

https://dspace.org/

Design of an intravaginal composite polymeric system for the reduction and prevention of STI and HIV transmission

Mashingaidze, Felix

2014-08-22
http://hdl.handle.net/10539/15217

Downloaded from a DSpace repository. https://dspace.org/

ABSTRACT

This dissertation discusses anti-HIV-1 microbicide research. In particular, it concentrates on microbicide formulation and delivery. Microbicides are anti-HIV-1 agents that when applied in the human vagina or rectum may prevent sexual HIV-1 transmission. Although most of the anti-HIV-1 agents being developed as microbicides are active *in vitro*, they have proved to be ineffective *in vivo*. A review of microbicide development over the last decade expounds the view that unsatisfactory microbicide failures may be a result of inefficient delivery systems employed. Thus, necessitating a thorough scientific qualitative and quantitative investigation of important aspects involved in HIV-1 transmission as a prerequisite for microbicide development. In this dissertation it is postulated that intravaginal targeting of HIV-1 increases the chances of microbicide success, wherein vaginal micro-environmental factors including pH would be maintained at HIV-1 prohibitive acidic levels to ward off other sexually transmitted diseases which compromise vaginal epithelial barrier properties. Furthermore, targeting early stages of the HIV-1 infection accompanied by computation and delivery of appropriate microbicide quantities could result in an effective microbicide formulation.

In an effort to address microbicide formulation challenges, an intravaginal delivery system able to deliver anti-HIV-1 agents (zidovudine and BP36) over 28 days was formulated. This delivery system is a caplet-shaped composite system comprising zidovudine (AZT) and BP36-loaded pectin-mucin-polyethylene glycol submicrospheres embedded within a poly(D,L-lactide), magnesium stearate, polyvinyl acetate/polyvinylpyrolidone (Kollidon® SR) and poly(acrylic acid) based polymeric caplet matrix. The delivery system was tested *in vitro* and *in vivo* in the pig model. X-ray imaging illustrated the delivery system swelling and its matrix contrast fading over time as vaginal fluid permeated the matrix's core. Plasma, vaginal fluid and tissue drug was detected and quantified using ultra performance liquid chromatography-tandem photodiode array detector. AZT plasma and vaginal fluid concentrations measured on days; 3, 7, 14, 21 and 28 decreased gradually with time. Vaginal tissue AZT concentrations (after 28 days) were higher than plasma AZT concentrations and were in the same range as vaginal fluid AZT concentrations. The herbal extract, BP36, was detected in plasma, vaginal fluid and tissue but was only qualitatively analysed due to its lack of standardization. Histopathological analysis of excised vaginal tissue revealed different scores of abnormalities comprising mild to moderate epithelial proliferation and exocytosis, subepithelial leukocyte influx, perivascular cell cuffing and isolated epithelial erosion, stromal fibrosis and isolated tissue necrosis.