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A REVIEW ON - NOVEL IN-SITU FLOATING GEL FOR STOMACH SPECIFIC DRUG DELIVERY SYSTEM, NEW VENTURE IN DRUG DELIVERY

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ABSTRACT

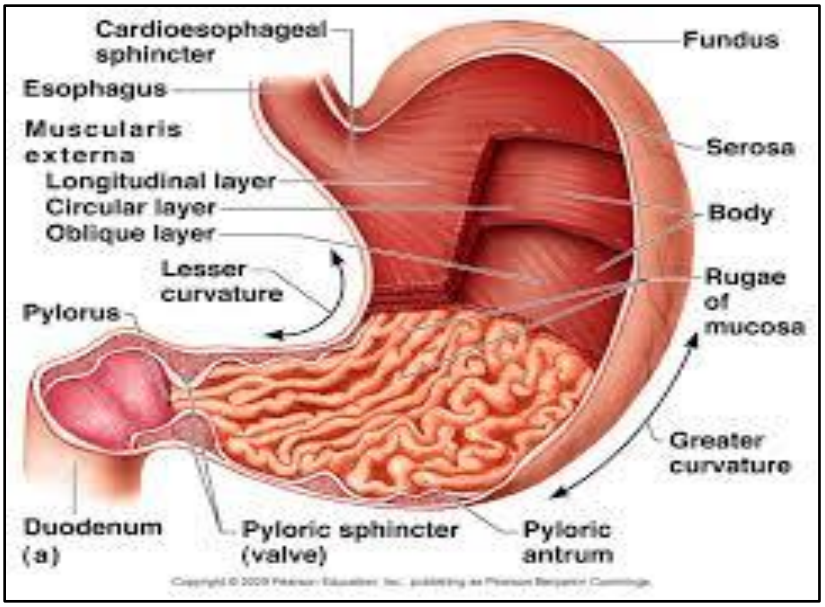
Gastro retentive floating in -situ gel is formulate to increase the residence time in stomach. And to sustain the release behavior of the drug that lead to increase drug bioavailability. Because of conventional liquid oral dosage forms are easy to administration as compared to unit solid dosage forms but sustain effect is not achieved due to less residence time in gastro intestinal track so to overcome this problem and to modulate the behavior of liquid dosage forms, in-situ gel is formulated.

INTRODUCTION

Aimed to formulate Floating drug delivery systems (FDDS) is retain the drug in the stomach and are useful for drugs that are poorly soluble or unstable in intestinal fluids. The principle is very simple i.e., to make the dosage form less dense than the gastric fluids so that it can float on them. Floating systems are low-density systems that have sufficient buoyancy to float over the gastric contents and remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. After release of drug, the residual system is emptied from the stomach. This result an increased gastric residence time and a better control of the fluctuations in plasma drug concentration. The principle of buoyant preparation offers a simple and practical approach to achieve increased gastric residence time for the dosage form and sustained drug release. Under certain circumstances prolonging the gastric retention of a delivery system is desirable for achieving greater therapeutic effect of the drug substance. For example, drugs that are absorbed in the proximal part of the gastrointestinal tract and drugs that are less soluble in or are degraded by the alkaline pH may benefit from prolonged gastric retention. In addition, for local and sustained drug delivery to the stomach and proximal small intestine to treat certain conditions, prolonged gastric retention of the therapeutic moiety may offer numerous

Advantages including improved bioavailability and therapeutic efficacy, and possible reduction of dose size.

Basic Gastrointestinal Tract Physiology:-



Basically stomach is divided into 3 regions 1) fundus 2) body, 3) antrum (pylorus). The proximal part made of fundus and body acts as a reservoir for undigested material, the antrum is the main site for mixing motions and act as a pump for gastric emptying by propelling actions it has four phages.

Phase I- (basal phase) lasts from 40 to 60 minutes with rare contractions.

Phase II- (pre-burst phase) lasts for 40 to 60 minutes with intermittent action potential and contractions.

Phase III - (burst phase) lasts for 4 to 6 minutes. It includes intense and regular contractions for short period.

Phase IV- lasts for 0 to 5 minutes and occurs between phases III and I of 2 consecutive cycles.

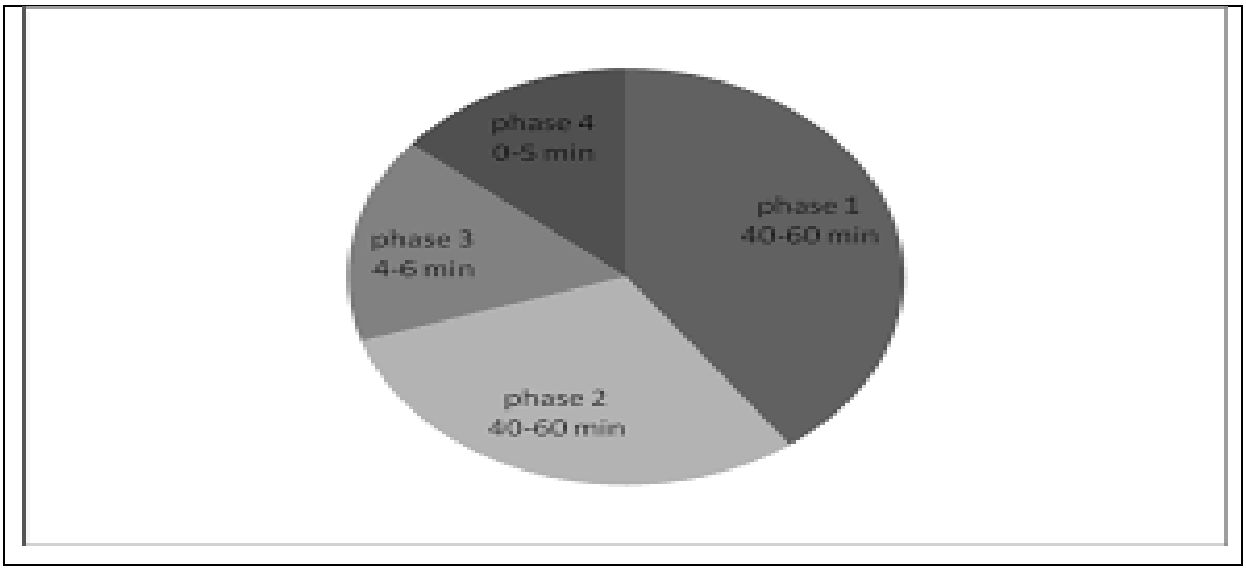


Fig:- different phages of gastric emptying.

Advantages:-

- Controlled delivery of drugs.
- Delivery of drugs for local action in the stomach.
- Minimizing the mucosal irritation due to drugs, by drug releasing slowly at controlled rate.
- Treatment of gastrointestinal disorders such as gastro-oesophageal reflux.
- Simple and conventional equipment for manufacture.
- FDDS improves patient compliance by decreasing dosing frequency.
- avoided; a desirable plasma drug concentration is maintained by continuous drug release

- Better therapeutic effect of short half-life drugs can be achieved.
- Gastric retention time is increased because of buoyancy.
- Enhanced absorption of drugs which solubilise only in stomach.
- Superior to single unit floating dosage forms as such microspheres releases drug uniformly and there is no dose dumping.
- Avoidance of gastric irritation, because of sustained release effect, floatability and uniform release of drug.

Disadvantages:-

- The major disadvantage of floating system is requirement of a sufficient high level of fluids in the stomach for the drug delivery to float.
- However this limitation can be overcome by coating the dosage form with the help of bioadhesive polymers that easily adhere to the mucosal lining of the stomach.
- These systems require a high level of fluid in the stomach for drug delivery to float and work efficiently.
- The drugs that are significantly absorbed through out gastrointestinal tract, which undergo significant first pass metabolism, are only desirable candidate.
- Some drugs present in the floating system causes irritation to gastric mucosa.
- Gastric emptying of floating forms in supine subjects may occur at random and becomes highly dependent on the diameter and size. Therefore patients should not be dosed with floating forms just before going to bed.
- Floating systems are not feasible for those drugs that have solubility or stability problems in gastric fluids.

Criteria for selection of candidate drug for FDDS:-

- Absorption from upper GIT.
- Drugs having low pKa, which remains unionized in stomach for better absorption.
- Drugs having reduced solubility at higher pH.
- The bioavailability of drugs that get degraded in alkaline pH can be increased by formulating gastro-retentive dosage forms.

Classification of floating drug delivery system:-

A. Single Unit Floating Dosage Systems

a) Effervescent Systems (Gas-generating Systems)

b) Non-effervescent Systems

B. Multiple Unit Floating Dosage Systems

a) Non-effervescent Systems

b) Effervescent Systems (Gas-generating Systems

c) Hollow Microspheres

C. Raft Forming Systems

A. Single Unit Floating Dosage Systems:-

a) Effervescent Systems (Gas-generating Systems.) –

These systems are prepared with sellable polymers. Like-HPMC polysaccharides like chitason. Effervescent component are, sodium bicarbonate citric acid and tartaric acid.

b) Non-effervescent Systems – this type of system, after swells unrestrained via inhibition of gastric fluid to an extent that it prevents their exist from the stomach.

B. Multiple Unit Floating Dosage Systems:-

Due to high variability of gastrointestinal transits time this system is developed

a) Non-effervescent Systems- in this system polymeric excipients indomethacin is used with chitason .chitason hydrates floats in acidic media.

b) Effervescent Systems (Gas-generating Systems.)- This system floats because of the carbon dioxide release in gastric fluids. And thus pepstatin resides in the stomach for prolong period of time.

c) Hollow Microspheres- hallows are considered as one of the most promising buoyant system as they possess a unique advantage of multiple unit system as well as better floating property. Because of the central hallow space inside the microspores.

C. Raft Forming Systems:-

The mechanism involved in the raft formation includes the formation of viscous cohesive gel in contact with gastric fluids, where in each portion of the liquid swells forming a continuous layer called a raft. This raft floats on gastric fluids because of low bulk density created by the formation of CO2.Usually, the system contains a gel forming agent and alkaline bicarbonates or carbonates responsible for the formation of CO2 to make the system less dense and float on the gastric fluids an antacid raft forming floating system.

EVALUATION PARAMETERS OF STOMACH SPECIFIC FLOATING DRUG DELIVERY SYSTEM

Measurement of buoyancy capabilities of the FDDS :-

The floating behaviour was evaluated with resultant weight measurements. The experiment was carried out in two different media, deionised water in order to monitor possible difference. The apparatus and its mechanism are explained earlier in this article. The results showed that higher molecular weight polymers with slower rate of hydration had enhanced floating behaviour and it was observed more in simulated meal medium compared to de-ionized water.

Floating time and dissolution:-

The test for floating time measurement is usually performed in stimulated gastric fluid or 0.1 moles/ lit HCl maintained at 37°C. It is determined by using USP dissolution apparatus containing 900 ml of 0.1mole/lit HCl as the dissolution medium at 37°C. The time taken by the dosage form to float is termed as floating lag time and the time for which the dosage form floats is termed as the floating or flotation time A more relevant in-vitro dissolution method pro-posed to evaluate a floating drug delivery system (for tablet dosage form) A 100 ml glass beaker was modified by adding a side arm at the bottom of the beaker so that the beaker can hold 70 ml of 0.1 mol/lit HCl dissolution medium and allow collection of samples. A burette was mounted above the beaker to deliver the dissolution medium at a flow rate of 2 ml/min to mimic gastric acid secretion rate. The performance of the modified dissolution apparatus was compared with USP dissolution. Apparatus 2 (Paddle): The problem of adherence of the tablet to the shaft of the paddle was observed with the USP dissolution apparatus. .

Drug release:-

Dissolution tests are performed using the dissolution apparatus. Samples are withdrawn periodically from the dissolution medium with replacement and then analyzed for their drug content after an appropriate dilution.

pH Measurement:-

In situ solution formulation pH measure by using calibrated digital pH meter at room temperature.

Pharmacokinetic studies:-

Pharmacokinetic studies are the integral part of the in vivo studies and several works has been carried out. The pharmacokinetics studies of gel compared with the conventional dosage forms the floating gel is comparatively higher than those obtained for the conventional dosage forms.

FACTORS CANTROLLING GASTRIC RETENTION OF DOSAGE FORMS:-

1) Size of dosage form :-

The size of the dosage form is another factor that influences gastric retention. The mean gastric residence times of non-floating dosage forms are highly variable and greatly dependent on their size, which may be small, medium, and large units. In fed conditions, the smaller units get emptied from the stomach during the digestive phase and the larger units during the housekeeping waves. In most cases, the larger the size of the dosage form, the greater will be the gastric retention time because the larger size would not allow the dosage form to quickly pass through the pyloric antrum into the intestine. Thus the size of the dosage form appears to be an important factor affecting gastric retention.

2) Density of dosage form :-

Dosage forms having a density lower than that of gastric fluid experience floating behaviour and hence gastric retention. A density of <1.0 gm/cm3 is required to exhibit floating property. However, the floating tendency of the dosage form usually decreases as a function of time, as the dosage form gets immersed into the fluid, as a result of the development of hydrodynamic equilibrium.

3) Food intake and nature of food:-

Food intakes, the nature of the food, caloric content, and frequency of feeding have a profound effect on the gastric retention of dosage forms. The presence or absence of food in the stomach influences the GRT of the dosage form. Usually, the presence of food increases the GRT of the dosage form and increases drug absorption by allowing it to stay at the absorption site for a longer time.

4) Effect of gender, posture and age:-

A study shows that females showed comparatively shorter mean ambulatory GRT than males, and the gastric emptying in women was slower than in men. The authors also studied the effect of posture on GRT, and found no significant difference in the mean GRT for individuals in upright, ambulatory and supine state.

APPLICATIONS:-

1) Sustained Drug Delivery

FDDS systems can remain in the stomach for long periods and hence can release the drug over a prolonged period of time. The problem of short gastric residence time encountered with an oral

CR formulation hence can be overcome with these systems. These systems have a bulk density of <1 as a result of which they can float on the gastric contents. These systems are relatively large in size and passing from the pyloric opening is prohibited

2) **Absorption Enhancement:-** Drugs that have poor bioavailability because of site specific absorption from the upper part of the gastrointestinal tract are potential candidates to be formulated as floating drug delivery systems, thereby maximizing their absorption.

3) **Site-Specific Drug Delivery:-**

These systems are particularly advantageous for drugs that are specifically absorbed from stomach or the proximal part of the small intestine.

4) **Enhanced Bioavailability:-**

Bioavailability is enhanced due to retention in gastric region for longer period of time.

5) **Absorption enhancement:-** due to retention in gastric region for longer period of time drug substance is more absorbs which leads to enhancement in absorption.

6) **Minimized adverse activity at the colon:-**

Retention of the drug in the HBS systems at the stomach minimizes the amount of drug that reaches the colon. Thus, undesirable activities of the drug in colon may be prevented.

CONCLUSION

A novel floating drug delivery system is helpful to increase the gastric retention time of the dosage form and to control drug release. One of the most feasible approaches for achieving a prolonged and predictable dug delivery profiles in the gastrointestinal tract is to control the gastric residence time, due to that decreased frequency of dose administration enough residence time in stomach increased bioavailability. Posses better patient compliance.

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