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

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Abstract

A series of 17 β -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-17 β -chloroacetamide-1,3,5(10)-triene (**5e**) and 2-methoxy-3-hydroxy-17 β -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-tmin} = 2068.20 \pm 315.74 $\mu\text{g}\cdot\text{ml}^{-1}\cdot\text{min}$) higher than 2-ME, respectively. Whereas **5e** had

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