
Correspondence: Professor H. J. T. Coelingh Bennink, Panthe biotics, PO Box 446, 3700 AL Zeist, The Netherlands

Climacteric 2008;11(Suppl 1):29

Estetrol, a pregnancy-specific human steroid, prevents and suppresses mammary tumor growth in a rat model


Pantethe Biosciences, Zeist, The Netherlands; †Division of Special Gynaecology, AKH Wien, Vienna, Austria; ‡Molecular and Cellular Gynecological Endocrinology Laboratory, Department of Reproductive Medicine and Child Development, University of Pisa, Italy; §Pharmconsul®, New York, NY, USA

Key words: ESTETROL, BREAST TUMOR, DMBA, PREVENTION, TREATMENT

Estetrol (E₄) is a pregnancy-specific D-ring metabolite of estradiol (E₂) and estril (E₃) produced by the human fetal liver and present in both male and female fetuses. In adults, female exposure is restricted to the gestational period.

We report that E₄, dose-dependently, prevents the growth of chemically induced (7,12-dimethylbenz(a)anthracene, DMBA) mammary tumors in female Sprague-Dawley rats and that E₄ has the potential to reduce the number and size of pre-existing mammary tumors.

We performed two prevention studies and one intervention study. In the prevention studies, we investigated the effect of oral doses of E₄ over a dose range of 0.5-3.0 mg/kg. The intervention study used oral dose levels of 1, 3 and 10 mg/kg. E₄ was dose-dependent, comparable to tamoxifen-treated animals, and at high dose levels E₄ was as effective as ovariectomy.

Estrogen doses pharmacologically equipotent to E₄, acted as control treatments in the second prevention study and in the intervention study.

Rats treated with DMBA develop estrogen-responsive breast tumors. This model has become the standard pharmacological model to investigate the effect of new compounds on breast tumors. When DMBA-induced rats were co-treated with E₄ for 8 weeks, this resulted in a dose-dependent reduction in the number and size of tumors, an effect that appeared equally effective as tamoxifen treatment or ovariectomy and was not seen with ethinylestradiol. When E₄ was administered to rats in which tumors had already developed, a significant decrease in the number and size of tumors was observed after 4 weeks. This decrease was dose-dependent, comparable to tamoxifen-treated animals, and at high dose levels E₄ was as effective as ovariectomy.