Published in: Journal of Steroid Biochemistry & Molecular Biology. 2006;98(1):90-6.

DT56a stimulates gender-specific human cultured bone cells in vitro.

Somjen D, Katzburg S, Lieberherr M, Hendel D, Yoles I.

Abstract

INTRODUCTION:

DT56a 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 (E_2), completely inhibited the E_2-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.

OBJECTIVE:

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.

RESULTS:

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 E_2, completely antagonized E_2-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.