Preliminary in Silico Studies on the Role of Nisin Cyclase in Food Preservation

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Abstract— This paper presents computational studies that estimate the RMSD distances of Nisin in its Cyclase form. Nisin Cyclase, the Cyclase of lantibiotic Nisin is a kind of bacterial toxin produced by lactococcus lactic and is widely accepted as a safe biological preservative. This paper showcases computational studies as an effective tool to estimate the docking affinities for 416ZN as an integral part of Nisin Cyclase which owning to a large RMSD distance with its binding sites proves its efficiency as a food preservative and also opens pathways for creation of model food preservatives from grid data accomplished by computational studies. Docking protocol for the RMSD distance was carried out using 416ZN conformation. These are preliminary studies that indicate a sequence and more sophisticated investigations are required for detailed analysis.

Key words: RMSD, Docking, Lantibiotic

I. INTRODUCTION

Nisin is a 34-residue lantibiotic widely used as a food preservative. Being made by lactococcus it is natural, non-poisonous, and effective food antiseptic. It inhibits certain strains of food pathogens such as clostridium botulinium, Staphylococcus aureus, Streptococcus hemolyticus, Listeria monocytogenes, Bacillus stearothermophilus, Bacillus subtilis, etc. [1, 2, 3, 4].
It was originally isolated in the late 1930s and produced since the 1950s as nisaplin from naturally occurring sources by Aplin and Barrett in laboratories in Beaminster in Dorset[5].Being a polypeptide it will be broken down into amino acid by protease in the digestive system, also it would not change the normal bacterial community in intestine or cause drug resistance of using other antibiotic substance [6].These cyclases are also classified underAMPs(antimicrobial peptides), Nisin being one of the well characterized one and is amphiphilic [7].

Nisin has no effect on the normal flora in the intestine and is not toxic to human [8].In this paper computational studies have been used to estimate the docking affinities for 416ZN as an integral part of Nisin Cyclase which owing to a large RMSD distance with its binding sites proves its efficiency as a food preservative and also opens pathways for creation of model food preservatives from grid data accomplished by computational studies.

The in-silico study done here includes the use of an open source software namely Argus Lab to carry out the preliminary docking and RMSD protocols.

II. METHODOLOGY

Docking and RMSD calculations attempt to place the ligands into binding sites. Before the procedure runs one needs to define the atoms that make up the ligands and the bonding sites wherein the outside moiety binds.

N-terminal moiety is responsible for insertion of Nisin in lipids [1,9].Zinc is essential for activity of Nisin Cyclase [10, 11] and thus here based on its action the large distances between ligand sites shows the outcome of preservation.

Thus, studies have shed light on the mechanism and substrate specificities of the enzymes that catalyze these transformations, and during these investigations, lantibiotic analogues have been generated that have been valuable for mode of action studies[12]. The structures used are from RCSB protein databank [13]; we made copies of catalyst and docked for RMSD distance onto the protein binding sites concluding preservation affinity.

A. RMSD Distance

This was the major observation to conclude how close is the bounded structure with the x-ray structure, creating an unusually higher distance verifying the preservation activity.

B. View Tool

Here the best grid positions and placements were observed giving us several dimensions where docking protocols are applicable or inapplicable with the binding distances in seconds of elapsed time.

III. RESULTS AND DISCUSSION

The residue incorporated namely 416ZN created 679ZN ligand group such that the RMSD distance between the binding site and the ligand came out in various docking protocols ranging between 8.236572-10.283646 Angstrom.

18.055556% of the protocol was recorded as the free space wherein 52 points of original Cyclase residue lied inside the docking grid and a large number, i.e., 236 lied outside. The effect of heavy atoms was recorded to be zero. NisC can be widely applied for the cyclization and stabilization of nonlantibiotic peptides [14].And hence using the RMSD value obtained its clear that the affinity for Nisin Cyclase is very low even for its own ligand copies so the food which is kept in its binding site will firmly stick with the residue of the Cyclase and wouldn't allow any foreign substance to invade its preservation.

Study of the mode of action of the lantibiotic Nisin has revealed its use of as a 'docking molecule' in the target cell to facilitate biological activities [15].

Nisin is produced as a fermentation product of a food grade bacterium and the safety and efficacy of Nisin as a food preservative have resulted in its widespread use throughout the world and is the only lantibiotic that has been well characterized for food preservation, it has a great potential for acting as a model to synthesize structural analogs [16] and more sophisticated work can be done using higher soft wares.

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