LOCAL DELIVERY OF DOXORUBICIN NANOCRYSTALS FROM ELECTROSPUN NANOFIBERS

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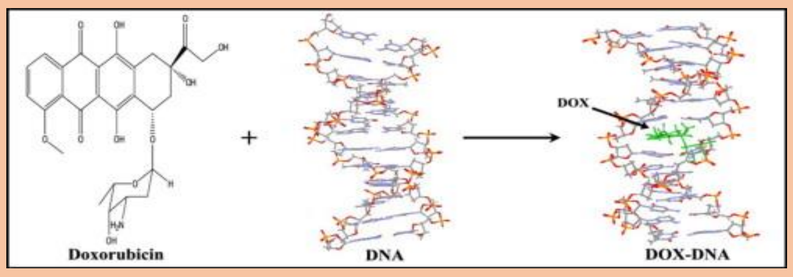
Introduction

Doxorubicin (DOX) → Class I: High permeability, High solubility

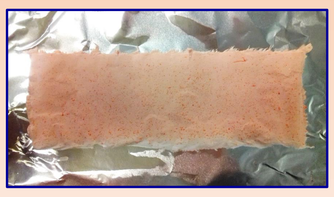


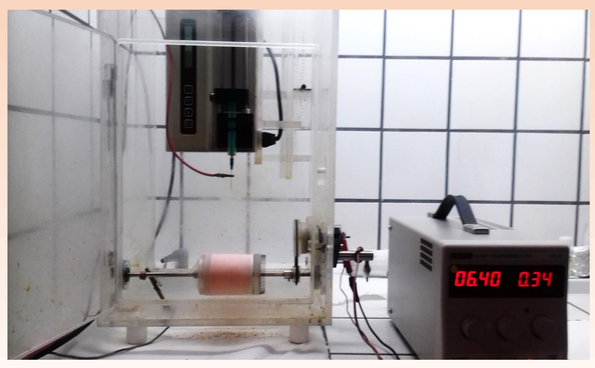
→ free DOX: low therapeutic index → repeated administration of high doses are required

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 polyoxyethilene (PEO) and polycaprolactone (PCL).

Experimental





Polymeric PEO solution
0.1 g/mL PEO in water
+
10 mg DOX

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

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

Electrospinning parameters
Flow rate: 0.6 mL/h
Voltage: 15 kV
Needle: 0.6 mm
Temperature: 20 ºC

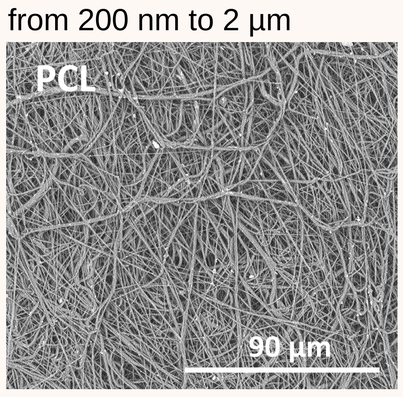
Characterization
SEM-EDS
XRD
ATR-FTIR
Controlled release assays in cancer tissues 'conditions (pH 5.5 at 37°C)

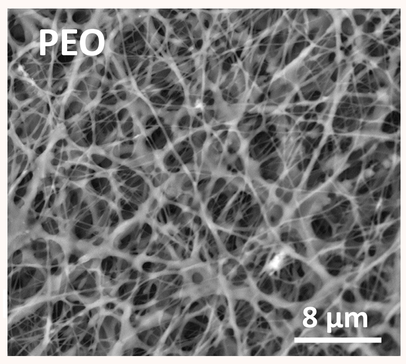
Results

SEM:

PCL or PEO nanofibers

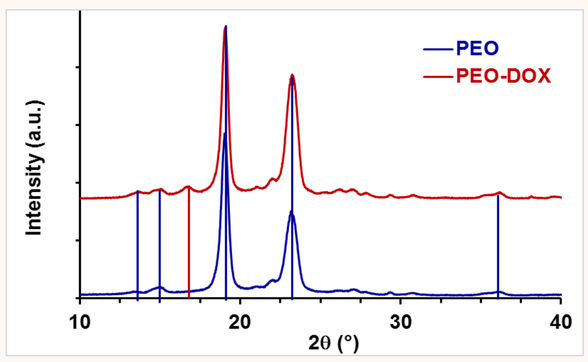
Estimated fiber diameters: from 200 nm to 2 µm

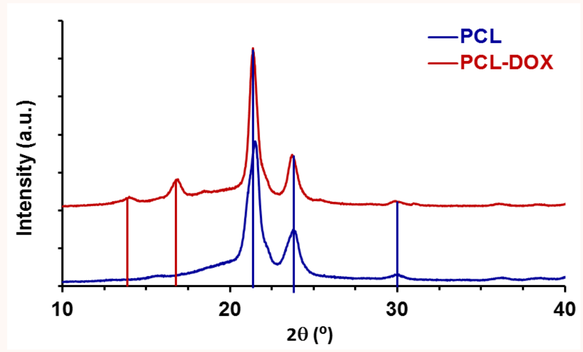




XRD:

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

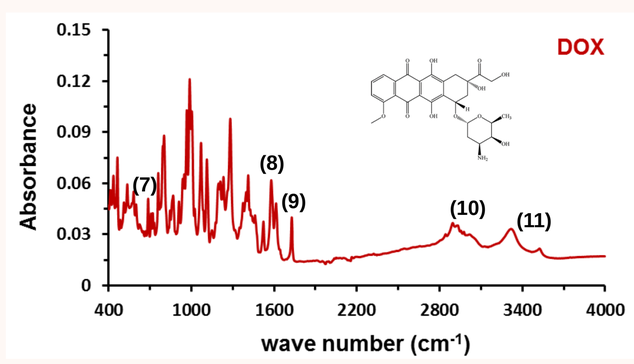




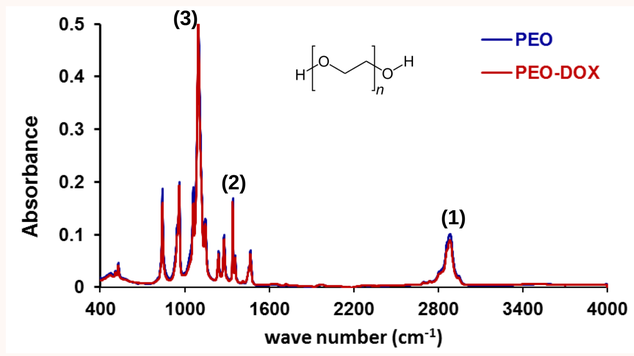
ATR-FTIR:

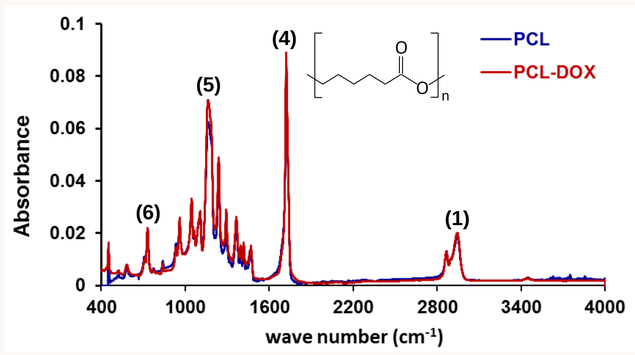
It was possible to identify the vibrations from the most important functional groups in the polymer fibers and in DOX (see table) but in fibers spectra, DOX peaks are not identified.

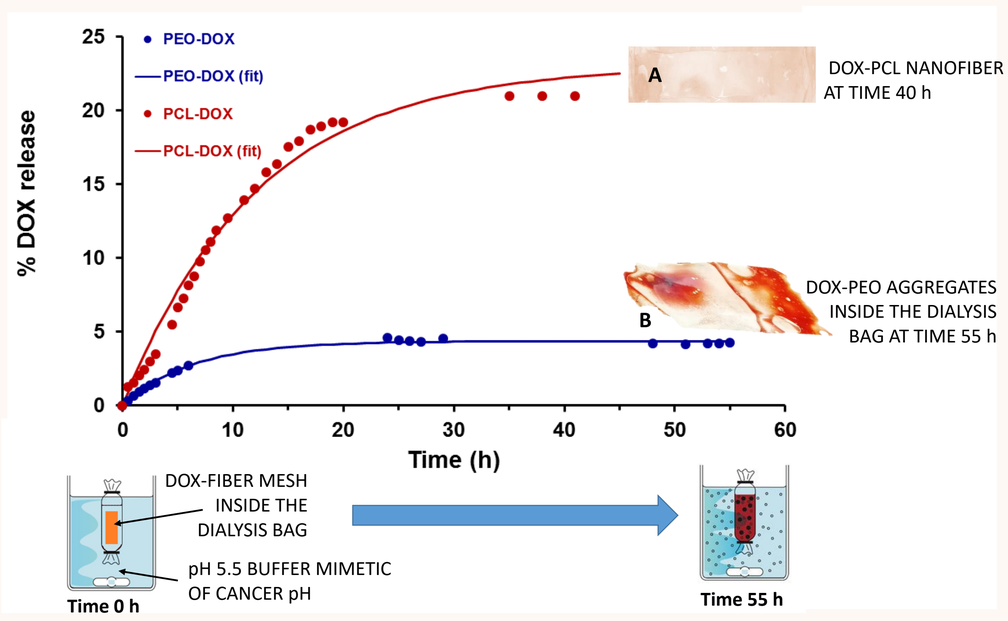
Why? 1. drug content is small (1.7-2.0%);
2. radiation penetration depth in the fibers is only around 1.7 µm;



	Functional group	Wave number (cm^{-1})	
(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.

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