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Antimycobacterial activity and QSAR studies of 2*H*-chromene and coumarin based hydrazones

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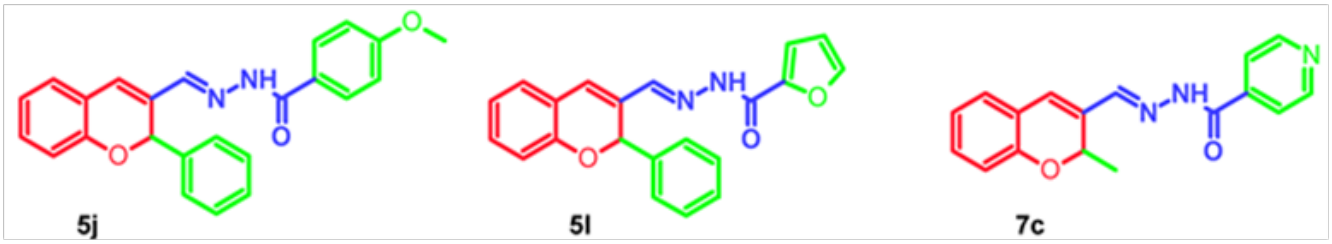
A series of 2H-chromene based hydrazones 5a-m, 6a-c and 7a-c were synthesized by condensation of 2H-chromene-3-carbaldehydes with varied substituted hydrazides. The structure of the newly synthesized compounds were confirmed by ^{1}H NMR, ^{13}C NMR, FTIR and HRMS (ESI) spectroscopy and the E-configuration of the compounds 7a and 7c was proven by X-ray crystal structure analysis.



MIC (exp)	**0.13 µM**	**MIC (exp)**	**0.18 µM**	**MIC (exp)**	**0.17 µM**
IC50	**90.66 µM**	**IC50**	**21.21 µM**	**IC50**	**76.32 µM**
SI	**697.38**	**SI**	**117.83**	**SI**	**448.94**

In vitro antimycobacterial activity of the newly synthesized hydrazones was tested against Mycobacterium tuberculosis H37Rv and compared to that of first-line antituberculous drugs isoniazid (INH) and ethambutol (EMB). The most active compounds 5j, 5h, 5l, 7b, 7c demonstrated a nanomolar inhibitory potency with MICs 0.13-0.74 µM, but noteworthy they proved to exert minimal associated cytotoxicity in the human embryonal kidney cell line 293 T. Hydrazone 5j was the most potent antituberculous agent with a minimal inhibitory concentration (MIC) of 0.13 µM. The activity of the tested compounds varied depending on the substituents and the log P values. Quantitative structure-activity relationship (QSAR) model was derived to guide the further lead optimization. Low log P values and 5 rings in the molecules proved to be optimal for nanomolar activity. These results could be considered a good starting point for further studies to develop new lead compounds.

Biography

Violina T Angelova has completed his PhD in 2004 from Bulgarian Academy of Sciences, Institute of Organic Chemistry with Centre of Phytochemistry, Sofia, Bulgaria. She is an Assistant Professor of Medical University of Sofia, Faculty of Pharmacy, Department of Chemistry. She has published more than 15 papers in reputed journals.

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