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

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Despite advances in treatment and prevention, novel strategies to reduce rectal and vaginal transmission of the human immunodeficiency virus (HIV) are still under development as a way to stop the infection. Oral pre-exposure prophylaxis (PrEP) with daily oral Truvada®, a commercial tablet comprising the antiretroviral drugs tenofovir disoproxil fumarate (TDF) and emtricitabine (EMT) has been shown successful in preventing sexual transmission of the virus [1]. This preventive option has already been approved in several countries, but its use still presents some caveats. For example, oral PrEP requires daily administration irrespective of sexual activity frequency and, despite overall safety, toxicity may still arise [2]. More important, the efficacy of Truvada® in women seems to be reduced as compared to men, a fact that may be related to poorer distribution of TDF/EMT into the female genital tract [3]. Thus, an alternative approach for women protection could be the administration of the drug combination as a vaginal microbicide (topical PrEP) in order to enhance local pharmacokinetics and reduce systemic drug exposure, ultimately resulting in better safety. Nanofibers, in particular, have been proposed as potential drug delivery systems for developing microbicides [4].

In this study nanofiber meshes composed by FDA-approved polymers, namely polyoxyethylene (PEO) and polycaprolactone (PCL), loaded with TDF or EMT or (TDF+EMT) have been produced by electrospinning. Nanofibers composition and preparation method were optimized for the two polymers and for the encapsulated drugs. Topographic analysis was done by Scanning Electron Microscopy (SEM) evidencing the fiber size and morphology. Structural characterization of the produced nanofibers were achieved by X-ray diffraction showing TDF and EMT nanocrystals inside the fibers. In order to elucidate the interactions between the polymer and the antiretroviral drugs, Attenuated Total Reflectance Fourier Transform Infrared Spectroscopy (ATR-FTIR) was used. Drug release assays were carried out using a simulated vaginal fluid (pH 4.2) [5] at 37 ºC and a dialysis tubing with a cut-off of 3.5 kDa. Simultaneous determination of TDF and EMT was achieved by using UV-vis derivative spectrophotometric based methods [6]. Owing to their drug loading (1.4-2% w/w) and preliminary drug release profiles (Fig. 1), the polymeric eletrospun nanofibers appear to be promising candidates for the topical delivery of TDF and EMT, and for further development as vaginal microbicide products.

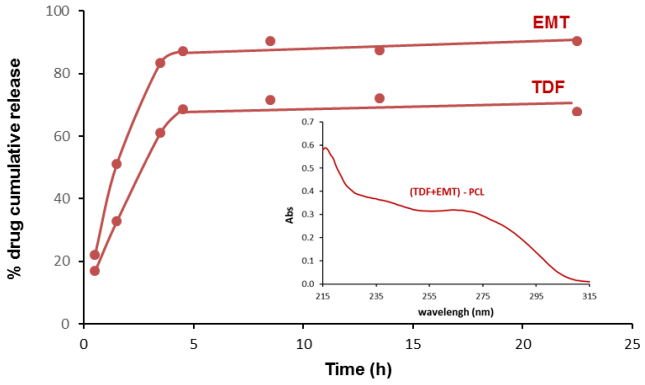

Fig. 1 Cumulative release of TDF and EMT from (TDF+EMT)-PCL nanofibers
(inset shows an absorption spectra of the eluant with (TDF+EMT) from which drugs concentration were calculated)

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