**BUOYANT OIL ENTRAPPED CALCIUMPECTINATE GEL BEADS OF FAMOTIDINE**

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**ABSTRACT**

In the present study, Buoyant oil entrapped calcium pectinate gel beads of Famotidine were prepared by emulsion gelation method. Oil entrapped calcium pectinate gel beads concept was applied to increase the gastric retention time of the drug. Famotidine is a histamine H2 receptor antagonist that inhibits stomach acid production and used in the treatment of peptic ulcer diseases. The obtained beads are capable of floating in the gastric fluid and thus increases the gastric retention time. Drug release was found to uniform and maximum for 24 hrs around 80%. The obtained beads were evaluated for size analysis, morphology, buoyancy test, dissolution profile. This approach is found to be one of the approach for gastro retentive drug delivery and thus increases the drug absorption and activity.

**Keywords:** Famotidine, calcium Pectinate Beads, Buoyant, Gastric residence time

**INTRODUCTION**

Famotidine is a histamine H2 receptor antagonist that inhibits stomach acid production and is commonly used in the treatment of peptic ulcer diseases. Here, we have prepared buoyant oil entrapped calcium pectinate gel beads to prolong the gastric retention time of the drug thus increasing drug absorption and drug activity. The obtained beads were capable of floating in the gastric fluid thereby increasing the gastric retention time of the drug.

Now days, gastro retentive dosage forms is an upcoming approach. Drugs which are locally active in the stomach, having absorption window in the stomach or in the upper small intestine and those which are unstable in the intestine or colonic environment can be used to prepared gastro retentive dosage forms1. Floating dosage forms can be made by a gelling process of hydrocolloid materials or by incorporating a vacuum or gas filled chamber. Floating properties of dosage forms can also be fabricated using oils, here we incorporated coconut oil3. Pectin is a structural heteropolysaccharide contained in the primary cell walls of terrestrial plants. It is an inexpensive, non toxic product produced commercially as a white to light brown powder, mainly extracted from citrus peel and has been used as a food additive, a thickening agent, and a gelling agent. It is also used in fillings, medicines, sweets as a stabilizer in fruit juice and milk drinks, as a source of dietary fibre. Pectin can reduce interfacial tension between oil phase and water phase and is efficient for the preparation of emulsion6. The central aim of the present study was to formulate and evaluate famotidine loaded oil entrapped beads using different concentration of coconut oil with low methoxy pectin to prolong the gastric retention time of the drug. To investigate their morphology and floating behavior, drug content and drug release.

**MATERIALS AND METHOD**

**Instruments**

Shimadzu-1700 Double beam UV-VIS Spectrophotometer, Microscope with stage and eye-piece micrometer, Scanning electron microscope.

**Materials**

Famotidine is obtained as a gift sample from Ajanta Pharma, Mumbai, India. All chemicals and reagents used were of analytical grade.

**Preparation of conventional calcium pectinate gel beads**

Conventional calcium pectinate gel beads were prepared by ionotropic gelation method. Low methoxy pectin was dissolved in water with agitation to make 100g solutions. The solution was extruded using a nozzle of 0.80-mm inner diameter into 5%w/v calcium chloride solution with gentle agitation. The gel beads formed were allowed to stand in the solution for 20 minutes, and then separated and washed with distilled water and dried at 37°C.

**Preparation of oil entrapped calcium pectinate gel beads**

The oil-entrapped calcium pectinate gel beads were prepared by emulsion gelation method. Low methoxy pectin was dissolved in water with agitation. Different amounts of coconut oil (10%, 20%, 30%) was added to the solution to make a 100g mixture. The homogenized mixture was extruded using a nozzle of 0.80mm into 5% calcium chloride solution w/v. Formed oil entrapped beads were separated and dried. Different formulations are listed in table no.1. Formulation F5 and F6 are not satable because they are not rigid enough and breaking down while touching2.

**EVALUATION OF PREPARED BEADS**

The obtained beads were evaluated for mean particle size, drug content, Buoyancy, Morphology, Leakage, FTIR study, in vitro drug release study and stability studies.

**Determination of particle size**

Mean diameter of 20 selected dried beads were determined by optical microscopy. The Eye-piece micrometer was calibrated and then means particle size was found out. The microscope eye-piece was fitted with a micrometer by which the size of the beads could be determined5.

**Morphology**

The external and internal morphology of oil entrapped calcium pectinate beads were studied by scanning electron microscopy.

**Estimation of drug content**

Drug content was analyzed by taking 10mg equivalent of beads in 100ml of 0.1N HCl and the absorption was taken by UV-Visible spectrometer at 272nm4.
Buoyancy effect
The in vitro floating study was performed using a USP dissolution apparatus II, having 500ml of 0.1 N HCl. The medium temperature was kept at 37±0.5°C. Selected 20 beads were soaked in the dissolution medium and the medium was agitated with a paddle at 50 rpm. After agitation, buoyancy (sink/float) was observed visually.

FTIR study
FTIR Study of formulation F2 was done to see the compatibility between drug and the polymer. The IR Spectra of calcium pectinate beads showed the characteristic band c=0 vibration of COOH group at 1740 cm⁻¹ and strong absorption band at 1617 cm⁻¹ belonging to the asymmetric stretching of vibration of COO⁻. The IR spectra of Famotidine showed the peak at 272 nm. The IR Spectra of drug loaded calcium pectinate beads of formulation F2 showed all the above mentioned peaks of calcium pectinate beads and Famotidine³.

In vitro study
In vitro drug release study was done for all the prepared formulation using USP type II dissolution apparatus. An accurately weighed equivalent to 50 mg of the formulation was kept in 900 ml of 0.1N HCl and conditions are maintained at a temperature of 37±0.5°C and stirred at a speed of 50 rpm. A 10 ml aliquot of the sample was withdrawn at 5, 10, 15, 20, 30, 35, 40, 50, 60 minutes for conventional beads and at 10, 20, 30, 60, 120, 180, 240, 300, 380, 420, 480 minutes for oil loaded beads respectively, and replaced with equivalent amount of the plain dissolution medium. The collected samples were filtered and analyzed at 272 nm using UV-Visible Spectrophotometer³.

Stability studies
All the formulations were subjected to stability studies at 25°C/60%RH and 40°C/75%RH for period of 2 months and evaluated for their physical appearance, drug content and In vitro drug release at specified interval of time.

RESULT AND DISCUSSION
Particle size and Morphology
The mean particle size of 4 formulations was between 1.97±0.9 and 2.82±0.06. Particle size of beads was found to increase with increase in percentage of oil incorporated. This can be attributed due to the increase in percentage of entrapped oil in polymer matrix with increase in percentage of oil incorporated. The drug loaded beads were studied for SCM. The surfaces of the beads are found smooth.

Drug entrapment efficiency
The percentage of drug entrapment efficiency of various formulations ranged between 54.23% and 58.3%. It was found that drug entrapment efficiency increases with increase in percentage of oil incorporated due to increased in porosity.

Buoyancy
Formulation F1 and F2 are not buoyant and sink immediately. Formulation F3 and F4 are found buoyant and floating for more than 12 hours. In F1 there is no incorporation of oil whereas in F2 10% of oil incorporated is not enough to attribute enough low bulk density and porosity for floating property. The floating properties of hollow/porous beads is may be due to low bulk density and the porosity of the beads; indicating that the beads will have the porosity to exhibit an excellent buoyancy effect in vivo.

Leakage
There is no leakage found in formulation F1, F2, F3. Leakage was observed in formulation F4. It may be due to larger pore size of beads because of more amount of oil incorporated.

FTIR Study
IR Spectra of pure drug, polymer and formulation F2 was done. It was found that, in IR Spectra of F2, all peaks of pure drug were found intact. Hence, no interaction between drug and polymer and they are found to be compatible.

Drug release study
In vitro drug release study was found for all formulation F1 – F4. Drug release was found to increase with increase in percentage of oil incorporated. Formulation F3 with 20% oil was found to give optimum drug release. F2 showed optimum drug release may be because F2 has enough porosity for entrapment of drug ad there is no leakage observed. On the other side F1 has not enough porosity because of that drug entrapment efficiency is less and leakage is observed in formulation F3 due to high porosity of beads.

Stability studies
All the formulations were subjected to stability studies as per ICH guidelines. It was found that there is no significant change in physical appearance, drug content and drug release for all the formulations. Further the stability of the drug in beads was confirmed by UV Scanning and they showed no change in the wavelength and confirmed by single peak.

CONCLUSION
Famotidine oil entrapped beads are found buoyant in nature and thus increases the gastric retention time thus prolongs the release of the drug. Buoyant oil entrapped beads of famotidine can be further subjected to in vivo studies for further studies. The beads showed excellent prolonged release as compared to the conventional beads and thus can be used as for prolonged delivery of suitable drugs.

ACKNOWLEDGMENT
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REFERENCES
Table 1 Formulation of beads

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Table 2 Physico-chemical characteristics of beads

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<td>Mean diameter (mm)</td>
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Fig 1 FTIR Spectra of formulation F2

Fig 2 Drug release profile of conventional beads (F1)

Fig 3 Drug release profile of formulations F2, F3, F4
SEM (CUT SECTION) OF F2 FORMULATION

Fig 4 Scanning electron microscope images of F2 formulation

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