



FORMULATION AND EVALUATION OF MAGNESIUM HYDROXIDE ALGINATE BEADS TO REDUCE ACIDITY

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ABSTRACT

Gastroesophageal reflux disease (GERD) affects individuals across various age groups, causing distressing symptoms such as heartburn, regurgitation, and chest discomfort. While conventional antacids offer rapid relief, their benefits are often short-lived, and gastrointestinal side effects can occur. Consequently, controlled-release drug delivery systems have been developed, providing a sustained release of medication over time. Notably, alginate-based delivery systems facilitate gradual medicine release, enhancing stability and absorption. This study focuses on developing and accessing magnesium hydroxide alginate beads as a controlled-release antacid formulation, aiming to alleviate acidity, prolong stomach retention for improved therapeutic outcomes, and achieve efficacy at lower doses.

KEYWORDS: Sodium Alginate beads, Magnesium Hydroxide, Calcium Chloride, Inotropic gelation, Gastro retentive drug delivery system (GRDDS).

1. INTRODUCTION

Many people suffer through acidity and gastroesophageal reflux, a condition involving acid reflux into the esophagus developing symptoms like burning sensation, acid reflux discomfort, food reflux, and chest tightness or discomfort. Additionally, some individuals may experience respiratory issues, including coughing, wheezing, hoarseness, or shortness of breath.¹

Traditional antacid formulations provide quick relief but have limitations including short life efficacy and gastro-intestinal side effects. To overcome such challenges Controlled Release Drug Delivery have emerged as a solution for GERD treatment. CRDDS ensure slow and steady release of medicine over time. So, it can keep stomach acid under control for a longer period, improve patient compliance, reduces side effects.

One such CRRDS system is Gastro retentive drug delivery system (GRDDS). GRDDS can be beneficial to treat GERD and reduce acidity for prolong period by extending antacid release in stomach and reduce symptoms of GERD.

GRDDS is classified as Floating and Non-floating, Bio-adhesive, Swellable Systems. Floating system is of two types Effervescent and Non-effervescent. FDDS have bulk density less than that of gastric fluid density so they can float on gastric fluid for prolong period of time and alter the gastric emptying rate for prolong period of time so the drug is released slowly at desired rate.^{2,3}

Alginate based drug delivery systems are beneficial for treating GIT diseases such as Gerd. This system releases medicines slowly and steadily making them more effective. Improve stability and absorption of antacids and other medicines. Alginate microbeads are popular for delivering medicines by

mouth. These are ideal for customized and sustained drug delivery in the gastrointestinal tract.⁴

Conventional antacids are limited by their brief therapeutic effect as the stomach constantly empties and secretes acid. Traditional medicines have poor utilization rates with only 10% to 15% being effective and have short lived effect. Controlled release antacid dosage form gives controlled and sustained release providing longer lasting neutralization of stomach acid.

Overdose of many antacids due to required frequent dosing can cause unwanted side effects like excess amount of magnesium can lead to Hyper magnesia and diarrhea.⁵ CRDDS help to get an antacid effect with low amount of antacid which cannot be obtained even after high doses of conventional antacids and help to neutralize stomach acid despite the stomach on going emptying and acid secretion. This controlled dosage form can be achieved with a gel forming and swelling system with sodium alginate as antacid encapsulating agent. Alginate alleviates acid reflux by thickening gastric fluids, thereby preventing acid from flowing into the esophagus. Magnesium Hydroxide does not dissolve well in neutral environment but it dissolves slowly in acidic environment so it can reduce stomach acid to some extent.⁶

The objective of this work is formulation and evaluation of Magnesium Hydroxide alginate beads to reduce acidity so as to improve drug retention in stomach, achieve antacid effect at low amount of drug, develop a patient friendly alternative to conventional antacid.

The beads were prepared by inotropic gelation method. Ionotropic gelation happens when two oppositely charged molecules interact forming connections or crosslink. Ionotropic gelation is a process used to create hydrogel beads. Hydrogels are network of polymer chain that can hold large amounts of

water. And were evaluated for physical appearance, swelling study, acidity reducing ability, floating test, percentage yield, bulk density and tapped density, stabilities study.⁷

2. NEED OF WORK

1. Need for Controlled-Release Formulation: To provide slow and steady release of medicine over time.
2. Improving Patient Compliance: To reduce frequency of dosing and improve patient adherence.
3. Reducing Side Effects: To minimize gastrointestinal side effects associated with traditional antacids.
4. Reducing Dose Frequency: To reduce the amount of magnesium hydroxide required, minimizing potential side effects.

3. OBJECTIVE

- To formulate magnesium hydroxide alginate beads by using the ionotropic gelation method to create a controlled-release formulation.
- To evaluate the formulated beads, including their physical appearance, swelling study, acid neutralization test, and floating test.
- To evaluate the effectiveness of the formulation in alleviating acidity and enhancing stomach retention.
- To investigate the stability and shelf-life of the formulated beads under storage conditions.

4. ADVANTAGES OF ALGINATE BEADS

- Biocompatible
- Non-toxic
- Low cost

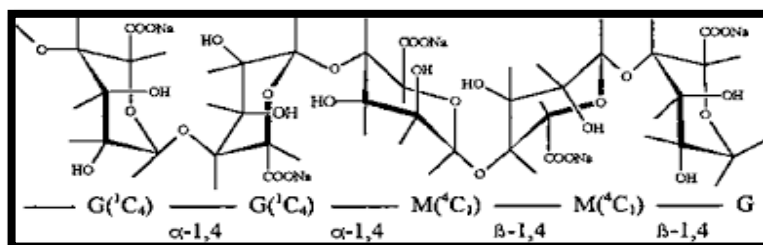


Fig. (1) Structure of Sodium Alginate

This building blocks are linked together in a specific way to form the alginate molecule.⁹ Most easy and common way to make alginate beads is to mix an alginate solution with special ions like calcium Ca^{2+} this helps to create a network of molecule and form hydrogels.

6. CALCIUM CHLORIDE

Calcium chloride CaCl_2 is often used to cross link sodium alginate. This process works by forming ionic bonds between calcium ions and carboxylate ions in the alginate solution. When alginate is placed in CaCl_2 solution calcium ions replace sodium ions in the alginate. Calcium ions bond with carboxylate ions forming cross-linking between polymer chains this creates a hydrogel network.¹¹

- Biodegradable.⁸

5. ALGINATE

Sodium Alginate was initially isolated from kelp in 1883 and since been the subject of extensive research. Alginate are anionic polysaccharides derived from brown seaweed composed of long unbranched chain.⁹ Sodium Alginate is a Marine plant polysaccharide which is naturally occurring carbohydrate extracted from Marine organisms. It also includes alginic acid, alginic starch, alginate gum etc.

Alginate has special groups (carboxyl groups) that get charged when the pH is above 3-4. In acidic environments, the carboxyl groups in alginate get protonated (gain a hydrogen ion) and becomes less soluble and reduces its ability to release drugs, effectively limiting drug release in acidic conditions.

This are usually water soluble and have strong gel thickening properties. Sodium alginate is a well-known member of hydrogel groups. This hydrogel absorb water due to presence of hydrophilic functional group in their structure and their resistance to dissolution is due to the cross-linking between the network chains.

The divalent cations are responsible to form alginate hydrogels by forming an ionic cross-link by guluronic acids from nearby chains.¹⁰ Alginates are Made up of two main building blocks. Figure 1

- Mannuronic acid (M)
- Guluronic acid(G)

7. MAGNESIUM HYDROXIDE [$\text{Mg}(\text{OH})_2$], CALCIUM CARBONATE [CaCO_3]

Magnesium Hydroxide, known as milk of magnesia, alleviates digestive discomfort by counteracting stomach acid. It's effective against heartburn, indigestion, and acid reflux. Meanwhile, Calcium Carbonate plays a crucial role in keeping medicinal beads afloat in the stomach, thanks to its gas-generating properties.^{12,13}

8. MATERIALS AND METHODS

➤ Material

1. Sodium Alginate
2. Calcium Chloride
3. Magnesium Hydroxide
4. Calcium Carbonate
5. Distilled water, syringe.

Table (1) Different formulations of alginate gel beads

Sr. No.	Formulation	Sodium alginate concentration	Calcium Chloride	Magnesium hydroxide	Calcium carbonate
1.	F ₁	1% w/v	2% w/v	2g	0.5g
2.	F ₂	2% w/v	2% w/v	2g	0.5g
3.	F ₃	2.5% w/v	2% w/v	2g	0.5g

➤ **Method**

Three concentrations of sodium alginate were made by dissolving 1 gram, 2gram, 2.5 gram of alginate each in 100 ml of distilled water with continuous stirring for 15 minutes to ensure that there is no clumping in the solution and refrigerated for 2 hours for removal of air bubbles. Add 2 grams of Magnesium Hydroxide and 0.5 grams of calcium carbonate as antacid and gas forming agent in each solution respectively. Add 2 gram of calcium chloride in 100 ml water with continuous stirring to prepare a cross-linking solution. Ensure calcium chloride is completely dissolved.^{13,14} Table 1.

➤ **FOLLOWING PROCEDURE IS FOLLOWED TO PREPARE SODIUM ALGINATE BEADS OF MAGNESIUM HYDROXIDE.**

A sodium alginate solution containing Mg (OH)₂ was carefully dropped or extruded into a calcium chloride solution using a syringe from a height of 5 cm to form uniform spherical beads. These beads were then allowed to stand in the calcium chloride solution for 15 minutes to develop a stable bead structure, during this time they were not disturbed to prevent damage. After 15 minutes, the beads were removed from the solution and washed twice with distilled water to eliminate excess calcium chloride and prevent unwanted cross-linking. The beads were dried. The beads were air-dried at room temperature, ranging from 20-25°C, for a duration of 12 hours. To preserve their stability and effectiveness, the alginate beads must be stored in a dry environment, such as airtight containers.^{18,19} Figure 2 and 3.



Fig. (2) Magnesium Hydroxide Bead



Fig. (3) Air Dried Beads

9. EVALUATION OF MAGNESIUM HYDROXIDE BEADS

9.1. Physical Appearance of Beads

Physical appearance test is used to determine the physical characteristics of alginate beads. This test is conducted by visual inspection of bead. Parameters evaluated in this are shape, color, texture, stickiness, mechanical strength.¹⁵

9.2. Swelling ratio

The swelling property of alginate beads was determined. 35 alginate beads of F₁, F₂, F₃ batch were taken and evaluated for swelling ability. Take the initial weight of the alginate beads

$$SI(\%) = \frac{W_s - W_d}{W_d} \times 100\%$$

(W_d). Prepare 0.1N HCl solution, add 20 ml 0.1N HCl in the petri dish and add beads gently in it for required time interval, remove the beads after a specific time interval and determine final weight (w_s) of swollen beads.^{15,20}

9.3. Percentage yield determination

The percentage yield of the beads indicates the preparation process's efficiency. To calculate this, the weights of all ingredients and the final product were recorded for each batch. The percentage yield is determined by dividing the actual product weight by the total weight of ingredients, then applying the formula.²⁰

$$\text{Percentage Yield (\%)} = \left(\frac{\text{Actual Weight of Beads Obtained}}{\text{Theoretical Total Weight of Ingredients Used}} \right) \times 100$$



9.4. Bulk density and Tapped density

Bulk density measures the mass of granules relative to their total volume, including the spaces between them. This helps predict whether the beads will float in gastric fluid by comparing their density to that of the gastric fluid. To measure bulk density, 20 grams of alginate beads are placed in a bulk density apparatus, and the initial volume is recorded.

$$\text{Bulk Density} = \frac{\text{Mass of Beads}}{\text{Bulk Volume of Beads}}$$

Tapped density the ratio of the mass of granules to their volume after tapping which includes the true volume of the granules and minimal void space. This are expressed in units of gram/cm³.²¹

$$\text{Tapped Density} = \frac{\text{Mass of Beads}}{\text{Tapped Volume}}$$

9.5. Diameter of beads

The diameter of 20 beads from each batch of F₁, F₂, F₃ concentration were measured to determine the mean diameter of the beads. Mean diameter is used to determine average size of alginate beads. This test is important to ensure that beads are formed of proper size and suitable for intended application. Vernier caliper was used to determine the bead diameter.²²

9.6. Impact on Gastric Acidity

It is conducted to check that formed beads are sufficient in increasing the pH of the acidic solution that mimic stomach acidic condition that is 0.1N HCl solution. Take 50 ml of 0.1 N HCl in 100 ml beaker measure initial pH it is around 1 to 2. Add

Magnesium Hydroxide beads with gentle stirring. Then check pH of solution with pH meter and pH strips and check the change at particular time.²³

9.7. Floating of beads

Floating test is conducted to check if beads can float in the solution for a long time that mimic the acidic environment of stomach (0.1 N HCl). If all beads float then they are considered to have buoyancy. In USP Paddle apparatus add 0.1 N HCl solution then add 1gram beads of all concentration F₁, F₂, F₃ in it. Record the time that beads take to float and observe beads for 24 hours to see how long they float.²⁴

9.8 Stability

The stability of Magnesium Hydroxide beads was studied under environmental conditions. The parameters for which it was observed during stability study were color, shape, stickiness, floating and swelling behavior.¹⁵ These parameters help to assess the beads stability over time.

10. RESULTS AND DISCUSSION

10.1. Physical Appearance of beads

It was observed that beads of F₂ and F₃ formulations had perfect shape, texture, color and mechanical strength. Beads of F₁ formulation showed poor mechanical strength they had very smooth surface and broke on applying slight pressure. F₂ beads exhibited moderate strength, retaining shape but slightly deformable. F₃ beads demonstrated good mechanical strength, maintaining integrity under pressure. The results indicate that F₂ and F₃ formulations are suitable for drug delivery. Table 2.

Table (2) Physical Appearance

Sr. No.	Formulations	Shape	Color	Texture	Stickiness	Mechanical strength
1.	F ₁	Non-spherical	White	Very smooth	Sticky	Breakable with poor mechanical strength
2.	F ₂	Spherical, round	White	Smooth	Non-sticky	Not easily breakable Good mechanical strength
3.	F ₃	Oval	White	Smooth	Non-Sticky	Not easily breakable High mechanical strength

10.2. Swelling Ratio

The prepared alginate beads of different concentration were evaluated for swelling behavior by soaking 30-35 beads of each batch in 20 ml of 0.1N HCL solution in petri dish. Beads were observed after 2 hours of soaking and their final weight was

determined and calculated their swelling ratio. All three-formulation exhibited high and consistent swelling capacity. F2 formulation beads offers best balance between swelling capacity and bead integrity making it ideal for control gastric drug delivery. Figure 4 swelling behavior of beads.



Fig (4A) Beads before swelling



Fig (4B) Beads After Swelling

10.3. Percentage Yield Determination

The percentage yield of beads ranges from 86.66% to 94.28% for different concentrations of alginate indicating efficient bead formation and minimal loss during the process. It was observed that as the concentration of alginate increased there was a slight decrease in percentage yield. Table 3.

10.4. Bulk Density and Tapped Density

Bulk Density

The ability of alginate beads to float in gastric fluid depends on their bulk density. Beads with a density lower than gastric fluid (1.004-1.010 g/ml) exhibit floatation. F₁ and F₂ alginate beads have densities of 0.8699 g/ml and 0.952 g/ml, respectively, allowing them to float well. F₁ beads have a higher tapped volume (22 ml), indicating a more porous structure, while F₃ beads have a lower tapped volume (19 ml), indicating a denser nature. Figure 5.



Fig. (5) Bulk Density Apparatus

Table (3) Percentage yield, swelling ratio, Bulk density, Tapped density, Carr's Index.

Sr. No.	Formulations	Percentage yield	Swelling ratio	Bulk density	Tapped density	Carr's Index
1.	F ₁	94.28 %	2.62	0.83g/ml	0.90g/ml	8.36%
2.	F ₂	86.66 %	2.12	0.95g/ml	1 g/ml	4.8%
3.	F ₃	90 %	2.29	1.05g/ml	1.05g/ml	3%

10.5. Diameter of beads

Diameter of 20 alginate beads of each batch was measured and mean diameter was found in range of 1.95mm, 2.30mm, 3.85mm and standard deviation 0.08mm, 0.07mm, 0.11mm respectively for F₁, F₂, F₃. The bead diameter evaluation revealed that there is a direct relationship between sodium alginate concentration and bead size. Beads prepared from F₂ formulation were of suitable size and easy to handle and suitable for antacid delivery system.

10.6. Impact on Gastric Acidity

pH meter and pH strips were used to assess the acid reducing effect of F₂ sodium alginate beads. At t = 0 minute the initial pH of 0.1N HCl was around 1 to 2. After 50 minutes the pH was around 6.5 to 6.9. This suggests effective gastric acid reducing behavior property of alginate beads of magnesium hydroxide.

10.7. Floating of beads

The floating behavior of all beads of different concentration was assessed using USP paddle apparatus and determined the floating lag time as less than 1 sec, in 1 sec, in 4-5 sec and total

floating duration of the beads in 0.1N HCL was found to be 8-12 hr., 12-16 hr., 16-24 hr. for F₁, F₂, F₃ respectively. The beads

demonstrated excellent in vitro floating properties in 0.1N HCl. Figure 6.



Fig (6) Floating Beads

10.8. Stability

The stability of formulated beads was assessed by observing key parameters like color, shape, stickiness, floating behavior, and swelling capacity were observed. The beads retained their spherical shape and color, indicating chemical stability. Surface stickiness remained unchanged, suggesting proper moisture balance. Floating behavior was preserved, confirming structural integrity. Swelling behavior in simulated gastric

conditions showed no significant deviations, demonstrating stability of the alginate matrix and magnesium hydroxide dispersion. Overall, the beads displayed excellent physical and functional stability, making them suitable for long-term use with consistent performance and efficacy. No significant changes were observed.

Table (4) Observation for F₂ formulation

Sr. No.	Test	Result
1.	Physical appearance: Shape Color Texture Stickiness Mechanical strength	-Spherical, round. -White -Smooth -Non-sticky -Good mechanical strength
2.	Swelling ratio	2.12
3.	Percentage yield	86.66 %
4.	Bulk density, tapped density	0.95g/ml, 1g/ml
5.	Floating	Floating for 12-16 hr.
6.	Stability	Stable

11. CONCLUSION

This study successfully formulated and evaluated magnesium hydroxide-loaded sodium alginate beads for gastro-retentive drug delivery to treat acidity and gastroesophageal reflux disease (GERD). The beads were prepared using the ionotropic gelation method, utilizing sodium alginate as the polymer matrix and calcium chloride as the cross-linking agent.

The results demonstrated that the formulated beads exhibited excellent physical and functional properties. The beads showed good mechanical strength, optimal swelling behavior, and excellent floating properties, which are essential for gastro-retentive drug delivery. The formulation F₂ showed the most promising results, with a mean diameter of 2.305 mm, a swelling ratio of 2.12, and a floating time of more than 12 hours.

The beads successfully reduced stomach acidity, increasing the pH from highly acidic (1-2) to near-neutral (6.5-6.8). Their density properties enabled formulations F₁ and F₂ to float well, making them ideal for prolonged stomach retention. Moreover,

the beads remained stable and effective, indicating a promising duration of viability.

Sodium alginate concentration affects the physical and functional properties of the beads. Formulation F₂ shows the most promising results for gastro-retentive drug delivery. The beads exhibit excellent floating properties, acid-neutralizing capacity, and stability. The formulated beads have potential as a treatment for GERD and acidity, providing sustained release of the antacid. Overall, this study demonstrates the potential of magnesium hydroxide-loaded sodium alginate beads as a gastro-retentive drug delivery system for treating acidity and GERD.

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