Design of Biodegradable Polyrotaxanes and Their Biomedical Properties

Tooru Ooya

School of Materials Science,
Japan Advanced Institute of Science and Technology

(Supervised by Associate Professor Nobuhiko Yui, Ph.D.)

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ABSTRACT

The design of biodegradable polyrotaxanes as advanced biomaterials are described in this dissertation. The synthesis of biodegradable polyrotaxanes includes three steps: the preparation of an inclusion complex consisting of α-cyclodextrins (α-CDs) and amino-terminated poly(ethylene glycol) (PEG), the introduction of L-phenylalanine (L-Phe) at each complex terminal via peptide linkages, and the hydroxypropylation of α-CDs in the polyrotaxanes. *In vitro* degradation of hydroxypropylated (HP-) polyrotaxanes revealed that HP-α-CDs threaded onto a PEG chain were completely released only when terminal peptide linkages were cleaved. Theophylline as a model drug was introduced to HP-α-CDs in the polyrotaxanes, and theophylline-α-CD release was observed in relation to the cleavage of terminal peptide linkages. Conjugation of the polyrotaxanes with insulin was found to increase physical stability of insulin in terms of preventing the aggregation and conformational change. Cellular response to the polyrotaxanes was investigated in terms of changes in cytoplasmic calcium levels in platelets. The polyrotaxanes regulated thrombin-induced calcium increase in platelets although constituent molecules of the polyrotaxanes showed fewer effect on the intracellular metabolism. Further, it was found that membrane fluidity of red blood cell ghosts were significantly enhanced by the polyrotaxanes. From light scattering measurements, it is suggested that supramolecular level interaction between the polyrotaxanes and cell membranes can regulate the intracellular metabolism. In addition, enhanced permeation of indomethacin through hairless rat skin was observed by the treatment of the polyrotaxanes, suggesting a feasibility of the polyrotaxanes as a biodegradable skin penetration enhancer. Thus, it is concluded that the biodegradable polyrotaxanes are feasible as novel biomaterials for drug delivery and/or blood-contacting devices.

List of Publication

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