Sustained release of the HIV microbicides maraviroc and emtricitabine from modified silicone elastomer vaginal gels


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

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.
Sustained Release of the HIV Microbicides Maraviroc and Emtricitabine from Modified Silicone Elastomer Vaginal Gels
C. F. McCoy, C. J. Forbes, R. K. Malcolm
Queen’s University Belfast

**Purpose**
Silicone elastomer gels (SEGs), consisting of lightly crosslinked polydimethylsiloxane (ST-Elastomer 10) and cyclomethicone, are commonly used in a range of cosmetic applications and are currently being developed for topical drug delivery applications. Recently, SEGs have been shown to provide sustained pharmacokinetics of the HIV entry inhibitor maraviroc (MVC) following vaginal administration in macaques. The objective of this study was to evaluate a range of second generation SEGs wherein the cyclomethicone component of the gel has been replaced with a low molecular weight (MW) hydroxyl-terminated, linear polydimethylsiloxane (h-PDMS). We anticipated that the resulting hydrophilic h-SEGs would offer enhanced release rates for HIV microbicide candidates MVC and emtricitabine (FTC) compared to conventional SEGs.

**Methods**
Continuous flow rheology was performed on h-SEGs prepared with different MW h-PDMS. In vitro release testing was performed on viscosity-matched gels containing either 5% w/w MVC or FTC in both simulated vaginal fluid (SVF) and a solvent/water system. Solubilities of MVC and FTC were determined in different MW h-PDMS.

**Results**
The viscosity of h-SEGs increased with ST-Elastomer 10 concentration. h-SEG gel compositions, viscosity-matched to a conventional 80:20% w/w SEG and a 2.2% w/w HEC gel (~50Pa.S), were chosen for in vitro release testing. Release of MVC and FTC from a low MW h-SEG was significantly increased in both dissolution media ((MVC; 18mg (SVF), 21mg (IPA/water), FTC; 4mg (SVF), 14mg (IPA/water)) compared to the conventional SEG gel (MVC; 3 mg (SVF), 12 mg (IPA/water), FTC; 2 mg (SVF), 9mg (IPA/water)). Release from high MW h-SEGs was comparable to the conventional SEG gel in both media. Solubility of MVC and FTC in the low MW h-PDMS (MVC; 40mg/mL, FTC; 0.4mg/mL) was significantly greater than in cyclomethicone (MVC; <5µg/mL, FTC; <1.1µg/mL).

**Conclusion**
The results demonstrated that SEG hydrophilicity can be readily modified by substituting the cyclomethicone component of the elastomer gel with low MW h-PDMS. Increasing the proportion of hydroxyl groups significantly enhanced release and solubility of both model hydrophobic (MVC) and hydrophilic (FTC) microbicides compared to the conventional SEG. The results highlight the potential of these second generation SEGs for vaginal delivery of HIV microbicides.