

Quantum-Chemical Evaluation of the Interaction Between Copper(II) Ions and Silk Fibroin Macromolecules

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Abstract

In this study, the interaction between copper(II) ions and silk fibroin macromolecules was investigated using quantum-chemical and molecular modeling methods. The main goal was to evaluate the structural and energetic stability of Cu(II)–fibroin complexes and to determine the amino acid residues responsible for metal coordination. Molecular docking and semi-empirical PM3 calculations with the CHARMM22 force field were employed to optimize the Cu–fibroin structures. The results demonstrated that Cu(II) ions preferentially bind to the $-\text{COO}^-$, $-\text{OH}$, and $-\text{NH}_2$ groups of Asp, Ser, and His residues, forming energetically favorable complexes with ΔG values ranging from -4.0 to -4.6 kcal/mol. Theoretical IR spectra were found to be consistent with experimental ATR–FTIR data. The study provides insight into the coordination behavior of silk fibroin and establishes a theoretical basis for the design of silk-based metal complexes with potential biomedical and environmental applications.

Keywords: silk fibroin, copper complex, quantum chemistry, molecular docking, PM3 method, CHARMM22, coordination bond, binding energy.

Introduction

In recent years, the study of biologically active natural polymers, particularly silk fibroin, and their interaction with metal ions has become a significant research direction. Such metal–protein complexes are of great importance in biotechnology, biosensor development, and medical materials science. Copper(II) ions are known to play a key role in the structural stabilization and reactivity of biomolecules. Therefore, understanding the mechanism of Cu(II) ion binding with silk fibroin at the molecular level through quantum-chemical calculations is of great scientific interest.

Aim and Objectives

The main aim of this research is to theoretically evaluate the interaction of silk fibroin macromolecules with copper(II) ions and to analyze the structural and energetic stability of the resulting “Cu–fibroin” complex using quantum-chemical methods. The following objectives were pursued: 1. To model the structures of the H-, L-, and P25 chains of silk fibroin using UniProt and Swiss-Model databases. 2. To determine the coordination sites of Cu(II) ions within amino acid residues of fibroin chains through molecular docking analysis. 3. To perform semi-empirical quantum-chemical calculations using the **PM3** method and **CHARMM22** force field implemented in *HyperChem 8.0.8*. 4. To calculate the Gibbs free energy (ΔG) values and assess the energetic stability of the Cu–fibroin complexes.

Methods

Molecular docking was applied to identify potential binding regions of Cu(II) ions with amino acid residues of silk fibroin. The most favorable configurations were further optimized using the **CHARMM22** force field and **PM3** semi-empirical method. The analysis focused on the interaction between Cu(II) ions and the functional groups of amino acids such as Asp, Ser, Gln, Lys, His, and Arg.

The calculations revealed that Cu(II) ions primarily form coordination bonds through $-\text{COO}^-$, $-\text{OH}$, and $-\text{NH}_2$ groups, stabilized by electrostatic and hydrogen bonding interactions. The lowest Gibbs free energy values ($\Delta G = -4.0$ to -4.6 kcal/mol) indicated that the Cu(II)–fibroin complexes are energetically favorable. The most stable complexes were found in the L-chain

(light chain) of fibroin, particularly involving Asp33, Asp48, and Ser44 residues.

Results and Discussion

The quantum-chemical modeling confirmed that the coordination of Cu(II) ions with silk fibroin occurs predominantly in the amorphous regions of the protein, such as the N-domain and A1, A7, A8, A10 segments. In contrast, the crystalline regions demonstrated lower binding affinity. The theoretical IR spectra of the Cu–fibroin complex exhibited good agreement with the experimental ATR–FTIR data, validating the computational results.

These findings provide detailed insights into the nature of metal–protein interactions and the stability of natural biopolymer-based metal complexes. The calculated ΔG values, coordination geometry, and interaction energies support the formation of stable Cu(II)–fibroin complexes, which could be useful for the design of biomaterials, biosensors, and catalytic systems.

Conclusion

The quantum-chemical evaluation of silk fibroin–Cu(II) complexes revealed that the coordination between metal ions and amino acid residues is energetically favorable and structurally stable. The results highlight the importance of L- and P25-chain amino acids (Asp, Ser, His, Arg) in the formation of copper coordination centers.

This theoretical investigation establishes a fundamental basis for the synthesis and practical application of silk-based copper complexes in biochemistry, biomaterials design, and environmental monitoring.