

Foaming Agents for Drug Delivery to Treat Inflammatory Bowel Disease

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Abstract:

About 1.6 million Americans suffer from Inflammatory Bowel Disease (IBD), a condition that includes Crohn's Disease and Ulcerative Colitis (2). Treatment of this condition focuses on reducing the inflammation caused by IBD either through anti-inflammatory drugs or immunosuppressants (4). Many times it is preferable to deliver these drugs topically, and foams provide several benefits over the common liquid enemas (as noted in Malchow 2002)(3). Furthermore, several foam products are already on the market to treat colitis including foams containing Mesalazine and Budesonide (1). Our experiment focuses on formulating an optimal foaming solution for lower gastrointestinal tract drug delivery. In addition to clinical treatment, we hope these foams will help researchers test new therapies for IBD and other disorders affecting the lower digestive system.

Methodology:

We made solutions of Polyethylene Glycol (PEG) or Alginic Acid (Alginate), and a foaming agent (pluronic, sodium caseinate, or I- α -phosphatidylcholine) and tested the following characteristics.

Half Life: We tested the stability of the foam by measuring the "half life" of a column of foam produced by bubbling compressed air at 1lpm through 10 ml of the solution in a 1½" chromatography column with a fritted glass filter in the base. After generation, the foam height was marked. A video camera was used to record the time it took for the foam to degrade to half of its original height.

Foamability: Using the same system we tested the volume of foam each solution was capable of generating. In separate trials the solution was allowed to foam until an air pocket formed in the bottom of the column. After waiting a minute the length of the foam was measured and a volume was calculated.

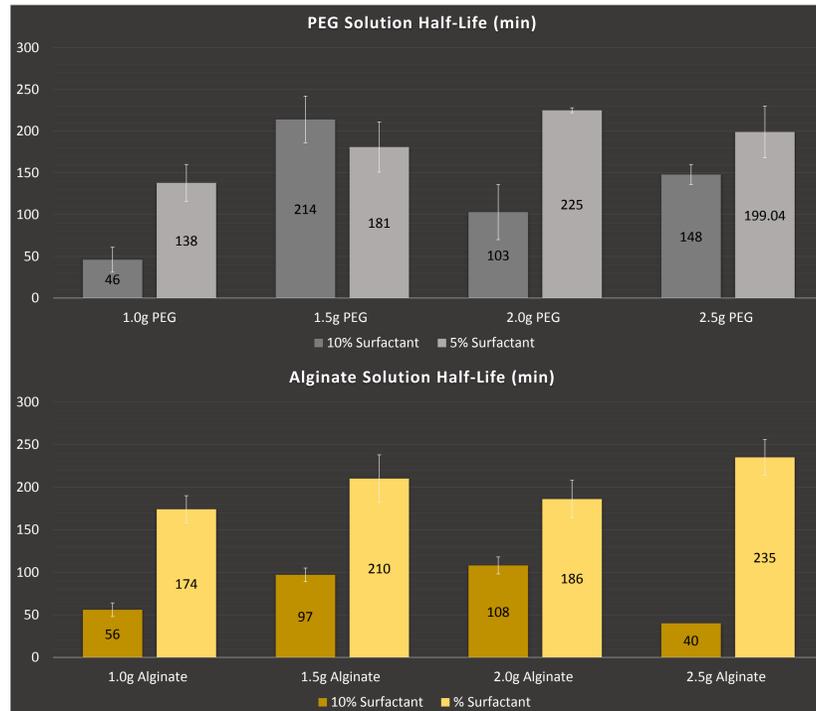
Drainage: To test drainage rate of the foam we completely foamed a 10 ml sample of the solution as described in the foamability test. This column was immediately inverted and allowed to drain into a 10ml graduated cylinder. Volume readings were taken every minute for ten minutes.

Density: We tested density along with the drainage test. After one minute, we measured the foam height and calculated the volume. Next we massed the drained solution and calculated the mass of solution still in the foam. Using these measurements we calculated the density of the foam.

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Background:

Drug delivery, to the gastrointestinal tract poses many unique problems. Topical delivery enemas minimizes systemic exposure and increases drug effectiveness. However, they present other problems including retention and patient compliance (4)(3). Foam enemas overcome some of these problems and have been shown to be as effective as their liquid counterparts (3). Still, foams have their own problems. One challenge is choosing a surfactant that will not irritate IBD (5). Many synthetic surfactants are irritants, and studies have shown that common surfactants may cause colitis in mice (6). Many times foam enemas use smaller concentrations of nonionic surfactants which are less irritating (5). Still, the situation is less than ideal both for patient comfort and for the condition itself. The other large concern is the density of the foam and drug holding capacity of the foaming solution (5)(7). In this experiment we attempted to overcome all three of these concerns using two alternative foaming agents; sodium caseinate, and I- α -phosphatidylcholine. By maximizing their foam half-life, foamability, drainage, and density, we hope to evaluate their use as a drug delivery method for IBD.



Future Direction:

Once we finish these trials and find the optimal foaming solution, there are many ways we can extend this project. For example, we can test how loading the foam with different active agents affects density and stability. We are especially interested in testing this foam for its ability to deliver nanoparticles.

Results:

This project is still very much a work in progress. Initially we didn't know that synthetic surfactants would irritate IBD, and we ran many tests with pluronic. You can see these results in middle charts. These trials taught us a lot about the procedure and the foaming properties of solutions. Firstly, we learned that higher concentrations of PEG and Alginate and surfactant did not necessarily produce longer lasting foams. We also saw that the foams could vary widely in their size and composition, a fact that led us to measure the extra parameters in the new trials. Finally, and perhaps most importantly, it showed us that the surfactant concentration was the most important factor in the foam half-life. Concentration of the PEG or Alginate played an important role, but surfactant concentration widely separated the different solutions. From this observation we decided to fix the concentration of these reagents to a value of 1.5% and focus on foaming agent concentration for the first part of this experiment. You can see our preliminary trials in the table below.

Substance	Foaming Agent 1	% wt. Agent 1	Foaming Agent 2	% wt. Agent 2	1/2 life (min)	Comments
PEG	I-a-P	0.1			-	
Alginate	I-a-P	0.1			-	The foam was stable, but the bubbles were too large and thin to do any good
PEG	Caseinate	1				
Alginate	Caseinate	1			170	
PEG	I-a-P	1			-	It seems like the phosphatidylcholine only stabilizes the foam and does not help its foamability
Alginate	I-a-P	1			24 + hrs	by this time most of the liquid had drained out. Additionally after the foam collapsed some of the I-a came out of solution
PEG	I-a-P	1	Caseinate	0.5	32	Again, something came out of solution after foaming. It seems like the I-a may have a minimal stabilizing effect at these concentrations
PEG	Caseinate	0.5			30	
Alginate	Caseinate	0.5			219	Non constant rate of collapse

Citation:

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