Novel Vaginal Ring Design for the Controlled Release of the Macromolecule Microbicide 5P12- RANTES


Document Version:
Publisher’s PDF, also known as Version of record

Queen's University Belfast - Research Portal:
Link to publication record in Queen's University Belfast Research Portal

Publisher rights
Copyright 2018 The Authors.

General rights
Copyright for the publications made accessible via the Queen's University Belfast Research Portal is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy
The Research Portal is Queen's institutional repository that provides access to Queen's research output. Every effort has been made to ensure that content in the Research Portal does not infringe any person's rights, or applicable UK laws. If you discover content in the Research Portal that you believe breaches copyright or violates any law, please contact openaccess@qub.ac.uk.
PD09.05

Novel Vaginal Ring Design for the Controlled Release of the Macromolecule Microbicide 5P12-RANTES

John McBride¹, Peter Boyd¹, Robin Offord³, Oliver Hartley², Vicky Kett¹, Karl Malcolm¹

¹Queen’s University Belfast, United Kingdom, ²Mentaka Foundation for Medical Research, Switzerland

Background: 5P12-RANTES, a chemokine analogue that potently blocks the HIV CCR5 coreceptor, is being developed as both a vaginal and rectal microbicide for prevention of sexual transmission of HIV. Development of low-cost intravaginal rings (IVRs) for controlled release of such protein molecules is significantly more challenging than for small-molecule antiretrovirals due to poor permeability. Here, we report a new reservoir-type IVR design comprising a drug-loaded/hydropropyl methylcellulose (HPMC) core and a non-medicated sheath with orifices for controlled release 5P12-RANTES.

Methods: Silicone elastomer IVRs containing model drug lysozyme or experimental drug 5P12-RANTES were manufactured via injection molding. HPMC particle size, HPMC molecular weight and HPMC loading, and number of orifices were varied across the IVR formulations. In vitro release testing was performed and 5P12-RANTES quantified using ELISA and HPLC-UV. Fluid ingress into the IVRs was assessed by weight increase and uptake of methylene blue.

Results: Using custom molds, the novel IVRs were easy to manufacture. Preliminary results with lysozyme revealed that a greater HPMC loading, molecular weight, and particle size correlated with a greater drug release rate and degree of swelling. Adjusting core surface area exposure, by increasing orifice size/number, correlated with greater swelling and 5P12-RANTES release (9.34 mm² surface area exposure, 3.5 ± 1.9 µg/day; 56.04 mm², 8.9 ± 1.8 µg/day; 210.90 mm², 39.3 ± 19.7 µg/day).

Conclusions: The ring design provided controlled release of 5P12-RANTES, and could be applied to a broader range of large molecule actives. This research supports continued development of the 5P12-RANTES IVR. Sheep pharmacokinetics studies are currently being conducted.