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Short Communication

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Computational Ferritin Nanocarrier Modification to Enhance Stability and Specific Drug Delivery

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ABSTRACT

The objective of this project was to assess the stability of the ferritin cage for drug delivery applications. Through molecular modeling, we evaluated the stability of the cage, demonstrating that ferritin has the potential to serve as an effective small drug carrier for future drug delivery and vaccine applications.

Keywords: Ferritin, Glycation, Molecular modeling, Nanocarrier

Introduction

Ferritin is a major iron-storage protein in the body consisting of 24 subunits that self-assemble to form spherical nanocages of around 12 nm in diameter [1,2]. Recently, Ferritin has gained attention as a potential vehicle for drug delivery. Nanocages have recently been employed in developing a SARS-CoV-2 vaccination eliciting long-term protective memory cells and a sustained antibody response [3]. Among all vaccination strategies, the nanoparticle vaccine has been shown to stimulate the immune system and provide optimal immunity to the virus in a single dose. Ferritin is a reliable self-assembled nanoparticle platform for vaccine production that has already been used in experimental studies [4]. Ferritin is also highly appealing as a carrier for delivering drug molecules and antigen proteins due to its distinctive structural and biochemical properties [5]. In this study, we investigated glycation's impact on ferritin nanocage to enhance its stability, binding, and recognition in the cell.

Material And Methods

The Ferritin structure was obtained from the Protein Data Bank (PDB ID: 4V6B)[6]. The 2D structures of glycans Fmoc-L-Thr(α-D-Man(Ac)4)-OH, GDP-MAN, and a-D-Man1-6a-D-Man1-benzyl obtained from Pubchem [7], and ChemBK[8]. The 3D structures of sugars were modeled and designed with the RCSB[9] program and were energy-minimized within Schrödinger [10] using OPLS3 forcefield. Schrödinger program was then used to dock the glycans and ferritin and visualize the results.

Results

The best docking score was represented by Fmoc-L-Thr(α-D-Man(Ac)4)-OH with a score of -5.1, followed by scores of -4.8785 D-Man1-6a-D-Man1-benzyl and -4.7 GDP-MAN, respectively. Also, the interactions of amino acids with glycans make the ferritin cage more stable.

The interactions are as follows:LYS101, LEU152, HIS156, ASP98, LYS95, PRO97, ALA163, LEU156, LEU158, GLY160, GLU162, PRO161, ARG157 and GLY159, pertaining to the sugar Fmoc-L-Thr(α-D-Man(Ac)4)-OH [Fig.1].

The amino acid residues ALA89, LEU106, LYS109, ALA30, GLN29, THR33, ALA102, LYS101, ASP98, TRP93, GLU90 and ALA105 are associated with the sugar D-Man1-6a-D-Man1-benzyl [Fig.2].

The amino acids GLU90, PRO88, ALA89, GLN29, LYS87, LYS86, LYS109, TRP93, ALA102, LEU106 and ALA105 are associated with the sugar GDP-MAN [Fig.3].Also, the presence of different interactions and the stability of cage ferritin show promising results. In this study, sugar Fmoc-L-Thr(α-D-Man(Ac)4)-OH showed the most stability.

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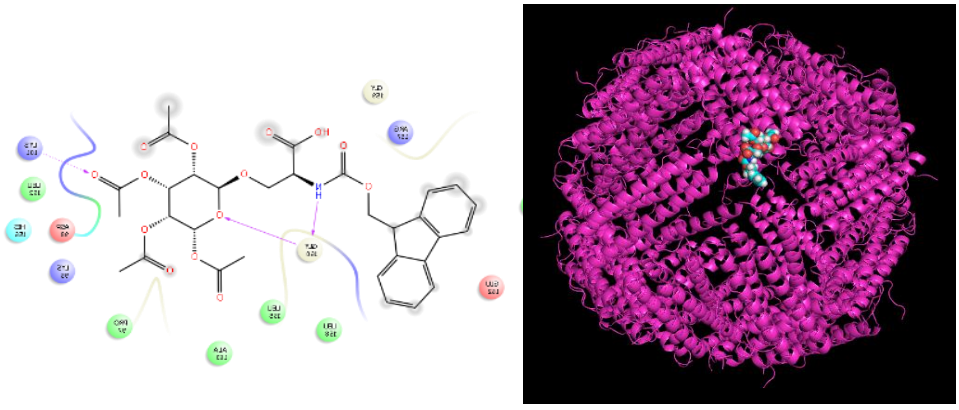
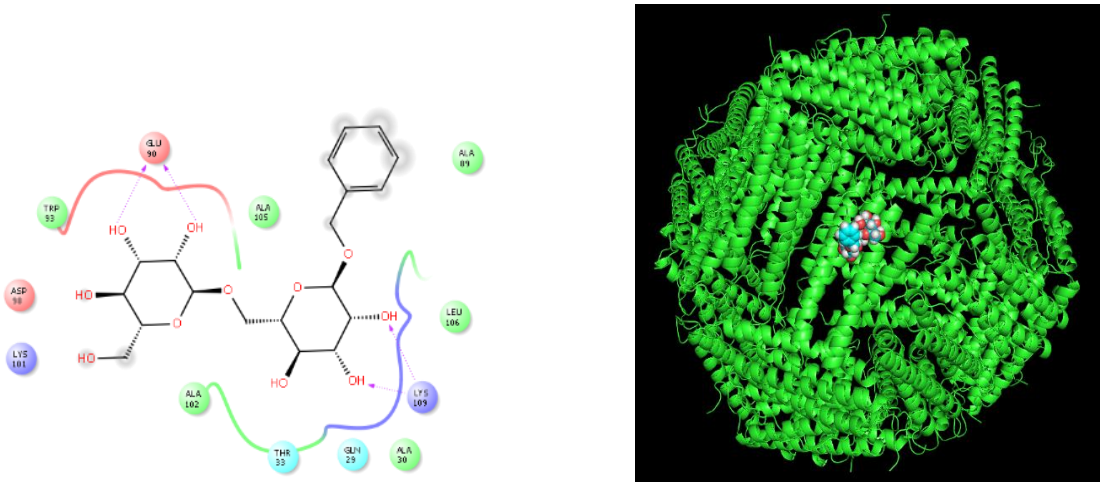


(A) (B)

Fig. 1. A. Interaction between one of Ferritin chains and Fmoc-L-Thr (α-D-Man (Ac)4)-OH
B. Interaction between full cage of Ferritin and Fmoc-L-Thr (α-D-Man (Ac)4)-OH



(A) (B)

Fig. 2. A. Interaction between one of Ferritin chains and D-Man1-6a-D-Man1-benzyl
B. Interaction between full cage of Ferritin and D-Man1-6a-D-Man1-benzyl

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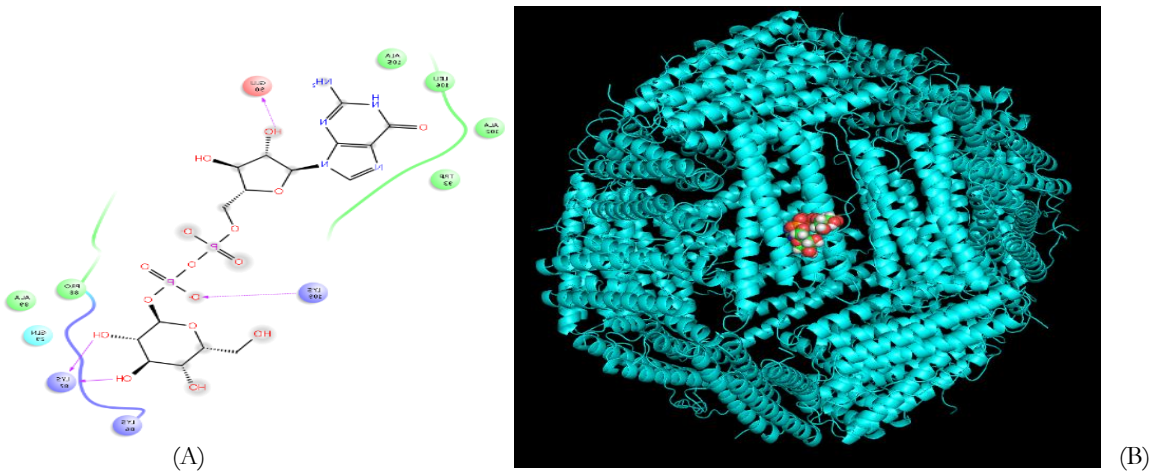

(A) (B)

Fig. 3. A. Interaction between one of Ferritin chains and GDP-MAN
B. Interaction between full cage of Ferritin and GDP-MAN

Conclusion

This study focused on model building and molecular docking of small molecule glycans with ferritin nanocage. The results showed that the defined nanocage is more stable due to the various formed atomistic interactions. These findings could have various applications in the field of drug transport and the new generation of nanocarriers.

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