EFFECTS OF DYSULFIDE BONDS ON LYSOZIM PROTEIN STRUCTURE AND PROPERTIES: MOLECULAR LEVEL STUDY

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INTRODUCTION

Lysozyme is one of the most important enzymes produced in large amounts in tears, saliva, and milk. Lysozyme destroys a peptidoglycan component of the bacterial cell wall and acts as an antimicrobial agent, leading to cell death. Lysozyme contains four disulfide bonds (DB), which play an important role in catalytic function. Using molecular dynamics, we studied the conformational changes for the case of DB (6Sis–127Sis, 30Sis–115Sis, 79Sis-94Sis va 64Sis – 80Sis) disruption and obtained results caused by 3D changes in various areas of lysozyme. These changes may affect the catalytic function of lysozyme[1].

In order to represent the changes that occur in Chicken Egg White (TTo) lysozyme after DBs are interrupted, native lysozyme and 6Sis–127Sis (OX1), 30Sis–115Sis (OX2), 79Sis–94Sis (OX3) and 64Sis–80Sis (OX4) performed standard MD simulations for lysozyme proteins with truncated DBs and compared the obtained results[2].

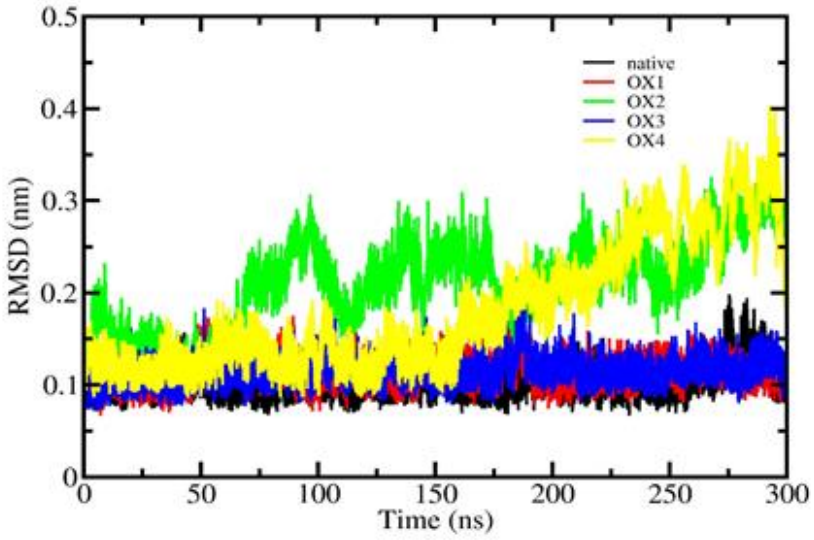
Material and Methods: To represent the changes that occur in Chicken Egg White (TTo) lysozyme after DBs are interrupted, native lysozyme and 6Sis–127Sis (OX1), 30Sis–115Sis (OX2), 6Sis–127Sis (OX1), 30Sis–115Sis (OX2), we performed standard MD simulations for lysozyme proteins with truncated DBs and compared the obtained results. MD simulations were performed using the GROMACS package version 2020.1. We obtained the initial coordinates of the TTo lysozyme molecule from www.rcsb.org (PDB code 1AKI) placed it in a dodecahedron box and surrounded it with water. NaCl ions at a concentration of 0.1 M were added to the system. AMBER99SB potential was used to represent interatomic interactions in the system. For water, the SPC/E model was used.

We created the same system for lysozymes with disconnected DBs. At first, using the "steepest descent" algorithm, we brought the system's potential energy to a minimum state. Then, freezing the lysozyme molecule with a potential force, we brought the water and ions around it to an equilibrium state in NVT and NPT conditions for 300 ps. Then, canceling the fixed potential, we simulated the system in NPT conditions for 300 ns MD. Both systems were simulated at the same steps, using the same files. We used the leap-frog algorithm to integrate the equations of motion of the system particles over time and set the time step (dt) to 2 fs. At the NVT equilibration stage, we gave the system a temperature of 310 K, used the V-rescale thermostat, and at the NPT stage, a pressure of 1 atmosphere was given in the

Berendsen barostat. In the 300 ns NPT simulation, we used the Parrinello-Rahman barostat to ensure isotropic constant pressure in the system. When calculating all intermolecular interactions (van der Waals, Coulomb), we set the particles' spherical radius (cutoff radius) to be 1.0 nm.

Results and Discussion: We analyzed the systems through trajectories obtained from MD simulations. In order to find out how the flexibility and mobility properties of the main chain of the protein change in the absence of DBs, we calculated the root-mean-square deviation (RMSD—Root-mean-square deviation) in the main chain of natural and DB-free lysozymes. In the same way, we also calculated the root-mean-square fluctuation (RMSF—Root-mean-square fluctuation) of the mobility of each amino acid in lysozymes during the simulation. If the macromolecule undergoes significant changes due to the breaking of bonds or mutations, this should be reflected in its secondary structure. Therefore, we analyzed the secondary structures of lysozymes during the simulation using the gmx do_dssp module of the

GROMACS program to study the 3D conformations more deeply. We compared the received analysis results and graphs.[3]



1 – Figure. Root mean square deviation (RMSD) plots of native, OX1, OX2, OX3, and OX4 lysozyme Cα-carbons

1 - Figure OX2 and OX4 have large changes in the model OX4 from about 150 ns to 300 ns, which is faster than natural lysozyme, the Cα-carbons deviate by 0.2 nm more than natural, and the vibrational amplitudes are also larger. No significant difference was observed in OX1 and OX3 compared to baseline. This graph means that conformational changes can be seen for native lysozymes and lysozymes with 6Sis–127Sis (OX1), 30Sis–115Sis (OX2), 79Sis–94Sis (OX3) and 64Sis –80Sis (OX4) DBs cleaved, and the DBs show the lysozyme structure. means that it has an important place to fulfill its unity and function.

Conclusion: So, lysozyme modified by changing its activity can be used for various purposes. For example, cleaning food from bacteria, treating cancer, etc[4].

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