# Biodegradable Polyester Hydrogels for Sustained Drug Delivery

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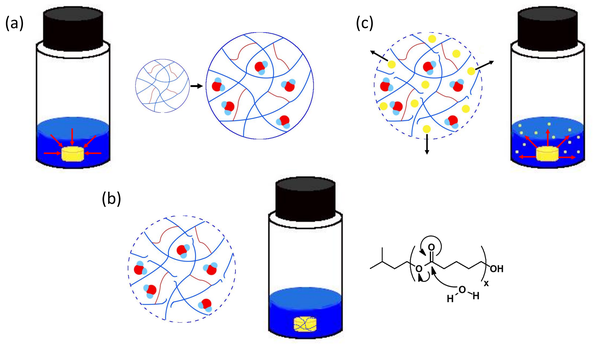
## Introduction

Polyester hydrogels created via oxime click chemistry are an attractive option as biocompatible and biodegradable drug delivery vehicles[1]. VL/OPD:AOPG polyester hydrogels can be formed in either water or DMSO without stimulus and are able to be modified by altering the polymer to cross-linker ratio. Hydrogels that degrade slowly and have a sustained linear release would allow for a reduction of invasive procedures for treating long term persistent illnesses.

The drug release rate can additionally be controlled by incorporating the drug in a complex with β-cyclodextrin or polyester nanoparticles, which would introduce an ancillary boundary that must degrade to release the drug.



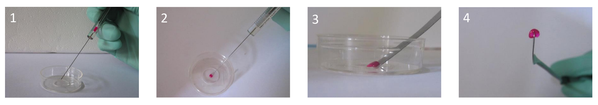

Representations of the (a) absorption, (b) degradation, and (c) drug release of VL/OPD:AOPG polyester hydrogels

**Objectives:**

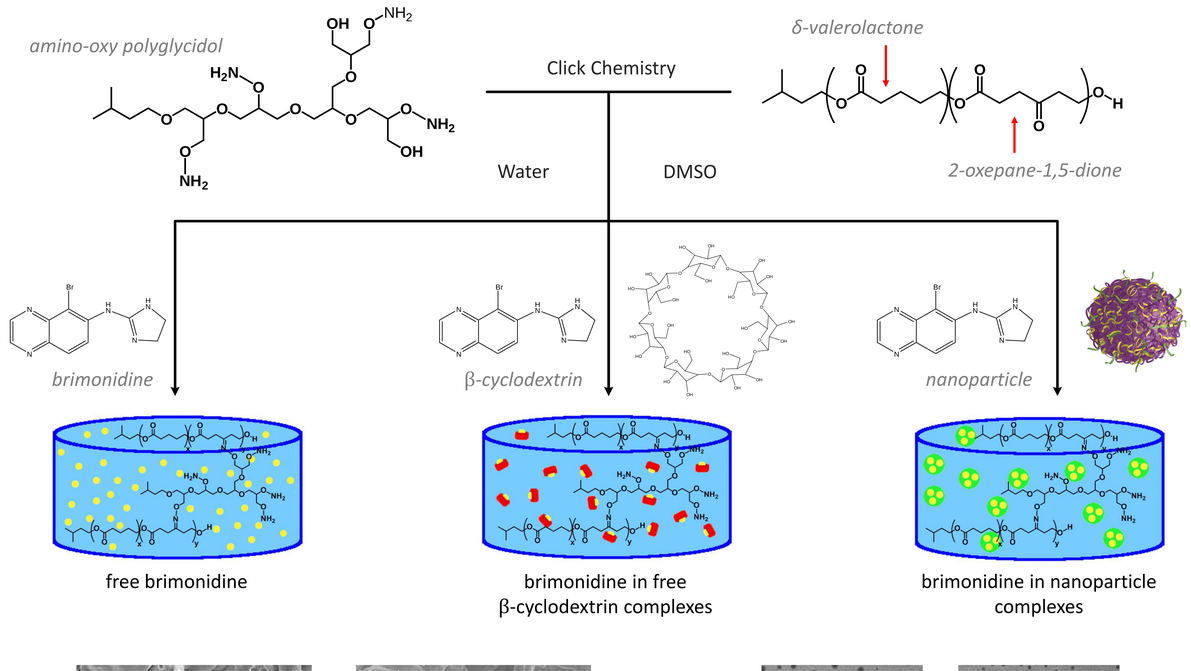
- Combine VL/OPD:AOPG in three ratios – 30:70, 50:50, 70:30
- Degrade and swell gel compositions in triplicate in PBS at 37 °C
- Brimonidine drug release profiles

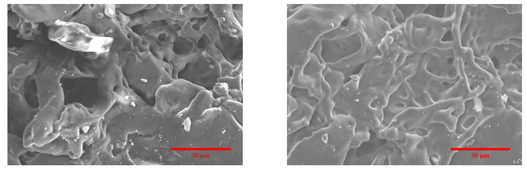
## Hydrogel Synthesis

- **Monomer Synthesis** – Creates repeat units with desired functional groups
- **Monomer Purification** – Removes impurities or byproducts from monomer synthesis
- **[1]Polymer Synthesis** – Creates polymer chains of desired molecular weight
- **[2]Crosslinker Injection** – Introduces amino-oxy functional groups to react with OPD ketones
- **[3]Gelation** – Creates network of AOPG and VL/OPD molecules
- **[4]Formed Hydrogel** – A stable, flexible hydrogel

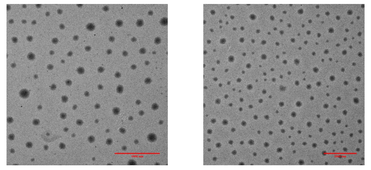



## Injectable Gel with Tailored Drug Release



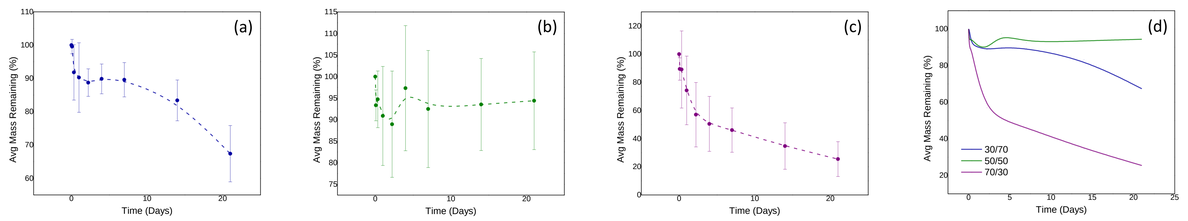



SEM images of the surface of a 50:50 VL/OPD:AOPG hydrogel. Taken at 10 kV.

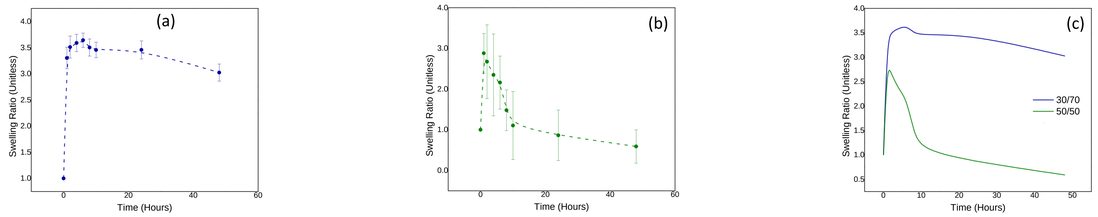


TEM images of polyester nanoparticles.

## Hydrogel Degradation and Swelling




Degradation curves of VL/OPD:AOPG hydrogels (a) 30:70 (b) 50:50 (c) 70:30 (d) all gels.




Swelling curves of VL/OPD:AOPG hydrogels (a) 30:70 (b) 50:50 (c) both gels.

## Conclusions

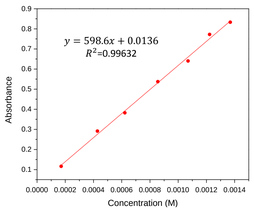
The degradation profiles show that the ester linkages in the hydrogels began to hydrolyze within the first few hours, but as they degraded, water was able to infiltrate the gels and increase the mass. After 21 days of degradation, it was shown that an equal ratio of polymer to cross-linker creates a sturdier gel due to the lack of ester bonds in the cross-linker.

The swelling profiles show that the maximum swelling ratio occurs within the first few hours of swelling before the hydrogel begins degrading. By increasing the amount of cross-linker, the hydrogels were able to stay swollen longer before degrading.

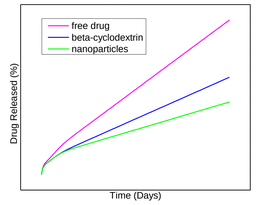
As the hydrogels form, they can be seen to form a porous network, allowing encapsulation of drug and water particles.

## Future Work

- Free brimonidine drug release profile
- Brimonidine incorporated within free β-cyclodextrin drug release profile
- Brimonidine incorporated within covalently bonded β-cyclodextrin drug release profile
- Brimonidine incorporated within polyester nanoparticles drug release profile
- Cell adhesion and proliferation




Standard curve for brimonidine at 388 nm.




Theoretical drug release profiles for brimonidine and brimonidine complexes.

## References

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[2] Van der Ende, et al., *J Am Chem Soc.* **2008,** *130* (27), 8706-13

[3] Spears, B.R., et. al., *Chem Comm*. **2013**, 49, 2394-2396.

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