NOVEL 1,2,4-OXADIAZOLE DERIVATIVES OF 18 β H-GLYCYRRHETINIC AND DEOXYCHOLIC ACIDS: SYNTHESIS AND BIOLOGICAL ACTIVITIES

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Oxadiazole derivatives, especially 1,2,4- and 1,3,4-regiostereoisomers, are widely represented in medical chemistry. These compounds have been shown to possess anti-inflammatory, anticancer, antidiabetic, among others [1]. A series of novel 18 β H-glycyrrhetic acid (GA) and deoxycholic acid (DCA) derivatives containing 3'-(alkyl/phenyl/pyridin(-2'', -3'', and -4'')-yl)-1',2',4'-oxadiazole moieties were synthesized by condensation of natural product's carboxyl group with corresponding amidoximes and further cyclization. Screening of the cytotoxicity of novel GA derivatives on a panel of tumor cell lines showed hit derivative pyridin-2''-yl-1',2',4'-oxadiazole-bearing GA. This compound marked proapoptotic activity and inhibitory effects on clonogenicity and motility of HeLa cervical carcinoma cells *in vitro*, and the metastatic growth of B16 melanoma *in vivo*. Additionally, the comprehensive *in silico* study revealed intermediate, bearing the *tert*-butyl moiety in *O*-acylated amidoxime, as a potent anti-inflammatory candidate, which was able to effectively inhibit inflammatory response induced by IFN γ in macrophages *in vitro* and carrageenan in murine models *in vivo*.

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References

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