The Effects Of (-)-epigallocatechin-3-gallate (egcg) On Fracture Healing

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Disclosures:

Introduction: Fractures greatly impair the quality of life of the affected individual. Delayed or impaired healing will occur in 5% to 10% of the 5.6 million fractures that occur annually in the United States, and up to 10% of all fractures will require additional surgical procedures for impaired healing. In our previous study, we found (-)-epigallocatechin-3-gallate (EGCG), a green tea catechin, enhanced osteogenesis in a murine bone marrow mesenchymal stem cell line, D1. In addition, we found that EGCG can increase osteoprotegerin (OPG) mRNA expression in D1 cells. Besides, we also found EGCG inhibit osteoclastogenesis via NF-κB. Our previous study showed EGCG increase proximal tibial and lumbar BMD and microarchitecture in age ovariectomized rats. Accordingly, we hypothesize that EGCG can enhance fracture healing.

Methods: The male Sprague-Dawley rats were randomized by body weight into 2 groups with 6 animals in each group treated with daily EGCG (20μL at the concentration of 10μM) or vehicle for 2 to 4 weeks. The animals were anesthetized with ether and unilateral, standardized fractures were produced in the right tibia by saw. Intra-medullary nailing were performed using #19 needles. X-ray and μCT, histology and bending tests were performed at the end of study.

Results: Daily local injection of 20μL EGCG at the concentration of 10 μM can increase callus formation in the X-ray examination at the 2nd to 4th week after treatment. In the μCT study, daily local injection of 20μL EGCG at the concentration of 10 μM can increase callus formation. In the histology study, EGCG can increase callus formation by increase callus volume. In the bending test, EGCG, 10 μM, can increase bone strength in tibia from 151 to 183 kN at the end of the 2nd week and from 154 to 198 kN at the end of the 4th week (P<0.05). Besides, Young’s module is also increased after EGCG treatment both at the end of the 2nd and 4th week (P<0.05). EGCG treatment also increased the energy resorption by increasing area under curve.

Discussion: We previously reported the dual effects of EGCG, and that EGCG enhances osteogenic differentiation of murine bone marrow mesenchymal stem cells at the concentration of 1 and 10 μmol/L, especially at 10 μmol/L.1 High concentrations of EGCG, 50 to 100 μmol/L, significantly suppressed RANKL-induced osteoclast differentiation and pit formation in murine RAW 264.7 cells and primary bone marrow macrophages.2 The bioavailability of EGCG is relatively low due to its short half-life, ranging from 1.87 to 4.58 hours.3 Drinking one cup of green tea could lead to a level of EGCG of 1 μmol/L in the circulation.4, 5 The maximum achievable EGCG concentrations in vivo have also been demonstrated.3, 5 A 1600 mg oral dose of EGCG under fasting conditions was reported to achieve a maximum human plasma level of 7.6 μmol/L,3 which is 8 times higher than the highest daily intake of EGCG from tea.3 It is likely that only pharmaceutically prepared formulations of green tea, such as capsule or injection, could reach the effective plasma levels of the catechin in an in vitro study. Daily local EGCG can enhance fracture healing by more callus formation with increase bone strength Young’s module and energy resorption. EGCG maybe a direction of fracture healing research for application.

Significance: Daily local EGCG can enhance fracture healing by more callus formation with increase bone strength Young’s module and energy resorption. EGCG maybe a direction of fracture healing research for application.

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