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A COMPREHENSIVE REVIEW ON TREATMENT OF RHEUMATOID ARTHRITIS USING VARIOUS HERBAL PLANTS

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ABSTRACT: The autoimmune illness rheumatoid arthritis is a chronic, progressive, and debilitating condition that causes systemic inflammation of the joints and damages the cartilage and bone around the joints. It is a systemic illness, which means that it may impact all of the body's internal organs, including the heart, lungs, and eyes. Despite the fact that many synthetic medications are utilised as the conventional treatment for rheumatoid arthritis, many treatments have side effects that might undermine the therapeutic approach. Unfortunately, there is currently no proven medical cure for rheumatoid arthritis. Instead, modern medicine can only alleviate the symptoms of this condition, such as joint discomfort and inflammation. It is possible to employ herbs and plants in a variety of ways to treat joint pain and inflammation. The ability of several medicinal plants to treat rheumatoid arthritis has been demonstrated. So, for the treatment of rheumatoid arthritis, plants and plant products with notable benefits are utilised. The focus of the current review is on medicinal herbs with anti-rheumatoid arthritis action.

***Index Terms*: Systemic inflammation, Autoimmune disease, Herbal plants, Rheumatoid arthritis.**

INTRODUCTION:

Rheumatoid arthritis is a systemic condition that manifests as rheumatoid nodules, vasculitis, ocular inflammation, and cardio pulmonary disease1. There is no genetic component to rheumatoid arthritis. According to researchers, some people have genes that predispose them to the illness. Rheumatoid arthritis does not necessarily occur in those who carry these genes. The genes are often activated by a "trigger," such as an infection or environmental influence. The immune system reacts incorrectly when the body is exposed to this trigger. The immune system starts to create chemicals that fight the joint rather than protecting it. That's what could cause rheumatoid arthritis to appear. It is an autoimmune illness, which means that healthy tissues are wrongly attacked by the body's immune system. In healthy joints, the lining is very thin and contains few blood vessels, but in joints affected by rheumatoid arthritis, the lining is thick and densely packed with white blood cells. Interleukin-1 (IL-1) and tumour necrosis factor alpha (TNF-alpha), which are released by the white blood cells, cause discomfort, joint swelling, and joint degeneration.

These cytokines trigger the secretion of proteoglycan- and collagen-degrading enzymes by synovial fibroblasts and chondrocytes in the surrounding articular cartilage, which results in tissue degradation and the production of RANK ligand (RANKL), a factor in the aetiology of chronic arthritis.4. The synovium begins to multiply and spread, a condition known as pannus, as a result of the release of numerous cytokines and inflammation-related mediators. The following stage, fibrosis, results in a lack of joint motion and is referred to as ankylosis.

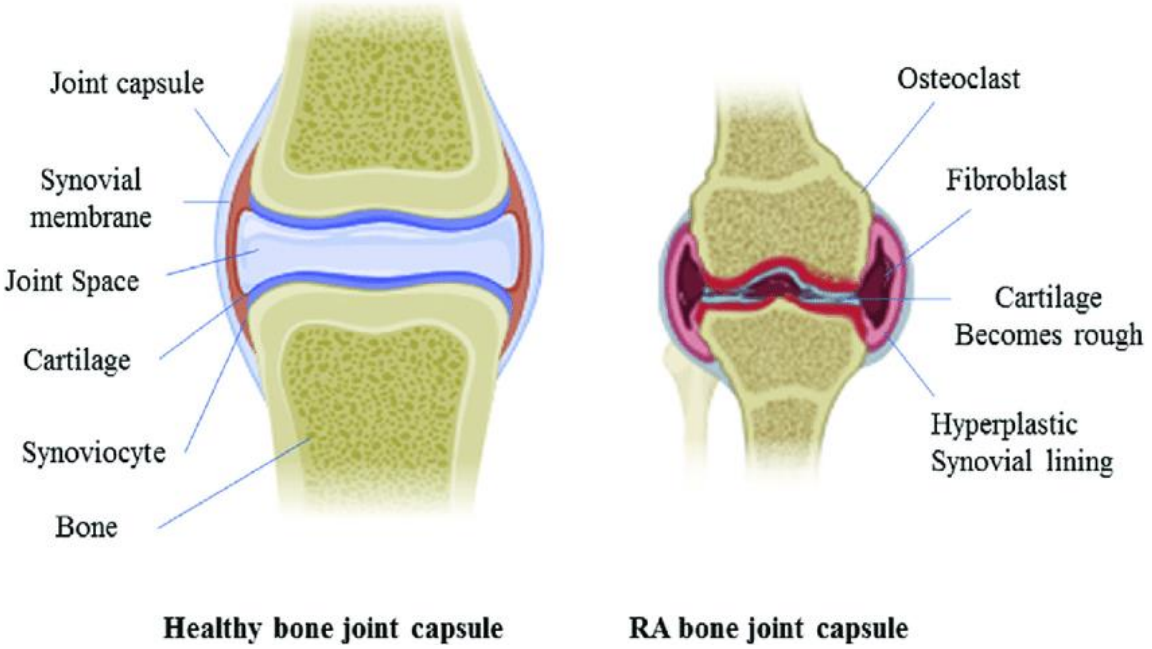

Fig. 1: Difference between normal joint lining and rheumatoid joint lining

The cartilages degrade and the synovial membrane thickens in rheumatoid arthritis. The synovial membrane encroaches on the joint space, causing swelling and discomfort while moving the affected joint.

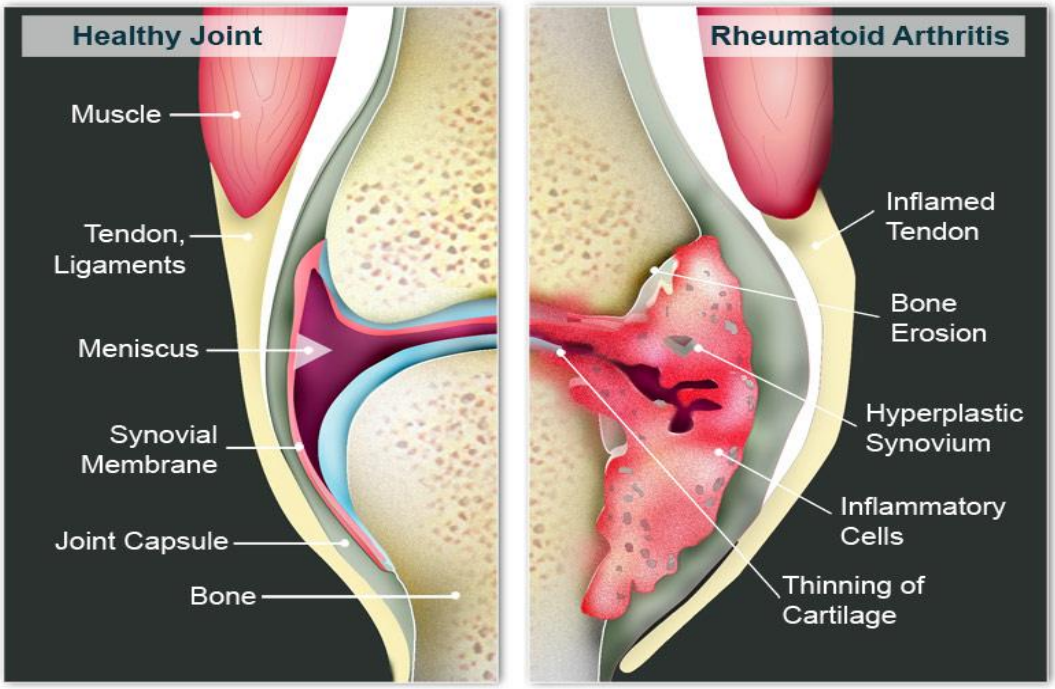

Fig.2: Rheumatoid arthritis joint

Joint discomfort, swelling, morning stiffness in the joints, lack of sleep, weariness, weight loss, and feeling like you have the flu are other symptoms. Rheumatoid factor, which are aberrant antibodies (IgG) found in blood, is used to diagnose rheumatoid arthritis. These react with the antigen to create an antigen-antibody complex, which causes the synovial membrane to become inflamed and painful. According to the American College of Rheumatology, the diagnosis must meet at least four of the following seven criteria. 6, 7

• Morning stiffness which lasts for at least an hour around the joint

• Three or more joints with arthritis for at least six weeks

• Hand joints have had arthritis for at least 6 weeks.

• Arthritis that has lasted at least six weeks on both sides of the body

• Skin-deep rheumatoid nodules

• Blood tests reveal the presence of rheumatoid factor

• X-ray results showing rheumatoid arthritis

Affecting around 1% to 2% of the world's population and committing attacks three times as many women than males. One of the most prevalent forms of such circumstances for which billions of dollars are paid annually the therapy and study.

Man was entirely dependent on medicinal plants before the invention of synthetic medications to treat illness. Every member of this civilization is aware of the healing properties of plants. Folk remedies were mostly generated from natural product extracts in the nineteenth and preceding centuries, especially those that were obtained from plant species. However, physiologically active organic compounds started to be extracted in reasonably pure form for medical application in the later half of the nineteenth century. Salicylic acid, the precursor to aspirin, for instance, was discovered from willow bark in 1874. There are several such instances. There are several synthetic medications which are utilised as the conventional treatment for rheumatoid arthritis, but these medications include side effects that might hinder the therapeutic treatment, increasing the likelihood that herbal plants will be employed instead. The medicinal plants which are utilised to treat rheumatoid arthritis are the focus of the current review.

Medicinal herbs utilised to treat rheumatoid arthritis include the following:

Here are some examples of plants with anti-rheumatoid arthritis characteristics:

1. **Myrobalan**

Botanical Nomenclature: Terminalia chebula Retz.

Vernacular Name: Haritaki

Family: Combretaceae

Deciduous tree Terminalia chebula Retz. It is indigenous to southern Asia, ranging from Sri Lanka, Malaysia, and Vietnam in the south to India and Nepal in the east, as well as southwestern China. It has phytochemical components such anthraquinone, resins, gallic acid, tannic acid, chebulinic acid, and sinnosides. It is utilised for cutaneous fungus infections, leucorrhea, and persistent ulcers. It serves as an antioxidant and neuroprotectant. The Terminalia chebula Retz. hydro-alcoholic extract has anti-arthritic action in full Freund's adjuvant or formaldehyde-induced arthritis. The modulatory impact of Terminalia chebula Retz. on the expression of pro-inflammatory cytokines in the synovium is responsible for the plant's anti-arthritic activity8, 9, and 10.

According to the review above, several plants have anti-rheumatoid arthritis characteristics that are equivalent to those of synthetic antidepressants. We can employ herbal based preparations for the therapy of anti-rheumatoid arthritis as they were lesser negative effects than synthetic antidepressants, which have significant unwanted effects. According to the review above, several plants have anti-rheumatoid arthritis characteristics that are equivalent to those of manufactured antidepressants. We can employ plant-based preparations for the therapy of anti-rheumatoid arthritis as they have lesser negative impacts than manufactured antidepressants, that have significant unwanted effects.

Fig. 3: *Terminalia chebula Retz.*

2. **Ashok**

Botanical Nomenclature: Saraca asoca Roxb.

Vernacular Name: Asok, Osaka

Family: Caesalpiniaceae

In sporadic sites throughout India's northern plains, Saraca asoca Roxb. may be found in the foothills of the central and eastern Himalayas. Carbohydrates, tannin, flavonoids, saponin, glycosides, proteins, and steroids are all present, according to preliminary phytochemical methanolic and ethanolic extracts. It is employed as an oxytoxic, uterotonic, spasmogenic, and anti-tumor agent. In rats given an adjuvant to develop arthritis, Saraca asoca Roxb. methanol extract decreased the thickness of the paws 11,12.

Fig. 4: *Saraca asoca Roxb*

3. Aloe vera Linn.

Botanical Nomenclature: Aloe barbadensis

Vernacular Name: Curacao aloe, Lily of the desert

Family: Liliaceae

Aloe barbadensis is grown in several regions of India, including the north-west Himalayan area, as well as in Europe. One of the most significant plants utilised in traditional medicine has been aloe vera. Aloe vera plants contain the compounds anthraquinone, anthracene, cinnamic acid, and anthranilic acid that give it its action. Aloe vera is used to treat a range of skin conditions, including eczema, minor scrapes, insect stings, bruises, and poison ivy. It is also utilized in the purification of blood, drug reducing swollen, diuretic and fever reducer. It also possesses antibacterial and antifungal qualities. Aloe vera's anti-arthritis properties are a result of the chemical anthraquinone. Aloe vera is a potent anti-inflammatory and immune system stimulant. Aloe vera extract used topically reduces swelling and arthritis in Sprague Dawley rats with adjuvant-induced arthritis 13, 14, 15.

Fig. 5: *Aloe barbadensis*

4. Ashwagandha

Botanical Nomenclature: Withania somnifera Linn.

Vernacular Name: Winter cherry, withania root

Family: Solanaceae

Ashwagandha, commonly referred to as Indian ginseng, is a very old plant. The roots of ashwagandha have been used in Ayurveda and Unani, two traditional medical systems in India. The subtropical states of Rajasthan, Punjab, Haryana, Uttar Pradesh, Gujarat, Maharashtra, and Madhya Pradesh are among the arid areas where it may be seen growing. Alkaloids and steroidal lactones are thought to be responsible for the root's pharmacological effect. Withanine, withanine, pseudo-withanine, tropine, pseudo-tropine, somniferine, and somnine are the most prevalent alkaloids. Sitoindoside-7 and Sitoindoside-8 are two acyl glucosides that have been isolated from roots. The herb has historically been used to treat asthma, ulcers, sleeplessness, and senile dementia as well as an aphrodisiac, liver tonic, and anti-inflammatory. The utilization of Ashwagandha for anxiety, neurological problems, inflammation, and Parkinson's disease is supported by clinical studies and animal research. The consumption of ashwagandha may stop or slow the development of cancers in people. For a variety of health issues like ageing, anaemia, arthritis, tiredness, sports fitness, and stress problems, it helps to provide gradual, long-lasting improvements. In adjuvant-induced arthritic rats, oral treatment of Withenia somnifera Linn., root powder has an anti-arthritic effect 16, 17.

Fig.6: *Withania somnifera Linn.*

5. Shallaki

Botanical Nomenclature: Boswellia serrata Linn.

Vernacular Name: Boswellia/Indian Frankincense

Family: Burseraceae

In India, Northern Africa, and the Middle East, you may find the medium-sized to giant branching tree known as Boswellia serrata Linn. It may be found in Gujarat, Madhya Pradesh, and Bihar in India. Peeling away sections of boswellia bark reveals gummy-oleo resins. The resin part of it includes boswellic acid, which has been proven to have anti-inflammatory, anti-atherosclerotic, and anti-arthritic properties. Astringent, stimulant, expectorant, antiseptic, juvenomimetic, anti-atherosclerotic, analgesic, and sedative are further uses for the extract of these gummy oleo resins. It is also known to restore the integrity of damaged or spasmed joints' blood vessels. Terpenoids, carbohydrates, and volatile oil are the primary components of boswellia. By turning off the pro-inflammatory cytokines and mediators that start the process, boswellia serrata extract has natural anti-inflammatory effects in areas where chronic inflammation is prevalent. While Boswellia serrata Linn. decreases the breakdown of glycosaminoglycan production, non-steroidal anti-inflammatory medicines (NSAIDs) can speed up the damage to the articular cartilage in arthritic situations. 18, 19, 20

Fig.7: *Boswellia serrata Linn.*

6. Black pepper

Botanical Nomenclature: Piper nigrum Linn.

Vernacular Name: Pepper

Family: Piperaceae

In South India, black pepper is both native to and grown there. Additionally, it is grown in Malaysia, Sri Lanka, Indonesia, Brazil, and Brazil. India is the top country for drug cultivation. Alkaloid piperine, volatile oil, spicy resins, piperidine, and starch are all components of pepper. As an aromatic, stimulant, stomachic, and carminative, it is utilised. Gastric juice secretion is increased by it. It also makes some medications more bio-available. extracted piperine from black pepper. In cases of carrageenan-induced acute paw arthritis, piperine given orally at doses of 20 and 100 mg/kg/day for eight days reduces arthritic symptoms 21, 22.

Fig.8: Piper nigrum Linn.

7. Black cohosh

Botanical Nomenclature: Actaea racemosa Linn.

Vernacular Name: Black snakeroot, bugwort

Family: Ranunculaceae

Smooth perennial herbaceous plant known as black cohosh. From the far south of Ontario to middle Georgia and west to Missouri and Arkansas, it is indigenous to eastern North America. Native Americans have traditionally employed black cohosh's roots and rhizomes as medicines. Acteina, cimigoside, steroidal terpenes, and 27-deoxyactein are among the chemical substances that have been taken out of the black cohosh plant. Salicylic acid, formononetine, and tannins are other components. It is used to treat snake bites, arthritis, diarrhoea, dieresis, dyspepsia, renal issues, and as an insect repellent. Menopause is one of the many female health issues that it is used to address. Black cohosh reduces the inflammation that arthritis causes 26, 27, 28.

Fig. 9: *Actaea racemosa Linn.*

8. Ginger

Botanical Nomenclature: Zingiber officinale

Vernacular Name: Ginger root

Family: Zingiberaceae

One of the most beneficial herbal supplements is ginger. It is grown throughout South East Asia, the Caribbean, Africa, Australia, Mauritius, Taiwan, and India despite being a South East Asian native. India produces more than 30% of the total. Volatile oil, starch, fat, fibre, inorganic material, and lingering moisture make up ginger. Monoterpine, sesquiterpine, oxygenated mono, and sesquiterpenes are all found in ginger oil. Ginger is utilised as a stimulant, flavouring agent, fragrant, carminative, and stomachic. It is used to treat diarrhoea, vomiting, and nauseousness. Additionally, it has anti-inflammatory, antiseptic, anticancer, antifungal, and anti-microbial properties. One of the powerful treatments for arthritic joint pain that doctors advise is ginger extract. Sesquiterpenoids, containing (-) zingiberene, are the primary components. Its anti-inflammatory properties are attributed to sesquiterpene lactones (SLs), which are natural compounds 29, 30, 31, 32.

Fig.10: *Zingiber officinale*

9. Turmeric

Botanical Nomenclature: Curcuma longa Linn.

Vernacular Name: Turmeric root, Indian saffron

Plant family: Zingiberaceae

For its rhizome, turmeric is grown in India, China, Sri Lanka, Indonesia, Jamaica, and Peru. There are curcuminoids, volatile oils, resins, starch grains, and resins in turmeric. Curcumin is the primary ingredient of curcuminoids. Curcumin, a natural substance found in the rhizomes of the Curcuma longa plant, has proven to have anti-inflammatory properties 33. It is useful for things like neuroprotection, hepatoprotection, and wound healing. It possesses anticancer, antispasmodic, antibacterial, and antimutagenic properties. In both the acute and chronic stages of arthritis, daily intraperitoneal treatment of the modest dosage of pure curcuminoids reduced joint swelling. 34, 35, 36.

Fig.11: Turmeric rhizome

10. Milkweed

Botanical Nomenclature: Calotropis procera Linn.

Vernacular n name: Giant Swallow Wort

Family: Asclepiadaceae

Calotropis procera Linn. is a species of flowering plant that is indigenous to North Africa, Tropical Africa, Western Asia, South Asia, and Indochina. It is a member of the dogbane family Apocynaceae. It has been noted that several portions of this plant contain anti-inflammatory, analgesic, antioxidant, and antifungal properties. In several animal models, this plant's latex has strong anti-inflammatory properties. The petroleum extract from latex has strong antibacterial activity 37. The entry of inflammatory cells and the development of edoema brought on by different inflammagens have both been demonstrated to be inhibited by latex and its methanolic extract. Additionally, it enhances locomotor activities in rats with experimentally induced monoarthritis. Roots of Calotropis Procera Linn. exhibit anti-inflammatory effect in cotton pellet-induced granuloma and carrageenan-induced paw edoema models at dosages of 180 mg/kg (methanol extract) and 200 mg/kg (other extracts) 38, 39, 40.

Fig.12: *Calotropis procera Linn.*

11. Green tea

Botanical Nomenclature: Camellia sinensis Linn.

Vernacular Name: Green tea extract, Chinese tea

Family: Theaceae

A little tree or shrub that is evergreen is called Camellia sinensis Linn. Originally from mainland China, South and Southeast Asia, Camellia sinensis Linn. is currently grown in tropical and subtropical areas all over the world.

Polyphenols (catechins and flavanols) are the Camellia sinensis Linn. plant's active ingredients. Caffeine and essential oils are additional ingredients. Green tea contains many catechins, but (-) epigallocatechin, a strong antioxidant, is the most significant. The inflammatory mediators COX-2, IFN, and TNF were significantly inhibited in the arthritic joints of mice given green tea, which was consistent with the decreased collagen-induced arthritis incidence and severity. 41, 42, 43.

Fig.13: *Camellia sinensis Linn*

12. Deodar cedar

Botanical Nomenclature: Cedrus deodara

Vernacular name: Marathi Deodar, Devadaru, Cedar

Family : Pinaceae

Cedrus deodara is a native of the western Himalayas, which may be found in western Nepal, south westernmost Tibet, eastern Afghanistan, northern Pakistan, and north-central India (Himachal Pradesh). Since the beginning of time, Cedrus deodara wood has been utilised in Ayurvedic medicine to treat inflammation and rheumatoid arthritis 44. Alkaloids, flavonoids, glycosides, phenolic

compounds, saponins, and proteins make up the majority of the ingredients. The herb Cedrus deodara has been used to treat rheumatoid arthritis and inflammation. As indicated by the paw swellings on the injected limbs in fully adjuvant-induced arthritis in rats, Cedrus deodara substantially reduced the polyarthritis phase 45, 46.

Fig.14: *Cedrus deodara*

13. Barringtonia

Botanical Nomenclature: Barringtonia racemose Linn.

Vernacular Name: Powder-puff tree

Family: Lecythidaceae

In the Ryukyu Islands, several Polynesian islands, the Indian Ocean, Sri Lanka, Malaysia, Thailand, Laos, southern China, and northern Australia are among the places where Barringtonia racemosa Linn. may be found in coastal swamp woods and on the borders of estuaries. Gallic acid, dihydromyticetin, bartogenic acid, stigmasterol, and 3, 3'-dimethoxyellagic acid are among the chemical components found in this plant. It possesses anti-inflammatory, antioxidant, and anti-microbial properties. It is used to treat rheumatoid arthritis, and bartogenic acid is the active ingredient responsible for its action (BA). Complete Freund's Adjuvant (CFA) causes haematological disturbances and primary and secondary arthritic lesions in rats that BA protects them against 47, 48, 49.

Fig.15: *Barringtonia racemose Linn.*

14. Tinospora gulancha

Botanical Nomenclature: Tinospora cordifolia Linn.

Vernacular name: Guduchi

Family: Menispermaceae

Tinospora cordifolia Linn. is found in tropical China and the Indian subcontinent. Tinosporidine, columbin, tinosporide, tinosporaside, cordifolide, cordifol, clerodane furano diterpene, diterpenoid furano lactone tinosporidine, and b-sitosterol are the main components. The plant is used to strengthen the body's defences against illness and the immune system. There are antiperiodic, antispasmodic, anti-inflammatory, and antipyretic effects in the bitter taste present. In order to treat rheumatoid arthritis, it is utilised. In rats with arthritis caused by collagen, paw volume is reduced at a dosage of 100 mg/kg 50, 51.

Fig.16: *Tinospora cordifolia Linn.*

15. Night jasmine

Botanical Nomenclature: Ncytanthes arbortristis Linn.

Vernacular name: Coral Jasmine

Plant family: Oleaceae

A tiny tree or shrub, Ncytanthes arbortristis Linn. It is found throughout southern Asia, from Nepal and northern Pakistan to northern India. Benjoic acid, mannitol, b-amyrin, b-sitosterol, and the benjoic ester of longanin, nycthanic acid, are all present in it. In addition to being used as a laxative, diuretic, and diaphoretic, it is also utilized to cure rheumatoid arthritis and to get rid of roundworm and threadworm in children. The rat hindpaw acute inflammatory edoema caused by carrageenin, formalin, histamine, 5-hydroxytryptamine, and hyaluronidase was prevented by the leaves of Nyctanthes arbortristis Linn.

Formaldehyde-induced arthritis is considerably reduced in both its acute and chronic stages. Additionally, it was shown that Nyctanthes arbortristis Linn. inhibits the inflammation brought on by immunological techniques, such as Freund's adjuvant arthritis 52, 53.

Fig.17: *Ncytanthes arbortristis Linn.*

16. Chhota halkusa

Botanical Nomenclature: Leucas aspera Linn.

Vernacular name: Gophaa, Tumba, Dronapushpi

Family: Lamiaceae

A tiny, erect, branching annual plant is called Leucas aspera Linn. It is found all throughout India, from the Himalayas to Ceylon.

The plant has historically been employed as a pesticide and antipyretic.

It has been demonstrated to have a variety of pharmacological effects in terms of medicine, including antifungal, antioxidant, antibacterial, antinociceptive, and cytotoxic action. It includes nicotine, sterols, glucoside, diterpenes, oleanolic acid, ursolic acid, triterpenoids, and b-sitosterol. Leucas aspera Linn. ethanolic extract has anti-rheumatoid arthritis activity in Complete Freund's adjuvant-induced arthritis 54, 55.

Fig.18: *Leucas aspera Linn.*

17. Headache tree

Botanical Nomenclature: Premna serratifoli Linn.

Vernacular name: Malbau

Family: Verbenaceae

Premna serratifoli, a large shrub or small tree, was named by Linn. Premna serratifoli Linn., which grows widely in tropical and subtropical Asia, Africa, Australia, and the Pacific coasts and islands. It is spreading over India in wild planes and flourishing there. Alkaloids, flavonoids, tannins, glycosides, steroids, and phenolics are among its constituents. It is employed to treat tumours, indigestion, constipation, fever, arthritis, and nerve discomfort. The ethanol extract reduced rat paw edoema in Freud's adjuvant-induced arthritic albino rats 56, 57.

Fig.19: *Premna serratifoli Linn.*

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