SYNTHESIS PHARMACOLOGICAL EVALUATION, MOLECULAR DOCKING AND CYTOTOXICTY STUDIES ON SOME N-SUBSTITUTED 5-[(4-CHLOROPHENOXY)METHYL]-1,3,4-OXADIAZOLE-2YL-2-SULFANYL ACETAMIDES

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ABSTRACT

The framework of our systematic efforts focuses on the synthesis of N-substituted 5-[(4 chlorophenoxy) oxadiazole-2yl-2-sulfanyl acetamides. 4-Chlorophenoxyacetic acid (1) was utilized as a precursor for the 1,3,4-oxadiazole moiety. Esterification of 1in the presence of catalytic amount of concentrated sulfuric alcohol generated ethyl 2-(4-chlorophenoxy)acetate (2) which was treated with hydrazine hydrate to yi chlorophenoxy)acetohydrazide (3). Ring closure reaction of 3 with carbon disulfide and alcoholic potass afforded [5-(4-chlorophenoxy)methyl)]-1,3,4-oxadiazole-2-thiol (4). Finally, substitution at thiol positior electrophiles, N-substituted-2-bromoacetamides (6a-p) in polar aprotic solvent and LiH yielded various chlorophenoxy) methyl]-1,3,4-oxadiazole-2yl-2-sulfanyl acetamides (7a-p). IR, 1H-NMR and EI-MS spect unequivocally confirmed all the substitutions on 1,3,4-oxadiazole-2-thiol core. It was recognized that th derivatives are potential anti-bacterial agents against both gram negative and gram positive bacteria an inhibitors of α-chymotrypsin enzyme. In vitro screening against various bacterial strains unleashed their potential, especially 5-[(4-chlorophenoxy)methyl]-1,3,4-oxadiazol-2yl-N-(3,4-dimethylphenyl)-2-sulfany exhibited marvelous activity when compared with standard ciprofloxacin against S.typhi (-), K.pneumon (+).Compounds were computationally docked with the α-chymotrypsin enzyme protein to unravel the a which displayed significant correlation with the bioactivity data. It can be envisioned that the amalgama chlorophenoxy)methyl]-1,3,4-oxadiazole-2-thiol with N-substituted-2-bromoacetamides generated N-su chlorophenoxy)methyl]-1,3,4-oxadiazole-2yl-2-sulfanyl acetamides having tremendous antibacterial act anti-enzymatic potential. Moreover, substitutions on the oxadiazole moiety lead to the discovery of less compounds as evident from the cytotoxicity data.

KEYWORS: N-Substitute5- [(4-Chlorophenoxy)Methyl]-1,3,4-Oxadiazole-2yl-2-Sulfanyl Acetamides, Spectral Analysis, Pharmacological Screening, Molecular Docking.