

LOCAL DELIVERY OF DOXORUBICIN NANOCRYSTALS FROM ELECTROSPUN NANOFIBERS

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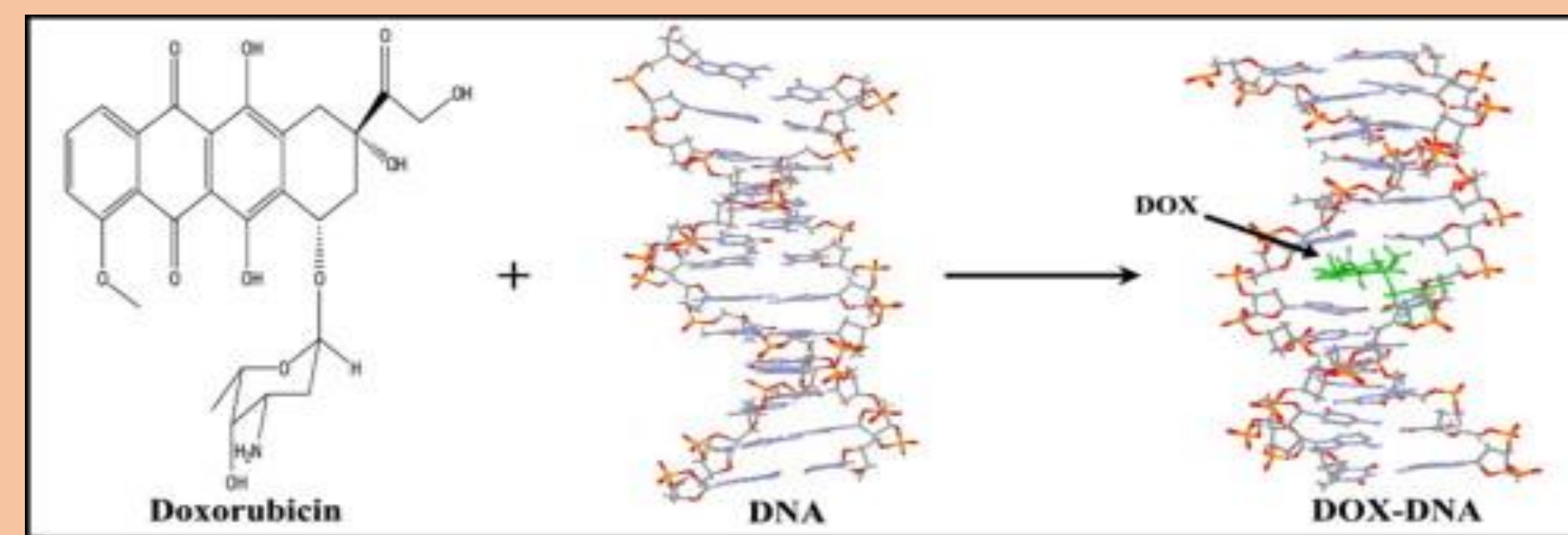
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Introduction

Doxorubicin (DOX)

Class I:
High permeability
High solubility



free DOX:
low therapeutic index

repeated administration of high doses are required

Objective

The objective of this study is to develop a novel system for local application of DOX either in surgical loci or in a topical application device enabling a controlled release of the drug. The developed system involves the encapsulation of DOX into electrospun polymeric nanofibers. Chosen polymers were polyoxyethylene (PEO) and polycaprolactone (PCL).

Experimental

Polymeric PEO solution

0.1 g/mL PEO in water
+
10 mg DOX

Polymeric PCL solution

0.12 g/mL PCL in
chloroform : metanol (5:1)
+
10 mg DOX

Electrospinning parameters

Flow rate: 0,03 mL/h
Voltage: 20 kV
Needle: 0.3 mm
Room temperature

Electrospinning parameters

Flow rate: 0.6 mL/h
Voltage: 15 kV
Needle: 0.6 mm
Temperature: 20 °C

Characterization

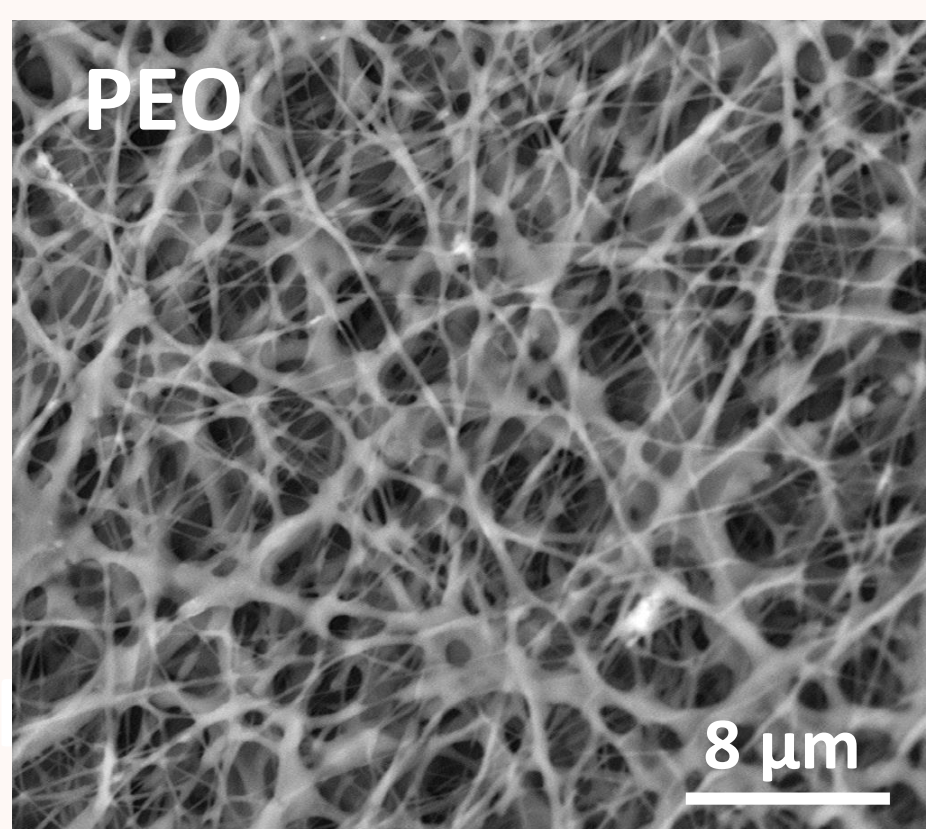
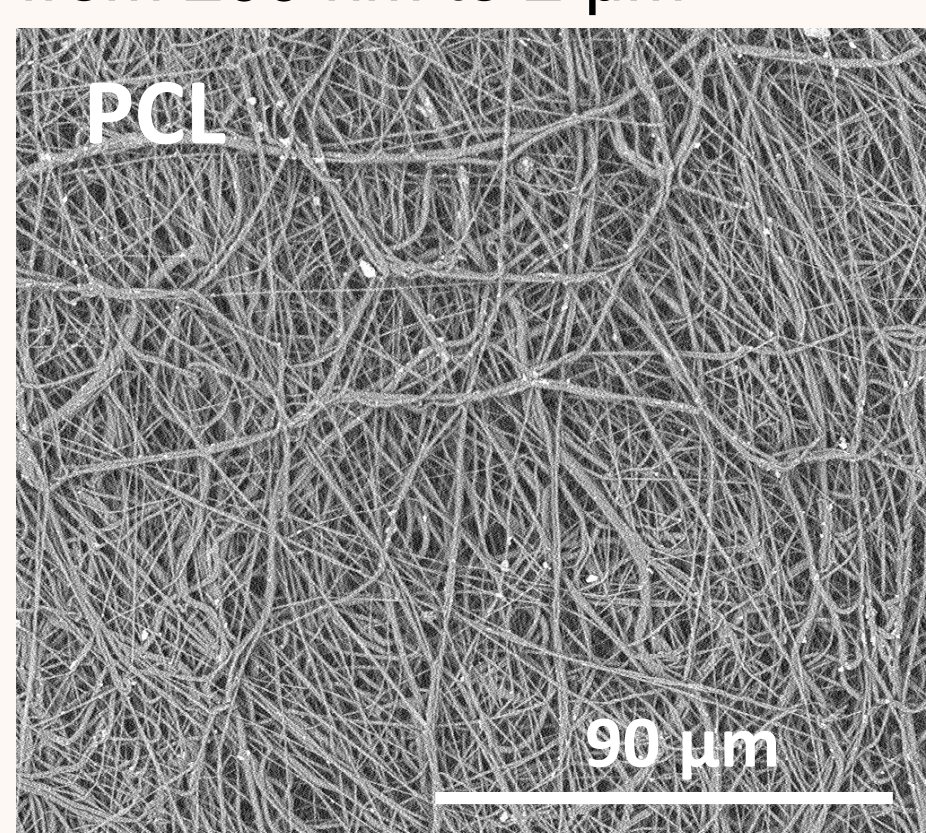
SEM-EDS
XRD
ATR-FTIR
Controlled release assays in cancer tissues 'conditions (pH 5.5 at 37°C)

Results

SEM:

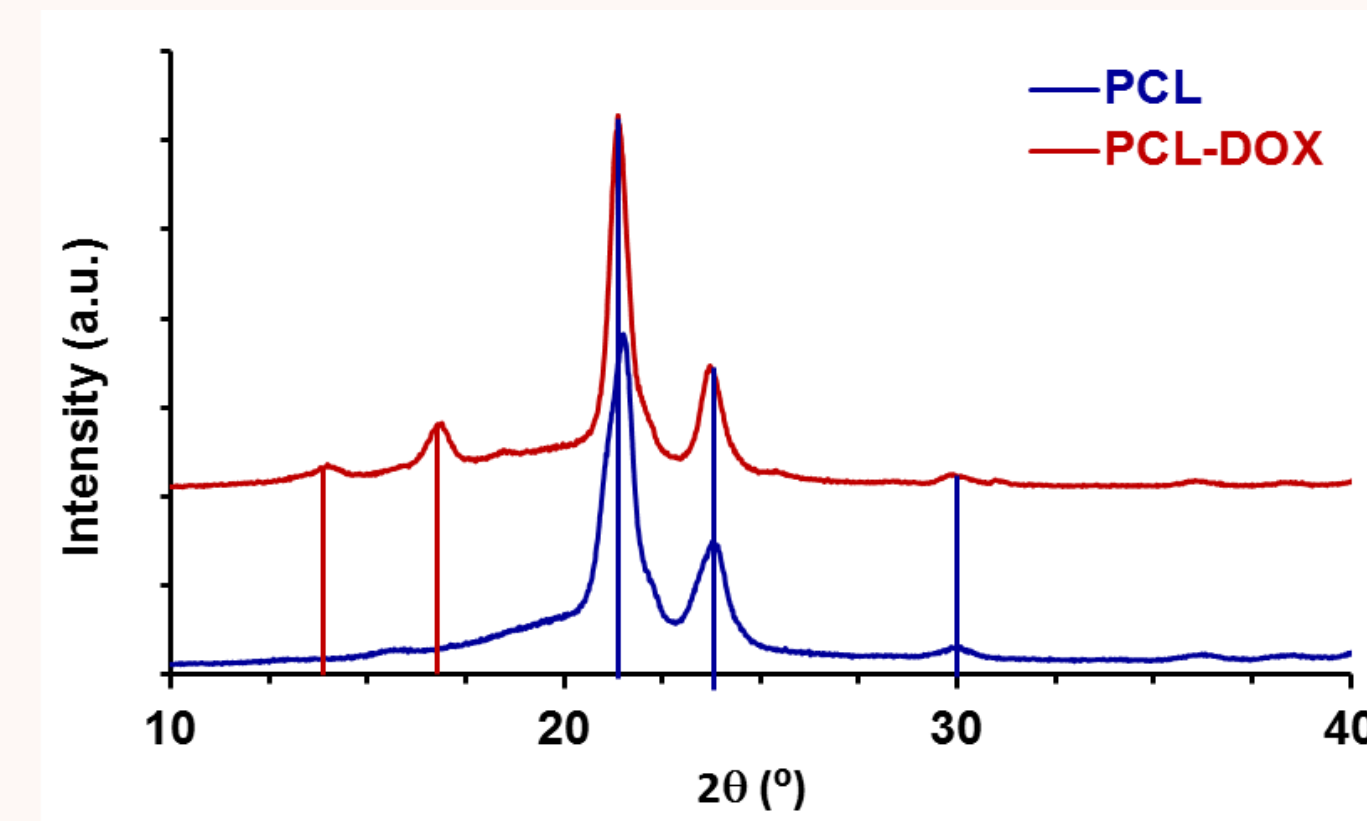
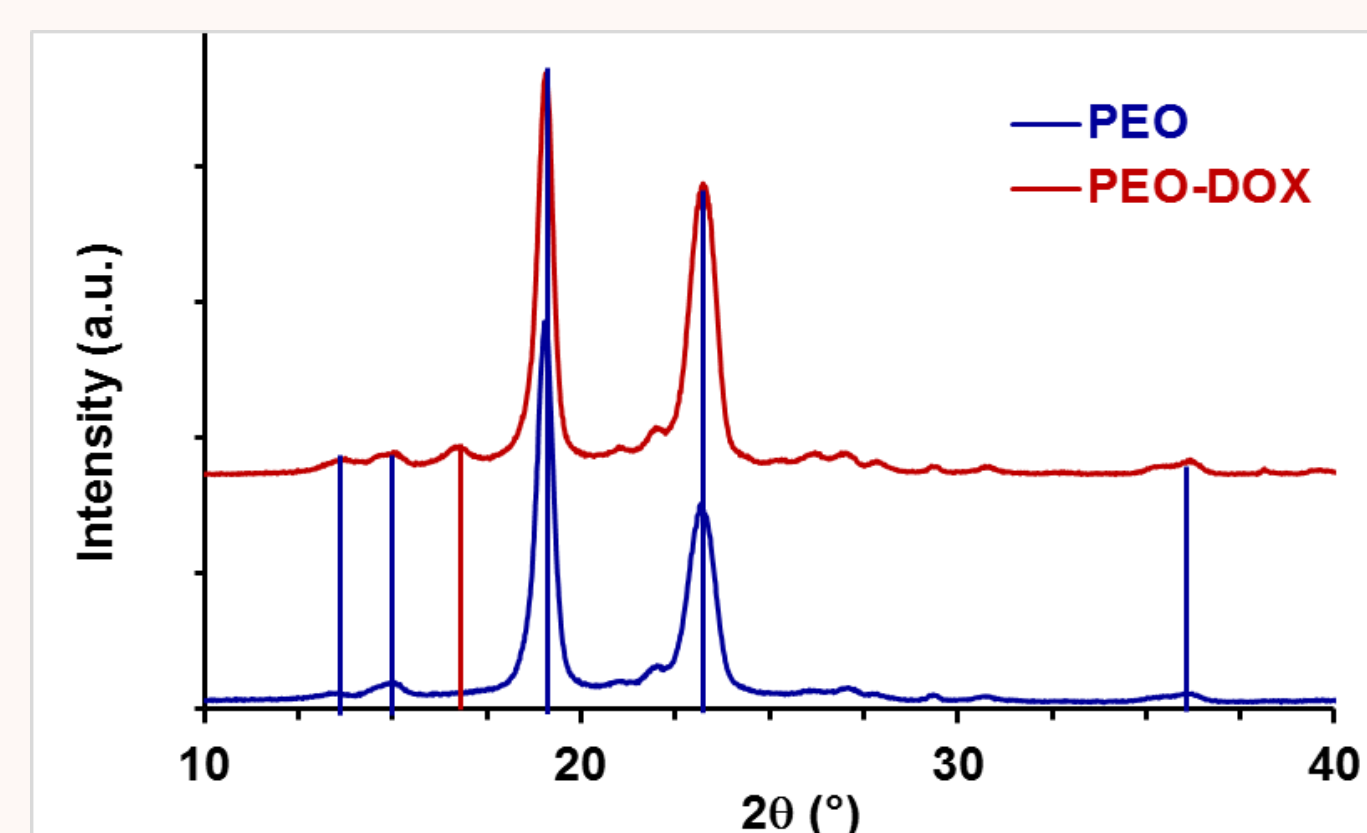
PCL or PEO nanofibers

Estimated fiber diameters:
from 200 nm to 2 μm



XRD:

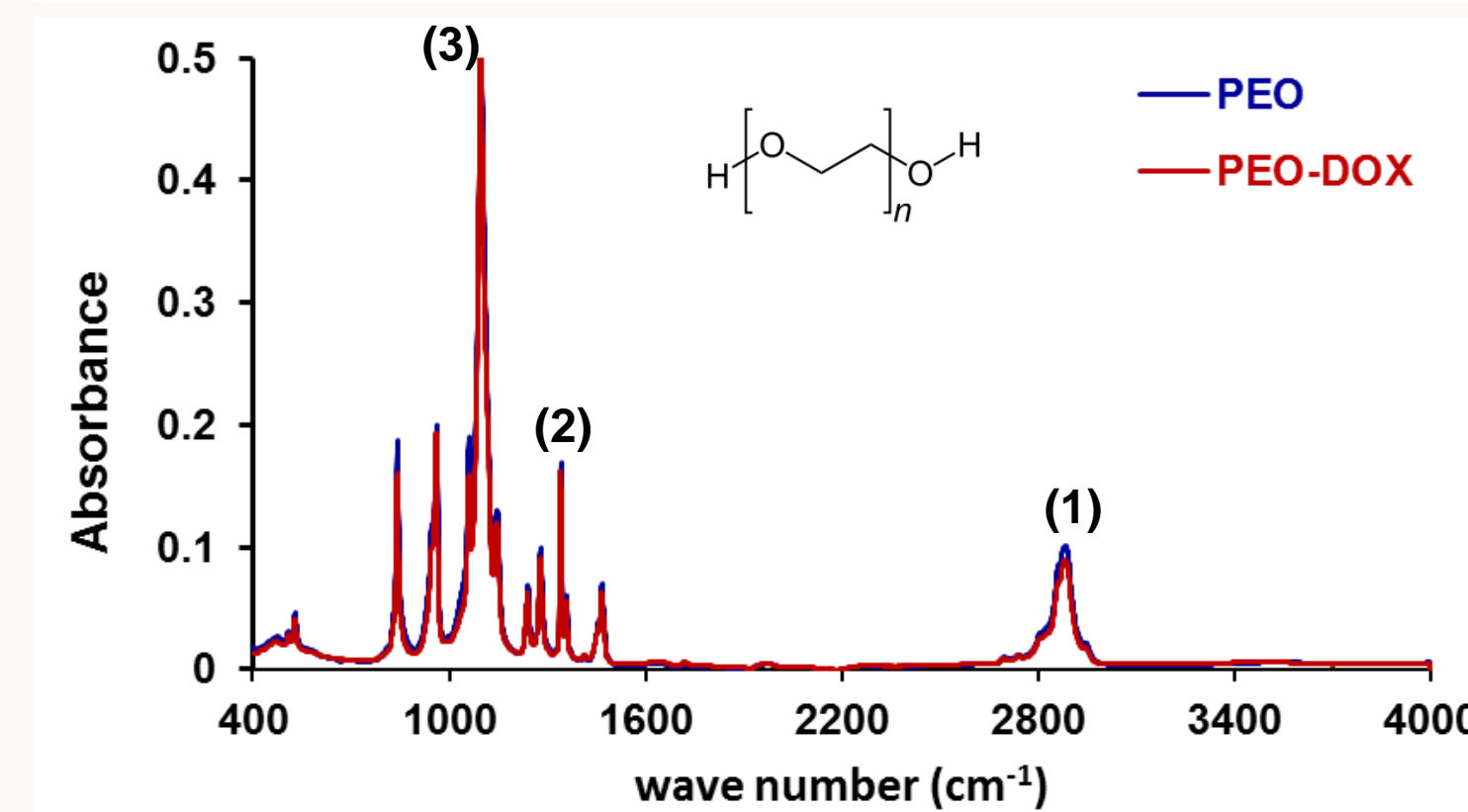
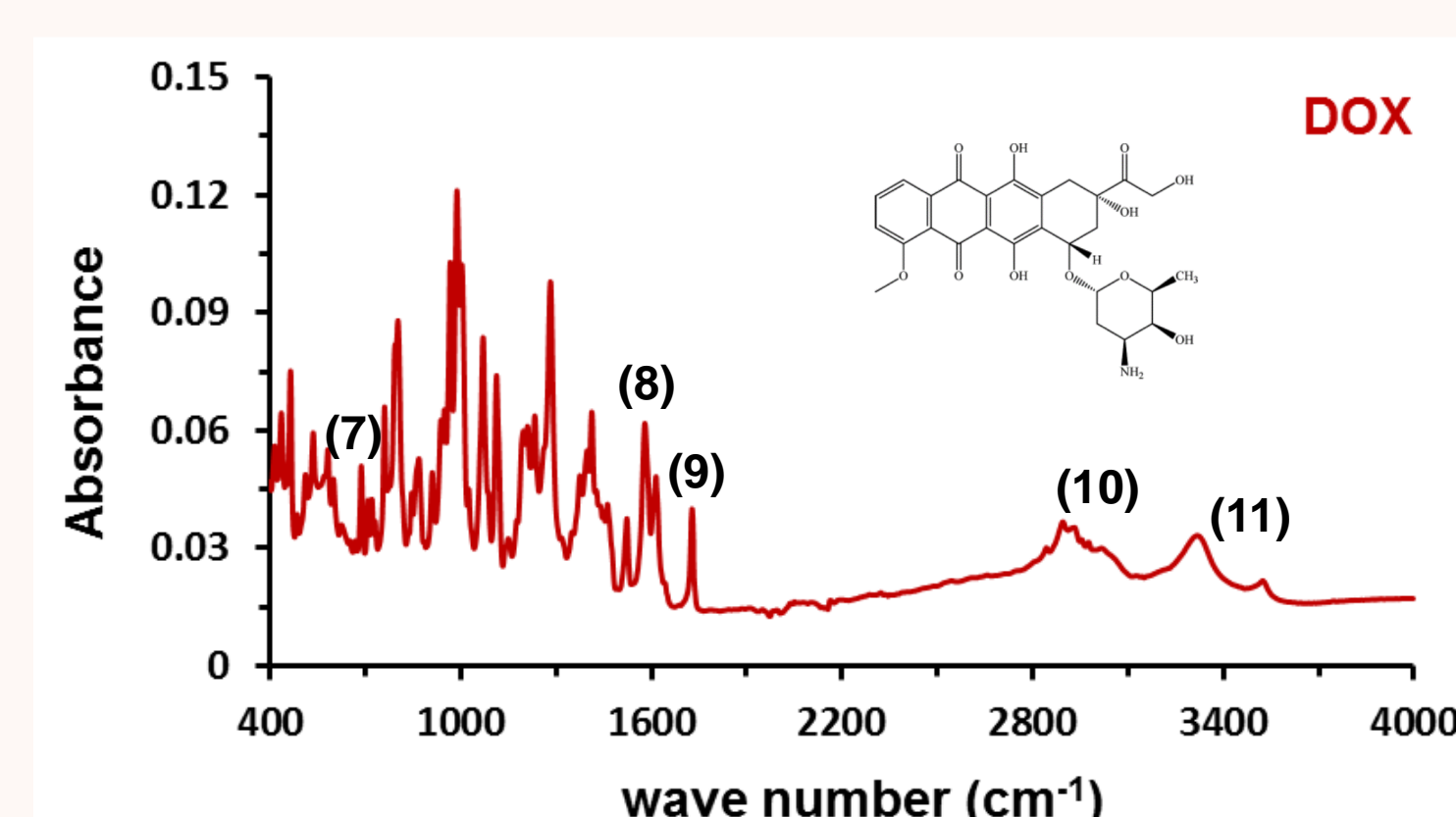
Crystalline structure of polymer nanofibers is not damaged by encapsulation of DOX. Diffraction peak around 17° should reveal the DOX within the fibers.



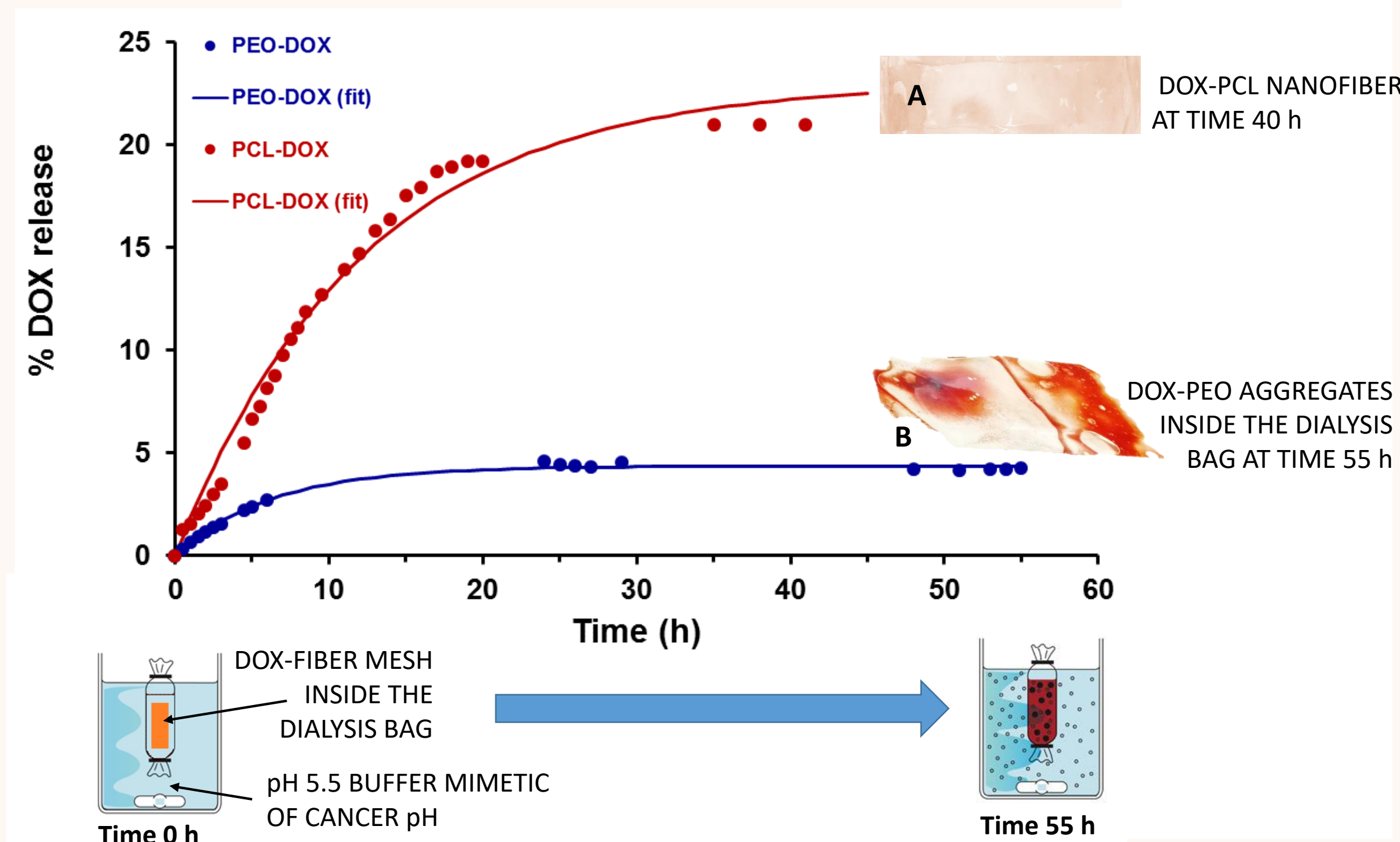
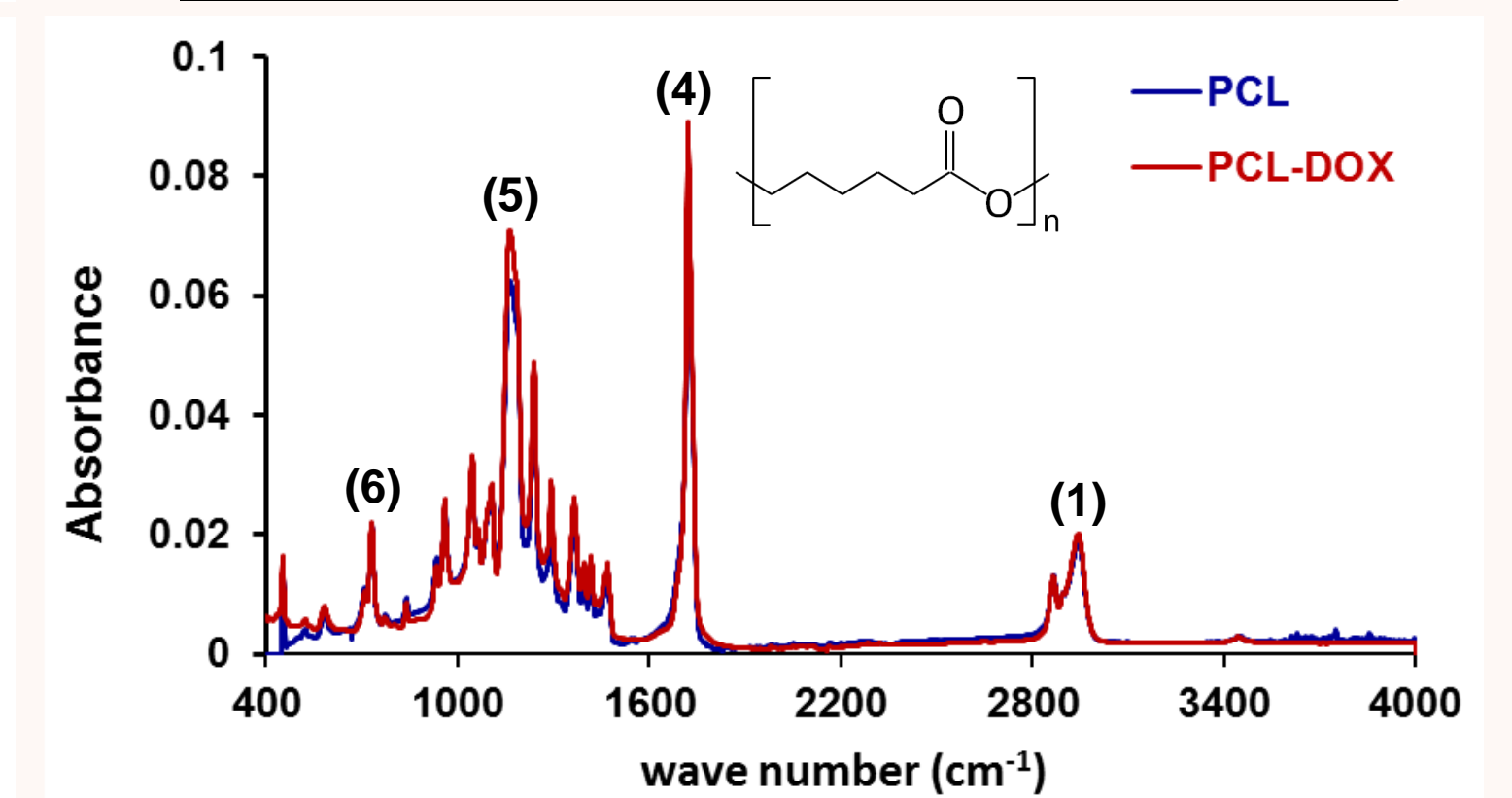
ATR-FTIR:

It was possible to identify the vibrations from the most important functional groups in the polymer fibers and in DOX (see table) but in fibers spectra, DOX peaks are not identified. Why?

1. drug content is small (1.7-2.0%);
2. radiation penetration depth in the fibers is only around 1.7 μm;



Functional group	Wave number (cm ⁻¹)	Assignment
(1) -(CH ₂) _n -	2850-2960	PEO and PCL
(2) -(CH ₂) _n -	1430-1470	PEO
(3) C-O ether	1070-1150	PEO
(4) C=O ester	1740-1750	PCL
(5) C-O ester	1050-1300	PCL
(6) -(CH ₂) _n -	≈ 720	PCL
(7) C-H aromatic ring	700-850	DOX
(8) C=O aromatic	≈ 1580	DOX
(9) C=O ketone	1700-1740	DOX
(10) N-H amine	3070-3500	DOX
(11) O-H	3200-3600	DOX



Control Release of DOX from polymer nanofibers

In the case of PCL-DOX nanofibers the fine mesh pores of nanofibrous scaffolds created by interconnected nanofibers and the diffusion of DOX through the nanofibrous layers as an additional barrier could cause a more controlled and prolonged release rate of about 20 % of drug in 40 h. Indeed at the end of controlled release assays, PCL nanofiber scaffold still reveals a great amount of color due to incorporated DOX (Image A). PEO nanofibers are water soluble and therefore one would expect an immediate release of DOX from the nanofibers, however a suspension with a gel appearance is formed inside the dialysis bag (Image B) suggesting aggregates formation between DOX and PEO monomers that hinder DOX release.

Conclusions

The electrospinning technique proved to be efficient in producing DOX loaded nanofibers. PCL nanofibers, by their mechanical resistance and elasticity when compared with PEO nanofibers, seem to be a promising approach to reach a sustained DOX release profile. DOX-PCL nanofiber meshes will be tested in colorectal cancer cells, for a therapeutic effect by topical application.



FCT Fundação para a Ciência e a Tecnologia
MINISTÉRIO DA CIÊNCIA, TECNOLOGIA E ENSINO SUPERIOR
Governo da República Portuguesa

Acknowledgements: This work was supported by the Portuguese Foundation for Science and Technology (FCT) in the framework of the Strategic Funding UID/FIS/04650/2013.

Marlene Lúcio acknowledges the exploratory project funded by FCT with the reference IF/00498/2012.