DISCUSSION

5.1. Introduction

The current focus of pharmaceutical research involves the development of new dosage forms or formulations using novel excipients for existing drugs that offer distinct benefit over the conventional formulations. These innovative formulations offer life extension to drugs in the form of new patents, extending the product life cycle. Besides this, these novel drug delivery systems provide certain advantage over the conventional formulation, which includes reduction in blood level fluctuations, reduction in dosing frequency and reduces the adverse effects associated with conventional therapy. In certain cases of cardiovascular diseases, successful treatment can be achieved by maintaining constant drug blood level in therapeutic range and for this a constant and uniform supply of drug is desired. Multiple dosing at frequent intervals is difficult for a patient, which can lead to patient non-compliance. This demands the need to develop a sustained release formulation.

Famotidine suffers from poor bioavailability (40-45%), as it is poorly soluble in the low pH of the stomach. Famotidine promotes confined supply of these drugs to the H₂ receptor of the parietal cell wall. Therefore, scholars are developing new formulations, such as gastro retaining drug delivery systems. Such formulations retained in the stomach for a extended period of time and thereby improve the bioavailability of drugs. The recommended adult oral dosage of Famotidine is 40 mg daily. The actual treatment of erosive oesophagitis requires administration of 40 mg of Famotidine per day. A conservative dose of 40 mg can hinder gastric acid secretion up to 5 hours but not up to 10 hours. Thus, a continuous release dosage form Famotidine is needed. The short biological half-life of drug (3–4 hours) also favors development of a sustained release formulation. Famotidine is a H₂ receptor blocker; these H₂ receptors are present in stomach. Floating beads of Famotidine retains in stomach, produces local action and thereby increasing bioavailability of drug. Famotidine shows improved solubility in acidic environment hence, it displays improved absorption from stomach thereby, reducing the dose of drug. The gastro retentive drug delivery system can be engaged in the stomach and supports in
Discussion

improving the oral sustained delivery of drugs that have an absorption window in a particular region of the GI tract. These systems help in continuously releasing the drug before it reaches the absorption window, thus ensuring optimal bioavailability. Several approaches are currently used to prolong gastric retention time. These include floating drug delivery systems, swelling and expanding systems, polymeric bioadhesive systems, high-density systems and other delayed gastric-emptying devices. The principle of buoyant research offers a simple and practical method to achieve improved gastric residence time for dosage form and continuous drug release. The present study describes the formulation development of intragastric floating beads of Famotidine.

5.2. Objective
The objective of present research study is to formulate and evaluate the multi-particulate floating drug delivery system for famotidine using natural polymer alginate, pectin and HPMC. This natural polymer offers several advantages like non-toxic, biocompatible, biodegradable and cost effectiveness. It exhibits suitable controlled release characteristic of the controlled drug delivery system. Famotidine is a competitive inhibitor of histamine H$_2$ receptors used in the treatment of gastric and duodenal ulcers, gastro-oesophageal reflux disease (GERD) and prophylaxis of stress ulcers. Its biological half-life is 3.5 to 4.5 hours with a bio-availability of 40 to 45% and is administered in divided doses (20-40mg). Hence, to increase the drug concentration at the gastric mucosa over an extended period of time, famotidine was formulated into a HBS. Famotidine inhibits H$_2$ receptors in the competitive-noncompetitive manner. In the gastric parietal cells the terminal enzyme H$^+$/K$^+$ATPase (proton pump) which secretes H$^+$ ions in the apical canaliculi of parietal cells can be activated by histamine, ACh and gastrin acting via their own receptors located on the basolateral membrane of these cells.

5.3. PRE-FORMULATION STUDIES
The study started with the characterization of the drug and polymer. The drug famotidin was a gift sample from cadila pharmaceuticals Ahmedabad, India. The
polymer sodium alginat was a gift sample from CDH (P) Ltd, New Delhi, Pectin SD fine chemicals, Mumbai, India. HPMC Gift sample from Colorcon India Ltd.

In the characterization study for drug, the melting point, solubility, loss on drying, UV, FTIR and DSC analysis were carried out to confirm the purity and quality of the drug. The results of these studies confirmed the purity of the drug. Famotidine is a light yellow and crystalline powder. Its melting point was determined by DSC method and it was found to be 167°C. The loss on drying was found to be 0.24%. The moisture content was found to be within the Pharmacopoeial specified limit. The UV scan of famotidine was performed and the absorbance maxima found to be at 265 nm in 0.1N HCl solution and 269 nm in phosphate buffer which is comparable with the standard values.

The FTIR spectroscopic studies of famotidine showed, the characteristic peaks appeared due to the different functional groups present in famotidine. The IR spectrum of famotidine exhibits a peak at 3402.40 cm\(^{-1}\) due to the N-H stretching of sulfonamide group and peaks at 1286.55 cm\(^{-1}\) and 1147.03 cm\(^{-1}\) due to C=\(\text{N}\)-strecthing and S-O stretching, confirms the structure of the drug. These observed principal peaks were comparable to the reference peaks of the famotidine. This observation confirmed the purity and authenticity of the famotidine (Fig. 4.1; Table 4.1).

The DSC thermo gram of the pure famotidine showed a single sharp endothermic peak at its melting point. At a scan rate of 10°C/min, the observed peak temperature was 167°C (Fig 4.4)

pH of the 1% aqueous solution of the drug when determined using Digital pH meter (systronics) found to be 7.35 and Partition coefficient was found to be 0.124. We had also found out the average partial size. The Average Particle size of Famotidine is found to be 2.452 µm.

This was followed by preparing the standard curve of famotidine in 0.1N HCl. The equation for the regression plot of pure drug in 0.1N HCl is: \(Y= (0.0381) X\) and the regression co-efficient \((R^2)\) was found to be 0.9996 and the curve has shown the linearity between the concentrations ranging from 2-25 mcg/ml and analyzed using UV spectrophotometer at 265 nm (Fig. 4.3; Table 4.2).
The regression line equation obtained was further used in in vitro evaluations for determining famotidine concentration in different formulated beads.

5.4. DRUG-EXCIPIENTS COMPATIBILITY STUDIES

Drug excipient interaction was determined using following methods:

**Thin Layer Chromatography (TLC):** Drug and excipients were mixed in ratio of 1:1 and kept under different conditions for 30 days and then analyzed by TLC for any possible interaction. At room temperature and at 40°C / 75% RH no interaction was found in any samples (Table 4.7)

**Visual observation:** Drug and excipients were mixed in ratio of 1:1 and kept under the different conditions for 30 days and analyze by visual observation. At the day of starting study and after 30 days above samples was observed visually. Drug was found to be compatible with all the excipients used in the formulation and there were neither any change in color nor any kind of lump formation in initial sample as well as sample kept in 50°C/80% RH for 30 days. And drug was found to be compatible with polymer used in formulation (Table 4.8).

**FTIR-Interpretation:**

IR spectroscopy was used as a means of studying drug-excipient interaction. The IR spectrum of famotidine exhibits a peak at $3402.40 \text{ cm}^{-1}$ due to the N-H stretching of sulfonamide group and peaks at $1286.55 \text{ cm}^{-1}$ and $1147.03 \text{ cm}^{-1}$ due to C=N– stretching and S-O stretching, confirms the structure of the drug. The FTIR spectrum of the pure drug was observed to be similar to the normal spectrum of Famotidine. It was detected that all the distinguishing peaks of Famotidine were present in blend spectra which specifies the compatibility of the drug with the polymers used. (Figure 4.7 to Figure 4.10)

5.5. FABRICATION OF FLOATING BEADS.
Various parameters had been optimized during the formation of beads and these are as follows:

**Optimizing the concentration of polymer:** As we increase the concentration of polymer (i.e. sodium alginate) the consistency of the gel formed were also increase and at higher concentration it is difficult for gel to pass from the syringe and at lower concentration the beads were not properly formed. From the prepared formulation P$_3$ was the optimized formulation having 3% concentration.

**Optimizing the height of syringe from the surface of curing agent:** When we keep the syringe at very low height above the surface of curing agent, perfect beads dose not attained as the beads become disk shape upon the gelling. Also there is no extra effect or advantage observed in increasing the height of syringe over the shape of beads. Here we have observed that the perfect shape is attained if we keep the syringe at 5 cm above the surface and so the formulation P$_8$ is optimized one.

**Optimizing the size of needle:** On the basis of size of needle it was observed that as we use the syringe without needle it was difficult to control the speed of drops. As we increase the gauze size the pore size will decrease consecutively and so it was difficult to exudate the beads from the syringe making almost impossible to exudate from gauze size 31. The optimized size was 28 used in formulation P$_{14}$ which gives the perfect size and uniform shape to the beads.

**Optimizing the rate of dropping:** When the speed of exudation was too fast, flaks were formed instead of drops. While perfect beads were formed when the speed was 2ml/min, so it is considered to be the optimized speed for further formulation

**Effect of speed of magnetic stirrer on the beads:** As there were no or slow agitation in the curing agent then the beads formed continuous to stick with each other and form a cluster, too high speed also disturb the perfect formulation of beads. 50 rpm is observed to be as optimized speed for providing gentle agitation and uniform shape of beads.

**Effect of different concentration of curing agent on the beads:** As such there is not any considerable change observed in the shape of beads by differing the concentration.
of curing agent but it has been observed that at lower concentration we have to keep the beads for longer duration for solidifications, and we get the properly shaped and solidified beads at 5% concentration of curing agent.

**Effect of different time of curing:** From the different batches prepared it has been observed that while removing the beads after 1 minute, beads were not properly solidify and it is still in solution form. It start attaining a proper shape after 10 or 30 minutes, as we have to give a proper time for reaction to perform i.e. for exchange of ions. Keeping the beads for longer time it may be possible that if the drug is water soluble then the drug may release out and dissolve and no proper encapsulation been done so it should be avoided. Accordingly formulation P$_{32}$ is having the optimized time i.e. 30 minute.

**Floating beads:**
After optimizing the seven different parameter of the manufacturing which requires 34 preliminary batches. We come to a conclusion and a common method was adopted for formulating the various formulations. Various blends of sodium alginate, pectin and HPMC were used as polymer and were dissolved in distilled water. Different formulations containing different concentrations of oil were fabricated by ion gelation technique and another 35 batches been fabricated according to the table 3.6. Various parameters have been evaluated of these batches and reported accordingly.

**5.6. PHYSICOCHEMICAL CHARACTERIZATION OF FORMULATION:**

The formulations were subjected to various physico-chemical evaluations. The formulated beads were subjected to the diameter measurement by using screw gauge. 20 randomly selected beads of each formulation were tested for their diameter. The average diameter was calculated. Percentage deviation from the mean diameter was determined. The formulations F$_1$, F$_2$, F$_3$, F$_4$, showed 1.59± 0.02, 1.48± 0.03, and 1.53± 0.01 and 1.52± 0.02 mm diameter respectively. The diameter of the beads varied from 1.33 to 1.64 mm. The diameter of the beads was found to increase with the increase in the polymer content and oil content. The shape and diameter of the beads vary from batch to batch (Table 4.17).
The shape of beads varies from spherical to disc shape with changing concentration and ratio of polymers, as the total concentration of the polymer reduces from 5\% to 3\% and 2\% w/v shape of beads also changes from spherical to dislike.

In the case of beads prepared with the combination of sodium alginate and pectin, as the part of alginate was reduced, the spherical shape was lost and beads became disk like or of irregular shape. (\textit{P}_{39} \& \textit{P}_{49}) (Fig 4.16) Result shows that that as the amount of oil increases, the size of beads increases gradually though there is not any significant change in the size of beads made of different types of polymer.

Beads appear to be white translucent and rigid. Color of the sodium alginate beads was white in solution but it changes to reddish brown after drying. The color of pectin beads prepared in similar way was somewhat darker than that of sodium alginate beads.

The color of the beads prepared with sodium alginate and pectin was off white and changed to dark brown when dried.

Upon air drying the conventional alginate and pectin gel beads of all formulation become dense, minor and flattened with crumpled circumference due to water diffusing gradually from the sphere under drying process. The oil entrapped beads were extra spherical with no hollow at the central of sphere (Fig 4.11 and Fig 4.12)

The SEM photo micrograph of the beads with HPMC & pectin depicts that the cavities inside the beads increased when the ratio of HPMC in the beads increased (Fig 4.15 & fig 4.16) True densities of drug loaded \textit{F}_1, \textit{F}_2, \textit{F}_3 and \textit{F}_4 gel beads was determined by suspending the gel beads in solvent in which the drug was insoluble. The findings reveal true density values to be less than the specific gravity of gastric fluid 1.004g/cc beads thus favoring floatation of beads in gastric fluid.

All the formulation exhibited good flow property with an angle of repose to be less than 30\°. Angle of repose of formulation \textit{F}_1, \textit{F}_2, \textit{F}_3, \textit{F}_4 comes to be 22.30, 22.88, 23.12 and 24.25 respectively.

The floating ability of the prepared beads was evaluated with or without oil. The beads without oil (\textit{P}_1-\textit{P}_{33}) sank immediately in HCl buffer (pH 1.2) while beads containing oil (mineral oil) demonstrates instantaneous and excellent floating ability.
It was also observed that floating ability was found to be directly related to the oil content of polymer.

It has been observed that there has been different floating time due to the differences in polymer and oil concentration. As the concentration of oil increases the floating time increases and the floating lag time decreases. We have taken separate test solution e.g. distill water, 0.1 mole/lit HcL, acid phthalate buffer and normal saline (ph. 6.8) it was observed that our optimized formulation F₁, F₂, F₃, F₄ floated in all test solution without any lag time and remain float for next 24 to 48 hrs without any sign of degradation and after 2-3 days they automatically burst and degrade by itself. Total floating cycle is been depicted in Fig 4.23 to Fig 4.6 giving clear idea about lag time and total floating time.

The drug entrapment efficiency of the dried beads was varied from 35.74% to 67.53 % (Table 4.19) as famotidine is a very slightly water soluble drug and the drug diffused into the surrounding aqueous medium is less quantity resulting in acceptable values for % entrapment efficiency. The second important parameter, which was utilized to improve % entrapment efficiency, was amount of oil used in preparation of each batch. As the amount of oil was increased from 10 to 20% the entrapment efficiency was also found to increase considerably. But at a higher concentration of oil (30%) the entrapment efficiency tends to decrease slightly. As when the amount of oil used was 10%, some amount of drug diffused in surrounding medium during jellification of beads. But when this amount was increased up to 20%, the barrier action of entrapped droplets of oil were increased and protected more drug against diffusion, resulting in increased entrapment efficiency of beads. When the amount of oil was increased up to 30% this enhanced volume of oil occupied the most of the volume of a single bead and prevented the entrapment of sufficient amount of drug. Thus it can be concluded that an intermediate optimum level of oil is necessary for preparation of beads with maximum entrapment efficiency.

The results indicate that the entrapment efficiency was less when the beads were prepared with a single type of polymer (sod. alginate) in comparison of the beads prepared with two types of polymers (sod. alginate and pectin). This might be due to the presence of two types of protective layers in beads, one of calcium pectinate and other one of calcium alginate, which prevented the diffusion of drug.
more effectively than a single type of layer only. But as the proportion of alginate was reduced in the combination of these two polymers, the entrapment efficiency of beads started to reduce. It can be explained that in combination of two layers calcium alginate layer was more effective in prevention of diffusion of drug than the calcium pectinate layer. The swelling index was found in the range of 0.27 to 0.431. In the present study it was observed that initially in every batch there was a sudden swelling of beads, followed by reduction in weight as we study further. This effect could be due to acid solubility of drug that might have influenced the swelling behavior of beads. The polymer mixture is also responsible for different swelling behavior of beads. As higher the proportion of alginate less will be the swelling behavior. It proves that alginate makes compact structured beads in comparison to pectin. When we compare the batches of high and low concentration of oil it has been observed that increasing the amount of oil leads to decrease in the swelling index. Thus the oil acted as a barrier for water absorption.

Dissolution study of our optimized batches i.e. F₁, F₂, F₃, F₄ were carried out. The entire four formulation shows sustained release pattern which last for more than 24 hrs. The drug release pattern was affected by polymer concentration, ratio of polymer mixture, and amount of oil. Earlier result shows that no single polymer was sufficient to sustained the drug release (P₃₅, P₃₆, P₃₇, P₄₇, P₄₈, P₄₉, P₅₉, P₆₀) after observing the release pattern it had been observed that beads having combination of polymer with alginate shows sustained effect. This could be due to presence of additional barrier layer of calcium pectinate or HPMC which caused the slow release of drug from beads. Although it had also been observed, that as we decrease the proportion of sodium alginate in comparison to pectin or HPMC, the release of drug become fast. So we can say comparatively sodium alginate is having more efficiency in providing sustainable beads as compare to pectin and HPMC not individually but in combination of other polymer i.e with pectin and HPMC. (F₁, F₂, F₃, F₄)

Another parameter which also affects the drug release from different batches was amount of oil. After analyzing the release pattern of different batches it has been observed that higher the amount of oil higher will be the efficiency to provide sustainability this is due to the formation of additional barrier of oil which slow down
the release of drug from beads. When we compare the dissolution profile of our optimized formulations we can conclude that F₁ is the most optimized formulation as far as sustainability is concern.

5.7. Drug Release kinetics of optimized formulation F₁

The in-vitro drug release data was subjected to accuracy of fit test by linear regression analysis according to first order, zero order kinetic equations, Higuchi and Korsmeyer models to determine the mechanism of drug release. The effects of linear regression study of data including regression coefficient are summarized in table 4.29. When the regression coefficient ‘R²’ value of first order plots and zero order were compared, it was observed that the ‘R²’ values of zero order were in the range of 0.898 whereas the ‘R²’ values of first order plots were found to be in the range of 0.965 indicating drug release from the formulations was found to follow first order kinetics.

As far as mechanism of dissolution is concern the dissolution profiles of all the formulations suggested that diffusion is the predominant mechanism. It was observed from the graphical data that the value of regression coefficient of Higuchi model was found to be 0.9741 which was closer to 1 as compared to regression coefficient of Korsmeyer and peppas model which was 0.9501. Therefore, the formulation F₁ follows Higuchi model (diffusion).

5.8. Accelerated stability studies

Stability study was shown only on optimized formulation. The formulation were filled in the aluminium foil and subjected to stability studies at different temperature and humidity condition as per the ICH guidelines i.e. room temperature (25⁰C / 45 % RH) and 40⁰C / 75 %RH. The sample was withdrawn at time intervals of 0, 15 & 60 days. The sample was evaluated for possible morphology, drug loading, % entrapment, floating time and in vitro release profile.

<table>
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<tr>
<th>Parameter</th>
<th>40⁰C ± 2⁰C / 75 % RH ± 5 %</th>
<th>Room Temperature</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>At 0 At 15 At 60</td>
<td>25⁰C ± 2⁰C / 45 % RH ± 5 %</td>
</tr>
<tr>
<td></td>
<td>At 0 days At 15 At 60</td>
<td></td>
</tr>
</tbody>
</table>

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Discussion

<table>
<thead>
<tr>
<th>Morphology</th>
<th>days</th>
<th>days</th>
<th>days</th>
<th>days</th>
<th>days</th>
<th>days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spheric and uniform</td>
<td>176</td>
<td>175</td>
<td>174</td>
<td>173</td>
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<td>171</td>
</tr>
<tr>
<td>Drug Loading (%)</td>
<td>11.21%</td>
<td>11.20%</td>
<td>11.15%</td>
<td>11.21%</td>
<td>11.15%</td>
<td>11.14%</td>
</tr>
<tr>
<td>% Entrapment Efficiency</td>
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<td>67.35%</td>
<td>67.66%</td>
<td>67.53%</td>
<td>67.57%</td>
<td>67.79%</td>
</tr>
<tr>
<td>Floating Time</td>
<td>18 hr</td>
<td>16 hrs</td>
<td>15 hr</td>
<td>18 hr</td>
<td>17 hrs</td>
<td>17 hr</td>
</tr>
<tr>
<td>Dissolution profile Formulation F1</td>
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<td>21.71%</td>
<td>21.97%</td>
<td>22.93%</td>
<td>21.71%</td>
<td>21.59%</td>
</tr>
<tr>
<td>4th hr</td>
<td>49.12%</td>
<td>49.76%</td>
<td>50.11%</td>
<td>49.12%</td>
<td>49.17%</td>
<td>49.22%</td>
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<tr>
<td>6th hr</td>
<td>57.54%</td>
<td>57.89%</td>
<td>58.37%</td>
<td>57.54%</td>
<td>58.14%</td>
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<tr>
<td>8th hr</td>
<td>60.75%</td>
<td>61.75%</td>
<td>62.11%</td>
<td>60.75%</td>
<td>60.98%</td>
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<tr>
<td>12th hr</td>
<td>73.89%</td>
<td>73.89%</td>
<td>74.98%</td>
<td>73.89%</td>
<td>74.11%</td>
<td>74.79%</td>
</tr>
</tbody>
</table>

Tables above indicated that there weren’t any major changes in the above parameter evaluated during stability studies and so it was inferred that the storage conditions have not significantly influenced the characteristic of optimized formulation. It was also revealed that dissolution pattern was not significantly affected by the storage condition and time of stability studies.

5.9 FLOATING STUDY WITH DIFFERENT OILS OF DIFFERENT DENSITIES:
Floating study with different oils of different densities such as Castor oil (R.D=0.96), Peppermint oil (R.D=0.90), Mineral oil (R.D=0.84), Sunflower oil (R.D=0.94), Soybean oil (R.D=0.92) and Olive oil (R.D=0.91) were performed. The effect of selected factors, such as type of oil, percentage of oil, on morphology and floating properties of optimized beads (F1) was investigated. (Table: 4.32) The kind and proportion of oil play an important role in controlling the floating of oil entrapped
beads. The result suggested that oil entrapped alginate pectin gel beads were favorable as a carrier for intragastric floating drug delivery.

Oil entrapped floating gel beads were more spherical in comparison to without oil. This sphere-shaped of oil captured could be maintained with high concentration of oil; also as we increase the amount of oil the size of pores found on beads also increases. There should be a proper homogenization of oil with solution without which the oil separated from the alginate pectin solution. However the emulsifying property is also having its limitation as when we increase the concentration of oil above 30% w/w oil began to leak. Polymer helped to emulsify the mixture of water and oil phase during the homogenization process as pectin and alginate act as a surface active agent and reduces the interfacial tension between an oil phase and water phase.

The beads containing mineral oil were spherical transparent and slightly yellowish whereas those containing peppermint oil soya been oil, sunflower oil, olive oil were less transparent and light yellowish as the original color of oil dominated over it.

The mean diameter of conventional alginate pectin gel beads was 130±0.07 mm. The mean diameter of oil entrapped alginate pectin gel beads containing different types and amount of oil is shown in table 4.32. The result shows that as we increase the amount of oil the mean diameter of beads also increase. The size of beads containing peppermint oil is comparatively smaller than other beads having same amount of oil. This could be the reason as being volatile in nature peppermint oil resulted in loss of mass during air drying.

Conventional alginate pectin gel beads without oil in all test solution sank, as no floating agent was there as shown in table 4.32. However oil entrapped beads containing different oil floats immediately and remains floating for 24 hrs, when sufficient amount of oil was used.

When we compare the floating characteristic of beads containing different oil it has been observed that at different concentration of oil, different oil act’s differently i.e. the floating behavior was different. This could be due to difference in densities of oil. At 10% only light mineral oil while at 20% olive oil, soya been oil, peppermint oil and at 30% sunflower and castor oil floats.

It has been observed that if we use oil with lower relative densities a very small amount of oil was required to keep the beads afloat, and if we use the oil of high
density then more amount of oil is required for beads to float. So density of oil plays an important role in floating characteristics.

5.10 STUDY THE EFFECT OF DIFFERENT CURING AGENT ON ALGINATE BEADS

In the present study the formation of famotidine beads through inotropic gelation method was investigated using several curing agent (several cations) and its various selected characteristics were studied such as size, wall strength, swelling ratio and drug encapsulation capacity. The type and percentage of cation plays an important role in physiological characterization of beads.

In this alginate pectin gel beads of our optimized batch was formulated using various curing agents such as Calcium chloride solution (CaCl$_2$), Magnesium chloride (MgCl$_2$.2H$_2$O), Barium chloride (BaCl$_2$.2H$_2$O), Lead nitrate (Pb(NO$_3$)$_2$) , SnCl$_2$, MnCl$_2$ maintained on gentle agitation at room temperature and various characteristics were evaluated of the prepared beads such as particle size and wall strength, drug entrapment efficiency and swelling ratio.

From the results observed from these preparations it can be concluded that the appearance of beads is influenced by the type of ions used. The average particle size of calcium-alginate bead was 1.63mm±0.02. The beads prepared from calcium, barium, & lead ions were found to be more acceptable in terms of shape, wall strength and formation. As no fraction was observed in these preparations and they are also having uniform in shape & size. Shape of calcium alginate beads can be seen in Fig 4.11

As far as drug encapsulation is concern the result shows that highest amount of drug entrapment was seen in beads formed by CaCl$_2$ as curing agent in comparison to other curing agent. We have also study the effect of different concentrations of calcium chloride on the entrapment efficiency and it has been observed that as we make the differences in concentration between polymer and CaCl$_2$ the entrapment efficiency also decrease.

As far as swelling study is concern a rapid swelling was observe in beads having 3% CaCl$_2$w/v.
5.11 EVALUATION OF CAPSULE FILLED WITH FLOATING BEADS AND COMPARING IT WITH PURE DRUG.

In the present study we have taken the capsule of size 18.3mm capsule no 2 into which famotidine loaded alginate pectin beads were filled (formulation F₁) and various evaluation parameters were evaluated such as floating lag time, floating time, dissolution study and comparing it with that of pure drug filled in capsule.

As the required dose of famotidine is approximately 40 mg per day so we have taken 200 mg of beads which contain the required dose of famotidine. This quantity of drug can be easily encapsulated in capsule of size No. 2 having volume of 18.3mm.

From the result above it has been concluded that due to an extra hard gelatin capsule shell the beads comes in contact with 0.1N HCl solution after another 15 minutes. So drug release delayed by another 15-30 minutes.

The floating lag time of both the capsules was 0 minutes. Floating time of F₉D observed to be 15 minutes after that the capsule degraded and dissolved in solution. While that of formulation F₉B floats more than 24 hrs. Formulation F₉B after 10 minute degraded and then beads itself floats for more than 24 hrs

As far as results of dissolution is concern pure drug capsule dissolves almost completely in early 2.5 hrs. And capsules filled with floating beads dissolves only 75% in 12 hrs of study. This suggested that oil entrapped alginate pectinate gel beads were promising as a carrier for intragastric floating drug delivery.