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Electrospun nanofibers loaded with Truvada® as a novel intravaginal delivery system for HIV prophylaxis

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HIV stands as an increasing global burden and sexual transmission remains the leading cause of new infections, particularly in women in the Sub-Saharan region [1]. New prevention strategies are urgent and vaginal microbicides have proven to be promising alternatives to prematurely fight and control its dissemination. In this study, we developed TDF/FTC-loaded fibers and tested their pharmacokinetics (PK) compared to oral Truvada® [2].

Hydrophobic and hydrophilic fibers were produced by electrospinning using polycaprolactone (PCL) and poly(vinyl alcohol) (PVA) with drug-loaded liposomes (DMPC:Chol:DOPE, 7:2:1), respectively. They were further characterized regarding their: (i) size and morphology; (ii) structure and mechanical properties; (iii) drug loading and in vitro drug release; (iv) interaction with mucin molecules; and (v) in vitro cytotoxicity using the MTT metabolic activity assay. Additionally, PK were assessed in medroxyprogesterone- treated ICR mice. Drug levels in vaginal lavages, vaginal tissues and blood plasma were determined by LC-MS/MS after vaginal administration of fibers (70 μg/50 μg of TDF/FTC) and compared to the continuous treatment with daily oral Truvada® (61.5 mg/mg per kg).

The mean section diameter of PCL and liposomes/PVA fibers was of ≈700 nm and ≈150 nm, respectively. Furthermore, the strong interactions observed with mucin molecules anticipate that all fibers may promote higher vaginal retention times. TDF/FTC release profiles were fast and almost all incorporated drug was released within 15-30 min in micellar medium (pH= 4.5). The toxicity of drug-loaded fibers to CaSki and HEC-1-A genital cell lines was negligible. In vivo experiments showed that liposomes/PVA fibers were able to significantly enhance the concentrations of TDF, tenofovir (TFV; resulting from TDF
®
hydrolysis) and FTC, as compared to PCL fibers and oral Truvada . Relative bioavailability
(Frel) values of TFV and FTC were 4.0 and 29.4, respectively, as compared to Truvada® (TDF was not detected for oral treatment). PCL fibers also featured higher drug levels in lavages than oral Truvada® (Frel values for TFV and FTC were 2.3 and 2.4, respectively).

Our results suggest that liposomes/PVA fibers may constitute an interesting system for the vaginal delivery of TDF/FTC in the context of topical pre-exposure prophylaxis.

References

[1] R. Nunes et al., Journal of Controlled Release 334, (2021).

[2] J. das Neves et al., Advanced Drug Delivery Reviews 103, (2016).

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