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Review

Mundi (*Sphaeranthus indicus* Linn): The best blood purifier and immunomodulatory Unani herb with versatile ethnomedicinal uses and pharmacological activities

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ABSTRACT

Sphaeranthus indicus Linn. (*Mundi*) belongs to the family Compositae, Indian aromatic weed. Since the ancient time, its whole plant and flowers have great medicinal value. It is used for medicinal purpose in Unani and other traditional medicines as a blood purifier, aphrodisiac, eye tonic, tonic for vital organs, and anti-inflammatory properties. Hence, useful for neurological, eyes, cardiac, gastrointestinal, integument and urogenital disorders. This article intent to highlight the Unani ethnomedicinal properties and therapeutic uses, other traditional medicinal properties, to signify its potential in the treatment of various ailments as mentioned in Unani medicine and likewise to survey its phytoconstituents, pharmacological and clinical studies. Thisplant details were explored in classical Unani texts for its ethnobotanical Unani description, temperament (*Mizaj*), medicinal properties and therapeutic uses. Further, for phytochemicals and pharmacological/clinical studies information various scientific search engines such as PubMed, Science Direct, Ovid, Springer, Medline, Research Gate and Google Scholar were browsed. All relevant articles up to 2020 were referred including 24 Classical Unani and Medicinal plant books, 60 research and review papers. *Mundi* has been used in Unani and other traditional medicine for ages and used in the aforementioned ailments. The organic phytoconstituents include alkaloids, glycosides, saponins, tannins, resins, flavonoids, steroids, proteins volatile oils, sterol and terpenoid. *In-vitro* or *in- Vivo* studies have proven pharmacological activities of *S. indicus* such as anti-oxidant, anti-inflammatory, antimicrobial, antimutagenic, immunomodulatory, anti-ulcer, anti-pyretic, neuroprotective, hepatoprotective, hypoglycemic, antiageing and anti-cancer

Hence, the aforesaid ethnomedicinal and therapeutic uses, pharmacological and clinical research studies rationalize the potential benefits of *S. indicus* mentioned in the classical Unani literature. However, future randomized clinical trials are proposed to approve its efficacy and safety for various ailments.

Keywords Antimicrobial, Antioxidant, Bicyclic sesquiterpene lactone, *Sphaeranthus indicus* Linn

INTRODUCTION

The traditional Unani system of medicine is a well-known complementary and alternative system of medicine founded on the philosophy of the Greek physicians Hippocrates and Galen that exist and sanctuaries its fundamental nature in this contemporary era (Sultana *et al.*, 2015). Globally, numerous texts/manuscripts of Unani traditional on medicine and pharmacopoeia literature are accessible for practice and various manuscripts have discussed regarding the herb, *Sphaeranthus indicus* Linn, Indian aromatic weed. It belongs to the family Compositae and commonly known as *East Indian Globe Thistle* (English).

Unani physicians mentioned that it is a very useful plant as it is used in various diseases. Hence, it is also called *Aab Hayat.* In authentic scriptures, it is mentioned to be one of the best herbs used for promoting intellect. Since antiquity, its whole plant and flowers have great medicinal value and are used for therapeutic purpose in *Unani* Medicine. The plant is used both internally as well as externally. It is used for medicinal purpose in *Unani* and other traditional medicines as a blood purifier, aphrodisiac, eye tonic, tonic for vital organs, and anti-inflammatory properties. Hence, useful for integument, cardiorespiratory, gastrointestinal, urogenital and locomotors diseases in folk medicine (Mohiuddin, 2004). Hence, for this purpose, a complete literature exploration to review the description of this medicinal herb in the traditional Unani literature and the contemporary era was comprehended for its ethnomedicinal uses, phytoconstituents and pharmacological studies.

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METHODOLOGY

All relevant articles up to 2020 were referred including 24Classical Unani and Medicinal plant books, 60 research and review papers. Plant *Mundi* details were explored extensively in classical Unani and medicinal plant texts for its ethnobotanical Unani description, temperament (*Mizaj*), ethnomedicinal properties, therapeutic uses and compound formulation. Standard Unani Medical Terminology (Anonymous, 2012) published by Central Council for Research in Unani Medicine in collaboration with World Health Organization was used to describe the appropriate Unani terminologies. Moreover, PubMed, Google Scholar, Medline, Research Gate and other search engines were browsed for ethnobotanical description, ethnomedicinal action and therapeutic used, phytoconstituents, and pharmacological and clinical research studies. The various MeSH terms such as "*S. indicus* and Unani", "*S. indicus* and pharmacological activities", "*S. indicus* and ethnomedicinal properties", "blood purifier in Unani', "anti-inflammatory", "antioxidant", "anti-microbial", and other pharmacological activities full-length paper were browsed.

CRITICAL EVALUATION

Criteria evaluation included surveying the literature for *Mundi* in all classical Unani texts such as *Busthan al-Muffradat, Khazainul Advia, Makhzan al-Mufradat, Rahuman-i-Aqaqeer, Muhit-i-Azam, Kinz al-Adwiya Mufridah, Ilmul Adwiya Nafeesi, Kanzul Mujarribat, Jamia ul Mufradat al Adviaal Aghiza, Al Qanoon fit Tibb (Canon of Medicine),* Unani Pharmacopoeia of India, Hamdard Pharmacopoeia of Eastern Medicine, Wealth of India, Glossary of Indian Medicinal Plants, Indian Medicinal Plants, etc were explored. The full-length papers were downloaded from the various scientific engines to review the ethnobotanical, phytoconstituent and pharmacological activities. After survey of the literature of *Mundi* a correlation of ethnomedicinal therapeutic use and its pharmacological activities was performed to ascertain the effect of Mundi on various ailments of different systems.

RESULTS

Description in Unani medicine and other traditional medicine

1) **Vernaculars:** The vernacular famous names are *Mundi* (Hindi and Urdu), *Aab Hayat* (Persian), *Kamazarijus* (Arabic), *Kotatakkarandai* (Tamil), *Badasorum* (Telugu) and *Mundirika, Pravrajita* (Sanskrit) (Chopra *et al.*, 2002). In Sanskrit word "*Mundi*" literally means that which "cuts off or "wards off".

2) **Etymology:** This plant is named *mundi* in Unani texts. In Persian, it is known as *Mahlaq al-Ras* as the flower looks like a bald head (Ghani, 2004).

3) **Description of the medicinal herb in Unani literature:** As per the Unani encyclopaedia and texts, *Mundi* is an Indian aromatic weed, found near water. The branches are thin and spread on the ground. Leaves are like *mint* (*Pudina)* but small, round and thick. Flowers are rounded, big and similar to wheat, flower reddish-blue with fragrance and mildly bitter taste. It's all parts that are aromatic. It is of two types small and big. The big one is called *Mahamundi* (*S. Africans*) (Ghani, 2004).

4) **Temperament (*Mizaj*):** The temperament of the plant is warm in 2nd degree and wet in 2nd degree (Kabir al-Din, 2007; Mohiuddin, 2004). Or cold in 1st degree and dry in 1st degree (Ghani, 2004).

5) **Ethnomedicinal properties (*Af'al*) in Unani medicine:** *Musaffī-i-Dam* (blood purifier) (Ghani, 2004; Kabir al-Din, 2007; Mohiuddin, 2004); *Mufattih* (deobstruent) (Kabir al-Din, 2007); *Muqawwī al-'Ayn* (eye tonic) (Kabir al-Din, 2007; *Muqawwī-i-A'dā' Ra'īsa* (tonic for vital organs) *Muqawwī-i-Bāh* (aphrodisiac), (Ghani, 2004; Kabir al-Din, 2007; Mohiuddin, 2004); Antitubercular properties (Ghani, 2004; Mohiuddin, 2004); *Muqawwī-i-Mi'da, Mukhrij wa Qātil-i-Dīdān-i-Am'ā', Muqawwī-i-Jigar* (Mohiuddin, 2004)

6) **Therapeutic uses in classical Unani texts:** The whole plant of *Mundi* is very useful in various diseases.

   a) **Effect on the nervous system:** The whole plant is employed to increase memory power. Its *'Arq* or *Sharbat* (distillate or syrup) is useful in melancholia and with *Lemoni Kagzi* (lemon) in epilepsy. Orally, its plant with sugar for 40 days is useful in *Saudavi* (black bile) cognitive diseases. Its powder is useful as *Muqawwī-i-A'dā' Ra'īsa* (tonic for vital organs) (Mohiuddin, 2004).

   b) **Effect on eye diseases:** Unani physicians described it as a specific medicine for eye diseases and used it to treat the itching of an eye in conjunctivitis and eye pain. It has *Muqawwī al-'Ayn* (eye tonic) property and hence useful in *Du'f al-Basar* (refractive errors). Powder of *Mundi* 6g twice daily for 40 days with honey is useful in blurred vision and/or due to catarrh. For redness and eye pain in conjunctivitis, tie pad soaked in the juice of *Mundi* (prepared by stirring juice of *Mundi* with fresh neem stick in a copper plate till it turns black). Its mashed flower juice is also useful in pain, cataract and blurring of vision. Further, the physician inscribed that swallowing one whole flower of *Mundi* prevents conjunctivitis. Orally, the powder of dried root (dried in shade) with an equal quantity of jaggery 7g with cow milk prevent all eye diseases. Oral administration of *'Arq* (distillate) 50 ml, is also credited to have *Muqawwī al-'Ayn* property (Mohiuddin, 2004).

   c) **Effect on oral cavity:** It is cooked as a vegetable and used in *Balghamī* (phlegmatic) diseases and halitosis (Mohiuddin, 2004).

   d) **Effect on respiratory tract:** It is useful in cough and chronic tuberculosis. (Kabir al-Din, 2007;Mohiuddin, 2004; Standardization of Single Drugs of Unani Medicine, 1987)

e) Effect on the cardiovascular system: It is useful in *Khafaqān* (palpitation) (Mohiuddin, 2004).

f) Effect on the gastrointestinal tract: In *Nafkh al-Mi'da* or *Riyāh Shikam* (flatulence), 7g of *S. indicus* with cow milk is advised. It has *Muqawwī-i-Mi'da* (strengths the stomach), appetizer effe-cts and helps in digestion. Its *Joshānda* helps to remove *Rutūbat Fuzla* (waste fluids) from stomach, antiemetic, and gastric pain. It is useful in diarrhoea caused by gastroenteritis. *Mundi* with *Roghan Zard* (ghee) is useful in diarrhoea. In worm infestation, *Mundi* powder *Mukhrij wa Qātil-i-Dīdān-i-Am'ā'* (kills and expels the worms). Daily use of the whole plant with sugar is effective in the *Bawāsīr* (haemorrhoids) treatment. Oral use of fresh *S. indicus* powder (6g) and blackpepper (4 in number) with water is also effective in *Bawāsīr Dāmiya* bleeding haemorrhoids. The application of a paste of leaf and flower with water is useful on piles mass and decreases its pain and bleeding. Its powder with curd or camphor is useful in haemorrhoids.

g) Effect on the liver: It is used in the correction of liver and intestine functions. It has *Muqawwī-i-Jigar* property (hepatotonic) and is useful in jaundice. With *Arandi*, it is useful in *Istisq ā'* (ascites) (Mohiuddin, 2004).

h) Effect on urinary tract: It is effective in burning micturition, urethral ulcer and gonorrhoea (Mohiuddin, 2004).

i) Effect on the male genital system: *S. indicus* has *Muqawwī-i-A'dā' Tanāsuliyya* (tonic to genital organs), *Tawlīd-i-Manī* (improves the production of semen), *Muharrik* and *Muqawwī-i-Bāh* (aphrodisiac) property and its use with milk is effective in *Jarayān Manī* (spermatorrhoea) and male organ dysfunction. Its juice and flowers for 40 dayswith neem are useful in oligozoospermia and to increase the viscosity of semen *(Mughalliz-i-Manī*). Its leaves and root powder with cow milk and jaggery for three consecutive days is effective *Muqawwī-i-Bāh* (Mohiuddin, 2004).

j) Effect on the female genital system: Its powder and decoction are used in vaginal discharge. Local application its root as a suppository is *Jazib* (absorbent), *Qabiz*, *Muqawwī* (tonic) and *Mujaffif* (desiccant). *Halwa Mundi* is effective in leucorrhoea, burning micturition and uterine inflammation.It is useful in gonorrhoea (Mohiuddin, 2004), and *Jarayān Manī* (Ghani, 2004). Further, to procreate a male baby, its use has been mentioned inclassical texts. Its use with *Myristica fragnans* is said to be effective in infertility treatment. It is useful for *Safrāwī wa Saudāwī Amrād al-Rahim* (yellow and black bile diseases of the uterus), *Sozish-i-Bawl* (micturition) and relieves uterine and vaginal pain (Ghani, 2004).

k) Effect on integument: It is used in *Jaraba wa Hikka*, (itching and scabies) (Ghani, 2004) (Standardization of Single Drugs of Unani Medicine, 1987), *Quba* (Ghani, 2004; Kabir al-Din, 2007), and other skin diseases (Hakeem, 2002; Kabir al-Din, 2007; Standardization of Single drug, 1987). It is a very effective *Musaffī-i-Dam* (blood purifier) and useful in various skin diseases. Its bloodpurifier activity is said to be equivalent to *Ushba Maghribi* (*Smilax aspera* L. root) and *Chobchini* (*Smilax china* root). It is useful in all *Fasad Khun* with sugar. Its local application is useful in thyroid glandular enlargement (*Khanazir*). *Joshānda Mundi* (30g) for a month is effective in *Khanazir*. In children, 10 g daily is effective for the same. Fresh *Mundi* juice in equal quantity with ghee is boiled till the juice dries, then filter the oil, it is effective in leprosy. It is useful in adenitis, urticaria, pruritis, eczema, leprosy andother diseases. Its root's oral use for consecutively one year prevents greying of hair (Mohiuddin, 2004).

l) Effect on general health: It is useful in fatigue as it has *Muqawwi* (tonic) effect. Its use with *Salib Misri* (*Orchis mascula* tubers) and *Zanjabeel* (*Zingiber officinale* rhizome) is effective to increase with weight in underweight individual as it has *Muqawwī-i-Aam* (general tonic) property (Mohiuddin, 2004).

7) Dosage: 15-20g as a powder; 12 g in the form of *Joshānda* (Hakeem, 2002; Kabir al-Din, 2007; Standardization of Single Drug of Unani Medicine, 1987)

8) Adverse effects: It adversely may affect to intestine and kidney

9) **Corrective:** Juice of *Bhangra Siyah* (*Eclipta prostrata* whole plant).

10) Substitutes: *Brahamdandi* (*Tricholepis glaburima*), *Sarphoka* (*Tephrosia purpurea* L.) (Kabir al-Din, 2007; Standardization of Single Drug of Unani Medicine, 1987)

11) Unani formulations: *Majun Mundi, Sharbat Ushba Khas, Arq Murakkab Musaffi Khoon.* The other important formulations, their preparation and uses are summarized in table 1 (Mohiuddin, 2004).

12) Ethnomedicinal uses in other traditional systems: The powder of root (40 grains) and seeds is usefulfor stomachic and anthelmintic properties (Kiritikar and Basu, 2003; Nadkarni, 2005). An oil prepared from the root by steeping it in water and then boiling it in sesamum oil until all the water is expelled is said to be a valuable aphrodisiac (Nadkarni, 2005). The roots and seeds are also used in intestinal worm's infestation, indigestion, and administered with honey in patients with cough (Nadkarni, 2005). The flowers are used as an alternative, depurative, cooling, tonic. It is employed in skin disorders(Chopra *et al.*, 2002; Kiritikar and Basu, 2003; Nadkarni, 2005). The rind of the fruit is useful in fishpoison. The whole plant is used in treating epileptic convulsions, mental illness and hemicranias. It is laxative, emmenagogue, increases the appetite, enriches the blood, lessens inflammation and resolves boils (Kiritikar and Basu, 2003). Antitubercular properties

have also been ascribed to the plant (Wealth of India, 2003).

In Ayurveda, it has been used as a laxative, digestible, tonic, fattening, alterative, anthelmintic, alexipharmic. It is employed in tuberculous glands, anaemia, diseases of spleen, elephantiasis, pain in the uterus and vagina, bronchitis, asthma, indigestion, biliousness, vomiting, dysentery, pain in the rectum, piles, insanity, hemicrania, epileptic convulsion, strangury, urinary discharges, looseness of the breasts, leukoderma, etc (Kiritikar and Basu, 2003).

Description of Mundi in scientific literature

1) **Plant Description**: It is an aromatic herb, 30-60 cm tall, with a stem with toothed wings. The leaves are obovate oblong, rounded or subacute, glandularhairy, spinous-serrate or dentate, narrowed at the base. The flowers in heads are 1-1.6cm in diameter, compound, globose-ovoid, bracteates on solitary glandular peduncles with tooted wings. Further, flowers are purple involucral bracts in several series; another tailed; style arms truncate and apically hairy;seeds small. It is found throughout India ascending the Himalayas up to 5000 feet from Kumaon to Sikkim. The herb is pungent, bitter and sweet. The part used are whole plant, especially flowers (Standardization of Single Drugs of Unani Medicine, 1987).

Phytoconstituents

Essential oil in the herb, an alkaloid in leaves, stems and flowers (Chopra *et al.,* 2002). The inorganic constituents are salts of iron and calcium. The organic phytoconstituents are alkaloids, glycosides, saponins, tannins, resins, flavonoids, steroids, proteins and volatile oils, sterol, and terpenoid. The alkaloid *Sphaeranthine* is present in the plants (Kiritikar and Basu, 2003). Other molecules are 7α-hydroxyeudesm-4-en-6,12-olide (sesquiterpene lactone), 2-hydroxycos-tic acid (sesquiterpeneacid), β-eudesmol and ilicic acid have been isolated from methanol extract. The major constituents were cadiene, ocimene, citral, p-methoxycinnamaldehyde, geraniol, eugenol and geranyl acetate. Methyl chavicol,α-ionone, d-cadiene, p-methoxycinnmaldehyde, α-terpinene, geraniol, geranyl acetate, β-ionoe, sphaerene, indicusene, sphaeranthol as essential oil and β-sitosterol, n-triacontanol, phenyl urethane,n-pentacosane isolated from the oil (Singh *et al.,* 2019). Hentriacontane, sesquiterpene lactone was isolated by Gogate *et al.,* (1986), sphaeranthanolide (Shekhani *et al.,* 1990) flavone and isoflavone glycosides were also isolated from this plant (Yadav *et al.,* 1998).

Pharmacological experimental studies

These uses in the Unani and other Traditional systems of medicine is evidenced by many explorative pharmacological and clinical research studies.

1) **Anti-asthmatic/Anti-allergic/Mast cell stabilizing activity:** Mathew and co-workers (2009). They found an ethanolic extract of *S. indicus* whole plant showed better protection of mast cell degranulation than ketotifen in the sheep serum model. Researchers concluded that *S. indicus* has potent mast cell stabilizing effects by inhibiting mediator release from mast cells in Wistar albino rats.

Prajapati *et al.,* (2010) reported that the methanolic extract of aerial parts of *S. indicus* has anti-asthmatic activity. The researchers found that significant increase in preconvulsion dyspnoea time, decreased differential leukocyte counts and serum bicarbonate level, with reduction in the inflammation and bronchodilation dilated. .

2) **Antibacterial /Antimicrobial activity:** Crude alcoholic extract of *S. indicus* flowers showed antibacterial activity against different species of Gram-negative and Gram-positive bacteria (Shaikh *et al.,* 1986). A bicyclic sesquiterpene lactone isolated from the aerial part of the plant demonstrated strong antimicrobial activity against *S. aureus, S. albus, E. Coli, Fusarum sp. Helmintho sporium* species and other microorganisms (Singh *et al.,* 1988). Alcoholic and aqueous extract of the plant was found to be highly effective in preventing the growth of *Alternoria solani, Fusarium oxysporum* and *Penicillium pinophitum* to a great extent (Dubey *et al.,* 2000). 7x – Hydroxyeudesm-4en-6, 12-olide exhibited antimicrobial activity (Rastogi, 2002).

3) **Antifungal activity:** High antifungal activity has been exhibited by essential oil obtained from leaves against *Trichoderma viride, Rhizopus nodosus, Aspergillus neger, Trichophyton rubrum 5s* and *Curvularia prasadie* (Garg and Kasara, 1982).

4) **Anxiolytic activity:** Petroleum ether extract of *S. indicus* flowers produced anxiolytic activity in mice (Amavade *et al.,* 2006).

5) **Anti-inflammatory activity:** Jain and Basal (2003) found inhibition of *Propionibacterium acnes*-induced mediators of inflammation by *S. indicus* extract. Aqueous extract *S. indicus* root caused significant suppression of reactive oxygen species (ROS), proinflammatory cytokine-induced monocytes, which are important inflammatory mediators in acne pathogenesis. Nanda *et al.,* (2010) found the ethanol and petroleum ether extracts showed significant (p<0.05) anti-inflammatory activity at the doses of 200mg/kg and 400mg/kg body weight from 1 hour onwards as compared to the standard drug diclofenac sodium. Whereas aqueous extracts exhibit activity from 2 hours onward when compared to the standard drug amongst various extracts.

In another study, 7- hydroxyfrullanolide a sesquiterpene lactone molecule isolated from fruit extract of *S. indicus* showed a significant and dose-dependent reduction in induced and spontaneous production 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. a. In collagen-induced arthritis in mice, 7-hydroxyfrullanolide significantly reduced disease associated increases in the 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. The authors concluded that these findings provide evidence of 7-hydroxyfrullanolide-mediated inhibition of pro-inflammatory cytokines in experimental models of acute and chronic inflammation (Fonseca *et al.*, 2010).

The ethanolic extract of leaves in different doses also exhibited dose-dependent and significant anti-inflammatory activity in acute (carrageenan induced hind paw oedema, $p< 0.05$) and chronic (cotton pellet granuloma formation, $P < 0.05$) inflammation model (Meher *et al.*, 2011).

Ali *et al.*, (2011) noted significant anti-inflammatory potency of ethanolic extract of flowers was 42.66 and 50.5% at doses of 300 and 500 mg/kg respectively at the end of one hour the inhibition of paw oedema.

Chakrabarti *et al.*, (2012) evaluated the standardized extract of flowering and fruiting heads and found that treatment reduced levels of pro-inflammatory cytokines from human macrophages and activated epidermal keratinocytes in a dose-dependent manner. They conclude that extract from *S. indicus* can be used as a therapeutic option in inflammatory and auto-immune conditions such as psoriasis.

6) **Analgesic activity:** The ethanolic extract of leaves (Ali *et al.*, 2011). and flower of *S. indicus* (Meher *et al.*, 2011) in different doses exhibited dose-dependent and significant analgesic activity in both models of pain

7) **Antiarthritic activity:** The petroleum ether extract of *S. indicus* flower at a dose of 100mg/day orally showed significant antiarthritic activity against complete Freund's adjuvant-induced arthritis in laboratory rats (Badgujar *et al.*, 2009).

8) **Attenuating effect on prostatic hyperplasia:** The petroleum ether, ethanol and aqueous extracts extract *S. indicus* flower head exhibited a significant attenuating effect on prostatic hyperplasia. Although the best attenuating activity was observed with petroleum ether. Urine output was also improved significantly in all extract groups (Nahata and Dixit, 2011).

9) **Antihyperlipidemic activity:** Alcoholic extract of *S. indicus* flower head showed a significant decrease in body weight, total cholesterol, triglyceride and low-density lipoprotein and very low-density lipoprotein whereas significant increases in the level of high-density lipoprotein were also obtained after treatment with *Sphaeranthus indicus* extract (Pande and Dubey, 2009).

Ramachandran and co-workers (2011) found that administration of ethanolic extract of *S. indicus* root in the STZ-induced diabetic rats of 200 mg/kg showed a significantly higher reduction in elevated TC, TG, LDL and an increase in HDL levels when compared to glibenclamide 100 mg/kg dose of extract.

10) **Anthelminthic activity:** Sharma *et al.*, (2011) found whole plant ethanolic and aqueous extract exhibits anthelmintic activity in a dose-dependent manner

11) **Antioxidant activity:** The ethanolic extract of the underground portion of *S. indica* at 1000µg/ml showed maximum scavenging of the free radical action, 2,2-azinobis-(3-ethylbenzothiazoline-6-sulphonate) (ABTS) observed up to 41.99% followed by the scavenging of the stable radical 1,1-diphenyl, 2-picryl hydrazyl (DPPH) (33.27%), superoxide dismutase (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%). The total antioxidant capacity of the extract was found to be 160.85 nmol/g ascorbic acid (Shirwaikar *et al.*, 2006).

Methanolic extract of flower head also exhibited a significant antioxidant effect (Tiwari and Khosa, 2009). The inhibitory concentration (IC50) in all models viz. ABTS, DPPH, superoxide dismutase, nitric oxide and iron chelating, were found. The total antioxidant capacity of extract was found to be 127.85 nmol/g ascorbic acids (Prabhu *et al.*, 2009).

Administration of ethanolic extract of *S. indicus* 200 mg/kg produced significant ($P < .01$) and higher antioxidant activity than 100 mg/kg dose in STZ-induced diabetic rats (Ramachandran *et al.*, 2011). Stems and leaves methanol extract showed a significant decrease in serum liver enzyme, total protein and antioxidant levels at the dose of 500 mg/kg and 750mg/kg in CCl4 induced liver damaged rats (Mathews *et al.*, 2012).

Krishna *et al.*, (2013) found that among the methanol extracts of leaf, flower, stem and root tested, flower and leaf extracts exhibited the highest free radical scavenging activity i.e., at 150µg/ml concentrations

12) **Antitussive activity:** The methanolic extract at the dose of 200, 300 and 400 mg/kg showed inhibition of cough by 71.24%, 76.84% and 77.92% on a cough induced by Sulphur dioxide gas in mice and also exhibited a synergistic effect of sleeping time induced by standard sedatives (Nayak *et al.*, 2010).

13) **Anti-ulcer activity:** Malairajan *et al.*, (2013) tested the ethanolic extract of the whole plant for antiulcer activity aspirin and pylorous ligation induced ulcer in Wistar albino rats. They found at 500 mg/kg dose significant reduction in gastric volume, free acidity, total acidity, and ulcer index. The ulcer protection of the extract was found to be 82.9% and 85.3%, in comparison to ranitidine showed 92.6%.

14) **Antiprotozoal activity:** The ethanolic extract of the flower was found to have an inhibitory effect on *Entamoeba histolytica* (Naqvi, 1997)

15) **Antipyretic activity:** Among whole parts petroleum-ether, benzene, chloroform, ethanol and triple distilled water extract; chloroform and ethanol extracts showed potential significant antipyretic activity from 1 hour onward whereas aqueous extracts exhibited activity from 2 h onward as compared to the standard drug paracetamol amongst various extracts (Nanda *et al.*, 2009)

16) **Antiviral activity:** The methanolic extract of *S. indicus* showed potent anti-MCV and anti HSV activities (low MIC_{100} and broad spectrum of activity) at a concentration as low as 0.4 µg/mL. (Vimalanathan *et al.,* 2009).

17) **Bronchodilator effect:** Whole plants methanolic extract and its fractions viz., petroleum ether, benzene, chloroform and ethyl acetate exhibited significant protection against bronchospasm, induced by histamine in guinea pigs at the dose of 87 and 174 mg/Kg, p.o. However, the methanolic extract showed a significant bronchodilatory effect comparable withChlorophenarmine maleate. Hence, *S. indicus* shows broncho dilatory activity (Sarpate *et al.,* 2009).

18) **Hepatoprotective activity:** Mansoori *et al.,* (2019) found that the petroleum ether, chloroform, ethyl acetate, ethanolic, and aqueous extract of *S. indicus* leaves had hepatoprotective activity against the carbon tetrachloride-induced hepatotoxicity in mice and *in-vitro* human live hepatoma cell line. Likewise, in the ethanol induced *in-vivo* study ethanolic and ethyl acetate extract showed a significant protectiveeffect at 400mg/Kg p.o.dose (Nayak *et al.,* 2007).

Pavan *et al.,* (2008) also reported that *S. indicus* methanolic extract at a dose of 500 mg/kg body weight exhibited hepatoprotective effect in CCl4 intoxicated rats, that were comparable with silymarin 100 mg/kg b.w.

Tiwari and Khosa (2009) found that the methanolic and aqueous extract of flower heads of *S. indicus.* Had hepatoprotective against carbon tetrachloride induced hepatic damage in rats. Another study found that at 500 and 750 mg/Kg dose extract statistically restored the serum

liver enzyme, total protein and antioxidant levels. Furth er, histopathological studies supported the biochemical assessment (Mathews *et al.,* 2012).

19) **Hypoglycaemic activity:** Oral administration of petroleum ether extracts of the flower head of *S. indicus* (200 mg/kg) showed significant hypoglycemic activity in alloxan induced Wistar rat (Jha *et al.,* 2010).

Arial part ethanolic extract showed that *S. indicus* increased the uptake of glucose by isolated rat hemidiaphragm significantly and was found to be more effective than insulin (Pareek *et al.,* 2010). Oral administration of alcoholic extract of *S. indicus* for 15 days at doses of 250 and 500 mg/kg significantly lowered fasting blood glucose in diabetic rats in a dose-dependent manner. The 500 mg/kg dose showed significantly better activity than the 250 mg/kg dose throughout the analysis (Prabhu *et al.,* 2008).

The methanolic extract *S. indicus* at the dose of 300 mg/kg body weight significantly reduced the blood glucose level, plasma total cholesterol, triglycerides and low-density lipoprotein in treated rabbits as compared to alloxan-induced diabetic rabbits; also, significantly increased the level of high-density lipoprotein. The extract also significantly decreased ALT and AST (Razi *et al.,* 2011). Muhammad *et al.,* (2011) and Kharkar *et al.,* (2013) has also reported the antidiabetic effect of *S. indicus.*

20) **Immunomodulatory effect:** The compound exhibited immune-stimulating activity (Shekhani *et al.,* 1990). The methanolic extract, its petroleum ether, chloroform and remaining methanol fractions, of flower heads of *S. indicus* Linn. was significantly effective in increasing phagocytic activity, haemagglutination antibody titre and delayed-type hypersensitivity in mice. The further, it probably stimulates stimulating both humoral and cellular immunity (Bafna and Mishra, 2007).

21) **Nephroprotective activity:** The ethanol and aqueous extract of *S. indicus* Linn. were showed nephroprotective activity in gentamicin induced nephrotoxic Wistar albino rats and significant improvement in blood urea, serum creatinine, serum protein and urine glucose level and reversed the kidney damage and restored normal kidney architecture in histopathological studies (Pradeep *et al.,* 2019). In another study, the ethanolic extract of the whole plant on cisplatin-induced nephrotoxicity in the albino rat showed significantreduction tion in the elevated serum creatinine and urea levels. Same time renal antioxidant defense systems, such as superoxide dismutase, catalase, glutathione peroxidase activities and reduced glutathione level that are depleted by cisplatin therapy were restored to normal by treatment with the extract (Mathew *et al.,* 2012)

22) **Neuroprotective and anxiolytic activity:** Ambikar and Mohanth (2013) evaluated the neuropharmacological activity of petroleum ether (SIP), methanolic (SIM) and aqueous extract (SIA) of *S. indicus* in mice. The SIP and SIM showed a significant decrease in locomotor activity but no effect on motor coordination at 200 and 400 mg/kg. All three extract showed significant anxiolytic activity at 100 mg/kg dose. Whereas, SIM showed significant anticonvulsant activity at SIM 100, 200 and 400 mg/kg/p.o. and prolonged haloperidol induced catalepsy at 400 mg/kg/p.o. in mice. Apart from this, SIP and SIM extracts also showed significant analgesic activity using the hot plate method. The authors concluded that the extract possesses anxiolytic, anticonvulsant and anti-stress activity.

23) **Psychotropic activity/ Sedative effect:** Whole plant extract of *S. indicus* significantly reduced spontaneous motor activity and prolonged pentobarbital induced hypnosis. The researcher suggests that effects might due to a mild neurosedative mechanism. The hydroalcoholic extract of *S. indicus* also reduced exploratory behaviour and decrease sedative activity (Galani and Patel, 2009).

24) **Wound healing activity:** The ethanolic extract (10%) cream prepared with aerial parts of *S. indicus* showed wound healing activity in Guinea pigs excised wounded models. After a 15-day application of cream researchers observed that wound area was reduced 88.9, 77.9 and 83.6% in extract, placebo and neomycin cream respectively (Sadaf *et al.,* 2006). Geethalakshmi *et al.,* (2013) reported that the excison wound healing activity

of methanolic extract (5% w/w) and flavonoid fraction of *S. indicus* in paste form in male Wistar rats. The authors also estimated the hydroxyproline content, collagen content and histopathology for fibroblast proliferation, collagen formation, epithelisation, and keratinisation of healed wound area skin. They found a very rapid closure of the wound in extract and flavonoid fraction treated groups which were comparable to the group treated with silver sulfadiazine. Likewise, rat wounds treated with methanol extract and flavonoid fraction ointments showed more fibroblastic proliferation and epithelisation as compared to the placebo-treated group.

An ointment prepared with the 2% alcoholic extract of the flower head of *S. indicus* also showed wound healing activity in the excision wound model, re-sutured incisional wound model, tensile strength measurement of healed tissue, and determination of hydroxyproline content in granular tissue. In addition to greater hydroxyproline content found in healed wounds as compared to control and standard formulation (Jha *et al.,* 2009).

Cream prepared with 5% and 10% ethanolic extract of flowers in Wistar albino rats observed significant wound epithelisation, contraction area and wound closure activity in the test drug which was comparable to standard i.e., framyctine sulphate cream Copda *et al.,* (2010).

Pharmacological clinical trials

1) **Efficacy in cervical erosion with cervicitis:** In the test group (n=30), *Safuf Mundi* (powder of flower) 6g orally in three divided doses and 5g cream of *Henna* (leaves of *L. inermis* Linn) with *Murdarsang* (*P. oxidum*) was applied intravaginally twice daily for 9 weeks showed that 26.7% complete healing of erosion whereas none of the patient had healing in the placebo group (n=15) ($p< 0.05$, statistically significant) in a randomized placebo-controlled single-blind study (Hashmi *et al.*, 2011).

2) **Effect on psoriasis:** Velaskar *et al.,* (2016) reported that the efficacy and safety of 12 weeks course of oral tablet of *S. indicus* extract (Tinefcon®) in 74 patients with moderate to severe plaque psoriasiss. They found that at 12 weeks, 65% and 31% patients achieved PASI-50 in the high and low dosegroup respectively. They also found marked mprovement in PGA status. Histopathological and biomarker data strongly support the improvement in the disease severity.

DISCUSSION

As per the Unani concept, Blood purification is the elimination of toxin and toxic metabolites from the blood consequently it comes at its optimal level, which strengthens the innate heat through physical activity and digestion faculty is enriched. Subsequently, abnormal humours will not be produced and toxin and impurities both will be prevented (Alam *et al.*, 2020). Blood purifying drugs have a warm and dry temperament in the second degree and are bitter. These drugs act as digestive, tonic to stomach and liver, general tonic, antipyretic, deobstruent and tonic to vital organs (Mushir *et al.,* 2019). The literature survey of Unani and ethnomedicinal plant texts showed *Mundi* has *Musaffī-i-Dam* (blood purifier) property, therefore has other properties such as *Mufattih*, *Muqawwī al-'Ayn*, *Muqawwī-i-A'dā' Ra'īsa* (tonic for vital organs) *Muqawwī-i-Bāh* wa *Mi'da wa Muqawwī-i-Jigar Mukhrij wa Qātil-i-Dīdān-i-Am'ā',* (Ghani, 2004; Kabir al-Din, 2007; Kiritikar and Basu, 2003; Mohiuddin, 2004). The mechanism of action of blood purifier drugs is they cause necessary changes in blood and remove its waste material hence, purifying it from impurities. They cause essential changes and sustain the blood composition by their moderate warm, cold, dry and wet properties. Hence, blood purifiers act as alterative and maintain the quality and quantity of blood thereby upholding the equilibrium. Further, they neutralize the disproportionate blood's heat due to their alterative and moderately warm and dry temperament thus normalize the blood composition. Moreover, blood purifier drugs boost the immune system and strengthen the defensive mechanism, prevent the body from toxins and strengths the sluggish liver and kidney dysfunction to its normal function because of *Muqawwī* property (Mushir *et al.,* 2019).

Mundi has blood purifier and other properties, hence, the mechanism of action will be the same. The blood purifying drugs contain saponins, phenols, phenolic glycosidees, alkaloids, minerals, etc (Mushir *et al.,* 2019). *Mundi* contains the phytoconstituent flavonoids that protect cells because of its powerful antioxidant property which prevents or repair the damage done to red cells by free radicals. Studies have shown that glycoside and saponins significantly increase the proliferation abilities of bone marrow cell. Mundi contains saponin so blood purifying drugs may prove the haematinic potentials due to the presence of these phytoconstituents. "*Triterpenic saponins stimulate the proliferation of lymphocytes for the production of interferon, hematopoietic growth factors and cytokines. Alkaloids enhance the restoration of haematopoiesis*." The drugs which contain flavonoid, saponins, and alkaloid have the antioxidant property (Mushir *et al.,* 2019). The Unani classical texts survey showed that *Mundi* not only has blood purifier action but other aforementioned properties hence, it is useful in various ailments of different systems of the body. Recent pharmacological and clinical trials prove its effect.

Unani physicians surmised that the *Mundi* is useful as a memory enhancer, epilepsy, melancholia, cough, chronic tuberculosis, worm infestation, flatulence, skin, liver, kidney, and intestinal diseases. It is also effective in male and female genital (leucorrhoea, gonorrhoea, uterine inflammation, infertility) diseases. The recent experimental studies have proven that *Mundi* has neuroprotective, anticonvulsant, sedative, anxiolytic, antitussive, bronchodilator, antiasthmatic, anti-inflammatory, antioxidant, anthelminthic, nephroprotective, hepatoprotective, antiulcer, wound healing, and anti-microbial activity. As it is the best blood purifier hence useful in diabetes, hyperlipidemia, infections, etc as it has antihyperlipidemic, antioxidant, antipyretic and antimicrobial activity. Further, *Mundi* have *Mufattih* and *Muqawwī* property hence, it is useful to improve hypertension and general health. Existing experimental studies proves that *Mundi* has antihypertensive, immunomodulatory, and antioxidant activities. Its effectiveness in various eye diseases however, no scientific studies are available hence, various experimental and clinical studies are requiring to prove its effect on eyes diseases.

CONCLUSION

S. indicus is the best blood purifier and immunomodulatory Unani herb with versatile properties that is useful in various ailments. Aforesaid pharmacological and clinical research studies rationalize the potential benefits of *S. indicus* in various disorders mentioned in the classical Unani literature. However, future randomized clinical trials are proposed to approve its efficacy and safety. Further, instead of using plant materials in the crude form, they may be formulated into elegant finished product provided with stability data so that they may be easy to use by patients and dispense by a pharmacist.

CONFLICT OF INTEREST

None to declare

ABBREVIATIONS

HDL: High level lipoproteins; LDL: Low density lipoprotein; PASI score: Psoriasis Area Severity Index score; PGA: Physician's Global Assessment; TD; Triglycerides; TC: total cholesterol

REFERENCES

Alam A, Siddiqui JI, Kazmi MH, Ahmad I, Moin MS. *Tasfiyaal-dam* (Blood purification) in Unani perspective: A comprehensive review. *International Journal of Herbal Medicine* 2020; 8(2):100-105.

Ali A, Naqvi S, Baqir G, Shahnaz, Rehana. Anti-inflammatory and analgesic activities of ethanolic extract of *Sphaeranthus indicus* Linn. *Pakistan J Pharm Sci.* 2011; 24(3): 405-409.

Amavade SD, Mhetre NA, Tate VD, Bodhankar SL. Pharmocological evaluation of the extracts of *Sphaeranthus indicus* flowers on anxiolytic activity in mice. *Indian J Pharmacol*, 2006;8(4):254-9.

Anonymous. Standardization of Single Drugs of Unani Medicine. Part 1. (New Delhi: Central Council for Research in Unani Medicine), pp. 230-1, 1987.

Anonymous. The Wealth of India. Vol X. (New Delhi: CSIR), pp. 107-111, 2003.

Badgujar LB, Ghosh, Gaur V, Bodhankar SL. Effect of petroleum ether extract of *Sphaeranthus indicus* Linn. On complete freunds adjuvant induced arthritis in laboratory rats. *Pharmacology Online*. 2009; 2:281-91.

Bafna AR and Mishra SH. Immunomodulatory activity of methanol extract of flower heads of *Sphaeranthus indicus* Linn. *Ars Pharmaceutica.* 2004;45(3): 281-91.

Bafna AR. and Mishra SH. Immunomodulatory activity of petroleum ether extract of flower heads of *Sphaeranthus indicus* Linn. J. *Herbal Pharmacotherapy*. 2007; 7(1):

Chakrabarti D, Suthar A, Jayaraman G, Muthuvelan B, Sharma S, Padigaru M. NPS31807, a standardized extract from *Sphaeranthus indicus*, inhibits inflammatory, migratory and proliferative activity in keratinocytes and immune cells. *Pharmacol Pharmacy*. 2012;(3)2 :178-194

Chopda M, Patole SS, Mahajan RT. Wound healing activity of *Sphaeranthus indicus* (Linn) in Albino rats, Bioresources for Rural Livelihood: Edited by: G.K. Kulkarni, B.N. Pandey and B.D. Joshi. (New Delhi: Narendra Publishing House), pp. 239-44, 2010.

Chopra RN, Nayar SL, Chopra IC. Glossary of Indian Medicinal plants. (New Delhi, India: National Institute of science communication and information resources), pp. 31, 151, 2002.

Dubey KS, Ansari AH, Hardaha. Antimicrobial activity of the extract of *Sphaeranthus indicus. Asian J Chem*. 2000; 12(2):577-8.

Fonseca LC, Dadarkar SS, Lobo AS, Suthar AC, Chauhan VS, Chandrababu S, Sharma SD, Dagia NM, Padigaru M. 7-hydroxyfrullanolide, a sesquiterpene lactone, inhibits pro-inflammatory cytokine production from immune cells and is orally efficacious in animal models of inflammation. *Eur J Pharmacol*. 2010; 644: 220-9.

Galani VJ and Patel BG. Psychotropic activity of *Sphaeranthus indicus* Linn. *In experimental animals. Phcog Res.* 2009;1:307–13.

Garg SC, Kasara HL. Antifungal activity of the essential oil of *Sphaeranthus indicus* Linn. *Pafal J.* 1982; 4 (4):23-24.

Geethalakshmi R, Sakravarthi C, Kritika T, Arul Kirubakaran M, Sarada DV. Evaluation of antioxidant and wound healing potentials of *Sphaeranthus amaranthoides Burm. f. BioMed Research International*. 2013 Jan 1;2013.

Ghani N. *Khazainul Advia*. (New Delhi: *Idarae Kitabus Shifa*), pp. 1263-1265, 2004.

Gogate MG, Ananthasubramanian L, Nargund KS, Bhattacharyya SC. Some interesting sesquiterpinoids from *Sphaeranthus indicus* Linn. (Compositae). *Indian J Chem.* 1986; 25B:233-8. 88.

Hakeem MA. *Bustanul Mufredat*. (Delhi: Idara Kitabus Shifa), pp. 599, 2002.

Hashmi S, Begum W, Sultana A. Efficacy of *Sphaeranthus indicus* and cream of *Lawsonia inermis* in cervical erosion with cervicitis. *Eur J Integr Med.* 2011;3:183-8.

Jain A and Basal E. Inhibition of Propionibacterium acnes-induced mediators of inflammation by Indian herbs. *Phytomedicine (Jena).* 2003;10:34-8.

Jha RK, Mangilal BA, Nema RK. Antidiabetic activity of flower head petroleum ether extracts of *Sphaeranthus indicus* Linn. *Asian J Pharm Clin Res*. 2010;3:16-19

Jha RK, Garud N, Nema RK. Excision and incision wound healing activity of flower head alcoholic extract of *Sphaeranthus indicus* Linn. in albino rats. *Glob J Pharmacol.* 2009; 3:32-7.

Kabir al-Din M. *Makhzan al-Mufridat*. (New Delhi: *Idarae Kitabus Shifa*), pp.581-3, 2007.

Kharkar R, Pawar DP, Shamkuwar PB. Anti-diabetic activity of *Sphaeranthus indicus* Linn. extracts in alloxan-induced diabetic rats. *Inter J Pharm Pharma Sci.* 2013;5(2): 524-6.

Kiritikar K and Basu BD. Indian Medicinal Plant. 2nd ed. Vol VI. (Dehradun: Oriental enterprises), pp. 1863, 2003.

Krishna TM, Thota SP, Jadhav M, Kamal KM, Venuganti A, Mrunalini D, Vadiari S, Mittapelli G. Studies on *in vitro* antioxidant and antibacterial activities of *Sphaeranthus indicus* (Linn). *Inter J Pharm Res Biomedical Anal.* 2013;2(1):1-9

Malairajan P, Venu Babu G, Saral A, Mahesh S, Gitanjali. Anti-ulcer activities of *Sphaeranthus indicus* Linn. *Int J Drug Dev Res*. 2013; 5(1): 43-46.

Mansoori MH, Gupta MK, Mishra V, Yadav N, Vyas. Estimation of antioxidant and hepatoprotective activity of *Sphaeranthus indicus* Linn leaves extract. *Int J Green Pharm.* 2019;12(04): S855-62.

Mathew JE, Srinivasan KK, Dinakaran V, Joseph A. Mast cell stabilizing effects of *Sphaeranthus indicus. J Ethnopharmacol.* 2009; 122(2):394-6.

Mathews LA, Dhanyaraj D, Prathibhakumari PV, Prasad G. Hepatoprotective and antioxidant potential of *Sphaeranthus indicus* [Linn] on liver damage in Wistar rats. *Int J Pharm Pharm Sci.* 2012;4(3):222-5.

Meher BR, Jena J, Rath BG. Evaluation of analgesic activity of ethanolic extract of *Sphaeranthus indicus*. *Scholars Research Library, Der Pharmacia Lettre*. 2011;3(3): 357-60.

Meher BR, Rath BG, Biswal S. Evaluation of anti-inflammatory activity of ethanolic extract of *Sphaeranthus indicus*. *J Chem Pharm Res*. 2011;3: 831-4.

Mohiuddin G, Fasihuddin. *Rahnuma-i-Aqaqeer*. Vol. II. (New Delhi: I'jaz Publishing House), pp. 309, 2004.

Muhammad RT, Malik S, Ghulam M, Waseem H. Determination of the antidiabetic effect of methanolic extract of *Sphaeranthus indicus* L. on alloxan induced diabetic rabbits. Lat Am J Pharm. 2011;30:378-82.

Mushir A, Jahan N, Sofi G. Exploration of Unani concept of blood purifying drugs and likely models for its screening. *Bangladesh Journal of Medical Science*. 2019; 18(2):312-21.

Nadkarni KM. Indian Plants and Drugs with their Medical Properties and Uses. (New Delhi: Srishti Book Distributor), pp. 374-5, 2005.

Nahata A, and Dixit VK. *Sphaeranthus indicus* attenuates testosterone induced prostatic hypertrophy in albino rats. *Phytother Res*. 2011;25:1839–48.

Nanda, BK, Jena, J, Rath, B, Behera, B. Anti-inflammatory activity of whole parts of *S. indicus. Der Pharmacia Lettre.* 2010;2(1):181-88

Nanda BK, Jena J, Rath B, Behera BR. Analgesic and antipyretic activity of whole parts of *Sphaeranthus indicus* Linn. *J Chem Pharm Research*. 2009;1(1): 207-12.

Naqvi SB. Studies on antibacterial activity of compounds of plants origin and isolation of active components from *Sphaeranthus indicus* Linn. Ph.D. Thesis. University of Karachi, Karachi, 1997.

Nayak SS, Maity T, Maiti BC. Hepatoprotective activity of *Sphaeranthus indicus* Linn. *Int J Green Pharm*. 2007;1:32–36

Nayak SS, Maity TK, Maiti BC. Antitussive and synergistic effects of sleeping time induced by standard sedatives of Sphaeranthus indicus plant extracts. *J Adv Pharm Res.* 2010; 1:123-32.

Pande VV and Dubey S. Antihyperlipidemic activity of *Sphaeranthus indicus* on atherogenic diet induced hyperlipidemia in rats. *Inter J Green Pharm*. 2009; 3(2):159-61.

Pareek A, Suthar M, Bansal VK. Chauhan RK, Batra N. *In vitro* study of *Sphaeranthus indicus* on glucose uptake by isolated rat hemi-diaphragm. *J Pharm Res*. 2010;3:2284-5.

Pavan P, Sathesh KS, Thirupathi K, Ravi KB, Krishna MG. Hepatoprotective properties of *Sphaeranthus indicus* on carbon tetrachloride induced acute liver damage in rats. *Biomed.* 2008; 2(4), 384-389

Prabhu KS, Lobo R, Shirwaikar A. Free radical scavenging activity of aqueous extract of *Sphaeranthus indicus. Pharmacology Online*. 2009; 2:468-76.

Pradeep S, Mahesh CD, Manjunath PM, Saraswathidevi HN. Nephroprotective activity of *Mundi (Sphaeranthus indicus* Linn)- an experimental study. *J Ayurveda Integr Med Sci*. 2019;5:143-51.

Prajapati MS, Shah MB, Saluja AK, Shah UD, Shah SK. Research Article Antiasthmatic Activity of methanolic extract of *Sphaeranthus indicus*. *Inter J Pharmacogn Phytochem Res*. 2010; 2(3): 15-19.

Ramachandran S, Asokkumar K, Uma Maheswari M, Ravi TK, Sivashanmugam AT, Saravanan S, Rajasekaran A, Dharman J. Investigation of antidiabetic, antihyperlipidemic, and *in vivo* antioxidant properties of *Sphaeranthus indicus* Linn. in type 1 diabetic rats: An identification of possible biomarkers. *Evid Based Complement Alternat Med.* 2011;2011:571721. doi: 10.1155/2011/571721.

Rastogi RP. Compendium of Indian Medicinal plants. Vol. IV. (Lucknow: Central Drug Research Institute), pp. 427, 690, 2002.

Razi MT, Saadullah M, Murtuza G, Hassan W. Determination of the anti-diabetic effect of methanolic extract of *Sphaeranthus indicus* L. on alloxan induced diabetic rabbits. *Lat Am J Pharm*. 2011;30(2): 378-82.

Sadaf F, Saleem R, Ahmed M, Ahmad SI, Zafar N. Healing potential of cream containing extract of *Sphaeranthus indicus* on dermal wounds in Guinea pigs. *J Ethnopharmacol*, 2006; 107(2):161-3.

Sarpate RV, Deore TK, Tupkari SV. Bronchodilatory effect of *Sphaeranthus indicus* Linn against allergen induced bronchospasm in guinea pigs. *Phcog Mag*. 2009; 5(19):74-7.

Shaikh D, Naqvi BS, Sheikh R. The antibacterial principles of *Sphaeranthus indicus*: Isolation purification and antibacterial action. *Pak J Sci Res*. 1986; 29(5), 366-371.

Sharma S, Jalalpure SS, Semwal B, Tandon S, Agarwal N. Anthelmintic activity of the whole plant of *Sphaeranthus indius* Linn. *Int J Ayur Herb Med*. 2011; 1:18-23/

Shekhani MS, Shah PM, Yasmin A, Siddiqui R, Perveen S, Khan KM, *et al.* An immunostimulant sesquitepene glycoside from *Sphaeranthus indicus. Phytochem* 1990; 29: 2573-6.

Shirwaikar A, Prabhu KS, Punitha ISR. *In vitro* antioxidant studies of *Sphaeranthus indicus. Ind J Exp* Bio. 2006;44(12): 993-6.

Singh S, Semwal BC, Kr Upadhaya P. Pharmacognostic study of *Sphaeranthus indicus* Linn. *A Review. Pharmacog J*. 2019;11(6):1376-85

Singh SK, Saroj VJ, Singh AK, Singh RH. Antimicrobial principle has been isolated from *Sphaeranthus indicus. Int J Crude Drug*. 1988;26(4) 235-9.

Sultana A, Rahman K, and Padmaja AR. Urinary Incontinence (*Salasal Bawl*) in Greco-Arabic Medicine: A Review. *Acta Medico-Historica Adriatica*. 2015;13 (Suppl. 2): 57-76.

Tiwari BK, and Khosa RL. Hepatoprotective and antioxidant effect of *Sphaeranthus indicus* against acetaminophen-induced hepatotoxicity in rats. *J Pharm Sci Res*. 2009; 1(2): 26- 30.

Velaskar S, Nayak CS, Torsekar RG, Viswanath V, Khopkar U, Saraf V, Kulkarni S, Shindikar A, Patil A, Patil S, Parikh H. Efficacy and safety of two doses of *Sphaeranthus indicus* extract in the management of plaque psoriasis: A randomized, double blind, placebo controlled phase II trial. *Am J Dermatol Venereol*. 2016;5(1):6-15.

Vimalanathan S, Ignacimuthu S, Hudson JB. Medicinal plants of *Tamil Nadu* (Southern India) are a rich source of antiviral activities. *Pharmaceutical Bio*. 2009; 47: 422-9.

Yadav RN, and Kumar S. 7-Hydroxy-3', 4',5,6-tetramethoxy flavones 7-O-b-D-(1-4)-diglucoside a new flavones glycoside from the stem of *Sphaeranthus indicus. J Inst Chem*. 1998;70:164-6.