Research in Pharmaceutical Sciences, 2012;7(5)
School of Pharmacy and Pharmaceutical Sciences
Isfahan University of Medical Sciences
Proceeding of 13th Iranian Pharmaceutical Sciences Congress

Evaluation of cytotoxic effects of some novel tetralin derivatives against human cancer cells

H. Sadeghi-aliabadi[1,2,*], F. Hassanzadeh[1,2], F. Shafiee[2]

[1]Department of Pharmaceutical Chemistry, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, I.R.Iran
[2]Isfahan Pharmaceutical Sciences Research Center, School of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Isfahan, I.R.Iran

Background and Aims: In postmenopausal women, the circulating estrone sulfate is nearly 10 fold higher than the free estrone and estradiol levels and thus constitutes a reservoir from which free estrogens could be synthesized in breast cancer tissues. The enzymes responsible for conversion of estrone sulfate to free estrone and then estradiol are estrone sulfatase and 17-β-hydroxysteroid dehydrogenase (17-β-HSD), respectively. Therefore, inhibitors of estrone sulfatase and 17-β-HSD could provide a means of blocking estrogen biosynthesis either peripherally or in situ leading to reduction of tumor estrogen level and promotion of tumor regression. Tetralin derivatives, 2-(4-halo-phenylmethylene)-3,4-dihydronaphthalene-1-ones, could be potential inhibitors of estrone sulfatase and 17-β-HSD due to similar backbone structure to estrone.
Methods: In this study, we evaluated the cytotoxicity of five tetralin derivatives (compounds 1 to 5) on MDA-MB-468 and MCF-7 as breast cancer cell lines, and Hela as a cervix carcinoma cell line. The cell lines were cultured in RPMI medium and the cytotoxic effect of each compound was screened at the concentrations of 1, 10, and 100 μM either alone or in combination with doxorubicin (0.5 mM), using MTT assay.
Results: None of these compounds exhibited cytotoxic effect (reduction of cell survival to less than 50%) on tested cell lines. However, statistically significant reduction in cell survival was observed for some compounds against particular cell lines. Among all tested combinations of compounds with doxorubicin against cell lines, only 100 μM concentration of compound 4 showed synergistic cytotoxic effect with doxorubicin against Hela cells.
Conclusions: In conclusion, with the exception of compound 2, other tested compounds have potential for further cytotoxicity evaluation. Synthesizing other tetralin derivatives similar to compound 4 and studying their structure activity relationships (SAR) would be encouraged.

Keywords: Cytotoxicity; Tetralin derivatives; Estrone sulfatase; 17-β-HSD; Cancer cell line