

The Possible Role of Annual Mugwort (*Artemisia Annua*) in Arthritis

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Abstract: Annual mugwort (*Artemisia annua*) is commonly found in Asia. Besides its antimalarial effect, *Artemisia annua* might have some roles in arthritis due to its bioactive components. **Objective:** The paper aims to describe the possible role of annual mugwort (*Artemisia annua*) in treating arthritis. **Methods:** This paper is a narrative literature review. Literature was chosen from PubMed, Science Direct, and Google Scholar. Selected journals were published within 10 years. **Results:** *Artemisia annua* is well known in Asia, Europe, Australia, and America. The sesquiterpene lactone artemisinin compound in this medicinal plant is related to the antimalarial effect. The main components are flavonoids, phenolic acids, sesquiterpene lactones, and coumarins. It is often used in the treatment for dysentery, malaria, jaundice, tuberculosis, hemorrhoids, and autoimmune disease. Recently, it was found that *Artemisia annua* has some unique properties such as antioxidant, analgesic, and anti-inflammatory. Based on these properties, *Artemisia annua* is developed as a natural remedy for osteoarthritis. *Artemisia annua* leaves also diminish the concentration of proinflammatory cytokines, interleukin-6, and interleukin-8. **Conclusion:** In conclusion, the possible role of *Artemisia annua* in arthritis might be related to its analgesic and anti-inflammatory properties. Further studies are needed to explore the possible dosage, contraindication, and side effects.

1 INTRODUCTION

Osteoarthritis is a degenerative joint disease. It is related to low-grade systemic inflammation and oxidative stress (Lambert et al., 2021; Yuan et al., 2021). Osteoarthritis is categorized as a chronic senescent process and caused low-grade inflammation (Chen et al., 2022). There is also muscle dysfunction related to osteoarthritis. Therefore, enhancing the function of muscle and minimizing the destruction of the joint could normalize muscle force capacity (Marks, 2023). It is characterized by cartilage destruction, pain, and joint stiffness. Some natural products with prophylactic effects have been studied lately, include *Artemisia* (Lee et al., 2020). In normal condition, there is a balance between the synthesis and degradation of Extracellular matrix (ECM). However, in abnormal condition such as degenerative disease, chondrocytes secrete a lot of degrading enzymes, namely matrix metalloproteinases (MMPs), a disintegrin and metalloproteinase with thrombospondin motifs (ADAMTSs). Those pro-inflammatory cytokines (such as interleukin (IL)-1 β) will induce abnormal conditions for chondrocytes and increase the up-regulation of catabolic factors (Lee et al., 2020).

Asia is a common place to find annual mugwort, or *Artemisia annua*. Owing to its bioactive components, *Artemisia annua* may have functions in arthritis in addition to its antimalarial effect. The annual mugwort, or *Artemisia annua*, has a long history of use in traditional medicine. Besides Asia, this species is also commonly found in Europe, Americas, and Australia. Since the 2015 Nobel Prize was given for discovering the sesquiterpene lactone can be impacted by their structural elements or matrix. The bioactive components of white mugwort are epoxide, artemisidiyne, polyphenols, and quercetin (Udomwasinakun et al., 2023).

A. vulgaris, another species of *Artemisia*, also shown effects against chronic inflammation by an animal experimental model. This plant grown in various altitudes related to the various pharmacological effects. The side effects are minimum. Nevertheless, thorough studies must be conducted to ensure the effect of the extract and the exact mechanism at clinical trials (Pandey et al., 2021).

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artemisinin in the species and demonstrating its antimalarial properties, the species has drawn special attention (Ekiert et al., 2021). Both the Vietnamese and Chinese pharmacopoeia list leaves as a raw material. The WHO's International Pharmacopoeia enzymes will degrade the ECM and also destruct cartilage (Blasioli & Kaplan, 2014). Furthermore, bacterial dysentery and jaundice, to treat wounds and hemorrhoids, to treat malaria and tuberculosis, and to treat autoimmune, viral, and bacterial illnesses. Professional pharmacological research carried out today has validated its well-known traditional uses and clarified hitherto unknown biological action mechanisms. It has also revealed evidence of novel biological activity directions, such as nephroprotective, antioxidant, antitumor, analgesic, and anti-inflammatory properties (Ekiert et al., 2021).

A. annua extract's safety and anti-inflammatory efficaciousness were evaluated in a randomized, double-blind clinical trial that was carried out in 2015 at Promisia Integrative Limited in Wellington, New Zealand. Supercritical CO₂ is used to extract the plant's herb, yielding the extract. It is advised to get ready if you have hip or knee osteoarthritis and are experiencing pain and stiffness (Ekiert et al., 2021). In a study by Ekiert et al., forty-two patients were divided into three groups at random as part of the experiment. The first group of patients received 150 mg of *A. annua* extract twice a day, the second group received 300 mg of *A. annua* extract twice a day, and the third group of patients served as the control group and were given a placebo twice a day for 12-week study. In patients receiving the lower dose of the extract (150 mg), there was a notable decrease in the pain score (Ekiert et al., 2021).

There were decreased joint stiffness, increased physical fitness, and decreased when *A. annua* was taken at the lower dose. Testing with the extract at a higher dose (300 mg) did not show any discernible improvement in the indicators. The study's authors demonstrated that administering 150 mg of *A. annua* extract for three months can lower inflammation and provide analgesic relief in patients with osteoarthritis. Subsequently, their impact on the human colon adenoma cell line Caco-2 was examined. Caco-2 cells form brush borders, or microvilli. Additionally, they are capable of producing the systems and enzymes needed to move substances. In the experiment, lipopolysaccharide and cytokines were used to cause inflammation in Caco-2 cells. It was also looked into how plant leaf extracts affected cytochrome P450 activity, which impacts artemisinin metabolism. Additionally, the extracts prevented CYP1A1 from being activated by benz- α -pyrene and CYP3A4 from being activated by Calcitriol. According to the findings, cytochrome P450 inhibition by extracts from *A. annua* leaves Asia for treating liver and menstrual issues. In Thailand, the stems and leaves are eaten raw or

can raise artemisinin's bioavailability and have an anti-inflammatory effect. It was established that the essential oil and every tested compound had dose-dependent analgesic effects (Ekiert et al., 2021).

Based on the various data of the previous research, this paper aims to describe the possible role of annual mugwort (*Artemisia annua*) in treating arthritis.

2 METHOD

This paper is a narrative literature review. Literature was taken from Science Direct, PubMed, and Google Scholar. Selected journals were published within 10 years.

a. DISCUSSION

Osteoarthritis happens due to multifactorial reasons. There is loss of balance between catabolic and anabolic of cartilage. Obesity, injury, genetic factors, gender (female), and aging are the common risk factors (Ma et al., 2020; Veronesi et al., 2022). Some pathological changes include synovial inflammation, cartilage erosion, and subchondral sclerosis. The therapy is divided into pharmacological and non-pharmacological treatment. Treatments are targeted to specific mediators to reduce the cartilage destruction due to an imbalance of catabolic and anabolic activity (Heikal et al., 2020).

In America, Australia, Europe, and Asia, *Artemisia annua* is highly recognized. The antimalarial activity of this medicinal plant is associated with the sesquiterpene lactone artemisinin component. Flavonoids, phenolic acids, sesquiterpene lactones, and coumarins are the principal constituents. It is frequently used to treat autoimmune diseases, hemorrhoids, malaria, jaundice, TB, and dysentery. It was recently discovered that *Artemisia annua* had several special qualities, including anti-inflammatory, analgesic, and antioxidant effects. *Artemisia annua* is created as a natural osteoarthritis therapy based on these qualities. Additionally, the leaves of *Artemisia annua* inhibit the release of interleukin-6 and interleukin-8, two proinflammatory cytokines (Ekiert et al., 2021).

Other type of *Artemisia* species, i.e. Jing-Ju-Chai, or white mugwort (*Artemisia lactiflora* Wall.), is edible and primarily found in Southeast Asia cooked into meals and beverages.

Products containing white mugwort can be found on the market

in a variety of forms for various uses, including liquid extract supplements and dried leaves and powder to blend with beverages. Generally speaking, the accessibility and digestibility of the bioactive chemicals found in plant-based meals Modern pharmacological research has established the antiprotozoal, immunosuppressive, antifungal, antibacterial, analgesic, antioxidant, anti-inflammatory, anti-cancer, nephroprotective, and essential oil properties of *A. annua*. Some clearly documented effects support this plant's long-known medicinal properties. Most of the proven analgesic, antioxidant, anti-inflammatory, and nephroprotective qualities are distinct. Up to twelve different variants of this species that could be used in cosmetic products can be discovered in the European CosIng (Cosmetic Ingredients) database (Ekiert et al., 2021).

A clinical trial with randomized control was conducted. The 80 cases in the control group and the 79 cases in the *Artemisia annua* L. (EAA) group were randomly assigned among the 159 participants who had active RA. For 48 weeks, individuals in the control group received medication in the form of leflunomide and methotrexate, whereas those in the EAA group received this medication along with 30 g/d of EAA. The objective pain score, number of painful joints and Erythrocyte Sedimentation Rate (ESR), all significantly improved ($P < 0.01$ or $P < 0.05$) in the EAA group after 12 weeks. At 24 and 48 weeks, the EAA group's overall efficacy was significantly higher ($P < 0.01$) than that of the control group. Within 12 weeks of treatment, the EAA group had a considerably greater rate of corticosteroid cessation ($P < 0.05$ or $P < 0.01$) and a significantly lower incidence rate of adverse effects compared to the control group. It was concluded that combination of EAA plus methotrexate and methotrexate and leflunomide in the treatment of active Rheumatoid. When discussing diagnoses and potential treatments, it is crucial for patients to consult healthcare specialists due to the variety of arthritis kinds and linked problems that may require different approaches. Medicine combination should be taken into account when administering *Artemisia annua* for patient who has certain comorbidities. Patients who consumes multiple QT prolonging medicines might have an increased risk of cardiac arrest or sudden death. This is why physician input is crucial to the prophylaxis and treatment of malaria in order to prevent resistance. The potential side effects such as hepatic injury and QT prolongation were seen in some cases in New Zealand (Medsafe, 2019).

4 CONCLUSIONS

In conclusion, the possible role of *Artemisia* in arthritis might be related to its analgesic and anti-

inflammatory properties, by reducing pro-inflammatory cytokines. Further studies are needed to explore the possible dosage, contraindication, and side effects.

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