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Research Article

Novel Synthetic Monothiourea Aspirin Derivatives Bearing Alkylated Amines as Potential Antimicrobial Agents

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A new series of aspirin bearing alkylated amines moieties **1–12** were synthesised by reacting isothiocyanate with a series of aniline derivatives in overall yield of 16–56%. The proposed structures of all the synthesised compounds were confirmed using elemental analysis, FTIR, and ^{1}H and ^{13}C NMR spectroscopy. All compounds were evaluated for antibacterial activities against *E. coli* and *S. aureus via* turbidimetric kinetic and Kirby Bauer disc diffusion method. Compound **5** bearing *meta* -CH_3 substituent showed the highest relative inhibition zone diameter against tested bacteria compared to *ortho* and *para* substituent. Furthermore, aspirin derivatives bearing shorter chains exhibited better bacterial inhibition than longer alkyl chains.

1. Introduction

Over the centuries many antibacterial drugs were used to treat bacterial-causing diseases including food poisoning, pneumonia and intestinal infection [1, 2]. The improper usage of these drugs has caused the bacteria to evolve into drug resistant bacteria which reduce the effectiveness of the drugs [3]. The continuing development of new antimicrobial agents therefore remains a priority [1].

Aspirin is a widely used medicine for antipyretic, analgesic, and anti-inflammatory [4]. The demand of aspirin and its derivatives for other biological properties is increasing due to its availability and reactivity as precursor for further modification *via* corresponding carboxyl group [5]. Aspirin derivatives have shown antibacterial activities against *Bacillus subtilis*, *Escherichia coli*, *Staphylococcus aureus,* and *Pseudomonas aeruginosa* [6, 7]. Other significant biological properties of aspirin derivatives are reported for antitumor, anticancer, antifungal, and antimicrobial agents [5, 7–9].

We have previously reported on aspirin with thiourea moieties bearing amino acid and aromatic amines with excellent antibacterial properties. The lipophilicity of the aromatic ring has contributed to the enhancement of the biological activities [5]. Thiourea is a type of reactive precursor due to the presence of C=S, C=O, and NH moieties which are essential in biological activities [10]. Several biological activities reported on thiourea are antibacterial, antifungal, anticancer, antitubercular, antimicrobial, and anti-HIV activities [11–17]. The synthesis of thiourea derivatives has also received great attraction due to their diverse application such as in textile processing and heavy metals extraction as chelating agent and agriculture as plant growth regulator [18–20].

2. Results and Discussion

Aspirin derivatives **1–12** with aryl side chain bearing alkyl substituents were prepared from the reaction of acetoxybenzoyl isothiocyanate with a series of commercially available