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Docking study of 2-aroyl-[1]benzopyrano[4,3-c]pyrazol-4(1H)-one derivatives and related hydrazide-hydrazones and their antimycobacterial activity

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A series of coumarin-linked hydrazide–hydrazones 4a-e and 2-aroyl-[1]benzopyrano[4,3-c]pyrazol-4(1H)-ones 5b-g were synthesized via an efficient one-pot protocol. All compounds demonstrated significant minimum inhibitory concentrations (MIC) ranging from 0.28 to 1.69 μM against reference M. tuberculosis H37Rv strain. The cytotoxicity against the human embryonic kidney cell line HEK-293 was also evaluated and the selectivity of the antiproliferative effects was thus assessed. All compounds displayed good SI values ranging from 33 to more than 645. In general, 2-aroyl-[1]benzopyrano[4,3-c]pyrazol-4(1H)-one derivatives 5b-g possessed potent antimycobacterial activity combined with low cytotoxicity what resulted into SI values higher than that of their open chain analogues 4a-e. The activity of the tested compounds may be attributed to the significant interactions with the inhibitor binding cavity of M. tuberculosis Enoyl-ACP reductase and\or related to ability of the tested compounds to penetrate mycobacterial cells.The above observations show that the novel hydrazide–hydrazones 4a-e and 2-aroyl-[1]benzopyrano[4,3-c]pyrazol-4(1H)-one derivatives 5b-g have potential as antimycobacterial agents. The results of the study can be utilized to further optimize and improve the potency and selectivity toward ENR enzyme by varying the basic skeleton and the substituents.

Biography

Valentin Karabelyov has completed his secondary education in 2013 from National High School of Maths and Science. Now he is studing in the Medical University of Sofia, Faculty of Pharmacy and he is a fourth year student of Faculty of Pharmacy. He works as an assistant in a pharmacy from 3 years ago. He is interested in the fields of LC-MS, Organic synthesis, Pharmacognosy, Pharmacology and Pharmacotherapy. Last year, Valentin participated in the European Chemistry Congress, where he presented a poster on the theme ,, Anticonvulsant activity of newly synthesized benzoylhydrazones with 2H-chromene and coumarin moieties in ICR mice.

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