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Bacterial Peptide Deformylase Inhibitors: A New Class of Antibacterial Agents

Bushra Yasmeen#, M. Shruthi*, K. Sirisha[1], K. Umasankar[2]

#Medicinal Chemistry Research Division, Department of Pharmaceutical Chemistry, Vaagdevi College of Pharmacy, Warangal-506001, Telangana.
*e-mail: nelofersultana40@gmail.com, *Medicinal Chemistry Research Division, Department of Pharmaceutical Chemistry, Vaagdevi College of Pharmacy, Warangal-506001, Telangana.*
e-mail: shruthi.mnd@gmail.com, [1]Medicinal Chemistry Research Division, Department of Pharmaceutical Chemistry, Vaagdevi College of Pharmacy, Warangal-506001, Telangana.
e-mail: ragisirisha@yahoo.com, [2]Department of pharmaceutical Chemistry, koneru lakshmaiah education foundation, vaddeswaram, Guntur -522502, Andhra Pradesh.
e-mail: umasankar@gmail.com

Abstract: Infectious diseases still remain the main cause of human premature deaths, especially in developing countries. Even though screening usually provided hits against selected targets, meeting the stringent requirements for a broad spectrum antibiotic turned out to be the real challenge. Only two new classes of antibiotics [Linazolid and daptomycin] have been introduced into the market during last three decades. Peptide deformylase inhibitors [PDFIs] appear to be one of the most exciting class of antibacterial agents discovered to date. PDF is a prokaryotic metalloenzyme that is essential for bacterial growth. Rapid progress in the development of PDFIs has been possible because PDF is a metalloprotease and this class of enzymes shows a high degree of structure function conservation. Although compounds with many different cheletors inhibit the cell free enzyme, only compounds containing hydroxamic acids (or) N-formyl hydroxylamine exhibit appreciable antibacterial activity. Several lead inhibitors have demonstrated invivo efficacy and an excellent safety profile. Actinonin is a naturally occurring compound that has demonstrated antibacterial activity by inhibiting PDF enzyme. Two new actinonin analogues VIC-104959(LBM415) and BB-83698 studied for their antibacterial activity target community-based bacterial infections and have progressed to phase I clinical trials, with a potential major pharmaceutical market. The present study is aimed to develop some new Pyrazolonyl-1-hydroxamic acids 4(a-c) as antibacterial agents. Molecular properties for designed molecules were predicted by different softwares (viz., Lipinski filters, PASS, Rigid Docking, Osiris molecular property explorer and the filtered non-toxic molecules were synthesized by appropriate schemes. In vitro studies was done against different Gram +ve and Gram –ve microorganisms.
In this presentation, design, synthesis and evaluation of some Pyrazolonyl-1-hydroxamic acids as antimicrobial agents targeting PDF enzyme shall we discussed

***Keywords**: Peptide deformylase, antibiotics, hydroxamic acids*

References:

1. M. Clements, R.P. Beckett, A. Brown, G. Catlin, M. Lobell, S. Palan, W. Thomas, S. Wood, S. Salama, P. J Baker and H.F. Rodgers. Antibiotic Activity and Characterization of BB-3497, a Novel Peptide Deformylase Inhibitor. *American Society of Microbiology* 2001,45(2):563-70, 2. S.Sharma1, S. Kaur, B Tania And G Jyoti, Review on Synthesis of Bioactive Pyrazoline Derivatives, *Chemical Science Transactions,* 2014, 3(3), 861-875.

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