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Research Paper

Synthesis, Characterization, and Antibacterial Activity of Some Mesalazine Derivatives

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Abstract
Mesalazine, often referred to as mesalamine or 5-aminosalicylic acid (5-ASA), and its derivatives are some of the first medications to be approved for treating digestive tract inflammations, including ulcerative colitis and mild to moderate Crohn's disease. Sulfasalazine, discovered in 1938 for therapeutic use, was the first mesalazine derivative. High yields of four different mesalazine derivatives were synthesized, including two Schiff bases and two azo compounds. The present study involved the synthesis of Schiff bases through the reaction of mesalazine with pyrrole-2-carbaldehyde or indole-2-carbaldehyde, resulting in the formation of 5-(((1H-pyrrol-2-yl)methylene)amino)-2-hydroxybenzoic acid (1) or 5-(((1H-indol-2-yl)methylene)amino)-2-hydroxybenzoic acid (2), respectively. The synthesis of azo compounds involved the coupling of mesalazine with sulfamethoxazole or pyridoxine, resulting in the formation of 5-amino-2-hydroxy-3-((4-(N-(5-methylisoxazol-3-yl)sulfamoyl)phenyl)diazenyl)benzoic acid (3) or 2-hydroxy-5-((5-hydroxy-3,4-bis(hydroxymethyl)-6-methylpyridin-2-yl)diazenyl)benzoic acid (4), respectively. The identification of the synthesized compounds was carried out using IR and 1H-NMR spectroscopy. Antibacterial assessment of the synthetic compounds was performed in vitro against gram-negative bacteria (such as *Escherichia coli* and *Pseudomonas aeruginosa*) and gram-positive bacteria (*Staphylococcus aureus*). The antibacterial activity studies demonstrated that against *Escherichia coli* and *Staphylococcus aureus*, the Schiff base compounds are more active than azo compounds. Compound 1 showed the highest activity, resulting in a 23 mm inhibition zone against *E. coli* at 1000 μg/ml. In contrast, the antibacterial activity of compound 2 was observed to be 25 mm against *S. aureus* at the same highest concentration.

Keywords
Mesalazine, Schiff Bases, Azo Compounds, Antibacterial Activity, Modification of Drug

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1. INTRODUCTION

Modifying the chemical molecules of commercially available medications is one of the most critical aspects of pharmacological development. Molecular modification involves changing the chemical structure of drugs away from their active site, which can impact their efficacy and ability to treat certain diseases. Thus, a new derivative of the drug molecule is prepared using different chemical reactions with physicochemical properties other than the original drug (Ye and van Langenberg, 2015). The substance mesalazine, used to treat inflammatory bowel diseases like Crohn's disease and ulcerative colitis, is one essential medicine whose chemical structure has undergone modifications (Yasutomi et al., 2019). Mesalazine has additional biological activities; it has been utilized as an antioxidant against oxygen and nitrogen free radicals (Yousefi et al., 2017), anti-ulcer (Beiranvand, 2021), against colorectal cancer (Dixon et al., 2021), and antimicrobial activity (Zhang et al., 2018; Cevallos et al., 2021).

Several pharmaceutical dosage forms of mesalazine derivatives are utilized in the drug market to treat UC, focusing on aminosalicylic acids and their associated derivatives. The most important derivatives are salazosulfapyridine (SASP), olsalazine, and mesalazine (Zhang et al., 2015).

The chemical structure of mesalazine is of great importance in the process of chemical modification on this molecule, as it contains in its structure two groups, carboxyl and amine groups, and these two groups are easily subject to many types of chemical reactions, allowing the formation of many types of derivatives (Yuri et al., 2020). Within the design of prodrugs as derivatives of the drug mesalazine, many polysaccharides were used by linking them using ester bonds of the carboxyl group because they are considered non-toxic. Through the polysaccharide compounds, it is possible to observe the mutation in the characteristics of these compounds through their