Concentration-dependent Antagonistic Persuasion of SDS and Naphthalene Derivatives on the Fibrillation of Stem Bromelain.

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Abstract:

Sodium dodecyl sulfate, a biological membrane mimetic, can be used to study the conversion of globular proteins into amyloid fibrils in vitro. Using multiple approaches, the effect of SDS was examined on stem bromelain (SB), a widely recognized therapeutic protein. SB is known to exist as a partially folded intermediate at pH 2.0, situation also encountered in the gastrointestinal tract (its site of absorption). In the presence of sub-micellar SDS concentration (500-1000 μM), this intermediate was found to exhibit great propensity to form large-sized β-sheeted aggregates with fibrillar morphology, the hall marks of amyloid structure. We also observed inhibition of fibrillation by two naphthalene-based compounds, ANS and bis-ANS. While bis-ANS significantly inhibited fibril formation at 50 μM, ANS did so at relatively higher concentration (400 μM). Alcohols, but not salts, were found to weaken the inhibitory action of these compounds suggesting the possible involvement of hydrophobic interactions in their binding to protein. Besides, isothermal titration calorimetry and molecular docking studies suggested that inhibition of fibrillation by these naphthalene derivatives is mediated not just through hydrophobic forces, but also by disruption of π-π interactions between the aromatic residues together with the inter-polypeptide chain repulsion among negatively charged ANS/bis-ANS bound SB.

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