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Research Article

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In silico analysis of interaction of silver nitrate with Braun lipoprotein in bacterial cell wall

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ABSTRACT

Silver nitrate with chemical formula of AgNO3 is an organic compound which have been used for a long times as an antibacterial agent with high antimicrobial and anti-fungi properties. The outer membrane of gram-negative bacteria contains abundant copies of a few proteins, the so-called ajorouter membrane proteins.In this study Molegro virtual docker (MVD) is used. The results obtained from docking showed that the best pose which is derived from MolDock score for Braun lipoprotein was -36.4966 with reranking score equal to-47. 8616. Bioinformatic studies show that silver nitrate has interaction with protein Braun lipoprotein.

Key words: AgNO3, Murein-lipoprotein, Braun lipoprotein, Bioinformatics

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INTRODUCTION

The antiseptic properties of silver salts have been demonstrated long times ago. Before the development of common antibiotics, solutions containing AgNO3 were used for preventing the contraction of gonorrhea from mother to newborn babies. This particle led to reduction in eye infection, but some extreme cases with incorrect dosage were resulted in blindness. This protection was used by Credé in 1881 for the first time [1]. The first studies on antimicrobial properties of silver nanoparticles performed during the years that silver containers have been used for water preservation. The disinfection properties of silver ions were studied for over a century. Before using a disinfectant as a water disinfectant, its inactivation kinetics must be recognized. The dosage of disinfectant and the time of application are two main parameters for determining the inactivation Kinetic. A good disinfectant is a compound that with the lowest dosage and minimum amount of time effectively inactive any pathogens in water. The researches in recent years are focused on generated silver ions or colloidal silver electrolytically. The adsorption of silver to glassware can lead to decrease in silver concentration and also release of the silver in subsequent experiment. So a glassware washing step is needed to minimize the خطای of experiment. Chambers, Proctor and Kabler established the importance of using an effective neutralizer solution which is made of a mixture of sodium thioglycolate and sodium thiosulfate, rather than sodium thiosulfate alone, which though it is effective in neutralizing other disinfectants does not satisfactorily stop the bactericidal action of silver nitrate. The researchers tested the effect of pH on the kinetics, finding that a higher pH increased the bactericidal action. Wuhrmann and Zobrist added that at a higher temperature, inactivation occurs faster [2]. Elemental silver and silver salts have been used as antimicrobial agents for a long time. Silver or silver ions have strong antimicrobial activity against pathogenic microbes such as bacteria, yeast, fungi and algae which is why they have long been used in many areas. It may be used for controlling different plant pathogens in a relatively safer way compared to synthetic fungicides [3]. Until now, limited studies have provided pieces of evidence of the applicability of silver for controlling plant diseases [3]. Lipopolysaccharide (LPS) and murein (Lpp) with a great importance in maintaining the integrity of the bacterial envelope are the most common parts of the outer membrane of gram-negative enteric bacteria. Glycerol

transferase (Lgt), *O*-acyl transferase, signal peptidase II, and *N*-acyl transferase (Lnt) are the main enzymes for modification of a lipid moiety to Lpp. A polysaccharide core, O antigen, and a lipid A domain are the main component of LPS. The fatty acids in Lipid A are believed to contribute to the low-permeability barrier of the outer membrane of gram-negative bacteria. The aim of present study is to study bioinformatic interaction of silver nitrate withBraun lipoprotein.

EXPERIMENTAL SECTION

2.1 Preparing 3 dimensional structures of silver nitrate and protein Braun lipoprotein:

In the first step, amino acid sequences of outer membrane lipoprotein with accession number of P69776were taken from NCBI website (www.ncbi.nlm.nih.gov/) (Figure1). In the next step, Silver Nitrate with AgNo3 molecular formula (number 22878) was provided from ChemSpider website (www.chemispider.com) (Figure2). Then the outer membrane lipoprotein with number of 1EQ7 was obtained from Protein Data Bank website (www.rcsb.com) (Figure3).

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MKATKLVLGAVILGSTLLAGCSSNAKIDQLSSDVQTLNAKVDQLSNDVNAMRSDVQAAKDDAARANQRLDNMATKY
RKQKKGN
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Figure 1: Amino acid sequence of structure of outer membrane lipoprotein

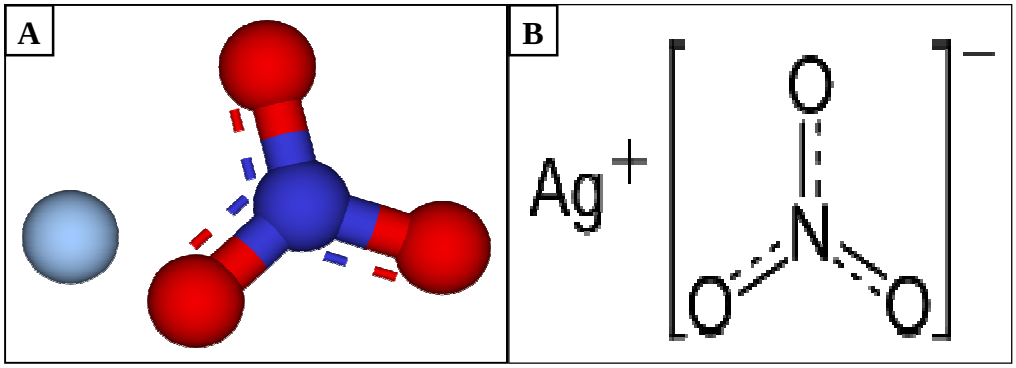

Figure 2: Structure of silver nitrate

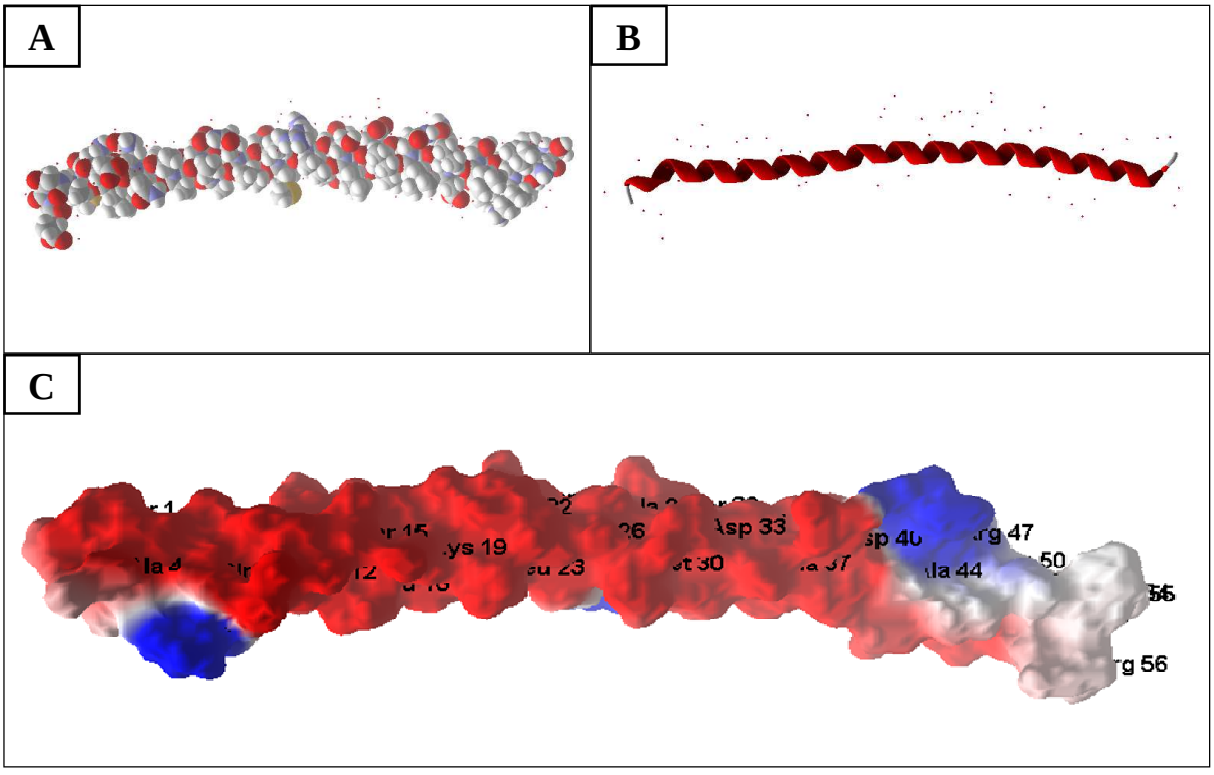

Figure 3:A and B: Structure of outer membrane lipoprotein from *Escherichia coli* .C: The hydrophobic regions and negative charge

2.2 Molecular docking study

For computer simulated study the Molegro virtual docker (MVD) 2011.4.3.0. Before initiation the docking operation, protein and ligand structures were prepared using MVD. For this purpose, charges assigned to the model of protein and ligands structures and flexible torsions in ligands were detected by this software (Figure 4).

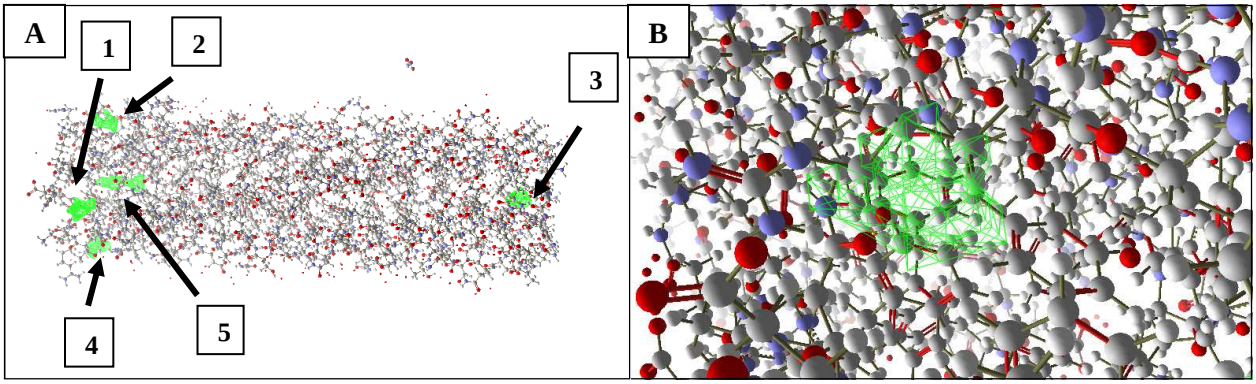

Figure 4: Cavities of outer membrane lipoprotein predicted model. MVD used for cavity detection. Detecting parameters: probe size 1.2, max number of ray checks was 16, minimum number of ray hits 12 and Grid Resolution 0.8

RESULTS AND DISCUSSION

MolDock score with a grid resolution of 0.30 Â was used as scoring function for docking. In the setting of program the internal electrostatic interaction and hydrogen bond between ligand and protein were ticked. The docking algorithm used in this study was MolDock SE and ten runs were carried outfor any ligands. The energy threshold of 100.00 was sued for energy minimizationand similar poses were ignored. Also optimization of hydrogen bonds were performed. The MolDock and reranking score are two parameters used for evaluating the docking results. For the defined docking radius in Pal protein, the best pose which is derived from MolDock score for Braun lipoprotein was -36.4966 with Reranking score equal to -47. 8616(Table 1).

Table 1: Binding energy level of top five poses of silver nitrate to outer membrane lipoprotein

		Outer membrane lipoprotein	
No	Ligand name	MolDock Score	Rerank Score
1	silver nitrat	-36.4966	-47. 8616
2	silver nitrat	-34.1189	-44.8951
3	silver nitrat	-33.0368	-44.534
4	silver nitrat	-32.8858	-38.7218
5	silver nitrat	-32.8726	-38.6887

3.2. Finding ligand binding sites:

3DLigand Site server (http://www.sbg.bio.ic.ac.uk) wasused for prediction of potentially binding sites of Braun lipoprotein. In the server output ASP, MET, GLN, SERand ILEwere predicted as present in binding site(Table 2). Table 4 showed the position and the percentage of each amino acids. Furthermore MVD is used for finding cavities of model. For this purpose, probe size of 1.2, 16 ray checks,12 ray hits and Grid Resolution of 0.8 were used. Five cavities were found by MVD (Figure 5).

Table 2: ligand binding sites by computing interactions with 3D Ligand Site server for Braun lipoprotein

No	Residue	Amino acid	contact	av distance
0.00	1	ASP	54	1
0.12	1	MET	72	3
0.00	1	GLN	43	4
0.23	1	SER	75	5
0.00	1	ILE	76	6

Silver ions are very reactive, which are known to cause the inhibition of microbial respiration and metabolism as well as physical damage [4,5]. Ionic silver has some disadvantages such as its high reactivity which made it unstable and thus easily oxidized or reduced into a metal depending on the surrounding environment. In addition, ionic silver causes discoloration by itself or allows other materials to cause undesirable coloration and it does not continuously exert antimicrobial activity. Also, silver in the form of a metal or oxide, which is stable in the environment, is applied in a relatively increased amount due to its low antimicrobial activity[3]. Today, the use of silver as a biocide has growing up significantly. Microcrystals and nanoparticles of silver are effective against many resistance

populations of microorganisms on the surfaces of bodies of water and inside water pipes [6,7,8].In general, specific binding with surface and metabolism of agents into the microorganism characterize the antimicrobial mechanism of any agent. Furthermore, it has been suggested that silver ions penetrate into bacterial DNA once entering the cell, which prevents further proliferation of the pathogen [9]. There is abundant number of a few proteins called major outer membrane proteins. One of the major outer membrane proteins in Escherichia coli and other gramnegative bacteria is the murein lipoprotein discovered by Braun and Rehn . The amino terminus of this lipoprotein consists of a novel lipoamino acid, N-acyl diglyceridecysteine[10]. Results obtained from this study showed that silver nitrate has interaction with Braun lipoprotein resulting to MolDock Score equal to -36.4966 and Rerank Score equal to -47. 8616. Results comparison form bioinformatic prediction similar to this study using Peptidoglycan-Associated lipoprotein (Pal) in 2014 revealed that Braun lipoprotein possesses a higher score compared to Pal[11].

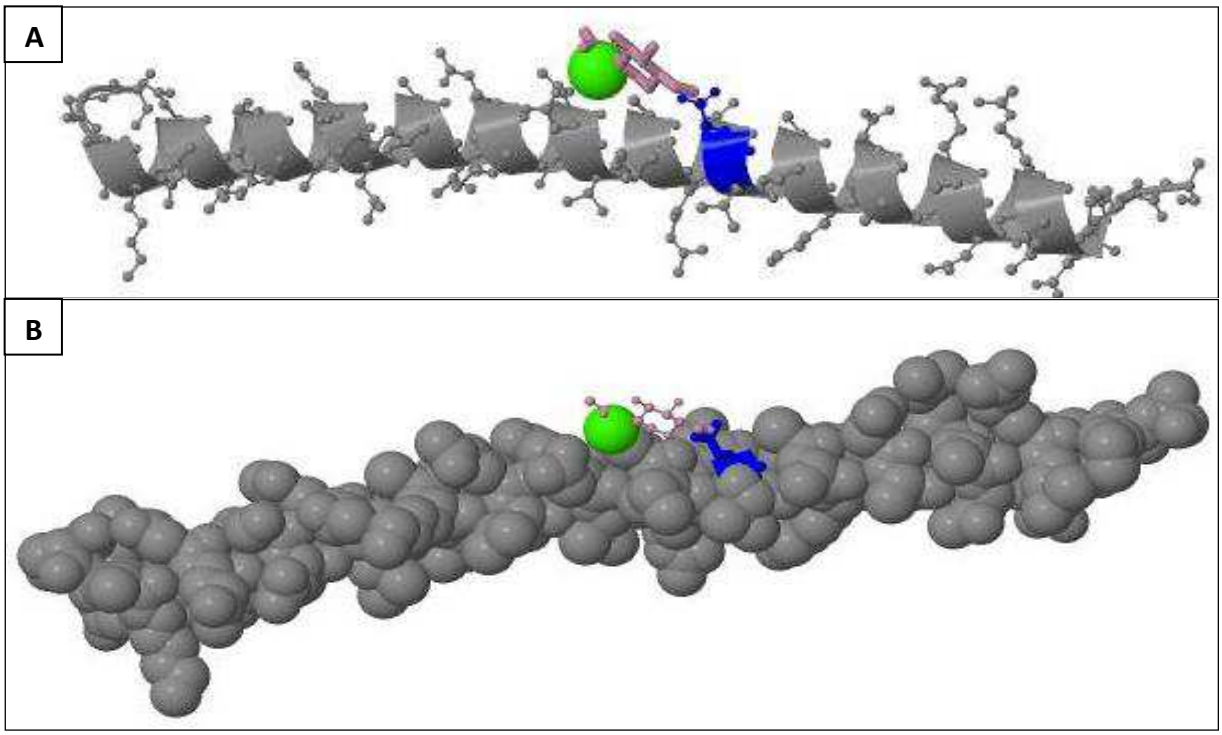

Figure 5: Ligand bound to amino acids located in A and B position in Braun lipoprotein

CONCLUSION

Silver nitrate possesses some toxic components which can cause some side effects on human health and environment. Hence using this inorganic compound in environment can be extremely harmful. This study showed that Silver nitrate has interaction with Braun lipoprotein and some related studies have already reported that silver nitrate is capable of making interaction with many proteins.

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