Poster abstract: Impact of Intermittent Use on In Vitro Release and Residual Content of 25 mg Dapivirine Rings

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Impact of Intermittent Use on In Vitro Release and Residual Content of 25 mg Dapivirine Rings

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Background: The current 25 mg dapivirine (DPV) matrix ring formulation is intended for continuous use over 28 days. However, poor user adherence remains a considerable challenge for the efficacy of microbicide-releasing vaginal products. Here, we report the impact of intermittent use on in vitro release and residual content of 25 mg DPV rings.
Methods: In vitro release testing of 25 mg DPV rings over 28-days was performed using different intermittent schedules, including: (i) continuous release, (ii) release on the first and last day, (iii) release for one day each week and (iv) release for the first and last week of the 28-day period. Release was performed using either isopropanol (IPA) and water (1:1 v/v) or simulated vaginal fluid (SVF) containing 0.2% w/v Tween 80. When periodically removed from the release medium, rings were stored at either ambient temperature or 4°C. Residual content analysis - using acetone extraction - was performed on rings after completion of in vitro release testing. DPV concentrations were quantified by HPLC.
Results: DPV release was significantly greater in IPA+water compared to SVF+Tween. The total amount of DPV released was proportional to the amount of time the rings spent in the release medium. No significant differences were observed in the release rates for rings stored at different temperatures. Residual content values were dependent on the total time of exposure to the release medium. Cumulative release values combined with residual content values gave mass balance values close to the mean content assay value provided for the ring batch.
Conclusions: In vitro release rates measured under intermittent in vitro release testing schedules were not significantly different from those observed under continuous release schedules, based on a direct comparison of release rates on equivalent days. Removal of rings from the release medium and subsequent storage did not substantially alter the in vitro release profiles when the rings were placed back into the release medium.

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Mechanical Testing Protocols for Vaginal Ring Formulations

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Background: There are currently no international standards regarding mechanical testing and properties of vaginal rings. Here, we report the development of a series of mechanical protocols aligned to ISO 8009:2014 ("Mechanical contraceptive - reusable natural and silicone rubber contraceptive diaphragms - requirement and tests") to aid evaluation and comparison of IPM's 25 mg dapivirine (DPV) matrix ring against a range of marketed vaginal ring (VR) products.
Methods: Based on the methodology described in ISO8009, various custom mechanical tests and test apparatus were designed and developed by Queen's University Belfast. Three marketed VR products (NuvaRing®, Femring® and Estring®) were evaluated alongside three batches of IPM's 25 mg DPV ring, one batch of 200 mg DPV rings and one batch of 200-320 mg DPV+levonorgestrel (LNG) rings. All rings were evaluated for weight, cross-sectional diameter, outer diameter (OD), hardness (Shore A and Shore M), mean tensile extension, 28-day static compression, 1000-cycle compression and twist during compression testing.
Results: IPM's 25 mg and 200 mg DPV rings recovered 90-100% of their original OD following 28-day static compression. Femring® was the only product to recover 100% of its original OD. During tensile testing, the 25 mg DPV ring batches endured mean tensile loads of 68-69 kg before fracture compared to 14 kg, 28 kg, and 71 kg for Nuvaring®, Femring® and Estring®, respectively. On completion of 1000-cycle compression testing, the 25 mg DPV rings, 200 mg DPV rings, 200-320 DPV-LNG rings and Femring® showed no visible deterioration and returned to 100% of their original OD. By comparison, the Nuvaring® devices were visibly deformed and recovered only 80% of their original OD.
Conclusions: ISO8009 was used as a framework to develop a series of mechanical tests for ring devices. The results indicate that IPM's 25 mg DPV, 200 mg DPV and 200-320 mg DPV-LNG ring formulations exhibit similar mechanical properties and performance to the commercially available rings.