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| **Feasibility of ultrasound mediated oral biopharmaceutical delivery: In-vitro gastrointestinal stability of lipid based microbubbles** |
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| **Background:** Despite a century of research, oral biopharmaceutical formulations are absent in the clinical setting. Ultrasound mediated gastrointestinal delivery has recently been demonstrated to improve macromolecule uptake ex-vivo and in-vivo using ultrasound alone. Ultrasound responsive agents, like microbubbles, cavitate when exposed to ultrasound and can transiently permeabilise membranes to improve drug absorption. There is no published data on microbubble stability in vitro or in vivo demonstrating microbubble formation and stability in the gastrointestinal tract. This study aims to assess the formation and stability of microbubbles in gastrointestinal relevant buffers and simulated gastrointestinal fluids. |
| **Methods:** Suspended DSPC-PEG40S (9:1) at a concentration of 4mg/ml in gastrointestinal relevant buffer/simulated media. Manufactured DSPC-PEG40S (9:1) microbubbles via agitation. Photographed microbubbles via light microscopy at timepoints across 24 hours and measured size and concentration using an ImageJ macro. |
| **Results:** The mean microbubble diameter increased over time while the microbubble concentration decreased over time which is the typical change of a microbubble population due to Ostwald ripening. 0.1M HCl (pH 1.2) had a statistically significant effect on microbubble concentration, indicating that acidic pH may have an effect on microbubble formation. Future work will address limitations of study by manufacturing microbubbles in standard media and removing non-incorporated shell components by leveraging centrifugal washing. |
| **Conclusions:** DSPC-PEG40S microbubbles manufactured via agitation were found to have a 24-hour stability maintained above 108 MBs/ml in biorelevant gastrointestinal buffers and simulated media but questions remain about role of non- incorporated shell components.  |