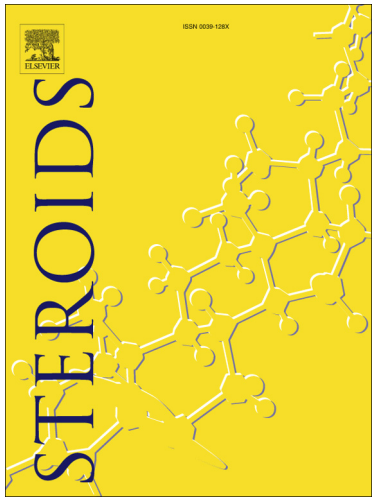

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Design, synthesis and antiproliferative effect of 17β-amide derivatives of 2-methoxyestradiol and their studies on pharmacokinetics

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Abstract

A series of 17β-amide-2-methoxyestradiol compounds were synthesized with an aim to enhance the antiproliferative effect of 2-methoxyestradiol. The antiproliferative activity of 2-methoxyestradiol analogs against human cancer cells was investigated. 2-methoxy-3-benzyloxy-17β-chloroacetamide-1,3,5(10)-triene (**5e**) and 2-methoxy-3-hydroxy-17β-butyramide-1,3,5(10)-triene (**6c**) had comparable or better antitumor activity than 2-methoxyestradiol. The elimination half-life of **6c** ($t_{1/2\beta}$ = 240.93 min) is ten times longer than 2-ME and the area under the curve was seven times ($AUC_{0\text{-}tmin}$ =2068.20 ± 315.74 $\mu g \cdot ml^{-1} \cdot min$) higher than 2-ME, respectively. Whereas **5e** had