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Review Article

Role of Floating Tablet In Oral Drug Delivery System

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A B S T R A C T

Oral delivery of drugs is the most commonly used mode of administration among all the routes explored for the systemic delivery of drugs by numerous different dosage forms. Many components play a significant role in the development of the drug delivery system. Differences in gastric physiology such as pH and motility, have been shown to have important effects on gastric retention time and drug delivery activity in both intra- and inter-subject variability. FDDS focuses on locally active drugs with a narrow stomach absorption window or a narrow upper small intestine absorption window, are unstable in the intestinal or colonic system, and have poor solubility at high pH values.For drugs that are locally active and have a narrow absorption window in the stomach or upper small intestine and which are unstable in the intestinal or colonic setting. FDDS is particularly interesting because it has a low solubility at high pH. The methods for constructing single and multiple unit floating structures. These systems can help with a variety of issues that arise during the production of a pharmaceutical dose.

Keywords: Types of floating tablets, Mechanism of floating tablets, Drug release.

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INTRODUCTION

Most common route for oral drug delivery is oral. Due to its ease of administration and patient enforcement. The oral route of administration has received more attention in the pharmaceutical industry than the drug delivery design for other routes owing to its greater flexibility in dosage form design. Floating multiparticulate are gastro-retentive drug delivery systems based on non-effervescent and effervescent approach.[1]Floating drug delivery systems have the advantage of minimising dose frequency while also improving patient compliance. As a consequence, the process is improved. Fluctuations in the plasma drug's concentration are minimised. Gastro retention continues to broaden the variety of products available to patients, including new treatment options and substantial benefits. To effectively modulate the gastrointestinal transit time of a drug delivery system using a floating drug delivery system (FDDS). For optimal drug gastrointestinal absorption and distribution, one must have a solid understanding of the anatomic and physiological features of the human gastrointestinal tract.[3]Any drug delivery systems goal is to deliver a therapeutic quantity of drug to the right part of the body at the right time to quickly achieve and then maintain the optimal therapeutic drug concentration that triggers the pharmacological activity and to reduce the occurrence and severity of unwanted side effect. Maintaining a dosing frequency of once or at most twice a day would be more effective and convenient for this reason. A correctly engineered extended release dose may be a big move forward in this direction. Drug concentration fluctuation over a critical concentration is reduced by floating drug delivery systems, which increases pharmacological effects and improved clinicalefficacy.

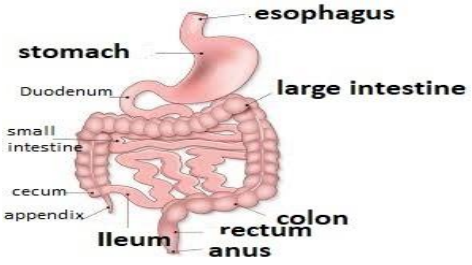

Fig 4: Anatomy of Gastrointestinal Tract.

Advantages:

- Sustained medication dose release can be achieved, and dose administration frequency can be decreased, resulting in improved bioavailability.
- It is possible to achieve targeted therapy for the stomach section local venue.
- In the case of FDDS, the problem of fluctuating drug concentration is reduced.
- In the activation of receptors, the floating system shows increased selectivity**.**
- The body decreased reaction time is achieved.
- A floating method of drug delivery demonstrates extended active concentration.
- Negative colon activity is minimised.
- The HBS mechanism is being incorporated into acidic drugs that irritate the stomach, thus reducing discomfort.

Disadvantages:

- Drugs that are unstable in an acidic setting are not appropriate candidates for this method.
- Drugs with solubility and consistency issues in the stomach are not appropriate for this system, since it needs a high amount of fluid in the stomach to float and function properly.
- Drugs that cause discomfort to the gastric mucosa are not appropriate for this system because of their solubility or stability issues in the GIT.
- The administration of the dosage form necessitated a minimum of 200 to 250ml of water.
- There is no major benefit of using a floating tablet over a traditional dosage type.

Classification of Floating Drug Delivery System

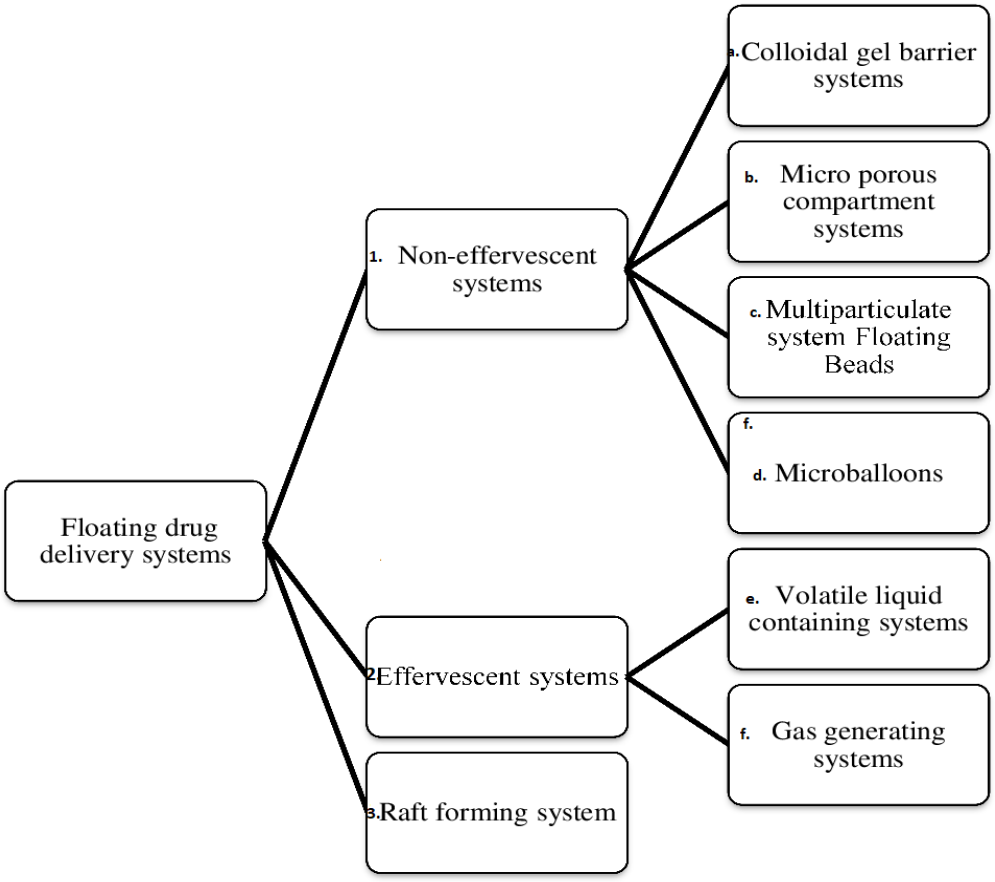

Figure 1: Classification of floating drug delivery systems

Non Effervescent System:

Noneffervescent system floating drug delivery system is based on swelling mechanism of polymer or bioadhesion to mucosal layer in the GI tract. The various types of non-effervescent systems are as follows:

a. Colloidal Gel Barrier System:

They are called as a hydrodynamically balanced system they remain in the stomach due to the presence of the gel

forming hydrocolloids due to this gastro retentive time is increased and at the site of the absorption amount of the drug is increased.They are highly soluble cellulose types hydrocolloids in which are hydroxypropyl cellulose, hydroxyethylcellulose, hydroxymethyl cellulose,

polysaccharides and matrixforming polymers such as polycarbophil , polystyrene.

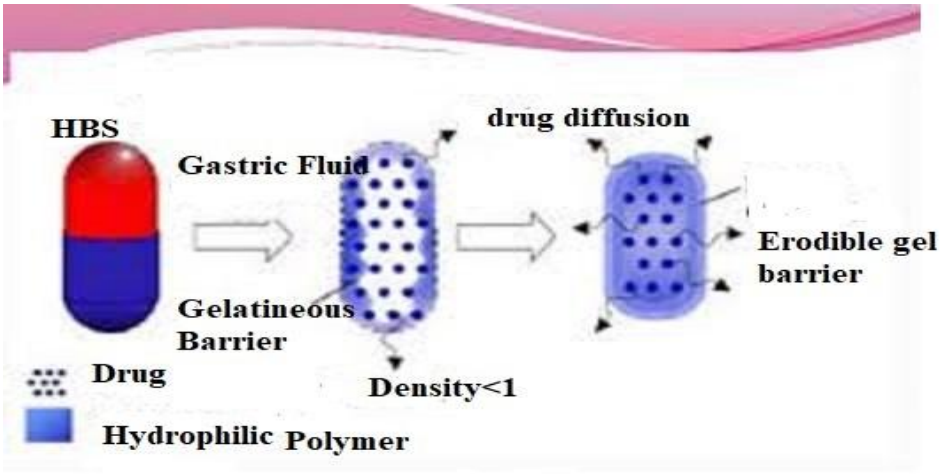

Fig 5: Colloidal Gel Barrier System

b. Micro porous compartment system:

The drug reservoir is encapsulated within a micro porous compartment with pores on the top and bottom surfaces in this form of device. The peripheral walls of the drug reservoir compartment are completely sealed to avoid any direct interaction with the gastric mucosal surface. The floatation chamber's entrapped air in the stomach.

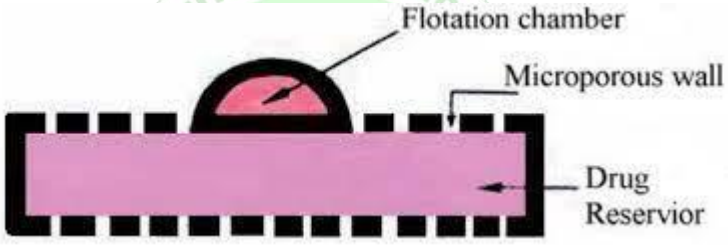

Fig 6: Micro porous compartment system

c. Multiparticulate system floating bead:

Freeze-dried calcium alginate has been used to create floating dosage types with multiple units. More than 5.5-10 hours of residence time was achieved with the floating beads.

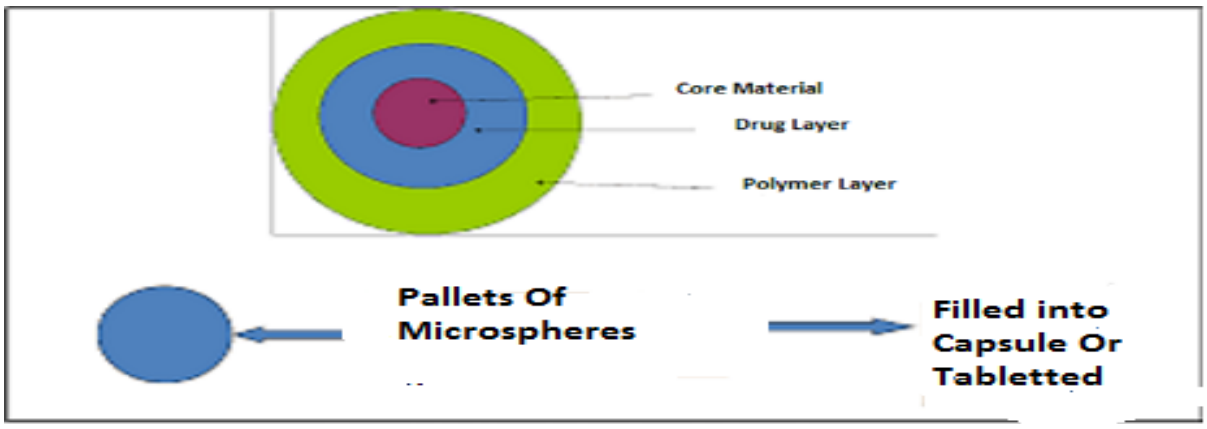

Fig 7: Multiparticulate system floating bead

d. Micro-balloons:

Hollow microspheres (micro balloons) for ibuprofen were prepared by novel emulsion solvent diffusion method. These micro balloons floated continuously for more than 12

hours over the surface of acidic solution media that contained surfactant.

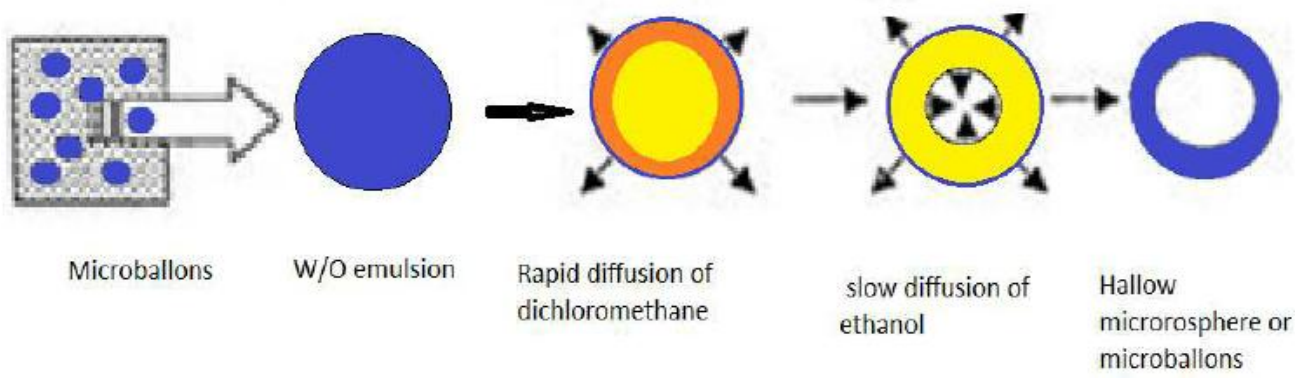

Fig 8: Micro-balloons

2. Effervescent systems: [8, 9]

A floating chamber, which can be filled with vacuum, air, or inert gas, can be used to make a drug delivery device float in the stomach**.**

Volatile Liquid Containing Systems (Osmotically Controlled DDS):

The device, which is an osmotically operated floating machine, consists of a hollow deformable unit that can be converted from a collapsed position after a period of time. The device has a bio erodible plug that allows the vapour to escape, allowing it to remove from the stomach.

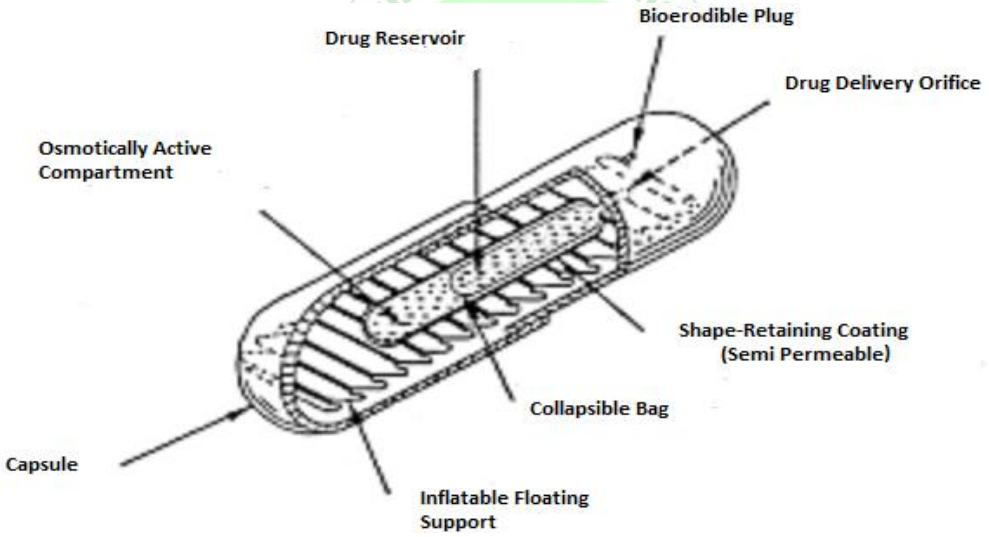

Fig 9: Volatile Liquid Containing Systems (Osmotically Controlled DDS)

Gas Generating Systems:

Low density FDDS are based on the formation of CO2 within the device following contact with body fluids. The medication type floats on the chyme due to a decrease in basic gravity. The CO2 generating components can be thoroughly mixed inside the tablet matrix, resulting in a single layer or bilayer containing the gas generating mechanism in one hydrocolloid-containing layer and the drug in the other, formulated for a sustained release effect.Volatile Liquid Containing DDS Systems (Osmotically Controlled DDS). As an osmotically controlled floating system, the device comprises of a hollow deformable unit that is convertible from a collapsed position after an extended period of time.

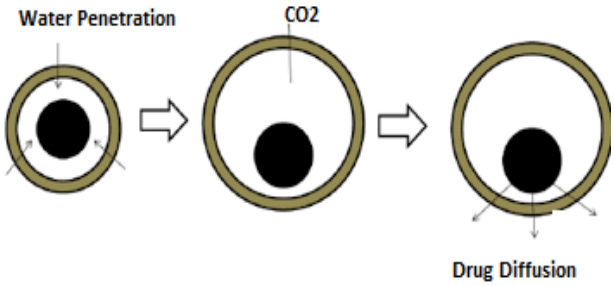

Fig 10: Gas Generating Systems

3. Raft forming systems: [9]

Raft forming devices have received a lot of publicity for the delivery of antacids and medications for gastro infection and disorders. As the gel-forming solution comes into contact with gastric fluid, it expands and forms a viscous cohesive gel with trapped CO2 bubbles. This forms a raft layer on top of the gastric fluid, slowly releasing the substance into the stomach. It's used to treat gastroesophageal reflux disease.

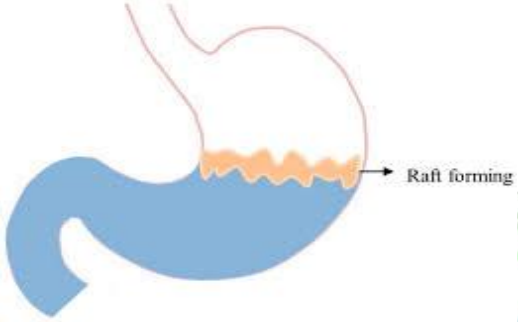

Fig 11: Raft forming systems

Mechanism of floating drug delivery system:[10]

FDDS is one of the most common methods for achieving gastric retention while maintaining optimum bioavailability of dosage forms. Only drugs with a window of absorption in the stomach or upper small intestine are eligible for this method. This has a lower density than gastric fluids and therefore remains buoyant in the stomach for a longer period of time without affecting gastric emptying volume and the drug is released slowly. The residual system is expelled from the stomach after the drug has been released. As a result, the gastric retention time is improved and the fluctuations in plasma drug concentration are better controlled.

Evaluation: [5,8, 11, 12]

1. Size and shape

The solubility rate of the drugs and therefore their possible bioavailability. It is largely determined by particle size and shape. Sieve analysis (Jayant, Mumbai), air elutriation (Bahco TM) analysis, photo analysis, and an optical microscope (Olympus (India) pvt.ltd) were used to assess the particle size of the formulation. Electro résistance counting methods (Coulter counter), Sedimentation techniques, Laser diffraction methods, ultrasound attenuation spectroscopy, Air Pollution Emissions Measurements etc.

2. Floating Properties:

Using a continuous floating monitoring system and a statistical experimental design. The effect of formulation variables on the floating properties of a gastric floating drug delivery system was calculated.

3. Surface Topography:

Scanning electron microscope (SEM, JEOL JSM – 6701 F, Japan) with 10k.v acceleration voltage was used to assess the surface topography and structures. Atomic force microscopy (AFM), contact angle meter contact profiliometer.

4. Floating microspheres and beads:

Drug loading is accomplished by crushing an appropriately weighted sample of beads or microspheres in a mortar, adding it to the suitable dissolution medium, centrifuged, filtered, and analyses using spectrophotometry or other analytical methods. The size and shape of the beads or microspheres are measured using an optical microscopy process and the percentage drug loading is calculated in beads or microspheres. Scanning electron microscopes are used to characterized by the external and cross-sectional morphology of the surface (SEM).The measured weight of prepared microspheres was divided by total amount of all non-volatile components used for the preparation of microspheres, in which will give the total percentage yield of floating microspheres.

5. Resultant weight determination:

The key parameters of a dosage forms buoyancy have been bulk density and floating length. While a single density determination does not predict the floating force evolution in dosage types. It is a good starting point. It works by applying a force(F) equal to that needed to hold the object fully submerged in the fluid. As shown in the equal, the magnitude, direction and resultant weight correspond to the Victoria sum of buoyancy (Fbuoy) and gravity (Fgrav) forces acting on the objects.

F = Fbuoy – Fgra
F = dfgV – dsgV = (df-ds) gV
Where,
F = total vertical force (resultant weight of theobject)

g = the acceleration due to gravity
df =the fluiddensity
ds = the object density is the object mass
V = the volume of the object.

6. X Ray/Gamma Scintigraphy:

The key measurement parameter for floating systems in in vivo studies is XRay/Gamma Scintigraphy. The animals are fasted overnight and have free access to water in each experiment and the formulation allows for indirect external observation with a camera or scintiscanner. The related ionising radiation for the patient, the limited topographic detail, low resolution inherent to the technique and the complicated and costly preparation of radiopharmaceutical are the key drawbacks of scintigraphy.

7. Buoyancy studies:

Floating lag time is the time, it takes for the tablet to rise to the surface and float. Total floating time was calculated as the amount of time the dosage type remained stable on the medium surface. To examine their in vitro floating behaviour, the tablets were put in a 900 ml plastic vessel filled with 500 ml of 0.1 N HCl (pH 1.2, 37.5 C). The floating lag times and durations of the tablets were measured using visual observation.

8. Angle of repose:-

Angle of repose used to calculate the frictional forces in a loose powder or granules. This is the greatest angle that a pile of powder or granules can be make with the horizontal plane. The granules were permitted to flow through a funnel that was fixed to a fixed height stand (h).Angle of repose was calculated by measuring the height and radius of the heap of granules formed.

tan θ = h/r θ = tan-1 (h/r)
Where,
θ= angle of repose
h= height of the heap
r= radius of the heap

9. Determination of *In Vitro* Dissolution Study

In vitro drug release experiments and buoyancy tests are normally performed in simulated gastric and intestinal fluids held at 37°C. In practise, floating time is measured using a USP dissolution apparatus with 900ml of 0.1 HCl as a measuring medium held at 37°C. The HBS dosage type has a floating time requirement.

Measurement of floating capacity

In a 400 ml flask containing 0.1(N) HCl solutions, three individual tablets are placed. The time, it takes for each tablet to travel from the bottom to the top of the flask (floating lag time) and for tablets to float on the water surface for an extended period of time (duration of floating) are then calculated in minutes. The HBS dosage forms are set to floating after the sample mean and standard deviation are measured.

Determination of drug content in tablets

Each batch has ten tablets selected at random and transferred to a 100 mL volumetric flask containing 0.1N HCL. Before transferring 1 ml from the volumetric flask to the test tube, stir and set aside for 2 hours. The samples are then filtered, sufficiently diluted and spectrophotometrically analysed at a suitable wavelength.

Factors affecting gastric residence time of the floating drug delivery system[7, 14, 15]

Factors ofFormulation

Size of tablets:

The tablet size has a direct impact on dosage type floating retention in the stomach. Small tablets pass through the stomach easily, while large tablets take longer to pass through the digestive system.

Density of tablets:

Density is also a factor that influences the time a dosage type spends in the stomach. Since it is long enough from the pyloric sphincter, a buoyant dosage with a density less than that of the gastric fluids would float, resulting in more accumulation in the stomach for a longer time. Density tablets with a density of 1.0 g/ml (less dense than gastric contents) have been found to be more effective. The floating force kinetics, on the other hand, have shown that the bulk density of a dosage product is not the most important factor influencing its buoyancy.

Shape of tablets:

One of the influencing factors is the shape of the dosage type, which interferes with gastric residence time. In this research, six different types of shapes (ring tetrahedron, cloverleaf, string, pellet, and disc) were screened in vivo for their gastric retention potential. The tetrahedron shape (each leg 2 cm long) rings (3.6 cm in diameter) passed approximately 100% retention 24 hours.

Viscosity of polymers:

The viscosity of different polymer grades, as well as their interactions, have a big impact on FDDS drug release and floating characteristics. Low viscosity polymers (e.g., HPMC K100 LV) have been found to be more efficient than high viscosity polymers in enhancing the dosage type's floating properties (e.g., HPMC K4M).Moreover, a decrease in the release rate was also found with an increase in polymer viscosity.

Idiosyncrasy factors

Gender:

It has been found that gastric emptying time in women is longer than men. Regardless of weight, height or body surface, men have a shorter mean ambulatory gastric retention time (3.40.4 hours) than women of the same age and race.

Age:

Furthermore, the elderly have a faster gastric emptying time than younger people. In addition, there are variations in

gastric and intestinal transit time between individuals. The elderly, particularly those over the age of 70, have a significantly longer gastric retention time.

Upright position:

Postprandial emptying is prolonged by upright posture since the floating form stays above the gastric contents regardless of its duration. Floating dosage forms have a longer and more stable gastric retention time than traditional dosage forms, which sink at the lower part of the distal stomach and are expelled by the pylorus through peristaltic movement.

Supine position:

This position does not offer any reliable protection against early and erratic emptying. In supine subjects, large dosage tablets (both conventional and floating) may experience longer retention. The gastric retention of floating forms appears to remain buoyant anywhere between the lesser and greater curvature of the stomach. On moving distally, these units may be swept away by the peristaltic movements that propel the gastric contents towards the pylorus, leading to a significant reduction in gastric retention time compared with upright subjects.

Concomitant intake of drugs:

Different drugs with a concomitant intake like prokinetic agents (e. g., metoclopramide and cisapride), anticholinergic (e. g. propantheline or atropine), opiates (e. g. codeine) may affect the performance of the floating drug delivery system. The co-administration of GI motility decreasing drugs can increase gastric emptying time and vice versa.

Feeding regimen:

In the presence of food, gastric residence time increases, resulting in a higher drug dissolution rate of the dosage type at the preferred absorption site. Following a fat-and-protein-rich diet, a gastric retention period of 4 to 10 hours has been recorded**.**

APPLICATIONS:[4,5,7,8,11,12]

Absorption Enhancement orBioavailability:

Since, drugs ingested from the upper gastrointestinal tract have low bioavailability due to site specific absorption, possible candidates are conceived as floating drug delivery systems with the aim of maximising absorption. A floating tablet containing Metoprolol Succinate in a mixture of hydrophilic and hydrophobic polymers increases bioavailability and gastric residence time.

Enhanced bioavailability:

The bioavailability of the medication is increased as compared to administration of the drug in Gastro retentive floating tablet and non-floating type of device polymeric formulations. The magnitude of drug absorption is influenced by a variety of processes related to drug absorption and drug transfer in the GI tract.

Fourier Transforms Infrared Analysis:

The technique of Fourier transform infrared spectroscopy (FT-IR; Shimadzu, Model-RT-IR-8300) is used to define functional groups and differentiate organic, polymeric and inorganic materials. Fourier Transform Infrared Analysis was used to quantify pure drug, polymer, and drug-loaded polymer formulations (FT-IR). Over a wave number range of 3600 to 400 cm-1, the spectra were scanned on a KBr-press at ambient temperature with a hydraulic pressure of 150kg/cm2.

Differential Scanning Calorimetry (DSC):

DSC (Shimadzu, Model-DSC-60/DSC-50/Metler Toldeo) is used to distinguish water of hydration in pharmaceuticals. Thermograms of formulated preparations were obtained using a DSC instrument with an intercooler. Indium/zinc standards were used to calibrate the DSC temperature and enthalpy scales. Over a temperature range of 25° C to 65°C, the sample preparations were hermetically sealed in an aluminium pan and heated at a constant rate of 10°C/min. Purging nitrogen gas at a rate of 50ml/min was used to preserve the inert atmosphere.

Site specific drug delivery systems:

These systems are especially useful for medications that are absorbed mainly through the stomach or the proximal part of the small intestine. The monitored, gradual delivery of the medication to the stomach ensures adequate local therapeutic levels while limiting the drug's systemic exposure. It decreases the drug's blood circulation-related side effects.Furthermore, a site guided delivery system's prolonged gastric availability can reduce dosing frequency.

Minimize adverse activity at the colon:

The amount of drug that enters the colon is decreased when the drug is stored in the HBS systems at the stomach. As a consequence, the drug's undesirable effects in the colon can be avoided. The explanation for GR resistance is based on this pharmacodynamic aspect.Beta lactam antibiotics that are only absorbed from the small intestine and whose existence in the colon contributes to the production of microorganism resistance have a DF (dry flowables) formulation.

Decrease the adverse activity of the colon:

When the dose form is held in the gastro retentive system, the amount of drug that enters the colon is decreased.

Minimize and fluctuation of drug concentration:

Drug effectiveness fluctuation is reduced and side effects can be avoided by adjusting the concentration. It's especially important for low-curative-index dosage types.

Reduced Fluctuations of Drug Concentration:

Continuous feedback of the medication after control release floating drug delivery dosages form administration induces blood drug concentrations within a narrower range as opposed to immediate release dosage forms. As a result, drug effect fluctuations are minimised, and side effects associated with peak doses that are concentration-dependent can be avoided. This is especially important for drugs with a small therapeutic index.

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