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Short Communication

DOCKING AGAINST NOSOCOMIAL INFECTION-*STAPHYLOCOCCUS EPIDERMIDIS*

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ABSTRACT

Objective: Nosocomial infections are acquired by immuno-compromised patients in hospitals which seem to be the serious health problem in recent times. *Staphylococcus epidermidis*, the commensal bacterium inhabiting human skin emerges as the most common opportunistic nosocomial pathogen due to its ability to form biofilms on medical devices. Biofilm acts as a mask against attacks from an immune system which leads in difficulty to eradicate. Several research works have been going on to find out the effective drug against hospital acquired infections since these pathogens are resistant to several antibiotics like methicillin, penicillin and amoxicillin. Using docking tools, an attempt has been made to find out the most potential drug against the nosocomial pathogen - *Staphylococcus epidermidis.*

Methods: Using mcule online docking server, several drugs like linezolid, ceftaroline, rastomycin, vancomycin, nitrofurantoin, trimethoprim sulfamethoxazole, allicin and gallic acid were selected to dock against epidermin decarboxylase (*Staphylococcus epidermidis).*

Results: Ceftaroline showed the lowest docking energy of -10.2 Kcal/mol against the target protein of *Staphylococcus epidermidis* (Table 1 and Figure 1) followed by Linezolid, Allcin and Rastomycin.

Conclusion: By comparing the docking scores against the selected target, ceftaroline could be suggested as potential drug against coagulase negative *Staphylococcus epidermidis* infection.

Keywords: Nosocomial infection, *Staphylococcus epidermidis,* Mcule, Epidermin decarboxylase, Ceftaroline.

A nosocomial infection is one for which there is no evidence that the infection was present or incubating at the time of hospital admission [1]. Coagulase negative *Staphylococcus epidermidis* is considered as the major frequent cause of these hospitals acquired infections other than Gram negative rods which remain in surgical site infections. Normally, it is a commensal bacterium that inhabits the human skin. In case of nosocomial infection, these commensals emerge as opportunistic pathogen. Due to increased use of antibiotics in hospitals, the strains of *Staphylococcus epidermidis* have become antibiotic resistant due to their ability to form biofilms, which results in chronic infection [2]. Biofilm acts as a mask against attacks from an immune system which leads in difficulty to eradicate. Several research works have been going on to find out the effective drug against these healthcare associated global infections since these pathogens are resistant to several antibiotics like methicillin, penicillin and amoxicillin.

Drug discovery process is time consuming since it includes many preclinical and clinical trials. In spite of all these trials, there occur drug failures most of the time. The reason might be due to pharmacokinetic properties of ligands and its poor drug-likeness with the target protein. Hence by using computer aided docking tools, an attempt has been made to find out the most potential drug against the nosocomial pathogen - *Staphylococcus epidermidis.*

Treating nosocomial infections have become very crucial nowadays. There are reports about the use of several antibiotics like linezolid, ceftaroline, rastomycin, vancomycin, nitrofurantoin and trimethoprim. Hence, their structures in SMILES format were retrieved from PubChem database. Online Marvin Sketch tool (http: //www. chemaxon. com/marvin/sketch/index. php) was used to draw the structures of the drugs for which the SMILES format was unavailable. The ADMET (Absorption, Distribution, Metabolism, Excretion and Toxicity) properties of these antibiotics were also checked in the PubChem database.

Epidermin is an antimicrobial peptide that consists of unusual amino acid residue S: -[(Z:)- 2-aminovinyl]-D-cysteine present in *Staphylococcus epidermidis.* Oxidative decarboxylation of cysteine leads to post-translational modification of Epi-A which leads to introduction of this unusual cysteine residue [3]. Hence, previous studies reported that epidermin decarboxylase present in *Staphylococcus epidermidis* is the virulent factor of its infection. Hence its 3D crystal structure (PDB ID: 1G63) was retrieved from RCSB protein data bank (www. rcsb. org/pdb).

Argus Lab (4.0) and online docking server (www. mcule. com) were used for docking analysis. Active sites were predicted using online active site prediction tool (www. scfbioiitd. res. in/dock/activesite. jsp). Molecular visualization of ligand and receptor interaction was carried out in Pymol software.

Table 1: Docking results of selected drugs against target protein of *Staphylococcus epidermidis*

Antibiotics	Docking energy (Kcal/mol)
Linezolid	-7.9
Ceftaroline	-10.2
Rastomycin	-7.7
Vancomycin	-6.9
Nitrofurantoin	-6.9
Trimethoprim	-7.2
Allcin	-7.7
Gallic acid	-7.1
Nimbin	No acceptable ligand poses were found
Emodin	No acceptable ligand poses were found
Aloin	No acceptable ligand poses were found
Meliantriol	No acceptable ligand poses were found
Gentamycin	No acceptable ligand poses were found
Azadirachtin	No acceptable ligand poses were found

Primary transporters of antimicrobial peptides have mainly been reported among Gram-positive bacteria producing bacteriocins themselves. For instance, *S. epidermidis* strains producing the lantibiotic epidermidin have evolved an additional protective system removing harmful peptides from the membrane after they have reached the lipid bilayer. This epidermidin resistance is mediated by the EpiEFG ABC transporter, which specifically binds only epidermidin [4].

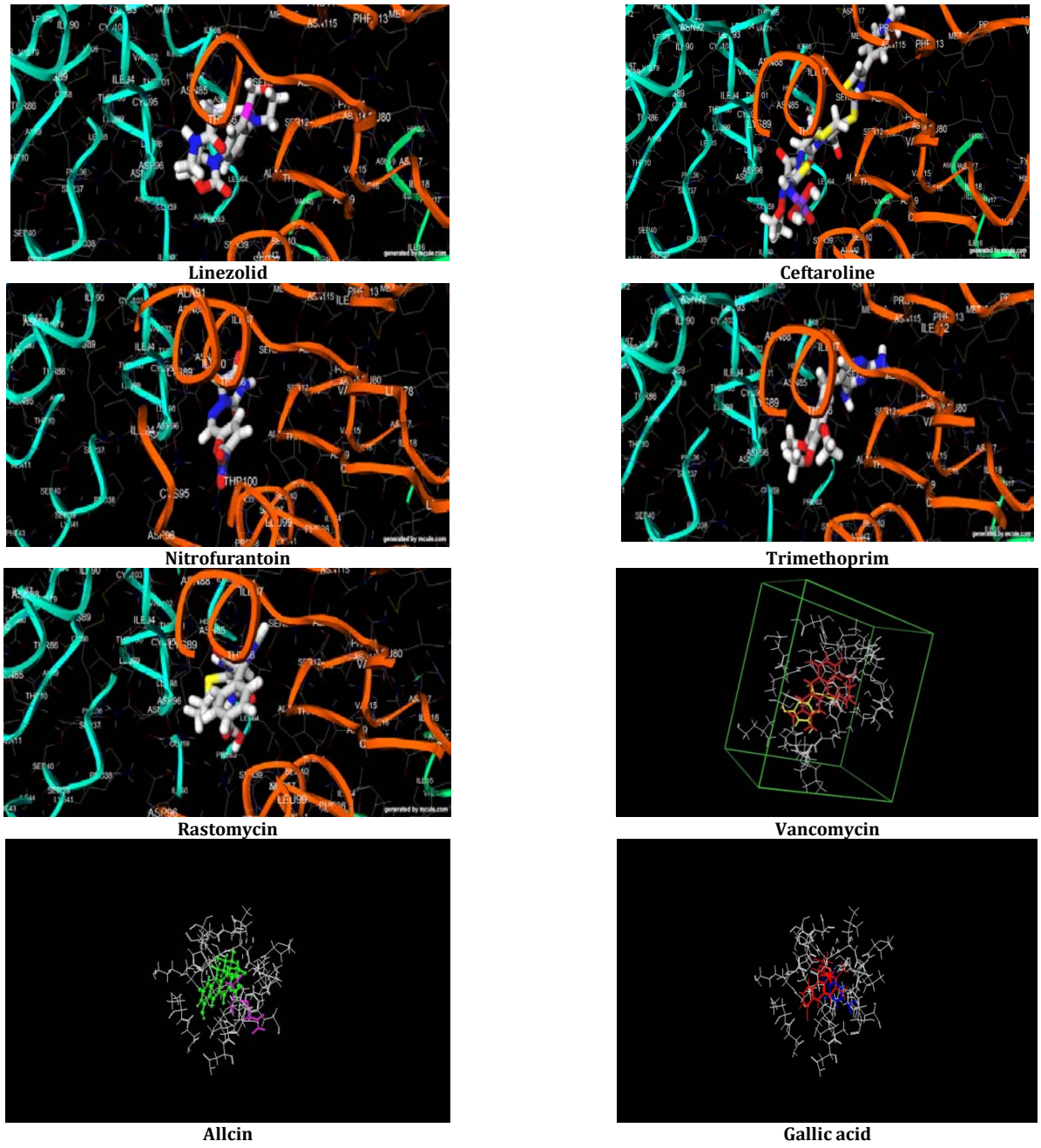

Fig. 1: Molecular interaction of target protein PDB ID: 1G63 with above antimicrobials

Ceftaroline showed the lowest docking energy of -10.2 Kcal/mol against the target protein of *Staphylococcus epidermidis* (Table 1 and Figure 1) followed by Linezolid, Allcin and Rastomycin.

In silico docking analysis revealed the comparative potentiality of antibiotics and phytochemicals as a promising source against nosocomial infections caused by *Staphylococcus epidermidis*. Out of seven phytochemicals and seven antibiotics screened, two phytochemicals and five antibiotics showed effective binding to the target proteins. Lower the docking score, higher is the binding affinity [5]. The results are effective not only for the pose construction and pose selection but also for virtual screening [5]. All the ligand molecules successfully passed the Lipinski filter, which shows its drug-likeliness.

The results of *in silico* docking study clearly revealed that Ceftaroline is the most potential antibiotic showing very strong interaction with epidermin target proteins as evident by its least binding energy compared to other tested ligands. Even the phytochemicals are promising resource which deserves further research in order to combat dreadful human diseases either singly or in combination with the commercial antibiotics.

Thus, the computer aided method plays a rapid and significant screening approach of drug discovery by selecting the lead molecules with good pharmacological and druggish properties in order to bind effectively with target protein.

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CONFLICT OF INTEREST

We hereby declare that there is no conflict of interest.

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