Synthesis and Characterisations of Functional Biomimetic Polymers for Intracellular Delivery

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Abstract

Intracellular drug delivery of therapeutics, particularly macrodrugs such as proteins and nucleic acids, is of great importance for modern therapy. A great variety of synthetic vectors, including lipids, recombinant virus and synthetic polymers, have been investigated to facilitate this process. Among them, hyper-branched polymers are of great interest because of many unique properties, such as complex macromolecular architecture and multivalency. However, current hyper-branched polymers either suffer from low loading capacity, poor biocompatibility or undesirable stability in biological environment. To reduce cytotoxicity and increase cell permeability, specific polyamides could be employed by mimicking the structure and pH-dependent membrane-disruptive behaviour of endosomolytic viral peptides.

In this study, hyperbranched pH-responsive polyamides based on L-lysine isophthalamide have been developed. By adjusting feeding ratios, the branching degrees of these polymers could be manipulated. pH-responsiveness of these polymers was investigated by different techniques. Results demonstrate that pH-induced conformational changes are branching degree-dependent. Furthermore, it is found that highly branched polymers were efficient in membrane disruption at late endosomal pH (5.0), but non membrane-lytic at physiological pH (7.4). Cytotoxicity study shows these polymers are biocompatible with negligible toxicity effects on Hela cells. This indicates the polymers are promising materials for intracellular drug delivery to facilitate drugs to escape from endosomes and release into cytoplasm.