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MURB INHIBITORS - INSIGHTS AND PERSPECTIVES IN THE ERA OF ANTIBIOTIC RESISTANCE

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Abstract

The rise of antimicrobial resistance constrain the renewal and potent exploration in antibacterial drug design. The bacterial peptidoglycan biosynthesis is a superior therapeutic target for antimicrobial drug discovery. The cytoplasmic steps of the biosynthesis of peptidoglycan precursor, catalysed by a series of Mur enzymes, are crucial site of action for combatting the emerging concern of resistant bacterias. Many studies were attempted to understand the detailed mechanisms and structural features of the key enzymes MurA to MurF . Among them, MurB is an attractive target, not only because of its critical and unique role in bacterial cell wall synthesis but also due to its presence in several bacterial species. MurB have been thoroughly characterized both biochemically and structurally and, interestingly, have no homologs in humans. Researchers have designed and reported many derivatives of 4-,Thiazolidinone, Dioxopyrazolidine, Thiazolyl urea as MurB inhibitors. However, none has yet made to clinical trials. Inactivity of designed inhibitors on whole-cell tests and high albumin binding of inhibitors were some of the commonly observed hindrance faced by researchers for development of potential MurB inhibitors. This review gives an insight on the strategies to overcome the draw backs of current inhibitors, structural characteristics required for potent MurBinhibitiors and attributes of active site of MurB.

Keywords: MurB, Petidoglycan, antibacterial agents,MurBinhibitors,antibiotic resistance

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IN-VITRO EVALUATION OF ANTICANCER ACTIVITY OF L-AMINO ACID OXIDASE FROM CROTALUS ATROX

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Abstract

Though snake venoms are deadly toxins, research reveals that they are treasure house of enzymatic and non-enzymatic peptides and proteins that are biologically and pharmacologically important with tremendous therapeutic potential. In this context, we evaluated anticancer potential of L-Amino Acid Oxidases (LAAO) from the venom of western diamond back rattle snake (*Crotalusatrox)* on human breast cancer cell line (MDA-MB-231). Preliminary cytotoxicity assays confirmed concentration dependent cytotoxic effect with an IC50 value of 8.98 µg/ml, suggesting the anticancer potential of LAAO from*Crotalusatrox*. Significant induction of apoptosis is exhibited by LAAO from*Crotalusatrox* in Annexin V-FITC apoptosis assay and the effect is further confirmed by TBARs assay. Effect of LAAO from*Crotalusatrox* on cell cycle was evaluated by flow cytometric analysis using propidium iodide and found that LAAO from*Crotalusatrox* significantly arrested the cell cycle at G0/G1phase. Further clarification with animal studies, toxicity as well as pharmacokinetic studies may help to confirm the chemotherapeutic potential of the compound.

Key words: Snake venom, L-amino acid oxidases,Crotalusatrox,Flow cytometry

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