



## 3D printed intravaginal rings

Based on public information

## Developer(s)

AnelleO, inc.

Originator

<https://anelleo.com/about-anelleo/>



United States

Anelleo, Inc. is located in Chapel Hill, North Carolina. Current support and funding is provided by NIH-NICHD (Phase I STTR) and strategic partners (Carbon, Inc. & undisclosed pharma partnerships) to allow AnelleO to complete prototyping, preclinical studies, and IND-enabling studies.

## Sponsor(s)



National Institute of Health (NIH-NICHD) (Phase I STTR funding)

<https://www.nih.gov>

## Partnerships

**Carbon<sup>®</sup>**

Carbon Inc.

<https://www.carbon3d.com/>

# Technology information

## Type of technology

Intra-vaginal ring

## Administration route

Topical (Vaginal)

## Development state and regulatory approval

### Active Pharmaceutical Ingredient (API)

Etonogestrel (ENG)

### Development Stage

Pre-clinical

### Regulatory Approval

Not provided

## Description

The 3D-printed intravaginal ring (IVR) represents a non-invasive, self-administered technology designed to provide localized, controlled drug release. This innovative device allows for the combination of various active pharmaceutical ingredients (APIs) within a single dosage form. Fabricated using a two-part silicone polyurethane resin (Silicone urethane from Carbon Inc.), the 3D IVR is capable of delivering drugs over an extended period of 8–10 weeks. The intricate geometries of the 3D-printed IVR enable precise and controlled drug release kinetics, enhancing its efficacy and reliability.

## Technology highlight

1) Self-administration: The IVR can be easily administered by the user, enhancing convenience and compliance. 2) Initial Burst Release: Upon administration, the IVR provides an initial burst release of 15% of the API. 3) Customizable Structure: The IVR can be tailored based on shape, size, volume, API loading capacity, and surface area to meet specific therapeutic needs. 4) Low Systemic Toxicity: The localized drug delivery system minimizes systemic toxicity. 5) Controlled Pharmacokinetics: The IVR is designed to deliver drugs with controlled pharmacokinetics, ensuring sustained release rate. 6) Dual API Delivery: The IVR has the potential to deliver two different APIs simultaneously, each with its own distinct release rate.

## Technology main components

1) Two part Polyurethane resin 2) 0.01 %wt Rhodamine 3) Pore forming agent (Eg: PEG 3000; PEG 6000; PEG 8000; Hydroxy cellulose; PVA 10000; PVA 10000) 4) Plasticizer 5) Stabilizer 6) Filler 7) API (added during or after 3D printing)

## Information on the raw materials sourcing, availability and anticipated price

The polyurethane material and the three dimensional printing technology is obtained from Carbon Inc.

## Delivery device(s)

No delivery device

# APIs compatibility profile

## API desired features

### Water-soluble molecules

### Water-insoluble molecules

### Small molecules

Both hydrophobic and hydrophilic small molecules are suitable for Intravaginal ring (IVR), however molecules must be able to withstand the heat and pressure of the manufacturing process. The selected pharmacological classes of interest encompass antivirals, antiretrovirals, microbicides, contraceptives, antibiotics, and hormones.

### Proteins

The IVR formulation is designed to target macromolecular drugs, including dendrimers, biopharmaceuticals, chemotherapeutics, and biologics (e.g., antibodies, peptides).

### Additional solubility data

Not provided

### Additional stability data

Not provided

### API loading: Maximum drug quantity to be loaded

75-90 wt%



## API co-administration

1 single API :

### LogP

Min: -1 Max: 5

# **Scale-up and manufacturing prospects**

## **Scale-up prospects**

The manufacturing of IVR is multistep process which limits the scalability of these 3D printed IVRs in time and cost efficient process.

## **Tentative equipment list for manufacturing**

1) Hot melt extrusion - Single/ Twin Screw Extruder 2) Injection Molding - Injection Molding machine (Injection unit and clamping Unit)

## **Manufacturing**

The fabrication of the IVR involves either hot melt extrusion or injection molding, requiring at least 3-4 steps to complete the process. Key manufacturing considerations include: 1) The API must be miscible in the melted polymer. 2) The API must remain stable and not undergo phase separation upon cooling. 3) The API must withstand high temperatures, specifically 120°C at 90 psi for injection molding and 150-160°C for hot melt extrusion.

## **Specific analytical instrument required for characterization of formulation**

1) Environmental Scanning Electron Microscope (ESEM) 2) Fluorescence Microscope 3) Carbon CLIP Printer 4) Instron 5566 Universal Test System and 100N load cell 5) High Performance Liquid Chromatography (HPLC)

**Clinical trials**

Not provided

# Excipients

## **Proprietary excipients used**

No proprietary excipient used

## **Novel excipients or existing excipients at a concentration above Inactive Ingredients Database (IID) for the specified route of administration**

No novel excipient or existing excipient used

## **Residual solvents used**

No residual solvent used

# **Additional features**

## **Other features of the technology**

- Drug-eluting
- Removable
- 3d-printed
- Molded
- Reservoir-type

## **Release properties**

In vitro studies conducted on animal models have demonstrated that the release of the drugs was sustained over a period of 150 days, with all drugs exhibiting a minimal burst release within the first 24 hours. Furthermore, the release kinetics varied significantly between hydrophilic drugs, such as islatravir, and hydrophobic drugs, such as hormones.

## **Injectability**

This formulation is non-injectable.

## **Safety**

Mild neutrophil infiltrates were observed in animals treated with intravaginal rings containing hormones; however, no other toxicity was detected.

## **Stability**

Not provided

## **Storage conditions and cold-chain related features**

Not provided



## Potential application(s)

### Therapeutic area(s)

HIV

Contraception

Other(s) : "Prevention of STD like HSV, HPV and other infections such as UTI, cystitis, chlamydia. Other indications are hormone replacement therapy, infertility, and other women health conditions."

### Use case(s)

Pre-Exposure Prophylaxis (PrEP)

Treatment

### Use of technology

#### Ease of administration

- Self-administered

#### Frequency of administration

Weekly, Monthly

#### User acceptance

Not provided

## Targeted user groups

### Age Cohort

- Adults
- Older Adults

### Genders

- Female
- Cisgender female
- Transgender female

### Pregnant individuals

Unspecified

### Lactating individuals

Unspecified

### Healthy individuals

Unspecified

### Comment

Not provided



## Potential associated API(s)

### Etonogestrel (ENG)

#### Class(es)

Synthetic Progestrone

#### Development stage

Pre-clinical

#### Clinical trial number(s)

Not provided

#### Foreseen/approved indication(s)

Hormone replacement therapy

#### Foreseen user group

Not provided

#### Foreseen duration between application(s)

Once monthly

#### Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

## Ethinylestradiol (EE)

### Class(es)

Synthetic estrogen

### Development stage

Pre-clinical

### Clinical trial number(s)

Not provided

### Foreseen/approved indication(s)

Hormonal replacement therapy

### Foreseen user group

Not provided

### Foreseen duration between application(s)

Once monthly

### Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

## Islatravir (ISL)

### Class(es)

Nucleoside Reverse Transcriptase Translocation Inhibitor

### Development stage

Pre-clinical

### Clinical trial number(s)

Not provided

### Foreseen/approved indication(s)

HIV

### Foreseen user group

Not provided

### Foreseen duration between application(s)

Once monthly

### Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

## Dapivirine (DPV)

### Class(es)

Non-nucleoside Reverse transcriptase inhibitors

### Development stage

Pre-clinical

### Clinical trial number(s)

Not provided

### Foreseen/approved indication(s)

HIV

### Foreseen user group

Not provided

### Foreseen duration between application(s)

Once monthly

### Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

## Levonorgestrel (LNG)

### Class(es)

Synthetic progestogen

### Development stage

Pre-clinical

### Clinical trial number(s)

Not provided

### Foreseen/approved indication(s)

Contraceptive

### Foreseen user group

Not provided

### Foreseen duration between application(s)

Once monthly

### Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided



## Patent info

## Description

Methods, Systems and Devices for Post-Fabrication Drug Loading

### Brief description

A post-fabrication method for drug loading a medical device with an active pharmaceutical ingredient (API). Such medical devices can include a polymer matrix, where the polymer matrix, after exposure to a loading solution with the API, can exhibit a degree of swelling of the polymer matrix and/or a degree of swelling in which the polymer matrix increases in a dimension along an axis. The medical devices include intravaginal rings (IVR). Medical devices including a polymer matrix and an API are provided, where the API is loaded into the polymer matrix by adsorption and/or swelling after fabrication of the polymer matrix, wherein the medical device provides a substantially sustained release of the API for an extended period of time.

### Representative patent

US20230338278A1

### Category

Not provided

### Patent holder

University of North Carolina at Chapel Hill

### Exclusivity

Not provided

### Expiration date

September 17, 2041

### Status

Granted



## Description

Methods Of Producing Polyurethane Three - Dimensional Objects from Materials having Multiple Mechanisms Of Hardening

## Brief description

A three-dimensional object made of polyurethane, polyurea, or copolymer thereof is created by: (a) providing a carrier and an optically transparent member with a build surface, the carrier and the build surface defining a build region therebetween; (b) filling the build region with a polymerizable liquid that contains at least one of the following: (i) a blocked or reactive blocked prepolymer; (ii) a blocked or reactive blocked diisocyanate; or (iii) a blocked or reactive blocked diisocyanate chain extender; (c) irradiating the build region with light through the optically transparent member to form a solid blocked polymer scaffold and moving the carrier away from the build surface to form a three-dimensional structure.

## Representative patent

US10647880B2

## Category

Technology

## Patent holder

Carbon , Inc.

## Exclusivity

Not provided

## Expiration date

February 7, 2039

## Status

Granted

## Description

Geometrically complex intravaginal rings, systems and methods of making the same

## Brief description

Geometrically complex intravaginal rings, systems and methods of making the same are provided herein. Disclosed herein are geometrically complex intravaginal rings with tunable and enhanced drug release, which in some embodiments can be fabricated by 3D printing technologies. The disclosed IVRs include a ring structure comprising a plurality of unit cells or macroscopic and/or microscopic architecture, which can be tuned to control the loading capacity of an active compound within the IVR, the diffusion of an active compound from the IVR, the surface area of the IVR, and/or the mechanical properties of the IVR. The geometrically complex IVRs can provide superior control over drug loading and drug release compared to conventional IVRs fabricated by injection molding.

## Representative patent

WO2017165624A1

## Category

formulation

## Patent holder

The University of North Carolina at Chapel Hill

## Exclusivity

Not provided

## Expiration date

March 23, 2037

## Status

Granted

## **Supporting material**

## Publications

Young, I. C., Srinivasan, P., Shrivastava, R., Janusiewicz, R., Thorson, A., Cottrell, M. L., Sellers, R. S., Sykes, C., Schauer, A., Little, D., Kelley, K., Kashuba, A. D. M., Katz, D., Pyles, R. B., García-Lerma, J. G., Vincent, K. L., Smith, J., & Benhabbour, S. R. (2023). Next generation 3D-printed intravaginal ring for prevention of HIV and unintended pregnancy. *Biomaterials*, 33, 301-312. <https://doi.org/10.1016/j.biomaterials.2023.122260>

Here we report the first 3D-printed multipurpose prevention technology (MPT) intravaginal ring (IVR) for HIV prevention and contraception. We utilized continuous liquid interface production (CLIP™) to fabricate MPT IVRs in a biocompatible silicone-based resin. Etonogestrel (ENG), ethinyl estradiol (EE), and islatravir (ISL) were loaded into the silicone poly(urethane) IVR in a controlled single step drug loading process driven by absorption. ENG/EE/ISL IVR promoted sustained release of drugs for 150 days in vitro and 14 days in sheep. There were no adverse MPT IVR-related findings of cervicovaginal toxicity or changes in vaginal biopsies or microbiome community profiles evaluated in sheep. ISL IVR in macaques promoted sustained release for 28 days with ISL-triphosphate levels above the established pharmacokinetic benchmark of 50-100 fmol/10<sup>6</sup> PBMCs. The ISL IVR was found to be safe and well tolerated in the macaques with no observed mucosal cytokine changes or alterations in peripheral CD4 T-cell populations. Collectively, the proposed MPT IVR has potential to expand preventative choices for young women and girls.

Janusiewicz, 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>

Intravaginal rings (IVRs) represent a sustained-release approach to drug delivery and have long been used and investigated for hormones and microbicides delivery. For decades, IVRs have been manufactured by injection molding and hot-melt extrusion with very limited design and material capabilities. Additive manufacturing (AM), specifically digital light synthesis (DLS), represents an opportunity to harness the freedom of design to expand control and tunability of drug release properties from IVRs. A novel approach to IVR design and manufacturing is reported that results in geometrically complex internal architectures through the incorporation of distinct unit cells using computationally aided design (CAD) software. A systematic approach is developed to design through the generation of an IVR library and the effects of these parameters are investigated on ring properties. The ability to precisely and predictably control the compressive properties of the IVR independent of the internal architecture with which control of drug release kinetics can be achieved is demonstrated, thus opening the door for a “plug-and-play” platform approach to IVR fabrication.

## Additional documents

No documents were uploaded

## Useful links

There are no additional links

# Access principles

## Collaborate for development



Consider on a case by case basis, collaborating on developing long acting products with potential significant public health impact, especially for low- and middle-income countries (LMICs), utilising the referred to long-acting technology

**Not agree**

## Share technical information for match-making assessment



Provide necessary technical information to a potential partner, under confidentiality agreement, to enable preliminary assessment of whether specific medicines of public health importance in LMICs might be compatible with the referred to long-acting technology to achieve a public health benefit

**Not agree**

## Work with MPP to expand access in LMICs



In the event that a product using the referred to long-acting technology is successfully developed, the technology IP holder(s) will work with the Medicines Patent Pool towards putting in place the most appropriate strategy for timely and affordable access in low and middle-income countries, including through licensing

**Not agree**



## **Comment & Information**

## Illustrations



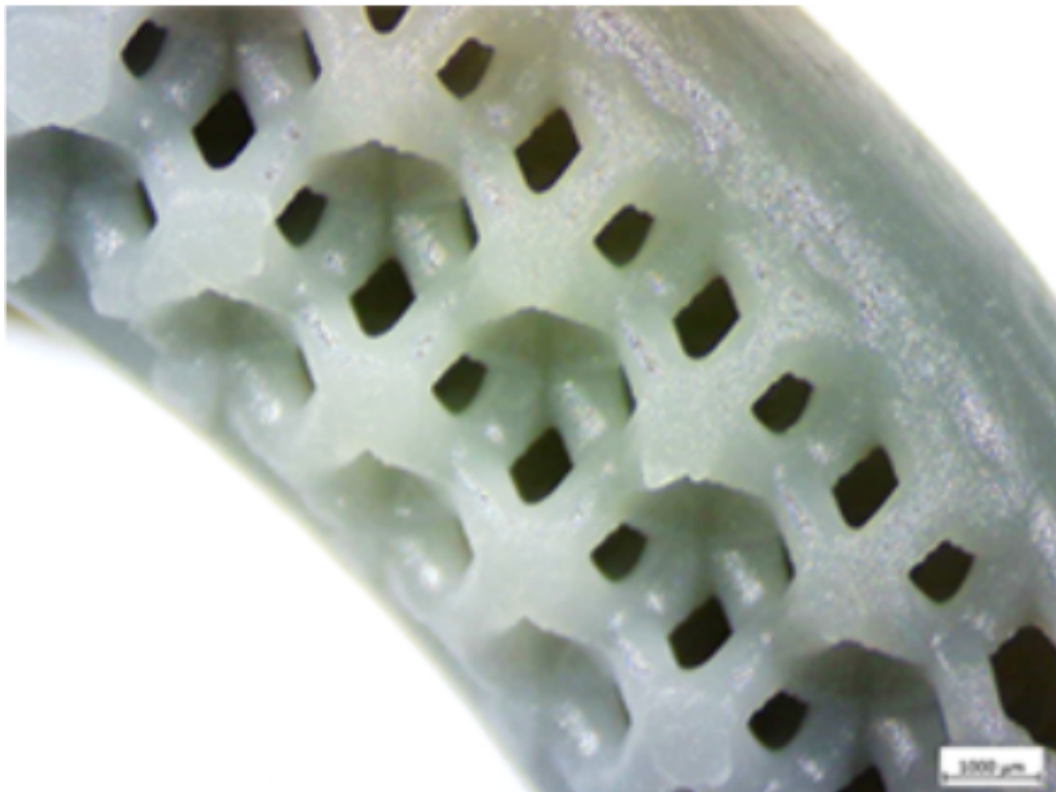
3-D intravaginal ring

AnelleO. (n.d.). Products. AnelleO. Retrieved July 3, 2024, from <https://anelleo.com/products/>



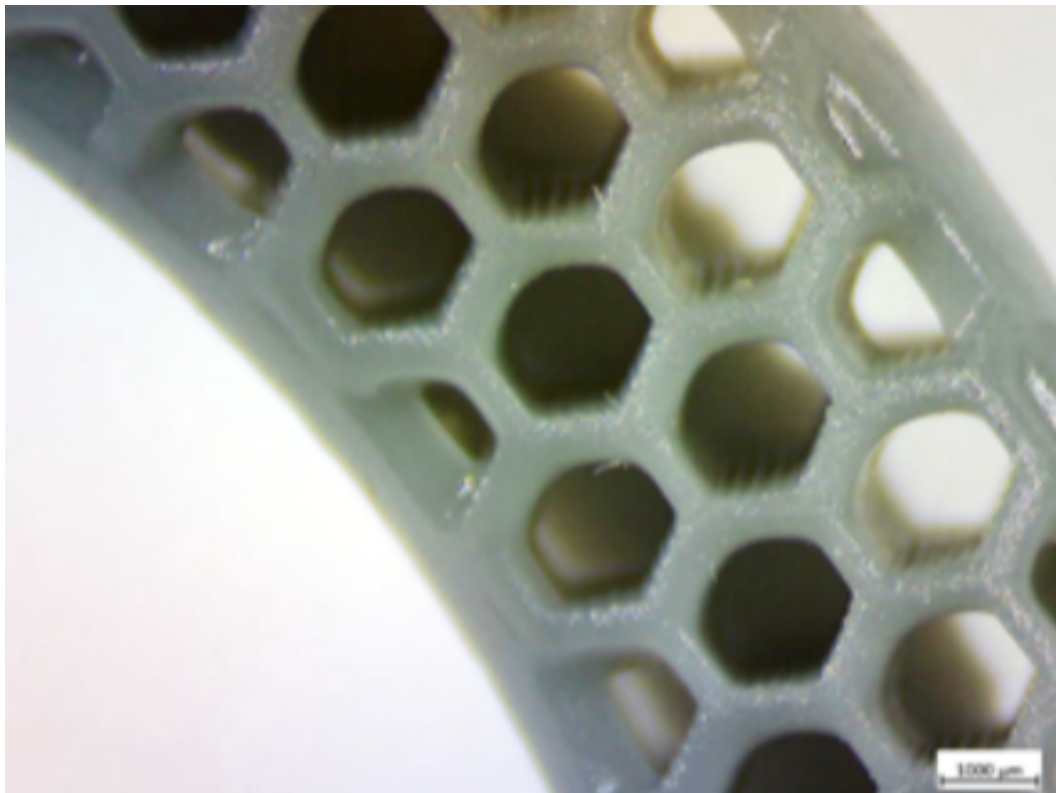
Geometric complex structure of intravaginal ring (Cylindrical type)

AnelleO. (n.d.). Products. AnelleO. Retrieved July 3, 2024, from <https://anelleo.com/products/>



### Geometric complex structure of intravaginal ring (Trident Type)

AnelleO. (n.d.). Products. AnelleO. Retrieved July 3, 2024, from <https://anelleo.com/products/>



### Geometric complex structure of intravaginal ring (Honey Comb Type)

AnelleO. (n.d.). Products. AnelleO. Retrieved July 3, 2024, from <https://anelleo.com/products/>