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Synthesis, Biological Properties and Comparative Molecular Docking Evaluation Studies of 1,3 and 1,4 *Bis*-Thiourea Derivatives as Potential Antimicrobial Resistant Agents

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ABSTRACT

Introduction: Thiourea is one of the promising class of compounds that possess various pharmacological activity including antibacterial properties.

Objective: The rise of microbial resistant drugs has triggered an alarming response among researchers to developed new drugs with effective biological properties. The position of substituents and active pharmacophores play an important role in designing a lead compound with effective biological properties.

Methods: In this study, two series of 1,3-*bis*-thiourea derivatives (3a-l) and 1,4 *bis*-thiourea derivatives (4a-l) were synthesised from the reaction of isophthaloyl diisothiocyanate intermediates with halogenated amines.

Results: The comparative studies of antibacterial properties of 3a-l and 4a-l against the growth of *E. coli* showed the minimum inhibition of 3g (7mm inhibition) and 4g (18mm inhibition) compared to standard drug ampicillin (16mm inhibition). Molecular docking evaluation against *E. coli* DNA gyrase B showed strong binding interaction of 4g with binding affinity -6.7 kcal/mol and more hydrogen bond compared to 3g with binding affinity -6.4 kcal/mol).

Conclusion: The study is significant in drug design in particular for the development of potential drugs with antimicrobial resistant properties.

Key Words: Anilines, Carbamothioyl, *Escherichia coliform*, Halogens

INTRODUCTION

Discovering new drugs has become a major concern nowadays due to the egression of pathogens with drug-resistant properties. The emergence of new drugs with improved antimicrobial properties has become a phenomenal alternative to overcome the issue. Drugs with active pharmacophores able to form strong interaction with the pathogen receptors and retard the growth of the microorganism[1]. Interest has grown rapidly in the preparation and studies of the critical effects of compounds containing an O-N-S set of atoms that have an energetic effect against different types of microbes and viruses.[1-3]

Thiourea is one of the promising class of compounds that possess good antibacterial, antifungal, anticancer, and other useful pharmaceutical properties.[3-5] The presence of N-H and C=S groups in the thiourea moieties act as active binding sites between the compounds with the protein receptor on the surface of microorganism.[1] The number of thiourea moieties in a molecular network plays a significant role in antibacterial properties. The ratio of binding sites in a compound with the surface of microorganism receptors increases as the number of thiourea moieties increases.[6,7] We have reported on series of mono-substituted thiourea[4], di-substituted thiourea derivatives bearing halogenated aryl groups (4a-l)[5], bearing amino acids[8] and bearing alkyl chains[8,9] with excellent antibacterial activities against *Escherichia coliform* (*E. coli*). The presence of two or more substituted thiourea moieties in the molecular network is believed to increase the biological

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