



# Indigenous Medicinal Plants Based Remedies in Management of Arthritis by *Irula* Tribals of Tamil Nadu – A Comprehensive Review

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## Abstract

Arthritis is a chronic autoimmune illness that causes joint dysfunction, and antibodies directed against self-neoepitopes. Globally more than 350 million peoples have arthritis and it is the second most rheumatological problem with a prevalence of 22% to 39% in India reported by World Health Organization. Considering the numerous synthetic therapeutic strategies that target immune cells and cytokines but drug administration of allopathic anti-arthritic medicaments is still difficult because of the persistent hazardous consequences. Presently, the use of medicinal plants as a trustworthy source of new therapy has become more popular due to the numerous side effects of synthetic drugs. One of the most significant foes in modern medicine, non steroidal anti-inflammatory drugs creates huge impact on human health, high influence on living quality and has significant economic implications. National Biopharma Mission primarily focus on the development of Bio-Therapeutics to achieve the sustainable health. According to the estimations based on various literatures, *Fabaceae* is the most significant herbal family which includes a vast range of plants having biological and therapeutic uses. This study presents the extensive knowledge about arthritis, immunomodulatory mechanism and existing drugs and therapies. The analgesic activity, potential active chemicals from the *Fabaceae* genus, as well as potential mechanisms of action for these plants are studied. The scientific information and evidences presented in this review paper is crucial for determining the precise effects of *Fabaceae* plants on pain modulation especially for arthritic pain and anti-inflammatory properties. This could be used to separate potentially active compounds from some of these medicinal plants in the future and create synthetic therapeutics.

**Keywords:** Anti-inflammatory, Arthritis, *Fabaceae*, Painkiller, Phytochemicals, Therapies

## 1. Introduction

Pain is the predominant symptom of many clinical disorders. It is associated with neurological and musculoskeletal issues, as well as with an individual's quality of life and general functioning. Pain can be classified as acute or chronic. Acute pain can be caused by inflammation, tissue damage, a wound, a disease, or a post-surgical condition. It usually lasts a few days to a

week, and the pain goes away after the underlying reason is addressed or remedied<sup>1</sup>. Chronic pain is pain that lasts longer than the typical recovery period or develops in association with a chronic health condition such as arthritis. Pain mechanisms are roughly classified into three types: nociceptive pain is caused by the activation of sensory nerve fibres that respond to potentially harmful stimuli (nociceptors) and is classified based on the mode of noxious stimulation. Neuropathic

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pain is caused by any illness or damage to any part of the nervous system, whereas Nociceptive pain is characterized by nociception changes but no evidence of true or threatening tissue injury, disease, or damage to the somatosensory system<sup>2</sup>. Nociceptive joint pain is most typically felt in the joint area, which is more likely utilized for basic routines and activities to perform a task. It can substantially impair joint function and impede an individual's ability to do essential survival tasks. Our immune system plays an important role in our human body. An overactive immune system can lead to fatal diseases due to a variety of hypersensitive or allergic reactions that cause massive disruptions; loss of natural capability to self from non-self, resulting in an immune reaction against our body cells and tissues known to be harmful<sup>3</sup>. Autoimmune disease, Arthritis is the second most frequent autoimmune illness, and it is regarded as a serious problem in the medical world due to its uncertain aetiology. Arthritis can affect people of any age, although it is most common between the ages of 25 and 50, with a higher risk between the ages of 40 and 50<sup>4</sup>. In addition to load-bearing joints, arthritis affects the peri-articular bone structure, synovial joint wall, and surrounding supporting connective tissue elements<sup>5</sup>. The worsening state of arthritis needs therapy as well as more financial concern for long-term treatment. Given the aforementioned, innovative therapeutic agents with great efficacy and low side effects are now more affordable, resulting in improved health, which is a primary aim in modern medicine<sup>6</sup>.

The use of plants as analgesic agents in folk medicine is a centuries-old practice that precedes contemporary medical research. Almost 7000 plant species are used ethnomedicinally for a range of ailments worldwide<sup>7</sup>. In recent decades, research into novel analgesic combinations derived from a diverse array of medicinal plant assets has expanded. The following data assures the development of novel therapeutic medications capable of suppressing, alleviating, or displaying pain alleviation. Plants are a rich natural supply of recognized chemicals that are essential for the development of novel medications. Because they are cost-effective and have fewer side effects, detailed evaluations of the effectiveness of plant-based medications used in folk medicine have shown considerable results<sup>8</sup>. The *Fabaceae* family, one of the most significant herbal groups, has a diverse range of plants with medicinal and

biological use. *Fabaceae* belongs to Kingdom: Plantae, Division: Magnoliophyta, Class: Magnoliopsida, and Order: Fabales<sup>9</sup>.

Medicinal plants of *Fabaceae* have anti-nociceptive, anti-atherogenic, anti-inflammatory, and anti-osteoporotic properties. They can also fight diabetes and cancer and have the potential to act as chemopreventive and neuroprotective, laxative, sedative, diuretic, digestive, and anti-nephritic. *Acacia*, *Albizia*, *Dichrostachys*, *Elephantorrhiza*, *Mimosa*, *Aspalathus*, *Erythrina*, *Indigofera*, *Lotononis*, *Pterocarpus*, *Afzelia*, *Bauhinia*, *Burkea*, *Caesalpinia*, *Cassia*, *Colophospermum*, *Peltophorum*, *Schotia*, *Senna* are well-known genera in this family<sup>10</sup>. The objective of present review to undertake a literature survey for the unique implications of the *Fabaceae* family species which are locally available as a same time predominantly used by various ethnic communities of India for arthritis and thereby contribute to ongoing research for finding new possible anti-arthritic drugs.

## 2. Types of Arthritis

The most common type of arthritis is osteoarthritis, which is a degenerative joint disease characterized by damage to the articular cartilage, changes in subchondral and minuscule bones, synovitis, and capsular thickening, and it primarily affects weight-bearing joints<sup>4</sup>. Rheumatoid arthritis is a systemic autoimmune disease that causes persistent pain, inflammation, and tissue loss in multiple joints<sup>11</sup>. Ankylosing spondylitis is a kind of inflammatory arthritis that affects the major joints and spine. Reactive arthritis, often known as Reiter's syndrome, is a condition that causes inflammation (redness and swelling) in many parts of the body. It is generally caused by an infection and cures in a few weeks with no long-term consequences<sup>12</sup>. The most well-known kind of chronic or long-term arthritis that affects young individuals is Juvenile Idiopathic Arthritis (JIA). JIA is a category of chronic disorders characterized by joint inflammation (arthritis), which can cause discomfort, edoema, stiffness, and loss of mobility in moving joints. JIAs differ in several ways, including the arrangement of joints involved and inflammation in locations other than the joints<sup>13</sup>. Other illnesses that can cause joint pain include Gout, a painful disorder in

which crystals from the body concentrate in the joint, producing extreme pain and swelling. The big toe is the most commonly affected part of the body. Bursitis is caused by misuse of joints and muscular strain. It is most frequently seen in the hip, knee, elbow, or shoulder<sup>14</sup>. The most common kind of lupus is systemic lupus erythematosus. SLE is an autoimmune illness in which the immune system attacks its tissues, causing widespread inflammation and tissue damage in the affected organs. It can cause damage to the joints, skin, brain, lungs, kidneys, and blood vessels<sup>15</sup>. In the Indian population, the prevalence of the two primary types of arthritis is roughly 22-39% for osteoarthritis and 5% for rheumatoid arthritis, respectively. Chronic joint pain can be caused by several conditions, the most prevalent of which are rheumatoid arthritis and osteoarthritis, which are more frequent in adults over the age of 55<sup>16</sup>.

### 3. Aetiology for the Most Common Type of Arthritis

Obesity is the primary cause of osteoarthritis. Obese people are more prone to joint pain as a result of the tension generated by their body weight. Poor health status of an individual with deficiency of vitamin D or lack of amino acid such as glucosamine plays a predominant role. The person's age may have a significant effect on Osteoarthritis (OA). The structural arrangement of joints exhibits abnormalities. Injured joints and joint hypermobility both contribute to OA<sup>17</sup>. Overloading joints owing to repeated impulse loading leads to decreased neuromuscular reflexes and poorly directed force, whereas underloading joints lead to OA. Ligamentous injury, endocrine illnesses like diabetes, inflammatory diseases like joint infections, hemochromatosis, and metabolic diseases (e.g., urate crystal deposits) can all contribute to OA. In menopausal women, a decrease in estrogen levels causes RA<sup>18</sup>.

The primary cause of rheumatoid arthritis is genetic susceptibility with a family history. Age is not a factor in RA, however, those between the ages of 40 and 60 are more prone to develop the disease. The degeneration of immune system tissues is a major cause of RA. Pain, swelling, cartilage, and bone degradation are the primary symptoms of RA, which

lead to lifelong disability. Although the exact etiology is uncertain, numerous studies propose that it is caused by a combination of genetic predisposition and being exposed to potentially hazardous elements such as viruses<sup>19</sup>. RA is a degenerative illness that causes continuing joint degeneration for the remainder of a person's life. There is no known cause of RA at this time. When a disease is discovered, therapy is provided to alleviate symptoms and reduce or stop disease development. Arthritis also has a substantial impact on people's life in terms of disability, health, and economic effects. Patients can continue working and caring for themselves with contemporary therapies, allowing them to live full lives<sup>20</sup>.

### 4. Epidemiology of Arthritis

According to WHO, persistent discomfort caused by Rheumatoid Arthritis (RA) affects the whole global population. According to the data, girls are three times more likely to get the condition than boys. According to the World Health Organisation, most individuals in industrialized nations will be unable to work full-time over the next ten years. Epidemiological studies in developing countries show a lower frequency of RA than in Caucasians<sup>6</sup>. RA is projected to have a median prevalence of 3.5 (range: 2.4-3.6). RA affects 0.16% of males and 0.75% of females in low- and middle-income countries. The prevalence of RA in India is 0.75% of the overall population, in which 0.28 to 0.7% is of rural peoples due to their overuse of joints compare to urban population. Some of these variables may increase the risk of RA, while others may prevent disease development. Men who smoke are three times as likely to acquire RA. Unbalanced hormone levels may contribute to the evolution of RA in women<sup>21</sup>. People with RA die at a greater rate than the general population. Life expectancy is decreasing by 3 to 10 years. Over the previous two or three decades, the increased mortality linked with RA has remained stable<sup>22</sup>.

### 5. Mechanism of Arthritis

Arthritis is caused by the dysregulation of pro-inflammatory enzymes and cytokines, which results in higher amounts of prostaglandins on synovium, as well

as nitric oxide and leukotrienes. In addition, a sticky molecule, matrix metalloproteinase, and fibroblast hyper multiplication are expressed in the synovium. A transcription factor termed Nuclear factor kappa-light-chain-enhancer of activated B-cells (NF- $\kappa$ B) regulates all of these variables. Although the exact pathophysiology is unknown, certain free radicals, such as nitrous oxide and superoxide radicals, are produced as consequences of cellular metabolic activities. The release of such free radicals may trigger the manufacture of interleukins (IL) and tumour necrosis factor (TNF- $\alpha$ ) from T-cells, which solely impact the production of growth-promoting factors, cytokines, and sticky molecules on immune cells, causing tissue damage and inflammation<sup>23</sup>. Synovial membrane hyperplasia, inflammatory cell infiltration, and neovascularization are all pathological alterations in RA that lead to cartilage deterioration and articular damage<sup>24</sup>.

Activation of immune-like cells such as monocytes (which play a role in the inflammatory process during immune response), macrophages (which secrete pro-inflammatory mediators), and synovial fibroblasts, as well as antigen-activated CD4+ T cells, all contribute to disease. When CD4+ T cells are activated, they produce cytokines such as interleukin-1, interleukin-6, and TNF- $\alpha$  (the major mediator of RA)<sup>25</sup>. These pro-inflammatory cytokines are important in the pathogenesis of RA, such as articular incorporation through increased inflammatory infiltration of immune cells, particularly B lymphocytes, T cells, and macrophages, and bone disintegration, which results in antibody production and the release of IL-6 and TNF- $\alpha$ <sup>26</sup>. Furthermore, pro-inflammatory cytokines hinder the production and degradation of proteoglycans and collagen. Cartilage erosion is caused by the activation of proteolytic enzymes such as collagenases and MMPs<sup>27</sup>. Furthermore, certain protein molecules, such as chemokines and cytokines, cause synovitis and tissue breakdown by attracting lymphocytes, monocytes, neutrophils, and the COX-2 enzyme, which activate hyperplasia and induce apoptosis in synovial fibroblasts<sup>28</sup>.

## 6. Rationality of Inflammation Associated with Arthritis

The gradual buildup of inflammatory mediators at the synovium of a joint causes pain, swelling, and bone

and cartilage degeneration. At the location of the inflammation, the cell variation is active<sup>29</sup>. Lymphocytes and macrophages enter the synovium from the circulation, and their numbers rise in the synovium as they develop, drawing additional inflammatory cells<sup>30</sup>. APCs in the region interact with and trigger T-cell signalling, as do other migratory macrophages and fibroblast-like synoviocytes that contribute to the hyperplastic synovial lining<sup>31</sup>.

Polymorphonuclear Neutrophils (PMN) are recruited by activated macrophages to migrate through the hyperplastic synovial lining and into the joint region, and inflammatory cytokines such as TNF- $\alpha$ , IL-1, and IL-6 enhance lymphocyte migration. The polymorphonuclear neutrophil (PMN) also produces the proteases MMP-1 and MMP-3, as well as Reactive Oxygen Species (ROS), which further degrades cartilage<sup>32</sup>. MMP-1 and MMP-3 are also released by fibroblast-like synoviocytes stimulated by pro-inflammatory cytokines, inducing cartilage degradation. Furthermore, RANKL (receptor activator for nuclear factor-kappa B ligand) is secreted by fibroblast-like synoviocytes in arthritis, which stimulates osteoclasts, which assault and destroy bone<sup>33</sup>.

## 7. Treatments and Therapies

Rheumatoid arthritis patients are treated to alleviate symptoms, delay the progression of the disease, and enhance their standard of life. As a result, before initiating RA medical care, specific goals must be kept in mind, such as relieving pain, lowering inflammation, protecting articular structure, maintaining function, and managing systemic involvement<sup>34</sup>. Nonsteroidal Anti-Inflammatory Medicines (NSAIDs) or Disease-Modifying Antirheumatic Drugs (DMARDs) are currently being substituted in the treatment of RA by new biological agents such as TNF monoclonal antibody<sup>35</sup>. To treat RA, five clinical techniques are used. To minimize inflammatory symptoms and disease development, the basic treatment is to utilize NSAIDs followed by low doses of glucocorticoids. DMARDs, such as methotrexate, sulfasalazine, gold salts, or D-penicillamine, can be utilized in the treatment of chronic conditions.

Chronic diseases can be treated with TNF-neutralizing pharmaceuticals such as infliximab,



etanercept, and others, IL-1 neutralizing medications such as anakinra, and T-cell activation inhibitors such as abatacept<sup>36</sup>. Finally, chronic patients are treated with immunosuppressive and cytotoxic drugs such as cyclosporine, azathioprine, and cyclophosphamide. The above-mentioned therapeutic drugs reduce joint degeneration and inflammation, but it is unclear what long-term risks they may pose. Drugs, on the other hand, can cause gastrointestinal ulcers, cardiovascular problems, hematologic toxicity, nephrotoxicity, pulmonary toxicity, myelosuppression, hepatic fibrosis, stomatitis, cirrhosis, diarrhoea, immunological reactions, and local injection-site reactions in the long run<sup>37</sup>. Additionally, there are increased costs and adverse effects that necessitate ongoing monitoring, notably significant chances of infections and pregnancies. The following simple home therapies are recommended by a practitioner as losing bodyweight, simple home remedies like applying heat or ice pads on painful joints, advice the patients to do exercise like low impact aerobic exercise to get back strength, wearing knee cap whether it is acute phase, counsel to take dietary supplements such as intake of Vitamin D to get rid of this ailment. In chronic phase, besides of therapeutic drugs supportive aids like brace, cane are also used, occupational therapies including acupuncture and physiotherapy being given regularly to the patient<sup>38</sup>. Anti-depressants and steroids are also recommended in low dosage in order to improve the sleep and provide short term relief from pain. Surgical method is also suggested which ultimately leads to wound infection, unexpected bleedings, nerve damage and stiffness in joints. In order to get away from the side effects of synthetic drugs herbal therapy was chosen<sup>38</sup>.

## 7.1 Herbal Therapy

According to ethnobotanical studies, 485 plant species offer to promise of anti-arthritis action. It is not an exaggeration to say that herbal treatments have been used since the dawn of time. They have long been used to cure a wide range of ailments. Herbal medicines are generated by combining the medicinal knowledge of generations of doctors who have long practiced an ancient medical system<sup>39</sup>. Because current medications have either undesirable side effects or are prohibitively expensive, researchers are now interested in therapeutic compounds derived from plants. The medicinally

relevant constituents of these herbal plants are chemical components that result in a favourable physiological action on the organism<sup>40</sup>.

For example, powdered root of *Withania somnifera* Dunal. (*Chooranam*) is a common type of internal medicine that is utilized as a foundational treatment for several illnesses, including arthritis. Another type of internal medicine is a potion, such as the seed of *Cuminum cyminum* Linn. potion (*Kudineer*), which is quickly absorbed by our bodies and allows speedier action, which is more crucial in the treatment of arthritis. Additionally, internal medications are given as pills (*Mathirai*), electuaries (*Legiyam*), oils (*Ennai*), ghees (*Nei*), etc. Examples are the fruit of *Piper nigrum* Linn. (pill form), and the seed of *Terminalia chebula* Retz. (oil form), and the seed of *Semecarpus anacardium* Linn. (*ghee*). Fomentation (*Ottradam*), poultice (*Patru*), oilation (*Thailam*), and other forms of external therapy for arthritis. To relieve the frequent pain sensation, this type of therapy is applied to the skin to relieve swelling or pain. Examples include the fomentation of *Vitex negundo* Linn. leaves, the poulticing of *Zingiber officinale* Roxb. roots, and the oiling of *Strychnos nux vomica* Linn. seeds<sup>39</sup>.

*Ayush Tulsi Jiwan Plus* oil: Polyherbal *Ayurvedic* formulation recommended by Ayush for musculoskeletal pain relief<sup>41</sup>. *Ayurvedic* medicaments such as *Eranda* oil, *Yograja Guggulu*, *Vatavidhwansak rasa*, *Agnitundi Vati*, *Rasanadikwath* and *Triphala* tablets were prescribed for arthritic patients<sup>42</sup>. *Rumalaya Forte* tablet, *Rumalaya* liniment, *Artha* cure oil, *Arthcure* capsule, *Rheumartho* gold capsule, *Ortho Joint Oil*, *SBS Biotech Ltd.*, and *Rheuma off Gold* from *Virgo UAP Pharma (P.) Ltd.* are some commercially available polyherbal formulations for rheumatoid arthritis. *Majoon Suranjan* (Qarshi herbal goods) *Dan Huo Luo Xiao (HLXL)*. *Sudard* (Bangalore, India's Anglo-French Drugs and Industries Ltd. *TBL-II* produced by Chinese business *Zhong-Yue Herbal Pharmaceutical Union*<sup>7</sup>.

## 8. Practising Mode of Selected Plants based on Ethnopharmacological Aspects for Arthritis and Painmodulation

Scientists are currently investigating the development of new polyherbal therapies or the use of old traditional

polyherbal formulations followed by various tribal groups. They were employed in ancient times, such as as Ayurveda, which dates back to 5000 years. At present ethno-medicinal plants values are evaluated for their therapeutic potential. There is a need to assess polyherbal formulation using scientific approaches identifying bioactive chemicals and determining its future clinical trials with mechanism of action<sup>7</sup>. Table 1 summarizes the Ethnopharmacological uses of Medicinal plant with potential anti-arthritic and pain relieving property.

Indigenous communities extensively utilise herbal plants as a supplemental therapy to standard drugs in the treatment of arthritis. The various portions of the plants mentioned in (Table 1) with various forms of usage such as infusion, decoction, extract, pills, poultice, and cocktail, etc., which are more beneficial in curing joint pain and inflammation linked with arthritis.

## 9. Potent Bioactive Metabolites and their Pharmacological Aspects

The potential use of plant secondary metabolites has grown, and research has demonstrated that they are more effective than synthetic medications. Unlike conventional medicines, this plant metabolite product has no negative effects. These have seen a significant improvement in healing the many feared ailments over the past few years as their production has expanded<sup>61</sup>.

The use of plant secondary metabolites as a substitute for synthetic medicines. The Fabaceae family's main chemical components are flavonoids. Isoflavones, prenylated flavonoids, flavanones, flavanols, saponins, glucosides, rotenoids, chalcones, alkaloids, and trypsin inhibitors are secondary metabolites present abundantly in most of the species

**Table 1.** Ethnopharmacological uses of Medicinal plant with potential anti-arthritic and pain relieving property

S. No.	Binomial name	Common name	Habit	Usage form	References
1	<i>Pterocarpus marsupium</i>	Indian kino	Deciduous tree	1. Decoction of heartwood possess anti-inflammation in the affected joint. 2. The stem bark extract is used to treat all kinds of body pain, especially in joints. 3. The heartwood of the plant has external applications for treating inflammation	43
2	<i>Cassia fistula</i>	Golden shower	Deciduous tree	1. Fruit poultice is used for frozen joints. 2. The herb is also traditionally used as a decoction, infusion, powder, or in combination with other medicinal plants.	44
3	<i>Vachellia leucophloea</i>	whitebark acacia	Large thorny tree	Bark oil and bark fomentation are used for joint diseases especially arthritic pain	39
4	<i>Butea monosperma</i>	Bastard teak	Deciduous tree	1. For lumbago pain (lower back pain) relief, the floral paste is ingested once daily on an empty stomach in the morning. 2. The informants stated that an osteoarthritic patient's shattered bone was treated with root bark paste of <i>B. monospermae</i>	45
5	<i>Trifolium species</i>	clover	Short lived perennial herb	Clove bud oil can be used in a massage oil blend or as a balm to treat arthritis, sprains, strains, and muscle pain, as well as rheumatism.	46
6	<i>Acacia catechu</i>	Black cutch tree	Deciduous tree	1. The anti-inflammatory capabilities of a blend of <i>A. catechu</i> roots or bark extract with <i>Scutellaria baicalensis</i> root extract. 2. Sometimes also use acacia's heartwood for blended formula.	47

**Table 1.** Continued...

S. No.	Binomial name	Common name	Habit	Usage form	References
7	<i>Pongamia pinnata</i>	Indian beech tree	Perennial tree	The seed oil has many uses, but it's most known for curing ulcers, rheumatism, and leucoderma	48
8	<i>Glycyrrhiza glabra</i>	Liquorice	Small perennial herb	1. Traditional applications for the herb include iron deficiency, gouty joints, asthma, epileptic seizures, fever, cough, skin diseases, rheumatic arthritis, paralysis, and bleeding disorders. 2. In inflammatory situations, roots can be used as a demulcent in the form of an infusion, decoction, extract, or pill.	49
9	<i>Pueraria tuberosa</i>	Indian kudzu	Perennial climber	A tuber of <i>Pueraria</i> used to make "mahavisagarbhataila" - a traditional remedy for joint disorders.	50
10	<i>Acacia nilotica</i>	Gum Arabic tree	Ever green tree	Leaves, root, stem, and bark are boiled in water and the resulting combination is ingested with soup two times a day for 14 days, or until the patient is well.	51
11	<i>Bauhinia racemosa</i>	Bidi-leaf tree	Flowering shrub	The bark extract are used for joint pain.	52
12	<i>Cajanus cajan</i>	Pigeon pea	Perennial woody shrub	Tea made from the seeds is used to treat inflammation.	53
13	<i>Lablab purpureus</i>	Hyacinth bean	Herbaceous plant	The seed decoction was used for rheumatism and sunstroke.	54
14	<i>Sesbania grandiflora</i>	Humming bird tree	Sparsely branched tree	All parts extract as internally and externally of <i>S. grandiflora</i> have been practically used in folk medicine as a traditional remedy for fever, dysentery, headaches, stomatitis, and dysentery.	55
15	<i>Bauhinia tomentosa</i>	Yellow bird tree	Many stemmed shrub or small tree	A leaf infusion is used against arthritis.	56
16	<i>Erythrina stricta</i>	Indian coral tree	Deciduous tree	1. Externally, a warm poultice of the leaves is given to ease rheumatic joints. 2. A bark decoction can help with arthritis pain.	57
17	<i>Smithiasensetiva</i>	Sensitvesmithia	Annual herb	The whole plant is used for anti-arthritis activity especially bark powder as paste.	23
18	<i>Acacia mearnsii</i>	Black wattle	Shapeless tree	Roots and stem bark boiled with water and eaten orally, one glass twice a day.	58
19	<i>Acacia mellifera</i>	Blackthorn	Thorny Shrub to small trees	Root and stem bark boiled in water and concoction taken orally. One glass 2 times daily, for 14 days or until the patient recovers.	59
20	<i>Vachellia seyal</i>	Red acacia	Thorny high tree	Boiled with water and administered orally, one glass 2-3 times each day of 1 or 2 weeks.	60

Scientific names and authorities of plants were validated with the "www.theplant.org database.

belonging to *Fabaceae*. Numerous characteristics of these plants have been clarified by *in vitro* and *in vivo* studies. *Fabaceae* are used to treat common bronchitis, treat ailments of the upper respiratory system, relieve rheumatic pain and treat the inflammation of glands, prevent sleeplessness, anxiousness, and irregular heartbeat due to nervousness, inhibit melanogenesis, and control metabolism and energy expenditure<sup>10</sup>. Table 2 summarizes the bioactive compounds and pharmacological potential of selected Medicinal plants.

## 10. The *In Vitro* and *In Vivo* Anti-Inflammatory Activities of Medicinal Plants

Preclinical studies were typically conducted in several different phases, starting with *in vitro* studies using cell cultures and progressing to animal studies designed to provide information on the drug's effectiveness and safety *in vivo*, as well as to determine optimal dosages and potential side effects. Table 3 summarizes the plants with *in vitro* and *in vivo* anti-inflammatory activities of those 20 plant species reported in various experimental

**Table 2.** List of bioactive compounds and pharmacological potential of selected medicinal plants

S. No.	Name of the plant	Phytochemicals reported	Pharmacological activity	References
1	<i>Pterocarpus marsupium</i>	Catechin, epicatechin, pterosupin, and pterostilbene	Anti-bacterial, anti-cancer, anti-diabetic, anti-oxidant, and anti-inflammatory activity. Especially the heartwood of kino possesses analgesic and anti-arthritic activity.	62-64
2	<i>Cassia fistula</i>	<i>Cassia</i> has been reported to have anthraquinone which is more potential to act against arthritis. apart from that sennosides, tannin, phlobaphenes, oxy anthraquinone compounds, emodin, chrysophanic acid, lupeol, beta-sitosterol, and hexacosanol and fistulic acid are also reported.	The plant has been shown to hold hepatoprotective, anti-inflammatory, antioxidant, and antidiabetic properties.	65-67
3	<i>Vachellia leucophloea</i>	Epicatechin, catechin, rutin, friedelin, lupeol, and quercetin reported in the bark of <i>Vachellia</i> contain promising anti-arthritic activity.	The plant's bark is an astringent and a remedy for biliousness, thirst, vomiting, burning, and bronchitis. The bark of the plant is used as an expectorant, blood purifier, antibacterial, and antihelmentic.	68,69
4	<i>Butea monosperma</i>	The bark includes pyrocatechin, gallic acid, and kino-tannic acid. Other prominent glycosides found in the plants are butrin, alanind, allophonic acid, butolic acid, cyanidin, histidine, lupenone, lupeol, medicarpin, miroestrol, palasimide, and shellolic acid. In flowers triterpene, butein, butin, isobutrin, coreopsin, isocoreospin, sulphurein, and monospermoside, as well as chalcones, auronas, flavonoids (palasitrin and prunetin), and steroids which has analgesic properties.	<i>Butea monosperma</i> used to treat tumours, bleeding piles, urinary stones, inflammations, aphrodisiacs, astringents, tonics, and skin and eye diseases. Additionally, it has anthelmintic, appetizing, and aphrodisiac properties.	45,70,71
5	<i>Trifolium</i> species	Estrogenic isoflavones daidzein, genistein, formononetin, biochanin A, coumestrol, and naringenin. Other minor compounds include flavonoids, pterocarpan, coumarins, and tyramine	The analgesic and antiseptic qualities of clover ( <i>Trifolium</i> ) species are employed in traditional medicine as a treatment for rheumatic disorders.	72,73



Table 2. Continued...

S. No.	Name of the plant	Phytochemicals reported	Pharmacological activity	References
6	<i>Acacia catechu</i>	Catechin, epicatechin, epicatechin-3-O-gallate, and epigallocatechin-3-O-gallate are the main catechins found in <i>A. catechu</i> . The extracts also included significant amounts of caffeine, flavonol glycosides, and flavonol dimers.	Antibiotic, antispasmodic, antifungal, and clotting agents of blood, to eliminate intestinal worms and antidiarrheal agents, as well as to cure diabetes, make free from obesity, and keep teeth clean.	47,74-76
7	<i>Pongamia pinnata</i>	Phytochemicals including sterol and its derivatives are found in seeds, whereas pongone, galbone, pongalabol, and pongagallon A and B are found in leaves and stems.	huge potential to fight against ulcers, and diarrhoea, which also acts as an antioxidant, anti-hypoglycemic, and has anti-microbial activity especially anti-viral, anti-bacterial, anti-plasmodium etc.	48,77,79
8	<i>Glycyrrhiza glabra</i>	Glycyrrhizin, which is present as the potassium and calcium salts of glycyrrhizic acid, is the active chemical component. GY also contains fat, sucrose, glucose, resins, mannites, and asparagines	GY has been shown to have antibiotics, hypolipidemic, antiviral, and hypotensive conditions, heals ulceration, and is known to inhibit-diuretic, anti-inflammatory, known to inhibit-mutagenic, expectorant, hepatoprotective, antioxidant, and antipyretic properties.	49,80-82
9	<i>Pueraria tuberosa</i>	Prominently puerarin, and quercetin, and also with additional phytocompounds irisolidone, biochanin, iso orientin, and mangiferin.	Cancer prevention, reducing the diabetic level, antifertility, anti-inflammatory, relieving hyperaesthesia, known to inhibit stress, antiulcerogenic, cardioprotective, hypolipidemic, hepatoprotective, immunomodulatory, nephroprotective, neuroprotective, and wound healing properties	50,83
10	<i>Acacia nilotica</i>	Epigallocatechin-7-gallate, epigallocatechin-5,7-gallate, flavonoids such as catechin-5-gallate, catechin-5,7-gallate, catechin-3,5- digallate, catechin-4,5-digallate, mollisacacidin, apigenin-6,8-bis-C- $\beta$ -D- glucoopyranoside (vicenin), leucocyanadin, kaempferol-7-glucoside, acacetin, umbelliferon, caffeic acid, protocatechuic acid, and m-catechol.	Anti-inflammatory, analgesic, antibacterial, antidiabetic, and antihypertensive characteristics.	51,84,85
11	<i>Bauhinia racemosa</i>	$\beta$ -sitosterol, Lupeol, catechin, Betulin, Rutin and $\beta$ -amyirin.	Antitumor activity, anti-inflammatory activity, analgesic effect, antipyretic, antihyperglycemic activity, hepatoprotective activity, antimicrobial activities, antiulcer activity, antihistaminic effect, anxiolytic activity, and anti-HIV activity.	52,86,87
12	<i>Cajanus cajan</i>	Polyphenols, quercetin, luteolin, apigenin, isorhamnetin, flavonoids and cajaninstilbene acid.	Anthelmintic, antibacterial hypocholesterolemic, antidiabetic, anti-oxidant, anti-inflammatory, anti-nociceptive, and anticancer effects.	53,88

**Table 2.** Continued...

S. No.	Name of the plant	Phytochemicals reported	Pharmacological activity	References
13	<i>Lablab purpureus</i>	Alcohols, phenols, steroids, essential oils, alkaloids, tannins, flavonoids, saponins, coumarins, terpenoids, pigments, glycosides, and anthnanoids.	Antidiabetic, anti-inflammatory, analgesic, antioxidant, cytotoxic, hypolipidemic, antimicrobial, insecticidal, hepatoprotective, antilithiatic, and antispasmodic effects.	54,89
14	<i>Sesbania grandiflora</i>	It contains arginine, cysteine, histidine, isoleucine, phenylalanine, tryptophan, valine, threonine, alanine, asparagine, aspartic acid, oleanolic acid, galactose, rhamnose, and glucuronic acid.	Antibacterial, antifungal, antioxidant, antiurolithiatic, anticonvulsant, ananxiolytic and hepatoprotective.	55,90,91
15	<i>Bauhinia tomentosa</i>	Phytol, rutin, n-hexadecanoic acid, squalene, ethyl ester-hexadecanoic acid and octadecanoic acid	<i>B. tomentosa</i> leaves possess antidiabetic, anticancer, antiobesity, antihyperglycemic, and antihyperlipidemic activities.	52,56,92
16	<i>Erythrina stricta</i>	It contains alkaloids and also contains sterols - like campesterol, $\beta$ -sitosterol, and $\beta$ -amyrin. Isoflavones -indicanines D and E together with 9 known compounds including isoflavones like genistein, alpinum isoflavones, dimethyl alpinum isoflavone, etc.	Traditionally the leaves are known to possess analgesic, anti-helminthic, antiulcer, and sedative properties. <i>E. stricta</i> bark is used medicinally as a febrifuge, anti-bilious, and anti-diarrheal antirheumatic.	57,93
17	<i>Smithia sensitiva</i>	Presence of alkaloids, sugars and Carbohydrates, steroids, tannins, and flavonoids.	An anti-inflammatory and antioxidant property.	94
18	<i>Acacia mearnsii</i>	Alkaloids, steroids, coumarins, essential oils, flavonoids, terpenoids, and anthraquinones.	Anticancer, anti-inflammatory, antiprotozoal, antibacterial, anthelmintic, analgesic, antimycobacterial, antifungal, and antioxidant	58,95
19	<i>Acacia mellifera</i>	Flavonoids, phenolics, saponins, alkaloids, cardiac glycosides, steroids, and terpenoids.	Anti-inflammatory, antinociceptive, and antipyretic properties. It possesses antimicrobial, antileishmanial, hepatoprotective, and antiviral activities.	59,96
20	<i>Vachellia seyal</i>	Catechin, epicatechin, lupeol, campesterol, stigmasterol, clionasterol, and oleamide.	Pneumonia, malaria, joint pain, bleeding, rheumatic arthritis, jaundice, chest pain, diarrhoea, skin necrosis, bleeding leprosy, dysmenorrhea, eye infection, stomach ulcers, and respiratory tract infection.	96-98

Scientific names and authorities of plants were validated with the "www.theplant.org database.

studies. The drug's effectiveness and safety *in vivo*, as well as to determine optimal dosages and potential side effects of the plant extracts. It also provides the potent bioactive compound and their mechanism of action against various pro-inflammatory cytokines such as Tumor Necrotic Factor (TNF), Interleukin 1 and 6 (IL) and Cyclooxygenase (COX) enzymes possess inhibitory effects.

## 11. Evaluation and Analysis of Reported Phytochemicals based on their Anti-Inflammatory Activity

Among the experimental studies, the selected plants contained the most active substances in terms of anti-arthritic and anti-inflammatory activity. Various

**Table 3.** Anti-inflammatory activities research results of selected plants based on *in vitro* and *in vivo* studies

S. No.	Name of the plant	Preclinical studies	References
1	<i>Pterocarpus marsupium</i>	Strong anti-inflammatory effects are possessed by <i>Pterocarpus marsupium</i> . In LPS-stimulated PBMC, the PGE2-inhibitory and COX-1/2-selective inhibitory effects of an extract containing pterostilbene were investigated. Methanolic and aqueous extracts exhibit anti-inflammatory properties in acute inflammation using the carrageenan-induced paw edoema model. Aqueous heartwood extract at doses of 100 mg/kg and 200 mg/kg decreases the high levels of inflammatory cytokines and TNF alpha in NIDDM diabetic rats. 500 mg of the PM bark's crude methanolic extract was tested in Swiss albino mice using the hot plate method, and the results were encouraging. Due to the existence of distinctive phytochemicals, <i>Pterocarpus</i> plays a significant role in folk medicine to treat a variety of disorders, but these cannot be properly investigated to produce natural medications and goods for arthritis.	99
2	<i>Cassia fistula</i>	An aqueous extract of <i>Cassia fistula</i> 's leaves and fruits was found to have anti-inflammatory properties. By denaturing proteins using the bovine albumin method, the alcohol (ethanolic) extracts of <i>Cassia fistula</i> 's leaves and Diclofenac (the reference medication) were examined for antiarthritic activity. where the percentage of arthritic protection was determined to be 89.1 for diclofenac and 93.1 for alcohol/ethanolic at 1000 cc concentration. When compared to Diclofenac, which was utilized as a standard drug for pain management, it may be considered that the alcoholic (ethanolic) leaf extract has significant and pronounced antiarthritic action. <i>In vivo</i> studies: Winstar albino rats were used to assess the anti-inflammatory properties of methanolic and aqueous extracts of <i>C. fistula</i> bark. The results showed that the extracts had notable anti-inflammatory activity in both chronic and acute phases. Commercial preparations nowadays and in any controlled therapeutic trials have typically been standardized extracts of the entire plant.	44,67
3	<i>Vachellia leucophloea</i>	The bark extract of <i>Vachellia leucophloea</i> was prepared using acetone, and its anti-inflammatory efficacy was tested in lipopolysaccharide-stimulated RAW 264.7 macrophage cells line of sight. The results showed that 25 g/ml was the most effective.	100
4	<i>Butea monosperma</i>	Studies on acute toxicity: The acute toxicity of <i>Butea monosperma</i> stem bark extract in its ethanolic and acetone fractions was determined. It was found that even at a level of 2000 mg kg <sup>-1</sup> , the ethanolic extract and the acetone fraction did not cause death. The ethanolic extract of <i>B. monosperma</i> aerial bark inhibited the COX-1 and COX-2 enzymes, respectively, in a cyclooxygenase assay. Compared to petroleum ether, benzene, and chloroform fractions, the acetone fraction showed greater inhibition, with COX-1 and COX-2 enzymes, compared to the common medication Celecoxib. The effect of <i>Butea monosperma</i> 's ethanolic stem bark extract and the acetone fraction in carrageenan-induced paw edema in rats show that the two constituents were found to have remarkable anti-inflammatory activity in rats.	101
5	<i>Trifolium</i> species	<i>In vivo</i> , studies show that giving red clover - <i>Trifolium</i> extract (500 mg/kg body weight) to female and normal (control) rats for about 90 and 180 days can restore pain threshold to normal levels, as measured by tail flicking and formalin test methods, in cases where pain threshold was reduced due to oestrogen deprivation. Although there are currently no clinical data available. Formononetin, an active component in clover, has also shown anxiolytic efficacy in mice <i>in vivo</i> in a chronic pain paradigm by decreasing inflammation and neuronal hyperexcitability.	102,103
6	<i>Acacia catechu</i>	A customized blend of extracts from <i>A. catechu</i> and <i>S. baicalensis</i> was tested using <i>in vitro</i> , cellular, and <i>in vivo</i> models of cyclooxygenase and 5-lipoxygenase enzyme activity. The anti-inflammatory activity of the unique blend of <i>S. baicalensis</i> and <i>A. catechu</i> was investigated using lipopolysaccharide as a pro-inflammatory agent in animal and human immortalized cell lines and primary human cells. The combined product normalized the pro-inflammatory genes cyclooxygenase (COX 1 and 2). Tumor necrosis factor (heart of RA), IL-1, and IL-6 in all cell cultures. A second study looked at the efficacy of UP446, a combination of catechin from <i>A. catechu</i> core wood and baicalin from <i>S. baicalensis</i> , in a clinical rat model of arthritis with rheumatoid. The 50 mg/kg dose of the combination product considerably reduced ankle diameter, paw edema, and pain sensitivity. It has been proven that the product reduces the expression of the pro-inflammatory cytokines TNF-, IL-1, and IL-6.	47

Table 3. Continued...

S. No.	Name of the plant	Preclinical studies	References
7	<i>Pongamia pinnata</i>	It has been demonstrated that <i>Pongamia pinnata</i> possesses anti-arthritic properties utilizing several animal models, including those that cause paw edema, such as those caused by formaldehyde and carrageenan. Anti-arthritic effects of a polyherbal formulation containing <i>Cissampelos pereira</i> Linn. roots, <i>P. pinnata</i> (L.) Pierre leaves, and <i>Vitex negundo</i> Linn. leaves against Freund's complete adjuvant-induced arthritis in rats. The degree of inflammation was determined using the size of the hind paw, body weight, and a hematological examination, as well as radiographic and histological investigations of the ankle joints. The polyherbal formulation with different dosage levels lowers bone degradation, pannus production, mononuclear infiltration, hind paw edema, and body weight considerably.	104
8	<i>Glycyrrhiza glabra</i>	The methanolic extract of <i>Glycyrrhiza glabra</i> rhizomes shows anti-arthritic activity in Wistar rats with male genders at 150 mg per kg by reducing the formation of autoantibodies and leukocyte migration. The study found that <i>Glycyrrhiza glabra</i> had significant anti-arthritic effectiveness.	49
9	<i>Pueraria tuberosa</i>	In the most accurate mouse air pouch model of inflammation, Mangiferin from the tubers of <i>Pueraria tuberosa</i> (PT-Mangiferin) was used to identify its anti-inflammatory mechanism. The anti-inflammatory efficacy of PT-Mangiferin was evaluated using the generation of ROS. The formation of ROS caused by lipopolysaccharides was considerably and dose-dependently decreased by PT-Mangiferin. The conventional ROS inhibitor, N-Acetyl Cysteine (NAC), was not as efficient at lowering the amount of ROS as PT-Mangiferin at a dose of 40 µM. The utterance of inflammatory proteins like cyclooxygenase especially COX-2, and TNF- is regulated by NF-B translocation. However, pre-incubation with <i>Pueraria tuberosa</i> -Mangiferin significantly and dose-dependently inhibited LPS-induced NF-B translocation in the cells.	105
10	<i>Acacia nilotica</i>	Based on these findings, the aqueous extract of <i>A. nilotica</i> pods may have anti-inflammatory properties that are beneficial when taken orally, supporting its usage in traditional medicine. Using several models of both acute and chronic inflammation, the anti-inflammatory properties of the aqueous extract of <i>A. nilotica</i> pods, delivered orally at doses of 50 and 100 mg/kg, were assessed <i>in vivo</i> . To assess the immediate impact of the plant extract, mouse models of paw and ear edema were produced with carrageenan and xylene, respectively. The greatest inhibition of the carrageenan- and cotton-pellet-induced granuloma in rats was 64.41 and 25.62%, respectively, at the highest dose of <i>A. nilotica</i> extract (100 mg/kg).	106
11	<i>Bauhinia racemosa</i>	The inflammatory activity of <i>B. racemosa</i> methanolic extracts in Wistar albino rats is investigated. To test <i>B. racemosa</i> 's anti-inflammatory activity, the extracts were combined with an ethanol solvent and administered to mice at dosages of 50, 100, and 200 mg. Indomethacin is a common medication. The inflammatory levels in 200 mg of <i>B. racemosa</i> are 44.8% and 51.5% in 10 mg of indomethacin.	52
12	<i>Cajanus cajan</i>	The anti-inflammatory activity of <i>Cajanus cajan</i> was tested in Albumin-induced paw edema in rats. Rats who were given the extract at a dosage of 500 mg/kg consistently showed the least change in paw sizes, with almost 50% prevention of edema development by 60 minutes after albumen injection (0.300.07 cm, 70%). The extract inhibited edema development at dosages of 300 mg/kg (64%) and 500 mg/kg (82%) for 120 minutes, which was substantially greater than that reported in rats given Indomethacin (55%).	53
13	<i>Lablab purpureus</i>	<i>In vitro</i> , anti-inflammatory studies revealed a linear relationship of % inhibition for <i>Lablab purpureus</i> (white bean pods) indicating good anti-inflammatory properties. The antinociceptive effects of methanol extract from <i>Lablab purpureus</i> beans (fruits including seeds) were tested in mice using an acetic acid-induced pain model.	107
14	<i>Sesbania grandiflora</i>	The ethyl acetate extract has inhibitory action at 200-1000 g/ml by preventing protein denaturation, and its impact was compared to that of the standard medication diclofenac sodium. Protein denaturation causes autoantigen formation in rheumatoid arthritis. According to the findings of this study, ethyl acetate extract of <i>Sesbania grandiflora</i> is capable of reducing autoantigen production and preventing protein denaturation in rheumatoid arthritis.	55
15	<i>Bauhinia tomentosa</i>	In anti-inflammatory experiments of <i>Bauhinia tomentosa</i> , the isolated component Rutin (10 mg/kgb.w.) inhibited paw oedema (92.6%) more effectively than crude extracts (88.7%).	56

**Table 3.** Continued...

S. No.	Name of the plant	Preclinical studies	References
16	<i>Erythrina stricta</i>	Anti-inflammatory action has been demonstrated for alkaloids isolated from the leaves of <i>E. stricta</i> . The bark and leaves are also used to treat fever and rheumatism. It has been found that methanolic extracts of <i>E. stricta</i> leaf exhibit substantial antinociceptive action.	57
17	<i>Smithia sensitiva</i>	The extracts of <i>Smithia sensitiva</i> acute toxicity analysis revealed that a dosage of up to 2000 mg/kg per b.w was harmless. At 200mg/ml, the methanolic extract inhibited hypotonicity-induced HRBC membrane lysis by 29.8%. <i>S. sensitiva in vitro</i> tests revealed substantial anti-inflammatory and anti-arthritis efficacy.	94
18	<i>Acacia mearnsii</i>	For the fresh leaves, dried leaves, fresh stem, and dry stem bark of <i>Acacia mearnsii</i> the primary components of the oil were octadecyl alcohol (25.5%) and phytol (10.5%); cis-verbenol (29.5%); and phytol (23.4%), respectively. In the albumin-induced test paradigm in rats, oral administration of essential oils at a concentration of 2% demonstrated strong anti-inflammatory activities. Oils extracted from fresh leaves and dry stems reduced inflammation for up to 4 hours after treatment.	58
19	<i>Acacia mellifera</i>	<i>Acacia mellifera</i> stem bark extract with dichloromethane showed anti-inflammatory, antinociceptive, and antipyretic properties. <i>A. mellifera</i> stem bark extract had a substantial anti-inflammatory effect in acute inflammation and considerably decreased pain feeling via both peripheral and central pathways.	59
20	<i>Vachellia seyal</i>	In carrageen-induced inflammatory models, the methanolic crude extract of <i>Vachellia seyal</i> from both ASG and PTC samples was inhibited at 150 and 300 mg/kg doses over 24 hours.	97

Scientific names and authorities of plants were validated with the “www.theplant.org” database. Abbreviations in the table include the following in alphabetical order: COX (cyclooxygenase), IL (Interleukin), LPS (lipopolysaccharide), NIDDM (Non-insulin dependent diabetes mellitus), PBMC (peripheral blood mononuclear cells), PGE2 (Prostaglandin E2), ROS (Reactive Oxygen Species), TNF (Tumour Necrotic Factor).

phytochemical elements of each plant have potential therapeutic roles in the relief of arthritic symptoms and even the disease itself. Further elucidation of the molecular mechanisms underlying the action of these phytochemicals is expected to lead not only to the discovery of new drugs for symptomatic relief of arthritis conditions such as inflammation and pain but also to the ability to stop or even reverse the damage caused by Arthritis. Based on plant cellular and animal investigations, different active phytochemical compounds obtained from the above medicinal plants may be effective against arthritis<sup>108</sup>. These phytoconstituents come from a variety of chemical groups, including flavonols, anthraquinones, terpenes, triterpenes, steroidal compounds, phytoestrogens, oxyanthraquinones, alkaloids, and others listed in Table 2, notably pterostilbene, catechin, epicatechin, butrin, and Pterostilbene, Pongone, Formononetin, and Rutin, in which all have the ability to block the binding receptors associated with arthritis. More study is needed to focus on the bioefficacy and safety aspects of these phytochemical compounds in order to find novel natural medicines. Clinical and preclinical studies on

these herbal formulations provided evidence-based data demonstrating the mechanism of such herbal plants and the active constituents of herbal plants responsible for suppressing the inflammatory mediators or the molecular signalling pathways involved in arthritis<sup>20</sup>.

## 12. Supremacy of Drugs Derived from Plants

Pain is a major worldwide public health concern because it is an unpleasant physiological and psychological experience that is connected to existing or potential tissue harm. Twenty percent of persons globally experience some level of pain, and ten percent are diagnosed with a new chronic pain condition each year. Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) are the cornerstone of contemporary pain treatment methods. When these medicines fail to provide enough pain relief, stronger opioids are employed as a second line of therapy<sup>109</sup>.

The various negative side effects of opioids, as well as the possibility of addiction, make their usage problematic. Fatigue, emesis/vomiting, bloating,



tolerance, physical reliance, and respiratory depression can all be caused by opioids. As a result, it is critical to develop pain treatment alternatives, particularly those manufactured from plants. Instead of basic components, plant extracts have synergistic properties or effectiveness against several targets<sup>110</sup>. Because phenolic plant components have strong antioxidant and anti-inflammatory activities, one of the key mechanisms of action of plant-derived medicines is the modulation of inflammation signalling pathways. Patients suffering from chronic pain frequently employ a variety of alternative treatments. These treatments are progressively being scrutinised in the same way that all other modern practises supported by scientific evidence are. More than 60% of chronic pain sufferers finally turn to non-drug therapy. When employing herbal remedies to treat acute or chronic pain, the capacity to react quickly is critical. Traditional treatment with NSAIDs or analgesics is rapid and effective, but drugs nearly usually have significant and unacceptable side effects. Herbal-based drugs may have less detrimental anti-inflammatory, analgesic, and muscle-relaxant effects in this scenario. The mechanisms of action of many herbs have already been recognised, and they are similar to those of synthetic drugs. While the efficacy of several herbal medications has been demonstrated via traditional usage, the specific mechanism by which they function remains unknown<sup>111</sup>. Furthermore, although traditional treatments are pure chemicals, plants frequently comprise component mixtures. Natural herbal remedies frequently have pain-relieving properties due to its many constituents, each of which has a distinct biochemical pathway via which it might function. Other herbal components, on the other hand, might be to blame for how the patient's other synthetic prescriptions interact with them<sup>112</sup>. To recap, plant-derived medications may be useful in controlling chronic pain with few side effects, but they are not appropriate for providing quick relief in situations of acute pain.

### 13. Future Perspectives and Conclusions

The *Fabaceae* family contains several well-known plants used in traditional medicine. *Pterocarpus marsupium*, *Cassia fistula*, *Vachellia leucophloea*,

*Butea monospermae*, *Trifolium species*, *Acacia catechu*, *Pureria tuberosa*, *Pongamia pinnata*, *Acacia nilotica*, and *Glycyrrhiza glabra*, *Bauhinia racemosa*, *Cajanus cajan*, *Lablab purpureus*, *Sesbania grandiflora*, *Bauhinia tomentosa*, *Erythrina stricta*, *Smithia sensitiva*, *Acacia mearnsii*, *Acacia mellifera*, *Vachellia seyal* and few more plants were studied in this review. According to the studies given, the medicinal herbs mentioned above have potent anti-arthritic and antinociceptive properties. The review's results on novel medicinal chemicals that can be adjusted to relieve pain generated by arthritis are promising. The majority of the extracts discovered were as least as effective as commonly used synthetic drugs and lacked any toxic qualities or unknown adverse effects. Overall, there is promising evidence that the Fabaceae genus may be effective in the treatment of pain-related illnesses associated with arthritis but the data is too preliminary and frequently excludes specific molecular and cell-based mechanisms of action, as well as crucial active components. The next stage of study should concentrate on knowing the mechanisms of action, precise doses, clinical pain management efficacy, and safety of extracts and active chemicals used to treat pain. This article outlines a feasible technique for uncovering more novel chemicals with painkilling potential from a variety of medicinal plants.

### 14. Acknowledgement

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