Fibril Formation Effect: The Case of the Islet Amyloid Polypeptide (IAPP) and other Segments Involved in Amyloidogenic Processes

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In a conceptual departure from approaches that have been applied for studying solute-solvent interaction of strongly aggregating peptides, we have focused on examining this process in the light of some physico-chemical properties of both components [Malavolta and Nakaie, *Tetrahedron* (2004), 58, 4383; Malavolta et al.(2006), *Prot. Sci.* 15,1476]. For instance, many amyloidogenic diseases share the common characteristic of containing heavily aggregated peptide segments. The present work intended to interpret the dissociation process of insoluble peptide sequences in the light of their secondary structures such as the electron acceptor (AN) and electron donor (DN) properties of the solvent systems, pH of the medium, etc. Amongst the peptides selected for the present study, the islet amyloid polypeptide (IAPP) Jayasinghe and Langen [*J. Biol. Chem*. (2004) 279, 48420], with the sequence KCNTATCATQ^{10}RLANFLVHSS^{20}NNFGAILSST^{30}NVGSNTY, that is the major protein constituent of amyloid deposits in non-insulin-dependent (type II) diabetic humans was examined as to the association tendency of chains when bound to solvated resins or free in solution. The ß-amyloid peptide (1-42) involved in Alzheimer disease, its N-terminal segment (1-21) and other model fragments were also evaluated through solubility measurements paralleled by fluorescence and light scattering measurements of the sample. Specifically for the case of IAPP, a clear sequence-dependent synthesis difficulty was verified. Moreover, a greater fibril formation tendency in the (20-28) region in comparison with other segments of this peptide was observed. Accordingly, It was also confirmed that the greater the difference between AN and DN values of the solvent, the higher is its solubility power of aggregated amyloidal sequences.