Formulation Development of Acyclovir/Tenofovir Loaded Two-Polymer (SR-2P) Bioadhesive Vaginal Gel
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Purpose
To develop and evaluate two-polymer (SR-2P) bioadhesive vaginal gel for the simultaneous delivery of acyclovir and tenofovir

Methods
Gel formulations were prepared with different combinations of temperature sensitive polymer (Pluronic® F-127) and mucoadhesive polymer (Noveon® AA1). The gel formulations were evaluated for pH, osmolality, buffering capacity and viscosity under simulated vaginal and semen dilutions, and bioadhesivity using ex vivo mini pig vaginal tissues. The vaginal irritation of the gels was evaluated in mouse vaginal irritation model. The compatibility of the combinations of acyclovir and tenofovir in two polymers was investigated by stressing the samples at 40°C/75%RH for up to 6 weeks. The chemical stability of the drugs was measured using a HPLC method. The thermal properties of the drug, polymers and gel formulations were characterized by differential scanning calorimetry (DSC). The in vitro release of drugs from the optimized gel formulation in simulated vaginal fluid was characterized using in-line Franz diffusion cell with regenerated cellulose membrane

Results
The pH of the polymeric gel formulations ranged from 5.1 to 6.4; the osmolality varied from 13 to 173 mOsm. Absolute viscosity ranged from 513 to 3780 cPS. Among the tested gels, only SR-2P retained gel structure upon dilution with simulated fluids and mild simulated coital stress. Among the tested gels, only SR-2P had shown high peak force of adhesion in mini pig vaginal tissue. Furthermore, SR-2P gel caused no or only minimal irritation in a mouse vaginal irritation model. Results of the compatibility studies have shown that tenofovir was compatible with Noveon® AA1 and acyclovir was compatible with Pluronic® F-127. However acyclovir and tenofovir were stable at both ambient and accelerated storage conditions in SR-2P gel base. As part of the dual syringe product development strategy, tenofovir needs to be in Noveon® AA1 and acyclovir in Pluronic® F-127 compartment. In vitro release of acyclovir and tenofovir from SR-2P gel in simulated vaginal fluid at the end of 6 h was about 10 and 35 %

Conclusion
The results of this study demonstrated the potential application of SR-2P as a vaginal microbicide vehicle for delivery of acyclovir and tenofovir