**A REVIEW OF PHYTOPHARMACOLOGY AND FORMULATION OF SPHAERANTHUS INDICUS**

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**Abstract**

*Sphaeranthus indicus* Linn., belonging to the Asteraceae family, it thrives abundantly in damp areas, including as a weed in rice fields across India. In traditional Indian medicine, many different components of the plant, including the leaves, cortex, wood, roots, flower, and seed, are used to cure a variety of illnesses. Astringent, stomachic, refreshing, and externally calming are some of the qualities associated with the herb. *Sphaeranthus indicus* is rich in diverse secondary metabolites, including eudesmanolides, sesquiterpenoids, sesquiterpene lactones, sesquiterpene acids, flavone glycosides, flavonoid C-glycosides, is flavone glycoside, sterols, sterol glycosides, alkaloids, peptide alkaloids, amino acids, and sugars. Essential oils extracted from its flowers and whole plants contain monoterpenic hydrocarbons, oxygenated monoterpenes, sesquiterpene hydrocarbons, and oxygenated sesquiterpenes. This comprehensive review encompasses the structure, botanical compounds composition, ethnomedical uses, and pharmacological activities reported for Sphaeranthus indicus. It underscores the vast medicinal potential of this plant and highlights its importance in traditional and modern medicinal practices.

**Keywords:** Secondary metabolites, essential oils, antimicrobial activity, antioxidant properties, antidiabetic potential, hepatoprotective activity.

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**Introduction**

*Koṭṭaikkarantai*, additionally referred to as *Sphaeranthus indicus* Linn., is a fragrant herb that typically grows 1-2 feet tall and is extensively dispersed throughout Asia’s valleys and hills. It holds significant medicinal importance, being used for treating a variety of conditions including gastric disorders, skin diseases, helminth infections, lymphoid swellings, depressing of the nerves, and acting as a bowel movement, a urinary tract antibiotic, and antimicrobial. The plant's preparation is reputed to be effective against a skin infection like yellowing of the skin leukoderma vulgar, pneumonia, along with lung disease. Powdered bark mixed with whey is utilized for treating piles, while the flowers are known for their alterative, depurative, and stimulant properties. Both roots and seeds act as anthelmintic, and fresh leaf juice is taken for cough relief. Additionally, the plant's insecticidal properties are utilized in preserving food grains. Although extensively reviewed in previous literature, this paper aims to explore its Siddha and Ayurveda uses, in addition to its biological effects and botanical compounds characteristics [1-5].

Herbal medicines have been integral to human health practices since ancient times. Ayurveda, India’s oldest traditional system of medicine, reflects a deep understanding of the medicinal properties of diverse plants. India's rich flora, influenced by diverse climates and geographical conditions, has contributed to a vast repository of medicinal plants. With advancements in science, many traditional herbal remedies have been subjected to scientific scrutiny [6-9].

A common therapeutic plant in Indian traditional medicine, *Sphaeranthus indicus* Linn, grows well in a variety of tropical Indian settings, including agriculture, dry waste areas, and farmed areas. Its range is from the level of the ocean to 1.2km, and it includes Africa, Australia, Sri Lanka, and India [10, 11].

**Morphology**

The herb *Sphaeranthus indicus* is characterized by its highly branched structure and strong aroma. It is an annual plant with erect stems and taproots that branch extensively. The cylindrical stems feature toothed wings, while the leaves are sessile and recurrent, measuring 2-7 cm in length and 1-1.5 cm in width. The leaves are obovate-oblong, rounded or subacute at the tip, glandular-hairy, and spinous-serrate or dentate along the margins. They are greenish-brown in colour and narrow towards the base.

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The flowers of *S. indicus* are clustered terminally in solitary, globose heads. The heads themselves are purple, with short, slender, and acuminate bracts. Each flower head consists of outer female flowers that are fertile, along with central bisexual flowers that can be fertile or sterile. The involucre is narrow, with alliaceous bracts that are spatulate, acute, and ciliate. The receptacle is small and naked.

**Figure 1:** *Sphaeranthus indicus* plant

The corolla of female flowers is purple, slender, tubular, and minutely two to three toothed, while the corolla of hermaphrodite flowers is purplish-white, tubular or funnel-shaped, and four to five toothed. The anther base is agitating with acute or tailed auricles, and the style is armed, filiform, and sometimes connate.

The fruits of *S. indicus* are oblong and contain compressed achenes, lacking a pappus. The herb emits a slightly aromatic odour, which diminishes with prolonged storage.

**Microscopic Characters**

**Stem**

The stem exhibits a thick epidermis with numerous multicellular, uniseriate glandular trichrome. Collenchymatous cells form a continuous layer beneath the epidermis, providing mechanical strength. Vascular bundles are collateral, arranged in a ring, composed of xylem and phloem tissues. The xylem consists of vessels and fibres, while phloem contains sieve tubes and companion cells. Parenchymatous ground tissue fills the spaces between vascular bundles and around the pith.

**Leaf**

The leaf epidermis is covered with cuticle and contains numerous glandular trichrome, which are multicellular and glandular-tipped. Stomata are present on both upper and lower epidermis, facilitating gas exchange. Palisade mesophyll is located beneath the upper epidermis, consisting of elongated cells arranged parallel to the leaf surface, optimizing photosynthesis. Spongy mesophyll is located beneath the palisade layer, comprising loosely packed, irregularly shaped cells with intercellular spaces for gas exchange [12].

**Figure 2:** T.S of Stem of *Sphaeranthus indicus*

**Root**

The root structure shows an outermost layer of epidermis with root hairs for absorption of water and minerals. Cortex consists of several layers of parenchymatous cells with intercellular spaces, facilitating storage and lateral movement of nutrients. Endodermis forms a single layer of cells with Casparian strips, regulating the movement of water and solutes into the vascular cylinder. Vascular cylinder (stele) includes xylem and phloem tissues. Xylem is composed of vessels and fibres, while phloem contains sieve elements and companion cells.

**Figure 4:** T.S of Root of *Sphaeranthus indicus*

**Flower**

Floral parts exhibit glandular trichrome on the outer surfaces. The receptacle is lined with epidermal cells, and the ovary contains ovules within locules. The corolla consists of epidermal cells with a cuticle, stomata, and glandular trichrome on the outer surface. Stamens and pistil show typical floral anatomy, with anther cells containing pollen grains and stigma adapted for pollen reception.

**Seed**

The seed structure includes an outer seed coat (testa) composed of thick-walled cells, providing protection. The test may exhibit sculpturing or ornamentation for additional protection and seed dispersal. Endosperm within the seed provides nourishment to the developing embryo. The embryo consists of cotyledons (seed leaves) and a radicle (embryonic root), enclosed within the seed coat [13].

**Pharmacognostic Study**

A pharmacognostic study was conducted on *S. indicus*, focusing on examining the physical and chemical characteristics and
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The flowering plant produced spathanthone, an organic compound having its molecular formula C13H19O5 with a melting temperature between 166 and 168°C. Physical and chemical characteristics of the essential oil isolated from young floral plants were characterised. These included the following: spectral rotation (none), specific gravity at 30°C (0.9419), index of refractive at 20°C (1.512), value of acid (2.4030), fatty acids value (47.80), and acetylated fatty acids value (14, 15).

The essential oil contained compounds such as estragole, cadinene delta, alpha-ionone, para-methoxyincinic aldehyde, alpha-terpinene, 3,7-dimethyl-2,6-octadienial, 3,7-dimethyl-2,6-octadien-1-ol, (2E)-3,7-dimethyleneocta-2,6-dienyl acetate, 4-(2,6,6-trimethyl-1-cylohexen-1-yl)-3-buten-2-one, 3,7-dimethylocta-1,3,6-triene, 4-allyl-2-methoxyphenol, 1,3,4-trimethyl-2,5-dihydro-1H-pyrazol-5-one, sphaeranthol, 1-allyl-4-methoxybenzene, and indicucine. Additionally, the solvent included Stigmast-5-en-3-ol, 1-triacontanol, Ethyl carbamate, and pentosane [15, 16].

Sterols such as 24-ethylcholesterol-5-en-3β-ol and 24-ethylcholesterol-5-en-3β-ol were present in the ethanol extract. Three noteworthy hydroxyl lactones and a valerenalactone were separated through the petroleum ether extract of the aerial component by botanical compounds testing. Together with well-known substances beta-eudesmol and ilicic acid, a novel valerenalactone, hydroxyeudesm-4-en-6,12-olide, and a novel sesquiterpenoid acid, costic acid, were discovered from the acetone extract. Additionally, reported were a sterol glycoside, beta-sitosterol glucoside, and 7-hydroxyfrullanolactone [17-23].

Further compounds isolated include a new sphaeranthanol [24].

With the flowers, three novel eudesmanolides have been found. Spectroscopy like 2D magnetic resonance and nuclear magnetic resonance were employed to clarify the structures of these substances. Together with two novel eudesmanolides, sesquiterpene lactone and Peptide alkaloids are a subclass of alkaloids that contain one or more peptide bonds within their structure, often contributing to their pharmacological properties and bioactivity. The two identified eudesmanolides and a novel eudesmanolides derivative were produced through photo-oxidization [25-28].

The stems and leaves were used to identify the following: sugars (Glucose, Fructose, Sucrose, Maltose, Galactose), amino acids (Valine, Leucine, Isoleucine, Phenylalanine, Tyrosine, Lysine). Isolated from the base of the stem and blossoms, respectively, are new flavone glycosides. From the entire plant, three novel eudesmanolides were extracted and characterised by comparing their spectrum data with those of known spathanthone [29-32].

Gas chromatography (GC) and GC/mass spectrometry of the hydro distilled essential oil identified 38 compounds, comprising 84.0% of the oil, with major components including 2,5-dimethoxy-α-cymene, α-agar furan, 10-epi-γ-eudesmol, and selin-11-en-4-ol. The sample contained various compounds, including (Z)-3-hexenol, (E)-2-hexenol, α-pinene, camphene, 6-methyl 5-hepten-2-one, β-pinene, myrcene, α-phellandrene, p-cymene, limonene, α-p-dimethyl styrene, linalool, camphor, borneol, terpen-4-ol, nerol, neral, geraniol, geranial, maaliene, β-cubebene, β-elemene, β-caryophyllene, 2,5-dimethoxy-1-isopropenyl-4-isopropylbenzene, α-humulene, dihydroagarofuran, indipone, carphophyllene oxide, globulol, cis-artemannic alcohol, guaiol, trans-artemannic alcohol, cubenol, α-muurolol, α-eudesmol, and valianol [33].

A new flavonoid C-glycoside 5-hydroxy-7-methoxy-6-C-glycosylflavone, was discovered in the aerial part of the plant. Its structure was determined using spectroscopic techniques [34].

Overall, S. indicus demonstrates a diverse array of chemical constituents, encompassing alkaloids, sesquiterpene lactones, sterols, flavonoids, and essential oils, underscoring its potential pharmacological significance. Several bioactive compounds have been identified from various extracts of Sphaeranthus indicus.

The acetone extract yielded 7-hydroxyeudesm-4-en-6,12-olide (a sesquiterpene lactone), 2-hydroxyxostic acid (a sesquiterpene acid), β-eudesmol, and ilicic acid. From other extracts, three 7-hydroxyeudesmanolides, a bicyclic sesquiterpene lactone, and additional sesquiterpene lactones were isolated [35-39].

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Fig 5: Pharmacological study

The powdered form of S. indicus contains a significant amount of hairs, seeds in sperm pockets, and apical openings in the leaves. A solution combination made up of n-hexane: diethyl ether (3:7) was utilised to quantify 7-hydroxy eudesmenolides (0.0658% w/w) [12].

determining the levels of 7-hydroxy eudesmenolides [1], a significant sesquiterpene lactone. S. indicus is described as an herb with branching, hairiness, and a strong scent. Its leaves are spatulate and sessile, while its flowers are pinkish purple. The leaf exhibits various types of trichrome including unimulticellular, club, and clavately types. The stem features a consisting of an established parenchyma that has some pitted cells and a circle of deltoid arteries and veins. The cortical region of the root exhibits alternating secondary channel arrangements, along with metaderm and radially organised fibres.
dimethylocta-1,3,6-triene, 4-allyl-2-methoxyphenol, 1,3,4-trimethyl-2,5-dihydro-1H-pyrazol-5-one, sphaeranthol, 1-allyl-4-methoxybenzene, and indicusene. Various carbohydrates such as Glucose, Fructose, Sucrose, Maltose, Galactose were reported from the leaves [43-53]. Phytoconstituents and its pharmacological activity mention in table 1.

Table 1: Phytoconstituents and its pharmacological activity

<table>
<thead>
<tr>
<th>S.no</th>
<th>Part Of The Plant</th>
<th>Method of Extraction</th>
<th>Phytoconstituents</th>
<th>Pharmacological activity</th>
<th>Journal</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.</td>
<td>Whole Plant</td>
<td>Steam Distillation</td>
<td>Three 7-hydroxyeudesmanolides and two sesquiterpenoids, cryptomeridiol and 4-epicryptomeridio 6</td>
<td><strong>7-Hydroxyeudesmanolides</strong>: Anti-inflammatory, antimicrobial, <strong>Cryptomeridiol</strong>: Anti-inflammatory, antimicrobial, <strong>4-Epicryptomeridio</strong>: Anti-inflammatory, antimicrobial.</td>
<td>Rojatkar SR, et al (1992)[55]</td>
</tr>
<tr>
<td>3.</td>
<td>Aerial Parts S.Indicus</td>
<td>Maceration or Soxlet Extraction</td>
<td>Eudesmanoids such as dihydroartemisinin, artemisinin and eudesm-3-one.</td>
<td><strong>Dihydroartemisinin</strong>: Anti-inflammatory, antimicrobial, <strong>Artemisinin</strong>: Anti-inflammatory, antimicrobial, <strong>Eudesm-3-one</strong>: Anti-inflammatory, antimicrobial.</td>
<td>Pujar PP, Sawaikar Diet al (2000) [54]</td>
</tr>
<tr>
<td>5.</td>
<td>Whole Plant</td>
<td>Maceration or Soxlet Extraction</td>
<td>Some other sesquiterpene lactones.</td>
<td><strong>Parthenolide</strong>: Anti-inflammatory, anticancer, <strong>Artemisinin</strong>: Anti-inflammatory, antimicrobial, <strong>Costunolide</strong>: Anti-inflammatory, antimicrobial, <strong>Helenalin</strong>: Anti-inflammatory, anticancer, <strong>Lactucin</strong>: Sedative, anti-inflammatory.</td>
<td>Gogte MG, et al (1986) [56]</td>
</tr>
<tr>
<td>8.</td>
<td>Flowers Of S.Indicus</td>
<td>Steam Distillation</td>
<td>The components of the plant’s rich cherry-colored essential oil are p-methoxyxinnamaldehyde, d-cadinene, estragole, and alph-ionone.</td>
<td><strong>Methyl chavicol</strong>: Antispasmodic, antimicrobial, <strong>d-Cadinene</strong>: Anti-inflammatory, antimicrobial, <strong>α-limonone</strong>: Antioxidant, antimicrobial, <strong>p-Methoxyxinnamaldehyde</strong>: Antimicrobial, anti-inflammatory, <strong>α-Terpinen</strong>: Antioxidant, antimicrobial, <strong>Citral</strong>: Antimicrobial, anti-inflammatory.</td>
<td>Baslas KK, et al (1959) [59]</td>
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<td>-------------------------------------------------------------------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>10.</td>
<td>Leaves Of S. Indicus</td>
<td>Maceration or Soxhlet Extraction</td>
<td>Carbohydrates such as arabinose, galactose, glucose, fructose, lactose, maltose, raffinose, and xylose.</td>
<td>Anti-inflammatory, antioxidant, antimicrobial, immunostimulant.</td>
<td></td>
</tr>
<tr>
<td>11.</td>
<td>Leaves</td>
<td>Maceration or Soxhlet Extraction</td>
<td>A novel isoflavone glycoside, 5,4′-dimethoxy-3′-prenylbiochanin 7-O-( \beta )-d-galactoside.</td>
<td>Antioxidant potentially anti-inflammatory</td>
<td></td>
</tr>
<tr>
<td>12.</td>
<td>Flowers Of S. Indicus</td>
<td>Maceration or Soxhlet Extraction</td>
<td>Eudesmenolide type of sesquiterpene glycoside, sphaeranthanolide.</td>
<td>Immuno-stimulant potential</td>
<td></td>
</tr>
<tr>
<td>13.</td>
<td>Flowers</td>
<td>Alcoholic extract</td>
<td>Eudesmenolides such as frullanolide,</td>
<td>Eudesmenolide: Anti-inflammatory, potentially cytotoxic. Peptide alkaloids: Various activities including antimicrobial, potential neuroactive effects</td>
<td></td>
</tr>
<tr>
<td>14.</td>
<td>Flowers</td>
<td>Alcoholic extract</td>
<td>Peptide alkaloids</td>
<td>Antidepressant effects</td>
<td></td>
</tr>
<tr>
<td>15.</td>
<td>Flowers</td>
<td>Alcoholic extract</td>
<td>The of contains stigmasterol and ( \beta )-sitosterol</td>
<td>Pharmacological activities: Anti-inflammatory, antioxidant, potential cholesterol-lowering effects</td>
<td></td>
</tr>
<tr>
<td>16.</td>
<td>Powdered Caputula</td>
<td>Alcoholic extract</td>
<td>Flavonoids include compounds such as vicenin-2 (5-hydroxy-7-methoxy-6-C-glycosylflavone) and other flavonoid glycosides known for their medicinal properties.</td>
<td>5-hydroxy-7-methoxy-6-C-glycosylflavone: Anti-inflammatory, antioxidant</td>
<td></td>
</tr>
<tr>
<td>17.</td>
<td>Stem Of S. Indicus</td>
<td>Maceration or Soxhlet Extraction</td>
<td>Harmine and harmaline, two alkaloids present in the extract</td>
<td>Neuroprotective effects, Antidepressant effects</td>
<td></td>
</tr>
<tr>
<td>18.</td>
<td>Stem And Leaves Of Spharanthus Indicus</td>
<td>Soxhlet extraction method</td>
<td>Neuroprotective effects, Antidepressant effects</td>
<td></td>
<td></td>
</tr>
<tr>
<td>19.</td>
<td>The Roots And Aerial Parts</td>
<td>Methanolic extraction</td>
<td>The primary phytoconstituents</td>
<td>Immunomodulatory activity</td>
<td></td>
</tr>
<tr>
<td>No.</td>
<td>Plant Part(s)</td>
<td>Extraction Method</td>
<td>Phytoconstituents Identified</td>
<td>Potential Activities</td>
<td></td>
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</tr>
<tr>
<td>20.</td>
<td>The Leaves And Flowers</td>
<td>Solvent Extraction</td>
<td>Gallic acid is the primary phytoconstituent</td>
<td>Anti-inflammatory activity, Antioxidant activity</td>
<td></td>
</tr>
<tr>
<td>21.</td>
<td>Flower</td>
<td>Alcoholic extraction</td>
<td>The primary phytoconstituent discussed in the article is β-sitosterol.</td>
<td>Anti-inflammatory, Antioxidant, Anticancer Immunomodulatory</td>
<td></td>
</tr>
<tr>
<td>22.</td>
<td>Leaves And Flowers</td>
<td>Solvent Extraction</td>
<td>The primary phytoconstituent discussed in the article is Kaempferol</td>
<td>Anti-cancer activity</td>
<td></td>
</tr>
<tr>
<td>23.</td>
<td>Whole Plant</td>
<td>Alcoholic extraction</td>
<td>Multiple including flavonoids, alkaloids, tannins, and saponins.</td>
<td>Anti-inflammatory, antioxidant, and antimicrobial effects.</td>
<td></td>
</tr>
<tr>
<td>24.</td>
<td>Leaves And Stems</td>
<td>Alcoholic extraction</td>
<td>The primary phytoconstituents identified in the extract were Tannins</td>
<td>Wound healing: Promotes tissue regeneration and reduces healing time.</td>
<td></td>
</tr>
<tr>
<td>25.</td>
<td>Leaves And Roots</td>
<td>Solvent Extraction</td>
<td>The primary phytoconstituents identified in the extract were Pyrrolizidine alkaloids</td>
<td>Hepatoprotective, anti-inflammatory, and antimicrobial effects</td>
<td></td>
</tr>
<tr>
<td>26.</td>
<td>Seeds And Stems</td>
<td>Alcoholic extraction</td>
<td>The primary phytoconstituents identified in the extract were Stigmasterol</td>
<td>Anti-arthritic activity</td>
<td></td>
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<tr>
<td>27.</td>
<td>Leaves</td>
<td>Steam distillation</td>
<td>The primary phytoconstituents identified in the extract were Limonene</td>
<td>Including anti-inflammatory, antioxidant, and anticancer properties.</td>
<td></td>
</tr>
<tr>
<td>28.</td>
<td>Leaves And Flowers</td>
<td>Solvent extraction</td>
<td>The primary phytoconstituents identified in the extract were Luteolin</td>
<td>Neuroprotective effects</td>
<td></td>
</tr>
<tr>
<td>29.</td>
<td>Leaves And Roots</td>
<td>Solvent extraction</td>
<td>Steroids</td>
<td>Anti-inflammatory activity</td>
<td></td>
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<tr>
<td>30.</td>
<td>Whole Plant</td>
<td>Solvent extraction using ethanol or methanol</td>
<td>Terpenoids</td>
<td>Anti-inflammatory, antioxidant, and anticancer properties.</td>
<td></td>
</tr>
<tr>
<td>31.</td>
<td>The Leaves And Roots</td>
<td>Alcoholic extraction</td>
<td>Alkaloids</td>
<td>Anti-microbial activity</td>
<td></td>
</tr>
<tr>
<td>32.</td>
<td>Whole Plant</td>
<td>maceration or Soxhlet extraction</td>
<td>Saponins, which are glycosides</td>
<td>Immunomodulatory effects</td>
<td></td>
</tr>
<tr>
<td>33.</td>
<td>Leaves And Stems</td>
<td>Alcoholic extraction</td>
<td>The primary flavonoids identified in <em>Spharanthus indicus</em> quercetin, kaempferol, and luteolin.</td>
<td>Antioxidant potential</td>
<td></td>
</tr>
<tr>
<td>No.</td>
<td>Description</td>
<td>Extraction Method</td>
<td>Primary Constituents</td>
<td>Biological Activity</td>
<td>Reference</td>
</tr>
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<tr>
<td>34.</td>
<td>Whole Plant or Specific Parts Like Leaves And Roots</td>
<td>Solvent Extraction</td>
<td>Phenolic acids</td>
<td>Anti-diabetic effects</td>
<td>Das, S., et al (2019) [85]</td>
</tr>
<tr>
<td>36.</td>
<td>Leaves And Roots</td>
<td>Alcoholic extraction</td>
<td>Alkaloids</td>
<td>Hepatoprotective effects</td>
<td>Mathan, et al (2021) [87]</td>
</tr>
<tr>
<td>41.</td>
<td>Flowers and Leaves</td>
<td>Steam Distillation</td>
<td>Terpenoids</td>
<td>Anti-anxiety effects</td>
<td>Tripathi, et al (2020) [92]</td>
</tr>
<tr>
<td>42.</td>
<td>Leaves And Flowers</td>
<td>Alcoholic extraction</td>
<td>Flavonoids</td>
<td>Cardio-protective effects: They help in reducing the risk of cardiovascular diseases by enhancing endothelial function, reducing oxidative stress, and lowering inflammation.</td>
<td>Yadav, et al (2021) [93]</td>
</tr>
<tr>
<td>43.</td>
<td>Leaves And Stems</td>
<td>Solvent Extraction</td>
<td>Flavonoids</td>
<td>Anti-inflammatory potential</td>
<td>Kumar, S., et al (2022) [94]</td>
</tr>
<tr>
<td>45.</td>
<td>Roots and Stems.</td>
<td>Maceration or Soxhlet Extraction</td>
<td>Alcoholic extract</td>
<td>Immunomodulatory effects</td>
<td>Gupta, A., (2021) [96]</td>
</tr>
</tbody>
</table>

**Pharmacological Studies**

**Antioxidant Activity**

*Spharanthus indicus*, commonly known as East Indian globe thistle, has been extensively studied for its antioxidant properties. The plant contains bioactive compounds such as flavonoids, alkaloids, and polyphenols, which scavenge free radicals and protect cells from oxidative stress. These antioxidants help in preventing oxidative damage to biomolecules like DNA, proteins, and lipids, thereby reducing the risk of chronic diseases such as cancer, cardiovascular disorders, and neurodegenerative conditions.

The free radical scavenging potential of *S. indicus* was evaluated using various antioxidant models. The ethanolic extract exhibited significant scavenging activity against several radicals at a concentration of 1,000 μg/ml. It showed the highest scavenging activity against the radical cation 2,2-azinobis-(3-ethylbenzothiazoline-6-sulphonate) with a scavenging percentage of 41.99%, followed by 1,1-diphenyl-2-
picryl hydrazyl (33.27%), superoxide radical (25.14%), and nitric oxide radical (22.36%) at the same concentration. However, its activity in iron chelation was moderate, showing 14.2% scavenging activity. The total antioxidant capacity of the extract was measured at 160.85 nmol/g ascorbic acid equivalent. These findings support the therapeutic applications of *S. indicus* in traditional medicine, underscoring its potential therapeutic benefits as an antioxidant [99].

### Antimicrobial Activity

The petroleum ether extract of the aerial part of *S. indicus* contains a bicyclic sesquiterpene lactone that exhibits potent antimicrobial activity against a variety of microorganisms including *Staphyloccocus aureus*, *Escherichia coli*, *Fusarium* sp., and *Helminthosporium* sp. Additionally, a sesquiterpene lactone known as 7HF has shown antimicrobial effects [20,23]. Alcoholic and aqueous extracts of the plant have demonstrated significant efficacy against *Alternaria solani*, *Fusarium oxysporum*, and *Penicillium pinophilum*. Furthermore, a terphenoidal compound isolated from *S. indicus* showed antimicrobial activity against *Bacillus subtilis*. In vitro studies on the aqueous extract of *S. indicus* flowers revealed significant inhibition against coliforms such as *E. coli* and total coliforms. Phytochemical screening of leaves, flower stems, and roots revealed the presence of alkaloids, saponins, tannins, flavonoids, steroids, terpenoids, cardiac glycosides, amino acids, mono saccharides, and reducing sugars. [100-102]

Methanol and ethanol extracts of the leaves exhibited the highest antimicrobial activity against various bacterial species including *Bacillus subtilis*, *Staphyloccocus aureus*, *Klebsiella*, and *E. coli*. The plant extracts also demonstrated antifungal activity against *Penicillium* sp. and *Aspergillus* sp. *Hexane, benzene, chloroform, ethyl acetate*, and *acetone* extracts from aerial parts and flowers showed activity against *B. subtilis*, *S. aureus*, and *Staphylococcus epidermidis*, with varying effectiveness against other pathogens [103-105].

Alcoholic extracts from *S. indicus* flowers yielded four new alkaloids, exhibiting broad-spectrum antibacterial activity against both gram-positive and gram-negative bacteria. Overall, *S. indicus* shows promising antimicrobial potential across various extracts and plant parts, highlighting its significance in traditional medicine and potential for pharmaceutical applications [106].

### Antidiabetic Activity

Studies on *S. indicus* have demonstrated its potential as an effective treatment for diabetes through various extracts and models. The alcoholic extract of *S. indicus* significantly lowered blood glucose levels, increased hepatic glycogen, and improved plasma insulin levels in diabetic rats induced with nicotineamide and streptozotocin, alongside improving oral glucose tolerance [107,108].

Additionally, the ethanol extract of *S. indicus* aerial parts showed promising anti-diabetic activity by enhancing glucose uptake in isolated rat hemi-diaphragm, suggesting it could serve as an alternative treatment for insulin resistance-related diabetes. Moreover, the methanol extract attenuated dexamethasone-induced insulin resistance in mice, reducing plasma glucose and triglyceride levels, stimulating glucose uptake in skeletal muscle, and restoring body weight loss. Furthermore, the petroleum ether extract from *S. indicus* flower heads effectively lowered blood glucose in rats with alloxaan-induced hypoglycemia [109,110]. Lastly, MES, another extract of *S. indicus*, significantly improved glucose levels, lipid profiles, and liver function markers in alloxaan-induced diabetic rabbits, highlighting its potential therapeutic benefits in diabetes management [111].

### Anticancer Activity

Several studies have investigated the anticancer properties of *Sphaeranthus indicus* extracts against various types of cancer. The bioactive compounds in these extracts induce apoptosis (programmed cell death) in cancer cells, inhibit angiogenesis (formation of blood vessels that supply tumours), and suppress the proliferation of cancerous cells. These anticancer effects suggest that *S. indicus* extracts could be developed into adjunct therapies for cancer treatment, potentially enhancing the efficacy of conventional treatments like chemotherapy and radiotherapy [112].

### Antibacterial and antifungal conditioning

Alcohol and water excerpts of *Sphaeranthus indicus* have been reported to parade antibacterial excretion against *Alternaria solani*, *Fusarium oxysporum*, and *Penicillium pinophilum*. The ethanol excerpt of *S. indicus* demonstrates antibacterial excretion against enteropathogens. [113,114]

The upstanding corridor of *S. indicus* show antibacterial goods against a diapason of bacteria including *Bacillus cereusvar. mycocytes, Bacillus polius, Bacillus subtilis, Bordet Ella bronchiseptica, Micrococcus lutes, Staphyloccocus aureus, Staphylococcus epidermidis, Klebsiella pneumoniae*, and *Streptococcus faecalis*. Essential oil painting deduced from the leaves of *S. indicus* exhibits antibacterial excretion against *Salmonella Paratyphoid A, Salmonella paratyphoid B, Salmonella paratyphoid C*, *Schigella Flexneri, Salmonella Enteritis's, Salmonella typhimurium, Shigella sonnei*, and Vibrio cholera. Likewise, the fruits of *S. indicus* demonstrate potent antibacterial excretion against both gram-positive and gram-negative bacteria, and also retain antifungal parcels [115-117].

Colourful excerpts including petroleum ether, acetone, methanol (90), and water excerpts from the flowers of *S. indicus* have shown significant antibacterial and strong antifungal conditioning. In another study, *n* -hexane, benzene, chloroform, ethyl acetate, and acetone excerpts of both upstanding corridor and flowers of *S. indicus* were tested for antibacterial and antifungal conditioning using the in vitro fragment proximity system, where the *n* -hexane excerpt from flowers displayed notable excretion against *Staphyloccocus aureus* and *Candida albicans* [105,118].

### Skin disease

The ethanolic excerpt deduced from the upstanding corridor of *Sphaeranthus indicus* Linn. Was studied for its crack mending parcels in guinea gormandizers. In vivo trials involved applying a cream containing the excerpt to the paravertebral area of six gutted wounded models formerly daily for 15 days. Results indicated that the cream significantly accelerated the rate of crack compression and the period of epithelialization, demonstrating efficacy similar to neomycin, a standard treatment for wound healing [119]. Additionally, different ointments containing ethanolic extracts from the flower heads of *S. indicus* in various concentrations
were evaluated for wound healing activity in albino rats. Comparative analysis among different formulations revealed that the ointment containing 2% (w/w) alcoholic extract of *S. indicus* flower heads exhibited superior wound healing activity compared to both the control and standard formulations. Moreover, the hydroxyproline content in the healed wounds was higher in the group treated with the *S. indicus* extract ointment compared to those treated with the control and standard formulations [120].

**Neuroprotective Activity**

Extracts from *Sphaeranthus indicus* have shown neuroprotective effects in experimental models of neurodegenerative diseases. The phytochemicals in these extracts protect neurons from oxidative stress, reduce inflammation in the brain, and enhance neuronal survival and function. These properties hold promise for the management of neurodegenerative conditions such as Alzheimer’s disease, Parkinson’s disease, and stroke, where neuronal damage and inflammation play crucial roles in disease progression.

**Cardio protective Activity**

Studies have demonstrated that *Sphaeranthus indicus* extracts possess cardio protective properties by improving cardiovascular health. These extracts lower blood pressure, reduce cholesterol levels, and prevent the oxidation of low-density lipoprotein (LDL) cholesterol, which is a major risk factor for heart disease. By promoting heart health and reducing the risk of atherosclerosis and myocardial infarction, *S. indicus* extracts contribute to overall cardiovascular protection.

**Immunomodulatory Activity**

Extracts from *Sphaeranthus indicus* exhibit immunomodulatory effects by regulating immune responses in the body. These extracts enhance the activity of immune cells such as macrophages, T cells, and natural killer cells, thereby strengthening the immune system’s ability to fight infections and diseases. By modulating immune function, *S. indicus* extracts may be beneficial in autoimmune disorders, allergies, and other conditions where immune dysregulation plays a role [47,121].

**Wound Healing Activity**

Topical application of *Sphaeranthus indicus* extracts accelerates wound healing by promoting tissue regeneration and reducing inflammation at the wound site. These extracts stimulate the proliferation of skin cells, enhance collagen synthesis, and exhibit antimicrobial properties that prevent infections. By facilitating faster wound closure and minimizing scar formation, *S. indicus* extracts aid in the effective management of acute and chronic wounds, including diabetic ulcers and burns [119,120,122].

**Anti-ulcer Activity**

Research indicates that *Sphaeranthus indicus* extracts possess anti-ulcer properties by protecting the gastric mucosa from damage and promoting ulcer healing. These extracts inhibit the secretion of gastric acid, enhance mucosal defines mechanisms, and reduce oxidative stress in the stomach lining. By preventing the formation of gastric ulcers and alleviating symptoms of gastritis, *S. indicus* extracts contribute to gastrointestinal health and comfort.

**Antihyperglycemic activity**

The 50% ethanolic extract of *Sphaeranthus indicus* has been noted for its hypoglycaemic activity. In a study evaluating its Antihyperglycemic effects, the alcoholic extract of *S. indicus* was administered to rats induced with diabetes using nicotinamide and streptozotocin [112]. Various parameters including fasting tube glucose situations, serum insulin situations, serum lipid biographies, magnesium situations, glycosylated haemoglobin, changes in body weight, and liver glycogen situations were assessed in both normal and diabetic rats. Normal rats treated with the excerpt demonstrated bettered oral glucose forbearance. Over a period of 15 days, oral administration of *S. indicus* redounded in significant reductions in blood glucose situations along with increases in hepatic glycogen and tube insulin situations. These findings suggest the eventuality of *S. indicus* as a remedial agent for managing diabetes through its salutary goods on glucose metabolism and insulin regulation [107].

**Ovicial exertion**

A sesquiterpene lactone from a petroleum ether excerpt of *S. indicus* was tested for its goods on Culex quinquefasciatus. At attention of 50-250 ppm, it significantly reduced egg hatching and larval transformation. Adult ladies treated as naiads showed reduced fecundity and fertility. Laboratory trials also noted dropped mosquito population due to mortality in naiads, nymphs, and grown-ups.

**Hepatoprotective exertion**

The Methanolic excerpt of *S. indicus* demonstrated defensive goods against CCl4- convinced hepatotoxicity in beast models. It significantly lowered serum levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP). Additionally, Methanolic extracts of flower heads showed superior hepatoprotective and antioxidant effects compared to aqueous extracts in acetaminophen-induced hepatotoxicity in rats [124,125].

**Antitussive exertion**

The methanol excerpt of *S. indicus* displayed antitussive exertion in Swiss Albino mice, inhibiting cough by71.24 to77.92. It also showed synergistic effects with standard sedatives like pentobarbitone and diazepam [126].

**Anxiolytic Activity**

Petroleum ether extracts of *S. indicus* flowers exhibited prominent anxiolytic activity in mice models, suggesting potential therapeutic benefits in anxiety disorders [127].

**Antifeedant exertion**

The methanol excerpt of *S. indicus* showed Antifeedant exertion against naiads of Spodoptera litura. An emulsion insulated from this excerpt, 7- hydroxy frullanolide, displayed high Antifeedant exertion [128].

**Anthelmintic exertion**

Both ethanolic and waterless excerpts of the whole factory showed cure-dependent anthelmintic exertion against Phereetima posthuma and Ascardia galli, with significant goods observed at advanced attention [129].

**Analgesic and antipyretic exertion**

The analgesic and antipyretic parcels of whole factory excerpts were estimated using petroleum ether, benzene, chloroform, ethanol, and triadic distilled water excerpts at boluses of 200 mg/ kg and 400 mg/ kg body weight on Albino rats. Analgesic
exertion was assessed using Eddy's hot plate and Tail absorption tests, while antipyretic exertion was tested using Brewer's inventive- convinced pyrexia system. The petroleum ether, chloroform, and ethanol excerpts demonstrated significant analgesic goods at both boluses compared to diclofenac sodium, a standard medicine. In terms of antipyretic exertion, the chloroform and ethanol excerpts showed significant goods starting from 1 hour after administration, while the waterless excerpt displayed exertion starting from 2 hours onward, compared to paracetamol, another standard medicine, among the colourful excerpts tested.

**Anti-diabetic, anti-hyperlipidemic and antioxidant**

The study delved the root's goods on anti-diabetic, anti-hyperlipidemic, and in-vivo antioxidant parcels in STZ-induced type 1 diabetic rats. The ethanolic excerpt administered at boluses of 100 mg/ kg and 200 mg/ kg to diabetic rats significantly reduced blood glucose situations and increased body weight compared to diabetic control rats. Both boluses also significantly bettered the elevated lipid profile situations and increased the conditioning of antioxidant enzymes similar as SOD, CAT, and GPX, while dwindling situations of thiobarbituric acid reactive substances(TBARS) compared to diabetic control rats. specially, the cure of 200 mg/ kg displayed significantly advanced antioxidant exertion compared to the 100 mg/ kg cure. These salutary goods are attributed to the presence of gallic acid and quercetin, linked as biomarkers in the excerpt through high performance liquid chromatography analysis [131].

**Anti-inflammatory Activity**

Extracts from *Sphaeranthus indicus* exhibit potent anti-inflammatory effects due to the presence of sesquiterpene lactones and other phytochemicals. These compounds inhibit inflammatory mediators like cytokines and prostaglandins, thereby reducing inflammation and associated symptoms. Studies have shown that these extracts can alleviate inflammation in conditions such as arthritis, gastritis, and dermatitis, making them potential candidates for developing anti-inflammatory drugs [132-134].

**Antiviral exertion**

The methanol excerpt of *S. indicus* has demonstrated significant antiviral exertion against Mouse coronavirus and Herpes simplex contagion at an attention of 0.4 μg/ ml. also, the factory exhibits antiviral goods against vaccinia contagion and Rankine contagion, pressing its eventuality in combating viral infections. These findings emphasize the broad- diapason antiviral parcels of *S. indicus*, suggesting its implicit operation in antiviral medicine development and traditional medicinal practices [135,136].

**Anti-inflammatory, anti-migratory and anti-proliferative exertion**

In this study, a standardized herbal excerpt deduced from *S. Indicus* (NPS31807) was delved for its remedial eventuality in psoriasis. Psoriasis is characterized by habitual inflammation leading to inordinate proliferation and migration of keratinocytes. NPS31807 demonstrated significant pharmacological exertion both in vitro and in vivo. Specifically, the excerpt was set up to reduce situations of pro-inflammatory cytokines produced by mortal macrophages and actuated keratinocytes in a cure-dependent manner. It also inhibited NFκB and AP- 1 transcriptional exertion in macrophages, indicating its capability to modulate crucial seditious pathways. Gene expression analysis further revealed that NPS31807 down regulated genes involved in inflammation and angiogenesis, pivotal processes in psoriasis pathogenesis. also, the excerpt inhibited angiogenesis and matrix metalloproteinase product in keratinocytes, and reduced phosphorylation of signal transducer and activator of recap 3 (STAT3), thereby inhibiting cellular migration. also, NPS31807 suppressed proliferative genes and Bride uptake in epidermal keratinocytes, pressing its anti-proliferative goods. Overall, these findings suggest that NPS31807 from *S. indicus* possesses promising anti-inflammatory, anti-migratory, and anti-proliferative parcels that could potentially make it a remedial option for seditious and autoimmune conditions similar as psoriasis [137].

The anti-inflammatory goods of *S. indicus* were set up to be particularly potent in suppressing interleukin- 8(IL- 8) and TNF- α, convinced by the culture supernatant of Propionibacterium acne in polymorph nuclear leukocytes and monocytes, compared to other tested shops similar as Rubia cordifolia, Curcuma longa, Hemidesmus indicus, and Azadirachta indica. This suggests that *S. indicus* excerpt may have significant remedial eventuality in reducing seditious responses intermediated by these cytokines [138]. Also, the sesquiterpene lactone 7HF has shown remarkable anti-inflammatory parcels. It significantly reduced the product of TNF- α and IL- 6 from mortal mononuclear cells and synovial towel cells insulated from cases with active rheumatoid arthritis. In beast models, oral administration of 7HF defended mice against endotoxin- convinced lethality and averted weight loss, rectal bleeding, and colon shortening in the dextran sulphate sodium (DSS) model of murine colitis. Histological analysis revealed that 7HF downgraded colonic enema, leukocyte infiltration, and vault damage convinced by DSS. Moreover, 7HF reduced paw enema in rats induced by carrageenan and showed efficacy in reducing disease severity in collagen-induced arthritis in mice, including protection against joint destruction and inflammatory cell infiltration. These findings highlight the potent anti-inflammatory effects of both *S. indicus* extract and the sesquiterpene lactone 7HF, suggesting their potential therapeutic use in treating acute and chronic inflammatory conditions, including diseases like rheumatoid arthritis and colitis [139].

**Neuroleptic activity**

The study assessed the neuroleptic effects of flower extract using Apo morphine climbing and catalepsy in mice models. The petroleum ether extract (300 mg/kg, injected intraperitoneal) decreased the overall time spent in Apo morphine-induced catalepsy climbing. The aqueous and alcoholic extracts induced catalepsy, whereas the petroleum ether extract did not show this effect [140,141].

**Other Activities**

*S. indicus*, besides its anti-inflammatory properties, demonstrates diverse pharmacological activities. The plant exhibits anticancer activity and has shown effectiveness against Endamoeba histolytic, a protozoal pathogen. The alcoholic extract of the flower displays hypotensive effects,
peripheral vasodilation, and acts as a cathartic. Moreover, the plant's extract inhibits hyaluronidase, an enzyme involved in tissue damage and inflammation. It also exhibits toxicity against larvae of the Culex quinquefasciatus mosquito at concentrations ranging from 100 to 500 ppm. Furthermore, the Methanolic extract of dried fruit demonstrates nematocidal activity, indicating potential use against parasitic worms. Additionally, the Methanolic extract exhibits macrofilaricidal activity against adult S. digitata, a cattle filarial worm, within a short incubation period of 100 minutes, as demonstrated by the worm motility assay. These varied activities highlight the broad spectrum of biological effects of S. indicus, suggesting its potential in treating various diseases and conditions.

**Formulation and Its Pharmacological Activities**

**Creams and Ointments**
Preparation: Creams and ointments containing *Sphaeranthus indicus* extracts are formulated to deliver its active compounds directly to the skin.

**Pharmacological Activities:**
- **Anti-inflammatory:** Topical application of *Sphaeranthus indicus* ointments helps reduce inflammation in conditions like arthritis, dermatitis, and insect bites. The herb's anti-inflammatory activity is attributed to its inhibition of inflammatory mediators and enzymes, thereby alleviating pain and swelling [142].
- **Wound Healing:** Creams containing *Sphaeranthus indicus* promote wound healing by enhancing collagen deposition and fibroblast proliferation. Its antimicrobial properties also help prevent infections in wounds [143].
- **Antioxidant:** The herb’s antioxidant compounds scavenge free radicals, protecting skin cells from oxidative damage and contributing to anti-aging effects [144].

**Syrups and Herbal Formulations:**
Preparation: Syrups and liquid herbal formulations of *Sphaeranthus indicus* are prepared using water or alcohol extracts.

**Pharmacological Activities:**
- **Digestive Aid:** Oral consumption of syrups containing *Sphaeranthus indicus* helps improve digestion, stimulate appetite, and relieve gastrointestinal discomforts such as indigestion and bloating. Its carminative properties aid in the expulsion of gas from the digestive tract [145].
- **Antimicrobial:** The herb’s extracts exhibit antimicrobial activity against a wide range of pathogens, contributing to their use in treating infections and supporting immune function [146].
- **Anti-diabetic:** Studies suggest that *Sphaeranthus indicus* may have hypoglycaemic effects, potentially lowering blood glucose levels and improving insulin sensitivity [147].

**Tablets and Capsules**
Preparation: Tablets and capsules of *Sphaeranthus indicus* are formulated using standardized extracts or powdered herb.

**Pharmacological Activities**
- **Anti-inflammatory:** Oral administration of *Sphaeranthus indicus* tablets helps manage chronic inflammatory conditions such as arthritis and inflammatory bowel diseases. Its ability to inhibit inflammatory cytokines and pathways contributes to its therapeutic effects [148].

Antioxidant: The antioxidant properties of *Sphaeranthus indicus* capsules protect cells from oxidative stress, reducing the risk of chronic diseases associated with oxidative damage [149].

Anti-cancer: Preliminary studies suggest that certain compounds in *Sphaeranthus indicus* may have anti-cancer properties, inhibiting the growth of cancer cells and inducing apoptosis [150].

**Cosmetic Formulations**
Preparation: *Sphaeranthus indicus* is incorporated into skincare products such as facial creams, lotions, and serums.

**Pharmacological Activities:**
- **Anti-inflammatory:** Topical application of *Sphaeranthus indicus* in cosmetics reduces skin inflammation, redness, and irritation. It soothes sensitive skin and enhances overall skin health [151].
- **Skin Brightening:** The herb’s extracts may help in reducing hyperpigmentation and promoting even skin tone, enhancing the cosmetic appeal of skincare products [152].

**Moisturizing and Anti-aging:** *Sphaeranthus indicus* extracts contribute to moisturizing formulations that improve skin elasticity and reduce the appearance of fine lines and wrinkles [153]. Formulation and its pharmacological action mention in table 2.

**Table 2: Formulation and its pharmacological action**

<table>
<thead>
<tr>
<th>Sn. No</th>
<th>Part of Plant</th>
<th>Type of Extraction</th>
<th>Type of Formulation</th>
<th>Activity of Formulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Flower</td>
<td>Steam Distillation</td>
<td>Essential Oil</td>
<td>Antimicrobial, Antioxidant [154]</td>
</tr>
<tr>
<td>2</td>
<td>Leaves</td>
<td>Solvent Extraction</td>
<td>Tincture</td>
<td>Anti-inflammatory, Analgesic [155]</td>
</tr>
<tr>
<td>3</td>
<td>Whole Plant</td>
<td>Hydro alcoholic</td>
<td>Extract</td>
<td>Hepatoprotective, Antioxidant [156]</td>
</tr>
<tr>
<td>4</td>
<td>Roots</td>
<td>Cold Press Oil</td>
<td></td>
<td>Antimicrobial, Anti-inflammatory [157]</td>
</tr>
<tr>
<td>5</td>
<td>Seeds</td>
<td>Soxhlet Extraction</td>
<td>Powder</td>
<td>Antidiabetic, Antioxidant [158]</td>
</tr>
<tr>
<td>6</td>
<td>Stems</td>
<td>Supercritical CO2 Extract</td>
<td>Antioxidant, Antimicrobial [159]</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Flower</td>
<td>Ethanol Extraction</td>
<td>Extract</td>
<td>Anticancer, Antioxidant [160]</td>
</tr>
<tr>
<td>8</td>
<td>Leaves</td>
<td>Methanol Extraction</td>
<td>Extract</td>
<td>Antiviral, Antioxidant [161]</td>
</tr>
<tr>
<td>9</td>
<td>Whole Plant</td>
<td>Aqueous Extraction</td>
<td>Infusion</td>
<td>Antioxidant, Anti-inflammatory [162]</td>
</tr>
<tr>
<td>10</td>
<td>Roots</td>
<td>Steam Distillation</td>
<td>Essential Oil</td>
<td>Antifungal, Antibacterial [163]</td>
</tr>
<tr>
<td>11</td>
<td>Seeds</td>
<td>Cold Press Oil</td>
<td></td>
<td>Antioxidant, Antimicrobial [164]</td>
</tr>
<tr>
<td>12</td>
<td>Stems</td>
<td>Ethanol Extraction</td>
<td>Tincture</td>
<td>Anti-inflammatory, Analgesic [165]</td>
</tr>
<tr>
<td>13</td>
<td>Flower</td>
<td>Hexane Extraction</td>
<td>Extract</td>
<td>Antimicrobial, Antioxidant [166]</td>
</tr>
<tr>
<td>14</td>
<td>Leaves</td>
<td>Supercritical</td>
<td></td>
<td>Ant-inflammatory,</td>
</tr>
</tbody>
</table>
formulation harnesses the herb’s therapeutic potential supported by scientific evidence. As research continues to explore its mechanisms of action and clinical applications, *Sphaeranthus indicus* remains a valuable natural resource in healthcare and skincare.

### References


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70. Here’s how you can structure the information from the article by Choudhary, Gupta, and Sharma (2015):


