Synthesis of amphiphilic hyaluronan containing-phenyl fatty acids for the preparation of polymeric micelles for applications in drug delivery

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Introduction

Polymeric micelles (PM) are particularly interesting for drug delivery applications because of their characteristic features e.g., size, surface, solubility under physiological conditions and enhanced permeability, which help them to penetrate and be taken up by cells. Hyaluronan (HA) is a natural polysaccharide, ubiquitous in the human body, therefore, it is suitable for medical applications. Moreover, HA allows specific targeting.

Methods

In this work, novel amphiphilic hyaluronan (HA) based polymeric micelles were prepared in base of HA grafted with omega-phenylalkanoic acids (ω-PAA), including 4-phenylbutyric, 6-phenylhexanoic, 8-phenyloctanoic or 11-tolylundecanoic acids, which are aromatic fatty acids normally occurring in fats of natural origin. The prepared derivatives were encapsulated of aromatic hydrophobic drugs in order to evaluate its loading capacity (ie. trans-resveratrol, retinyl palmitate and quercetine).

Results

The synthesis of HA-grafted with ω-PAA (HA-g-PA) was mediated by mixed anhydrides1 that allows HA modification without degradation or formation of toxic subproducts. The reactivity of ω-PAA towards esterification has decreased with the increasing length of the aliphatic spacer between the aromatic ring and carboxylic moiety. The novel HA derivatives were found to be not cytotoxic and self-assemble from very low CMC. Furthermore, Polymeric micelles (PM) were characterized by small size (cca 30 nm, PDI; 0.2).

Discussion

Comparing to our previously reported work2, the drug loading capacity of HA-g-PA. The drug loading content increased substantially likely because of pi-pi interactions between the micelle core and loaded aromatic hydrophobic drug. The formation of well-defined hydrophobic nanodomains can be reached by defining the degree of modification of HA. This work describes a facile strategy to achieve well defined HA derivatives possessing an effective drug loading content, which is a critical factor for designing polymeric micelles3.

References

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