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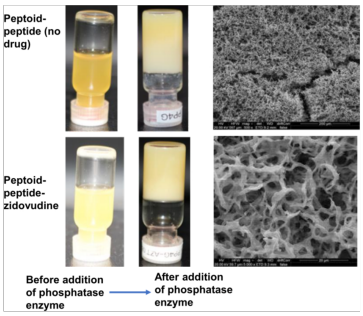


Peptide-like hydrogels as a long-acting injectable drug delivery platform

Verified by the innovator, on Nov 2023

Developer(s)

Queen's University Belfast
https://www.lavertylab.com/

N. Ireland

Queen's University Belfast is a leading UK university for knowledge exchange, and commercialisation. The School of Pharmacy is one of Queen's University Belfast's most prestigious departments and a global leader in drug delivery. It is the top ranking UK School of Pharmacy (Complete University Guide 2024) and 39th in the world (2023 QS Rankings).

Sponsor(s)

EPSRC

https://gtr.ukri.org/projects?ref=EP%2FS031561%2F1

Invest NI

https://www.investni.com/

Wellcome Trust

https://wellcome.org/

The Royal Society

https://royalsociety.org/

Innovate UK

https://www.ukri.org/councils/innovate-uk/?_ga=2.249041671.1434978779.1695123556-567133346.169167901

MRC

https://www.ukri.org/councils/mrc/

The Institut Laue–Langevin

https://www.ill.eu/

Science and Technology Facilities Council

https://www.ukri.org/councils/stfc/

Partnerships

ViiV Healthcare

https://viivhealthcare.com/

Technology information

Type of technology

Peptides and peptide-like molecules, In-situ forming gel/implant

Administration route

Subcutaneous, Intramuscular, Intra-vitreal

Development state and regulatory approval

Active Pharmaceutical Ingredient (API)

Anti-infectives for systemic use, Antivirals for systemic use, Cabotegravir (CAB), Lamivudine (3TC)

Development Stage

Pre-clinical

Regulatory Approval

Not provided

Description

We have created a soluble injection that is able to incorporate multiple drugs in a water-based solvent. This forms a hydrogel implant in response to enzymes present within the skin to release drugs long-term, removing the need for daily dosing. Our injectable implant is composed of peptide-like molecules which are capable of forming tissue-like hydrogels that can be tailored to gradually release drugs. This will remove the need for patients to comply with complex drug dosing regimens on a daily basis and improve their adherence to medication

Technology highlight

We have so far proven our technology can deliver the HIV drug zidovudine to rats at IC90 values for at least 35 days. We believe protection can be lengthened i.e. to 84 days by using more potent HIV antiretrovirals and are currently working on this goal. These results formed part of a recent publication in Advanced Healthcare Materials (2023). DOI: doi.org/10.1002/adhm.202203198. We have also demonstrated hydrogel formation and sustained release using several drugs/diseases (doxorubicin [cancer], haloperidol [antipsychotic]) and as a single injectable multipurpose technology (HIV prevention + contraception). Our most promising technology has formed part of a patent submission to the UK Patent Office on 31st March 2023 (2304871.3).

Technology main components

Low molecular weight peptide and peptide-mimetic (peptoid, D-peptide) molecules covalently attached to drugs.

Information on the raw materials sourcing, availability and anticipated price

Fmoc protected amino acids, primary amines

Delivery device(s)

No delivery device

APIs compatibility profile

API desired features

Small molecules

This formulation works best with drugs of low molecular weight (<~1200 Da) as it allows precise covalent attachment of drug to the peptide/peptide-like molecule. There is the potential to study delivery of larger biologics but these would likely have to be physically mixed with peptide/peptide-like molecule.

Additional solubility data

Not provided

Additional stability data

Not provided

API loading: Maximum drug quantity to be loaded

We have tested up to 5%w/v so far. We see no reason why this could not be increased as the peptide provides increased water solubility to drugs.

API co-administration

3 different APIs : We have tested up to 3 hydrophobic drugs successfully so far (2xHIV antiretrovirals + 1 contraceptive hormone)

LogP

Not provided

Scale-up and manufacturing prospects

Scale-up prospects

The formulation's peptide/peptide-like molecule is low molecular weight and can be readily synthesised using common solid phase synthesis protocols. The impact of manufacture on synthetic factors should be considered e.g. yield, raw material availability, novel vs. established methods of chemical conjugation, chemical orthogonality, analysing to regulatory requirements e.g. Pharmacopoeial, green chemistry and overall cost.

Tentative equipment list for manufacturing

Preparative LC with Mass Spec capability for efficient purification

Manufacturing

The peptide is made by chemical synthesis, requirements will depend mainly of drug of interest. e.g. a steroid drug for contraception will required increased safety considerations in line with cGMP.

Specific analytical instrument required for characterization of formulation

Analytical HPLC, preferably with Mass Spec capability. Hydrogen and Phosphate NMR.

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

Not provided

Additional features

Other features of the technology

- Biodegradable
- Single-use

Release properties

Zidovudine drug burst release reduced by 30% (from 79% released at 72 hrs, physical encapsulation) to 48% release upon attachment of drug to our most promising molecule a peptoid-peptide.

Injectability

Injected as a solution, rapidly forms a hydrogel upon administration. Hydrogel begins to form within 1-2 minutes, fully forms ~20 minutes. The low viscosity and volume of the dissolved formulations permit use of narrow bore needles to improve patient acceptance.

Safety

No signifiicant toxicity (L929 cells) via Live/Dead, MTS and LDH assays. Studies in rats (histological, mass) show no adverse effects for study period (at least 2 months currently).

Stability

Currently undergoing ICH stability assays. Type 1 glass vials preferred packaging choice as they offer the highest hydrolytic resistance.

Storage conditions and cold-chain related features

In practice, this formulation – prepared as highly stable freeze-dried powders – will be first readily dissolved in sterile water/buffer and then immediately administered via injection.

Potential application(s)

Therapeutic area(s)

Malaria

Contraception

Multipurpose technology : "Combined HIV prevention and contraception in one injectable product"

HIV

Oncology

Substance use disorders

Mental health

Use case(s)

Pre-Exposure Prophylaxis (PrEP)

Post-Exposure Prophylaxis (PEP)

Treatment

Use of technology

Ease of administration

- Administered by a community health worker
- Administered by a nurse
- Administered by a specialty health worker
- Self-administered

Frequency of administration

Monthly, We are aiming for a minimum dosgae interval of every 3 months (84 days)

User acceptance

We have performed studies with UK HIV charity Positive Life NI. Patients demonstrate a high interest in the use of such technology to replace oral medicines.

Targeted user groups

Age Cohort

- Adolescents
- Adults

Genders

- All

Pregnant individuals

Unspecified

Lactating individuals

Unspecified

Healthy individuals

Unspecified

Comment

Main target group would be within adolescent and young women who require a discrete technology to provide combined HIV prevention and contraception.

Potential associated API(s)

Anti-infectives for systemic use, Antivirals for systemic use, Cabotegravir (CAB), Lamivudine (3TC)

Class(es)

antiviral

Development stage

Pre-clinical

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

HIV prevention

Foreseen user group

Not provided

Foreseen duration between application(s)

Not provided

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

Genito-urinary system and sex hormones, Progestogens

Class(es)

Contraceptive

Development stage

Pre-clinical

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

Combined HIV prevention and contraception

Foreseen user group

Not provided

Foreseen duration between application(s)

Not provided

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

Haloperidol

Class(es)

Not provided

Development stage

Pre-clinical

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

Not provided

Foreseen user group

Not provided

Foreseen duration between application(s)

Not provided

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

Antineoplastic and immunomodulating agents

Class(es)

Anthracycline chemotherapy

Development stage

Pre-clinical

Clinical trial number(s)

Not provided

Foreseen/approved indication(s)

Cancer

Foreseen user group

Not provided

Foreseen duration between application(s)

Not provided

Applications to Stringent Regulatory Authorities (SRA) / regulatory approvals

Not provided

Patent info

Description

Patent application submitted to UK Patent Office on 31st March 2023. • United Kingdom Priority Patent Application No. 2304871.3 AN INJECTABLE DELIVERY SYSTEM FOR LONG-ACTING ADMINISTRATION OF DRUGS "Peptoid-peptide hydrogel drug delivery platform" filed 31/03/2023.

Brief description

Not provided

Representative patent

Patent Application No. 2304871.3

Category

Formulation/platform

Patent holder

Garry Laverty, Sreekanth Pentlavalli, Sophie Coulter, Emily Cross, Queen's University Belfast

Exclusivity

Not provided

Expiration date

Not provided

Status

Applied awaiting approval

Supporting material

Publications

** Advanced Healthcare Materials **

Eradicating HIV/AIDS by 2030 is a central goal of the World Health Organization. Patient adherence to complicated dosage regimens remains a key barrier. There is a need for convenient long-acting formulations that deliver drugs over sustained periods. This paper presents an alternative platform, an injectable in situ forming hydrogel implant to deliver a model antiretroviral drug (zidovudine [AZT]) over 28 days. The formulation is a self-assembling ultrashort d or l-α peptide hydrogelator, namely phosphorylated (naphthalene-2-ly)-acetyl-diphenylalanine-lysine-tyrosine-OH (NapFFKY[p]-OH), covalently conjugated to zidovudine via an ester linkage. Rheological analysis demonstrates phosphatase enzyme instructed self-assembly, with hydrogels forming within minutes. Small angle neutron scattering data suggest hydrogels form narrow radius (≈2 nm), large length fibers closely fitting the flexible cylinder elliptical model. d-Peptides are particularly promising for long-acting delivery, displaying protease resistance for 28 days. Drug release, via hydrolysis of the ester linkage, progress under physiological conditions (37 °C, pH 7.4, H2O). Subcutaneous administration of Napffk(AZT)Y[p]G-OH in Sprague Dawley rats demonstrate zidovudine blood plasma concentrations within the half maximal inhibitory concentration (IC50) range (30–130 ng mL−1) for 35 days. This work is a proof-of-concept for the development of a long-acting combined injectable in situ forming peptide hydrogel implant. These products are imperative given their potential impact on society.

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 provided

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 provided

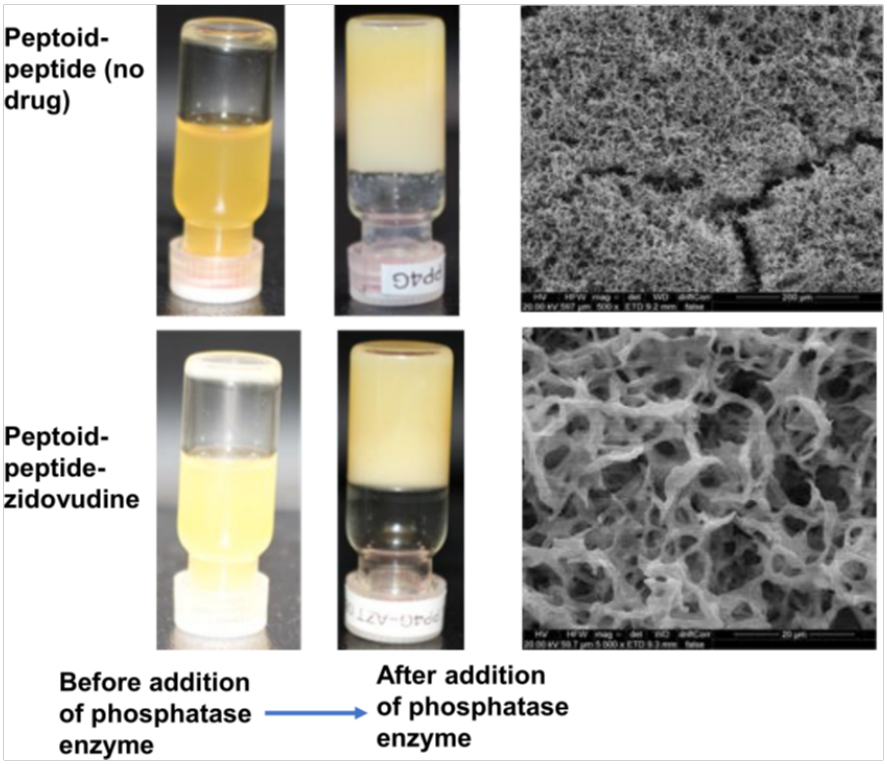
Work with MPP to expand access in LMICs

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 provided

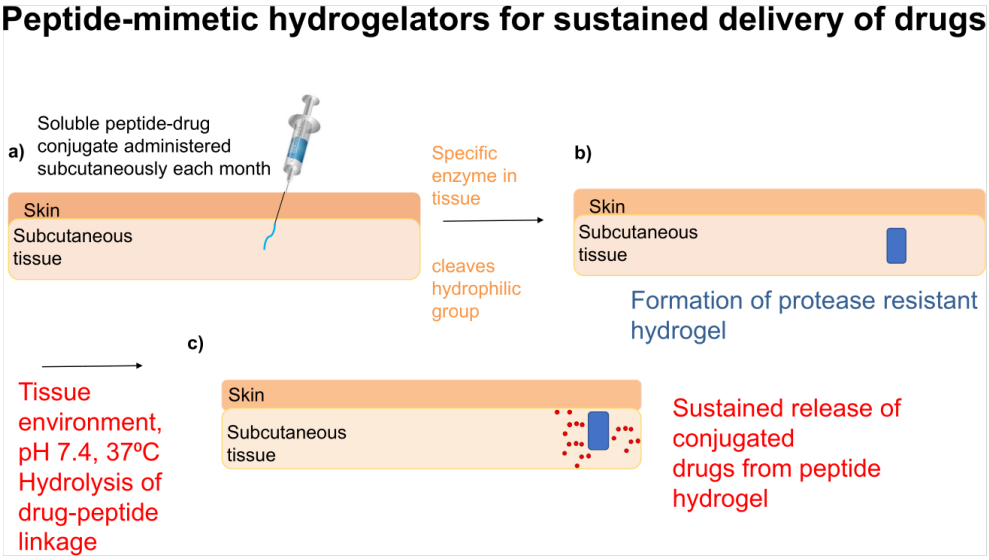
Comment & Information

Illustrations



Peptoid-peptide hydrogel formation in response to phosphatase enzyme

G Laverty



Concept peptide-like/peptide-mimetic hydrogels as long-acting injectable drug delivery systens

G Laverty