Abstract

Candidate: Md. Anas (Index No.: 157/18/Chem./26]

Senior Research Fellow (SRF), School of Chemical Sciences, IACS

Registration No.: SCHEM 1415 718 (Jadavpur University)

Title of the thesis: "FUNCTIONALIZED POLYPEPTIDES AND THEIR COPOLYMERS: SYNTHESIS, PROPERTIES AND APPLICATIONS".

Synthetically prepared functionalized polypeptides are one of the most challenging areas for synthetic chemist to impart specific functional groups or modifications to artificially designed or modified polypeptides for both fundamental understanding and technology development. Ring opening polymerization (ROP) of α-amino acid N-carboxyanhydride (NCA), is mostly used by the researchers for synthesis of long chain polypeptides. Subsequent post-functionalization enables the production of polypeptides with tailored properties such as improved stability, enhanced solubility, stimuli-responsiveness, good self-assembly property, or specific interactions with other molecules. This functionalization can be achieved through various chemical reactions, such as coupling reactions, click chemistry, or post-translational modifications. The specific functional groups or modifications added to the polypeptides can impart unique properties that are useful for specific applications in various fields, including biotechnology, biomedical research, materials science, and drug delivery.

Overall, synthetically prepared functionalized polypeptides offer a versatile platform for designing and engineering customized biomolecules with desired functionalities, opening up opportunities for numerous scientific and technological advancements.

The aim of this thesis is to synthesis, exploration and study the solution properties of differently modified polypeptides exhibiting diverse functionalities and self-assembled structures. The focus is on investigating the potential of these functionalized polypeptides to enhance therapeutic effectiveness, biocompatibility, and materialistic applications. This thesis is divided into four chapters based on the results obtained by the experiments conducted during the period of research.

Chapter 1: It provides complete literature review on developments of functionalized polypeptide through the ROP of NCA and their application as biomaterials. Different available methods of ROP using different initiators for the synthesis of functional polypeptide with different architectures have been discussed in detailed. A brief emphasis also has been made on the stimuli-responsiveness of these functionalized polypeptides which include different stimuli such as thermo, pH, photo, redox and others. This chapter also concentrates on the self-assembly behaviours of the synthetically prepared polypeptides to form different micro-/nano-structured aggregates in different solvents in a systematic way. Finally, in the last section of this chapter, the potential applicability of these functionalized responsive polypeptides as a biomaterial have been classified into three main category such as, drug/gene delivery application, tissue engineering and as antimicrobial agents.

Tarun Kumar Mandal
01.08.2023

Chapter 2: This chapter deals with the synthesis and solution properties of a novel amphiphilic graft copolypeptides (PCys-*g*-P^{i}POx) with hydrophobic polycysteine backbone and hydrophilic pendant poly(2-isopropyl-2-oxazoline) side chain. The amphiphilic copolypeptides are synthesized using polymerization techniques such as ROP, cationic ring opening polymerization (CROP), click grafting etc. Propargyl functionalized polycysteine is synthesized via ROP of corresponding NCA and azide end functionalized poly(2-isopropyl-2-oxazoline) is synthesized via CROP and these two polymers are then conjugated via click reaction (CuAAC) to obtain the final graft copolypeptides. PCys-*g*-P^{i}Pox(s) show tunable 'lower critical solution temperature' (LCST) type thermoresponsive behaviour in water. Self-assembly of these amphiphilic copolypeptides in aqueous and nonaqueous media, resulted in vesicular morphologies with different size distribution. These vesicles can encapsulate different types of dye/drugs with high efficiency. Those encapsulated dye/drug further can be released from the vesicular system simply by heating or treating with concentrated HCl.

Chapter 3: This chapter describes the synthesis of polycysteine based responsive polypeptide synthesized via ROP of corresponding NCA monomer followed by cationization using triphenyl phosphine to produce cationic homopolypeptides ([PCys-PPh_3]$^{+}$[Br^{-}]). The ionic polypeptides also show tunable 'upper critical solution temperature' (UCST) type thermoresponsiveness in water in the presence of externally added chaotropic salts. Ionic nature of the [PCys-PPh_3]$^{+}$[Br^{-}] makes it potent candidate for DNA intercalating agent as confirmed by fluorescence spectroscopy and gel electrophoresis study.

Chapter 4: This chapter illustrates the synthesis a long alkyl chain functionalized poly(L-glutamate) based functionalized polypeptides by combining the ROP of NCA and successive click reaction. Propargyl functionalized poly(L-glutamate)s are clicked with long chain alkyl azides by Cu-AAC reaction. The resulting polypeptides (PGlu-C_n, [n = 10, 12, 16, 20]) shows UCST-type thermoresponsiveness in $CHCl_3$, and THF. The cloud point can be tuned by varying the pendant alkyl chain length and solvent polarity. In comparison to their monomeric analogues (Glu-C_n [n = 10, 12, 16, 20]), some of the PGlu-C_n(s) show poor crystallinity due to the presence of long alkyl groups in their side chain. PGlu-C_n(s) further form vesicular aggregates in both $CHCl_3$, and THF due to their self-assembly and those vesicles can encapsulate dye molecules.

Tarun Kumar Mandal
.....
01.08.2023
(Signature of the Supervisor)

Md. Anas
.....
01/08/2023
(Signature of the Candidate)

Dr. Tarun K. Mandal
Senior Professor
School of Chemical Sciences
Indian Association for the Cultivation of Science
Jadavpur, Kolkata - 700 032