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The Isoflavone Intake for Preventing Osteoporosis in Menopausal Women: A Systematic Review and Meta-Analysis

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ABSTRACT
Osteoporosis is a condition marked by reduced bone mass and structural deterioration, increasing the risk of fractures. Isoflavones have been proposed as an alternative treatment to manage osteoporosis-related symptoms. This study aimed to evaluate the effectiveness of the isoflavones in improving bone health. A systematic search was conducted using PubMed, ScienceDirect, and Google Scholar, following PRISMA 2023 guidelines to identify relevant studies. Articles were selected based on their investigation of isoflavones' effects on osteoporosis. A meta-analysis using a random-effects model was performed, with outcomes reported as odds ratios and 95% confidence intervals (CI). Two studies (total participants = 251) met the inclusion criteria. The findings indicated that isoflavones had a positive effect on increasing bone mineral density (BMD) in postmenopausal women with osteoporosis, showing a mean difference of 0.87 (95% CI: 0.42 to 1.78; p = 0.78). However, the improvement was not statistically significant compared to the placebo group. In conclusion, while isoflavones appear to support BMD, they did not show a significant advantage over placebo. Nonetheless, they may still be considered a potential complementary therapy for managing osteoporosis symptoms, especially in postmenopausal women.
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1. INTRODUCTION

Osteoporosis is a pathological condition of the bones characterized by decreased bone mass and deterioration of the bone microarchitecture, resulting in an increased risk of fractures (1). It is estimated that more than 100 million adults worldwide are affected by osteoporosis (2,3), and more than 10 million osteoporotic fractures occur each year (4). One of the primary causes of osteoporosis is estrogen deficiency, which contributes to a higher incidence of the disease in postmenopausal women compared to younger women and men (3,5).

Long-term management of postmenopausal osteoporosis, including regular supplementation with nutrients that cause minimal or no side effects, is preferable to treatment options associated with serious side effects. Phytoestrogens, which are plant-derived compounds, are known to cause fewer side effects than synthetic drugs and offer a promising alternative for the long-term management of postmenopausal osteoporosis (6). These polyphenolic compounds come from legumes, nuts, and beans and have an affinity for estrogen receptors. Phytoestrogens are categorized into four major groups: *isoflavonoids*, flavonoids, lignans, and stilbenes (7).

Isoflavonoids are a subclass of polyphenolic compounds derived from the FABA family and are known for their estrogenic potential, cholesterol-lowering, chemotherapeutic, and antioxidant activities. Different isoflavones exhibit distinct bioactivities, and provide a unique profile of isoflavones, particularly rich in

formononetin and biochanin A (8). Enzymatic and probiotic methods can be employed to enhance isoflavone absorption.
Fermented isoflavone formulations (aglycone-rich) demonstrate higher bioavailability compared to non-fermented (glycoside-rich) formulations.) (9–11). In vivo studies on female rats with induced bone loss (via ovariectomy) support the theory that formononetin, in particular, may possess both anti-resorptive and anabolic properties (12). (12). Randomized controlled trials (RCTs) in humans have also shown promising effects of isoflavones in reducing markers of bone resorption. (13).

Genistein aglycone, a plant-derived nutrient belonging to the isoflavone class, has been shown to prevent bone loss in osteopenic postmenopausal women through modulation of estrogen receptors (14,15). Post-hoc analyses of RCTs suggest that genistein may also be effective in patients with osteoporosis by promoting a favorable balance in bone turnover, shifting it towards bone formation.

This review presents a current expert analysis of data on isoflavone intake and its role in increasing bone mineral density (BMD) compared to placebo in women with osteoporosis.

2. METHOD

This systematic review and meta-analysis were conducted to ascertain the relationship between isoflavone intake and postmenopausal osteoporosis. A comprehensive literature search was carried out using databases such as Google Scholar, ScienceDirect, and PubMed. The following Medical Subject Headings (MeSH) terms were used individually or in combination during the search: “Osteoporosis,” “Postmenopausal,” and “Isoflavone.” The review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The PRISMA flowchart for study inclusion in the review is shown in Figure 1.

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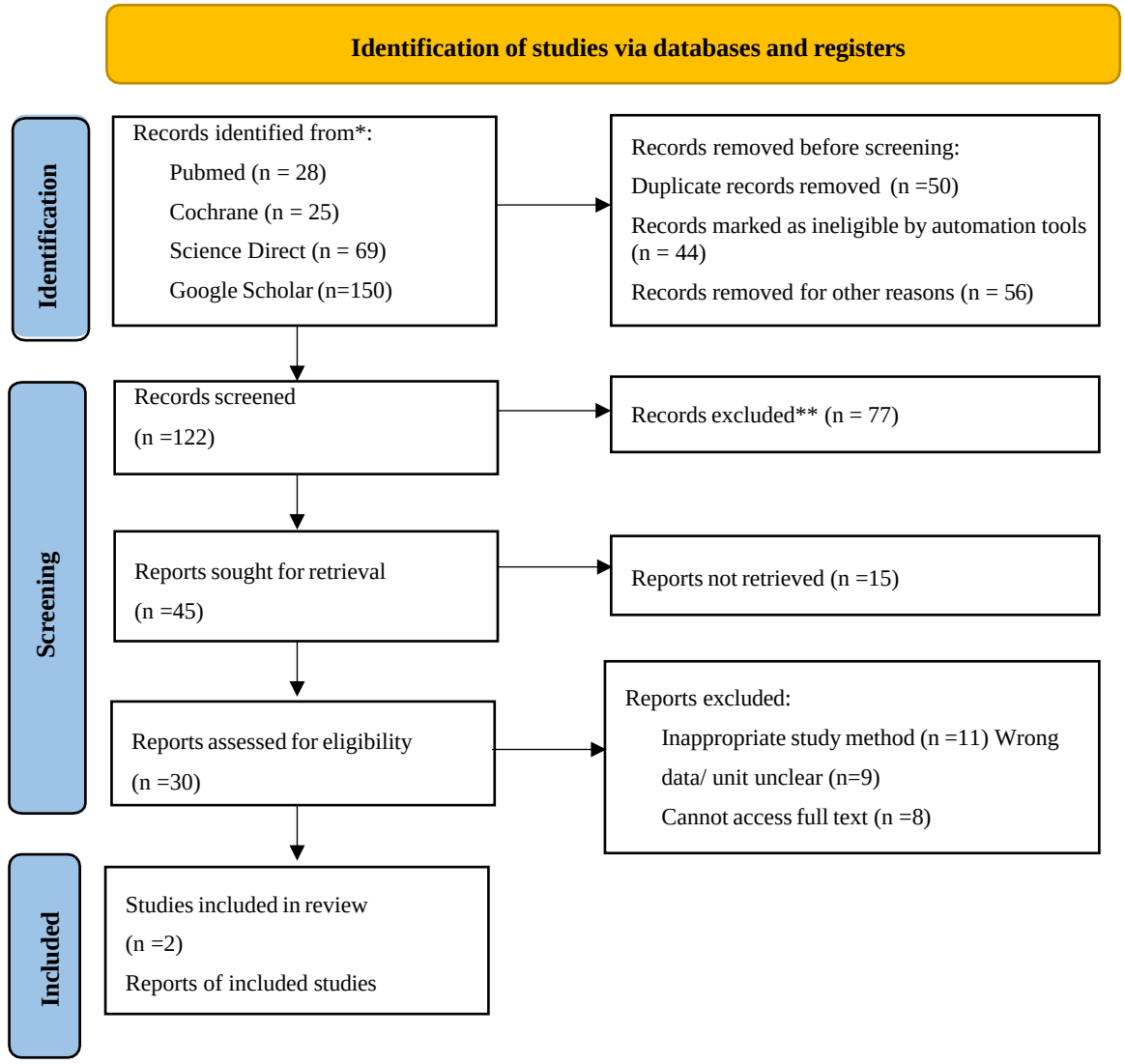

Figure 1. PRISMA flowchart of the literature selection

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3. RESULTS AND DISCUSSION

Summary of Mean Differences in Subgroup Analysis of Isoflavone and Osteoporosis Improvement. In this subgroup analysis, two studies compared the improvement in bone mineral density (BMD) in osteoporosis between the isoflavone group and the placebo group. Two studies comparing osteoporosis in menopause between the isoflavone group and the placebo group were included.

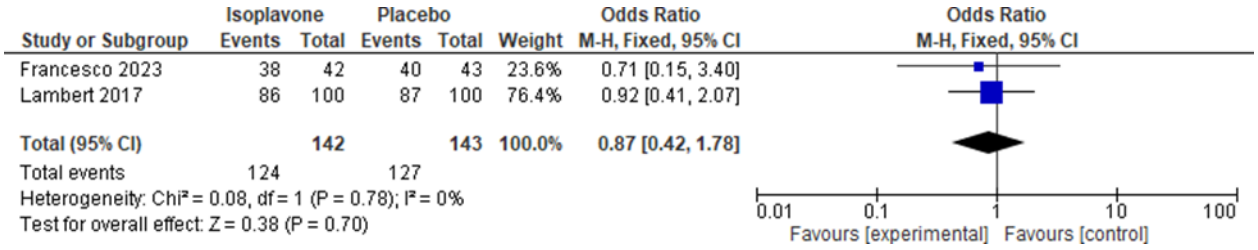

Figure 2. Bone mineral density (BMD) in osteoporosis between the isoflavone group and the placebo group

The isoflavone group showed an effect in increasing bone mineral density (BMD) in postmenopausal women with osteoporosis, with a mean difference of 0.87 (95% CI: 0.42–1.78; p = 0.78). However, treatment with isoflavone did not result in a significantly greater improvement in osteoporosis compared to the placebo group (mean difference: 0.87; 95% CI: 0.42–1.78; p = 0.78), as shown in Figure 3.

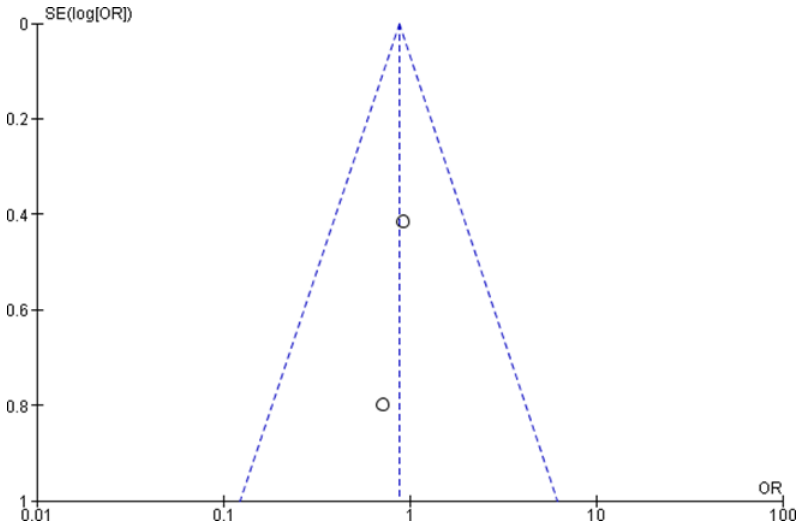

Figure 3. Funnel plot diagram for the improvement in bone mineral density (BMD) in osteoporosis between the isoflavone group and the placebo group

Osteoporosis is a degenerative condition associated with aging and characterized by low bone mass and reduced bone microstructure, thereby increasing the risk of fractures (16). According to a report on osteoporosis in Indonesia, approximately 32.3% of women aged 50 and above know more about osteoporosis than 50 (17). The World Health Organization (WHO) reports that osteoporosis can cause lifelong disability in 50% of those affected (17).

There are various factors that influence the onset of osteoporosis. In postmenopausal women, more pronounced than in men, with estrogen considered a contributing factor to osteoporosis. Isoflavones are

compounds that have a chemical structure and function similar to estrogen hormones. They are classified as phytoestrogens and are commonly found in soybeans and non-fermented soy products (18,19). Isoflavones act as selective estrogen receptor modulators (SERMs) and produce effects similar to those of raloxifene (20,21). They play a role in stimulating bone formation and inhibiting bone resorption, thereby helping to maintain bone health.

A previous randomized clinical trial demonstrated that a diet rich in isoflavones was more effective in reducing the risk of bone loss in postmenopausal women compared to a placebo (19,22). Another study has shown that the inclusion of 60 mg/day of isoflavones for 8 weeks can reduce the risk of bone loss in postmenopausal women (23). These results suggest that isoflavone supplementation serves as a preventive treatment in postmenopausal women.

Treatment with isoflavones showed a slightly better improvement in bone mineral density (BMD) in postmenopausal women with osteoporosis, with a mean difference of 0.87 (95% CI: 0.42–1.78; p = 0.78). However, this improvement was not statistically significant when compared to the placebo group. These results are consistent with previous trials supporting the beneficial effects of isoflavones in significantly preventing and reducing the risk of osteoporosis in postmenopausal women. (21,24).

It should be noted, however, that this study included only two related articles. Therefore, further testing is needed to determine the actual effect of isoflavone supplementation on bone mineral density (BMD) in postmenopausal women with osteoporosis. Nonetheless, this study highlights the potential of isoflavones as a natural alternative therapy to estrogen replacement for postmenopausal women.

4. CONCLUSION

In short, osteoporosis is a pathological condition of the bones, characterized by a decrease in bone mass and degradation of bone microstructure, increasing the risk of fractures. One of the main factors contributing to osteoporosis is estrogen deficiency, which increases the incidence of osteoporosis in women during menopause. In a double-blind trial, treatment with isoflavones demonstrated potential in the prevention and treatment of osteoporosis compared to placebo. Isoflavones should be considered as an alternative treatment for symptoms associated with osteoporosis.

However, it is important to note that only two studies met the inclusion criteria, which significantly limits the generalizability and strength of the conclusions. This narrow dataset may not adequately represent the broader population, and the observed outcomes should therefore be interpreted with caution. Future studies with larger sample sizes and diverse populations are needed to confirm these findings. This meta-analysis is limited by the small number of eligible studies (n=2), which restricts the statistical power and external validity of the results. Hence, while isoflavones appear promising, stronger evidence is required.

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