Research in Pharmaceutical Sciences, 2012;7(5)
School of Pharmacy and Pharmaceutical Sciences
Isfahan University of Medical Sciences

Triazolothiadizoles and triazinothiadizoles: synthesis and their toxicity evaluations

M. Tayarani Najaran[1,*], Z. Tayarani Najaran[1], M. Bakavoli[2], A. Shiri[2]

[1]*Department of Pharmacodynamics and Toxicology, School of Pharmacy, University of Medical Sciences, Mashhad, Iran*
[2]*Department of Chemistry, Faculty of Science, Ferdowsi University of Mashhad, Mashhad, Iran*

Background and Aims: In this study, triazolothiadiazoles and triazinothiadiazoles are synthesized and tested on different cancer cell lines including ACHN, HeLa, HL-60, MCF-7, and PC3.
Methods: Considering of this principle that combinations of bioactive substructures with each other have the potential of pharmaceutical activities, we are aimed to synthesize various new derivatives of substituted-[1,2,4]triazolo[3,4-b][1,3,4]thiadizoles (AMTT) and [1,2,4]triazino[3,4-b][1,3,4]thiadizoles (AMTTO) by the condensation of 4-amino-3-methyl-1H-1,2,4-triazole-5(4H)-thione and 4-amino-6-methyl-3-thioxo-3,4-dihydro-1,2,4-triazin-5(2H)-one with various carboxylic acids and phosphorus oxychloride under reflux conditions. All the newly synthesized compounds were identified by spectroscopic and microanalytical data. Malignant cells were cultured in RPMI medium and incubated with different concentrations of the titled compounds. Cell viability was quantitated by MTS assay.
Results: A cell-based screening method were performed on the compounds in three different concentrations (60, 125 and 250 mcM). Studies on AMTT and AMTTO derivatives revealed promising activity against cancerous cells. The cytotoxicity on AMTTO derivatives was generally more noticeable than AMTT derivatives. Of all the fourteen compounds, 4-methylphenyl, 3,4-dichlorophenyl and cynnamyl derivatives of AMTTO were promising, while diphenylmethyl and cynnamyl derivatives of AMTT were inactive. The other compounds did not show any considerable toxicity.
Conclusions: We have described the synthesis and antiproliferative activity of new substituted-[1,2,4]triazolo[3,4-b][1,3,4]thiadizoles (AMTT) and [1,2,4]triazino[3,4-b][1,3,4]thiadizoles (AMTTO).

Keywords: Triazolothiadizoles; Triazinothiadizoles; Synthesis; Toxicity