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Review

Green tea and bone health: Evidence from laboratory studies

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ABSTRACT

Osteoporosis is a major health problem in the elderly. Epidemiological evidence has shown an association between tea consumption and the prevention of bone loss in the elderly population. Ingestion of green tea and green tea bioactive compounds may be beneficial in mitigating bone loss of this population and decreasing their risk of osteoporotic fractures. This review describes the effect of green tea with its bioactive components on bone health with an emphasis on the following: (i) the etiology of osteoporosis, (ii) evidence of osteo-protective impacts of green tea on bone mass and microarchitecture in various bone loss models in which induced by aging, sex hormone deficiency, and chronic inflammation, (iii) discussion of impacts of green tea on bone mass in two obesity models, (iv) observation of short-term green tea supplementation given to postmenopausal women with low bone mass, (v) possible mechanisms for the osteo-protective effects of green tea bioactive compounds, and (vi) a summary and future research direction of green tea and bone health.

1. Introduction

The trend of increased life expectancy is accompanied with an increase in the prevalence of osteoporosis and concomitant complications in the elderly population. Osteoporosis, a degenerative bone disease, is characterized by low bone mass and microstructural deterioration of bone tissue that results in bone fragility and an increased susceptibility to fractures [1]. Hip fracture is the most severe consequence of osteoporosis, resulting in decreased activities of daily living, lowered quality of life, and increased mortality [2].

Osteoporosis occurring in postmenopausal women and elderly men represents a major health and economic burden in our fast growing elderly population. In the United States, approximately 44 million or 55 percent of the people 50 and older have osteoporosis or low bone mass [3]. It is estimated that by 2020, there will be over 61 million women and men in this age category that are affected [3]. By the year 2025, experts predict that the costs of osteoporosis-related expenses will rise to approximately $25.3 billion [4].

Although there are a variety of agents available for the prevention and/or treatment of low bone mass (also called osteopenia) and osteoporosis, some patients select complementary and alternative therapies, such as dietary supplements or functional foods, for this purpose [5]. Tea, the dried leaves of the *Camellia sinensis* species of the Theaceae family, is a popular beverage with an annual production of three billion kilograms worldwide [6]. In the past decade, epidemiological evidence has shown an association between tea consumption and the prevention of age-related bone loss in the elderly population. The impact of tea consumption on bone mass and risk of osteoporotic fractures in humans has been comprehensively reported in our previous review paper and we found that among different forms of tea (green tea, black tea, white tea, and Oolong tea), drinking green tea and/or ingesting green tea bioactive compounds may mitigate bone loss in elderly women and men, thereby decreasing their risk of osteoporotic fractures

Abbreviations: BMC, bone mineral content; BMD, bone mineral density; EC, (−) epicatechin; ECG, (−) epicatechin gallate; EGC, (−) epigallocatechin; EGCG, (−) epigallocatechin gallate; ER, estrogen receptor; ERK, extracellular signal-regulated kinases; LF, low fat; GTC, green tea catechins; GTP, green tea polyphenols; HF, high fat; IL, interleukin; LPS, lipopolysaccharide; M-CSF, macrophage-colony stimulating factor; NF-κB, receptor activator of nuclear factor-κB; ORX, orchidectomized; OVX, ovariectomized; RANKL, receptor activator of nuclear factor-κB ligand; ROS, reactive oxygen species; Runx2, Runt-related transcription factor-2; SH, sham; TNF-α, tumor necrosis factor-α; TRAP, tartrate-resistant acid phosphatase.

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[7]. Therefore, in this review, we focus on animal studies in various models with an emphasis on bone health. In addition, a short-term translational study employing green tea supplement given to post-menopausal women with low bone mass is also discussed.

2. Bone biology and metabolic disorders

Bone is a highly specialized support tissue which is characterized by its rigidity and hardness. As a material, bone has strength similar to cast iron, while its density is as low as wood. Calcium and phosphorus mineral crystals are deposited around the protein strands. The flexible protein strands provide the tensile strength that holds the structure together and the brittle minerals provide the solid structure. The two main categories of bone cells are osteoblasts that form the bone and osteoclasts that resorb (dissolve) the bone. The combined and cooperative activities of osteoblasts and osteoclasts result in a bone architecture that provides mechanical support and protection for the body. In addition, bone serves as a vital reservoir of minerals, principally calcium and phosphorus, necessary for maintaining normal cellular, neurologic, and vascular activities of the body [8].

Table 1
Effect of green tea supplementation on bone health in various animal models.

First author, yr reference	Model	Animals	Treatments	Main results
Shen, 2008 [16] Shen, 2010 [21]	Aging-induced bone loss model Aging plus estrogen deficiency-induced bone loss model	Sham and OVX, 14-mo-old female F344 × BFN1/NIA rats	GTP: 0.1% or 0.5% (wt/vol) in drinking water for 16 weeks	↑ Femur BMD[a] ↑ Serum OC, ↓ serum TRAP, ↓ urinary Ca via ↓ 8-OHdG (a marker of oxidative stress DNA damage), ↑ GPX activity (a marker of antioxidant capacity), and ↑ SOD1 expression (a marker of antioxidant capacity)
Shen, 2009 [17]	Aging-induced bone loss model Aging plus estrogen deficiency-induced bone loss model	Sham and OVX, 14-mo-old female F344 × BFN1/NIA rats	GTP: 0.1% or 0.5% (wt/vol) in drinking water for 16 weeks	↑ BV/TV, BFR, Tb.N and Tb.Th of proximal tibia[b] ↑ Cortical thickness and area of femur[d] ↓ Tb.Sp and bone erosion of proximal tibia[b] ↓ Endocortical bone eroded surface of tibia shaft[b]
Shen, 2010 [23]	Aging-induced bone loss model Aging plus testosterone deficiency-induced bone loss model	Sham and ORX, 15-mo-old male F344 rats	GTP: 0.5% (wt/vol) in drinking water for 16 weeks	↑ BV/TV, Tb.Th and bone formation rates in both proximal tibia and periosteal tibial shafts[b] ↓ Eroded surface in both proximal tibia and endocortical tibial shafts[b] via ↑ GPX activity
Shen, 2010 [25]	Chronic inflammation (LPS)-induced bone loss model	3-month-old female CD rats	GTP: 0.5% (wt/vol) in drinking water for 12 weeks	↑ Femur BMD[a] ↑ Serum OC, ↓ serum TRAP via ↓ 8-OHdG production and ↓ COX-2 and TNF-α mRNA expression (makers of pro-inflammatory cytokine)
Shen, 2010 [26]	Chronic inflammation (LPS)-induced bone loss model	3-month-old female rats	GTP: 0.5% (wt/vol) in drinking water for 12 weeks	↑ BV/TV, Tb.N and Tb.Th of femur[d] and tibia[b] ↑ Periosteal bone formation rate in tibial shafts[b] ↓ Tb.Sp in proximal tibia and eroded surface in endocortical tibial shafts[b] ↓ Osteoclastic number of tibia shafts[b] ↑ Bone strength of femur via ↓ TNF-α protein expression in trabecular bone
Nakamura, 2010 [27]	Topically LPS-infected gingival inflammation model	7-wk-old male BALB/c mice	GTC: injection (10 μg/mL) into infected gingival, once every 48 h for 10 times	↓ LPS-induced alveolar bone resorption[b,c] (as shown by increased TRAP-positive osteoclasts) via ↓ IL-1β production (a marker of pro-inflammatory cytokine) or ↓ osteoclastogenesis directly
Maruyama, 2010 [28]	Topically LPS-infected periodontal inflammation model	8-wk-old male Wistar rats	GTC: 1% in dentifrice for the last 4 weeks in a total of 8 weeks study period	↓ LPS-induced inflammation cell infiltration in connective tissue via ↓ hexanoyl-lysine (a maker of lipid peroxidation), nitrotyrosine (a maker of oxidative protein damage), and TNF-α (a maker of pro-inflammatory cytokines) No impact on LPS-induced bone resorption
Shen, 2010 [30]	High-fat-diet induced obesity model	3-mo-old CD female rats fed a high-fat diet for 4 months	GTP: 0.5% (wt/vol) in drinking water 16 weeks	↑ Femur BMC and BMD[a] ↓ Weight gain (↓ fat mass and ↑ fat-free mass) ↓ Serum leptin production via ↑ GPX activity