

Abstract Content:

ELECTROSTATICS REGULATE EPIGALLOCATECHIN-GALLATE EFFECTS ON BOVINE SERUM ALBUMIN AGGREGATION.

Daniele Gulli¹, Giuseppe Sancataldo¹, Caterina Alfano², Bruno Giuseppe Pignataro¹, Valeria Vetri¹.

¹Physics and Chemistry, University of Palermo, Palermo, Italy, ²Structural Biology and Biophysics Group, Fondazione Ri.MED, Palermo, Italy.

Protein aggregation processes are complex phenomena often involved in the etiology of several pathologies. It is now assessed that all proteins, in suitable conditions, may undergo supramolecular assembly. Aggregation pathways are known to be controlled by solution conditions which regulate protein-protein and protein-solvent interactions affecting occurring binding mechanisms, morphology and inherent toxicity of the aggregate species. In this context, the presence of small molecules was indicated as a promising method to modulate protein-protein interactions reducing pathogenic aggregation. In the light of the idea that common mechanisms regulate anti-aggregogenic properties of small molecules, we here investigate Epigallocatechin-Gallate (EGCG) effects on thermal aggregation pathway of Bovine Serum Albumin, a well-known model protein. EGCG is a small molecule extracted from green tea, which is known to reduce aggregation of key proteins involved in neurodegenerative diseases. Fundamental mechanisms which regulate EGCG effectiveness as therapeutic molecule are still not clearly elucidated.

The interaction of EGCG with BSA and its effects on thermal aggregation pathway were investigated by means of spectroscopic methods and Isothermal Titration calorimetry as a function of solution conditions. Results show that electrostatic forces modulated by pH play a key role in regulating EGCG interactions with BSA. Data show that close to the isoelectric point of the protein, EGCG is found to promote the supramolecular assembly, whilst away from the isoelectric point, EGCG is found to reduce aggregation mechanisms increasing protein conformational stability. These results reveal the large impact of electrostatics in small molecules effects on the protein aggregation phenomena requiring larger investigation aimed at rationalizing their effects on related pathogenic mechanisms.