adipogenic, osteoblastogenic, and anti-photoaging properties have been found in *S. orientalis*. The ethyl acetate extract of *S. orientalis* may prevent human cervical cancer HeLa cells from proliferating. Its ethanol extract has been shown to inhibit the growth and spread of endometrial cancer cells [17].

Chemical constituents [18, 19, 20]

- **Sesquiterpenoid**
  - Orientalide
  - Orientalide 4a
  - Orientalide 1b
  - Germacranolide
  - Melampolide

- 8β- Isobutyryloxy-14-al-costunolide
- 9α,15-Dihydroxy-8β-isobutyryloxy-14-oxo-melampolide
- 8β-Isobutyryloxy-1β,10αepoxycostunolide
- 9β-Hydroxy-8β-isobutyryloxy-1β,10αepoxycostunolide
- 8β,9β-Dihydroxy-1β,10α-epoxy-11β,13-dihydrocostunolide
- 14-Hydroxy-8β-isobutyryloxy-1β, 10αepoxycostunolide
- 9β-Hydroxy-8β-isobutyryloxycostunolide
- 14-Hydroxy-8β-isobutyryloxycostunolide
- 9β,14-Dihydroxy-8βisobutyryloxycostunolide
- 9β-Hydroxy-8βmethacrcryloyloxycostunolide
- 15-Hydroxy-8β-isobutyryloxy-14-oxomelampolide
- Orientin
- Siegenolides A
- Siegenolides B

- **Pimarenoids**
  - Ent-2β,15,16-trihydroxy-pimar-8(14)-ene
  - Ent-15,16-dihydroxy-2-oxo-pimar-8(14)- ene
  - Ent-15,16,18-trihydroxy-2-oxo-pimar-8 (14)-ene
  - Orientalin A
  - Orientalin B
  - Ent-2α,15,16,19-tetrahydroxypimar-8 (14)-ene
  - Ent-2-oxo-15,16-dihydroxypimar-8(14)- en-16-O-β-glucopyranoside
  - Ent-2-oxo-15,16,19-trihydroxypimar-8 (14)-ene
  - Ent-2-oxo-3β,15,16-trihydroxypimar-8 (14)-en-3-O-β-glucopyranoside
  - Ent-2β,15,16,19-tetrahydroxypimar-8 (14)-en-19-O-β-glucopyranoside
  - Ent-15-oxo-2β,16,19-trihydroxypimar-8 (14)-ene
  - Ent-12α,16-epoxy-2β,15α,19- trihydroxypimar-8(14)-ene
  - Ent-12α,16-epoxy-2β,15α,19- trihydroxypimar-8-ene
  - Hythiemoside B
  - 7β-Hydroxydarutigenol
  - 9β-Hydroxydarutigenol
  - 16-O-Acetyldarutigenol
  - 15,16-Di-O-acetyldarutoside
  - 16-O-Acetyldarutoside
  - Ent-14β,16-epoxy-8-pimar-ene2α,15α,19-triol
  - Ent-14β,16-epoxy-8-pimar-ene-3β,15αdiol

- **Kaurenoids**
  - Siegesesteric acid
  - Siegesetheric acid

- **Chain diterpenoids**
  - 19-Acetoxy-12-oxo-10,11- dihydrogeranylnerol
  - 19-Acetoxy-15-hydroxy-12-oxo-13,14Edehydro-10,11,14,15-tetrahydrogeranylnerol
  - 19-Acetoxy-15-hydroperoxy-12-oxo13,14E-dehydro-10,11,14,15-tetrahydrogeranyln-erol

- **Flavonoids**
  - 3,7-Dimethylquercetin

- **Other components**
  - Heneicosanol

Phytochemical screening of *Siegesbeckia Orientalis* [10, 11]
Phytochemical screening of *Siegesbeckia Orientalis*leaves possess high content of saponins, alkaloids and flavonoids, oxalates, tannins, phytates and phenols. The leaf contains a significant amount of vitamin A, indicating that it is critical for mammalian eye development. Its consumption has the potential to affect the transcription of a wide range of genes. Similarly, the presence of vitamin C in the plant extract suggests that, when used, the extract could act as an antioxidant by donating electrons to various anti-oxidative enzymatic and non-enzymatic reactions, reducing the effects of free radicals.

Physicochemical propertiesof *Siegesbeckia Orientalis* [11]
The moisture content, crude lipid content, crude fiber content, protein content, carbohydrate content of the extracts was determined. The total ash, acid insoluble ash was also determinedby standard procedure.

Pharmacological actions

Anti-inflammatory activity [21]
Anti-inflammatory efficacy in rats was assessed by complete Freund's adjuvant (CFA)-induced chronic inflammation, carrageenan-induced acute inflammation and the formalin test. As a positive control, piroxicam gel was used. 4 hours after carrageenan injection, the piroxicam gel was used to compare the anti-inflammatory effect of the kirenol 0.4 to 0.5 percent w/w.

Analgesic activity [21]
The goal of the study was to examine the topical analgesic effects of the compound derived from *Siegesbeckia orientalis* in order to support its traditional use. Kirenol was extracted from a *Siegesbeckia orientalis* EtOH extract. The analgesic properties of many topical preparations containing kirenol were examined in rats. Carrageenan-induced acute inflammation in rats, CFA (complete Freund's adjuvant) induced chronic inflammation in rats, and a formalin test in rats were used to investigate the effects. As a positive control, methyl salicylate ointment was investigated. In the late phase, analgesic effect of topical preparations containing greater than 0.4 percent w/w was detected.

Anti-allergic activity [22]
The effect of S. orientalis on IgE production was investigated in this study. The plasma levels of IgE generated by antigens were decreased by S. orientalis. S.orientalis reduced IL-4-dependent IgE production in whole spleen cells treated with lipopolysaccharide (LPS). S.orientalis reduced the generation of IgE triggered by LPS plus IL-4 in U266B1 human IgE-bearing B cells.

Immunosuppressive activity [23]
The immunosuppressive action of the EtOH extract of *S. orientalis* on immunological reactions in mice was examined in vitro and in vivo. *S. orientalis* inhibited splenocyte proliferation driven by lipopolysaccharide (LPS) and concanavalin A (Con A) in vitro in a concentration dependent manner. ICR On days 0 and 14, mice were inoculated subcutaneously with ovalbumin (OVA). In OVA-immunized mice, *S. orientalis* considerably inhibited LPS, Con A and OVA-induced splenocyte proliferation in a dose

dependent manner.

Anti hyperuricemic activity [24]

The aerial component of *S. orientalis* was collected in Vietnam's hilly region. The plant components were used to make the crude ethanol extract and its Butanol fraction. The anti-hyperuricemic properties of the crude ethanol extract and Butanol fraction were investigated in vivo by using oxonate-induced hyperuricemia rats model, with serum uric acid levels and inhibitory effects on xanthine oxidase (XO) in the rat liver being measured. A uricase inhibitor, Potassium oxonate was used to cause hyperuricemia in rats.The BuOH fraction was discovered to be the important active component of the *S. orientalis* CEE, which has anti-hyperuricemic action. In vivo investigations on this fraction revealed a reduction of 31.4 percent in serum uric acid levels and a 32.7 percent inhibition of xanthine oxidase (XO).

Neuroprotective effect [25, 26]

Phytochemical screening for alkaloids, tannins, cyanogenicglycosides, oxalates, saponins, flavonoids, phenols andphytates in aqueous extracts were investigatedAfter surgery, a small percentage of people have immediate or even long-term cognitive impairment, a condition known as PCOD ie. Postoperative Cognitive Dysfunction. The goal of this investigation was to see if prior treatment with *Siegesbeckia Orientails*before surgery has any neuro protective effects in terms of lowering inflammation and moderating cognitive damage in postoperative mice. Before undergoing a laparotomy, three-month-old male C57BL/6N mice were fed varying doses of *S. Orientails* extract for 14 days. They were sacrificed on postoperative day (POD) 3 after cognitive tests. When compared to control rats, the results showed that extract pretreatment improved memory in a dose-dependent way. In addition, the medicated mice showed indications of reduced systemic and neuroinflammation, as well as suppression of inflammatory pathways and dramatically reduced tau phosphorylation in the hippocampus. Taken together, our findings showed that *S. Orientails* has a neuroprotective effect in postoperative rats, implying that *Siegesbeckia Orientails* may have therapeutic potential in reducing the postoperative pain.

Anti-Proliferative activity

- **Endometrial cancer [27, 28]**

It is a common genital tract cancer in women. The proliferation of RL95-2 human endometrial cancer cells was greatly suppressed by *Siegesbeckia orientalis* ethanol extract (SOE), according to this study. By up-regulating Bad, Bak, and Bax protein expression while down-regulating Bcl-2 and Bcl-xL protein expression, SOE triggered cell arrest in the G2/M phase and induced apoptosis in RL95-2 cells. Treatment with SOE enhanced caspase-3, -8, and -9 protein expression in a dose-dependent manner, showing that apoptosis occurred via both intrinsic and extrinsic mechanisms. SOE was also effective against the cell lines A549 (lung cancer), Hep G2 (hepatoma), FaDu (pharyngeal squamous carcinoma), MDA-MB-231 (breast cancer), and LNCaP (prostate cancer). Gas chromatography-mass analysis found a total of ten SOE components. SOE's cytotoxic action against RL95-2 cells is mostly due to caryophyllene oxide and caryophyllene.

- **Cervical cancer [29]**

The goal of this research was to look into the cytostatic effects of *Siegesbeckia orientalis* L. on human cervix cancer HeLa cells. HeLa cells were given varying doses *of S.orientalis* extracts. The MTT assay was used to determine the level of growth inhibition. HeLa cells

were significantly suppressed by the ethyl acetate and n-butanol extracts of *S.orientalis*. Conclusion In vitro, *S.orientalis* inhibits human cervical cancer HeLa cells.

Antifeedant and insecticidal effects [30]
Extract of *Siegesbeckia orientalis* was tested for the antifeedant and insecticidal effects on third-instar larvae of the cabbage webworm, Crocidolomia binotalis, which is presently one of the most important pests of cruciferous crops in Mauritius. The plant extract investigated showed significant antifeedant properties. *Siegesbeckia orientalis* at 1.0% showed significant antifeedant activity.

Antimicrobial effect [31]
The goal of this work was to develop a dependable kirenol manufacturing procedure using *S. orientalis* converted root cultures and to look into the antibacterial properties of hairy root, kirenol and *S. orientalis*. The transformation of Agrobacterium rhizogenes A4 resulted in transformed root cultures of S. orientalis. Polymerase chain reaction (PCR) with rolB specific primers was used to confirm the roots' transgenic status. Hairy root clones' biomass and kirenol accumulation were measured using four different culture media: MS, MS/2, B5, and white. The disc diffusion method was used to assess the antibacterial activity of kirenol, hairy root, and *S. orientalis.*

Xanthine oxidase inhibitory activity [32]
The aerial portions of *S. orientalis* L. yielded five unknown chemicals (four guaianolide sesquiterpenes and a benzoate ester derivative) and seven recognised compounds. Extensive investigation of HR-ESI-MS and NMR spectroscopic approaches was used to establish their chemical structures. Experimental and TD-DFT computed ECD spectra revealed absolute configurations. Twelve identified compounds with IC50 values ranging from 0.76 0.17 M to 31.80 0.97 M showed potential xanthine oxidase inhibitory action. Molecular docking studies predicted that all identified drugs had lower binding energies with xanthine oxidase than the positive control allopurinol. With IC50 values of 0.76 0.17 M and 0.98 0.26 M, respectively, benzyl 2-hydroxy-6-O—D-glucopyranosylbenzoate and benzyl 2-methoxy-6-O—D-glucopyranosylbenzoate had the best docking score as well as the highest in vitro xanthine oxidase inhibitory activity.

Conclusion
This review is conducted to provide comprehensive information on *S. orientalis* L. regarding its botany, microscopy, traditional uses, chemical constituents, pharmacological activities. As a Chinese herbal medicine, *S. orientalis* L. is mainly used for relieving rheumatoid arthritis, pains and aches in the legs and sides, hemiplegia, hypertension, sciatica, weeping dermatitis and mastitis, traumatic bleeding. Various studies demonstrated that S. orientalis posses anti-inflammatory, antiproliferative, antiallergic, antimicrobial, Immunosuppressive, Anti hyperuricemic, neuroprotective, analgesic activity. A number of compounds were reported belonging to the category of sesquiterpenoids, diterpenoids, flavonoids, Kaurenoids, pimarinoids, and other compounds.

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Conflicts of Interest:
There are no conflicts of interest among the authors

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