Abstract:

Introduction: Amyloid fibrils are associated with lots of diseases such as Alzheimer, Parkinson, spongiform encephalopathies and diabetes. Unordered polypeptide chains assemble together and form ordered packed B-parallel structures. Their crucial role in initiation of toxic process in neurodegenerative disorders is well known. Diverse sequences of amino acids can form the amyloid state of proteins.

Methods: In this study, the spectroscopy methods used were NMR spectroscopy, CD spectroscopy and Infrared spectroscopy. Kinetic measurements of amyloid fibril elongation were done using Thioflavin-T (TThT) and quartz crystal microbalance (QCM). Solution small angle x-ray scattering (SAXS) and differential scanning calorimetry (DSC) combined with some annealing of the protein were applied. Computational studies help to understand the application and analysing the obtained results.

Results and discussion: Experimental kinetic measurements and theoretical analysis, showed that electrostatic effects control protein aggregation. Furthermore, the magnitude of binding of a variety of ions to protein molecules was determined. Our results suggest that longer amyloid fibrils are more stable. Our spectroscopy tools confirmed that the formation of amyloid fibrils are a generic property of polypeptide chains, and for different peptides and proteins, the mechanism of formation is similar.

Conclusions: Amyloid fibrils cause neurotoxic effects in neurodegenerative disorder. Detailed biophysical studies of amyloid fibrils can elucidate new aspects and features of this diseases and help our understanding on the prevention of these fibril formation and treatment of related diseases to be more effective.

Discussion:

- Amyloid fibrils are highly ordered protein aggregates.
- They play a crucial role in the initiation and progression of various neurodegenerative disorders, including Alzheimer’s disease, Parkinson’s disease, type 2 diabetes.
- Under certain conditions these disease proteins can undergo structural rearrangements resulting in misfolded proteins that can lead to the formation of aggregates with a fibrillar amyloid-like structure.

- The excellent agreement between the four techniques confirms that the process of fibril elongation along a surface is equivalent to the elongation in bulk solution.
- The plots illustrate that the observed screening effects have no detectable temperature dependence in the investigated temperature range.

- Electrostatic effects control protein aggregation.
- Longer amyloid fibrils are more stable.
- The formation of amyloid fibrils is a generic property of polypeptide chains.
- Magnitude of binding of a variety of ions to protein molecules.

Biophysical aspects of amyloid fibrils

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