LAPaL
THE LONG-ACTING THERAPEUTICS PATENTS AND LICENCES DATABASE

Developed by

medicines patent pool

UNIVERSITY OF LIVERPOOL

CELT

Supported by

Unitaid
SAVE LIVES FASTER

leap

3D printed intravaginal rings

Based on public information

Developer(s)

AnnelleO, 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 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., Janusziewicz, 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, 301, 122260. 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/106 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.

** 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</p>

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

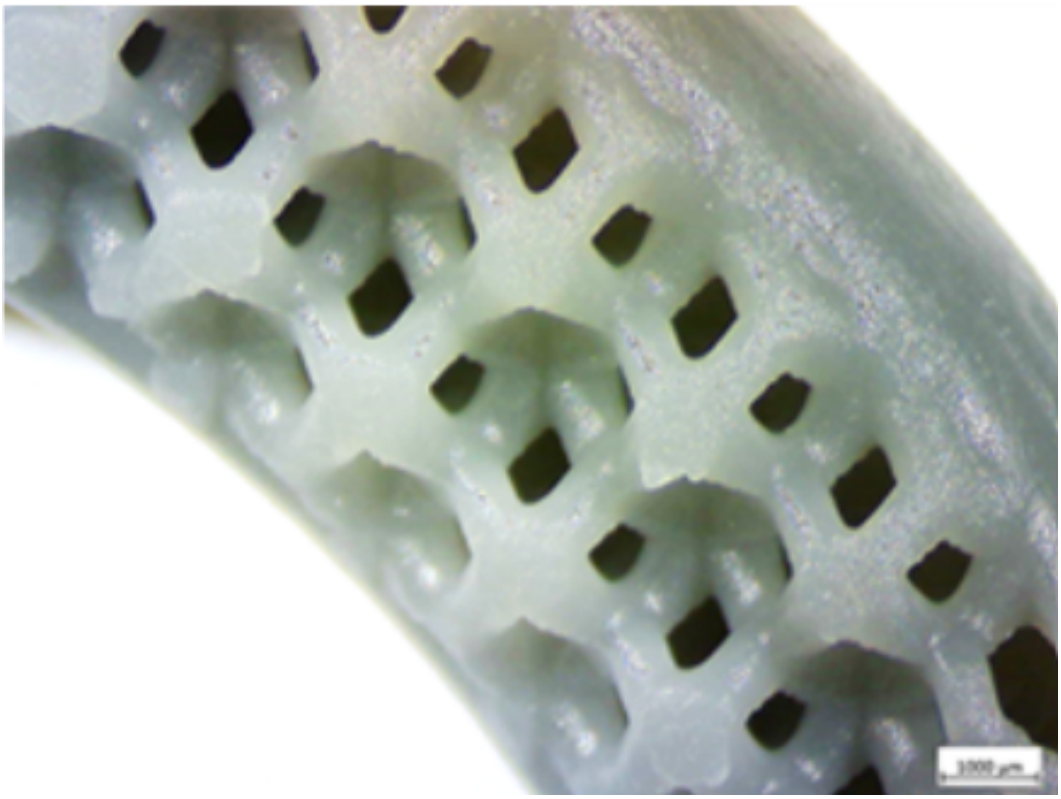
Illustrations

3-D intravaginal ring

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

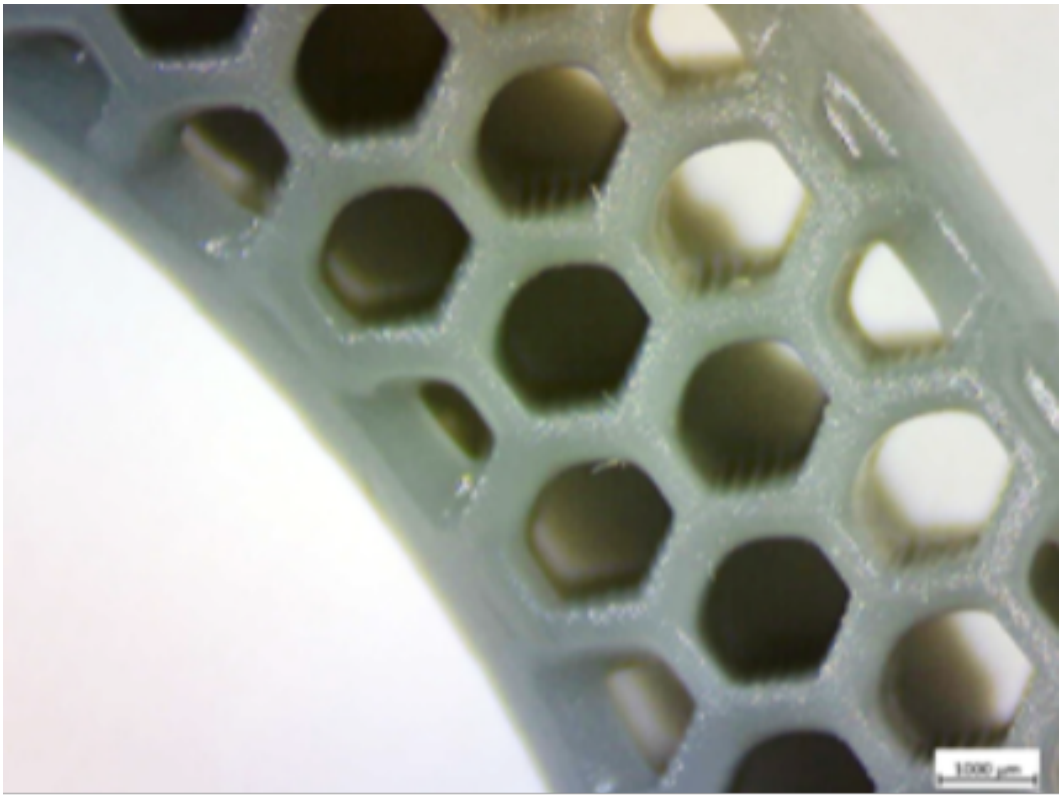
Geometric complex structure of intravaginal ring (Cylindrical type)

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/