"*Synthesis and Antibacterial Activity of 1,3,4-thiadiazines*"

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1,2,4-Triazolo [3,4-*b*]- 1,3,4-thiadiazine is a bicyclic compound consisting of a five-membered 1,2,4-triazole ring fused with a six-membered 1,3,4-thiadiazine ring which also an important class of heterocycles in organic chemistry due to its various biological activities such as analgesic, anti-inflammatory, anti-cancer, anti-fungal, anti-bacterial and anti-malarial. The indole ring system is the prominent structural component in many drugs. Due to the increasing occurrences of multi-drug resistant bacteria, it is an urgent need to search for new antibiotics. This project aims to synthesize and characterize five series of some new 1,2,4-triazolo[3,4-*b*]-1,3,4-thiadiazines incorporating an indole moiety and evaluate their antibacterial activity. Various types of 1,2,4-triazolo[3,4-*b*]-1,3,4-thiadiazines had been synthesized via cyclocondensation reaction of 4-amino-5-mercapto-1,2,4-triazole with mono-substituted phenacyl bromides. The crude products obtained from the reactions were purified by recrystallization. The structures of the 1,2,4-triazolo[3,4-*b*]-1,3,4-thiadiazines were characterized by ^{1}H NMR, ^{13}C NMR, DEPT, HMQC, HMBC, IR and LC-MS spectral data. The antibacterial activity of the 1,2,4-triazolo[3,4-*b*]-1,3,4-thiadiazines was evaluated against a panel of Gram-positive strains: *Bacillus cereus* (ATCC: 13061), *Bacillus subtilis* subsp*. spizizenni* (ATCC: 6633), *Staphylococcus aureus* (ATCC: 6538), *Micrococcus luteus* (ATCC: 4698), methicillin-resistant *Staphylococcus aureus* (ATCC: 43300) and methicillin-sensitive *Staphylococcus aureus* (ATCC: 29213) and Gram-negative strains : *Escherichia coli* (ATCC: 25922), *Pseudomonas aeruginosa* (ATCC: 27853), *Salmonella typhimurium* (ATCC: 14028), *Proteus vulgaris* (ATCC: 29905) by using a broth microdilution technique. The minimum inhibitory concentration (MIC) values were determined colorimetrically using *p*-iodonitrotetrazolium violet (INT) as an indicator. A potent compound 3-[(5-chloro-2-methyl-1*H*-indol-3-yl)methyl]-6-phenyl-7*H*-1,2,4-triazolo [3,4-*b*]-1,3,4 thiadiazine exhibited excellent MIC and minimum bactericidal concentration (MBC) at 3.91 µg/mL against Gram-positive strains: *Bacillus cereus*, *Bacillus subtilis* subsp. *spizizenni* and *Staphylococcus aureus*. In addition, it showed potential inhibitory activity against methicillin-sensitive *Staphylococcus aureus* (MSSA) ATCC 29213 at MIC 7.81 µg/ml and methicillin-resistant *Staphylococcus aureus* (MRSA) ATCC 43300 at MIC 31.25 µg/ml.

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