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"DT56a (Femarelle®): a Natural Selective Estrogen Receptor Modulator (SERM)"

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Abstract

A selective estrogen receptor modulator (SERM) is defined as a substance with dissimilar effects on different tissues: agonist in some and antagonists in others. The natural compound DT56a (Femarelle®) was shown to activate estrogen receptors in human cultured female derived osteoblasts. It was also shown to relieve menopausal symptoms and to increase bone mineral density with no effect on sex steroid hormone levels and on the endometrial thickness. DT56a, similarly to estradiol-17beta (E₂), stimulated the specific activity of creatine kinase (CK) in skeletal and vascular tissues of female rats, as a marker of estrogen receptor (ER) activation. However, in the uterus, CK was activated only by E₂ but not by DT56a. In order to prove that DT56a is a SERM, we examined the mutual interaction between DT56a and E₂, at supra physiological doses, in different tissues in both intact and ovariectomized female rats, as well as in human cultured vascular and bone cells. Administration of DT56a or E₂ stimulated CK in all tissues tested, but when given simultaneously, in intact immature female rats, DT56a completely abolished E₂ stimulation of CK in all organs except in the diaphyseal bone where the inhibition was partial. In ovariectomized female rats, DT56a abolished E₂'s stimulation of CK in diaphyseal bone, thymus, uterus and pituitary but caused a partial inhibition in aorta, left ventricle and epiphyseal cartilage. In human bone cells E₂ stimulation of CK, of alkaline phosphatase (AP) activity and of DNA synthesis was completely abolished by DT56a in post-menopausal cells and partially inhibited in pre-menopausal cells. In human vascular cells, inhibition of DNA synthesis by E₂ was completely abolished by DT56a and E₂-induced CK was partially inhibited by DT56a. The results support the finding that DT56a is a SERM; it stimulated different parameters similar to E₂, but when given simultaneously, at supra physiological doses, inhibited these E₂'s effects. Further investigations regarding intra and extra cellular mechanism of action of DT56a are currently performed.