Dendrimer effects on peptide and protein fibrillation

Dendrimers are synthetic, symmetrically branched polymers that can be manufactured to a high degree of definition and therefore present themselves as monodisperse entities. Flexible and globular in shape and compartmentalized into a partly inaccessible interior and a highly exposed surface, they offer numerous possibilities for interactions with and responses to biological macromolecules and biostructures including cell membranes and proteins. By way of their multiple functional surface groups, they allow the design of surfaces carrying a multitude of biological motifs and/or charges giving rise to quite significant biological and physico-chemical effects. Here we describe the surprising ability of dendrimers to interact with and perturb polypeptide conformations, particularly efficiently towards amyloid structures; that is, the structures of highly insoluble polypeptide aggregates involved in a range of serious and irreversibly progressive pathological conditions (protein-misfolding diseases). Interesting as this may be, the interaction of dendrimers with such generic peptidic aggregates also offers a new perspective on the molecular mechanisms governing assembly and disassembly of amyloid structures and thereby on determinants of protein and peptide folding. Despite the potent disaggregative nature of various dendrimers, they have variable effects on the stability of different proteins, suggesting that they do not act as generic denaturants, but rather exert their effects via specific interactions with individual parts of each protein.
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