学 位 論 文 内 容 の 要 旨

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学 位 論 文 題 名

Topology-Dependent Complexation of Cyclic Poly(Ethylene Glycol) with Nanoparticles and Proteins
（環状ポリエチレングリコールのトポロジーに基づいたナノ粒子およびタンパク質との複合化）

Influence of polymer topology has gained attention and application in various fields in recent years. Topology defined as the shape and connectedness of the polymer backbone is taking into considerations as polymer properties. Polymer topologies include the branched, comb, monocyclic, multicyclic, graft, dendritic, helical star, among others. In the new era, attention has been drawn to polymer properties such as melting, diffusion, rheology, crystallization, and phase separation because of distinct topological differences. Of the various polymer topologies, cyclic polymers without polymer termini have shown potential in various applications resulting from their physical and chemical properties in bulk and solution states, such as increased glass transition temperature, higher refractive index, less entanglement, slow hydrolytic degradation, smaller hydrodynamic volume and radius of gyration, lower intrinsic viscosity, high critical solution temperature, accelerated rate of crystallization, high refractive indices and self-assembling behaviors etc., which are different from their linear counterparts with the same molecular weight. Cyclic polymers also have promising potentials in biomedical applications because of their biological properties such as higher gene transfection, longer circulation time in vivo, controlled release of drugs, etc. Dumbbell-shaped amphiphilic copolymers with cyclic moieties as the two bells enhanced performance for controlled drug release. Also, topology-controlled particle disassembly for the controlled release of an anti-cancer drug in vitro has been reported. Of recent time cyclized PEG (c-PEG) without any chemical inhomogeneity was found to endow gold nanoparticles (AuNPs) with high dispersion stability by physisorption. On the other hand, silver nanoparticles (AgNPs) are unstable unlike AuNPs and thiol chemisorption sulfidates the surface of AgNPs to form an AgS2 shell which further degrades leading to dissolution, aggregation etc. A steady PEGylation of AgNPs have been sort after for various applications. Moreover, the various applications of proteins in therapeutics and drug delivery are high desirable. In recent time, topology-dependent interaction of polymers with proteins has given rise to various unique applications. Suppression of thermal aggregation of lysozymes by PEG of triangular geometry has been reported. A new dimension to cyclic PEG applications in AgNPs stabilization and interactions with bovine serum albumin when complexed with AuNPs was examined and reported in this dissertation.

Chapter 1 gives an introduction encompassing the polymer topology, current state of research on polymer topology and applications of cyclic polymers, metal nanoparticles, issues in their applications, polymer–protein interactions, advantages and research on this interaction, objectives, and outline of this dissertation.

Chapter 2 describes the first steady PEGylation method for AgNPs conferred by physisorption of c-PEG, which cannot be attained with linear PEG even HS–PEG–OMe due to the formation of silver sulfide. Various conditions including physiological condition, white light, high temperature, and as well as biological applications were investigated. Physisorption of c-PEG provided outstanding dispersion stability to AgNPs, against the above-mentioned conditions whereas HO–PEG–OH or MeO–PEG–OMe did not provide such dispersion stability. This method further exhibited persistent antimicrobial activity and cytotoxicity, which are one of the most important properties of AgNPs. Coupled with the excellent biocompatibility

of PEG and the simple physisorption method, these results highlighted potential applications of c-PEG in biological and medical fields.

Chapter 3 demonstrates unique sensitivity of c-PEG to BSA, which in the presence of AuNPs, a colorimetric change was evident. The interaction between c-PEG and BSA was investigated by various instruments and techniques and further effect of complexation to AuNPs. The interaction between BSA and c-PEG arose from the cyclic topology as it was not attainable by the linear counterparts. Aggregation of AuNPs was evident in c-PEG/BSA/AuNPs system. The concentration effect of each of BSA, AuNPs, and c-PEG was also investigated as well as the incubation time for the interacting properties. The results showed incubation time as a major factor for interaction and aggregation of AuNPs. The sensitivity of c-PEG towards BSA was also found to be a factor of the c-PEG concentration. An equilibrium tends to be attained with a high c-PEG concentration. This research gives an insight into a new topology effect of c-PEG.

Chapter 4 summarizes the results. This dissertation has shown a new method of AgNPs stabilization by physisorption of c-PEG while maintaining its biological properties. This was not attainable by HS–PEG–OMe or any other linear PEGs. Usage of c-PEG in biomedical fields is underway in tandem with concerns of biocompatibility. On the other hand, a new effect of c-PEG on proteins is reported in this dissertation. Sensitivity of c-PEG towards BSA and further aggregation of AuNPs when complexed has given insight to the possibility of biosensing ability of c-PEG in biomedical fields. When corona formation is important, c-PEG could be useful in further studies.