Co-delivery of two anti-HIV drug nanocrystals from electrospun nanofibers

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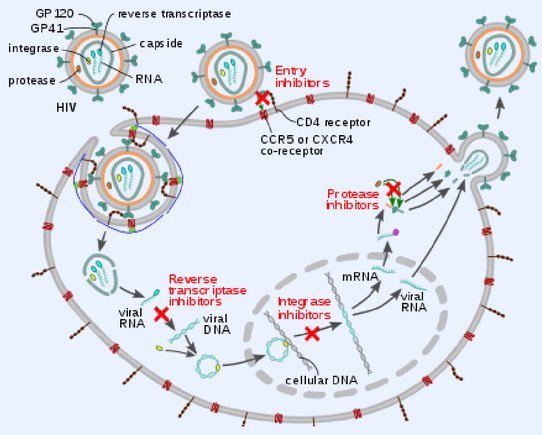
Introduction and Objective



Truvada®

- The only medication approved by FDA for pre-exposure prophylaxis of the HIV infection
- Tablets with fixed dosages of two antiretroviral compounds for **daily oral uptake:** Tenofovir disoproxil fumarate (TDF) + Emtricitabine (EMT) – reverse transcriptase inhibitors

Consequences

↓ renal function

↓ bone mineral density

↑ hepatic enzymes

Objectives:

- Incorporate TDF and EMT drugs in polymeric nanofibers produced by electrospinning; chosen polymers were polyoxyethilene (PEO) and polycaprolactone (PCL).
- Characterize the nanofibers and study the *in vitro* release profile of the drugs.
- Evaluate the possibility of a topical administration of the loaded fibers , by rectal or genital route, for HIV infection prophylaxis.

Method

1. Polymeric PEO solution

10 mg TDF + 7 mg EMT + 0,5 g PEO + 5,0 mL H_2O

2. Parameters of electrospinning

Flow rate: 0,05 mL/h
Voltage: 20 kV
Needle: 0,3 mm
Room temperature

1. Polymeric PCL solution

10 mg TDF + 7 mg EMT + 0,5 g PCL+ 5,0 mL H_2O

2. Parameters of electrospinning

Flow rate: 0,6 mL/h
Voltage: 15 kV
Needle: 0,6 mm
Room temperature

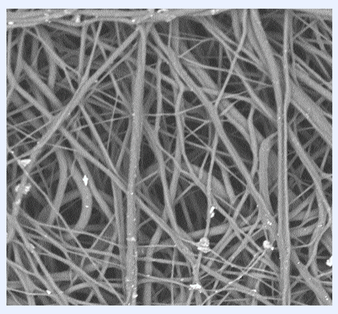
3. Characterization

SEM
XRD
ATR-FTIR
Controlled release assays in simulated vaginal fluid (VFS) (pH 4,2 at 37°C)

Results and Discussion

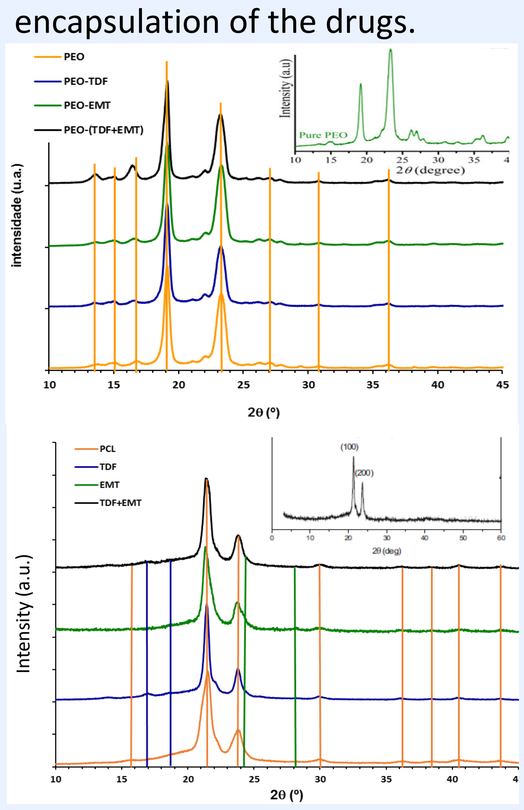
SEM

Estimated fiber diameters: from 200 nm to 2 µm



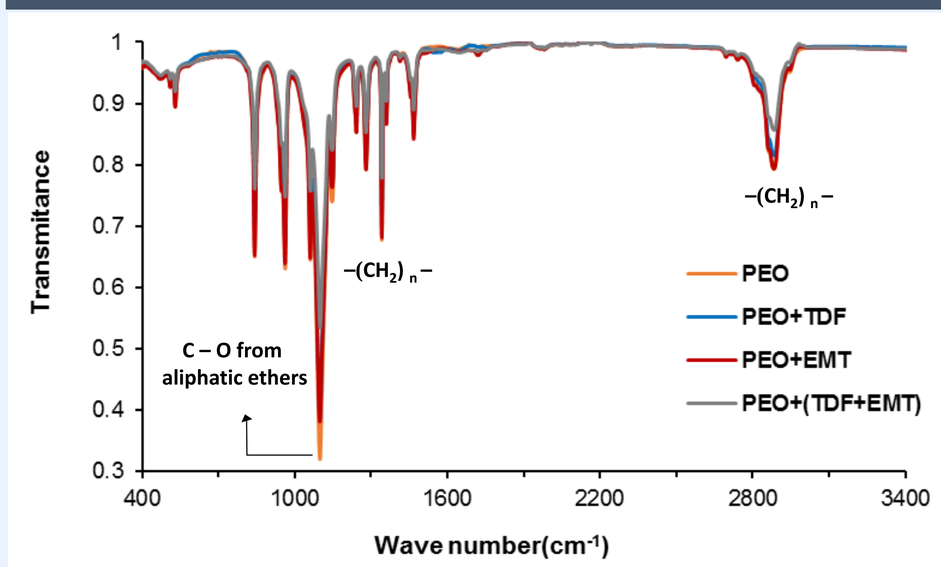
XRD

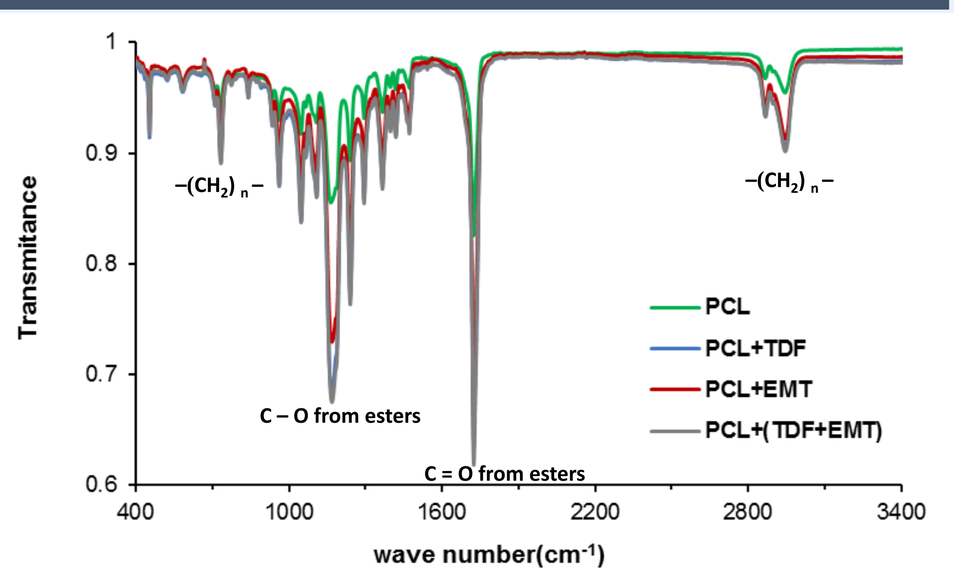
Crystalline structure of polymeric nanofibers is not damaged by encapsulation of the drugs.



Blue and green lines in XRD of PCL can reveal the presence of the drugs within the fibers.

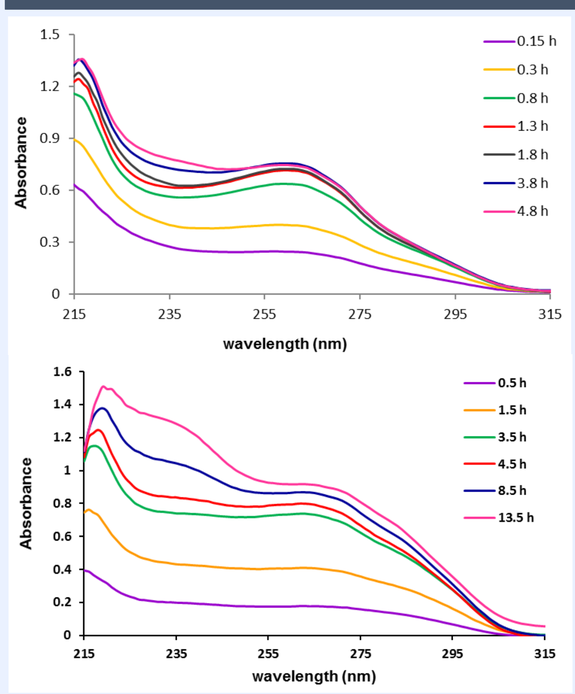
ATR-FTIR



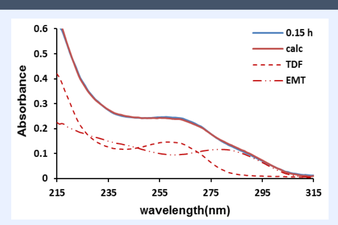


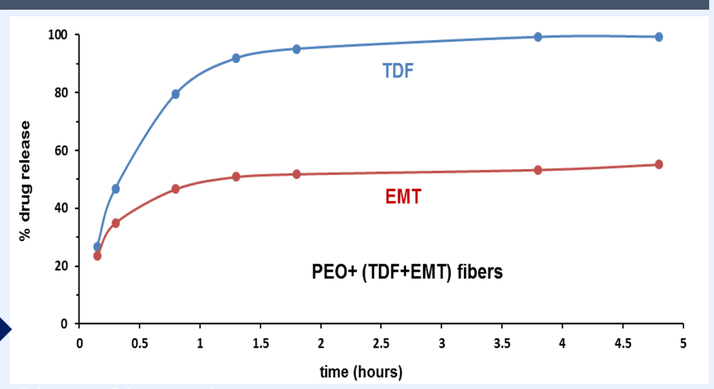
In the fibers it was possible to identify the vibrations from the most important functional groups of the polymers but not of the drugs. Why? 1. because drug content is small (1.7-2.0%);
2. because radiation penetration depth in the fibers is only around 1.7 µm.

Control Release of TDF and EMT from PEO and PCL nanofibers



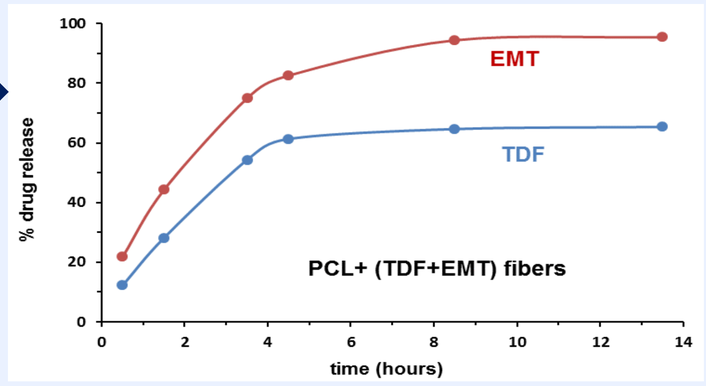
Each measured spectrum, resulting from the release of both drugs from the polymer nanofibers, was simulated by considering variable and adjusted contributions of each drugs.





TDF is more easily released from PEO nanofibers fibers than EMT.

By contrast, from PCL nanofibers the release of EMT is more efficient.



IN CONCLUSION
By varying the hydrophobicity of the polymer, it is possible to tailor the drug release kinetics

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