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Synthesis and antimycobacterial activity evaluation of novel 1-substituted indole-3-carboxaldehyde 1,3,4-thiadiazol-2-yl hydrazones

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Background and Aims: Based on the previous studies conducted by the group of the authors leading to the discovery of 1,3,4-thiadiazol-2-yl hydrazones as potent antimycobacterial derivatives with safe toxicity pofile, in the present study a series of indole-based 1,3,4-thiadiazol-2-yl hydrazones have been synthesized and tested against Mycobacterium bovis BCG.
Methods: The final derivatives were prepared by a two-step procedure. The first step was the reaction of indole-3-carboxaldehyde at N-1 position with various benzylic and aliphatic halides. The resulting intermediates were used in the second step which was a Schiff base formation reaction with 2-hydrazinyl-1,3,4-thiadiazole. The final derivatives were tested against Mycobacterium bovis BCG by the Alamar Blue microdilution assay using ethambutol and thiacetazone as standard drugs and DMSO as negative control.
Results: Amongst the derivatives some exhibited excellent biological activity comparable to those of the tested standard drugs. Moreover, it was found that there were some correlations between the observed MICs of the tested derivatives and the physicochemical parameters of the substituents (majorly lipophilicity) and also their aliphatic/aromatic nature.
Conclusions: In this study a series of indole-3-carboxaldehyde 1,3,4-thiadiazol-2-yl hydrazones with substitution at indole N-1 position have been synthesized and evaluated for their antimycobacterial activity. Some of the derivatives exhibited promising biological activity and therefore could be considered as new lead compounds for further lead optimization studies targeting tuberculosis.

Keywords: Antimycobacterial; 1,3,4-Thiadiazol-2-yl Hydrazones; Indole