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Review Article

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Phytopharmacology of some indigenous medicinal plants used in arthritis

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ABSTRACT

Over last few decades, there have been a marked in casements in the field of traditional or herbal system of medicine. It is fuelled by increased number of research papers, research funding agency, venture capital and the number of start-ups. As a result of this research data and different funding agency has led to novel systems of treatment with incorporation of herbal drugs given to the diseased conditions to the patients. Due to increased number of publications and research activities are clearly a sign of proliferation of the herbal treatment. This increased the clinical and commercial translation of medicine from the early-stage research ideas to commercialization of products for future growth and interest in the field. The present review work would emphasize on designing and estabilising the synergistic effects of plants or plants part i.e. Sphaeranthus indicus fruit (gorakhmundi). Here, we will highlight some of the examples of treatment of arthritis with herbal drug that have undergone transitional system of medicine. Current review is finally addressing an answer for the problem of modern system of medicine with an ethnopharmacological approach as an alternative therapy. This will help in enhance the safety, efficacy and quality of traditional medicines with new drug discovery in global health.

Keywords: Rheumatoid arthritis (RA); Traditional medicine; Ethnopharmacology

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INTRODUCTION

Rheumatoid arthritis (RA) is one of the most common inflammatory disease, which affects 0.5% to 1% of the general population throughout the world [1]. RA is a musculoskeletal, autoimmune chronic disorder characterised by synovial inflammation, pain and debility [2]. The reason of occurrence of rheumatoid arthritis is unknown but several hypotheses said that it is triggered by the combination of genetic predisposition, exposure to environmental factors like viruses and the prognosis is marked. However, advances in understanding the pathogenesis of the disease have fostered the development of new approachable therapeutics, with improved outcomes. The exact pathophysiology is not clear but release of certain free radicals such as nitrous oxide and superoxide radicals generated as by-products of cellular metabolism. The release of such free radicals may induce the production of interleukins (IL) and tumor necrosis factor (TNF-α) from T-cells which ultimately influence the production of growth factors, cytokines and adhesive molecules on immune cells as such factors may cause tissue destruction and inflammation [3]. The main reason behind the occurrence of RA is due to synovial hyperplasia which further leads to massive irreversible bone destruction [4]. Progression of RA is followed by the destabilization of normal coupling between degradation and synthesis within articular cartilage through mechanical and biological [5]. RA can affect individuals of any age group, but the people of age-group 25-50 years are more prone with a peak in the age group of 40-50 years. Incidence rate of occurrence is very high to Indian followed by Americans. As compared to other categories, mainly two types of arthritis are common among Indian population i.e. osteo-arthritis and rheumatoid arthritis. The percentage occurrence of osteo-arthritis is 22-39% and rheumatoid arthritis is 5% [6-7].

Before starting the treatment of RA certain goals must be kept in mind such as relief from the pain, reduction of inflammation, protection of articular structure, maintenance of function and control of systemic involvement. Over

the decades or even today, conventional treatment available for the treatment of rheumatoid arthritis are changed from traditionally used non-steroidal anti-inflammatory drugs (NSAIDs) or disease modifying antirheumatic drugs (DMARDs) to novel biological agents, like TNF monoclonal antibody [8]. The above-mentioned therapeutic agents used for the reduction of the inflammation and joint destruction but their long-term risks are still unknown. However, long-term risks of drugs includes gastrointestinal ulcers, cardiovascular complications, hematologic toxicity, nephrotoxicity, pulmonary toxicity, myelosuppression, hepatic fibrosis, stomatitis, cirrhosis, diarrhea, immune reactions, and local injection-site reactions. Moreover, higher costs and side effects which include high risks of infections and malignancies requires continuous monitoring [9]. Results are very dangerous. It worsen the condition of the patients. An aspect that has been largely ignored is that of the side-effects associated with these maintain the drug concentration within the therapeutic effective range needed for the treatment, it is mandatory to take this dosage forms several times a day, which results in fluctuation of drug levels. Over few decades, several technical advancements have been made, which resulted into new drug delivery techniques. Treatment of an acute and chronic illness have been made possible on development of novel systems by phyto-constituents or plant extracts.

HERBAL THERAPY FOR THE TREATMENT OF ARTHRITIS

Ayurveda, the oldest system of medicine in the Indian history for treatment of various ailments. It reveals that ancient Indians had a rich knowledge of medicinal value of different plants [10]. These system of medicines are on great demand in the developed and developing countries because of its wider biological and medicinal applicability's, higher safety margins and lesser costs [11]. Nature has blessed human with enormous wealth of herbal plants and as a source of therapeutic agents for the prevention and cure of various diseases [12] According to WHO, 80% population of the world uses herbal medicines for their primary health care needs. Herbal medicines will act as parcels of human society to combat disease from the dawn of civilization [13]. There is a number increasing evidences in the literature which give an idea that modern drug therapies (allopathic) suppresses the symptoms of disease and ignore the underlying disease processes. In comparison to allopathic system of medicines herbal formulations have more beneficial effects and less side-effects. Unfortunately, due to lack of evidences many doctors and patients are not even aware that these alternatives system exist.

Table 1: List of anti-arthritis plants

S.No.	Plant	Family	Reference
1.	*Alstonia scholaris* Linn.	Apocynaceae	14
2.	*Aloe vera* Linn.	Solanaceae	15
3.	*Withania somnifera* Linn.	Solanaceae	16
4.	*Boswellia serrata* Linn.	Burseraceae	17
5.	*Piper nigrum* Linn.	Piperaceae	18
6.	*Actaea racemosa* Linn.	Ranunculaceae	19
7.	*Uncaria tomentosa*	Rubiaceae	20-21
8.	*Zingiber officinale*	Zingiberaceae	22-23
9.	*Curcuma longa* Linn.	Zingiberaceae	24-25
10.	*Calotropis Procera* Linn.	Asclepiadaceae	26-27
11.	*Camellia sinensis* Linn.	Theaceae	28-29
12.	*Ficus bengalensis* Linn.	Moraceae	30-31
13.	*Cedrus deodara*	Pinaceae	32-33
14.	*Barringtonia racemosa* Linn.	Lecythidaceae	34-35
15.	*Mangifera indica* Linn.	Anacardiaceae	36-37
16.	*Tinospora cordifolia* Linn.	Menispermaceae	38-39
17.	*Ncytanthes arbortristis* Linn.	Oleaceae	40-41
18.	*Hemidusmus indicus* Linn.	Asclepiadaceae	42-43
19.	*Vitex negundo* Linn.	Verbanaceae	44-45
20.	*Cissampelos pareira* Linn.	Menispermaceae	46-47
21.	*Ammania baccifera* Linn.	Lythraceae	48-49
22.	*Justicia gendarussa* Linn.	Acanthaceae	50-51
23.	*Premna corymbosa* Rottl.	Verbenaceae	52
24.	*Terminalia paniculata* Roxb.	Combretaceae	53
25.	*Tripterygium wilford*	Celastraceae	54
26.	*Cleome gynandra* Linn.	Capparaceae	55-56
27.	*Leucas aspera* Linn.	Lamiaceae	57
28.	*Premna serratifoli* Linn.	Verbenaceae	58
29.	*Strychnos potatorum* Linn.	Loganiaceae	59-60
30.	*Saraca asoca* Roxb.	Caesalpiniaceae	61
31.	*Terminalia chebula* Retz.	Combretaceae	62
32.	*Sphaeranthus indicus*	Asteraceae	63
33.	*Ficus religiosa*	Moraceae	64

To overcome the limitations of the traditional drug delivery systems it is found that phyto-herbal based drug delivery system is a very good alternative for an effective therapy. The main purpose of developing alternative therapy is to increase efficiency and safety in the process of drug delivery and provide more convenience for the patients. This review article summarizes various plants or plants part as whole for the treatment of arthritis.

Number of scientific research and scholarly articles are referred throughout the paper for specification. These research or review articles are incorporated by reference herein to describe the art to which this review pertains. To collect the data which support this idea we performed a systematic review using PubMed, ACS, Science Direct, RSC, Springer, Cochrane, Ovid, Wiley online, Patent Search Google and MEDLINE databases. All English-language articles published in last 15 years. The data which are relevant would be considered. The botanical correct names and families were mentioned after verification from published literature and databases. The detailed information on research status of plants or plant parts having anti-arthritis properties was gathered from multiple references. **Table 1** showing the list of plants used for Rheumatoid arthritis (RA).

Above listed plants are available in the literature having anti-arthritis properties. The present review aims to update information on the phytochemistry and pharmacological activities of *Sphaeranthus indicus*.

SPHAERANTHUS INDICUS

Sphaeranthus indicus Linn belongs to family Asteraceae. It is a medicinally important plant used as folk medicine [65].

Boatanical Description

Taxonomy

Kingdom: Plantae
Division: Phanerogamae
Sub division: Angiospermae
Class: Dicotyledonae
Sub class: Gamopetalae
Order: Asterales
Family: Asteraceae
Genus: Sphaeranthus
Species: indicus

VERNACULAR NAMES

In different parts of India *S. indicus* is known by different names [66].
Sanskrit: *Mahamundi, shravani, tapasvini, mundi, hapus*
Marathi: *Barasavodi, gorakhmundi*
Oriya: *Murisa, bokashungi*
Panjabi: *Ghundi, khamadrus, mundibuti*
Telugu: *Boddatarupa, boddasoram*
Gujarati: *Bodiokalara, mundi, dorakhmundi*
Tamil: *Kottakaranthai*
Urdu: Malayalam: *Adakkamanian*
Hindi: *Gorakhmundi, mundi*
Bengali: *Chagulnadi, ghorkmundi*
Santal: *Belaunja*
Undari: *Mundi*
English: *East Indian globe thistle*

Fig1: Fruits of *Sphaeranthus indicus Linn*

Phytochemistry:

Carbohydrates, proteins, amino acid**s,** tannins, phenols, steroids, fats and oils are obtained from the dried roots and rhizome from the **m**ethanolic extract of *S. Indicus [67]*. 7α-hydroxyfrullanolide and three eudesmanolides, 11α, 13-dihydro-3α, 7α-dihydroxyfrullanolide, 11α, 13 - dihydro - 7α, 13-dihydroxyfrullanolide and 11α, 13-dihydroxy-7α-hydroxy-13-methoxyfrullanolide was isolated from the flower heads of *S. Indicus [68]*. An alkaloid sphaeranthine and an isoflavone 5,4-dimethoxy-3-prenylbiochanin 7-O-β-galactoside, sesquiterpenes and a new flavone glycoside were isolated from *S. Indicus [69]*. Ocimene, α-terpinene, methyl-chavicol, α-citral, geraniol, α-ionone, β-ionone, δ-cadinene, p-methoxycinnamaldehyde and an alkaloid sphaeranthine are obtained from the stem distillation of whole herbs. And the alcoholic extract of powdered drug contains stigmasterol, β-sitosterol, hentriacontane, n-triacontanol, sesquiterpene lactone, sesquiterpine glycoside, sphaeranthanolide, flavone and isoflavone glycosides [70].

Table 2: Pharmacological properties of *S. Indicus*

S.No.	Pharmacological properties	Reference
1	Anxiolytic activity	71
2	Analgesic and antipyretic activity	72
3	Antioxidant activity	73
4	Antihyperlipidemic activity	74
5	Antimicrobial activity	75
6	Hepatoprotective activity	76
7	Immunomodulating activity	77
8	Wound healing activity	78
9	Psychotropic activity	79
10	Bronchodialatory activity	80
11	Anti-macrofilaricidal activity	81
12	Anti-allergic activity	82
13	Antidiabetic activity	83

1. Anxiolytic activity: Ambavade et al., in 2006 reported anxiolytic activity of flowers of *Sphaeranthus indicus.* In this study, 10 mg/kg of petroleum ether extract, 10 mg/kg of alcoholic extract and 30 mg/kg of water extract resulted in prominent anxiolytic activity in the mice. Petroleum ether extract (10 mg/kg) resulted in more prominent anxiolytic activity in the EPM and OFT than ethanolic or water extracts, but was less than that produced by diazepam (1 mg/kg) [71].

2.

Hydroalcoholic extract of *Sphaeranthus indicus plants* 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 [84].

3. Analgesic and antipyretic activity: Nanda et al., 2009 reported analgesic and antipyretic activity of *Sphaeranthus indicus* plants. The different extracts at (200mg/kg) and (400mg/kg) dose were subjected to analgesic and antipyretic activity. The petroleum ether, chloroform and ethanol extracts showed significant analgesic activity in both doses ($p<0.001$ & $p<0.01$) from 1 h onwards as compared to the standard drug diclofenac sodium. The chloroform and ethanol extracts showed potential significant antipyretic activity ($p<0.05$) from 1 hour onwards where as aqueous extracts exhibit activity from 2 h onward as compared to the standard drug paracetamol amongst various extracts [72].

Ali et al., 2012 reported the anti-inflammatory and analgesic activities of Sphaeranthus indicus on albino mice and rat of either sex. In this study, the ethanolic extract of S. indicus in doses of 300 and 500 mg/kg was used. The analgesic activity was tested against acetic acid induced writhing response using albino rats. Result of the study shows that at the end of one hour the inhibition of paw edema was 42.66 and 50.5% respectively and the percentage of protection from writhing was 62.79 and 68.21 respectively [85]

4. Antioxidant activity: The free radical scavenging potential of the plant was studied by using different antioxidant models of screening. 1,000 µg/ml of ethanolic extract 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. 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 [73].

MuraliKrishna et al., in 2013 reported the antioxidant activity of methonolic extract of *Sphaeranthus indicus.* Antioxidant activity was conducted by using different reported methods i.e. DPPH, hydroxyl radical, nitric oxide, superoxide anion and hydrogenperoxide. Extracts of flowers and leaves showed highest scavenging activity at 150 µg/ml [86].

5. Antihyperlipidemic activity: Hyperlipidemia at the dose of 500 mg/kg/day p.o. for 8 days in rats were investigated. The extract effectively suppressed the hyperlipidemia by decreasing total cholesterol, triglyceride, LDL and very low density lipoprotein (VLDL); a significant increase in the level of high-density lipoprotein was observed after treatment with *S. indicus* extract [74].

6. Antimicrobial activity: Antimicrobial activity of alkaloidal and nonalkaloidal fractions of alcoholic extract of flowers has also been reported [87]. *Sphaeranthus indicus* L. were tested against the uropathogenic organisms *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabils*, and *Pseudomonas aeroginosa*. From the above results it can be concluded that plant *Sphaeranthus indicus* extracts have great potential as antimicrobial compounds against micro-organisms and that they can be used in the treatment of infectious diseases caused by resistant micro-organisms [88].

7. Hepatoprotective activity: Ethanolic extract of aerial parts of *S. indicus* L. in the doses 200 and 300 mg/kg of body weight 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 [89].

Aqueous extract of root of *S. indicus* L. at the dose of 200 and 300 mg/kg bodyweight 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) [90].

The protective effect of methanolic extract of *S.indicus* Linn. (MES) against CCl_4induced hepatotoxicity was studied in animal models. It showed a significant protective effect by lowering the serum aspartate aminotransferase, alanine aminotransferase and alkaline phosphatase (ALP) [91].

8. Immunomodulating activity: Shekhani in 1990 reported that *S. indicus* have immunostimulant activity. It was tested by Jerne plaque assay method. This compound was found to be an immune modulator [92].
The bioactive fraction exhibited dose dependent increase in immoral and cell-mediated immunity and offers protection against immunosuppression induced by the cytotoxic agent cyclophosphamide [93].

9. Wound healing activity: Jha et al., 2009 reported that the ointments comprising of various percentage of alcoholic extract of *S. Indicus* flower head has wound healing activity. It was tested for protection against microbial invasion by providing better tissue formation [94].

10. Bronchodialatory activity: Sarpate in 2009 reported bronchodialatory activity of *S. Indicus.* The methanolic extract and its fractions exhibited significant protection against bronchospasm induced by histamine in guinea pigs [95].

11. Antidiabetic activity: Extracts of *S. indicus* were screened for activity against alloxan induced hypoglycemea in Wistar rats. The oral administration of flower head extract at doses of 200 mg/kg lead to a significant blood glucose reduction [96].

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 [97].

12. Anti-inflammatory activity: The extract of *S. indicus* at different doses (100, 200 and 400 mg/kg, p.o.) exhibited dose dependent and significant anti-inflammatory activity in acute and chronic condition [98].
The aqueous extract obtained from the root of *S. indicus* was found to be moderately active in down-regulating *P. acnes* induced TNF-α and IL-8 production [99].

13. Anti-arthritic activity: The petroleum ether extract of the flowers of *S. indicus* in the doses of 10, 30 and 100 mg/kg/day p.o. was investigated against complete Freund's adjuvant induced arthritis in laboratory rats. The dose of 100 mg/kg/day p.o. showed significant anti-arthritic activity [100].

CONCLUSION

S. indicus Linn. is widely distributed throughout India. The plant appears to have a broad range of activities on several ailments. Various parts of the plant have been explored for the treatment of different diseases. Presently, herbal medicines is an increasing interest throughout the accompanied by increased laboratory investigation into the pharmacological properties of the bioactive ingredients and their ability to treat various diseases. These plants are our heritage with the global importance in terms of economic. Medicinal plants also play an important role in the lives of rural people, particularly in remote parts of developing countries with few health facilities. Although scientific studies have been carried out on a large number of Indian botanicals and number of drugs have entered the international market through exploration of ethnopharmacology and traditional. Efforts are therefore needed to establish and validate evidence regarding safety and practices of Ayurvedic medicines for the treatment of arthritis.

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