



Biophysical insights into the interaction of hen egg white lysozyme with therapeutic dye clofazimine: modulation of activity and SDS induced aggregation of model protein.

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Abstract:

The present study details the binding process of clofazimine to hen egg white lysozyme (HEWL) using spectroscopy, dynamic light scattering (DLS), transmission electron microscopy (TEM) and molecular docking techniques. Clofazimine binds to the protein with binding constant (K_b) in the order of 1.57×10^4 at 298K. Binding process is spontaneous and exothermic. Molecular docking results suggested the involvement of hydrogen bonding and hydrophobic interactions in the binding process. Bacterial cell lytic activity in the presence of clofazimine was increased to more than 40% of the value obtained with HEWL only. Interaction of the drug with HEWL induced ordered secondary structure in the protein and molecular compaction. Clofazimine also effectively inhibited the SDS induced amyloid formation in HEWL and caused disaggregation of preformed fibrils, reinforcing the notion that there is involvement of hydrophobic interactions and hydrogen bonding in the binding process of clofazimine with HEWL and clofazimine destabilizes the mature fibrils. Further, transmission electron microscope (TEM) images confirmed that fibrillar species were absent in the samples where amyloid induction was performed in the presence of clofazimine. As clofazimine is a drug less explored for the inhibition of fibril formation of the proteins, this study reports the inhibition of SDS induced amyloid formation of HEWL by clofazimine, which will help in the development of clofazimine related molecules as the treatment for amyloidosis.

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