MOLECULAR DYNAMICS SIMULATION OF HEAVY METAL ION BINDING TO β-LACTOGLOBULIN AND 7S SOYBEAN GLOBULIN

Zhytniakivska O. A., Tarabara U. K., Vus K. O., Trusova V. M., Gorbenko G. P.
V. N. Karazin Kharkiv National University, Kharkiv, Ukraine
olga.zhytniakivska@karazin.ua

Industrialization and rapid urban development have drastically increased heavy metal pollution in water sources worldwide. Even minimal exposure to these metals can pose severe health risks, affecting different systems in the human body. Biosorption is currently considered one of the most efficient and inexpensive methods for removing heavy metals from contaminated water using biomass as sorbents. Protein-based nanomaterials have emerged as highly promising biosorbents for heavy metal adsorption due to their diverse amino acid functional groups demonstrating exceptional metal-binding capabilities. Numerous studies demonstrated the effectiveness of whey and soybean proteins in formulating protein-based nanomaterials for heavy metal removal. However, to the best of our knowledge, a gap exists in understanding the intermolecular interactions between heavy metal ions and proteins in the various proteins-based nanomaterials. The study of the metal-protein interactions is an important step in the development of protein-based nanomaterials for heavy metal sorption.

In the present study, molecular dynamics (MD) simulations were employed to investigate the molecular details of interactions between β-lactoglobulin and soybean 7S globulin with Cd^{2+}, Ni^{2+} and Co^{3+} heavy metal ions. A series of 200-ns MD simulations for the metal-protein systems containing 5, 50, 100, and 500 heavy metal ions was conducted at 300 K using GROMACS software and the CHARMM General Force Field. The three-dimensional X-ray crystal structures of proteins were obtained from the Protein Data Bank (https://www.rcsb.org/) using the PDB IDs 3AUP and 1QG5 for 7S globulin from soybean and bovine β-lactoglobulin, respectively. The chain A of the three-dimensional X-ray crystal structure of 7S globulin was selected for the MD studies. Input files for the molecular dynamics (MD) simulations were generated using the Solution Builder module of the web-based CHARMM-GUI interface and a TIP3P water rectangular solvation box, maintaining a minimum distance of 10 Å between the protein and the box edges. Heavy metal ions in different concentrations were incorporated into the system and randomly distributed. To provide comprehensive insights into the system's structural stability and dynamics, we analyzed the key structural parameters namely the backbone root-mean-square deviation (RMSD), radius of gyration (Rg), solvent-accessible surface area (SASA), and root-mean-square fluctuations (RMSF).

Our results demonstrated the stability of the simulated systems, since the calculated RMSD values for all systems remained below 0.2 nm, except for brief fluctuations observed in the Ni^{2+}-containing system during the first 50 ns. Notably, the binding affinity of Cd^{2+}, Ni^{2+}, and Co^{3+} heavy metal ions to proteins under identical simulation conditions varies significantly and depends on the protein type and heavy metal ion concentration, highlighting the strong correlation between the increasing heavy metal concentration and number of binding sites. The results also demonstrated the destabilization effect of Cd^{2+}, Ni^{2+} and Co^{3+} on the protein's structure, with a magnitude of the effect more pronounced at higher heavy metal ions concentration. The degree of destabilization varied depending on the specific heavy metal ion. Moreover, the residue-level root-mean-square fluctuations (RMSF) analyses revealed that metal binding particularly affected regions important for β-lactoglobulin's and 7S globulin stability.

The findings from this study can contribute to the development of protein-based nanomaterials for the effective detection and removal of heavy metal ions.