NOVEL CHITOSAN POLYMERIC MICELLES AS A DELIVERY VEHICLE OF HYDROPHOBIC ANTICANCER DRUGS

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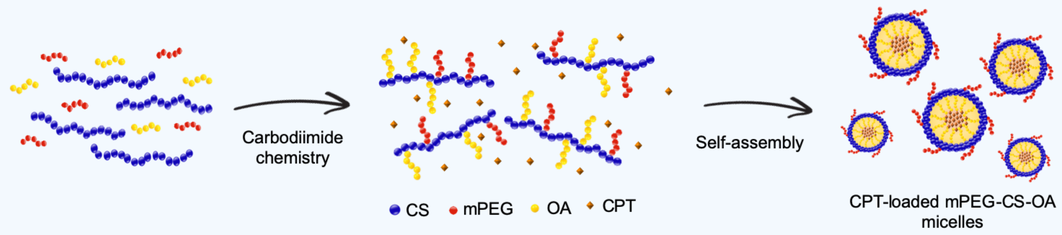
PURPOSE

Chitosan (CS) is a natural polymer well known for its biocompatibility, biodegradability and mucoadhesive properties. Once CS has reactive groups in its backbone, it is easily used to be modified into amphiphilic polymers to produce polymeric micelles by self-assembly [1-3].

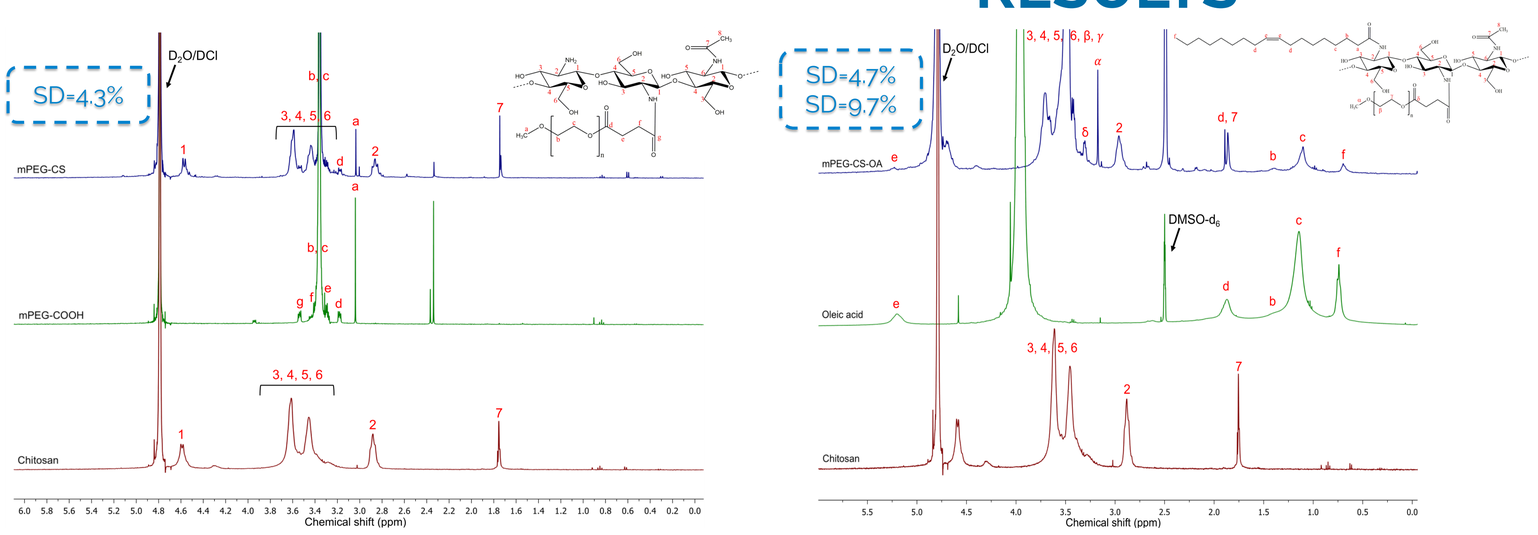
Polymeric micelles (PM) have the ability to encapsulate hydrophobic drugs efficiently, as the case of many anticancer drugs as camptothecin (CPT), improving its water solubility and reducing its drastic side effects [4]. Additionally, PM are stable drug delivery systems and can protect the drug against degradation upon its administration.

AIM

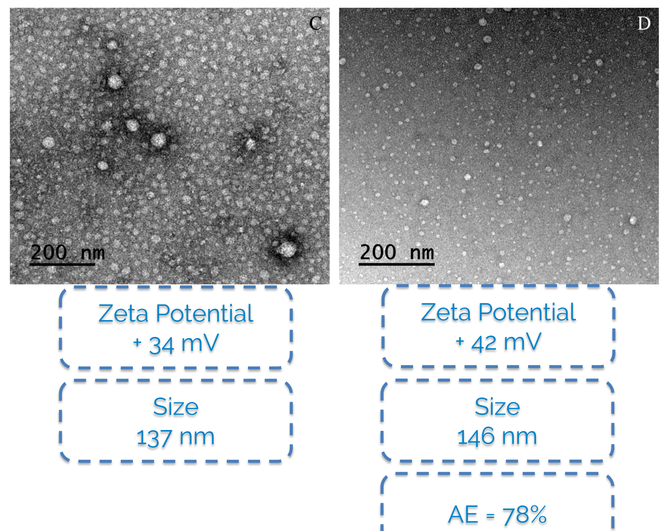
CS was chemically modified into an amphiphilic polymer with **mPEG** and **oleic acid** (OA) in order to encapsulate hydrophobic anticancer drugs, as CPT, by self-assembly.



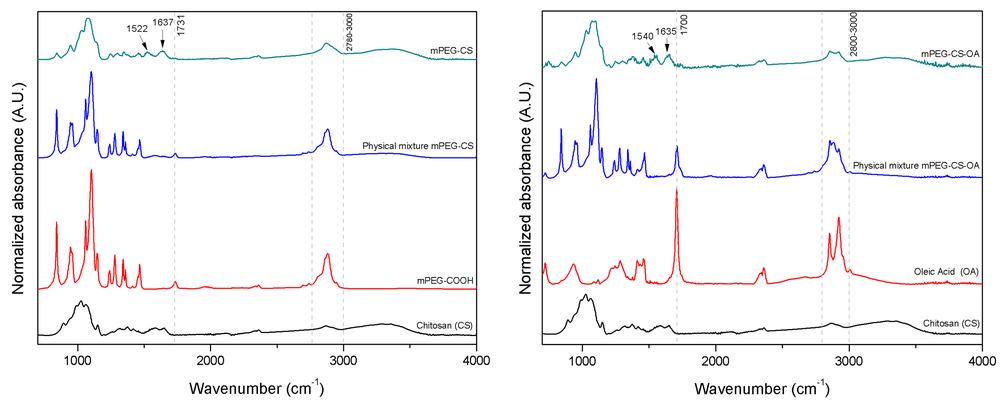
RESULTS



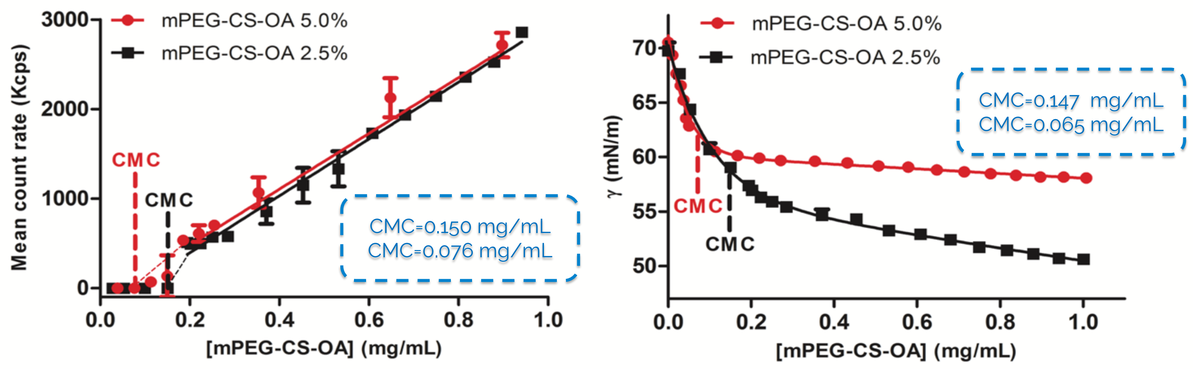
^{1}H NMR confirmed the success of the mPEG and OA grafting into CS backbone



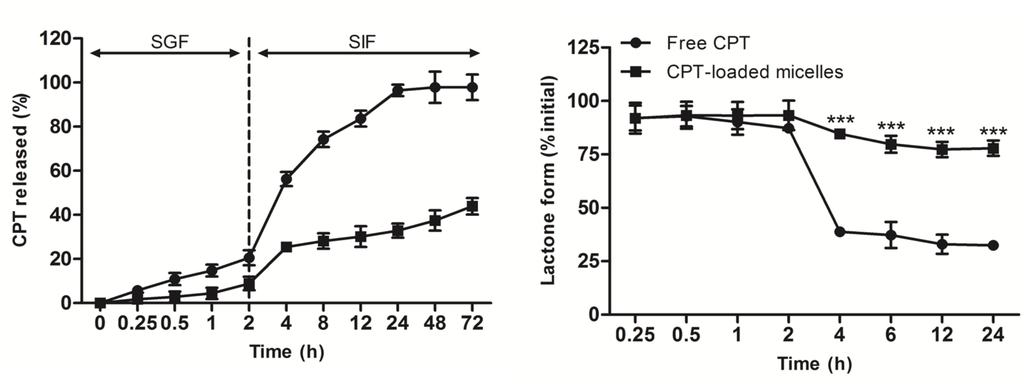
TEM microscopy showed round and smooth surface for both empty (left) and CPT-loaded (right) micelle.



FTIR showed the presence of amine groups as result of the carbodiimide reaction

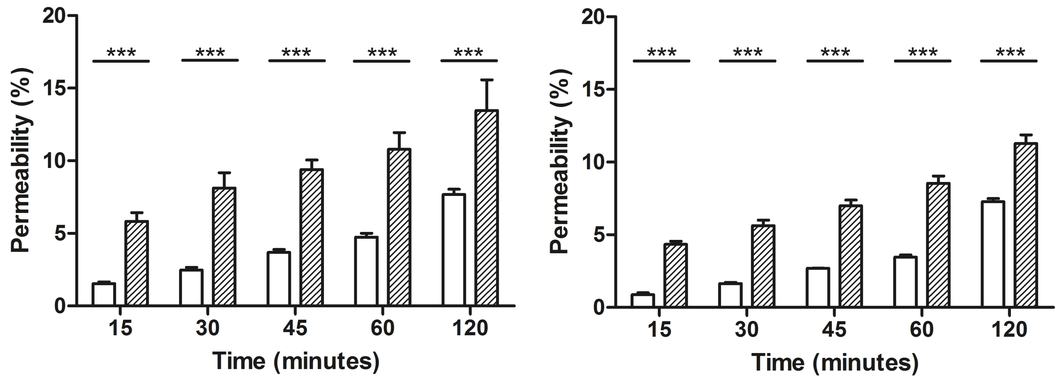


CMC determined by DLS and surface tension.



A sustained and controlled release of CPT from mPEG-CS-OA micelles in simulated GIF was observed.
Micelles protected CPT from hydrolysis up to 75% in simulated GIF.

Caco-2 **3D**



CPT permeability across Caco-2 model and 3D model composed by a collagen layer with human intestinal fibroblasts embedded providing the 3D support for the epithelium composed by Caco-2 and HT29-MTX cells

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ACKNOWLEDGMENTS

This work was financed by Portuguese funds through FCT – Fundação para a Ciência e a Tecnologia/Ministério da Ciência, Tecnologia e Ensino Superior in the framework of the project "Institute for Research and Innovation in Health Sciences" UID/BIM/04293/2019. Andreia Almeida would like to thank FCT for financial support (SFRH/BD/118721/2016).

CONCLUSIONS

- CS was successfully modified into an amphiphilic polymer;
- PM presented an average size around 140 nm and a positive surface;
- PM were able to protect CPT from hydrolysis up to 75% of its initial lactone form;
- CPT-loaded micelles improved significantly its *in vitro* intestinal permeability, as compared with free CPT.