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College of Pharmacy

Synthesis, Characterization and Antibacterial Evaluation of some of 2-Oxoazetidin-benzenesulfonamide Derivatives as Possible Hybrid Antibiotics

A Thesis
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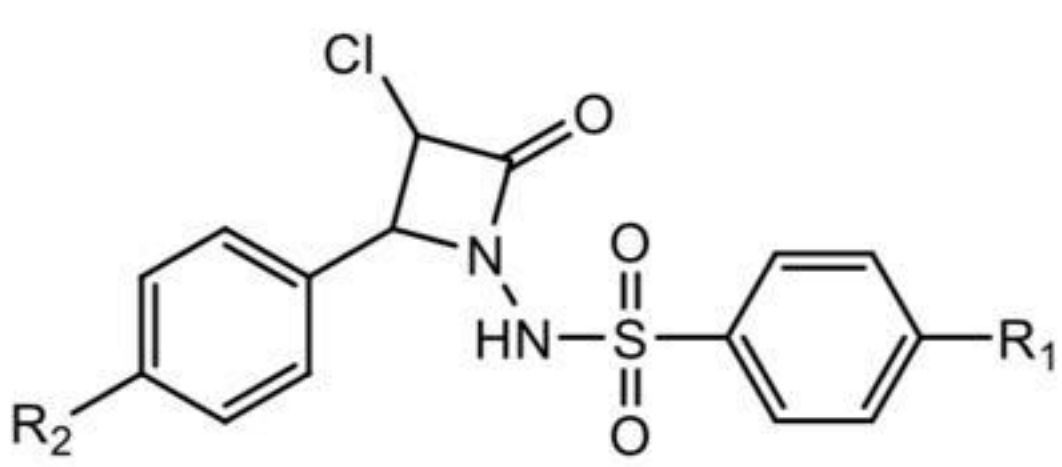
Abstract

An antibiotic is a compound that is active against bacteria and is the most significant form of antibacterial agent for bacterial infection control. In the therapy and prevention of such diseases, antibiotic medicines are commonly used. Antibiotics can either kill or deter bacteria's production.

This research involves the synthesis of a new antibiotic that is effective against a broad range of Gram-positive and Gram-negative bacteria as well as penicillin-resistant Pseudomonas aeruginosa. The target compound to be synthesized is a hybrid molecule from sulfonamide skeleton and a beta lactam heterocyclic ring (as shown in the figure below), both of which are known to have antibacterial activity.



R_1: H, CH_3
R_2: H, Cl, NO_2, OCH_3

The synthesis procedure involves several reactions. The first step is the reaction of benzene (or toluene) with chlorosulfonic acid in a cool water bath to produce the sulfonyl chloride derivatives.

The second step is the production of sulfono hydrazides derivatives which were prepared from reaction of a sulfonyl chloride derivative with hydrazine hydrate in tetrahydrofuran.

The third group of compounds are Schiff bases prepared by reaction of a sulfono hydrazide derivative with benzaldehyde derivatives in glacial acetic acid solution.

The final compounds were synthesized from cycloaddition reaction of chloroacetyl chloride with a Schiff base in tetrahydrofuran and in the presence of trimethylamine.

All the compound produced in the synthesis procedure were identified by FT-IR analysis. The final compounds were further identified by ^{1}H-NMR and elemental microanalysis.

Antibacterial activity evaluation of the synthesized compounds was performed to screen the effectiveness of these new compounds as antibacterials and to compare their activity with the activity of standard antibiotics. The in-vitro evaluation process was carried out by the disc diffusion method. Amoxicillin and cefotaxime were used as standards.

The antibacterial activity was screened against 4 species of bacteria obtained from clinical samples. The tested bacteria species include the Gram-positive *Staphylococcus aureus*, the Gram-negative Enterobacterecea species *Escherichia coli* and *Klepsiella pneumonia* along with the penicillin resistant *Pseudomonas aeruginosa*.

Of the eight synthesized compounds, compound 4b4 showed good activity against all types of tested bacteria, compound 4a4 also had a good action against all species tested. Compounds 4a1, 4b1, 4a2, 4b2 showed a greater activity against Gram-negative bacteria as compared to amoxicillin.