Long-acting injectable D and L-α peptide hydrogels for HIV/AIDS treatment and prevention

Poster P13

Yuming An[1], Sophie Coulter[1], Sreekanth Pentlavalli[1], Emily Cross[1], Lalitkumar Vora[1], Ralf Schweins, Garry Laverty[1]*

[1] Biofunctional Nanomaterials Group, School of Pharmacy, Medical Biology Centre Queen's University Belfast, 97 Lisburn Road, BT9 7BL.

[2] Institut Laue-Langevin, Grenoble Cedex 9 - France

Rationale

- E.g. HIV/AIDs: Sexual transmission and mother to child transmission, two major causes of HIV/AIDS infection.
- The challenge is overcoming patient medication adherence issues with drugs for HIV/AIDs.
- Need for a convenient and effective long-acting formulation to deliver drugs over a sustained period of time e.g. 28 days.

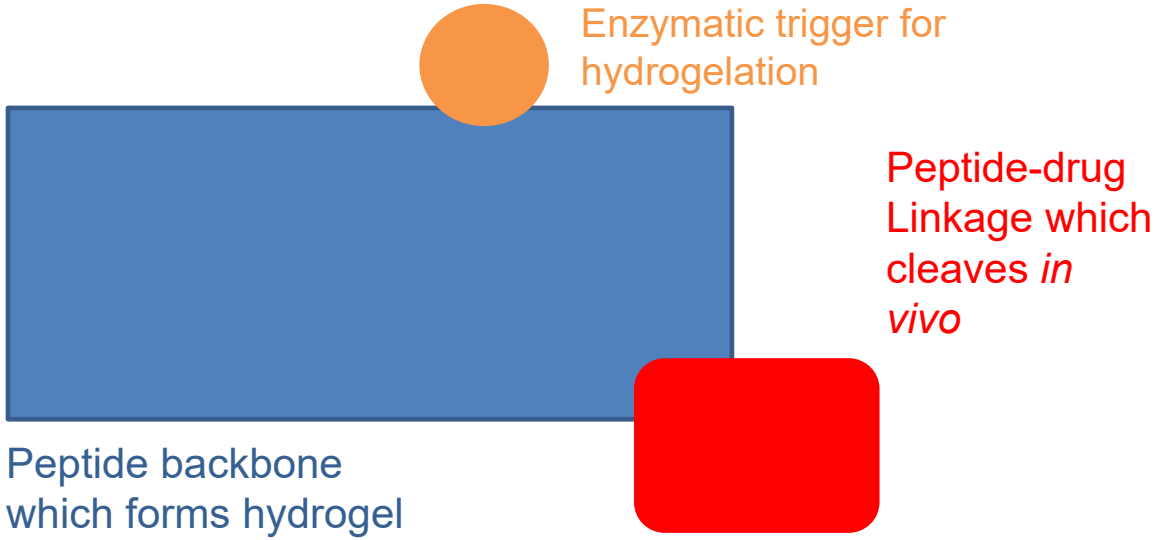


Figure 1. Structural overview of our enzyme responsive peptide drug delivery implant

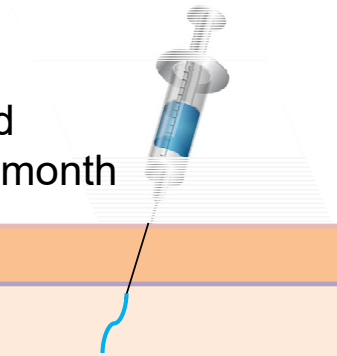
EPSRC Engineering and Physical Sciences Research Council

MRC Medical Research Council

QUEEN'S UNIVERSITY BELFAST

Peptide hydrogelators for sustained delivery of drugs

a) Soluble peptide-drug molecule administered subcutaneously each month



Skin

Subcutaneous tissue

Enzymes in tissue

cleaves group to decrease water solubility

b)

Skin

Subcutaneous tissue

Formation of protease resistant hydrogel: remains in body >28 days

Tissue environment, pH 7.4, 37ºC breaking of drug-peptide linkage

c)

Skin

Subcutaneous tissue

Sustained release of drugs from peptide hydrogel

QUEEN'S UNIVERSITY BELFAST

Advantages compared to current long-acting injectables

Limitations of current long-acting injectable technologies	Our approach
Fast drug/"burst" release after insertion leading to potential toxicity issues/concerns over-dose received	Combination of hydrogel formation and breakage of peptide-drug bond = significant reduction in "burst" release.
Need for surgery for implant insertion and removal.	Administered as a soluble injection. Hydrogel breaks down to non-toxic products *in vivo* after 28 days
A requirement for large needles (e.g. nanosuspensions)	Formulation is fully soluble in water. Enables use of narrow bore needles improving ease of administration to variety of body sites.
Stability issues upon storage/transport (e.g. due to temperature changes) which can result in clogging of syringes and incomplete dosing of drugs for suspension-based products.	Can be transported as powder for mixing with water prior to injection. Increased stability to temperature fluctuations.
Limit on type and amount of drug that can be incorporated, e.g. suspensions limited to use of water-insoluble drugs.	Drug precisely attached to peptide. Therefore, increased drug loading to meet therapeutic need for e.g. 28 days. Vast range of hydrophobic and hydrophilic drugs can be attached.

QUEEN'S UNIVERSITY BELFAST