FORMULATION AND IN VITRO EVALUATION OF FLOATING MULTIPARTICULATE DRUG DELIVERY SYSTEM OF AMOXICILLIN

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ABSTRACT

Gastro retentive drug delivery system have been developed for prolonged gastric residence time (GRT), extended release devices with reduced frequency of administration and also improved patient compliance. The purpose of designing gastro retentive floating multiparticulate beads of Amoxicillin dosage form is to develop a reliable formulation that has all the advantages of a single unit formulation and yet devoid of the danger of alteration in drug release profile and formulation behavior. The reason for selection of Amoxicillin as a candidate for the study was Amoxicillin has the absorption window in upper part of GIT. Amoxicillin along with excipients sodium alginate, hydroxyl propyl methyl cellulose, calcium chloride, calcium carbonate was prepared as gastro retentive floating beads. The beads were evaluated for drug encapsulation efficiency, buoyancy test, FTIR study, scanning electron microscopy analysis, in vitro dissolution studies and drug release kinetics. Optimised formula of F4 showed better release profile and extended the drug release for longer duration of time upto 12 hours. The drug release pattern from the optimized formulation followed zero order kinetics. The floatation was accomplished by incorporating gas generating agent calcium carbonate into a swellable polymer. FTIR studies of the pure drug and formulation showed that there was no drug polymer interaction. The physio chemical properties of all the formulations were found to be within the prescribed official limits. The optimized formulation have 99.87% of drug release upto 12 hours in a controlled manner.

KEYWORDS: Gastro retentive, Floating multi particulate, Amoxicillin, Controlled release, FTIR.
INTRODUCTION
Oral route is the most popular and convenient route for various drugs. Oral route generally consider an ideal drug delivery system that will possess two main properties
a) It should be in a single dose for prolonging action.
b) It should deliver the active drug directly to the target site.

An important requisite for the successful performance of oral controlled release drug delivery system is that the drug should have good absorption throughout the gastrointestinal tract (GIT).

Gastro Retentive Drug Delivery Systems (GRDDS)
Dosage forms that can be retained in the stomach are called gastro retentive drug delivery systems (GRDDS). GRDDS can improve the controlled delivery of drugs that have an absorption window by continuously releasing the drug for a prolonged period of time before it reaches its absorption site thus ensuring its optimal bioavailability.

Gastric retention will provide advantages such as the delivery of drugs with narrow absorption windows in the small intestinal region. Also, longer residence time in the stomach could be advantageous for local action in the upper part of the small intestine, for example treatment of peptic ulcer disease.

Furthermore, improved bioavailability is expected for drugs that are absorbed readily upon release in the GI tract. These drugs can be delivered ideally by slow release from the stomach. Certain types of drugs can benefit from using gastric retentive devices. These include:

- Drugs acting locally in the stomach
  Ex. Antacids and drugs for H. Pylori viz., Misoprostol
- Drugs that are primarily absorbed in the stomach Ex. Amoxicillin
- Drugs that is poorly soluble at alkaline pH
  Ex. Furosemide, Diazepam, Verapamil, etc
- Drugs with a narrow window of absorption
  Ex. Cyclosporine, Methotrexate, Levodopa, etc
- Drugs which are absorbed rapidly from the GI tract.
  Ex. Metonidazole, tetracycline
- Drugs that degrade in the colon.
Ex. Ranitidine, Metformin HCl

- Drugs that disturb normal colonic microbes
  Ex. antibiotics against Helicobacter pylori

Thus, small intestinal transit time is an important parameter for drugs that are incompletely absorbed. Gastro retentive systems can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs. Prolonged gastric retention improves bioavailability, reduces drug waste, and improves solubility for drugs that are less soluble in a high pH environment. It has applications also for local drug delivery to the stomach and proximal small intestine. Gastro retention helps to provide better availability of new products with new therapeutic possibilities and substantial benefits for patients.

**Basic gastro-intestinal tract physiology**

The GI tract is essentially a tube about nine metres long that runs through the middle of the body from the mouth to the anus. The wall of the GI tract has the same general structure through out most of its length, with some local variations for each region. The stomach is an organ with a capacity for storage and mixing. Anatomically the stomach is divided into 3 regions: fundus, body, and antrum (pylorus).

![Figure 3: Anatomy of stomach](image)

**Motility patterns of the GIT**

The various phases are as below

*Phase I* (basal phase) – Period of no contraction (40-60 minutes),

*Phase II* (pre burst phase) – Period of intermittent contractions (20-40 minutes),

*Phase III* (burst phase) – Period of regular contractions at the maximal frequency that travel
distally also known as house keeper wave; includes intense and regular contractions for short period. It is due to this wave that all the undigested material is swept out of the stomach down to the small intestine (10-20minutes).

*Phase IV-* Period of transition between phase III and phase I (0-5minutes).[18]

![Figure 4: Motility patterns of the GIT in the fasted state](image)

1.2 Factors controlling gastric Retention of dosage forms

The stomach anatomy and physiology contain parameters to be considered in the development of gastroretentive dosage forms. To pass through the pyloric valve in to the small intestine the particle size should be in the range of 1 to 2 mm. The most important parameters controlling the gastric retention time (GRT) of oral dosage forms include :density, size and shape of the dosage form, food intake and its nature, caloric content and frequency of intake, posture, gender, age, sex, sleep, body mass index, physical activity and diseased states of the individual (e.g. chronic disease, diabetes etc.) and administration of drugs with impact on gastrointestinal transit time for example drugs acting as anticholinergic agents (e.g. atropine, propantheline), Opiates (e.g. codeine) and prokinetic agents (e.g. metclopramide, cisapride.). The molecular weight and lipophilicity of the drug depending on its ionization state are also important parameters.
1.2.1. Density of dosage forms
1.2.2. Shape and size of the dosage form
1.2.3. Effect of gender, posture and age

1.3 Approaches to gastric retention

![Diagram of Approaches to Gastric Retention]

Types of Gastro retentive Dosage Forms

1.4. Advantages of floating drug delivery system
- Improves patient compliance by decreasing dosing frequency.
- Better therapeutic effect of short half-life drugs can be achieved.
- Gastric retention time is increased because of buoyancy.

1.5. Disadvantages
- Floating system is not feasible for those drugs that have solubility or stability problem in GIT.
- These systems require a sufficiently high level of fluids in the stomach.

**MECHANISM**
- The mechanism of drug release from multiparticulates can be occur in the following ways:
  - **Diffusion** On contact with aqueous fluids in the gastrointestinal tract (GIT), water diffuses into the interior of the particle. Drug dissolution occurs and the drug solutions diffuse across the release coat to the exterior.
• **Erosion** Some coatings can be designed to erode gradually with time, there by releasing the drug contained with in the particle.

• **Osmosis** In allowing water to enter under the right circumstances, an osmotic pressure can be built up within the interior of the particle. The drug is forced out of the particle into the exterior through the coating.

**Formulation aspects**
The design of novel controlled release dosage forms should take into account three important criteria, viz., drug delivery and destination. The various aspects which have to be considered while formulating FDDS (floating microspheres in particular).\(^{34}\) are;

a) Drug:
b) Polymer:
c) Solvent:
d) Processing medium:
e) Surfactant:
f) Cross linking agent:
g) Hardening agent:

**1.6.1. Applications**
1. **Sustained Drug Delivery**
2. **Site-Specific Drug Delivery**
3. **Absorption Enhancement**
4. **As carriers**

**Pharmacokinetic advantages and future potential**
Drugs that have poor bioavailability because their absorption is restricted to the upper GI tract can be delivered efficiently there by maximizing their absorption and improving their absolute bioavailabilities.\(^{16,18}\)

**1.7 EVALUATION OF FLOATING MICROSHEMERES**
**1.7.1. Micro-meritic properties**
Floating microspheres are characterized by their micromeric properties such as angle of repose, tapped density, compressibility index, true density and flow properties. True density is determined by liquid displacement method; tapped density and compressibility index are calculated by measuring the change in volume using a bulk density apparatus; angle of repose
is determined by fixed funnel method. The hollow nature of microspheres is confirmed by scanning electron microscopy. The compressibility index is calculated using following formula:

\[ I = \frac{V_b - V_t}{V_b} \times 100 \]

Where, \( V_b \) is the bulk volume and \( V_t \) is the tapped volume.

The value given below 15% indicates a powder which usually give rise to good flow characteristics, where as above 25% indicate poor flow ability.

### 1.7.2. Particle size and shape

The most widely used procedures to visualize microparticles are conventional light microscopy (LM) and scanning electron microscopy (SEM). LM provides a control over coating parameters in case of double walled microspheres.

SEM allows investigations of the multiparticulate surfaces and after particles are cross sectioned, it can also be used for the investigation of double walled systems.

### 1.7.3. Floating behavior

Appropriate quantity of the floating microparticulates is placed in 100ml of the simulated gastric fluid (SGF, ph 2.0), the mixture is stirred with a magnetic stirrer. The layer of buoyant microparticulate is pipette and separated by filtration. Particles in the sinking particulate layer are separated by filtration. Particles of both types are dried in a desiccator until constant weight is achieved. Both the fractions of microspheres are weighed and buoyancy is determined by the weight ratio of floating particles to the sum of floating and sinking particles.

\[ \text{Buoyancy(\%)} = \frac{W_f}{W_f + W_s} \]

Where, \( W_f \) and \( W_s \) are the weights of the floating and settled microparticles.

### 1.7.4. Entrapment efficiency

The capture efficiency of the multiparticulate or the percent entrapment can be determined by allowing washed multiparticulate to lyse. The lysate is then subjected to the determination of active constituents as per monograph requirement. The percent encapsulation efficiency is calculated using equation

\[ \% \text{Entrapment} = \frac{\text{Actual content}}{\text{Theoretical content}} \times 100 \]
1.7.5. *In-vitro* drug release studies

The release rate of floating microspheres is determined using United States Pharmacopoeia (USP) XXIII basket type dissolution apparatus.

1.7.6. *In-vivo* studies

The *in-vivo* floating behavior can be investigated by X-ray photography of hollow micro particulate loaded with barium sulphate in the stomach of beagle dogs. The *in-vitro* drug release studies are performed in a dissolution test in a dissolution media. The *in-vivo* plasma profile can be obtained by performing the study in suitable animal models.[14-15]

2. REVIEW OF LITERATURE

Ichikawa M, et al.[43] reported a multiple unit type of floating dosage form containing Aminobenzoic acid for which the floating ability and sustained release characteristics were evaluated in-vitro.

Floating force kinetics of per oral polymeric matrix dosage forms by a novel in-vitro resultant-weight measuring system was reported by Timmermans J. et al.[44] Results indicated that the magnitude of floating strength may vary as a function of time and usually decreases after immersion of the dosage form into the fluid consequently to the evolution of its hydrodynamic equilibrium.

Baumgartner S, et al.[50] developed floating matrix tablets containing Hydroxypropyl Methyl Cellulose, which after oral administration are designed to prolong the gastric residence time, increase the bioavailability and diminish the side effects of irritating drugs.

3.1 Aim of Designing Multiparticulate Dosage Forms

The purpose of designing multiparticulate dosage form is to develop a reliable formulation that has all the advantages of a single unit formulation and yet devoid of the danger of alteration in drug release profile and formulation behavior due to unit-to-unit variation. For the optimum design of a CR oral dosage form, the key step is to understand the principles of GI dynamics such as gastric emptying, small intestinal transit, colonic transit, etc. The concept of multiple-unit systems is characterized by the fact that the dose is administered as a number of subunits, each containing the active ingredient. The dose is then the sum of the individual subunits, and the functionality of the entire dose is directly correlated to the functionality of the individual subunits. When multiple-unit systems are taken orally, the
subunits of multiple-unit preparations distribute readily over a large surface area in the gastrointestinal tract and these small particles behave like liquids leaving the stomach within a short period of time. Their small size also enables them to be well distributed along the GI tract that could improve the bioavailability, which potentially could result in a reduction in local drug concentration, risk of toxicity, and side effects. Inter and intra-individual variations in bioavailability caused by, for example food effects, are reduced. Multiple-unit systems are a common way of obtaining well-controlled regulation of the drug release rate from oral drug formulations, partly because they minimize the risk of dose dumping, and partly because the reproducibility in release profile is better than that of single-unit devices. The main advantage of multiple unit dosage forms is related to their in vivo behavior, e.g., increased uniformity of plasma levels and better reproducible bioavailability. The multiple-unit system, the total drug is divided into many units.

3.2 Objective of the study
1. The present work is aimed to design and evaluate gastroretentive floating multiparticulate drug delivery system of Amoxicillin.
2. To study the effect of polymer, oil on buoyancy studies and drug release.
3. To determine the kinetics and mechanism of drug release.

DRUG PROFILE
Amoxicillin (INN, BAN), or amoxycillin (AAN) and abbreviated amox, is an antibiotic useful for the treatment of a number of bacterial infections.

It is a moderate-spectrum, bacteriolytic, β-lactam antibiotic in the aminopenicillin family used to treat susceptible Gram-positive and Gram-negative bacteria. It is usually the drug of choice within the class because it is better-absorbed, following oral administration, than other β-lactam antibiotics.

Structure of Amoxicillin
Medical Uses
Amoxicillin is used in the treatment of a number of infections, including acute otitis media, streptococcal pharyngitis, pneumonia, skin infections, urinary tract infections, Salmonella infections, Lyme disease, and chlamydia infections.

4. EXPERIMENTAL METHODOLOGY

4.1 Plan of research work

- Literature Survey.
- Selection of Excipients.
  1. Sodium alginate
  2. Hydroxy Propyl Methyl Cellulose K4 M
  3. Calcium chloride
  4. Calcium carbonate
- Compatibility tests.
  1) FT IR studies for pure drug, optimized formulation.
- Preparation of floating multiparticulate drug delivery system of Amoxicillin.
- Evaluation of the prepared multiparticulate system for Amoxicillin
  1. Drug encapsulation efficiency
  2. Buoyancy test
  3. FTIR study
  4. Scanning electron microscopy (SEM) analysis
  5. In vitro dissolution studies
- Drug release kinetics studies.

4.2 Materials and Sources

Table 6: Materials required and their suppliers

<table>
<thead>
<tr>
<th>S.No</th>
<th>Ingredients</th>
<th>Supplier</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Amoxicillin</td>
<td>Spectrum Pharma-Hyderabad.</td>
</tr>
<tr>
<td>2</td>
<td>Hydroxypropyl methylcellulose</td>
<td>Narmada chemicals</td>
</tr>
<tr>
<td>3</td>
<td>Sodium alginate</td>
<td>Narmada chemicals</td>
</tr>
<tr>
<td>4</td>
<td>Calcium chloride</td>
<td>Drugs India-Hyderabad.</td>
</tr>
<tr>
<td>5</td>
<td>Calcium carbonate</td>
<td>Drugs India-Hyderabad.</td>
</tr>
</tbody>
</table>
4.3 Instruments used

Table 7: Instruments used and their manufacturer

<table>
<thead>
<tr>
<th></th>
<th>Instrument</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Electronic single pan balance</td>
<td>Dona-Mumbai</td>
</tr>
<tr>
<td>2</td>
<td>pH meter</td>
<td>Lab India-Mumbai</td>
</tr>
<tr>
<td>3</td>
<td>Dissolution test apparatus</td>
<td>Sistronics</td>
</tr>
<tr>
<td>4</td>
<td>U.V Visible spectrophotometer</td>
<td>Lab IndiaLabindia-Mumbai</td>
</tr>
<tr>
<td>5</td>
<td>Homogenizer</td>
<td>Karnavthi</td>
</tr>
<tr>
<td>6</td>
<td>FTIR</td>
<td>Shimadzu</td>
</tr>
</tbody>
</table>

4.4 METHODOLOGY

4.4.1 Standard graph of Amoxicillin

The UV scanning of drug sample was carried out using a solution of drug dissolved in 0.1 N Hcl solution at concentration of 100 µg/ml. The $\lambda_{\text{max}}$ was observed at 228 nm. The calibration curve of Amoxicillin was obtained by dissolving the drug in 0.1 N Hcl solutions and absorbance was measured at 228 nm in 0.1 NHcl solution used as blank.

4.4.2 Method of preparation of 0.1N Hcl

8.5 ml of concentrated hydrochloric acid dissolved in 1000ml of demineralized water to give 0.1N HCL.

4.4.4 Master formulation of floating beads

Table 8: Master formulation of floating beads

<table>
<thead>
<tr>
<th>Ingredients (gm)</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
<th>F5</th>
<th>F6</th>
<th>F7</th>
<th>F8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>HPMC K4M</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Sodium alginate</td>
<td>0.5</td>
<td>1.0</td>
<td>1.5</td>
<td>2.0</td>
<td>2.5</td>
<td>3.0</td>
<td>3.5</td>
<td>4.0</td>
</tr>
<tr>
<td>Calcium chloride</td>
<td>0.5</td>
<td>1.0</td>
<td>1.5</td>
<td>0.5</td>
<td>1.0</td>
<td>1.5</td>
<td>0.5</td>
<td>1.0</td>
</tr>
<tr>
<td>CaCO$_3$</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
</tr>
</tbody>
</table>

4.4.5 Evaluation parameters for multiparticulate delivery system

1. Determination of drug encapsulation efficiency
2. Buoyancy test
3. Scanning electron microscopy (SEM)
4. FT-IR study

Principle

Electromagnetic radiation ranging between 500cm$^{-1}$ and 4000cm$^{-1}$ is passed through a sample and is absorbed by the bonds of the molecules in the sample causing them to stretch or bend. The wave length of the radiation absorbed is characteristic of the bond absorbing it.$^{[16]}$
Table 9: FTIR absorption peaks

<table>
<thead>
<tr>
<th>Region</th>
<th>Wavelength(µm)</th>
<th>Wave number(cm⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Near IR</td>
<td>0.78-2.5</td>
<td>12500-4000</td>
</tr>
<tr>
<td>Mid IR</td>
<td>2.5-25.0</td>
<td>4000-400</td>
</tr>
<tr>
<td>Far IR</td>
<td>25-200</td>
<td>400-10</td>
</tr>
</tbody>
</table>

Table 10: FTIR absorption peaks and their functional group

<table>
<thead>
<tr>
<th>S.No</th>
<th>Peaks</th>
<th>Functional group</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3668.62 &amp; 3346.30</td>
<td>OH (Alcohol)</td>
</tr>
<tr>
<td>2</td>
<td>3051.96</td>
<td>Aromatic C-H Stretching</td>
</tr>
<tr>
<td>3</td>
<td>3015.42</td>
<td>Alkene C-H Stretching</td>
</tr>
<tr>
<td>4</td>
<td>2950.80 &amp; 2893.72</td>
<td>Alkane C-H Stretching</td>
</tr>
<tr>
<td>5</td>
<td>1730.91 &amp; 1709.46</td>
<td>Ketone</td>
</tr>
<tr>
<td>6</td>
<td>1621.74</td>
<td>NH (Amine)</td>
</tr>
<tr>
<td>7</td>
<td>1396.31, 1372.09, 1351.93 &amp; 1325.98</td>
<td>C-O (Phenol)</td>
</tr>
<tr>
<td>8</td>
<td>1081.22, 1159.04, 1182.78</td>
<td>C-N Vibrations</td>
</tr>
<tr>
<td>9</td>
<td>600-900</td>
<td>C-H Bending (Aromatic)</td>
</tr>
</tbody>
</table>

5. In vitro dissolution studies.

Dissolution Medium: 900ml of simulated gastric fluid

Number of baskets : 6 baskets

Medium : 0.1N Hcl

Type : USP –II (Paddle assembly)

RPM : 50

Volume : 900ml

Run time : 16hr

Temp : 37± 0.5º C.

4.4.6 Kinetic Studies

A) Zero Order Release Equation

- The equation for zero order release is

\[ Q_t = Q_0 + K_0 t \]

Where

- \( Q_0 \) = initial amount of drug
- \( Q_t = \) cumulative amount of drug release at time “t”
- \( K_0 \) = zero order release constant
- \( t \) = time in hours
• It describes the systems where the drug release rate is independent of its concentration of the dissolved substance.
• A graph is plotted between the time taken on x-axis and the cumulative percentage of drug release on y-axis and it gives a straight line.

![Zero order kinetics graphs](image1.png)

**Figure 24: Zero order kinetics graphs**

C) Higuchi Release Equation

\[ Q = K_H t^{1/2} \]

Where

- \( Q \) = cumulative amount of drug release at time “\( t \)”.  
- \( K_H \) = Higuchi constant.  
- \( t \) = time in hours.

• The Higuchi equation suggests that the drug release by diffusion.  
• A graph is plotted between the square root of time taken on x-axis and the cumulative percentage of drug release on y-axis and it gives a straight line.

![Higuchi Release Equation graphs](image2.png)

**Figure 26: Higuchi Release Equation graphs**
5. RESULTS AND DISCUSSION

5.1. Standard calibration curve of Amoxicillin

Standard Curve of Amoxicillin was determined by plotting absorbance (nm) versus concentration (µg/ml) at 228 nm. The results obtained are as follows.

Table 13: Standard calibration curve of Amoxicillin

<table>
<thead>
<tr>
<th>Conc. in µg</th>
<th>Absorbance at 228 nm</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>0.110</td>
</tr>
<tr>
<td>10</td>
<td>0.224</td>
</tr>
<tr>
<td>15</td>
<td>0.367</td>
</tr>
<tr>
<td>20</td>
<td>0.488</td>
</tr>
<tr>
<td>25</td>
<td>0.532</td>
</tr>
<tr>
<td>30</td>
<td>0.661</td>
</tr>
<tr>
<td>35</td>
<td>0.772</td>
</tr>
<tr>
<td>40</td>
<td>0.869</td>
</tr>
</tbody>
</table>

![Figure 28: Standard calibration curve of Amoxicillin](image)

The linear regression analysis was done on absorbance data points. A straight-line equation was generated to facilitate the calculation of amount of drug. The equation is as follows.

\[ Y = mx + c \]

Where \( Y \) = Absorbance, \( m \) = slope, \( x \) = Concentration, \( c \) = Intercept.
5.2. Micromeritic property evaluation

Table 14: Results of micromeritic property evaluation

<table>
<thead>
<tr>
<th>Powders/Drugs</th>
<th>Angle of Repose ($\theta$) $= \tan^{-1}(h/r)$</th>
<th>Loose bulk Density (LBD) (g/ml)</th>
<th>Tapped bulk Density (TBD) (g/ml)</th>
<th>Carr's index %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin</td>
<td>27” 15’</td>
<td>0.348</td>
<td>0.421</td>
<td>17.33</td>
</tr>
<tr>
<td>Amox + Ca. chloride</td>
<td>26” 91’</td>
<td>0.321</td>
<td>0.372</td>
<td>13.70</td>
</tr>
<tr>
<td>Amox + Sod. Alginate</td>
<td>22” 01’</td>
<td>0.318</td>
<td>0.364</td>
<td>12.63</td>
</tr>
</tbody>
</table>

All the micromeritic properties were within normal limits which indicates good flow properties (Table 14).

5.3. Compatibility Studies

![Figure 29: FTIR Analysis of pure drug Amoxicillin](image-url)
Figure 30: FTIR analysis of pure drug Amoxicillin
Figure 31: FTIR analysis of optimized formulation
FTIR STUDY: Fig. 29 Shows FTIR spectra of Amoxicillin Trihydrate. There are many peaks observed at 3039 cm⁻¹ (–OH) and amoxicillin major peak observed at 3387 cm⁻¹ (amide NH and phenol OH stretch), 3034 cm⁻¹ (benzene ring CH stretch), 1726 cm⁻¹ (beta lactam CO stretch), 1614 cm⁻¹ (amide I, CO stretch), 1519 cm⁻¹ (benzene ring C=C stretch), 1483 cm⁻¹ (NH bend CN stretch combination band and NH3+ symmetric deformation), 1120 cm⁻¹. When peaks were observed in amoxicillin loaded alginate beads
that 3527 cm\textsuperscript{-1}, 3471 cm\textsuperscript{-1}, 3323 cm\textsuperscript{-1}, 3168 cm\textsuperscript{-1}, 3140 cm\textsuperscript{-1}, 3141 cm\textsuperscript{-1}, 1774 cm\textsuperscript{-1}, 1616 cm\textsuperscript{-1}, 1519 cm\textsuperscript{-1}, 1487 cm\textsuperscript{-1}, 1452 cm\textsuperscript{-1}, 1120 cm\textsuperscript{-1} comply with peaks of amoxicillin trihydrate, indicate that amoxicillin compatible with the excipients.

5.4: Determination of drug encapsulation efficiency
The drug encapsulation efficiency was increased with the increment of drug to polymer ratio. In case of Formulation-1, the % of encapsulation was 75\%, where the drug to alginate ratio was 1:0.5. But, this was increased in F-2 to F-8 where entrapment efficiency was 80.8\% to 88.9\%. (Table 15).

Table 15: Encapsulation efficiency, Floating lag time, Total floating time of F1-F8

<table>
<thead>
<tr>
<th>Parameters</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
<th>F5</th>
<th>F6</th>
<th>F7</th>
<th>F8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encapsulation efficiency</td>
<td>75.45</td>
<td>78.12</td>
<td>85.43</td>
<td>92.34</td>
<td>87.21</td>
<td>76.34</td>
<td>81.34</td>
<td>88.45</td>
</tr>
<tr>
<td>Floating lag time (Seconds)</td>
<td>132</td>
<td>129</td>
<td>120</td>
<td>118</td>
<td>134</td>
<td>143</td>
<td>129</td>
<td>135</td>
</tr>
<tr>
<td>Total floating time (Hours)</td>
<td>10.34</td>
<td>10.21</td>
<td>11.10</td>
<td>12.2</td>
<td>10.88</td>
<td>10.10</td>
<td>10.23</td>
<td>10.12</td>
</tr>
</tbody>
</table>

5.5 Buoyancy test: Floating properties of beads were studied by determining buoyancy and time required for sinking all the beads under study. The surfactant was used in medium to simulate surface tension of human gastric juice. Beads of all formulations floated immediately (very short lag time) and remained floating up to 12 hours. (Table 15).

5.6 Scanning electron microscopy (SEM)

![Figure 33: SEM photographs of optimized formulation of Amoxicillin I](image-url)
In vitro release kinetics: After 12 hours the percent of drug release (Figure 35) for eight formulations were 86.92% (F1), 85.76% (F2), 88.97% (F3), 95.64% (F4), 82.12% (F5), 86.34% (F6), 88.97% (F7), 87.97% (F8). The decrease in drug release was due to simultaneous increase in alginate amount. Because the more the amount of alginate, more would be the cross-linking between sodium alginate and calcium chloride; thus more drug would remain entrapped and decrease the release. In the absence of gas-forming agent the release rate was very slow. CaCO3 is present as an insoluble dispersion in neutral pH aqueous alginate solution. However in acidic media, the CaCO3 becomes water soluble.

Table 16: In vitro Dissolution profiles of floating beads F1-F8

<table>
<thead>
<tr>
<th>Time Hrs.</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
<th>F5</th>
<th>F6</th>
<th>F7</th>
<th>F8</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>21.94</td>
<td>24.34</td>
<td>26.45</td>
<td><strong>22.98</strong></td>
<td>28.43</td>
<td>27.34</td>
<td>28.12</td>
<td>26.43</td>
</tr>
<tr>
<td>4</td>
<td>24.65</td>
<td>29.45</td>
<td>34.56</td>
<td><strong>40.13</strong></td>
<td>34.67</td>
<td>36.56</td>
<td>35.56</td>
<td>33.56</td>
</tr>
<tr>
<td>6</td>
<td>35.24</td>
<td>34.56</td>
<td>46.56</td>
<td><strong>56.02</strong></td>
<td>39.56</td>
<td>45.67</td>
<td>45.56</td>
<td>44.56</td>
</tr>
<tr>
<td>8</td>
<td>48.56</td>
<td>49.63</td>
<td>57.87</td>
<td><strong>72.04</strong></td>
<td>46.23</td>
<td>57.87</td>
<td>58.87</td>
<td>56.87</td>
</tr>
<tr>
<td>10</td>
<td>76.45</td>
<td>75.65</td>
<td>78.89</td>
<td><strong>84.92</strong></td>
<td>74.56</td>
<td>76.56</td>
<td>79.89</td>
<td>77.89</td>
</tr>
<tr>
<td>12</td>
<td>86.92</td>
<td>85.76</td>
<td>88.97</td>
<td><strong>99.87</strong></td>
<td>82.12</td>
<td>86.34</td>
<td>88.97</td>
<td>87.97</td>
</tr>
</tbody>
</table>
5.8. Zero order release kinetics for F4

After studying the drug release kinetics, it was observed that all the formulation follows zero order release kinetics (Table 17).

Table 17: Zero order kinetics data For F4

<table>
<thead>
<tr>
<th>Time in hrs</th>
<th>0</th>
<th>2</th>
<th>4</th>
<th>6</th>
<th>8</th>
<th>10</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td>%CDR</td>
<td>0</td>
<td>22.98</td>
<td>40.13</td>
<td>56.02</td>
<td>72.04</td>
<td>84.92</td>
<td>99.87</td>
</tr>
</tbody>
</table>

6. SUMMARY AND CONCLUSION

Gastric emptying of the dosage forms is an extremely variable process and is the ability to prolong and control the emptying time which is a valuable asset for dosage forms, which reside in the stomach for a longer period of time than conventional dosage forms.
Gastroretentive floating beads of Amoxicillin were prepared with an aim to provide the drug for prolonged period of time in the stomach. Amoxicillin was targeted to stomach because it has the absorption window in upper part of GIT.

The floatation was accomplished by incorporating gas generating agent, calcium carbonate into a swellable polymer.

FTIR studies of the pure drug and formulations showed that there was no drug polymer interaction.

The physico chemical properties of all the formulations were found to be within the prescribed official limits.

The increase in polymer concentration and viscosity causes retarding of the drug release. Formulations containing higher polymer concentration had slower drug release when compared to formulations with lower concentration of polymers.

From all the formulation F4 formulation showed better release profile and extended the drug release for longer duration of time. Hence F4 formulation is optimized.

The drug release pattern from the optimized formulation followed zero order kinetics.

REFERENCES