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OPTIMIZED FLOATING ALGINATE BEADS OF NITROFURANTOIN

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ABSTRACT: This research enhances the quality of floating alginate particles that have been infused with nitrofurantoin. These beads must remain in the stomach for an extended period in order to gradually discharge the medication. We generated buoyant alginate particles by employing ionotropic gelation. Sodium alginate polymer crosslinked with calcium chloride. In order to produce beads with the desired chemical and physical properties, as well as a gas-forming agent, we modified the polymer composition and other formulation components. In vitro, we evaluated the drug release, flotation, inflation, medication retention, surface morphology, and particle size of bead. Formulations that were optimized for buoyancy, latency time, floating capacity, and drug entrapment demonstrated superior performance. Nitrofurantoin release was observed to be gradual and consistent in in vitro dissolution experiments. The results indicate that stomach-bound medications may be delivered by custom-made floating alginate nitrofurantoin particles. They can be administered less frequently and assimilated more rapidly.

Keywords: *Nitrofurantoin; Floating alginate beads; Gastroretentive drug delivery system; Ionotropic gelation; Sustained drug release; Sodium alginate; Buoyancy; Entrapment efficiency*

1. INTRODUCTION

Oral administration continues to be the most effective pharmaceutical delivery method due to its simplicity, cost-effectiveness, and increased adherence. It is difficult to synthesize oral dosage forms for drugs that are unstable in the stomach, cross membranes, or have limited water solubility. These limitations indicate that the medication is less effective when administered orally, necessitates more frequent dosages, and performs inadequately.

Therapeutic medication concentrations are preserved by pharmaceutical delivery methods that are both adaptable and durable. By doing so, these complications are resolved. Treatment adherence is enhanced by reducing dosages. GRDDSs prolong the duration of the medicine's body presence by retaining it in the stomach. These methods are effective for medications that are absorbed primarily in the upper gastrointestinal system and have a limited duration of action.

Nitrofurantoin is capable of eliminating numerous microorganisms. Frequently employed to treat urinary tract infections. In the Biopharmaceutics Classification System (BCS), Class II indicates that the substance is capable of surmounting obstacles and has a low solubility in

water. Nitrofurantoin has a biological half-life of 0.5–1 hour. Patients may be discouraged by an increased frequency of administration. Nitrofurantoin, an imidazolidinedione derivative, is converted into reactive intermediates by flavoproteins in bacteria. Ribosomal proteins and DNA are destroyed by these intermediates, which results in the death of bacteria. This disrupts DNA, RNA, proteins, and membranes in order to either limit the growth of cells or kill bacteria.

Floating medication delivery methods are employed to prolong stomach retention due to their buoyancy in gastric fluid. These biocompatible floating alginate beads are low-density, spherical multiparticulate devices that release medications gradually, thereby reducing dose dumping and enhancing accessibility. Their large particle size facilitates the uniform distribution of medications throughout the gastrointestinal tract.

Polyelectrolyte complexation, ionotropic gelation, and emulsion gelation results in the formation of floating alginate particles. Emulsion gelation is a frequently employed method of medication release. In order to establish a continuous oil phase, agitation is necessary for a drug-polymer solution in water. A cross-linking agent, such as calcium chloride, is then employed. These gel-like particles are unyielding.

Sodium alginate establishes a gel matrix when combined with calcium ions. This is indispensable for beading. This regulates the discharge of medication. Carbopol stabilizes and buoys beads, while HPMC alters their release.

The most effective floating alginate particles of nitrofurantoin will be produced and evaluated through emulsion gelation. Consequently, the medication will be more effective, require fewer dosages, discharge more slowly, remain in the stomach for a longer period, and assist patients in adhering to their treatment regimen.

2. METHODOLOGY

Determination of Melting Point: Nitrofurantoin's melting point was determined through capillary fusion. A modest quantity of nitrofurantoin was used to obstruct one capillary terminal. The melting point device was directed toward the sealed end by twisting the capillary. A sample is transformed into a liquid at the melting point.

Drug- excipient Compatibility: We conducted a comparison of spectra from various equipment using an FTIR spectrophotometer. Potassium bromide was pelletized in this experiment. FTIR spectra are available for carbopol 934, HPMC K100, sodium alginate, purified medication, and their combination. Software spectrum is interpreted by readers.

Solubility Studies: Nitrofurantoin is dissolved in distilled water, dimethylformamide, ethanol, and 0.1N HCl (pH 1.2).

Method of Preparation of Floating Alginate Beads of Nitrofurantoin:

A solution of sodium alginate (2.5% w/v) was prepared in distilled water with gentle stirring.

- Hydroxypropyl methylcellulose (HPMC K100) and Carbopol 934 were incorporated at different concentrations and mixed until they were fully hydrated.
- A precisely weighed amount of Nitrofurantoin (100 mg) was added to the polymer mixture and dispersed uniformly using a magnetic stirrer.
- To aid emulsification, 3 mL of castor oil along with Tween 20 was introduced into the drug-polymer blend.
- The resulting mixture was loaded into a syringe and released drop by drop through a 23-gauge needle into a calcium chloride solution under mild agitation.

- The beads formed were kept in the calcium chloride bath for a defined period, then collected by filtration and dried in air.

Table 1: Formulation Design of Floating Alginate Beads of Nitrofurantoin

Formulation Code	Nitrofurantoin (mg)	Sodium Alginate (% w/v)	HPMC K100 (mg)	Carbopol 934 (mg)	Castor Oil (mL)	Tween 20 (mL)	Calcium Chloride (% w/v)
F1	100	2.5	150	150	3	2	2
F2	100	2.5	150	100	3	2	2
F3	100	2.5	150	200	3	2	2
F4	100	2.5	200	150	3	2	2
F5	100	2.5	100	200	3	2	2
F6	100	2.5	150	150	3	2	2
F7	100	2.5	100	100	3	2	2
F8	100	2.5	200	200	3	2	2
F9	100	2.5	150	150	3	2	2
F10	100	2.5	100	150	3	2	2
F11	100	2.5	150	150	3	2	2
F12	100	2.5	200	100	3	2	2
F13	100	2.5	150	150	3	2	2

3. EVALUATION OF FLOATING ALGINATE BEADS

Micromeritics Properties: The prepared beads were evaluated for Carr's index, bulk density, tapped density, and angle of repose.

Bulk Density: Powder mass divided by bulk volume yields bulk density. The bulk density machine included a weighed sample of particles. It was possible to calculate the granule volume without moving the cylinder. We used the equation and g/cm3 to get the bulk density.

Bulk density = Mass of beads/ Bulk volume of beads

Tapped Density: Tapping can be used to indicate touched densities. After 100 and 1000 strikes, the volume of the weighed beads was measured using a tapping density device.

Tapped density = Mass of beads / Tapped volume of beads

Angle of Repose: The utmost angle between the horizontal plane and the surface of the powder pile. The flow is enhanced as the angle of repose decreases. Utilize this equation to determine the answer.

$$\tan(\theta) = h / r \text{ Therefore, } \theta = \tan^{-1}(h / r).$$

r is the radius, θ is the angle of repose, and h is the height in centimeters.

At h, beads are allowed to flow through a funnel that is set up on a stand. The height and radius of the bead accumulation were measured in order to estimate the angle of repose.

Carr's Index: This demonstrates how the bead moves. shown in percentage form.

% compressibility index = Tapped density – Bulk density / Tapped density × 100

Hausner's Ratio: Hausner's ratio can be used to measure bead flow indirectly. The formula for calculating it.

Hausner's ratio = Tapped density / Bulk density

Particle size: The particle sizes of the beads were measured using an optical microscope and an eyepiece micrometer that was calibrated using a stage micrometer.

Determination of Swelling Index: By adding the right amount of Nitrofurantoin particles to 0.1 N HCl at pH 1.2, the swelling index was calculated. Before using a microbalance to weigh the beads, we used blotting paper to remove any liquid particles. A 60°C oven was used to desiccate the swollen beads for five hours until they reached a constant weight. By comparing the bead's enlargement before and after drying, the swelling index was calculated. We used the equation that follows:

Swelling index = (Mass of swollen Beads - Mass of dry beads /Mass of dried beads) x 100

Entrapment Efficiency: Repeated extraction with 0.1 N HCl was used to assess the drug content of crushed beads.

After that, 0.1 N HCl was added to the extract after it had been moved to a 100 ml volumetric flask. After filtration, the solution's absorbance was measured with a blank in a UV spectrophotometer. The following calculation was used to calculate how much medication was in each bead:

% Drug entrapment efficiency = Calculated drug concentration / Theoretical drug concentration × 100

Percentage Yield: By dividing the product's weight by the total of all non-volatile ingredients used in its manufacture, the percentage yield of beads was calculated:

Practical yield (%) = [Practical Mass / Theoretical Mass(Drug+ Carrier)] × 100

Buoyancy Studies: 100 mg of beads were weighed and then transferred to a USP type II dissolve apparatus with 900 ml of simulated stomach fluid (0.1N HCl) at 37°C for the buoyancy test. After being separated, the beads were dried until they had a constant weight. Use the following calculation to determine the buoyancy percentage:

Buoyancy % = Initial weight of floating beads x100/ Weight of floating beads

In-vitro Drug Release Studies: Using the USP dissolving apparatus II, 100 mg of floating beads were mixed with 900 ml of 0.1N HCl at a speed of 100 rpm in order to assess the nitrofurantoin floating particles. At regular intervals, aliquots were filtered and combined with the same medium. Finally, a twin beam spectrophotometer was used to evaluate them at 360 nm. After being reintroduced into the same dissolving solvent, all isolated samples were examined.

Formulation Optimization via Doe: To determine the most important components, their interactions, and the ideal process conditions for getting the intended results, statistical design of experiments and computer-aided optimization were used. To attain the best possible formulation, we used Design Expert Stat Ease Software. The optimization technique involved the implementation of a central composite design. In this work, drug entrapment efficiency and in vitro drug release were the dependent variables, whereas carbopol934 and HPMC K100 were the independent factors. Thirteen investigations were carried out. Using optimization criteria, contour maps were produced, and the best formulation was chosen.

Drug Release Kinetics: To ascertain the mechanism of drug release, we analyzed the medicine release data from enhanced floating beads using a variety of kinetic models. The Higuchi model, first order, zero order, and Korsmeyer Peppas plots are the four types. R2 values were found.

- **Zero Order Kinetics Model –** proportion of the overall material discharge over time T.
- **First Order Kinetics Model -** Track the remaining quantity of medication throughout the designated time interval, T.
- **Higuchi's model –** Proportion of drug emission concerning the square root of time T.

- **Korsmeyer-** Comparing the proportion of medication release over time 17.
- **Stability Studies:** The stability tests were performed using high-quality beads, which were subsequently placed in screw-cap borosilicate glass containers. Thereafter, they were preserved at different temperatures: 40±2°C with 75%±5% relative humidity in the oven, 25±2°C with 60%±5% relative humidity at ambient temperature, and 4-8°C in the stability chamber. To evaluate the effectiveness of the beads in drug retention and release, we performed tests at 30, 60, and 90 days.

4. RESULT AND DISCUSSION

Determination of Melting Point: Pure nitrofurantoin had a melting point of 228 ± 1.8°C (n=3).

Drug – excipient Compatibility: We analyze the infrared spectra of both the pure pharmaceuticals and the excipients.

This analysis demonstrates that the peaks remain mostly unchanged, demonstrating an absence of physical interaction between the drug and excipients through bond formation.

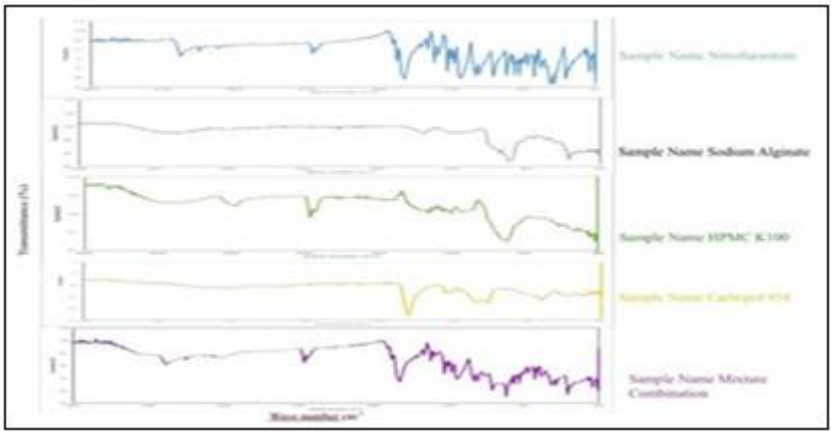

Fig. 1: Ftir Spectrum Of Nitrofurantoin, Sodium Alginate, Hpmc K100, Carbopol 934, Physical Mixture (Nitrofurantoin+Sodium Alginate+Hpmc K100+Carbopol 934)

Solubility Studies:

TABLE 2: SOLUBILITY PROFILE OF THE DRUG

Name of the Medium	Solubility of Nitrofurantoin
Water	Slightly soluble
Ethanol	Slightly soluble
Dimethylformamide	Soluble
0.1 N HCl	Soluble

Standard Calibration Plot of Nitrofurantoin: The λ_{max} of nitrofurantoin in 0.1 N HCl was 360 nm. The curve from 1 to 10 µg/ml is a linear relationship that conforms to Beer-Lambert's law. The regression coefficient is 0.9986. Table 3 presents the absorbance values.

Table 3: Calibration Curve Data of Nitrofurantoin In 0.1n HCL

Concentration (µg/mL)	Absorbance (Mean ± SD)
0	0
2	0.161 ± 0.002
4	0.286 ± 0.004
6	0.463 ± 0.001
8	0.617 ± 0.003

10	0.762 ± 0.002

All values expressed as mean of ± SD, n = 3

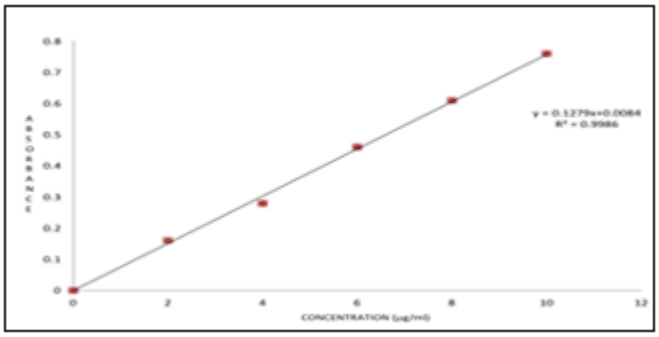

Fig. 2: Standard Calibration Curve of Nitrofurantoin In 0.1n Hcl At 360 Nm

5. CONCLUSION

This Research effectively illustrated the methodology for developing, statistically enhancing, and elucidating nitrofurantoin floating alginate beads as an efficient means of delivering drugs that remain in the stomach. The formulation factors were methodically enhanced using a statistical design approach. This produced beads that were appropriately sized, very buoyant, possessed a significant drug entrapment rate, and maintained buoyancy for an extended duration. Characterization studies indicated that the beads were round, stable, and exhibited suitable physicochemical properties. Nitrofurantoin exhibits a sustained and regulated release profile, as demonstrated by in vitro assays. This is advantageous as it extends the medication's residence time in the stomach and enhances its efficacy. Ultimately, the novel floating alginate bead formulation possesses significant potential to enhance bioavailability, reduce the required dosage frequency, and assist patients in adhering to their treatment protocols. This is a fantastic choice for individuals who prefer not to administer nitrofurantoin in the conventional manner.

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