Engineering Phase Separation to Induce Microstructures in Biomaterials for Controlled Release of Cancer Drugs

Naya Leslie, Saniya Yesmin Bubli, Dr. Linqing Li

Department of Bioengineering and Chemical Engineering

Background

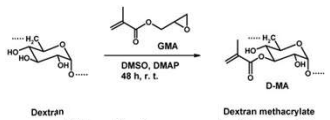
- **1 in 5** people will develop cancer within their lifetime
- Breast cancer is the most common form of cancer
- One treatment option is **chemotherapy,** but it requires frequent hospital visits and has many harmful side effects
- Hydrogels offer a promising drug delivery system but raise their own concerns like:
  - Lack of precision
  - Burst/slow release
  - Effectiveness decline
- Creating engineered hydrogels will help **resolve** these issues
- **Dextran Methacrylate (DEX-MA)** hydrogels offer a good gel synthesis material due to its tunability and **hydrophobic** nature matching the **hydrophobic** drugs used
- **Phase separation** allows for pores or domains to be formed that drugs can be encapsulated into that will allow for more controlled drug release

Materials

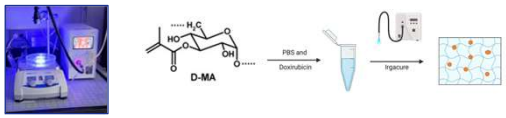
- **Doxorubicin (DOX)** is a hydrophobic chemotherapy drug
- **Phosphate Buffer Solution** is a solution with the pH of 7.4
- **Dextran** is an uncharged hydrophilic FDA-approved material
- **Irgacure 2959** is a photo-initiator that induces the photopolymerization of the dextran methacrylate hydrogel

Methods

- Dextran Methacrylate synthesis

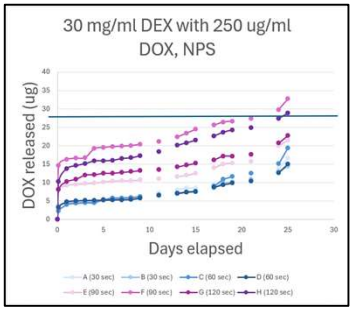


- Gel formation at 30mg/ml concentrations with doxorubicin

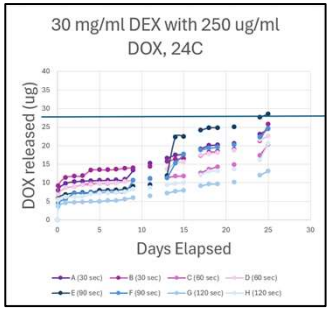


- UV vis to test drug release using UV visible light spectroscopy

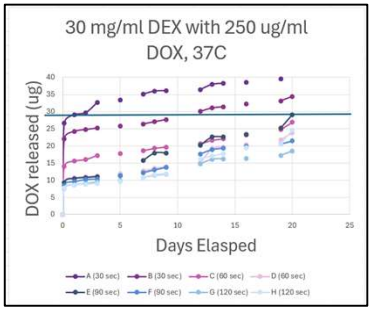
Drug Release studies



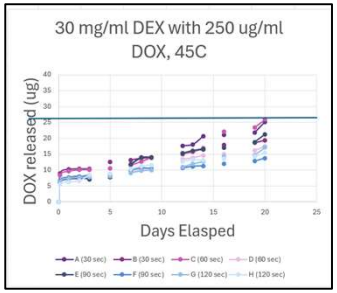
- The lower the curing time the longer the release
- Slight burst release



- The longer the curing time the longer the release
- Large jump releases in the 90 second gels



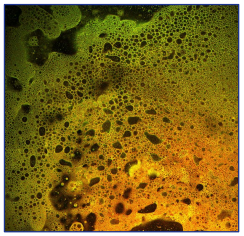
- There was an initial burst release



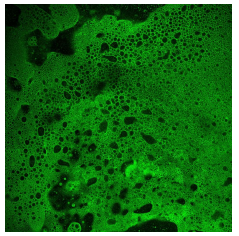
- The longer the curing time the longer the release
- More continuous release without large jumps

Imaging

Non phase separated



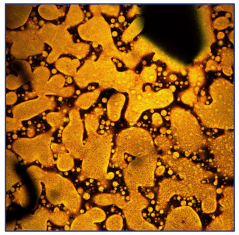
120 second cure time merged



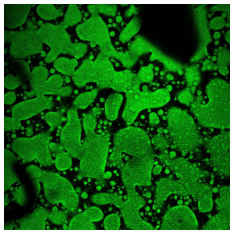
120 second cure microstructure

120 second cure time DOX

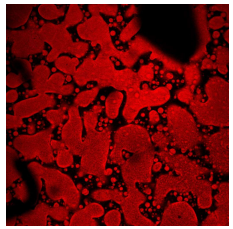
Phase separated



120 second cure time merged



120 second cure microstructure



120 second cure time DOX

Discussion

The gels lasted about 26 days for the 24c and NPS and about 21 for the 37C and 45C. During gel formation the gels were a bit soft and some broke during the first wash (37C and 45C) causing the high initial release. The non-phase separated gels had longer release times with the shorter curing times, but all phase separated gels displayed the opposite trend.

Future work

Throughout the rest of the summer more dextran concentrations in each gel will be tested, and then once all of the release profiles are known the optimal concentration will be chosen. Once the optimal dextran concentration is chosen, the doxorubicin within the test gels will be replaced with a statin drug. Then the statin-filled gels will be placed in transwell plates with SKBR3 cancer cells lined along the bottom. SKBR3 is a HER2-positive breast cancer strain.

Acknowledgements

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References

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