

An *In silico* Approach to Battle with NDM-1 Superbug: From Wet to Dry

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The spread of multi-drug resistant strains in the hospital setting has become a serious problem for clinicians and physicians world-wide [1,2]. Therefore, carbapenems are the drug of choice to treat infections, both in nosocomial and community acquired infections. These are the important class of antimicrobial agents for the treatment of members of enterobacteriaceae, producing ESBLs [3]. However, the emergence of carbapenem resistance has also changed the scenario of therapeutic approach in serious nosocomial infections. Carbapenemases are carbapenems hydrolyzing enzymes, are now extensively identified in Gram-negative rods. One of the latest enzymes, NDM-1 (New Delhi Metallo beta lactamase) has been first identified from Swedish patient of Indian origin in 2008. This patient travelled to New Delhi and while there, acquired a urinary tract infection [4]. In August, 2010 a study was published in Lancet Infectious Diseases identifying the widespread of NDM-1 in the Indian subcontinent and imported into UK. The emergence of NDM-1 producers has been identified in the US and many other countries almost worldwide [5,6].

The spread of Carbapenemases among enterobacteriaceae is an alarming threat to the clinical and hospital settings. It is not only because these enzymes confer resistance to carbapenem and other betalactam antibiotics, but also other classes of antibiotics are getting ineffective, leaving only limited treatment options [3,7]. This level of resistance may have serious public health implications because the current therapeutic approaches are not able to treat infections [3,8,9].

In the current scenario all pharmaceutical industries and independent research laboratories need for a novel and effective drugs to control infections, caused by drug resistance mutant strains. *In vitro* technologies of high-throughput screening (HTS) has become a keystone for pharmaceutical research since 1980 [10]. Such experimental approaches to carry out the biological screening of billions of compounds are cost effective and time consuming therefore, computer-aided drug design has become attractive alternatives. Now a days virtual screening has emerged as an important tool in pursuit of novel compounds for interested target from available chemical databases. Increasing availability of databases for small molecules and their free online distribution has enabled not only private industries but also large number of research groups to use virtual screening methodology in early stages of drug discovery. A wide range of software are available for screening the lead like compounds from chemical databases which are based on comparative and contrasting methodological protocols. These approaches are reliable, cost-effective and time-saving for the novel lead discovery.

Therefore, we have proposed an effective structure based virtual screening approach to identify the most potential drug candidates. The three dimensional structures of the target molecules by X-ray and NMR studies have opened a new vista to the structure based drug designing. These predicted structures were analyzed for their active site which may act as an assembly site with another macromolecule or a communication site [11]. The docking is another key step in the protocol of structure based virtual screening (SBVS). This is a crucial step needs significant attention among all the virtual screening steps. The stability of the complex should be evaluated at this step which determines the specific biological target site. Different scoring

functions are to be used for the evaluation of ligand-target affinity for the conformation of ligands. These functions may be categorized as empirical-based, force-field based, knowledge-based and consensus scoring [12]. These scoring functions rank the compounds by an exhaustive conformational consensus scoring approaches.

This editorial gives a new turn to the researcher to design a new lead molecule against various disease targets in general and specifically to combat infections caused by multi-drug resistant strains of bacteria. The clinicians and physicians are worried after the emergence of NDM-1 superbug since no drug of choice is left to treat patients with these infections. The only antibiotic left is Aztreonam which may not be continued to support the infections. Therefore, we have proposed a computational approach to screen new inhibitor molecules against NDM-1 as well as other resistant targets. These molecules can be the future drug candidates. The work has already in progress in my laboratory.

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