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Study of Cosolvent-Induced α-Chymotrypsin Fibrillogenesis: Does Protein Surface Hydrophobicity Trigger Early Stages of Aggregation Reaction?

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Abstract The misfolding of specific proteins is often associated with their assembly into fibrillar aggregates, commonly termed amyloid fibrils. Despite the many efforts expended to characterize amyloid formation in vitro, there is no deep knowledge about the environment (in which aggregation occurs) as well as mechanism of this type of protein aggregation. Alpha-chymotrypsin was recently driven toward amyloid aggregation by the addition of intermediate concentrations of trifluoroethanol. In the present study, approaches such as turbidimetric, thermodynamic, intrinsic fluorescence and quenching studies as well as chemical modification have been successfully used to elucidate the underlying role of hydrophobic interactions (involved in early stages of amyloid formation) in α-chymotrypsin-based experimental system.

Keywords Fluorescence · α-Chymotrypsin · Aggregation · TFE · Hydrophobicity

Abbreviations

BSA	Bovine serum albumin
DSC	Differential Scanning Calorimetry
PSH	Protein surface hydrophobicity
TFE	2,2,2-Trifluoroethanol
CR	Congo red
ThT	Thioflavin T
α-CD	α-Cyclodextrin
TNBS	2,4,6-Trinitrobenzenesulfonic acid
ANS	1,8-Anilinonaphtalenesulfonate
BTEE	*N*-Benzoyl-L-tyrosyl-ethyl ester
PMSF	Phenyl methyl sulphonyl fluoride

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1 Introduction

Protein aggregation and misfolding have gained great deal of attention due to their undesirable consequences both in vivo and in vitro [10, 53, 62]. Furthermore, protein misfolding followed by fibrillar aggregation is now well recognized to be a major contributing factor in a group of pathologic states known as amyloid diseases [40, 55]. It is estimated that ~50% of the human diseases, including cancer and degenerative diseases, are caused by folding defects in a variety of organs and tissues [16]. One of the holy grails in understanding the molecular mechanism of protein fibrillogenesis lies in identifying, characterizing and kinetically controlling the formation of the partially folded aggregate species [25, 56]. Therefore, there is now a strong motivation to elucidate the types of involved interactions and characterize the conditions where the formation of aggregation-prone species can be kinetically controlled [42, 54]. Within the past 10 years, induction/inhibition of partially folded aggregation-prone species as well as the kinetic mechanism of amyloid-type aggregation by several (disease and non-disease related) proteins has been frequently investigated [22, 31, 36, 42, 45, 48]. Also, the