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Synthesis and Antitumor Assessment of Novel N_1-(Phenoxy Ethyl)3,7-Dimethyl-3,7-Dihydro-1*H*-Purine-2,6-Dione Derivatives as Potential Anticancer Agents

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Here we report synthesis of 12 novel N_1 substituted phenoxy ethyl 3,7-dimethyl-3,7-dihydro-1H-purine-2,6-dione derivatives. Moreover, their cytotoxic activities were measured. Then, molecular docking studies were used to predict and propose the possible mechanism of action. The route comprises the reaction of theobromine with 2-Chloroethanol followed by the addition of *p*-toluenesulfonyl chloride. Then relative phenoxy ethyl derivatives (**5a-5l**) were obtained by the reaction of the different phenols with the previous product. All newly synthesized compounds were subjected to study their cytotoxicity activity by MTT based colorimetric assay method against 4 human cancer cell lines.

The results of IR, ^{1}HNMR and ^{13}CNMR spectra showed that all derivatives were successfully synthesized in the laboratory. The results of cytotoxicity assay showed that the greatest effect of cell cytotoxicity occurred on cell lines of A549 (viability percent 40.08 compound **5e**) and MCF7 (viability percent 41.37 compound **5d**), and the lowest viability percent (viability percent 40.08 compound **5e**) observed on A549 cell line in the presence of **5e** compound. The calculated IC_{50} was found to be 86.65 µM against cell line of A549. Finally, molecular docking was performed to propose which anticancer target protein the synthesized compound may work. The results of molecular docking showed the acceptable binding energy against the enzyme ecto-5'-nucleotidas. Among the synthesized derivatives, compound **5a** with the lowest ΔG was chosen as the best inhibitor of this enzyme. The high effects of cell toxicity at various concentrations of synthesized compounds on MCF7 A549 cell lines were observed.

Biography:

Ehsan Faghih-Mirzaee was born in Kerman, Iran, in 1981. He received PhD degrees in Medicinal Chemistry from Shiraz University, Iran, in 2012. He has been faculty member of the Pharmacy, Department at Kerman University of Medical Sciences, since 2013. His research interests include: Biotransformation of chemical compounds and Design, Synthesis, and Molecular modeling of novel synthesized compounds.