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Arylquinolinecarboxamides: Synthesis, *in vitro* and *in silico* studies against *Mycobacterium tuberculosis*

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Abstract

A series of fourteen 6-substituted-2-(methoxyquinolin-3-yl) methyl)-*N*-(pyridin-3-ylmethyl) benzamides was prepared from commercially available anilines in five simple and convenient synthetic steps. The structures of all new products were confirmed by routine spectroscopic methods: IR, ^{1}H and ^{13}C NMR, and HRMS (electrospray ionization). The resulting arylquinolinecarboxamides were subjected to biological screening assay for *in vitro* inhibitory activity against *Mycobacterium tuberculosis* (*Mtb*) H37Rv strain. Several compounds exhibited modest antitubercular activity with compounds **8–11**, **15** and **19** exhibiting MIC_{90} values in the range of 32–85 μM. The antitubercular data suggested that inhibition of *Mtb* can be imparted by the introduction of a non-polar substituent on C-6 of the quinoline scaffold. Further, to understand the possible mode of action of the series, the reported compounds and bedaquiline were subjected to *in silico* docking studies against *Mtb*ATPase to determine their potential to interfere with the mycobacterial adenosine triphosphate (ATP) synthase. The results showed that these compounds have the potential to serve as antimycobacterial agents. *In silico* ADME pharmacokinetic prediction results showed the ability of these arylquinolinecarcboxamides to be absorbed, distributed, metabolized and excreted efficiently.

KEYWORDS

antitubercular, arylquinolinecarboxamides, *Mtb*ATPase, *Mycobacterium tuberculosis*