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Design ,synthesis and In-vitro antitumor evaluation of new 2, 3-diaryl-indenopyrazole and 2,3-diaryl-benzofuropyrazole derivatives as selective cyclooxygenase (COX-2) inhibitors

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Background and Aims: The non-steroidal anti-inflammatory drugs (NSAIDs) are widely used as analgesic, anti-pyretic and anti-inflammatory agents.. The mechanism of action of these drugs is the inhibition of Cyclooxygenase (COX) enzyme. There are at least two COX isozymes. The COX-1 is expressed in many tissues and plays an important role in protection of gastric mucosa. In contrast, the COX-2 isozyme is induced by stimuli such as mitogenes and grows factors linking its involvement to pathological process such as inflammation and various cancer types. Nowadays it is proved that selective COX-2 inhibitors can be used in treatment of cancer diseases. in this regard A new group of 2,3-diaryl-indenopyrazoles and 2,3-diaryl-benzofuranopyrazoles, possessing a methyl sulfonyl pharmacophore, were designed and synthesized in order to specify the effects of these compounds and decrease the adverse reactions, and regarding to the point that COX-2 plays decisive roles at different stages of tumor development.
Methods: These derivatives were synthesized using different reactions. The chemical structures were confirmed by IR, NMR and Mass spectra , the Molecular modeling studies was done by Vina software and invitro anti tumor evaluation was performed by colonogenic assay on MCF7 and A549 cell lines. Results and discussion:. Docking studies display that the SO2Me pharmacophore is well oriented into the COX-2 secondary pocket. The results of the anti cancer effects of the synthesized compounds show that COX-2 pathway is an important strategy in prevention and treatment of tumors.
Conclusions: Based on the results of biological evaluations, most of the synthesized compounds as selective COX-2 inhibitors, inhibited COX-2 selectively and some of them showed the potent cytotoxicity effects on MCF7 and A549 cell lines.

Keywords: COX-2 inhibition; 2,3-Benzofuropyrazole; 2,3-Indenopyrazole; Selectivity