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## From Ethnomedicine to Drug Discovery: Phytochemical and Pharmacological Insights into *Sphaeranthus indicus*

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### ABSTRACT

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*Sphaeranthus indicus* Linn. (Asteraceae), commonly known as East Indian Globe Thistle, is a medicinally important plant widely distributed across the Indian subcontinent. Traditionally employed in Ayurveda, Siddha, and Unani systems of medicine, it has been used to treat neurological disorders, hepatic ailments, skin diseases, and inflammatory conditions. Modern phytochemical investigations have revealed a diverse array of bioactive constituents, including sesquiterpene lactones, eudesmanolides, sesquiterpenoids, flavonoids, sterols, alkaloids, glycosides, amino acids, and sugars. Essential oils derived from flowers and whole plants contain monoterpenes, sesquiterpenes, and oxygenated derivatives, with compounds such as methyl chavicol, citral, geraniol, and  $\beta$ -eudesmol contributing to its chemical richness.

Pharmacological studies have demonstrated that *S. indicus* possesses significant anti-inflammatory, antioxidant, antimicrobial, hepatoprotective, immunomodulatory, and neuropharmacological activities. Its extracts have shown potential in reducing oxidative stress, modulating immune responses, and protecting hepatic function against toxic insults. The plant also exhibits anticancer and antimitotic properties, with sesquiterpene lactones and alkaloids interfering with tumor cell proliferation and inducing apoptosis. Neuroactive effects, including anxiolytic, antidepressant, and anticonvulsant activities, further validate its traditional use in neurological disorders. Additional studies highlight its antidiabetic, wound healing, cardioprotective, and anti-arthritic potential, making it a versatile candidate for drug discovery.

Despite promising findings, most studies remain limited to preliminary in vitro and in vivo models, with scarce clinical validation. Future research should emphasize bioassay-guided fractionation, mechanistic studies, and clinical trials to establish standardized phytopharmaceuticals. Overall, *Sphaeranthus indicus* represents a valuable medicinal resource, bridging traditional knowledge with modern biomedical research, and offering scope for novel therapeutic interventions.

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## 1. INTRODUCTION

*Sphaeranthus indicus* Linn., commonly known as East Indian Globe Thistle, is a well-recognized medicinal plant belonging to the

family Asteraceae. It is widely distributed across the Indian subcontinent, thriving in moist deciduous forests, grasslands, and cultivated fields (1, 2). Traditionally, the plant has been employed

in Ayurveda, Siddha, and Unani systems of medicine for its diverse therapeutic properties. Various parts of the plant, including flowers, leaves, and roots, have been utilized in formulations aimed at treating neurological

disorders, hepatic ailments, skin diseases, and inflammatory conditions. Its ethnomedicinal relevance has made it a subject of growing scientific interest in recent decades (3, 4).



**Figure 1: Sphaeranthus indicus Linn.**

Phytochemical investigations of *Sphaeranthus indicus* have revealed the presence of bioactive constituents such as flavonoids, alkaloids, glycosides, sesquiterpene lactones, and essential oils (5, 6). These compounds are believed to contribute to its wide spectrum of pharmacological activities, including antioxidant, anti-inflammatory, antimicrobial, hepatoprotective, and immunomodulatory effects (7, 8). Notably, the plant has also demonstrated promising anticancer and antimitotic potential in preliminary studies, supporting its traditional use in managing proliferative disorders. The hydroalcoholic and methanolic extracts, in particular, have shown significant biological activity, warranting further exploration through *in vitro* and *in vivo* models (9, 10).

Given the increasing global demand for plant-based therapeutics, *Sphaeranthus indicus* represents a valuable candidate for drug discovery and development. Its rich phytochemical profile and traditional applications provide a strong rationale for systematic scientific evaluation (11, 12). Moreover, the plant’s accessibility and adaptability to diverse agro-climatic conditions enhance its potential for sustainable utilization. Current research trends emphasize the need to validate traditional claims with modern pharmacological evidence, establish standardized extraction protocols, and elucidate mechanisms of action at the molecular level (13, 14). Thus, *Sphaeranthus indicus* stands as a promising medicinal resource, bridging traditional wisdom with contemporary biomedical research, and offering scope for novel therapeutic interventions.

**Table 1: Taxonomical classification**

|              |                 |
|--------------|-----------------|
| Kingdom      | Plantae         |
| Subkingdom   | Viridaeplantae  |
| Phyllum      | Tracheophyta    |
| Subphylum    | Euphyllophytina |
| Infraphyllum | Radiatopses     |

|                   |               |
|-------------------|---------------|
| <b>Class</b>      | Magnoliopsida |
| <b>Subclass</b>   | Asteridae     |
| <b>Superorder</b> | Asteranae     |
| <b>Order</b>      | Asterales     |
| <b>Family</b>     | Asteraceae    |
| <b>Genus</b>      | Sphaeranthus  |
| <b>Species</b>    | indicus       |

## 2. MORPHOLOGICAL CHARACTERS

Sphaeranthus indicus is anaromatic annual spreading herb with branches, 30cm to 60 cm tall. Stems and Branches have toothed wings, more or less covered with glandular hairs. Leaves are spatulate, sessile, decurrent, obovate-oblong, glandular dentate and narrowed at the base. Flowers are in compound; heads, globose, ovoid in shape, ebracteate, borne on solitary glandular peduncles with toothed wings. They purple in colour. Involucre of bracts are linear in shape, acuminate apex, pubescent and ciliate near the ends. Fruits are achenes are glabrous and stalked. Roots are 5 to 15cm long and 0.3 to 0.5 cm thick, a few branching; smooth, slender, somewhat laterally flattened, grayish-brown; fracture, short; odour, not characteristic; taste is slightly bitter (15, 16).

## 3. CHEMICAL CONTENTS OF SPHAERANTHUS INDICUS LINN. (ASTERACEAE)

Phytochemical investigations of Sphaeranthus indicus have revealed a remarkably diverse array of secondary metabolites distributed across its anatomical parts. The plant is rich in eudesmanolides, sesquiterpenoids, sesquiterpene lactones, sesquiterpene acids, flavone and flavonoid glycosides, isoflavone glycosides, sterols, sterol glycosides, alkaloids, peptide alkaloids, amino acids, and sugars (17, 18). Essential oils derived from flowers and whole plants have been extensively analyzed, showing the presence of monoterpene hydrocarbons, oxygenated monoterpenes, sesquiterpene hydrocarbons, and oxygenated sesquiterpenes. Among these, 7-hydroxy eudesmanolide has been

identified as a major sesquiterpene lactone, while sphaeranthine, an alkaloid, represents another significant constituent (19). The essential oil profile includes compounds such as methyl chavicol,  $\delta$ -cadinene,  $\alpha$ -ionone, citral, geraniol, geranyl acetate,  $\beta$ -ionone, eugenol, estragole, and indicusene, highlighting its chemical complexity. Sterols like stigmasterol and  $\beta$ -sitosterol have been isolated from alcoholic extracts, while petroleum ether and acetone extracts yielded novel sesquiterpene lactones and acids, including 7 $\alpha$ -hydroxyeudesm-4-en-6,12-olide, 2-hydroxycostic acid,  $\beta$ -eudesmol, and ilicic acid (20). Additionally, unique glycosides such as sphaeranthanolide and sterol glycosides have been reported. Further studies identified multiple hydroxy lactones, eudesmanolides, sesquiterpenoids, and peptide alkaloids, along with amino acids (glycine, alanine, valine, leucine, histidine, cysteine, lysine, aspartic acid, glutamic acid) and sugars (D-arabinose, L-rhamnose, lactose, raffinose, galactose, maltose, fructose, glucose). Novel flavonoid and isoflavone glycosides have also been isolated from stems and leaves, enriching its phytochemical profile (21). Gas chromatography and GC-MS analyses of hydro-distilled essential oil identified 38 compounds accounting for 84% of the oil, with major constituents such as 2,5-dimethoxy-p-cymene,  $\alpha$ -agarofuran, 10-epi- $\gamma$ -eudesmol, and selin-11-en-4 $\alpha$ -ol. Collectively, these findings underscore the chemical richness of Sphaeranthus indicus, providing a strong foundation for its pharmacological potential and therapeutic applications (22, 23).

**Table 1: Chemical Constituents of *Sphaeranthus indicus* Linn. (Asteraceae)**

| Class of Compounds                             | Representative Molecules                                                                                                                                                                                                     | Source (Plant Part/Extract)                             |
|------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------|
| <b>Sesquiterpene Lactones / Eudesmanolides</b> | 7-Hydroxy eudesmanolide, 7 $\alpha$ -hydroxyeudesm-4-en-6,12-olide, 7-hydroxyfrullanolide, sphaeranthanolide, 11 $\alpha$ ,13-dihydroxyfrullanolides, 5 $\alpha$ ,7-dihydroxyeudesmanolide                                   | Flowers, aerial parts, acetone/petroleum ether extracts |
| <b>Sesquiterpenoids / Sesquiterpene Acids</b>  | $\beta$ -Eudesmol, ilicic acid, 2-hydroxycostic acid, cryptomeridiol, 4-epicryptomeridiol                                                                                                                                    | Aerial parts, acetone extract                           |
| <b>Essential Oils (Volatile Constituents)</b>  | Methyl chavicol, $\delta$ -cadinene, $\alpha$ -ionone, citral, geraniol, geranyl acetate, $\beta$ -ionone, eugenol, estragole, indicusene, $\alpha$ -agarofuran, 2,5-dimethoxy- <i>p</i> -cymene, selin-11-en-4 $\alpha$ -ol | Flowers, whole plant, hydro-distilled oil               |
| <b>Sterols / Sterol Glycosides</b>             | Stigmasterol, $\beta$ -sitosterol, n-triacontanol, sterol $\beta$ -D-glucoside                                                                                                                                               | Alcoholic extract, oil                                  |
| <b>Alkaloids / Peptide Alkaloids</b>           | Sphaeranthine (C <sub>13</sub> H <sub>19</sub> O <sub>5</sub> ), peptide alkaloids (two reported)                                                                                                                            | Whole plant, flowers                                    |
| <b>Flavonoids / Glycosides</b>                 | 7-hydroxy-3',4',5,6-tetramethoxy flavone diglucoside, 5-hydroxy-7-methoxy-6-C-glycosylflavone                                                                                                                                | Stem, aerial parts                                      |
| <b>Isoflavone Glycosides</b>                   | 5,4'-dimethoxy-3'-prenylbiochanin galactoside                                                                                                                                                                                | Leaves                                                  |
| <b>Amino Acids</b>                             | Glycine, alanine, valine, leucine, histidine, cysteine, lysine, aspartic acid, glutamic acid                                                                                                                                 | Leaves                                                  |
| <b>Sugars</b>                                  | D-arabinose, L-rhamnose, lactose, raffinose, galactose, maltose, fructose, glucose                                                                                                                                           | Leaves                                                  |

#### 4. PHARMACOLOGICAL ACTIVITIES

*Sphaeranthus indicus* Linn. (Asteraceae) has been extensively investigated for its broad spectrum of pharmacological activities, many of which validate its traditional use in Ayurveda, Siddha, and Unani medicine. The plant exhibits anti-inflammatory and analgesic properties, attributed largely to its sesquiterpene lactones and flavonoids, which modulate inflammatory mediators and reduce pain perception. Its antioxidant activity has been demonstrated through free radical scavenging and lipid peroxidation inhibition, supporting its role in preventing oxidative stress-related disorders (24, 25). The plant also shows significant antimicrobial and antifungal effects, with extracts inhibiting pathogenic bacteria and fungi, thereby justifying its ethnomedicinal use in treating skin infections and wounds. Hepatoprotective activity has been reported, where extracts safeguard liver function against chemical-induced toxicity, likely due to antioxidant and membrane-stabilizing mechanisms (26). In addition, *S. indicus* demonstrates immunomodulatory potential,

enhancing both humoral and cell-mediated immune responses, which may contribute to its traditional application in chronic diseases. Notably, the plant exhibits anticancer and antimetabolic activity, with sesquiterpene lactones and alkaloids interfering with cell cycle progression and inducing apoptosis in tumor cells. Neuropharmacological studies reveal anxiolytic, antidepressant, and anticonvulsant effects, suggesting modulation of neurotransmitter systems and supporting its traditional use in neurological disorders (27, 28). Furthermore, antidiabetic activity has been observed, with extracts lowering blood glucose and improving lipid profiles in experimental models. Other reported activities include anti-arthritic, wound healing, anti-ulcer, and cardioprotective effects, highlighting the plant's multifaceted therapeutic potential. Collectively, these findings establish *Sphaeranthus indicus* as a promising medicinal resource, with its diverse phytoconstituents contributing to multiple pharmacological actions. Continued research focusing on mechanism elucidation, bioactive compound isolation, and

clinical validation will further strengthen its role in modern phytomedicine.

#### **Ovicidal activity:**

Sesquiterpene lactone, isolated from a petroleum ether extract of *S. indicus*, at concentration of 50-250 ppm, decreased rates of fecundity and fertility in the larval-treated adult females, *Culex quinquefasciatus*. Egg hatching was also significantly lowered. Mortality in the larvae, pupae and adults caused a marked decrease in mosquito populations in laboratory experiments.

#### **Hepatoprotective activity:**

Methanolic extract of *S. indicus* showed a protective effect against  $\text{CCl}_4$  induced hepatotoxicity. The aqueous and methanolic extracts of flower head of *S. indicus* exhibited hepatoprotective and antioxidant effect on acetaminophen-induced hepatotoxicity in rats. Ethanolic extract (200 and 300 mg/kg) of aerial parts of *S. indicus* demonstrated marked hepatoprotective activity against paracetamol induced liver damage in rats with maximum effect at 300 mg/kg.

#### **Anti-inflammatory activity:**

Ethanolic extract of *S. indicus* leaves (100, 200 and 400 mg/kg, p.o.) exhibited dose-dependent anti-inflammatory effect in acute (carrageenan induced paw edema) as well as chronic inflammatory (cotton pellet induced granuloma) models in rat. The methanol extract of *S. indicus* flowers and its standardized fraction, NPS31807 decreased release of proinflammatory cytokines like  $\text{TNF-}\alpha$ , IL-6 and IL- $1\beta$  from human monocytic cell line (THP-1). It also reduced  $\text{TNF-}\alpha$  and IL-8 expression in normal human epidermal keratinocytes (NHEK). Administration of petroleum ether extract of *S. indicus* (100 mg/kg/day) for a period of 21 days to arthritic animals suppressed the chronic phase of inflammation as well as elevation of WBC count significantly without any gastrointestinal side effects like ulcers. Anti-inflammatory effect of ethanolic extract was evaluated. The extract in different doses (100, 200 and 400 mg/kg, p.o.) exhibited dose dependent and significant anti-inflammatory activity in acute (carrageenan induced hind paw edema,  $P < 0.05$ ) and chronic (cotton pellet granuloma formation,  $P < 0.05$ ) model of inflammation.

#### **Attenuation effect on prostatic hypertrophy:**

The attenuating effect of petroleum ether, ethanolic, aqueous extracts and  $\beta$ -sitosterol on prostatic hyperplasia induced by testosterone in Albino rats. Finasteride was used as a positive control (1 mg/kg p.o.). The petroleum ether extract exhibited the best activity, although the ethanol and aqueous extracts also exhibited significant activity thereby indicating the potential use of *S. indicus* in the treatment of prostatic hyperplasia.

#### **Antitumor activity:**

The petroleum ether extract of flower heads of *S. indicus* demonstrated potent cytotoxic effects on human colon (Colo- 205), prostate (PC-3 and DU-145), lung (A-549), breast (MCF-7) and acute lymphoblastic leukemia (HL-60) cell lines but not in ovarian cancer (IGROV- 1) cell line as assessed by sulforhodamine B assay. In HL 60 cell line, the extract caused cell cycle arrest at subG0 phase and induced apoptosis by causing DNA laddering. Further, the petroleum ether extract caused mitochondrial damage leading to loss of their membrane potential and increase in caspase 3 and caspase 9 activities. A cancer activity of chloroform extract of whole plant of *S. indicus* against Ehrlich ascites carcinoma in Swiss albino mice.

#### **Anti-oxidant activity:**

The ethanolic extract showed maximum scavenging of, 2,2-azinobis-(3-ethylbenzothiazoline-6-sulphonate) and 1,1-diphenyl, 2-picryl hydrazyl (33.27%) radicals, superoxide (26.14%) and nitric oxide radical (22.36%) suggesting the therapeutic applications of the plant in free radical mediated pathologies.

#### **Immunomodulatory effect:**

Methanol extract, its petroleum ether, chloroform and remaining methanol fractions, of flower heads were found effective in increasing phagocytic activity, hemagglutination antibody titer and delayed type hypersensitivity, whereas only remaining methanol fraction was found active in normalizing total white blood cell levels in case of cyclophosphamide induced myelosuppression in mice. The study revealed that the drug holds promise as immunomodulatory agent. Methanolic extract of whole plant of *S. indicus* has immunomodulatory potential in both



humoral and cell mediated immunity as well as phagocytic function.

#### **Anti-feedant activity:**

Methanol extract of *S. indicus* and 7-hydroxy frullanolid isolated from its fraction showed anti-feedant activity against 4<sup>th</sup> instar larvae of *Spodoptera litura*.

#### **Anti-tussive activity:**

Methanol extract of *S. indicus* (200, 300 and 400 mg/kg) exhibited anti-tussive activity and synergistic effects of sleeping time induced by standard sedatives pentobarbitone and diazepam in Swiss Albino mice.

#### **Wound healing activity:**

A cream containing ethanolic extract of aerial parts of *S. indicus* exhibited wound healing activity in guinea pigs and enhanced the rate of wound contraction and the period of epithelialization comparable to neomycin. Similarly, an ointment containing 2% (w/w) alcoholic extract of flower head showed wound healing activity and protection against microbial invasion.

#### **Analgesic and antipyretic activity:**

The topical application of essential oil from flower heads of *S. indicus* demonstrated significant analgesic effect at 90 and 120 minutes of application. Petroleum ether, chloroform and ethanol extract of whole plant showed significant analgesic effect while petroleum ether and chloroform extract demonstrated antipyretic action [Nanda et al., 2009]. The ethanol extracts of the whole plant *S. indicus* exhibited dose dependent analgesic activity at 250 mg and 500 mg/kg in tail immersion method in rat.

#### **Anti-diabetic activity:**

Oral administration of alcoholic extract of *S. indicus* for 15 days in nicotinamide and streptozotocin (STZ) induced diabetic rats exhibited significant reduction in blood glucose levels and increased in hepatic glycogen and plasma insulin levels with significant improvement in oral glucose tolerance test. In in-vitro study, the ethanol extract of aerial part of *S. indicus* increased the uptake of glucose by isolated rat hemi-diaphragm significantly ( $P < 0.01$ )

#### **Anti-microbial activity:**

Methanol and aqueous extracts of leaf showed the highest inhibitory effect compared to all other extracts and it showed good inhibitory

activity against *Bacillus* sp., followed by *Staphylococcus* sp. The gram-positive bacteria were found to be more susceptible than gram-negative bacteria. Antifungal activity of methanol and ethanol extracts were tested against *Penicillium* sp., and *Aspergillus* sp. and the growth was found to decrease with increase in concentration of the extracts. The plant also exhibited antifungal activity. The petroleum ether, acetone, methanol (90%) and aqueous extracts of flowers also exhibited remarkable antibacterial and strong antifungal activities. The hexane, chloroform, ethyl acetate, ethanol, methanol and aqueous extract of entire part including flower heads exhibited antimicrobial activity compared with gentamycin and nystatin as standards.

#### **Anti-viral activity:**

The methanol extract exhibited inhibitory activity against Mouse corona virus and Herpes simplex virus at a concentration of 0.4 µg/ml. The plant also showed antiviral activity against vaccinia and ranikhet viruses.

#### **Larvicidal activity:**

Acetone extract of root and leaf showed > 50 % mortality in Indian mosquito specie, which acts as a vector of filarial worm. Root extract was more active than leaf extract. Purified fraction of acetone extract showed mosquito larvicidal effect. Methanolic extract showed repellent and feeding deterrent activities against *Tribolium castaneum* in the lower concentration of 1%; complete feeding deterrent activity at 5 ml and repellent activity at 4 ml dose.

#### **Antihelmenthic activity:**

The ethanolic and aqueous extracts (10, 50, 100 mg/ml concentration levels) of the whole plant exhibited anthelmintic activity against *Pheretima posthuma* and *Ascaridia galli* in a dose-dependent manner. The most significant activity was observed at the highest concentration of 100 mg/ml against both types of worms.

### **5. CONCLUSION**

The comprehensive exploration of *Sphaeranthus indicus* Linn. (Asteraceae) underscores its immense potential as a medicinal plant of significant pharmacological and phytochemical importance. Traditionally revered in Ayurveda, Siddha, and Unani systems, the plant has now gained recognition in modern scientific research owing to its diverse bioactive

constituents and wide-ranging therapeutic activities. The chemical investigations reveal a rich reservoir of secondary metabolites, including sesquiterpene lactones, eudesmanolides, flavonoids, sterols, alkaloids, glycosides, amino acids, and sugars, along with a complex profile of volatile oils. These compounds collectively contribute to the plant's multifaceted pharmacological actions, validating its ethnomedicinal applications.

The pharmacological studies highlight *S. indicus* as a potent anti-inflammatory, antioxidant, antimicrobial, hepatoprotective, immunomodulatory, and neuroactive agent. Its ability to modulate oxidative stress, inflammatory pathways, and immune responses positions it as a promising candidate for managing chronic diseases such as arthritis, diabetes, hepatic disorders, and neurological conditions. Furthermore, the anticancer and antimitotic properties of its sesquiterpene lactones and alkaloids open avenues for developing novel chemotherapeutic agents. The plant's anxiolytic and antidepressant effects, coupled with anticonvulsant activity, provide scientific support for its traditional use in neurological and psychiatric disorders. Such broad pharmacological relevance emphasizes the importance of integrating *S. indicus* into contemporary phytomedicine.

Despite these promising findings, several challenges remain. Most studies have been limited to preliminary in vitro and in vivo models, with scarce clinical validation. Standardization of extracts, identification of lead compounds, and elucidation of molecular mechanisms are essential to translate traditional knowledge into evidence-based therapeutics. Additionally, sustainable cultivation and conservation strategies must be prioritized to ensure consistent availability of quality plant material, given its widespread use and growing demand. Advances in analytical techniques, such as HPLC, GC-MS, and NMR, can further aid in characterizing novel compounds and establishing quality control parameters.

In conclusion, *Sphaeranthus indicus* represents a valuable bridge between traditional wisdom and modern biomedical research. Its chemical diversity and pharmacological versatility

make it a strong candidate for drug discovery and development. Future research should focus on bioassay-guided fractionation, mechanistic studies, and clinical trials to validate its therapeutic efficacy and safety. By integrating ethnopharmacological knowledge with modern scientific approaches, *S. indicus* can be developed into standardized phytopharmaceuticals, contributing significantly to global healthcare. Thus, the plant stands not only as a testament to the richness of Indian medicinal flora but also as a promising resource for innovative therapeutic interventions in the future.

## 6. CONFLICT OF INTEREST

None

## 7. REFERENCES

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