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RESEARCH ARTICLE

Synthesis of 2-Hydroxynaphthyl Pyrazolines Containing Isoniazid Moiety: A Potential Antitubercular Agent

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Abstract: The new series of pyrazolines derivatives containing isoniazid moiety were synthesized from 2-hydroxynaphthyl functionalized chalcones and isoniazid using sodium hydroxide as a base in 2-ethoxy ethanol. We evaluated their antitubercular activity against *Mycobacterium tuberculosis* strain ($H_{37}R_v$) by Microplate Alamar Blue Assay (MABA). Some of the tested compounds **3a**, **3b**, and **3c**, were found to have higher antitubercular activity than the selected standard drugs, whereas compounds **3d**, **3e**, **3i** and **3j** were found to have higher antitubercular activity than Streptomycin and same as that of Pyrazinamide and Ciprofloxacin, while remaining compound showed moderate activity. Whereas it is found that the disubstituted halogen compound and electron-withdrawing group on the phenyl ring are important substitutions for an increase in antitubercular activity.

Keywords: Chalcones, pyrazolines, isoniazid, antitubercular activity, 2-hydroxynaphthyl pyrazolines, antitubercular agent.

1. INTRODUCTION

Tuberculosis (TB) is the significant continual transmissible bacterial disease caused by *Mycobacterium tuberculosis*. One of the main causes of TB is morbidness which results in death all over the world. More or less 33% of the world's population is presently living with this disease [1]. Almost two billion people are infected and about 8.7 million new cases and 1.4 million deaths were reported by the World Health Organization (WHO) in 2013 and has predicted that by the year 2020 there will be one billion new active cases if new anti-TB drugs or treatments are not developed [2-4].

A recent survey indicates that the leading mortality caused by HIV/AIDS is closely associated with tuberculosis. Improved therapy for tuberculosis is reorganized as a major need for developing countries as well as developed countries [5]. Current chemotherapy of tuberculosis is not likely to be successful in retroviral infected patients throughout the world. Resistance of *Mycobacterium tuberculosis* strains by existing antitubercular agents is also an increasing problem worldwide [6]. Therefore powerful novel antitubercular agents, being new mechanism of action, is needed to develop for the treatment of complex tuberculosis cases [7]. Hence, selected nitrogen containing heterocyclic compounds such as pyrazolines have received notable awareness in the recent years due to their diverse pharmacological and biological activities such as antitubercular [8-12], antidepressant [13], antifungal [14-17], antimoebic [15], anticonvulsant [16-17], antitumor [18], anti-TB [19-22], anti-HIV [23], anticancer [12, 24] and anti-inflammatory [25]. Pyrazoline and its derivatives occupied a unique place in the chemistry of nitrogen heterocyclic compounds because of their varied biodynamic properties [26-28] and isoniazid containing pyrazolines reported to possess diverse biological activities [29-31], it is also a long familiar pharmacologically active antitubercular compound which is a forefront drug employed in the treatment of tuberculosis.

The structure-activity relationship is the link between the structure of a synthesized compound and its biological activity. Chemists use various synthetic techniques to introduce different groups of the bioactive compound and test for biological activity [32, 33]. Pyrazolines also influence the substitution pattern on the structure activity relationship (SAR). This study on the effect of different pyrazolines exposed some significant remarks on the influence that structural changes may affect the antitubercular and antibacterial activity [34, 35]. The present study investigates the influence of the different substitution patterns in pyrazolines on their antitubercular activity against *Mycobacterium tuberculosis*.

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