

A Novel Controlled Release System for GERD Drugs Using Immobilization Techniques

Abstract

Gastroesophageal reflux disease (GERD) is commonly treated with over-the-counter (OTC) GERD medications that dissolve quickly in the stomach, often resulting in rapid drug release, short-lasting relief, and frequent dosing. To address these limitations, this study investigates a novel controlled-release system using immobilization techniques to slow and regulate the delivery of GERD drugs. Sodium alginate, a natural polymer, was combined with calcium chloride to form gel beads capable of encapsulating acid-reducing agents through ionic crosslinking. Drug-loaded beads were tested in solutions of varying pH to simulate gastrointestinal conditions, and drug release was monitored using pH-based measurements as an accessible analytical method. Results showed that immobilization significantly modified the release profile of the drug, with slower, sustained release observed at stomach acid pH levels and more release in basic conditions. This project demonstrates that simple polymer-based immobilization systems can enhance drug stability by forming a raft on top of the stomach acid, reduce dosing frequency, and provide a more controlled therapeutic effect for GERD management.

Key Words: GERD Drugs, Drug Immobilization, Calcium Chloride, Sodium Alginate

Statement of Purpose

- The purpose of this project is to study whether sodium alginate immobilization can be used to achieve sustained release of GERD drugs.
- By encapsulating an over-the-counter GERD medication in calcium alginate beads, this project investigates how the drug release rate changes under different pH conditions that simulate the human stomach and intestine.
- My goal was to understand how polymer-based immobilization can control drug release and explore its potential application in improving drug delivery systems for acid reflux treatment.

Background Research

Stomach Acid

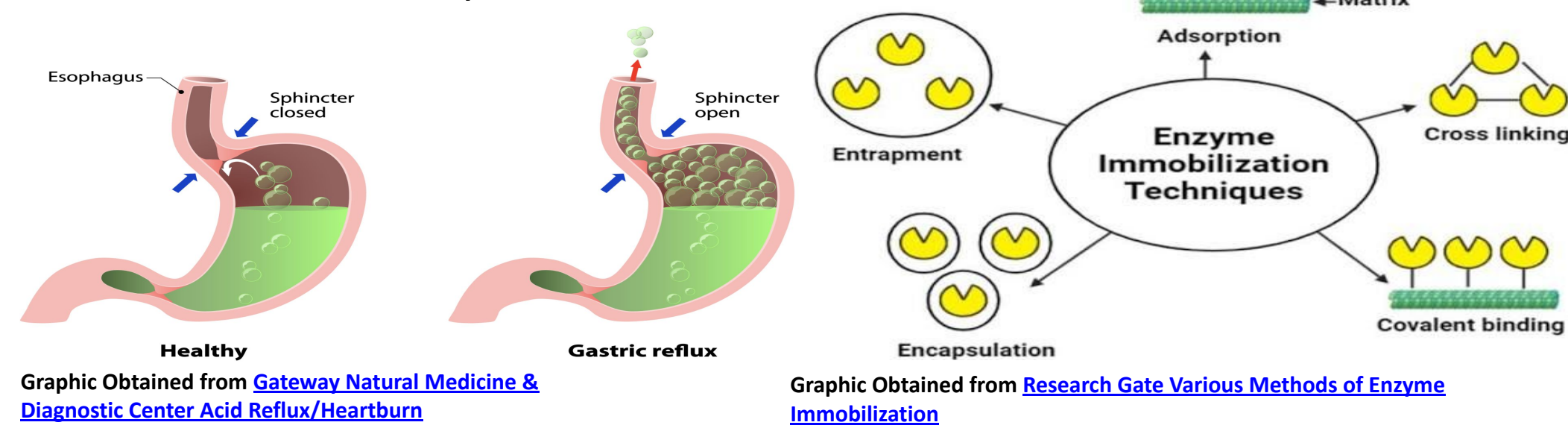
- Stomach Acid, which is made of hydrochloric acid, has a highly acidic pH of 1-2.
- The lining of the stomach secretes stomach acid, which is controlled by hormones and the nervous system.
- When the stomach creates too much acid, it can cause many irritating symptoms like vomiting, abdominal discomfort, bloating, heartburn, diarrhea, decreased appetite, & unexplained weight loss.

Antacids

- Antacids are used to treat heartburn and indigestion.
- This medicine works fast to both reduce the amount of acid in the stomach to relieve symptoms and neutralize the stomach acid by raising the stomach pH, inhibiting the activity of pepsin.

Immobilization

- Sodium alginate reacts with Calcium chloride to form calcium alginate gel beads that can trap drugs.
- The gel forms through ionic crosslinking, creating a stable and controlled-release system.



Hypotheses

- Increasing the sodium alginate concentration and increasing the volume of the syringe and the bead size will provide better bead stability.
- The beads will have more physical stability when placed in an acidic pH environment than when placed in a neutral or basic pH environment.
- In basic pH, the immobilized bead will dissolve quickly and release the drug. In acidic or neutral pH, the beads remain more stable, so the drug is released more slowly.
- The GERD drug encapsulated in sodium alginate beads will have a slower and more controlled release compared to the free drug.

Variables

- Constant Variables:** GERD Drugs, Distilled Water, and Duration of the Experiment
- Independent Variables:** pH of the Set Medium, Time of Exposure, and Formulation Variables
- Dependent Variables:** pH Change Over Time in Set Medium, Drug Release, Drug Stability, and Swelling/Erosion Behavior
- Controlled Variable:** Free Drug Actions/Effects

Materials

- Electronic Balance (Accurate to the Gram) and pH Meter
- Water Bath
- Sodium Alginate and Calcium Chloride
- Tums, Calcium Carbonate, Milk of Magnesia, and Gaviscon
- Distilled Water, 0.1 Molar Hydrochloric Acid (HCl), Vinegar and Baking Soda
- Safety Goggles and Nitrile Gloves

Methodology

Experiment 1: Preparation of Calcium Alginate Beads

- I prepared Calcium Alginate beads in two concentrations, using two syringe volumes: 1 mL & 10 mL.
- I dissolved 1 gram of sodium alginate in 100 mL of distilled water at 40°C (1% Sodium Alginate).
- I dissolved 2 gram of sodium alginate in 100 mL of distilled water at 40°C (2% Sodium Alginate).
- I prepared a 2% Calcium Chloride solution by dissolving 0.4 gram of Calcium Chloride in 20 mL of distilled water.
- I dropped the alginate mixture into a calcium chloride solution using a syringe and allowed the beads to harden for 30 minutes.
- I finally strained the beads using filter paper & rinsed the beads with distilled water.
- I decided to use the 2% sodium alginate solution for immobilizing the drugs.

Experiment 2: Testing the Stability of Calcium Alginate Beads in Different pH Conditions

- First, I prepared the pH 2 (0.01 M HCl), the pH of 6 (vinegar + baking soda), the pH of 7 (distilled water), and the pH of 9 (baking soda) solutions.
- I added 10 beads to 5, 20 mL replicates of all the pH solutions, and I observed the bead stability at 5, 10, 20, 30, 45, and 60-minute time intervals.

Experiment 3: The Immobilization of GERD Drugs

- I dissolved Sodium Alginate (0.4 grams) in 20 mL of distilled water.
 - Tums - The powdered tablet equivalent was mixed into the alginate solution.
 - Milk of Magnesia - 15 mL was mixed into the alginate solution.
 - Gaviscon - 5 mL was mixed into the alginate solution.
- Each mixture was dropped into a 2% Calcium Chloride solution to form immobilized beads.
- I wasn't able to make beads with Tums, but was able to form CaCO₃ encapsulated beads.

Experiment 4: Conducting a Drug Release Study With a Free Drug Vs. the Immobilized Drugs

- Drug-Immobilized Beads - The Milk of Magnesia & Gaviscon beads were placed in 25 mL of 0.01 M HCl and pH 6.8 solutions.
- Free Drug- I placed Milk of Magnesia and Gaviscon antacids in 25 mL of 0.01 M HCL and pH 6.8 solutions.
- I measured the pH at 0, 5, 10, 20, 30, 45, and 60-minute intervals, and at 3, 6, 9, 12, 18, 21, & 24 hour time intervals.
- I performed 5 trials for each one.

Photo Taken by Finalist



Figure 1:- Calcium alginate Beads

Photo Taken by Finalist



Figure 2:- Bead Stability Studies



Figure 3:- Calcium Carbonate antacid encapsulated Beads
Photo Taken by Finalist

Figure 4:- Tums and Sodium alginate solution.
Photo Taken by Finalist

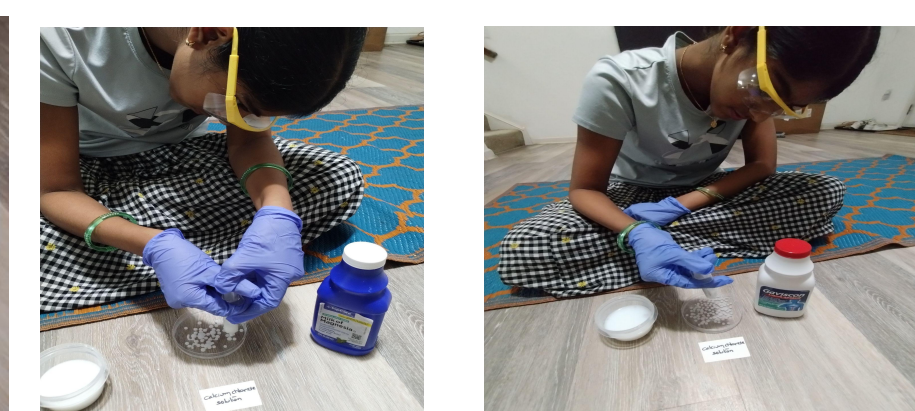


Figure 5:- Preparation of immobilized beads with Milk of Magnesia by Finalist.
Photo Taken by Another Individual

Figure 6:- Preparation of immobilized beads with Gaviscon by Finalist. Photo Taken by Another Individual

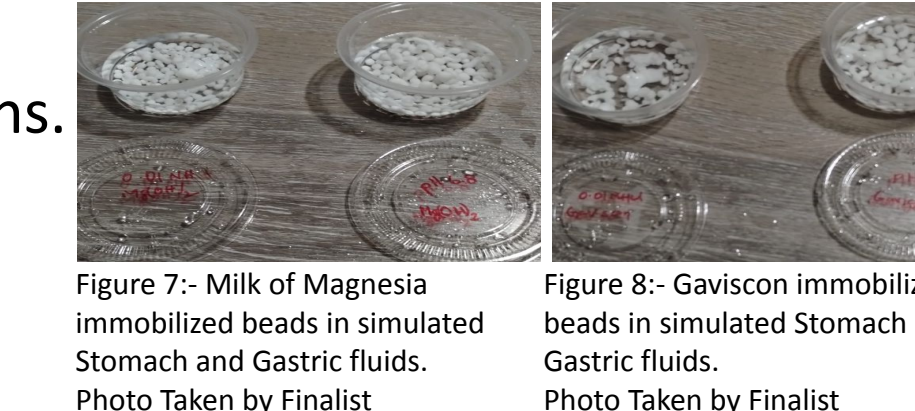


Figure 7:- Milk of Magnesia immobilized beads in simulated Stomach and Gastric fluids.
Photo Taken by Finalist

Figure 8:- Gaviscon immobilized beads in simulated Stomach and Gastric fluids.
Photo Taken by Finalist

Data & Results

1% Sodium alginate	2 % Sodium alginate
Smooth beads & some with tails	Dense & uniform beads
Easily drops through syringe	Thick jelly nature



Figure 9:- Beads with 1% Sodium alginate
Photo Taken by Another Individual



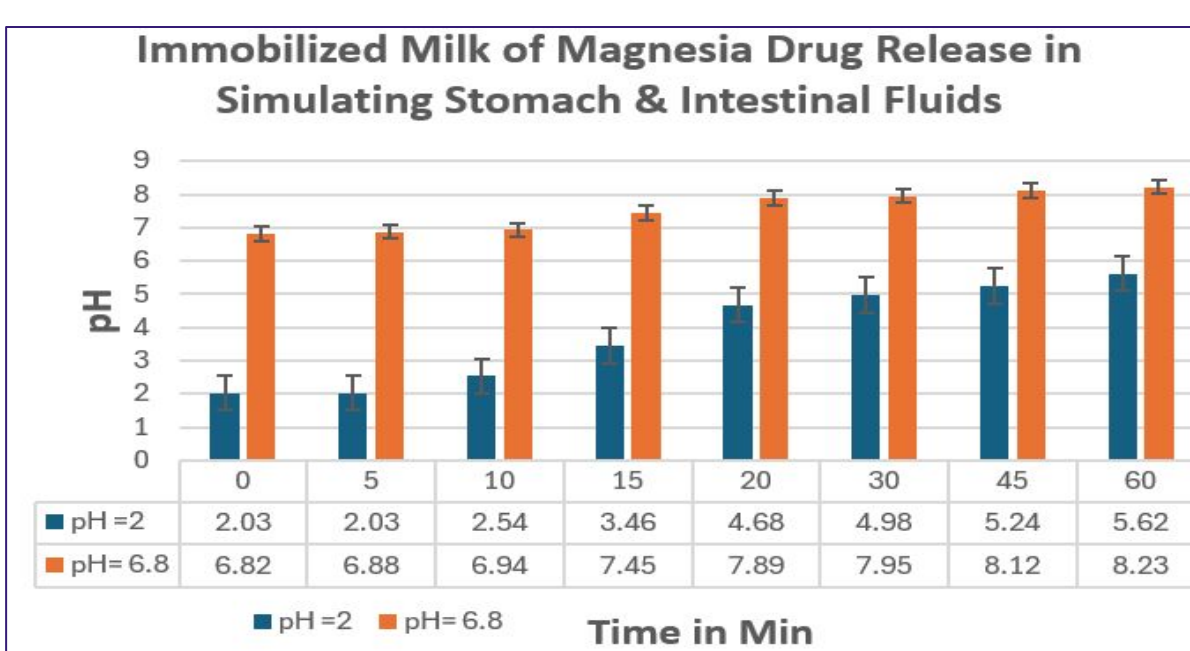
Figure 10:- Beads with 2% Sodium alginate
Photo Taken by Another Individual

Stability of Calcium Alginate Beads in Different pH Conditions

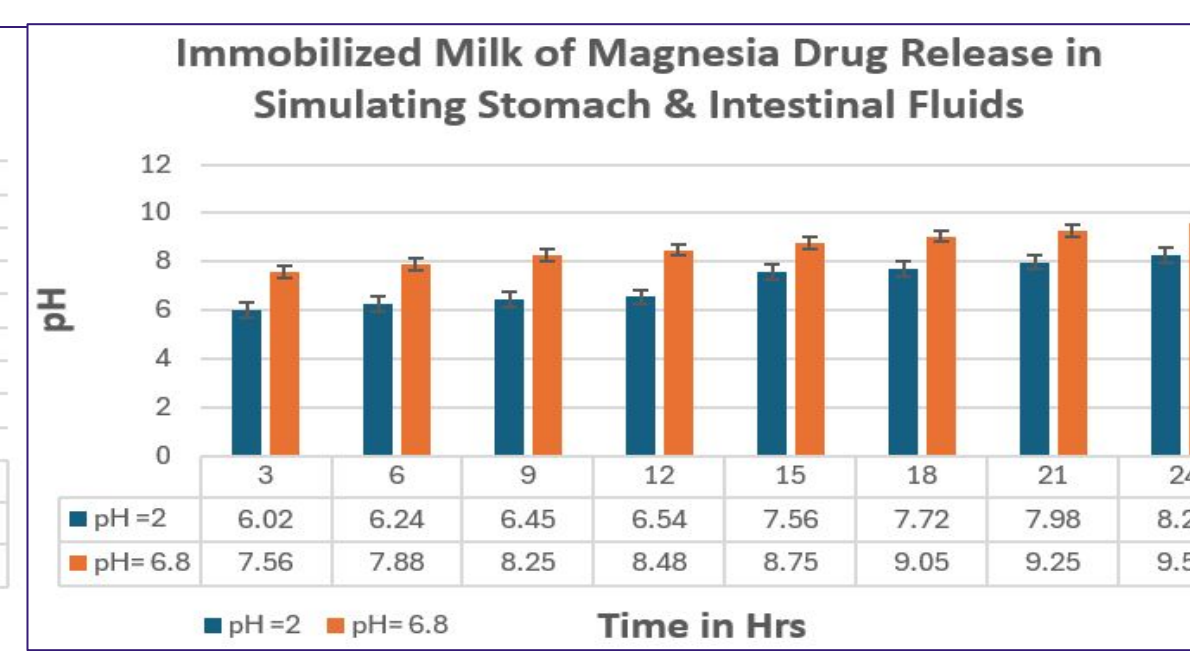
- The beads stayed stable & slowly shrank at acidic pH
- The beads were stable at neutral pH
- The beads showed a gradual size reduction at intestinal pH
- The beads swelled and dissolved rapidly at alkaline pH

Time (min)	pH 2 (0.01 M HCl)	pH 5.8 (NaHCO ₃ 0.1M HCl)	pH 7 (Distilled water)	NaHCO ₃ (pH=9)
5	Stable	Stable	Stable	Starting to Swell
10	Stable	Stable	Stable	Getting bigger
20	Stable	Stable	Stable	Getting bigger
30	Stable	Some are small	Stable	15% beads dissolved
45	Stable	50% small beads	Stable	40% beads dissolved
60	Some beads are small	All beads are small	Stable	90% dissolved

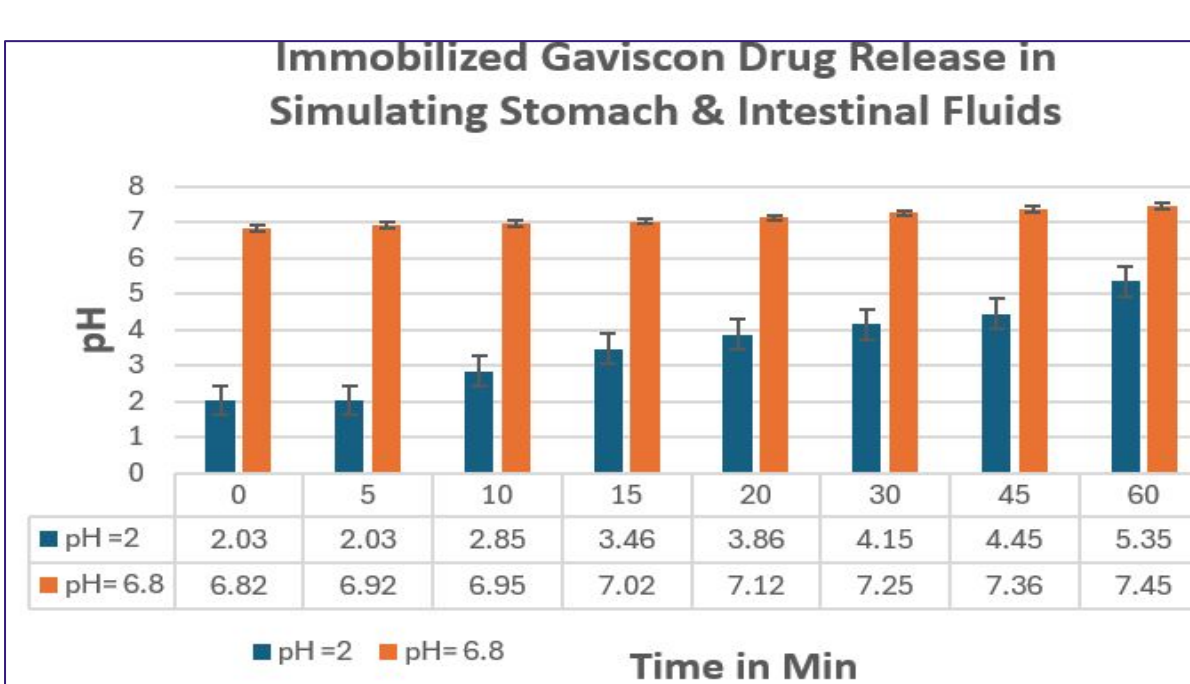
- Conversion of pH to Hydrogen Ion Concentration: $[H^+] = 10^{-pH}$
- Percent Acid Neutralized: $\% \text{ Neutralized} = \frac{[H^+]_0 - [H^+]_t}{[H^+]_0} \times 100$



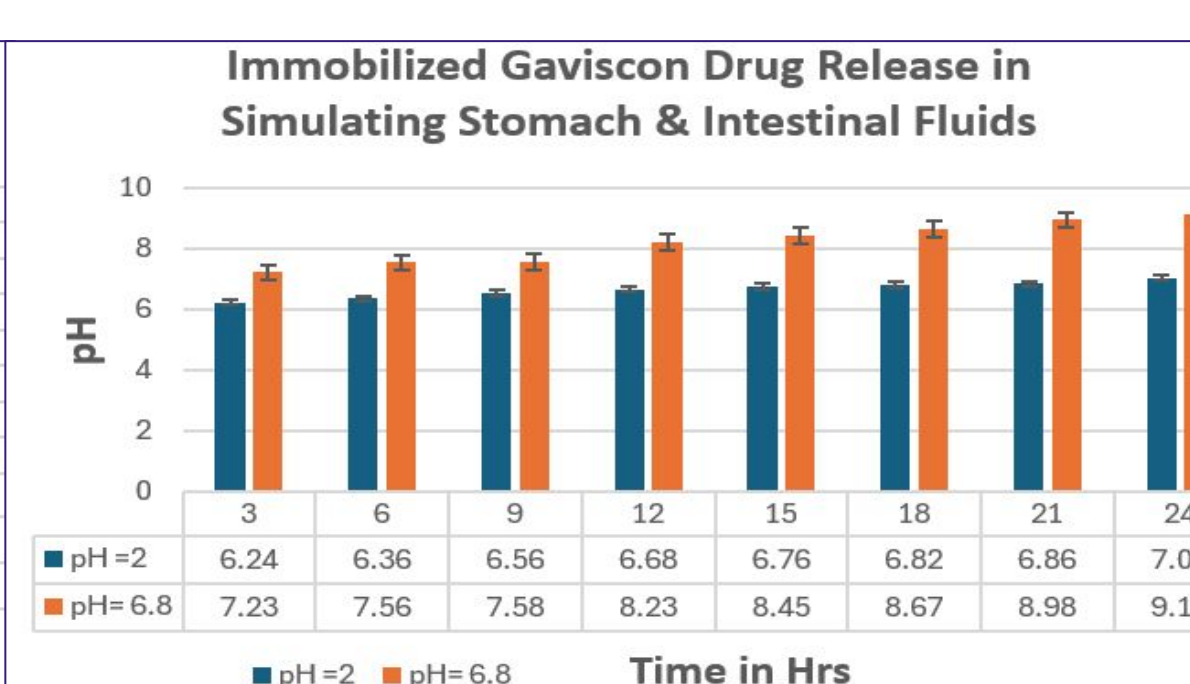
Graph created by Finalist using Microsoft Excel



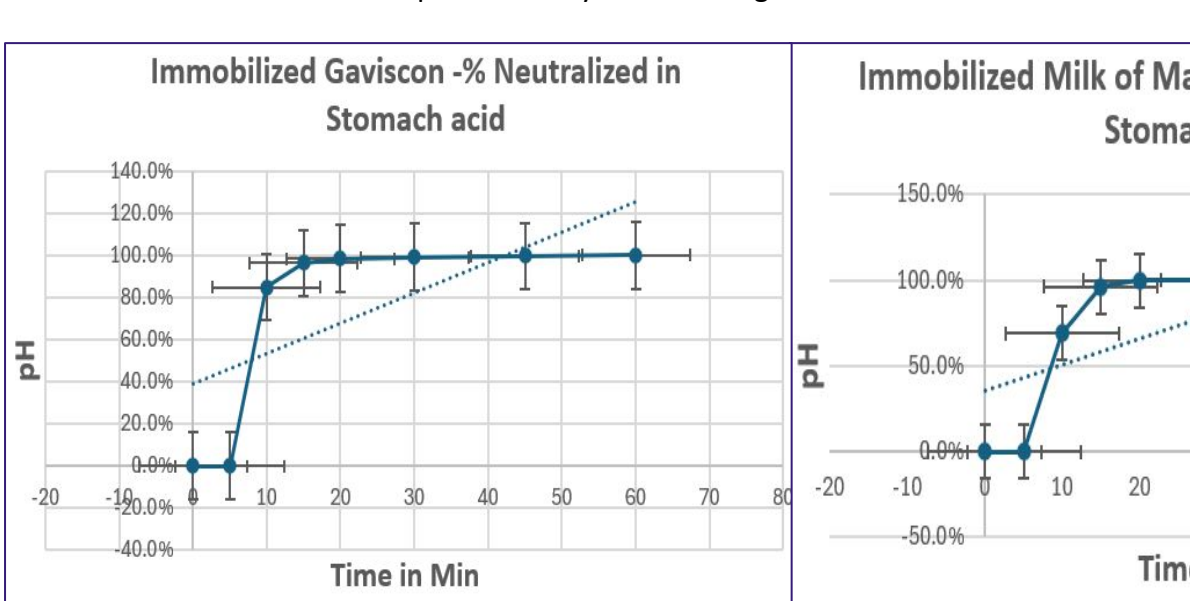
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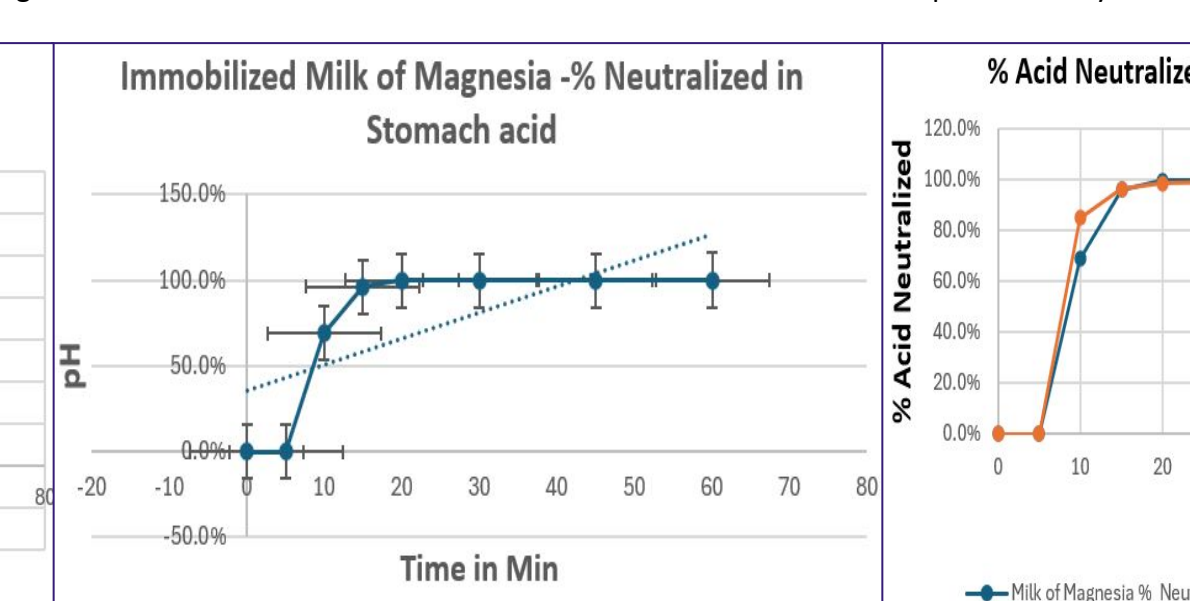
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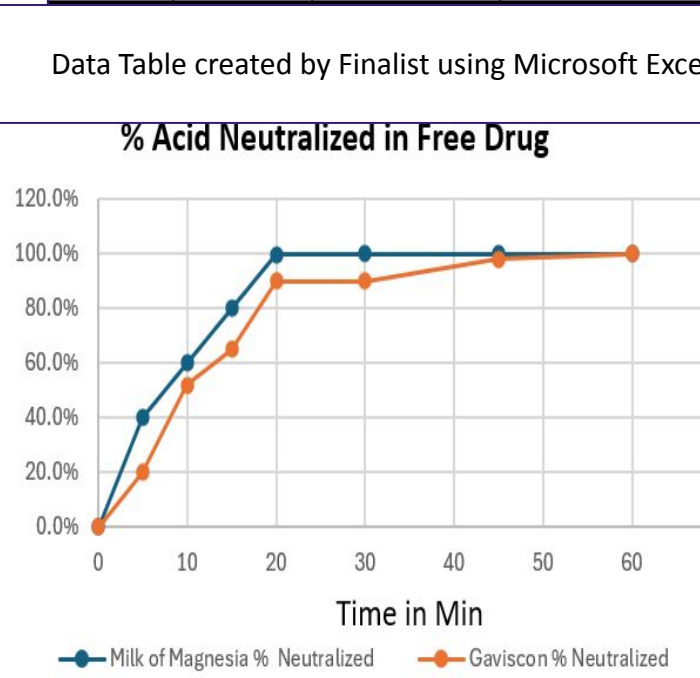
Graph created by Finalist using Microsoft Excel



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Milk of Magnesia - Neutralization			
Time (min)	pH	$[H^+]$ (M)	% Neutralized
0	2.03	9.33×10^{-3}	0.0%
5	2.03	9.33×10^{-3}	0.0%
10	2.54	2.88×10^{-3}	69.0%
15	3.46	3.47×10^{-4}	96.0%
20	4.68	2.09×10^{-5}	99.8%
30	4.98	1.05×10^{-5}	99.9%
45	5.24	5.75×10^{-6}	99.9%
60	5.62	2.40×10^{-6}	100.0%

Gaviscon - Neutralization			
Time (min)	pH	$[H^+]$ (M)	% Neutralized
0	2.03	9.33×10^{-3}	0.0%
5	2.03	9.33×10^{-3}	0.0%
10	2.85	1.41×10^{-3}	84.9%
15	3.46	3.47×10^{-4}	96.3%
20	3.86	1.38×10^{-4}	98.5%
30	4.15	7.08×10^{-5}	99.2%
45	4.45	3.55×10^{-5}	99.6%
60	5.35	4.47×10^{-6}	100.0%



Graph created by Finalist using Microsoft Excel

Data & Results (Continued)

Free Drug Vs. Immobilized Drug Analysis

- I observed a gradual and sustained neutralization between pH 2.5 and 4.5
- At pH ≥ 5.6 , almost all of the acid was already neutralized
- At pH > 7 , the solution is basic, and the antacid was no longer reacting with the acid
- Further pH increase is due to the basic nature of the drug
- This confirms pH-dependent, controlled-release behavior

Conclusion

- My experimental data supported all proposed hypotheses.**
- Increasing the sodium alginate concentration and the bead size improved bead stability due to a stronger cross-linked polymer network.
- Beads were more physically stable in acidic conditions than in basic environments. At basic pH, the beads dissolved faster, leading to quicker drug release.
- At acidic and near-neutral pH, the beads remained stable, resulting in slower drug release.
- The encapsulated drug showed a more controlled and sustained release compared to the free drug.

Discussion

- I observed random errors such as...
 - Small fluctuations in pH meter readings.
 - Slight variations in bead size and/or shape.
- I minimized these random errors by taking five measurements and calculating the average value. I have also calculated the 95% confidence intervals.
- In the future, I would like to expand on this project by evaluating the long-term stability and storage conditions of the beads. I also want to investigate multi-layered or coated beads for more precise pH-responsive drug delivery.

Resources

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