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Kaempeferol (Elaeagnus angustifolia) Supplementation in Osteoarthritis: A Review

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KEYWORDS:

Kaempferol, Elaeagnus angustifolia, rheumatic diseases, osteoarthritis.

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ABSTRACT

Background: Kaempferol supplementation (KS) has been used in Iranian medicine to treat several conditions, including rheumatic diseases.
Aim: To review the use of KS in rheumatic diseases.
Methods: PubMed and Scielo databases were searched for articles on KS and rheumatic diseases until September 2024.
Results: There are 3 articles with 162 patients. Age varied from 52 to 56.31 ± 8.90 years old, and female gender ranged from 32% to 100%. The kaempferol dosage went from 300 mg to 15 g/day. The study follow-up ranged from 4 to 8 weeks. Concerning outcomes, no significant clinical differences were detected comparing kaempferol and control. A reduction in proinflammatory parameters was observed after kaempferol supplementation: a decrease in tumor necrosis factor and matrix metalloproteinase-1 levels and an increase in interleukin-10.
Conclusion: This review shows that KS does not seem to have a significant clinical impact on OA treatment. One study showed decreased cytokine levels and a reduction in metalloproteinase. Future studies are, however, needed to confirm the present data.

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INTRODUCTION

Elaeagnus angustifolia (EA), commonly known as Russian olive, has been traditionally utilized in Iranian folk medicine for the treatment of various ailments, including fever, amoebic dysentery, and gastrointestinal issues such as nausea, vomiting, and jaundice. Additionally, it has been used for treating asthma and rheumatic diseases [1]. Phytochemical analysis of EA identified kaempferol-3-O-(6″-trans-p-coumaroyl)-β-D-glucopyranoside as one of its most significant compounds [1,2]. Research has demonstrated that extracts from EA possess potent anti-inflammatory, analgesic, and muscle relaxant properties, further supporting its use in traditional medicine [3].

This study's purpose was to conduct a review on the use of EA as a treatment for rheumatic diseases.

METHODS

Literature review: A systematic search of articles published in PubMed and Scielo until September 2024 using the following MeSH entry terms: "kaempferol" AND " Elaeagnus angustifolia " OR "rheumatologic" OR "fibromyalgia" OR "rheumatoid arthritis" OR "spondyloarthritis" OR "osteoarthritis" OR "gout." Was done. The search had no language restriction. The reference lists of the selected articles were analyzed to identify other publications.

The authors (JFC and RPCA) initially performed the literature search and independently selected the study abstracts. Then, in the second stage, the same reviewers independently read the full-text articles selected by abstracts. Finally, a standardized form was designed to extract the information from relevant articles, including authors, year of publication, number of patients studied, demographic data, disease duration, study follow-up, kaempferol posology, outcomes, and side effects.

RESULTS

Table 1 summarizes the search results on kaempferol treatment in knee OA studies [7-12]. There are 3 articles in this field, including 162 patients. All studies were performed in Iran. All trials had a randomized, double-blind, controlled design. Age varied from 52 to 56.31 ± 8.90 years old, and female gender ranged from 32% to 100%. Only one study showed the disease duration that was 6.35 ± 4.39 years. The kaempferol dosage went from 300 mg to 15 g/day. The study follow-up ranged from 4 to 8 weeks.

Concerning outcomes, no significant clinical differences were detected comparing kaempferol and the control. However, it was demonstrated that this substance is not inferior to ibuprofen in reducing clinical parameters, including a reduction in proinflammatory parameters observed after kaempferol supplementation: a decrease in tumor necrosis factor and matrix metalloproteinase-1 levels and an increase in interleukin-10 [re].

Only one study detected side effects, which were mild and similar to the placebo.

DISCUSSION

This is the first study to review the therapeutic effects of KS in rheumatic diseases.

Two studies have demonstrated the efficacy of EA in reducing clinical parameters in knee OA [5.6]. In fact, kaempferol had significant lowering effects on the Visual Analogue Scale (VAS), Pain-Function Index (LPFI), and Patient Global Assessment scores similar to those of ibuprofen use [5,6].

One study demonstrated that supplementation with Elaeagnus angustifolia L. (using medulla powder and whole fruit) in patients with osteoarthritis (OA) significantly reduced serum levels of TNF and MMP-1, while also increasing levels of the anti-inflammatory marker IL-10 [6]. Although the placebo group showed some improvement in the studied biomarkers, these changes were not statistically significant. The improvements in the placebo group may be attributed to the effects of conventional treatments these patients were receiving.

Several mechanisms have been proposed to explain the effects of E. angustifolia extracts. An animal study indicated that aqueous plant extracts inhibit the cyclooxygenase-1 (COX-1) and COX-2 enzymes like indomethacin [7]. Additionally, it has been suggested that Elaeagnus extracts may reduce the production of free radicals in OA-affected tissues due to their antioxidant properties, which are attributed to the flavonoid components present in the plant [8].

This study's strengths are (1) the inclusion of studies with patients with international criteria for rheumatic diseases and (2) the inclusion of all kinds of study designs for using KS in rheumatic diseases, except reviews, animal studies, and *in vitro* studies. In this way, the authors believe all published cases of KS in rheumatic patients were collected.

This study had some limitations. For instance, the number of participants was still low. More importantly, only one rheumatic disorder was studied more—OA. It is reasonable to evaluate the effect of KS in other rheumatological conditions. Therefore, future studies should include larger patient samples with more long-term observation, enabling a better understanding of the course of KS in rheumatic diseases.

CONCLUSION

Few evidence exists of the use of kaempferol supplementation in treating OA. Nevertheless, almost all analyzed studies demonstrated that KS use is efficacious in treating signs and symptoms of this rheumatic disease (pain, joint tenderness, swelling, quality of life) with rare and minor side effects.

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Conflicts of interest:

None

Author contributions:

JFC: Conception, analysis, literature searching, writing, submission, supervision.

RBCA: analysis, literature searching, writing, revision.

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Table 1. Summary of the studies that evaluated kaempferol in osteoarthritis;

Author, reference	Study design	Country	N	Age (years old)/gender	Disease duration	Kaempferol dose (mg/day)	Follow-up	Outcome	Side effects
Karimifar et al., 2017 [4]	Randomized double-blind controlled clinical trial	Iran	75	52 ND	ND	ND (EA, EA/BT vs. Ibuprofen)	4 weeks	All interventions had significant lowering effects on Visual Analogue Scale (VAS), Pain-Function Index (LPFI), and Patient Global Assessment scores, but no significant difference between groups.	2 patients in EA, 3 in EA/BT and 4 ibuprofen had dyspepsia and constipation
Panahi et al., 2016 [5]	Randomized, double-blind, active-controlled, and parallel group trial	Iran	97	55.0 32% females	ND	300 mg or 600 mg vs. 800mg ibuprofen	7 weeks	No differences between Western Ontario and McMaster Universities' Osteoarthritis Index (WOMAC), Visual Analogue Scale (VAS) of pain, Lequesne's Pain-Function Index (LPFI).	None
Nikniaz et al., 2014 [6]	Double-blind randomized placebo-controlled stud	Iran	90	56.31 ± 8.90 100% females	6.35 ± 4.39 years	15g of EA whole fruit vs. 15g medulla powders of EA vs. placebo	8 weeks	Decrease in tumor necrosis factor and matrix metalloproteinase-1 levels and increase in interleukin-10.	None

N: number; ND: not described; EA: Elaeagnus angustifolia; BT: Boswellia thurifera