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RESEARCH ARTICLE

BENTHAM SCIENCE

Synthesis of Coumarin-benzotriazole Hybrids and Evaluation of their Anti-tubercular Activity

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Abstract: ***Background***: Tuberculosis is one of the top ranked airborne infectious diseases caused by the bacillus *Mycobacterium tuberculosis* with high mortality rate from a single infectious agent. In the present article, we aimed to synthesize oxadiazole-coumarin-triazole based small molecules and evaluate for their possible anti-mycobacterial activity.

Method: Herein, we describe the facile synthesis of 5-((1H-benzo[d][1,2,3]triazol-1-yl)methyl)-1,3,4-oxadiazole-2-thiol-tethered substituted 4-(bromomethyl)-7-methyl-2H-chromen-2-one derivatives and evaluated for their anti-mycobacterial activity against H37Rv strain of *M. tuberculosis*. We also evaluated the cytotoxic effect of new compounds on normal cells.

Results: Among the 14 novel oxadiazole-coumarin-triazole derivatives, 4-((5-((1H-benzo[d][1,2,3]triazol-1-yl)methyl)-1,3,4-oxadiazol-2-ylthio)methyl)-6-methoxy-2H-chromen-2-one (5f) displayed good antimycobacterial activity towards *M. tuberculosis* with an MIC value of 15.5 μM. Pyrazinamide was used as reference drug. Our investigation also revealed that, 5f is not cytotoxic to normal cells.

Conclusion: In summary, the findings suggested that novel 1,3,4-oxadiazole coumarin-triazole hybrids are promising antimycobacterial agents against *M. tuberculosis*.

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1. INTRODUCTION

Tuberculosis is an infectious and airborne bacterial disease caused by the bacillus *Mycobacterium tuberculosis* (Mtb) and one of the leading killers globally [1]. According to the 2014's report of World Health Organization, 9.6 million new TB cases were identified with the mortality rate of 1.5 million deaths worldwide [2]. Based on the affected organ, TB is broadly classified into pulmonary TB (lungs) and extrapulmonary TB (pleura, central nervous system, bones, lymphatic system) [3]. Several studies have indicated the development of drug-resistance by Mtb against first-line and second-line drugs including isoniazid, rifampicin, ethambutol and pyrazinamide is making the regimen complicated [4]. In multidrug-resistance TB (MDR-TB), Mtb do not respond to first-line drugs. On the other hand, in extensively drug-resistance TB (XDR-TB), the bacillus no longer responds to the most effective second-line anti-TB drugs [2]. Development of resistance by mycobacterial strains against the conventional anti-TB agents demands the discovery of new therapeutic agents which can effectively target Mtb.

Benzotriazoles have been considered as privileged structures in medicinal chemistry because of their diverse pharmacological properties including anticancer, antitubercular, antibacterial, antiviral, antiparasitic and antioxidants [5]. Evidently, benzotriazole-oxazolidinone conjugates have displayed excellent anti-mycobacterial activity against drug-

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