Evaluating Agar Hydrogels With Bupivacaine as a Potential Local Anesthetic for Post-Operative Patients

Sergio Rico-Ochoa, Biomedical Engineering
Dr. Brent Vernon, Associate Professor
School of Biological and Health Systems Engineering

Research question

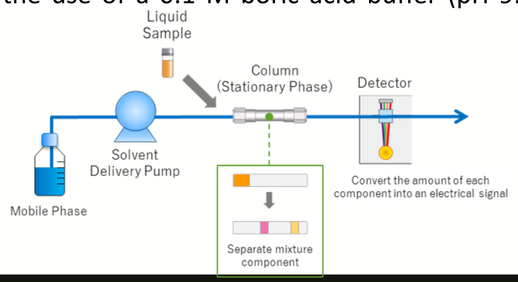
Can agar hydrogels serve as an effective test platform to quantify the release of bupivacaine, a local anesthetic, for optimizing injectable polymer matrices in post-operative pain management?

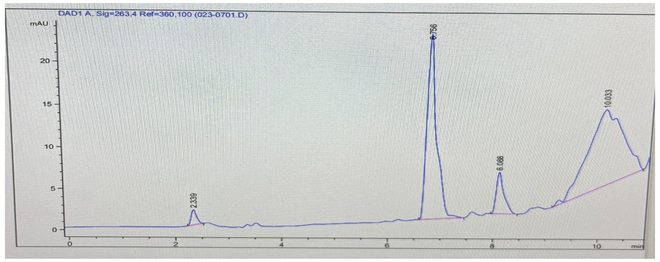
Background

-The opioid epidemic claims over 76% of U.S. drug-overdose deaths, driven largely by post-operative opioid prescriptions for procedures like knee or spinal surgeries [1].
-Local anesthetics, such as bupivacaine, offer a non-opioid alternative for pain management.
-This study uses agar hydrogels as a model system to develop and refine extraction methods for measuring bupivacaine release, supporting the design of injectable polymer matrices for sustained delivery.

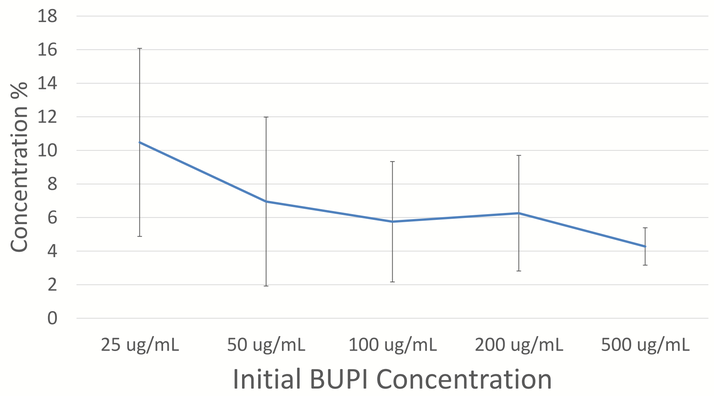
Methods

-Agar hydrogels (3% w/v) were prepared in deionized (DI) water with varying bupivacaine concentrations.
-To measure release, gels were homogenized into a liquid phase, filtered to remove agar residue, and analyzed via High-Performance Liquid Chromatography (HPLC) [2].
-Recovery percentage was calculated by comparing extracted bupivacaine to a standard concentration, with triplicate samples per condition (mean ± standard deviation).
-Initial binding between agar and bupivacaine was observed, prompting the use of a 0.1 M boric acid buffer (pH 9.18) to improve extraction.





Results



-HPLC analysis revealed low bupivacaine recovery (<10%) across all concentrations, with high variability between replicates (large standard deviations).
-Agar-bupivacaine binding reduced extractable drug levels; the boric acid buffer improved recovery slightly but remained insufficient.
-Graph: Bar chart of recovery % vs. bupivacaine concentration, showing mean ± SD for triplicate samples.

Conclusion

-Agar hydrogels bind bupivacaine, complicating extraction and reducing recovery efficiency, even with a boric acid buffer.
-While agar served as a useful test platform to identify release challenges, its binding affinity limits its utility for precise release rate quantification.
-Methods were refined throughout, laying the groundwork for alternative systems.

Next Steps

- Explore polymeric systems (e.g., gelatin or synthetic polymers) with weaker drug-binding properties to improve bupivacaine release and extraction.
-Test agar synthesis with boric acid as the solvent (vs. DI water) to reduce binding during gel formation, despite potential biocompatibility concerns.
- Validate release rates in a physiological model to bridge the gap to injectable matrices.

Acknowledgements

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[1]https://www.cdc.gov/overdose-prevention/about/understanding-the-opioid-overdose-epidemic.html
[2] https://www.ssi.shimadzu.com/service-support/technical-support/analysis-basics/basic/what_is_hplc.html

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Ira A. Fulton Schools of Engineering
Arizona State University