CONTROL RELEASE OF ACYCLOVIR NANOCRYSTALS FROM ELECTROSPUN NANOFIBERS: COMPARISON OF TWO POLYMERIC MATRICES

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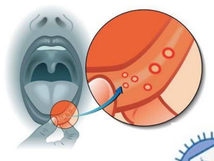
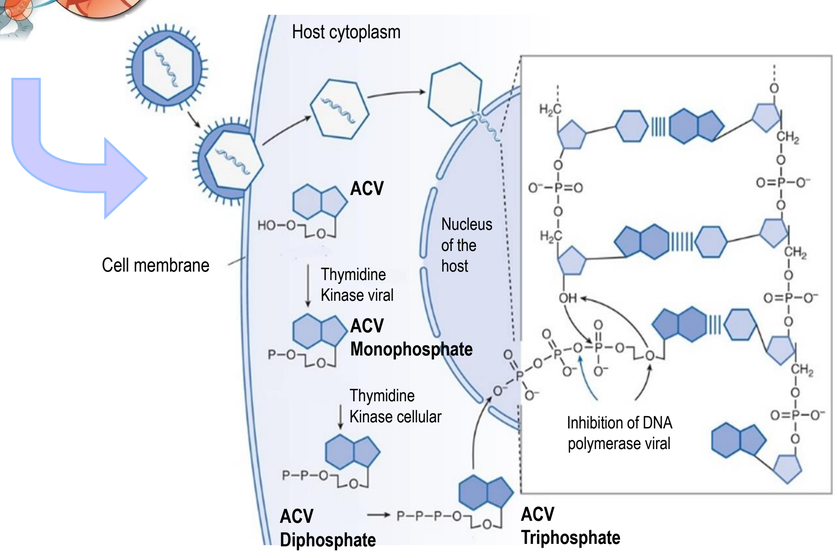
INTRODUCTION and OBJECTIVE:

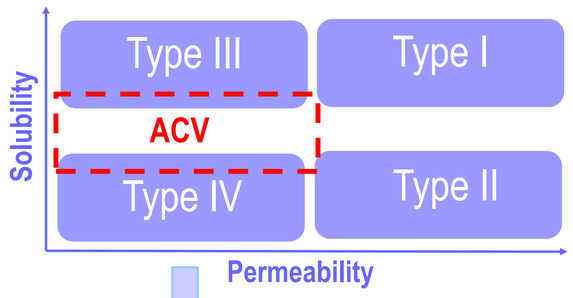


Herpes simplex virus (HSV) type 1 and 2
Varicella-zoster virus
Epstein–Barr virus



The **objective** of this study is to develop a novel system for cutaneous application of ACV that is capable of a controlled release of the drug overcoming the limitations of the conventional topical formulations.

Biopharmaceutical Classification System



ACV: intermediate/low aqueous solubility;
low permeability in biological tissues.

consequently
- Low bioavailability;
- Repeated administration of high doses.

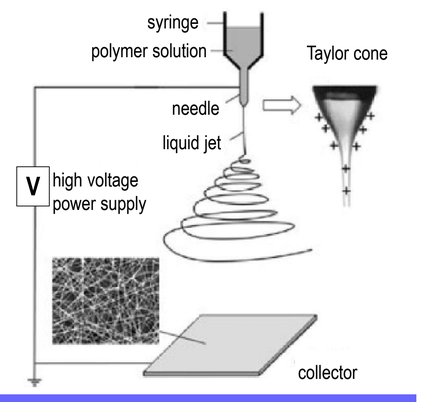
METHOD:

Encapsulation of ACV into different polymeric nanofibers

Zein from maize | Polycaprolactone (PCL)

Electrospinning tecnhique

Optimization of two polymeric systems

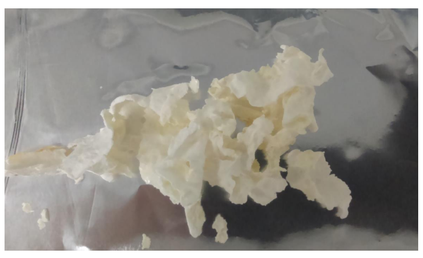


Controlled release assays at physiological conditions and evaluation of mechanical properties

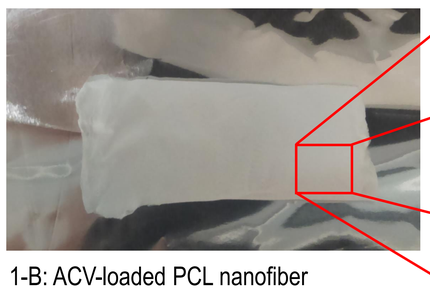
Characterization of the best system

RESULTS and DISCUSSION:

1. SELECTION OF THE BEST SYSTEM



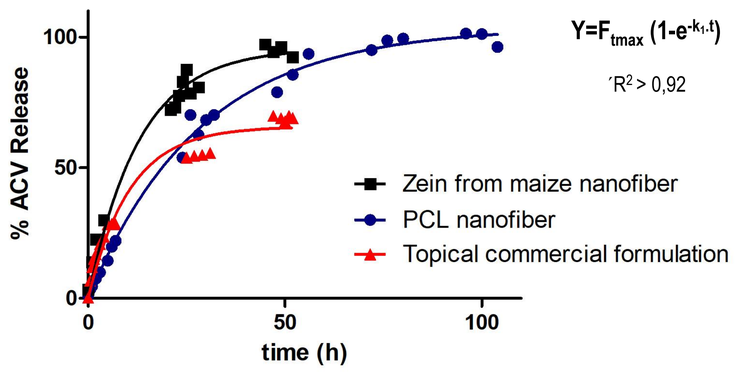
1-A: ACV-loaded zein nanofiber



1-B: ACV-loaded PCL nanofiber

1.1 Control Release Assays

(pH 5.5 at Temp=37 ºC in micellar environment)



$Y=F_{tmax}\,(1-e^{-k_1.t})$

$R^2 > 0,92$

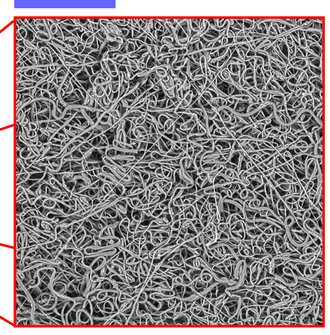
DISCUSSION:

1) The developed systems present a more sustained drug release profile when compared with commercial formulation. **The system that presents better resistance and mechanical properties is the PCL nanofibers matrix.**

2) Characterization of **ACV-Loaded PCL Nanofibers:**

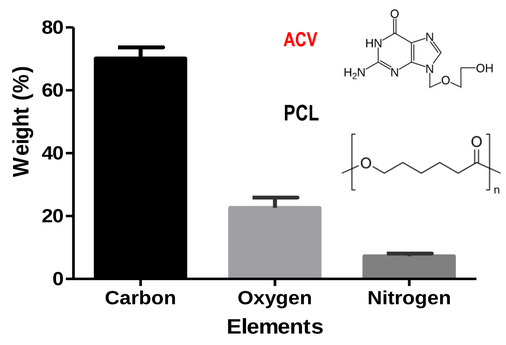
2.1) SEM-EDS shows the presence of ACV in the nanofiber. ACV loaded nanofibers have an average **size of 595 nm**.
2.2) X-ray diffraction shows the **presence of nanocrystals of ACV** in the nanofiber.
2.3) ATR-FTIR shows the **presence of ACV in the nanofiber**.
2.4) DSC indicates that ACV reduces the melting enthalpy without changing Tm of the PCL polymer. This suggests **presence of ACV within PCL nanofiber** reducing PCL crystallinity but preserving its melting temperature high over body temperature. Thus ACV incorporation in PCL nanofiber preserves its integrity.
2.5) The nanofibers presented acceptable **cell viability up to a concentration of 25 mg/mL**.

2. CHARACTERIZATION THE BEST SYSTEM

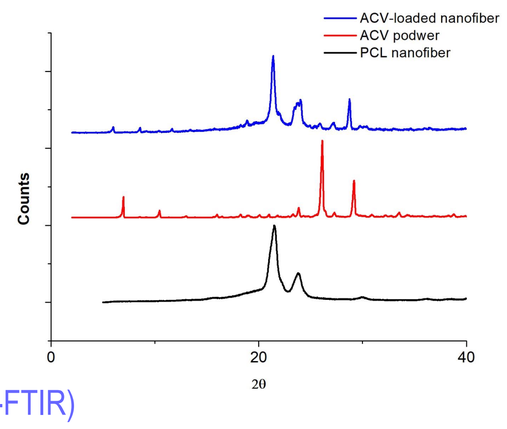


Visualization of ACV-loaded PCL nanofibers by Scanning Electron Microscopy with Energy-Dispersive X-ray Spectroscopy (SEM-EDS) with 15 kV, dimensions 380 x 380 µm.

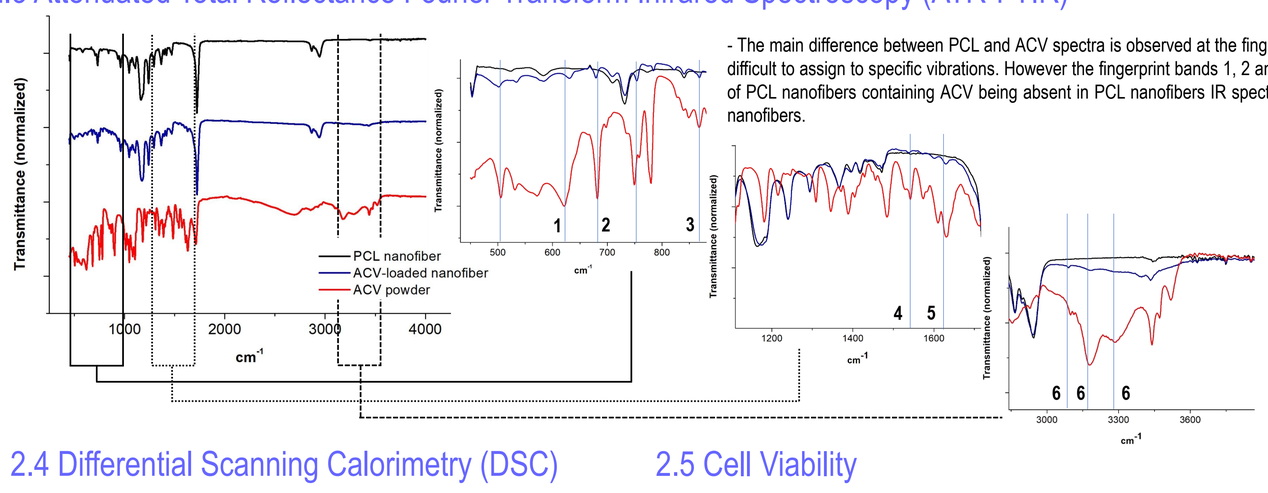
2.1 Scanning Electron Microscopy Elemental Analysis (SEM-EDS)



2.2 Structural Characterization by X-ray Diffraction



2.3 Attenuated Total Reflectance Fourier Transform Infrared Spectroscopy (ATR-FTIR)

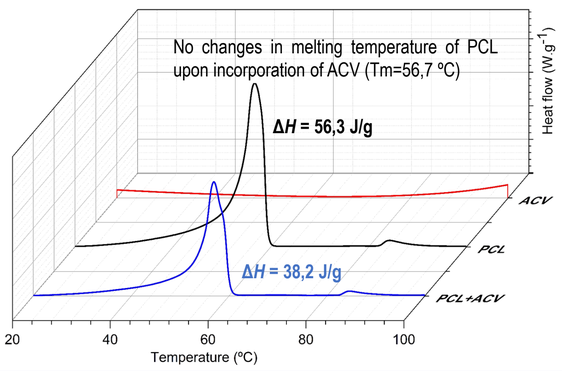


- The main difference between PCL and ACV spectra is observed at the fingerprint IR region (600-1000 cm^{-1}) which can be difficult to assign to specific vibrations. However the fingerprint bands 1, 2 and 3 are present both in IR spectra of ACV and of PCL nanofibers containing ACV being absent in PCL nanofibers IR spectrum which is a proof of ACV presence at PCL nanofibers.

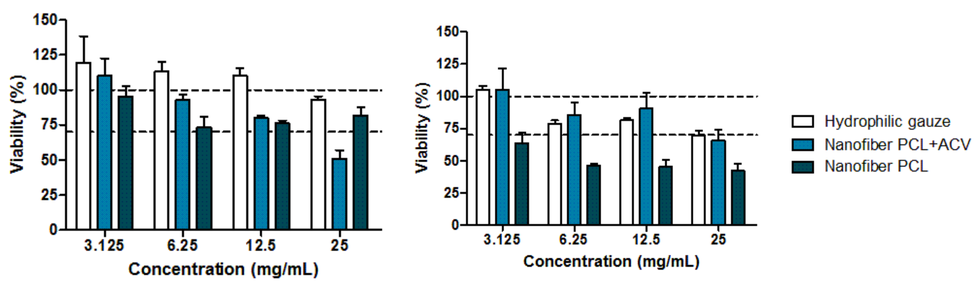
- Another distinctive region is the region of 1400-1750 cm^{-1} where it is possible to assign vibrations due to ACV monosubstituted amide (CO-N-H). CNH stretch-bend appears at 1570-1510 cm^{-1} (4) and C=O stretch band of ACV appears at 1630-1680 cm^{-1} (5)

- At 3200 to 3600 cm^{-1}, the N–H vibration of ACV primary and secondary amines can be found and do not appear at PCL nanofibers IR spectrum, but are present at IR spectrum of PCL nanofibers containing ACV.

2.4 Differential Scanning Calorimetry (DSC)



2.5 Cell Viability



Viability of epidermal keratinocytes - HaCaT (left) and human foreskin fibroblasts HFF-1 (right) assessed by the MTT assay after 24 h incubation with extracts of PCL fibers and hydrophilic gauze. Columns represent mean values and error bars the standard deviation (n=3).

CONCLUSION:

The electrospinning technique proved to be efficient in producing high-loaded ACV nanofibers. The PCL nanofibers are very resistant and elastic (Fig. 1-B) when compared with zein nanofibers, being a promising approach to reach a sustained drug release profile.

References:

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2) J. W. Gnam *et al*., *Pharmacotherapy*, 1983, 20, 275-283.
3) M. Parsa *et al*., Pharmacophore, 2014, 5, 483-493.
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