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Anti-Fibrillation Propensity of a Flavonoid Baicalein against the Fibrils of Hen Egg White Lysozyme: Potential Therapeutics for Lysozyme Amyloidosis

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Abstract : More than 20 human diseases involve the fibrillation of a specific protein/peptide which forms pathological deposits at various sites. Hereditary lysozyme amyloidosis is a systemic disorder which mostly affects liver, spleen and kidney. This conformational disorder is featured by lysozyme fibril formation. In vivo lysozyme fibrillation was simulated under in vitro conditions using a strong denaturant GdHCl at 3M concentration. Sharp decline in the ANS fluorescence intensity compared to the partially unfolded states, almost 20 fold increase in ThT fluorescence intensity, increase in absorbance at 450 nm suggesting turbidity, negative ellipticity peak in the far-UVCD at 217 nm, red shift of 50 nm compared to the native state in congo red assay and appearance of a network of long rope like fibrils in TEM analysis suggested HEWL fibrillation. Anti-fibrillation potency of baicalein against the preformed fibrils of HEWL was investigated following ThT assay in which there was a dose dependent decrease in ThT fluorescence intensity compared to the fibrillar state of HEWL with the maximum effect observed at 150 µM baicalein concentration, loss of negative ellipticity peak in the far-UVCD region, dip in the Rayleigh scattering intensity and absorbance at 350 nm and 450 nm respectively together with a reduction in the density of fibrillar structure in TEM imaging. Thus, it could be suggested that baicalein could prove to be a positive therapeutics for hereditary human lysozyme amyloidosis.

Keywords : amyloid fibrils, baicalein, congo red, negative ellipticity, therapeutics
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