

MIGHT FENUGREEK SEED EXTRACT BE A PROPHYLACTIC THERAPY FROM OSTEOPOROSIS?

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Abstract

Osteoporosis is a systemic bone disease characterized by reduced bone mass and the deterioration of bone microarchitecture leading to bone fragility and an increased risk of fractures. Fenugreek regulates osteogenic markers and upregulates osteoblast differentiation by stimulating extracellular calcium concentrations as well as osteoblast differentiation. Experimental studies have shown that it increases osteocalcin and bone morphogenic protein-2 (BMP-2) levels in treated cells. Fenugreek causes DNA damage of osteoclasts. Also, fenugreek steroidal saponins hinder osteoclastogenic bone resorption. Trigonelline, a known constituent of fenugreek seeds, showed significant improvement and prevent the progression of osteoporosis. We conclude that fenugreek seed extract might be of benefit for prophylaxis from osteoporosis. However, a well-planned randomized controlled trial is needed to have level I evidence of its efficacy.

Keywords: Osteoporosis, Fenugreek, Osteoclast, Osteoblast, bone resorption.

1. Introduction

Osteoporosis is a systemic bone disease characterized by reduced bone mass and the deterioration of bone microarchitecture leading to bone fragility and an increased risk of fractures [1]. The pathogenesis of osteoporosis involves an imbalance between osteoblast-mediated bone formation and resorption [2]. The normal remodeling cycle begins by osteoclastic bone resorption. This, then is repaired with an ingrowth of osteoblasts replacing the bone. In individuals older than 40 years, the osteoblasts rarely bring the original bone surface back to the starting point, and, thus, every remodeling cycle leaves a small deficit of bone. So, the discrepancies in the rate of

bone for resorption and formation lead to the gradual onset of osteoporosis [3]. Osteoporosis-associated fragility fractures constitute a major health problem all over the world. It is estimated that more than 40 million American citizens over 50 years of age are at risk of osteoporotic fractures, and that due to the demographic changes, this number will at least double until the year 2040 [4]. It is also predicted that 25% of people over 50 who have experienced osteoporotic hip fracture will die within a year [4]. The current treatment options for osteoporosis include bisphosphonates, hormone replacement therapy, selective estrogen receptor mod-

ulators (SERMs), and Denosumab. All of them not without side –effects [2]. Fenugreek (*Trigonella foenum -graecum*) is an annual herb with a long history as a traditional medicinal plant [5].

2. Fenugreek and Osteoporosis

Fenugreek seeds are useful for the treatment and prevention of different ailments [6]. Flavonoids, such as apigenin 6,8-di-C-glucoside, apigenin-6-C-glucosyl-8-C-galactoside, 6-Cgalactosyl- 8-C-arabinoside as well as rhaponticin, and isovitexin, are the main components of fenugreek seeds. Moreover, fenugreek seeds contain phosphorus, which is categorized into different classes such as inorganic phosphorus, phospholipids, phytates, phosphor-proteins, and nucleic acids. Germinated seeds contain amino acids, proteins, ascorbic acid, vitamin E and sugars [6-9]. The results of a previous study showed that feeding camels fenugreek (100 g / camel / day for two weeks) accelerated mandibular fracture healing [5]. Recently, we reported a case in which fenugreek seed extract enhanced healing of a fracture [10]. Previous studies have suggested several mechanisms by which fenugreek promotes bone formation. Fenugreek regulates osteogenic markers and upregulates osteoblast differentiation by stimulating extracellular calcium concentrations as well as osteoblast differentiation. Experimental studies have shown that it increases osteocalcin and bone morphogenic protein-2 (BMP-2) levels in treated cells. It also causes DNA damage of osteoclasts [8]. Also, Fenugreek steroidal saponins hinder osteoclastogenic bone resorption by targeting CSF-1R which diminishes the RANKL/OPG ratio [11]. Trigonelline, a known constituent of fenugreek seeds was investigated to determine the action on bone mechanical

properties in 12 weeks old non ovariectomized and ovariectomized rat model, and results displayed that receiving 1 % fenugreek seeds enhances tibial metaphysis strength of cancellous bone in non - ovariectomized rats and femoral diaphysis power of compact bone in ovariectomized rats [12]. In a rat model of dexamethasone-induced osteoporosis, Trigonelline showed significant improvement and prevent the progression of osteoporosis by enhancing the bone mineral density (BMD) and restoring bone physiology [13]. Anjaneyulu et al. Investigated the action of fenugreek seed extract on bone anatomy and mechanical activity in ovariectomized rats. The result showed that fenugreek seed extract improves the tibial dry weight as well as increases the cortical bone thickness and trabecular bone thickness [6, 14]. Fenugreek contains free amino acids, such as histidine [7] and calcium [15], both of which are important in bone formation [1,9]. Alkaline phosphatase (ALP) participates in the biological processes of bone healing. Fenugreek stimulates ALP activity in bone marrow-derived stem cells [11,16]. Dyslipidemia (mainly elevated total and low-density lipoprotein cholesterol concentrations) is associated with low bone mass and an increased fracture risk. This effect may be directly mediated by increased oxidative stress and systemic inflammation associated with dyslipidemia, leading to increased osteoclastic activity and reduced bone formation. Increased cholesterol inhibits osteoblast differentiation and prevents bone formation. Therefore, enhanced osteoclastogenesis might be involved in this process. Low high-density lipoprotein C (HDL-C) concentrations have been associated with the development of an inflammatory micro-environment and increased bone marrow

adiposity, which restrains the differentiation and function of osteoblasts, leading to reduced bone mass [17,18]. Experimental studies have shown that fenugreek significantly reduces triglyceride levels and causes a significant increase in HDL-C levels [19,20]. Other experimental study has shown that oxidative stress affects osteoblasts, osteoclasts, and osteocytes, causing an imbalance between bone formation and resorption in favor of bone resorption as well as impairing bone mineralization [21]. Several studies have suggested fenugreek as a potential antioxidant. Bhatia et al. [22] demonstrated the defensive effects of fenugreek on lipid peroxidation and enzymatic antioxidants in cyclophosphamide-treated mice by evaluating lipid peroxidation and antioxidants in the mouse urine bladder. Khole et al. [23] isolated two flavonoid compounds, vitexin and isovitexin, from germinated fenugreek seeds that were shown to have antioxidant activity. Some side effects were reported after use of fenugreek like abdominal distension, dyspepsia, hypersensitivity reaction, [15,24], hypoglycemia [15,25] and risk of bleeding due to coumarin content [15,26]. It should be taken into consideration that most of the old age patient has comorbidities, and receiving other drugs. Drinking fenugreek extract potentiates the effect of anticoagulant drug [9,26] and may reduce potassium serum level [15,28]. Additionally, it may increase the hypoglycemic effect of antidiabetic treatment [15,29]. An important consideration of drinking fenugreek seed extract is the characteristic odor of the sweet that might have a social effect.

3. Conclusion

Fenugreek seed extract might be of benefit for prophylaxis from osteoporosis. However, a well-

planned randomized controlled trial is needed to have level I evidence of its efficacy

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