Extended Abstract

Can Short Peptides Be Inhibitors of Serum Amyloid a Protein Aggregation? [†]

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One of the approaches in the design of anti-amyloid drugs is to find compounds that are able to hamper self-association of amyloidogenic protein molecules. There is an idea that aggregation inhibitors can be sought in the amyloidogenic sequence itself and prevent protein oligomerization due to shielding the interaction site [1,2]. We have focused our studies on inhibitors of the aggregation of serum amyloid A protein (SAA). SAA is an acute phase protein whose increased production occurs in response to injury, inflammation or infection [3]. Prolonged high concentration of circulating SAA may lead to its aggregation and accumulation of deposits of the protein in the cellular matrix of various organs and finally cause a death of the affected tissues and organs [4]. In our research, we used the 1–5 fragment of SAA as a lead compound to design aggregation inhibitors. We modified the sequence of this fragment by introducing various natural and unnatural aromatic residues. The inhibitory capacity of the saa1-5 analogs was studied using two fragments of the most amyloidogenic N-terminal region of the SAA protein, SAA1-12 and SAA1-27. In order to determine the impact of the inhibitor on the model peptide structure and the type and morphology of aggregates, circular dichroism spectroscopy, quantitative chromatographic analysis of the soluble fraction, and transmission electron microscopy were employed, respectively.

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