Designing potential inhibitors against NDM-1 type metallo-β-lactamases: to overcome antimicrobial effect

Asad U Khan [1], Abid Ali [2]

Interdisciplinary Biotechnology Unit, Aligarh Muslim University, Aligarh, India[12]
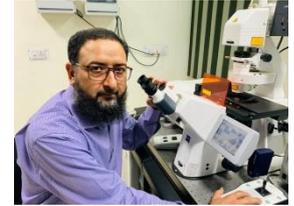
Abstract

NDM-1 is the most prevalent types of metallo-β-lactamases, hydrolyse most of the antibiotics of β-lactam group which may lead to multiple-antibiotic resistance in bacteria. A few inhibitors have been identified against NDM-1 or other class of metallo-β-lactamases but their efficacies are in question. Hence, we initiated to adopt strategies to identify novel anti-β-lactamase agents with specific mechanisms of action which are utmost need of society. In this study, we have reported the discovery of novel non-β-lactam inhibitors against NDM-1 by multi-step virtual screening approach. The potential for virtually screened drugs was estimated through in vitro cell assays. Five compounds were finally identified and procured for evaluation and experimentally testing for their efficacies to inhibit NDM-1 producing bacterial cells, in vitro. The kinetic parameters were evaluated. The dissociation constants (K_d), association constant (K_a), stoichiometry (n) and binding energies (ΔG) of compounds with the respective targets were determined using isothermal titration calorimetry (ITC). Molecular dynamic simulation carried out for 50 ns revealed that these complexes were quite stable throughout the simulation with relative RMSD in acceptable range. Moreover, Microbiological and kinetic studies further confirmed high efficacies of these inhibitors by reducing the minimum inhibitory concentration (MIC) and catalysis of antibiotics by β-lactamases in the presence of inhibitors. Therefore, we strongly conclude that these potential inhibitors may be used as lead molecule for future drug candidate after validation in vivo settings.

microbiology with special reference to multiple drug resistance in bacteria and its therapeutics approaches through Nanoparticle based medicine and effect of antineoplastic drugs on transcription machinery. He has discovered NDM-4 superbug in India. Dr Khan has recently received Visitor's Award of 2019, Wockhardt Excellence award of 2018 "Outstanding Research Award of the year 2014 and National Bioscience Award of department of Biotechnology Government of India 2012, for Career Development".

Speaker Publications:

1. "Etiology and antibiotic resistance patterns of community-acquired urinary tract infections in JNMC Hospital Aligarh, India"
2. "Antimicrobial activity of five herbal extracts against multi drug resistant (MDR) strains of bacteria and fungus of clinical origin"
3. "Aminoglycosides versus bacteria–a description of the action, resistance mechanism, and nosocomial battleground."
4. "Interaction of mitoxantrone with human serum albumin: spectroscopic and molecular modeling studies"
5. "Prevalence of Candida species and potential risk factors for vulvovaginal candidiasis in Aligarh, India"

International Conference on Molecular Microbiology; Webinar- December 07, 2020.

Abstract Citation:

Asad U Khan, Designing potential inhibitors against NDM-1 type metallo-β-lactamases: to overcome antimicrobial effect, Microbiology Conf 2020, International Conference on Molecular Microbiology; Webinar- December 07, 2020.

https://molecularmicrobiology.conferenceseries.com/

Biography:

Prof. Asad U Khan did post doc in RUTGERS University New Jersey, USA during 2000-2003 for three years. Currently he is Professor and head Biotechnology Unit, AMU, Aligarh India. Dr Khan has multiple research interest in the area of medical