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"DT56a (Femarelle[®]) Stimulates Gender-Specific Human Cultured Bone Cells In Vitro"

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Abstract

DT56a (Femarelle[®]) found to have SERM-like properties is used for the treatment of menopausal symptoms and osteoporosis. In vivo experiments demonstrated that DT56a displayed selective estrogenic activity; it stimulated creatine kinase (CK) specific activity in the skeletal tissues but not on the uterus of ovariectomized rats. DT56a, when applied together with estradiol-17beta (E₂), completely inhibited the E₂-stimulated CK, as demonstrated by other SERMs. DT56a stimulated bone formation in a rat model as measured by histological and histomorphometrical parameters. In a clinical study, administration of DT56a (Femarelle[®]) resulted in a considerable elevation of bone mineral density and relief of menopausal symptoms. The aim of the present study was to analyze the effects of DT56a in vitro on human-derived bone cultured osteoblasts (Ob), by measuring its effects, at different concentrations, on DNA synthesis, CK and alkaline phosphatase (ALP) specific activities as well as changes in intracellular [Ca(2+)](i) concentrations. DT56a stimulated CK and DNA synthesis in both pre- and post-menopausal female Ob with maximal effect at 100 ng/ml for both age groups. In addition, DT56a stimulated ALP in Ob from both pre- and post-menopausal women with maximal effect at lower dose of 50 ng/ml, with higher response of pre-menopausal cells. Raloxifene (Ral) inhibited all DT56a-stimulated changes in Ob from both age groups. DT56a, when given together with E₂, completely antagonized E₂-stimulated effects demonstrating its nature as a phyto-SERM. DT56a also, dose dependency, stimulated the intracellular levels of [Ca(2+)](i) with maximal effect at 10 ng/ml. Male-derived Ob did not respond to DT56a in any parameter. In summary, DT56a stimulated sex-specifically female-derived Ob, indicating its unique nature compared to the compounds currently used for postmenopausal osteoporosis by being bone-forming and not only an anti-resorptive agent.