SYNTHESIS AND CHARACTERIZATION OF AMPHIPHILIC CHITOSAN DERIVATIVES AS NANO/MICROSTRUCTURES

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Introduction

Among the most popular drug delivery systems (DDSs), dendrimers and polymeric micelles have gained attention due to certain structural advantages and features that they offer. Dendrimers are characterized by a precise molecular weight, high density of surface functionalities and well-defined structure that allow a high payload and provide toxicity control and release properties [1]. While, polymeric micelles based on amphiphilic polymers with self-assembly properties have the unique core-shell structure, a micro or nanoscale size, and thermodynamic stability [2].
One of the most abundant biomaterials - chitosan can also be an amphiphilic, by a hydrophobic modification, and create the proper derivatives for the above purpose. Moreover, most chitosan derivatives due to unique properties as low toxicity, excellent biocompatibility and biodegradation are suitable as a drug delivery vehicle [3].
The structural combination of those two systems i.e. polymeric micelle and dendrimer, named as dendrimeric micelle (DM), might allow creating a new multifunctional and multidrug delivery system.

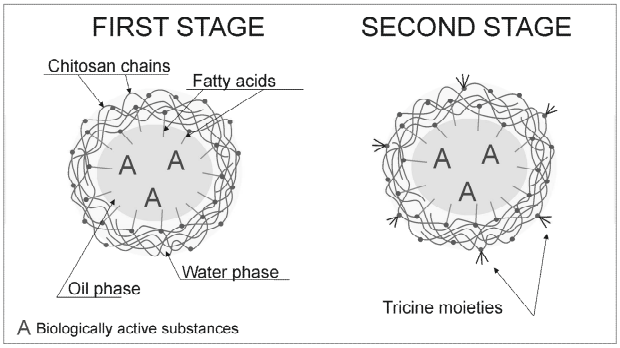

FIG. 1. Scheme of the dendrimeric micelle architecture.

In the study, amphiphilic chitosan derivatives were synthesized, characterized and tested for micelle formation abilities for the first step of a designed DM construction.

Materials and Methods

Series of amphiphilic chitosan derivatives were synthesized using carbodiimide EDC or EDC/NHS catalysis. The modifications were proceeded by introducing long fatty acid chains as hydrophobic moieties and/or tricine (*N*-(tri(hydroxymethyl)methyl)-glycine) as hydrophilic moieties.
Application of different reaction conditions allowed to obtain various *O*- or *N*- and *O*-,*N*- substituted derivatives.
The structures of the obtained materials were confirmed by ^{1}H NMR and ATR FT-IR spectroscopy.
Micelles formed from the derivatives were obtained by the O/W emulsification technique using dichloromethane (DCM) and 1wt% acetic acid (and ethylene glycol (EG)) as oil and water phases, respectively. The influence of the derivative concentration, DCM, and EG ratio on the micelle properties was investigated. The characterization of the micelles was performed using the dynamic light scattering technique by Zetasizer Nano-ZS (Malvern) apparatus determining the hydrodynamic diameter of the micelles.

Results and Discussion

The chemical structures of synthesized polymers were determined by ^{1}H NMR and ATR FT-IR spectroscopy. The successful incorporation of the fatty acid groups and/or tricine moieties onto the chitosan backbone was confirmed by ^{1}H NMR assay. The FT-IR spectra of the derivatives showed characteristic absorption bands for *N*- or *O*- and both *N*-, *O*- substitution depending on the reaction condition used.
The amphiphilic character of derivatives facilitated the micelles formation. By changing the solvents ratio as well as the derivative concentration, different micelles diameters were obtained, ranging from micro (ca. 55 μm) to nano (ca. 42 nm).

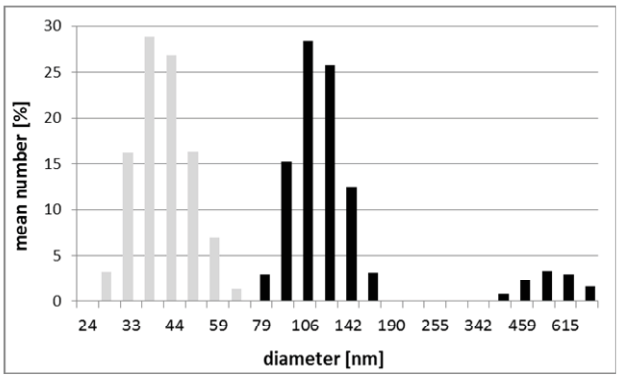

FIG. 2. Dynamic Light Scattering results of micelles prepared from 1g/L (black) and 0.8g/L (grey) chitosan derivative concentration in 1wt% of AA and 3v% of DCM.

Conclusions

As a part of the ongoing multifunctional polymeric drug delivery systems project (NanoEnCap), we reported herein the synthesis of amphiphically modified chitosan molecules with fatty acid chains as hydrophobic moieties and/or tricine group as hydrophilic ones. Providing the different O/W emulsification conditions, the self-assembly process was controllable and led to micelles with tunable sizes, which are suitable for further development of the dendrimeric micelle construction.

Acknowledgments

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References

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