Exploring the future of shaping protein assembly systems for pharmaceutical formulations

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Keywords: bovine serum albumin, polyphenols, fibrils, aggregation

Introduction: Current trends and challenges in pharmacology are focused on protein models designed for sustained drug delivery systems, with applications in the food and healthcare industry. Under unfavorable conditions, proteins form unfolded and partially misfolded intermediates, generating cross β-sheet-rich fibrillar aggregates called amyloid. Protein aggregates have negative impact when involved in amyloidosis diseases, and a positive action when amyloid-like fibrils are used to develop new biomaterials like hydrogels [1]. Bovine serum albumin (BSA), a widely investigated globular protein, is involved in the binding and transport of ligands and drug delivery. The influence of two polyphenols, resveratrol (RESV) and morin (MOR), on the BSA thermal stability with application in obtaining amyloid hydrogel was explored.

Methods: The thermal behavior of BSA in the presence of RESV and MOR was studied by differential scanning microcalorimetry (μDSC). Congo red (CR) and Thioflavin T (ThT) binding assays were used to detect protein fibrils. Dynamic light scattering (DLS) measurements were carried out to monitor the changes in the protein size due to aggregation. For rheological characterization, the storage modulus (G') and loss modulus (G'') were measured. New features of the polyphenol–albumin interaction were revealed by correlating the experimental data with molecular docking.

Results: The analysis of the μDSC thermograms revealed the effect of RESV and MOR on protein thermal stability. DLS results support the stabilizing effect of MOR on the protein structure and the role of RESV as aggregation promoter. The red-shift in the absorbance maximum of CR and the enhanced ThT fluorescence indicated amyloid fibril formation. The rheological properties of protein fibrils–polyphenol assembly systems were investigated.

Conclusions: A deeper insight into the action of polyphenols on the protein aggregation process is essential for understanding the features of aggregates and amyloid–polyphenol hydrogels with applications in healthcare.

Acknowledgements

This work was supported by a grant of the Ministry of Research, Innovation and Digitization, CNCS-UEFISCDI, contract number 93TE/3.01.2025, project code PN-IV-P2-2.1-TE-2023-0189, within PNCDI IV.

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