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Title: PH-Induced conformational isomerization of bovine serum albumin studied by extrinsic and intrinsic protein fluorescence

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Abstract: Serum albumins are multi-domain all α -helical proteins that are present in the circulatory system and aid in the transport of a variety of metabolites, endogenous ligands, drugs etc. Earlier observations have indicated that serum albumins adopt a range of reversible conformational isomers depending on the pH of the solution. Herein, we report the concurrent changes in the protein conformation and size that are inherent to the pH-induced conformational isomers of bovine serum albumin (BSA). We have investigated the fluorescence properties of both intrinsic (tryptophan) and extrinsic (ANS, pyrene) fluorophores to shed light into the structural features of the pH-dependent conformers. We have been able to identify a number of conformational isomers using multiple fluorescence observables as a function of pH titration. Our results indicate that at pH 3, a partially-folded, 'molten-globule-like' state is populated. Moreover, equilibrium unfolding studies indicated that the 'molten-globule-like' state unfolds in a non-cooperative fashion and is thermodynamically less stable than the native state. The fluorescence-based approach described in the present work has implications in the study of pH-induced conformational plasticity of other physiologically relevant proteins.

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