

## Exploring the release of proteins encapsulated in a degradable PEG hydrogel.

We experience the complex world of drug delivery in our everyday lives, whether it is by taking a pill for a bothersome headache or rubbing ointment on a sprained ankle. Controlled release of the drug is essential for effective and safe, 'side effect-free' treatment. A drug cannot be given to a patient in any amount or at any moment, since the patient could be at risk of overdosing or suffering from severe side effects. I will therefore explore the use of hydrogels as a system for controlling drug delivery, hoping to contribute to a crucial area of research in medicinal chemistry.

These materials will be designed to encapsulate proteins that promote the regeneration of damaged tissue, such as FGF (Fibroblast Growth Factor). These proteins can help tissue heal as they are released from the hydrogel scaffold that is broken down by specific proteases in the tissue. Controlled release can ensure long-lasting and effective repair. Since this project may be applied in the biomedical field, it is closely aligned with the University's research themes 'Technologies for the Future' and 'Health and Wellbeing'.

In this project, I will design and build hydrogels, encapsulating different model proteins in their pores and explore their release by simulating the environment inside the human tissues. I will begin by synthesising hydrogels made from PEG (Polyethylene glycol). PEG is widely used to form hydrogels for biomedical applications as it is biologically inert.

The hydrogels will be cross-linked with peptides via nucleophilic thiol-'ene' reactions(1) via a cysteine residue at each end. The peptide will be designed to be degraded by different proteases: trypsin, chymotrypsin (used as models since they are already found in the human body) and MMP-9 (overexpressed in many cancers, making the system relevant). I will research the sequence specificity of each protease used and will design the peptides according to them.

I will investigate the encapsulation of three different model proteins of different sizes and structures (insulin, equine myoglobin, and bovine serum albumin) with different medical effects to understand how their behaviours differ. I will monitor their release after being exposed to proteases that specifically break down the gel structure, mimicking the series of events that would take place inside the human body, where these enzymes are naturally found. Each protein will be released from the gel at different rates allowing me to study the relationship between protein size/structure and release. To monitor protein release, I will use optical methods, in particular, fluorescence, adding a fluorophore (fluorescein) to the proteins and observing the release of fluorescent molecules from the hydrogel upon addition of the enzymes.

If, due to COVID-19, I have to carry out my project remotely, I would theoretically model the rate of release of the protein based on known data from previous reports.

### References:

1. Lutolf MP and Hubbell JA. *Biomacromolecules* 2003; 4: 713-722