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# The Probable Impact of Soy Isoflavones in Bone Fracture Downturn: A Systematic Review

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#### **ABSTRACT**

Background: There is a direct relationship between taking soy isoflavones and higher bone density, but there is a paucity of studies examining the relationship between flavonoid consumption and fracture risk. This study aimed to assess the bone fracture and its relationship to soy product intake by performing a systematic review. Methods: Scopus, PubMed, and Web of science were searched to find studies on the effect of soy isoflavones on bone fracture, without any time and language of publication restrictions. Key words of SoyMilk, soymilk, soybeans, soybean, soy, soya, Isoflavones, Isoflavone, ipriflavone, equol, genistein, daidzein, glycitin, fractures, and broken bone were used. **Results:** From a total of 1675 articles, 27 studies (cross-sectional studies (n=1), case-control studies (n=1), cohort (n=11), and randomized control trials (n=14)) were identified, and their quality was assessed. Eighteen studies highlighted mainly positive results in preventive influence of soy bone fractures. Two papers reported a positive effect was observed in men with cancer. No significant association was found between soy intake and bone prevention fracture in eight distinct papers. Conclusion: Intake of soy isoflavones can make a significant preventive effect on bone fracture; however, the results of some studies are controversial. Therefore, it is necessary to survey more studies to identify the relationship between isoflavones and bone fracture.

**Keywords:** *Isoflavones; Bone; Fracture* 

#### Introduction

Bone with frequent renovation during the lifespan is an active tissue (Shetty et al., 2016). Bone renovation contains two stages including formation of new bone tissue and reabsorption of the old bone tissue (Eastell and Szulc, 2017). During growth, the amount of new bone tissue formation surpasses that of

reabsorption of old bone tissue, but with age, this trend is reversed. Augmented and non-stop bone reabsorption in aging causes osteoporosis. Osteoporosis is categorized by decreased bone mass related to augmented bone fragility and vulnerability to fracture (Shetty *et al.*, 2016).

Pelvic fractures increase the financial burden by

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postmenopausal women (Zhang et al., 2005). They also increased bone mineral density (BMD) (Abdi et al., 2016). Soy isoflavones might affect the bone by decreasing bone resorption while motivating bone formation (Arjmandi and Smith, 2002). Soy products stimulate the osteoblastic formation of osteoprotegerin, which prevents bone resorption (Viereck et al., 2002). They also have a function and structure similar to tamoxifen, which can be effective in reducing bone loss after menopause (George et al., 2020). Soy isoflavones, with their antioxidant effect, suppress angiogenesis by inhibiting the protein tyrosine kinase and cell growth by interfering with signal transmission. Isoflavones are also thought to inhibit aromatase and 5a reductase and induce estrogen synthesis (George et al., 2020).

Soy also increases the production of insulinlike growth factor 1, an indicator recognized to increase osteoblastic activity related to bone formation (Arjmandi and Smith, 2002). The amount of IGF-I in both sexes decreases with age, which intensifies in menopause (George et al., 2020). IGF-I, like growth hormone, stimulates bone formation (George et al., 2020). It may also increase the production of 1,25 (OH)2 vitamin D by regulating 1α-hydroxylase activity (George et al., 2020). Soy consumption in postmenopausal women has caused a reduction in urinary excretion of bone indicators (Nikander et al., 2004). Menaquinone-7 (MK-7) enables osteocalcin y -carboxylation (Shetty et al., 2016), and mineralization (Bruge et al., 2011). In a study in the Caucasus, MK-7 consumption was effective in preventing bone fractures in postmenopausal women (Knapen et al., 2013). Thus, soy products prevent bone fractures by preserving bone mass and bone microarchitecture (Rønn et al., 2016). Soy products can decrease bone loss (Wong et al., 2009) and provoke bone formation (Ma et al., 2008b, Marini et al., 2007); this association was not found in 8 studies. This can be attributed to different types of isoflavones in different soy products (Kojima et al., 2020). Isoflavone aglycones in unfermented soy products, such as tofu, are absorbed faster and have more bioavailability than other soy products (Izumi et al., 2000). The phytoestrogens in soy reduce the process of bone loss (Ma et al., 2008a). The effect of soy in avoiding osteoporosis in men has not been determined (Newton et al., 2006). The exact mechanism of genistein in men is unknown (Piekarz and Ward, 2007). Genistein prevents bone loss by increasing the activity of osteoblasts in male rodents (Khalil et al., 2005). Decreased testosterone is observed in men with age (Orwoll et al., 2006), since testosterone helps maintain bone health in men (Amin et al., 2006). Therefore, isoflavones can be effective in preventing bone fractures in older men and soy products, due to the mentioned properties, can be effective in preventing bone fractures.

### **Opposing effects**

Isoflavones have structures similar to estrogens, so they increase the risk of breast cancer in susceptible individuals or general survival from breast cancer (Qiu and Jiang, 2019, Touillaud *et al.*, 2019).

#### Limitation

This review study had some limitations. Each study had different interventions, evaluating different results, which made impossible to compare the results. Also, confounding factors such as age, BMI, and dietary calcium intake were not investigated.

#### Conclusion

Various diseases and factors that affect bone fractures mainly affect the quality of life of people. Therefore, the results of this review revealed that soy consumption may have a beneficial effect on preventing bone fraction. More studies with a longer time of intervention on a larger sample size are recommended to approve these results.

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