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Floating drug delivery system: A review

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ABSTRACT

The main location of functioning on that article on floating drug delivery systems (FDDS) is to make a compiled report on the recent studies and analysis with special thought on the principle mechanism of flotation to achieve internal organ retention. The scientific and technological advancements were created inside the previous few of years inside the analysis and development of rate-controlled oral drug delivery systems by overcoming physiological difficulties, like short gastric residence times (GRT) and unpredictable internal organ evacuation times (GET). This review conjointly epitomized the in-vitro procedure, in-vivo to assess the pursuance and implementation of floating systems, and applications of those systems. These ways are helpful to varied queries knowledgeable throughout the event of a pharmaceutical dose type.

Keywords: Floating drug delivery system; internal organ duration; rate management; internal organ removal time.

INTRODUCTION

The orals route of drug administration system is the easiest mode of drug delivery system and this route of drug administration also very comfortable for the patients. Although the oral drug delivery has very limited use for some important drugs, from the various pharmacological class, that some drugs having very poor bioavailability because of their imperfect absorption and their poor degradation in the alimentary canal. Q\dft some of these medicines are distinguished by Narrow Absorption Window (NAW) at the superior part of the alimentary canal, as of the adjacent part of the small intestine reveals the extended absorption properties. Remove fast from the blood circulation and utilize recurrent dosing of the drugs. To keep away these complications, the oral controlled release drug delivery system is introduced in an investigation to free the drug at a slow pace into the GI tract and keep pace with a persistent drug concentration in the blood for an expanded phase of time. To extend gastric retention i.e. very important to gain control on GRT, as of these helps to hold on to the controlled drug release system in the stomach for a longer period in an awaited manner [1]. The preparation floating system in the stomach content due to its lesser density than that of the gastric juice. A floating system built of manifold establishments' forms has aligned merits correspondence to a simple unit preparation next to a different formulation. The favored circumstances of oral controlled drug delivery systems crucial the three sides of the methodology, which is the physiochemical, attribute of the drug [2], Anatomy and physiology of the alimentary canal and feature of dosage forms [3].

STOMACH ANATOMY

The main role of the abdomen is to figure and convey food within the gut. The abdomen may be a stomachic organ placed between the esophagus and also the small intestine. The stomach has a 'J' shape in structure. The antecedent and back surfaces are fluently orbicular with a serous membrane wrapping the stomach has four main anatomical divisions; the orifice, fundus, body, and pylorus:

Cardia–surrounds the surpassing gap of the abdomen.

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Fundus – The rounded, typically gas-filled portion superior to and left of the cardia.

Body – It's situated lowly to the fundus. The body is the large median portion of the stomach.

Pylorus – The pylorus is situated between the abdomen and small intestine. It is divided into the pyloric antrum, pyloric canal, and pyloric sphincter [4]. The adjacent part fundus and the average value of pH in a rapid healthy person are 1.1± 0.15, after intake of food the pH may raise to levels within the 3.0 to 4.0 because of the buffering capacity of protein. However, in a fasted state, gastric secretion in women is slightly lower under that of men [5].

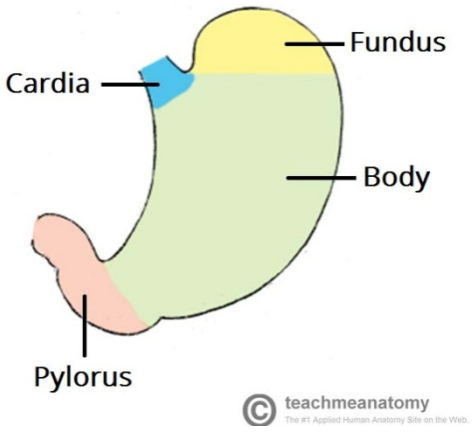

Fig 01: Parts of the stomach

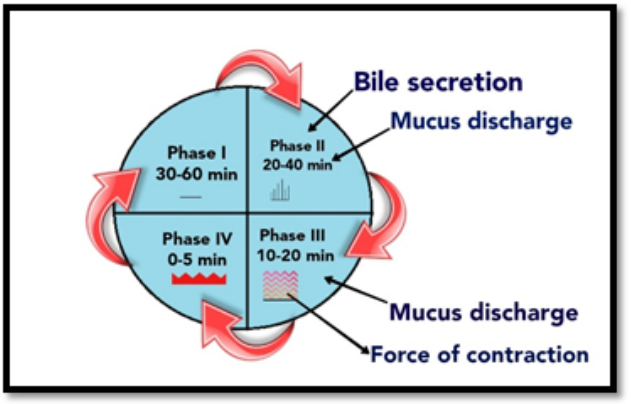

Fig 02: Motility pattern in the gastrointestinal tract.

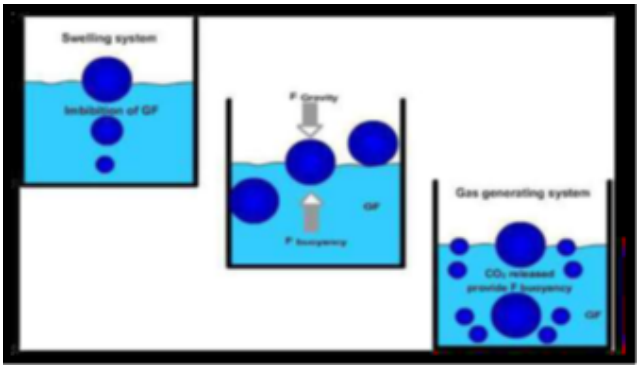

Fig 03: Mechanism of floating systems, GF= Gastric fluid.

MECHANISM OF FLOATING SYSTEMS

To enhance the gastric retention time in the stomach various methods are used. It assimilates establishing floating dosage forms (gas-generating systems and mucoadhesive systems, expanding systems), High-density systems, modified shape systems, gastric emptying delaying devices, and co-direction of gastric-emptying delaying drugs. The Floating drug delivery systems (FDDS) have every time lesser bulk density than gastric fluid and so encounter floatable in the stomach without showing any effect on the gastric emptying rate for a prolonged period. This set-up is floating on the stomach contents the drug is released slowly at the seek rate from the system [6]. The apparatus handle by computing constantly the force equivalent to F (a function of time) that is used to maintain the submerged object. This apparatus helps in adjusting the floating drug delivery system concerning inflexibility and resilience of floating effect prompted in order to avert the disadvantage of unforeseeable propensity to float potentiality variability [7].

$$F = F\,\text{buoyancy} - F\,\text{gravity} = (Df - Ds)gv \qquad (1)$$

Where, F= total vertical force, Df = fluid density,

Ds =Object density, v = volume and g = acceleration due to gravity.

Based on the mode of action of effervescent FDDS can be classified into:

1. **Single Unit Floating Dosage Systems**
   (a) Effervescent Systems
   (b) Non-effervescent Systems
2. **Multiple Unit Floating Dosage Systems**
   (a) Non-effervescent Systems
   (b) Effervescent Systems
   (c) Hollow Microspheres
3. **Raft Forming Systems**

A. Single unit floating dosage systems:

a) Effervescent Systems (Gas-generating Systems):

The arrays which are produced by the helping of expansible polymers like HPMC, polysaccharides like chitosan and effervescent elements are: tartaric acid, sodium bicarbonate, citric acid, or assembly embracing a liquid that annihilate at body temperature. The superlative stoichiometric proportion of citric acid and sodium bicarbonate for gas production is recorded to be 0.76:1. Thus, carbon dioxide is declared which causes the beads floating in the stomach [8]. Commonly contents incorporate polyvinyl acetate, Carbopol,

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calcium chloride sodium alginate, HPMC, polyethylene oxide, and polycarbonates.

b) Non-effervescent Systems

This type of system, after swallowing, gets expend with in the stomachic fluid which averts their exit from the stomach. One of the formulation techniques involves the blending of drugs with a gel, which expands in contact with the gastric fluid and maintains a relative rectitude of shape and a bulk density of less than one among the outer gelatinous barrier. Some samples of this drug delivery system are colloidal gel barrier; small porous compartment method, alginate beads, and vacant microspheres. Another type is a fluid-filled floating chamber [9], which keeps up the incorporation of a gas-filled floatation chamber into a micro porous constituent that causes a drug accumulation. The fluid present could be air, underneath restricted vacuum, or any other acceptable liquid, gas or solid having appropriate explicit gravity associated an inert behavior. Succeeding this drug is enlargement and starts floating. Up to the minute self-correcting floatable unsymmetrical design of drug delivery system [10]. The production of ciprofloxacin comprised of 1.03% xanthum gum, ciprofloxacin base 69.9%, 0.34% sodium alginate, 13.7%sodium bicarbonate, and 12.1% cross-linked polyvinyl pyrrolidine. The cross-linked polymer PVP initially and also the gel-forming polymers, at last, formation of a hydrated gel matrix that captured the gas, cause the tablet to float and behold in the stomach. The hydrated gel matrix prompted a diffusion pathway for the drug, followed within the slow release of the drug [11].

B. Multiple Unit Floating Dosage Systems

In the chronology to control the trouble multiple-unit floating systems were expanded, which reduces the inter-subject flexibility and terminated dose-dumping. The enlargement of both non-fizzy and fizzy multiple unit systems [12]. Much experiment has been focused and the scientists are still prospecting the field of hollow microspheres, proficient of floating on the gastric fluid and having better gastric retention properties.

a) Non-effervescent Systems:

Some employees have discovered the chance of developing such a way having indomethacin, and using chitosan as the polymeric excipient. A multiple-unit HBS containing indomethacin as a model drug ready by the extrusion method is rumored [13]. A mixture of drugs, chitosan, and acetic acid is extruded through a needle, and also the extrudate is cut and dried. Chitosan hydrates and floats in the acidic media and also the needed drug release could be obtained by modifying the drug-polymer quantitative relation [14].

b) Effervescent Systems (Gas-generating Systems):

These floating system utilize matrices created from swelling polymers like methocel, polysaccharides (e.g., chitosan), effervescent constituent (e.g., sodium bicarbonate, citric acid, or salt acid) [15]. Those Gas-generating system unit ready in such a way that upon arrival in the abdomen, carbon dioxide gas is obtaining free, that causes the formulation to float in to the abdomen. The other material and perspectives that have been appeared are a blend of sodium bicarbonate and sodium alginate, multi-unit buoyant pills that initiate carbon dioxide when devoured floating mini capsules with a core of sodium bicarbonate, polysaccharide and polyvinyl pyrrolidone coated with hydroxypropyl

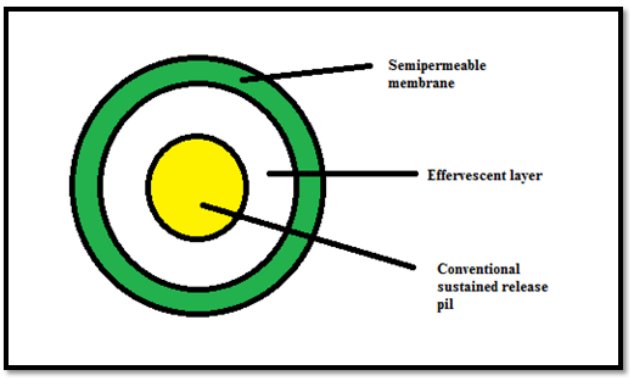

Fig 04:

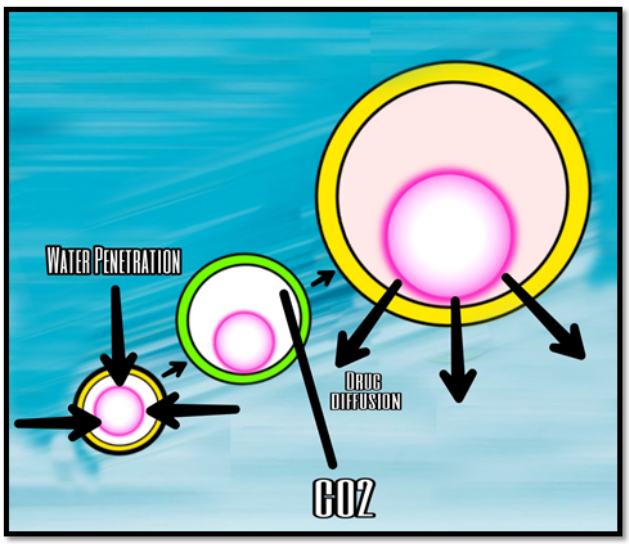

Fig 05: a) Different layers (i) Semi-permeable membrane, (ii) Effervescent Layer (iii) Core pill layer
b) Mechanism of floatation via CO2Generation. (c)Hollow Microspheres:

The most buoyant structure is vacant microspheres. The common method in their composition includes simple solvent evaporation [15], and also includes solvent diffusion or evaporation. The liberation of drug and a good buoyant property mainly depends on the variety of plasticizer, solvents, and a polymer such as polycarbonate, Eudragit, and cellulose acetate were used in the construction of empty

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microspheres sustained-release boyanting microspheres by using polycarbonate [16], employing solvent evaporation method Aspirin, Griseofulvin was used as standard drugs. Dispersed phase having polycarbonate in dichloromethane and micronized drug were mixed into to the dispersion medium incorporating sodium chloride, polyvinyl alcohol, and methanol. The dissemination was blended for 3-4 hours to persuade the complete solvent evaporation, and the microspheres established were filtered, washed and clean with cold water, and make it moisture free. The spherical and vacant nature of the microspheres was verifying by examine electron microscopic studies [17]. It is produced by an original emulsion solvent diffusion system. To achieve o/w emulsion, with continues rotating a solution of drug and enteric acrylic polymer in a mixture of ethanol and dichloromethane is put into the aqueous phase having polyvinyl alcohol (0.75% w/v). The microspheres achieve were filtered, and water washed, then dried. After collecting the microspheres exhibited better flow and have packing quality, and floating time is more than 12 hours on acidic medium carrying, surfactant [18, 19].

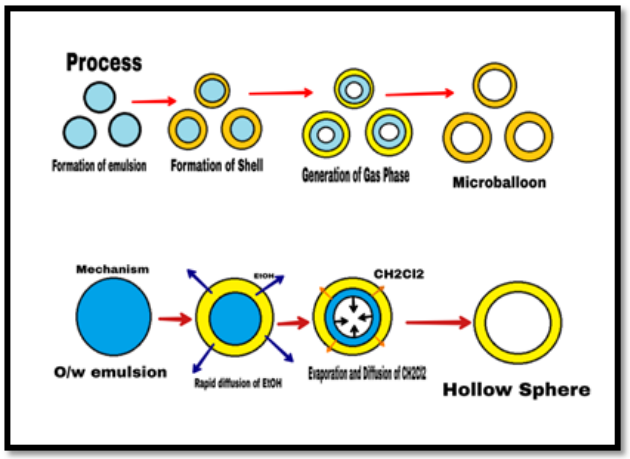

Fig 06: Preparation technique (Emulsion-solvent Diffusion Method) and Mechanism of 'Micro balloon' Formation.

C. Raft Forming Systems

Raft forming method has collect much noticed to the transporting of antacids and drug transporting for GI infections and disorders. The process involve in the raft development includes that the formation of viscous cohesive gel in exposure with gastric fluids, where in each portion of the liquid enlarge development a continuous layer called a raft. This raft floating on the gastric fluids because it's having low bulk density generate by the formation of CO2. Usually, the system carrying a gel-forming agent and carbonates or alkaline bicarbonate responsible for the development of CO2 to form a low density system and on the gastric fluids [20]. The system having a gel-forming agent, acid neutralizer and sodium bicarbonate, which makes a foaming sodium alginate, gel once come in exposure with gastric fluids. A patent allot to Reckitt and Colman Products Ltd. narrate a raft forming formulation for the therapy of helicobacter pylori contamination in the GIT. The composition has drugs, mannitol, sodium bicarbonate, sweetener, alginic acid, calcium carbonate then the citric acid add on which drift in the fluid.

FACTORS AFFECTING GASTRIC RETENTION

Some factors including like shape of dosage form, size, and density, concomitant intake of food and drugs such as anticholinergic agents (e.g.Propantheline, atropine), opiates (e.g. codeine) and prokinetic agents (e.g. metoclopramide) and some biological factors are: - age, disease state, gender, body mass index and posture (e.g. diabetes). The buoyancy strength kinetics of some dosage forms has appear that the bulk density of a dosage form is not the most favorable framework for describe its buoyancy. This is because the magnitude of floating power may differ as a purpose of time and normally decreases after involvement and its hydro dynamical equilibrium. The extending of gastric residence time by food is anticipated to increases drug absorption from floating drug delivery system (FDDS) because of increased dissolution of drug and overlong residence at the most approving sites of absorption.

Drugs Used In the Preparation of Stomach Specific Floating Dosage Forms:

Floating microspheres –Ketoprofen, Griseofulvin, pnitroaniline, Aspirin, Ibuprofen21, Piroxicam, Verapamil, Theophylline Nifedipine, Nicardipine, Tranilast [22], and Terfinadine [23].

Floating granules - Diclofenac sodium, Indomethacin, and Prednisolone.

Films – Cinnarizine [21], Albendazole

Floating tablets and Pills - Acetaminophen, Acetylsalicylic acid, Ampicillin, Atenolol, Fluorouracil, Isosorbide-mononitrate, Piretanide, Theophylline, Chlorpheniramine maleate, Aspirin, Calcium Carbonate, Fluorouracil, Prednisolone, Sotalol.

Floating Capsules - Chlordiazepoxide hydrogen chloride, Diazepam [21], Furosemide, Misoprostol, L Dopa, Ursodeoxycholic acid, Pepstatin , and Propranolol.

APPROACHES TO GASTRORETENTION

Different methods are described which are used to increase the gastric retention of drugs.

1) High-density systems:

All systems, having a density of ~3g/cm3, are keeping in the stomach and ability of resist its peristaltic movements. The crucial disadvantage of certain systems which is technically strenuous to manufacture them having great quantity of drug (>50%) and achieve the required density of2.4-2.8g/cm3. Diluents like: barium sulphate (density= 4.9), zinc oxide, and titanium oxide must be used to manufacture such high-density formulation.

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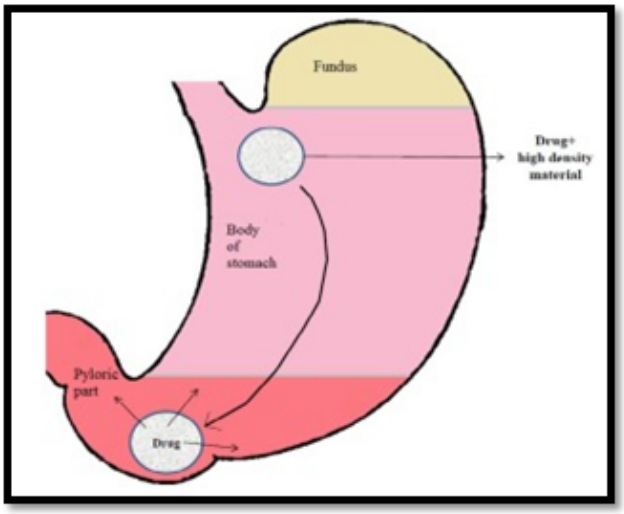

Fig 07: High-density systems

2) Swelling and expanding systems:

This methodology is also termed as "Plug type system" because they exhibit a propensity to remain logged in the pyloric sphincters. The polymeric matrices go on in the gastric cavity for some hours. The polymer having molecular weight and enlargement properties controlled and sustained drug discharge it can be reached the polymer soaked-up water and Swells. This cross-link stops the dissolution of polymer and also continued the physical honesty of the dosage form. A high degree of cross-linking delayed the enlargement capability of the system and maintains its physical integrity for an extended time duration. However, a less degree of cross-linking outcome will be large-scale swelling followed by the quick dissolution of the polymer [22].

3) Incorporating delaying excipient:

It takes more time for gastric emptying approach of attentiveness include feeding of easily digestible polymers or fatty acid salts that helps to impose the motility design, of the stomach to a fed point thereby reducing the gastric dumping rate and extending of the drug discharge with the help of delivery system including slow working excipient like tri etanolamine militate in a delivery system [23].

4) Modified systems:

The non-fragmenting geometric form molded from Silastic elastomers and ejected from polyethylene blends, that expand the GRT depending on the size, design, and flexural modulus of the drug transporting machine.

5) MUCOADHESIVE & BIOADHESIVE SYSTEMS:

The Bio adhesive transportation method is used to localize for conveyance device within the lumen to expand the drug immersion in a site-specific manner. A number of favorable excipients which is used regularly in these systems involving lectins, carbopol, polycarbophil, chitosan, CMC and gliadin 24, etc.

EVALUATION PARAMETERS OF GASTRORETENTIVE SYSTEM

Several studies including in the literature which indicate that pharmaceutical dosage forms demonstrate gastric residence in vitro floating deportment show extend gastric residence in vivo.

1) Assay, friability, hardness, content uniformity (Tablets):

These essays are executed as reported in particular monographs.

2) Floating delay time and total floating time Determination:

It is well-known by the time in the middle of the introduction of the tablet into the medium and its increases to the upper one-third of the dissolution container is called as floating lag time and the time for which the dosage form floats is known as the floating or flotation time. All the tests are commonly performed in gastric fluid or 0.1 moles.lit-1 Hydrochloric acid maintained at 37o C, with the help of using the USP dissolution equipment containing 900 ml of 0.1 molar Hydrochloric acid as the dissolution medium.

3) Drug release:

It is a necessary test for in vitro drug liberation study and carried out in gastric fluids and intestinal fluids temperature should maintained at 370 C. Termination tests are perform educing the USP termination equipment. Latest methodology as described in USP XXIII states that the dosage unit is having permission to sink to the lower portion of the vessel before starting rotation of the blade and standard dissolution process found on the USP or British Pharmacopoeia (BP) have been seen to be bad predictors.

4) Floating microspheres and beads:

Firstly take a drug sample then crushing it properly after this weighed accurately sample of beads or microspheres in a mortar pastel and then added sample to the appropriate dissolution medium and then centrifuged, filtered, and observed by different analytical methods like spectrophotometry. The percentage of drug taken is calculated in beads ormicrospheres and the shape and size should be calculated by the optical microscopy technique. The outer and cross-sectional morphology which is surface describing is done by scanning electron microscope (SEM). The calculated weight of produced microspheres was split by the total quantity of all non-volatile constituent used for the construction of microspheres, which gives the total percentage yield of floating microspheres [23].

5) Result of weight determination:

Bulk density or floating period of time has been the leading parameters of a dosage form's buoyancy. However,

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single-density measurement does not project the floatability development of the dosage forms. It administers by a force equivalent to the force (F) needed to keep the thing totally immersed in the fluid. The magnitude, govern the force and the resulting weight equivalent to the Victoria sum of buoyancy (Fbuoy) and gravity (Fgrav) forces acting on the objects as shown in the equal-

F = Fbuoy – Fgra

F = dfgV – dsgV = (df-ds) gV

F = (df – M/V) gV

In which the F is the total vertical force (resultant weight of the object), g is the acceleration due to gravity, dfs if the fluid density, ds is the object density is the object mass and V is the volume of the object.

6) Ray/Gamma scintigraphy:

For in vivo studies the main evaluation parameter for identification of floating system is X-Ray gamma scintigraphy. In each demonstration, the animals should fast overnight with free entrance of water in body, in a formulation that gives permit for indirect external monitoring by using a γ-camera. But the major disadvantage of γ- scintigraphy is the connected ionizing radiation for the patient, the restricted topographic details, short resolution inherent to the methodology, and the tangled or high-priced preparation of radio pharmaceutical [23].

7) Specific Gravity:

The displacement study is used to identify the particular gravity of floating system using compound benzene as a displacing medium [24].

APPLICATIONS OF FLOATING DRUG DELIVERY SYSTEMS

1. Enhanced Bioavailability
2. Sustained Drug Delivery
3. Sit-specific Drug Delivery System
4. Absorption Enhancement
5. Minimized adverse activity at the colon
6. Reduced fluctuations of drug concentration

CONCLUSION

Drug osmosis in the GI tract is extremely complex mechanism. Lengthen gastric remembrance of the dosage form prolonged the time duration for drug absorption is currently a convenient buoyancy drug delivery system. Floating command DDS are engaged to solve this issue. It also comes up with bosom contact in the middle of a dosage form, and the absorbing tissue which can result in higher drug concentration in a provincial area and therefore, high drug flow with the help of the absorbing tissue, manufacture the pharmacological effect for a long duration of time with maximum bioavailability and some side effects for drugs that are analyzed primarily in the superior part of gastrointestinal tract, i.e., the stomach, jejunum, and duodenum. The enhancing delivery techniques will make sure the development of enhancing the number of gastro retentive drug delivery to improve the transportation of molecules that display absorption window, less bioavailability, and large-scale first-pass metabolism.

ABBREVATIONS

KEY WORDS	FULLFORMS
1. FDDS	Floating Drug Delivery System
2. GRT	Gastric Residence Time
3. GET	Gastric Emptying Time
4. NAW	Narrow Absorption Window
5. GI Tract	Gastro intestinal Tract
6. HPMC	Hydroxypropyl Methylcellulose
7. PVP	Polyvinylpyrrolidone
8. BP	British Pharmacopoeia
9. USP	United States Pharmacopoeia
10. CMC	Carboxymethyl Cellulose
11. SEM	Scanning Electron Microscope

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CONFLICT OF INTREST

The authors declare that they have no conflict of interest

AUTHOR CONTRIBUTIONS

Dr. Arpita Singh (faculty of pharmaceutics department from goel institute of pharmacy & sciences) she guided me how to write this article.

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