Differential effects of genistein, estradiol and raloxifene on rat osteoclasts in vitro

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Abstract:
Genistein, a major phytoestrogen of soy, is considered a potential drug for prevention and treatment of postmenopausal osteoporosis. It is not clear whether mechanism of action of genistein on bone turnover is distinct from that of estradiol or raloxifene. The aim of the present study was to investigate the effects of genistein on the formation of osteoclasts from neonatal rat bone marrow cells in vitro, and compare them with those of estradiol and raloxifene. Formation of osteoclasts was stimulated by 1,25-dihydroxyvitamin D₃, added to the culture media on the second day after plating, together with genistein (10⁻⁹–10⁻⁶ M), estradiol (10⁻⁹–10⁻⁷ M) or raloxifene (10⁻⁹–10⁻⁸ M). The bone marrow cell culture lasted 7 or 9 days. Number of osteoclasts and number of osteoclast “ghosts” (necrotic giant cells) were determined.

Genistein, estradiol and raloxifene, at some concentrations, decreased the number of osteoclasts after 9-day culture of bone marrow cells. Genistein decreased the number at 10⁻⁶ M because of decreasing the viability of osteoclasts, whereas at 10⁻⁷ M due to attenuation of osteoclast formation. Estradiol decreased the osteoclast number at 10⁻⁷ M due to decreasing their viability, whereas at 10⁻⁸ and 10⁻⁹ M it was the effect of both decreasing the viability and inhibition of the formation. Decreases in the number of osteoclasts caused by raloxifene (10⁻⁷, 10⁻⁸ M) were the effect of decreasing the viability of these cells.

Key words:
osteoclasts, genistein, estradiol, raloxifene, rat

Introduction

Postmenopausal osteoporosis is the most common type of the bone loss. The main pathogenetic factor of postmenopausal osteoporosis is a hormone-dependent increase in bone resorption and accelerated loss of bone mass in the first 5–10 years after the menopause [20]. Estrogen deficiency leads to the increased rate of bone remodeling (both resorption and formation). The imbalance between bone resorption and formation in favor of the former observed in postmenopausal osteoporosis is due to changes in the working lifespan of osteoclasts and osteoblasts, as estrogen exerts pro-apoptotic effects on osteoclasts and anti-apoptotic effects on osteoblasts and osteocytes [17].

Estrogen replacement therapy (ERT) has been widely used to prevent or treat post-menopausal osteoporosis. However, ERT increases the risk of breast cancer and may have other undesirable side effects [6, 9]. There is growing interest in the discovery or development of compounds that provide the benefits of ERT but do not lead to estrogen-dependent risks and side effects [5]. Selective estrogen receptor modula-