www.ThePharmaJournal.com

The Pharma Innovation

ISSN: 2277- 7695
TPI 2017; 6(2): 77-84

www.thepharmajournal.com
Received: 11-12-2016
Accepted: 12-01-2017

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Sphaeranthus indicus Linn: A pharmacological update

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Abstract
Sphaeranthus indicus Linn is a well-known plant used in Indian system of medicine and is from the aroma family Asteraceae. It is abundantly distributed in damp areas, plains and also as a weed in the rice fields. In the Indian system of medicine, the plant as a whole plant or its different parts like leaf, stem, bark, root, flower and seed are widely used for curing many diseases. The plant has been reported with different types of secondary metabolites such as eudesmanolides, sesquiterpenoids, sesquiterpene lactones, sesquiterpene acids, flavone glycosides, flavonoid C-glycosides, isoflavone glycoside, sterols, sterol glycoside, alkaloid, peptide alkaloids, amino acids and sugars. Essential oil has been isolated from flowers and whole plant. The whole plant, its isolated secondary metabolites and different parts have been reported for ovicidal, antifeedant, anthelmintic, antimicrobial, antiviral, macrofilaricidal, larvicidal, analgesic, antipyretic, hepatoprotective, antitussive, wound healing, bronchodilatory, mast cell stabilizing activity, anxiolytic, neuroleptic, immunomodulatory, anti-diabetic, antihyperlipidemic and antioxidant, antioxidant, central nervous system depressant, anti-arthritic, nephroprotective, anticonvulsant activities and many other activities. It is also effective for psoriasis. The present paper is a compilation of data on experimentally confirmed biological activities.

Keywords: *Sphaeranthus indicus*, Asteraceae, pharmacological activities, traditional uses

1. Introduction
Plants have played a significant role in maintaining human health and improving the quality of human life for thousands of years and are valuable components of medicines, seasonings, beverages, cosmetics and dyes. Herbal medicine is based on the fact that plants contain natural substances that can promote health and abate illness. In recent times, plant research has increased all over the world and a mass evidence has been collected to show immense potential of medicinal plants used in various traditional systems. Today, we are witnessing a great deal of public interest in the use of herbal remedies. Furthermore, the toxicity and adverse reactions of allopathic medicines, has led to increased riving of public interest towards the herbal lore of native healers. Hence, the need for documentation of traditional knowledge on medicinal plants and further scientific investigations are significant to develop more trust and faith towards this potential wisdom and also to the herbal remedies [1]. Numerous drugs have been entered into the international market through exploration of ethnopharmacology and traditional medicine. Ethnopharmacological studies of herbs or medicinally important plant have attracted the investigators throughout the world. One such plant, *Sphaeranthus indicus*, invites attention of the researchers worldwide for its biological activities. *Sphaeranthus indicus* Linn belongs to family Asteraceae; is a medicinally important plant used as folk medicine.

2. Botanical Description
2.1 Taxonomy
Kingdom: Plantae
Division: Phanerogamae
Sub division: Angiospermae
Class: Dicotyledonae
Sub class: Gamopetalae
Order: Asterales
Family: Asteraceae
Genus: Sphaeranthus
Species: indicus

2.2 Synonyms
English: East Indian Globe Thistle
Sanskrit: mahamundi, mundi, hapusa
Hindi, Bengali, Marathi, Gujarathi: mundi, gorakh mundi
Telugu: Boddatarupu, boddasoramu
Tamil: kottakaranthai
Malayalam: mirangani, adakkamaniyan
Oriya: Murisa, buikadam, bokashungi
Punjabi: ghundi, khamadrus; Santal

2.3 Morphological characters
It is a multi-branched aromatic herb 1-2 feet in height, annual with winged stem and the wings toothed. Leaves obovate oblong, narrowed at the base, dentate and serrate. Flowers compound heads, globose avoid, purple in colour. Flowering time November to January in Indian conditions; glandular hairy. The plant is distributed widely in plains all over India and up to an altitude of 50 feet in hills. It is an important medicinal plant used for the treatment of styptic gastric disorders, skin diseases, anthelmintic, glandular swelling, nervous depression, analgesic, antibiotics, antifungal, laxative and diuretic properties [2]. The decoction of the plant is said to be active against bronchitis, asthma, leucoderma, jaundice and scabies. The powdered bark along with whey is useful in the treatment of piles. Flowers have alterative, depurative and stimulant characters. Roots and seeds are anthelmintic. Juice of fresh leaves is taken for cough. The plant is also useful in preservation of food grains as it possesses insecticidal property [3, 4].

2.4 Traditional Uses of Plant
2.4.1 Against piles: The bark grounded and mixed with whey, to be useful in application for piles.
Bark Powder is given orally and applied externally to cure piles.
Leaf, flower and seeds are grounded into paste and applied topically to treat skin diseases and piles [5].

2.4.2 Piscicidal: Whole plant is used as Fish-poison.

2.4.3 Crabicidal: Whole plant is stuffed into nesting furrows to kill crabs [5, 6].

2.4.4 Anthelmintic: Whole plant paste mixed with oil is an anthelmintic.
Roots and seeds: Used as stomachic and anthelmintic. Root and seed Powder is given orally to kill intestinal worm's in children.
Leaf decoction is taken in the morning 8 time once in 2 day.
Whole plant paste with a pinch of common salt is taken as an anthelmintic [6].

2.4.5 Cough: Root Decoction of root is useful for Chest-pain, cough, and bowel complaints.
Leaf juice is boiled with milk and sugar-candy is prescribed for cough [7].

2.4.6 Tonic: Flowers are used as refrigerant and tonic.

2.4.7 Gastric disorder: Whole plant juice is styptic and useful in liver and gastric disorders.
Inflorescence paste is given in empty stomach for curing excess bile.

2.4.8 Dysuria: Root paste and black peppers (5 to 7) are taken 2 times a day against dysuria.

2.4.9 Jaundice: Leaves Decoction is used by the tribes, for the treatment of jaundice [6].

2.4.10 Mouth ulcer: Raw leaf is chewed or leaf juice is administered orally during mouth ulcer, and other mouth diseases.

2.4.11 Stomachache: Amulet of root is worn in Stomachache.

2.4.12 Leucorrhoea: One teaspoonful of root powder is taken with a cup of water 2 times daily in the treatment of leucorrhoea for 30 days [7].

2.4.13 Elephantiasis: Leaf juice (5ml) with long pepper and common salt (3:1:1) is given for 10 days.

2.4.14 Swelling: Whole plant paste mixed with coconut oil is used for painful swelling.

2.4.15 Scabies: Leaf juice mixed in water is used for bath.

2.4.16 Skin diseases: Whole plant powder is taken internally to treat skin diseases.
Leaf, Flower and seeds are ground into paste and applied topically to treat skin disease. Whole plant Paste is topically applied for skin irritation. Root Paste is made by grinding root with juice of tender pericarp of coconut or lemon juice [7- 9].

2.4.17 Diarrhoea and dysentery: Flower, Leaf paste is given in empty stomach to cure dysentery, diarrhoea and indigestion. Leaf juice is also given to cure diarrhoea and vomiting. Fresh leaves with cumin seeds are taken internally to treat dysentery. Whole plant Children suffering from dysentery are exposed to fumes of whole plant [9].

2.4.18 Eye infection: Inflorescence is kept in water for whole night. Then the juice is used as an eye drop for eye infection or eye cleaning.

2.4.19 Toothache: Stem and leaf is chewed to get relief from toothache.

2.4.20 Blood purifier: Inflorescence Juice is given orally for purification of blood and itching [10].

2.4.21 Earache: Leaf Extract mixed with black pepper powder is dropped into ears.

2.4.21 Viral hepatitis: Leaf 50g. powdered drug given once a day with water to cure viral hepatitis**.**

2.4.22 Aphrodisiac: Shade dried plant at flowering stage powder with Deshi ghee and honey taken orally for 38 days to develop sexual power. Root powder mixed in hot *Sesamum indicum* (Til) oil is massaged on male sex organ for perfect erection [9-11].

2.4.23 For retaining pregnancy: Handful of leaves made in to juice, taken 200 ml internally for three days to retain pregnancy.

2.4.24 Rheumatic pain: Leaf is cooked together with rice and eaten to check rheumatic pains.

2.4.26 Scabies: Whole plant (Decoction) studies showed significant reduction in the signs and symptom of scabies after 15 days of treatment [11-14].

2.5 Pharmacological Studies

2.5.1 Ovicidal activity

Sesquiterpene lactone, isolated from a petroleum ether extract of *S. indicus*, was screened for its effects on the hatching of eggs and the metamorphosis of larvae of *Culex quinquefasciatus* at concentration of 50‑250 ppm. Rates of fecundity and fertility were found to be affected in the larval‑treated adult females. Egg hatching was also significantly lowered. Mortality in the larvae, pupae and adults produced a marked decrease in mosquito populations in laboratory experiments [15].

2.5.2 Hepatoprotective activity

The protective effect of methanolic extract of *S. indicus* Linn. (MES) against CCl_4 induced hepatotoxicity was studied in animal models. It showed a significant protective effect by lowering the serum aspartate aminotransferase, alanine aminotransferase and alkaline phosphatase (ALP).

The aqueous (AQS) and methanolic (MES) extracts of flower head of *S. indicus* L. were evaluated for the hepatoprotective and antioxidant effect on acetaminophen (APAP)‑induced hepatotoxicity in rats. Oral dose of MES (300 mg/kg) showed a significant hepatoprotective effect (serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), acid phosphatase (ACP) and ALP than aqueous extract. MES exhibited significant antioxidant activity showing increasing levels of superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX) by reducing malondialdehyde levels.

Ethanolic extract in the doses 200 and 300 mg/kg bw, of aerial parts of *S. indicus* L. was investigated for hepatoprotective activity against paracetamol induced liver damage of rat. 300 mg/kg of extract showed significant protection against paracetamol-induced hepatocellular injury.

Aqueous extract (200 and 300 mg/kg b/w) of root of *S. indicus* L. was evaluated for hepatoprotective activity against APAP induced hepatotoxicity in rats. The activity of 300 mg/kg of the extract was comparable to standard drug, silymarin (50 mg/kg body weight) [16, 17].

2.5.3 Antitussive activity

The successive methanol extract of *S. indicus* (MESI) exhibited antitussive activity and synergistic effects of sleeping time induced by standard sedatives using Swiss Albino mice. The MESI of (200, 300 and 400 mg/kg) showed maximum inhibition of cough by 71.24%, 76.84% and 77.92% and also exhibited significant synergistic effect ($P < 0.001$) at the dose levels of 200, 250 and 300 mg/kg when compared with control and standard sedative pentobarbitone and diazepam. The MESI produced significant synergistic effects three times greater than that of standard sedatives [18].

2.5.4 Wound healing activity

A cream containing ethanolic extract of aerial parts of *S. indicus*, L. (Asteraceae) was evaluated for wound healing activity in guinea pigs. The cream was applied *in‑vivo* on the paravertebral area of six excised wounded models once a day for 15 days. The cream significantly enhanced the rate of wound contraction and the period of epithelialization comparable to neomycin [19].

The wound healing activity of ointments comprising various percentage of alcoholic extract of *S. indicus* flower head was tested for protection against microbial invasion by providing better tissue formation. The formulation comprising of 2% (w/w) alcoholic extract was found to be superior to control and standard formulation.

A randomized placebo controlled single blind study was conducted on 45 patients (n = 30 test and n = 15 control groups) to test the efficacy and safety of *S. indicus* L., cream of *Lawsonia inermis* L. and *Plumbi oxidum*. The test drug formulations were found to be effective in healing and relieving the symptoms of cervical erosion with cervicitis [20].

2.5.5 Anxiolytic activity

The petroleum ether (10 mg/kg), alcohol (10 mg/kg) and water extracts (30 mg/kg) of flowers were tested to assess the anxiolytic activity in mice. Petroleum ether extract of *S. indicus* flowers produced prominent anxiolytic activity [21].

2.5.6 Neuroleptic activity

Neuroleptic activity of extract of flowers was evaluated in apomorphine induced cage climbing and catalepsy in mice models. The petroleum ether extract (300 mg/kg, i.p.) reduced total time spent in apomorphine induced cage climbing. Aqueous and alcoholic extracts showed catalepsy while petroleum ether extract was devoid of it [22].

2.5.7 Neuroprotective effect

Flower heads [Petroleum ether (SIP), methanolic (SIM) and aqueous extract (SIA)]. SIM and SIA were found to be an effective neuroprotective agent which could reverse D-galactose-induced oxidative damage and acceleration of aging [22].

2.5.8 Central nervous depressant and anticonvulsant activities

Hydroalcoholic extract of whole plant decreased locomotor activity but did not affect emotional activity parameters in the open field test, suggesting a possible central nervous depressant activity. Hydroalcoholic extract also increased the immobility time in the forced swimming test at an oral dose of 500 mg/kg but did not significantly modify the activity in the tail suspension test. Hydroalcoholic extract protected rats against MES-induced convulsions and mice against PTZ-induced convulsions [23].

Whole parts of the plant (Petroleum ether, Benzene, Chloroform, Ethanol extract, water (200- 400 mg/kg) significantly reduced the duration of seizures induced by maximal electroshock (MES). However, only 200 and 400mg/kg of the extract conferred protection (25 and 50%, respectively) on the mice. The same doses also protected animals from pentylenetetrazole-induced tonic seizures and significantly delayed the onset of tonic seizures produced by picrotoxin and N- methyl-dl-aspartic acid. The extract had no effect on bicuculline induced seizures. The aqueous extract (400mg/kg) significantly reduced the latency, but did not alter the incidence of seizures elicited by maximal electroshock to any significant extent [24].

2.5.9 Immunomodulatory activity

Immunostimulant activity of sphaeranthanolide was tested by Jerne plaque assay method. This compound was found to be an immune modulator.

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, therefore, revealed that the drug holds promise as immunomodulatory agent, which acts by stimulating both humoral as well as cellular immunity and phagocytic function.

The bioactive fraction exhibited dose dependent increase in immoral and cell-mediated immunity and offers protection against immunosuppression induced by the cytotoxic agent cyclophosphamide.

The petroleum ether extract from the flower heads of *S. indicus* Linn. was found to be effective in increasing phagocytic activity, hemagglutination antibody titer and delayed type hypersensitivity. The extract acts by stimulating both humoral and cellular immunity as well as phagocytic function [25].

2.5.10 Antifeedant activity

MESI showed antifeedant activity against 4th instar larvae of *Spodoptera litura*. Among the compounds isolated from this fraction, 7-hydroxy frullanolide had high antifeedant activity at 1,000-ppm. Deformities in larvae, pupae and adult were also observed [26].

2.5.11 Anthelmintic activity

The anthelmintic activities of ethanolic and aqueous extracts (10, 50, 100 mg/ml concentration levels) of the whole plant were tested against *Pheretima posthuma* and *Ascaridia galli*. Both extracts exhibited anthelmintic activity in a dose-dependent manner. The most significant activity was observed at the highest concentration of 100 mg/ml against both types of worms [26].

2.5.12 Analgesic Activity

The ethanol extracts of the whole plant *S. indicus* Linn. exhibited dose dependent analgesic activity with 66.6 and 67.4% of protection when tested with 250 mg and 500 mg/ kg b.w. by tail immersion method in rat models using pentazocine 10 mg/kg as standard [27].

2.5.13 Analgesic and antipyretic activity

The analgesic and antipyretic activity of the successive taking petroleum ether, benzene, chloroform, ethanol and triple distilled water extracts (200 mg/kg and 400 mg/kg b.w) of whole plant was screened for analgesic and antipyretic activities on Albino rats by Eddy's hot plate, Tail immersion and Brewer's yeast induced pyrexia method. The petroleum ether, chloroform and ethanol extracts showed significant analgesic activity in both doses as compared to the standard drug diclofenac sodium. The chloroform and ethanol extracts showed potential significant antipyretic activity from 1 h onward whereas aqueous extracts exhibited activity from 2 h onward as compared to the standard drug paracetamol amongst various extracts [28].

2.5.14 Anti-diabetic activity

The anti-hyperglycemic effect of *S. indicus* extract was carried out in diabetic rats induced by nicotinamide (120 mg/kg i.p.) and streptozotocin (STZ) (60 mg/kg i.p). Oral administration of alcoholic extract of *S. indicus* for 15 days exhibited in significant reduction in blood glucose levels and increases in hepatic glycogen and plasma insulin levels and significant improvement in oral glucose tolerance test. Glibenclamide was used as a reference standard.

The ethanol extract of aerial part was evaluated for anti-diabetic activity using the glucose uptake by isolated rat hemi-diaphragm *in-vitro* model. *S. indicus* increased the uptake of glucose by isolated rat hemi-diaphragm significantly ($P < 0.01$) and was found to be more effective than insulin and it will be alternative choice for the treatment of diabetes mellitus caused in the consequences of resistance to stimulatory effect of insulin on glucose transporter type 4 protein.

The effect of the methanol extract in dexamethasone-induced insulin resistance in mice was studied. The mice were treated with dexamethasone for 22 days. The *S. indicus* extract showed significant decrease in plasma glucose and serum triglyceride levels at doses, of 400 and 800 mg/kg, p.o. and stimulated insulin assisted and non-insulin assisted glucose uptake in skeletal muscle. The extract significantly restored dexamethasone induced body weight loss thereby suggesting its effect in the treatment of type II diabetes mellitus.

Dried petroleum ether (60-80 ‹C) extract of flower head of *S. indicus* was screened for activity against alloxan induced hypoglycemia in Wistar rats. The oral administration of flower head extract at doses of 200 mg/kg lead to a significant blood glucose reduction [29].

The anti-diabetic effect of MES in alloxan induced diabetic rabbits in comparison with 80 mg/kg of diamicron standard was studied. The extract at the dose of 300 mg/ kg body weight significantly reduced the blood glucose level, plasma total cholesterol, triglycerides and low density lipoprotein (LDL) in treated rabbits as compared to diabetic rabbits; also, significantly increased the level of high density lipoprotein (HDL) (36.95 ± 2.95); SGOT and SGPT also significantly decreased [29].

2.5.15 Anti-diabetic, antihyperlipidemic and antioxidant

The anti-diabetic, antihyperlipidemic and *in-vivo* antioxidant properties of the root in STZ-induced type 1 diabetic rats was studied. The ethanolic extract 100 and 200 mg/kg to the diabetic rats showed significant reduction in blood glucose and increase in body weight compared with diabetic control rats. Both doses showed significant alteration in elevated lipid profile levels, significant increase in SOD, CAT, GPX and decrease in thiobarbituric acid reactive substances levels than diabetic control rats. 200 mg/kg produced significant higher antioxidant activity than 100 mg/kg. These activities are possibly due to the presence of biomarkers gallic acid and quercetin revealed by high performance liquid chromatography analysis of the extract [30].

2.5.16 Antimicrobial activity

The bicyclic sesquiterpene lactone isolated from the petroleum ether extract of the aerial part has been found to be potent against *Staphylococcus aureus, Escherichia coli, Fusarium* sp., *Helminthosporium* sp., and other microorganisms.7HF, a sesquiterpene lactone showed antimicrobial activity. Alcoholic and aquous extracts of the plant were highly effective against *Alternaria solani, Fusarium oxysporum* and *Penicillium pinophilum* by preventing their growth to a greater extent. Antimicrobial

activity of terphenoidal compound isolated from *S. indicus* showed activity against *Bacillus subtilis*. The *in-vitro* antimicrobial activity of aqueous extract of flower was evaluated against coliforms *E. coli* (10,536) and total coliforms by using disc diffusion method. The extracts showed significant inhibition against coliform strains.

Leaves, flower stem and roots were extracted separately with methanol, ethanol, chloroform, petroleum ether and hot water and the extracts were screened for its phytochemical constituents. The plant revealed the presence of alkaloids, saponins, tannins, flavonoids, steroids, terpenoids, cardiac glycosides, amino acids, mono saccharides and reducing sugar. Leaves extracts showed significant number of phytochemicals and hence antimicrobial studies of leaves extracts were carried out against bacterial species such as *Bacillus* Sp. *Staphylococcus* sp., *Klebsiella* sp., *E. coli*, *Pseudomonas* sp., using filter paper and agar well diffusion method at 4 different concentrations. MES and AQS 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.

Hexane, benzene, chloroform, ethyl acetate and acetone extracts of the aerial parts and flowers showed activity against *B. subtilis, S. aureus* and *Staphylococcus epidermidis.* Benzene and chloroform extracts of flower and benzene and acetone extracts of aerial parts were not active against *Enterococcus faecalis;* all extracts of flower and aerial part were not active against *E. coli* and *Klebsiella pneumonia* when tested by disc diffusion method.

Four new alkaloids have been isolated from the alcoholic extract of flowers. The crude extract showed antibacterial activity against 18 different gram-positive and gram-negative bacteria. Both alkaloidal and non-alkaloidal fractions showed the activity. The isolated two alkaloids showed broad spectrum activity.

Ten Indian medicinal plants were screened for antibacterial activity specific to enteropathogens. Diffusion and dilution methods were used to measure the antibacterial activity. *Allium sativum*, *Camellia sinensis* and *Chamaesyce hirta* showed higher activity when compared to the rest. They had a minimum bactericidal concentration of <100 µg/ml and gave inhibition zones of more than 2 cm. Among the pathogens studied, *Vibrio cholerae* and *Shigella flexneri* were found to be highly susceptible to the plant extracts. [68] The essential oil from the leaves exhibited antibacterial activity against *Salmonella paratyphi* A, B and C, *S. flexner, Salmonella enteritidis, Salmonella typhimurium, Shigella sonnei* and *Vibrio cholera.* The fruits showed very good antibacterial activity against gram-positive and gram-negative bacteria. 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. The chloroform, methanol and aqueous extracts showed high antibacterial activity against *S. aureus*; chloroform, methanol and ethanol extract against *P. aeruginosa*, methanol, chloroform and hexane against *B. substilus*, aqueous, methanol, ethyl acetate and chloroform against *E. coli* [18, 20].

2.5.17 Antiviral activity

The methanol extract was found to exhibit inhibitory activity against *Mouse corona* virus and *Herpes simplex* virus at a concentration of 0.4 µg/ml [74]. The plant also showed antiviral activity against vaccinia and ranikhet viruses [20].

2.5.18 Macrofilaricidal activity

The methanolic extract showed macrofilaricidal activity (4 mg/ml) against adult *Setaria digitata*, the cattle filarial worm when tested by worm motility assay method [18, 20].

2.5.19 Larvicidal action

Acetone extract of root and leaf caused >50% mortality in an 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 [20].

2.5.20 Antioxidant activity

The free radical scavenging potential of the plant was studied by using different antioxidant models of screening. The ethanolic extract at 1,000 µg/ml showed maximum scavenging of the radical cation, 2,2-azinobis-(3-ethylbenzothiazoline-6-sulphonate) observed up to 41.99% followed by the scavenging of the stable radical 1,1-diphenyl, 2-picryl hydrazyl (33.27%), SOD (25.14%) and nitric oxide radical (22.36%) at the same concentration.

However, the extract showed only moderate scavenging activity of iron chelation (14.2%). Total antioxidant capacity of the extract was found to be 160.85 nmol/g ascorbic acid. The results justify the therapeutic applications of the plant in the indigenous system of medicine, augmenting its therapeutic value [21].

2.5.21 Attenuation effect on prostatic hypertrophy

The attenuating effect of petroleum ether, ethanolic, aqueous extracts and β-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 [31].

2.5.22 Effect on psoriasis

The effect of *S. indicus* on psoriasis was studied and found to exhibit the potent activity [32].

2.5.23 Bronchodilatory effect

The methanolic extract and its fractions viz. petroleum ether, benzene, chloroform and ethyl acetate exhibited significant protection against bronchospasm, induced by histamine in guinea pigs. Significant protection exhibited by methanolic extract was comparable with the standard chlorpheniramine maleate (2 mg/kg) [33].

2.5.24 Mast cell stabilizing activity
The protective effect of different extracts of whole plant against the compound 48/80 and sheep serum induced mast cell degranulation was evaluated. The ethanol extract at the dose levels of 150 mg/kg and 300 mg/kg and ethyl acetate extract at the dose levels of 100 mg/kg, 150 mg/kg and 300 mg/kg showed slightly better protection of mast cell degranulation (77-86%) than ketotifen (75%) in the sheep serum model. These extracts also showed better mast cell stabilizing activity (77-88%) than the standard drug (69%) when peritoneal mast cells are treated with compound 48/80. These results suggest that *S. indicus* has potent mast cell stabilizing effects thereby inhibiting mediator release from mast cells [34].

2.5.25 Antihyperlipidemic activity
The alcoholic extract of flower heads in atherogenic diet induced hyperlipidemia in rats was investigated for the dose of 500 mg/kg/day, p.o. for 8 days. The extract effectively suppressed the hyperlipidemia by decreasing total cholesterol, triglyceride, LDL and very low density lipoprotein (VLDL); increasing the HDL [35].

2.5.26 Anti-arthritic activity
The anti-arthritic activity of the petroleum ether extract of the flowers in the doses 10, 30 and 100 mg/kg/day p.o. was investigated against complete Freund's adjuvant induced arthritis in laboratory rats. Indomethacin (2 mg/kg/day p.o.) was the standard drug. The dose of 100 mg/kg/day p.o. showed significant anti-arthritic activity.

2.5.27 Anti-inflammatory activity
The 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 [36].

2.5.28 Anti-inflammatory and analgesic activity
The anti-inflammatory and analgesic activities of ethanolic extract of *S. indicus* flowers in doses of 300 and 500 mg/ kg was tested on Albino mice and rat of either sex. Anti-inflammatory activity was evaluated by measuring the mean decrease in hind paw volume after the sub planter injection of carrageenan. The analgesic activity was tested against acetic acid induced writhing response using Albino rats. At the end of 1 h, the inhibition of paw edema was 42.66 and 50.5% respectively and the % of protection from writhing was 62.79 and 68.21 respectively [36].

2.5.29 Anti-inflammatory, anti-migratory and anti-proliferative activity
Chronic inflammation induced hyper-proliferation and migration of keratinocytes are pathological hallmarks of psoriasis. Extracts from *Sphaeranthus* spp. Demonstrate pharmacological activity *in-vitro* and *in-vivo*. However, the activity in modulating disease relevant pathways in psoriasis has not been reported. In the current study a standardized herbal extract from *S. indicus* (NPS31807) was used to study the mechanistic activity under conditions of inflammation, keratinocyte proliferation and migration using cell based and gene expression assays. NPS31807 treatment reduced levels of pro-inflammatory cytokines from human macrophages and activated epidermal keratinocytes in a dose dependent manner. Treatment with NPS31807 diminished NFκB and AP-1 transcription activity in human macrophages. Lowered nuclear translocation of p65 sub-unit in macrophages by treatment confirmed reduced activity of NFκB. Gene expression profiling showed attenuated expression of genes involved with inflammation such as tumor necrosis factor (TNF) signaling and angiogenesis by NPS31807. Inhibition of angiogenesis and matrix metalloproteinase production in keratinocytes was confirmed using real-time quantitative-polymerase chain reaction assays. Pre-treatment with NPS31807 led to significant reduction of signal transducer and activator of transcription 3 phosphorylation and mitogen induced cellular migration. NPS31807 induced inhibition of proliferative genes and BrdU uptake in epidermal keratinocytes. In summary, our study provides novel molecular insights into the anti-inflammatory, anti-migratory and anti-proliferative properties of NPS31807. In summary, NPS31807, an extract from *S. indicus* can be used as therapeutic option in inflammatory and auto-immune conditions such as psoriasis [35, 36].
The anti-inflammatory effect *S. indicus* was found to be potent in suppressing the proinflammatory cytokines interleukin-8 (IL-8) and TNF-α induced by the culture supernatant of *Propionibacterium acnes* in polymorphonuclear leukocytes and monocytes than that of other tested plants, viz., *Rubia cordifolia, Curcuma longa, Hemidesmus indicus* and *Azadirachta indica*.
7HF significantly reduced the production (induced/spontaneous) of TNF-α and IL-6 from freshly isolated human mononuclear cells, synovial tissue cells isolated from patients with active rheumatoid arthritis and BALB/c mice. Oral administration of 7HF significantly protected C57BL/6J mice against endotoxin-mediated lethality. In the dextran sulfate sodium (DSS) model of murine colitis, oral administration of 7HF prevented DSS-induced weight loss, attenuated rectal bleeding, improved disease activity index and diminished shortening of the colon of C57BL/6J mice. Histological analyses of colonic tissues revealed that 7HF attenuated DSS-induced colonic edema, leukocyte infiltration in the colonic mucosa and afforded significant protection against DSS-induced crypt damage. 7HF was also significantly efficacious in attenuating carrageenan-induced paw edema in Wistar rats after oral administration. In the collagen-induced arthritis in DBA/1J mice, 7HF significantly reduced disease associated increases in articular index and paw thickness, protected against bone erosion and joint space narrowing and prominently diminished joint destruction, hyperproliferative pannus formation and infiltration of inflammatory cells. These results provide evidence that 7HF-mediated inhibition of pro-inflammatory cytokines functionally results in marked protection in experimental models of acute and chronic inflammation [37].

2.5.30 Nephroprotective effect
The ethanolic extract was screened for nephroprotective in gentamicin induced acute renal injury in rats. The extract in the dose of 300 mg/kg was found to increase blood urea, serum creatinine and decrease the total protein and serum albumin of the treated group compared to normal group [38].

3. Other activities

The plant was also found to exhibit anticancer activity and antiprotozoal activity against *Entamoeba histolytica* [39]. The alcoholic extract of the flower exhibited hypotensive, peripheral vasodilatory and cathartic activities. The extract of the plant was found to inhibit hyaluronidase. The extract effected toxicity on second and fourth instar larvae of *Culex quinquefasciatus* mosquito at 100–500 ppm concentration [15]. The methanolic extract of dried fruit exhibited nematocidal activity. The methanolic extract (<4 mg/mL) showed macrofilaricidal activity within an incubation period of 100 min by the worm motility assay against adult *S. digitata,* a cattle filarial worm [40].

4. Conclusion

From the literature survey, it is evident that *Sphaeranthus indicus* Linn. has been exhaustively worked out for both chemical and pharmacological studies. In all the reported pharmacological activities, it is found to be more effective for various disease conditions. It finds a broad spectrum of therapeutic usage. As the plant is widely distributed, it could be considered for new drug formulations as well as for further pharmacological studies.

5. References

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