Next Generation Multipurpose Prevention Technology (MPT) IVR: Effect of Geometric Design on *In-Vitro* Release

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BACKGROUND

Multipurpose Prevention Technologies (MPTs) are single strategy technologies, or formulations that address multiple reproductive health conditions[3]

A long-acting MPT to prevent Human Immunodeficiency Virus (HIV), Herpes Simplex Virus-2 (HSV-2) , and unintended pregnancy could overcome acceptability and adherence-related limitations to improve adherence and efficacy outcomes.

38M
People Living with HIV[3]

45%
Of All Pregnancies are Unintended[3]

Over 1M
New STIs Each Day[3]

HSV-2 increases risk of HIV infection fivefold[3].

Active Pharmaceutical Ingredients (APIs)

- **Dapivirine (DPV):** non-nucleoside reverse transcriptase inhibitor; HIV prophylaxis[1]
- **Levonorgestrel (LNG)**: progestin; hormonal contraceptive[1]
- **Pritelivir (PTV):** antiviral helicase-primase complex inhibitor; HSV-2 prevention[1]

Intravaginal Rings (IVRs)

Torus-shaped devices comprised of silicon-based, biocompatible resin capable of sustained release for one or multiple APIs. Highly acceptable as a user-controlled system that allows for facile insertion and removal at-will.

OBJECTIVE

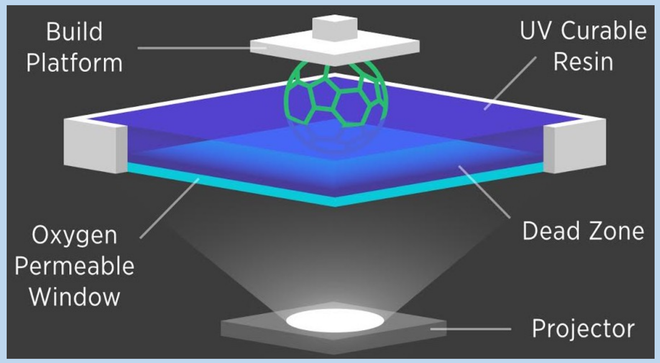
Determine which IVR designs enable sustained release of multipurpose prevention technology drugs for ≥30 days.

Targets: DPV – 200 µg/day LNG – 20 µg/day PTV – 200 µg/day

METHODS

Three ring designs, one solid (Solid) and two with varying geometric complexity (GCD1, GCD2), were designed in CAD and fabricated using Continuous Liquid Interface Production (CLIP™), a novel 3D-printing process utilizing photopolymerization[4]

- 3D-Printing enables geometrically complex ring designs to alter drug release properties[2]
- CLIP overcomes limitations with conventional injection molding IVR production



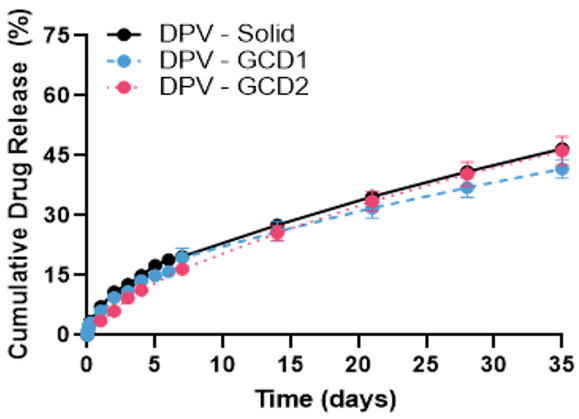
Ring Design	*Solid*	*GCD1*	*GCD2*
Specific Surface Area (SSA; mm^{-1})	0.53	0.57	6.28

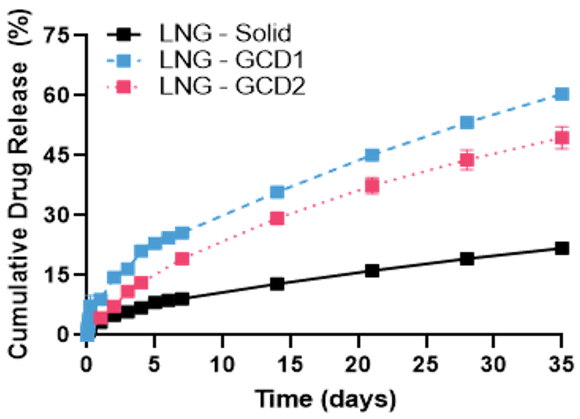
APIs were loaded onto rings by post-fabrication swelling in acetone solution. Solution concentrations to achieve target loading were determined using a weight-based loading equation.

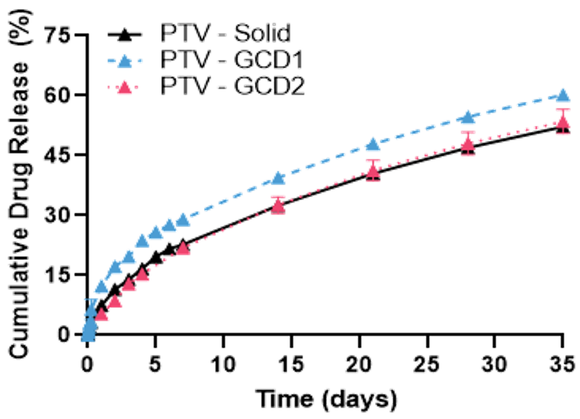
In-Vitro release studies were performed as follows:

- Rings (n=4) were submerged in 200 mL of Simulated Vaginal Fluid (NaOAc + 2% Solutol pH 4.2) and placed in an orbital shaking incubator at 37°C.
- 1 mL aliquots were removed and quantified with HPLC analysis to assess API release across 42 days.
- In the first day, samples were taken more frequently to assess burst release
- Complete media changes were performed weekly to ensure sink conditions were maintained.

RESULTS







	Ring Design	24-Hour Burst (%)	24-Hour Burst (µg)	Avg. Release Days 2-28 (µg/day)	Release Rate R^2
Dapivirine (DPV)	Solid	7.19± 0.07	2145.75 ± 20.96	318	0.99
30mg/ring	GCD1	6.02 ± 0.12	2120.21 ± 40.80	340	0.97
Target Rate: 200µg/day	GCD2	3.59 ± 0.37	1076.45 ± 109.999	387	0.99
Levonorgestrel (LNG)	Solid	3.19 ± 0.11	55.26 ± 1.93	8	0.99
2mg/ring	GCD1	8.93 ± 0.21	214.34 ± 4.94	33	0.99
Target Rate: 20µg/day	GCD2	4.37 ± 0.37	87.35 ± 7.37	28	0.98
Pritelivir (PTV)	Solid	7.45 ± 0.09	1267.34 ± 15.44	206	0.97
20mg/ring	GCD1	12.36 ± 0.82	2541.37 ± 168.98	263	0.97
Target Rate: 200µg/day	GCD2	5.34 ± 0.49	1067.66 ± 97.82	296	0.98

CONCLUSIONS

- Dapivirine release was well above target in all ring designs.
- Pritelivir release was at or above target in all ring designs.
- Levonorgestrel release in solid ring failed to meet target.
- No rings achieved 100% release within the 30-day timeframe.

FUTURE DIRECTIONS

- Continue monitoring release for extended duration (60+ days)
- Alter drug loadings to achieve optimal release rates

References

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2. Janusziewicz, R., Mecham, S. J., Olson, K. R., & Benhabbour, S. R. (2020). Design and Characterization of a Novel Series of Geometrically Complex Intravaginal Rings with Digital Light Synthesis. *Advanced materials technologies*, *5*(8), 2000261. https://doi.org/10.1002/admt.202000261

3. Young, I. C., & Benhabbour, S. R. (2021). Multipurpose Prevention Technologies: Oral, Parenteral, and Vaginal Dosage Forms for Prevention of HIV/STIs and Unplanned Pregnancy. *Polymers*, *13*(15), 2450. https://doi.org/10.3390/polym13152450

4. Carbon3D