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Exploring the future of shaping protein assembly systems for pharmaceutical formulations

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INTRODUCTION & AIM

Actual trends and challenges in the pharmacology domain are focused on designing protein models for sustained drug delivery systems, with applications in the food and healthcare industries. Under unfavorable conditions, proteins can generate unfolded and partially misfolded intermediates, and implicitly cross β-sheet-rich fibrillar aggregates called amyloids. Protein aggregates have both a negative impact when are involved in amyloidosis diseases, and a positive action, when are used to develop novel bio-based materials like hydrogels [1]. Bovine serum albumin (BSA), represents a key and widely investigated globular protein, which takes part in the drug delivery process. Starting from the above considerations, the influence of resveratrol (RESV) and morin (MOR) on the BSA thermal stability with application in obtaining amyloid hydrogels was explored.

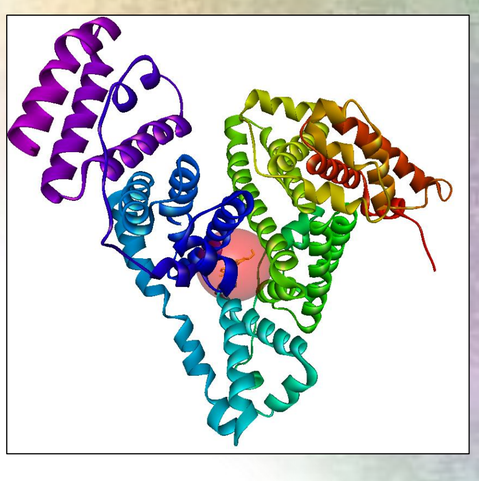
MATERIALS & METHODS

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 & DISCUSSION

Tabel 1. Molecular interactions between RESV/MOR and the amino acid residues of BSA binding site.

polyphenol	Aminoacid residue	Type of interaction	Binding affinity, kcal/mol
RESV	GLU339, ALA341	Hydrogen bond, hydrophobic	-7.2 (site I)



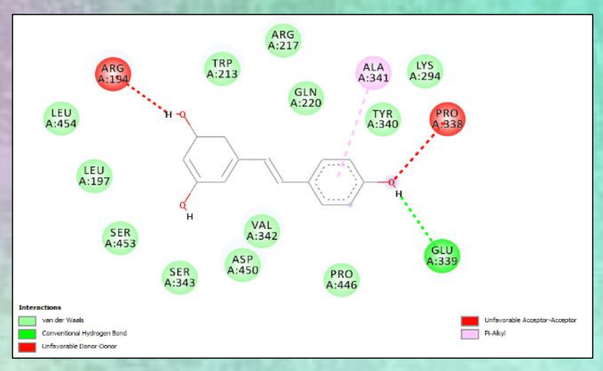


Fig.1. Molecular docking of RESV with BSA. BSA structure is shown by line ribbon; Polyphenol is presented by ball and stick model; hydrogen bonds are displayed by green lines and electrostatic interactions by orange lines; 2D representation of interactions between aminoacid residues and ligand.

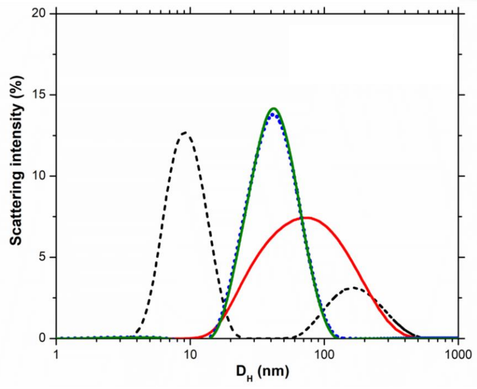


Fig.2. DLS measurements of neat BSA samples (**black**- 2 mg/mL- in 20 mM 7.4 Tris buffer and **red**- 2 mg/mL, incubated for 96 h); BSA-RESV at different molar ratios (1:1- **blue** and 1:4- **green**).

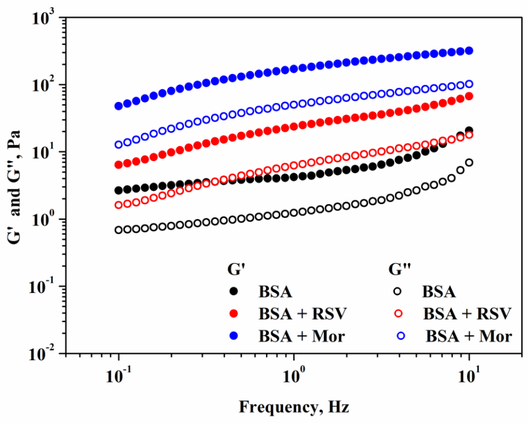
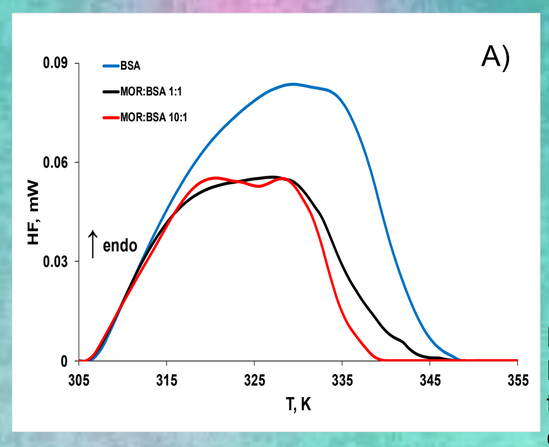


Fig.3. Rheological characterization as a function of frequency: G′ and G″ values measured at 25 °C, for the following systems: BSA, BSA-RESV and BSA-MOR.



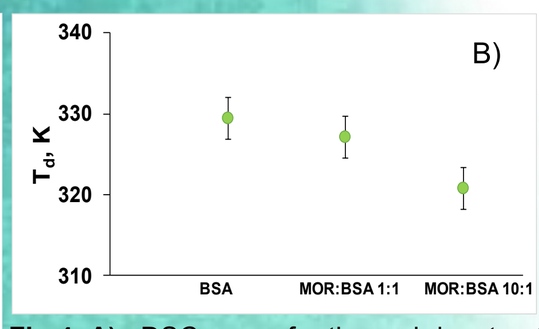
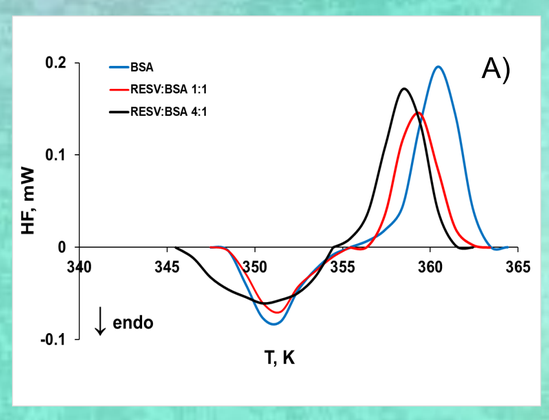


Fig.4. A) μDSC scans for thermal denaturation of BSA (1.05×10^{-4} M), Gly-HCl buffer 0.1 M, pH 3, in the absence and presence of different concentrations of MOR; **B)** thermodynamic parameters of denaturation (temperature) of BSA in the absence and presence of MOR.



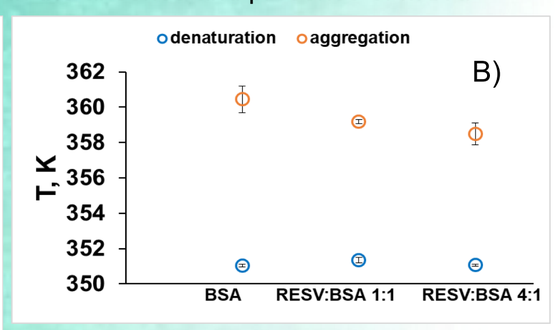


Fig.5. A) μDSC scans for the thermal denaturation of BSA (1.05×10^{-4} M), in Tris buffer 25 mM, pH 7.4, in the absence and presence of different concentrations of RESV**; B)** thermodynamic parameters of denaturation (temperature) of BSA in the absence and presence of RESV.

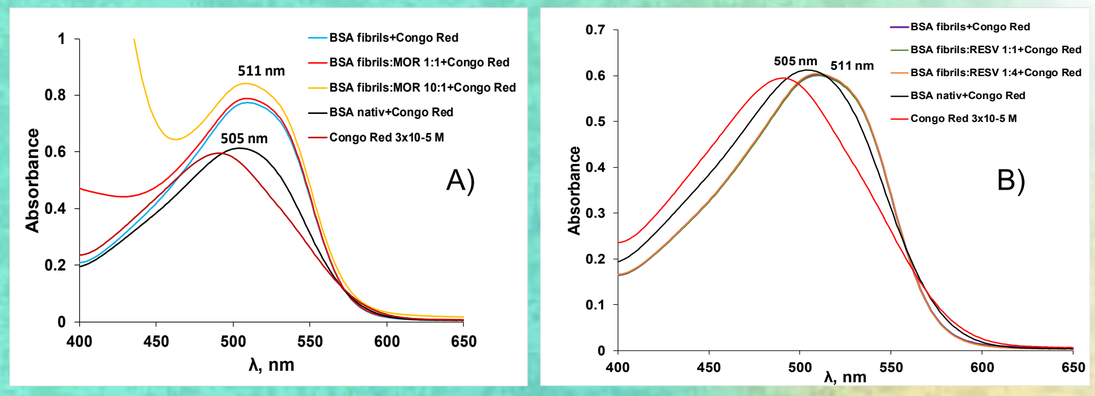


Fig.6. Congo Red binding assay for incubated BSA samples (96 h at 338 K, Tris buffer 25 mM, pH 7.4) in the absence and presence of different concentrations of A) MOR and B) RESV.

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. Molecular docking showed the type of interaction and the amino acids involved in the binding of polyphenols with the native structure of BSA. μDSC results revealed lower values of denaturation temperature in the presence of MOR, pointing to the destabilizing effect of polyphenol on the protein structure, while RESV promotes aggregation. The amyloid specific dye, CR, displayed red-shift in the absorbance spectrum upon binding with incubated BSA solution in the presence of RESV and MOR, indicating typical β-sheet structures in amyloid aggregates.

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REFERENCES

[1]. S. S. Yadav, P. K. Padhy, A. K. Singh, S. Sharma, Tanu, S. Fatima, A. Sinh, R. Tariq, Varsha, S. K. Sharma, S. Priya, Advancements in amyloid-based biological materials for healthcare, environmental and sensing applications, Mater. Adv., 2024, 5, 4078-4090, https://doi.org/10.1039/D3MA00969F.

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