Original Article

Influence The Study On The Need Of Floating Tablets For The Treatment Of Hypertension

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Abstract

The most convenient and widely used drug delivery method is the oral drug delivery system. Oral administration accounts for more than half of all OTC drugs. Conventional drug therapy can cause fluctuations in drug concentrations, leading to toxicity and therapeutic efficacy. However, recent research has led to the development of new techniques. These advanced technologies have led to the development of floating drug delivery systems. When studying airborne drug delivery systems, it is important to understand the functions and functions of the gastrointestinal tract. The stomach is divided into three parts. fundus, body, pylorus. The sinuses act as pumps that empty the stomach by propulsive movements, while the fundus and proximal body region act as reservoirs for undigested material. Gastric emptying is caused by fasting and other factors. Rapid-acting treatment is essential for mild symptoms, but conventional therapies do not have the desired effect due to insufficient drug bioavailability. As a result, this project aimed to arrive at an FDD with low drug elimination potential and high therapeutic efficacy. Against this background, this review should be carried out. Hypertension (HTN or HT), also known as hypertension (HBP), is a long-term condition characterized by persistently elevated arterial blood pressure. Symptoms of hypertension are rare. On the other hand, long-term hypertension is a significant risk factor for stroke, coronary heart disease, heart failure, atrial fibrillation, peripheral artery disease, blindness, and chronic kidney disease.

KEYWORDS- FDDS, Tablets, Hypertension, Pathophysiology, GRDDS.

INTRODUCTION-

For the majority of medications, oral administration was the preferred method of delivery. Numerous oral delivery systems have been developed over the past 20 years to function as drug reservoirs that can release active drugs at a controlled pace over a predetermined amount of time. There is widespread use of controlled-release oral dose versions of several significant medications with better therapy. Designing controlled release methods to increase absorption and bioavailability presents a number of difficulties. The difficulty to limit the dose form to the desired area of the gastrointestinal tract is one of these challenges. There are numerous factors that affect the complicated process of drug absorption from the gastrointestinal tract. [1].

The length of time a drug spends in contact with the small intestinal mucosa determines how much of the drug is absorbed in the digestive system. Changing the GI transit time is a significant obstacle in the development of oral controlled medication delivery devices. The rate at which different medications leave the stomach varies greatly. Depending on the dosage type and the stomach's fed or fasted state, the normal gastric residence period ranges from 5 minutes to 2 hours. Prolonged stomach retention lengthens the time that a drug is released, enhances bioavailability, decreases drug waste, and makes medicines that are only partially soluble in high pH conditions more soluble. Additionally, extending the gastric retention time (GRT) in the stomach might help with upper small intestine local effects. such as the treatment of gastric ulcers [2].

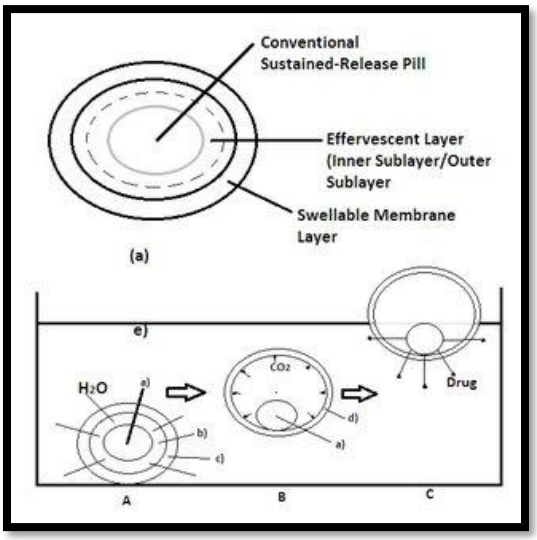

Figure number 01- Diagrammatic representation of Floating Tablet

The method of gastric retentive medication delivery lengthens the stomach retention period. These dosage forms can target site-specific drug release for local or systemic effects in the gastric tract and stay there for a long time. There have been many different strategies for gastro retentive medication administration established over the years. Low-density (floating) systems that create buoyancy inside the stomach and high-density (sinking) systems that are retained at the base of the stomach are included in this. An injectable, mucoadhesive system that promotes adherence to the gastric mucosa [3,4].

Magnetic systems, expandable, stretchable, or sealable systems that prevent the release of the dosage form via the stomach's pyloric sphincter, super porous hydrogel systems, and similar devices. the stronger therapeutic impact of active ingredients. For instance, longer gastric retention may be beneficial for medications that are absorbed into the proximal gastrointestinal system and medications that are poorly soluble or destroyed by alkaline pH. [5].

Additionally, the possibility for local and sustained drug administration to the stomach and proximal small intestine for the treatment of specific illnesses may increase bioavailability and therapeutic efficacy when therapeutic substances are retained for an extended period of time in the stomach. It has been demonstrated to enhance dosage advantages, including size reduction. The vestibule is the main location of mixing movements, acting as a pump to empty the stomach with propulsive energy. The body serves as a reserve for undigested material. [6].

CLASSIFICATION OF FLOATING DRUG DELIVERY SYSTEM-

Effervescent Systems (Gas-generating Systems):

These systems remain buoyant in gastric juice and contain effervescent substances like sodium bicarbonate, tartaric acid, or citric acid, swelling polymers like hydroxy propyl methyl cellulose (HPMC), polysaccharides like chitosan, or liquids that evaporate at body temperature. contains chamber-made matrices [7].

These systems are created by first coating resin beads with ethylcellulose and then loading them with bicarbonate. Water cannot dissolve this layer but can travel through it. The carbon dioxide that is released as a result causes the beads to float in the stomach. Excipients such HPMC, polyvinyl acetate, polyacrylic acid polymers, sodium alginate,

polyethylene oxide, calcium chloride, Carbopol®, agar, and polycarbonate are most frequently utilised in these systems. [8].

On-effervescent Systems-

The non-foaming FDDS system is based on the bioadhesion to the gastrointestinal tract's mucosal layer and polymer swelling mechanisms. In non-foamed FDDS, hydrophilic cellulose gums, hydrocolloids, polysaccharides, and matrix-forming substances such polymethacrylates, polystyrenes, polycarbonates, and polyacrylates as well as bioadhesive polymers like carbopol and chitosan are the most often utilised excipients. This dosage form has a bulk density of 1. reach 1 and expands when in contact with stomach fluid. The air that has been trapped in the enlarged matrix is what gives the dose form its buoyancy. The reservoir-like, inflated gel-like structure that results from this process allows for continuous drug release through the gelatinous bulk. [9,10].

BASIC GASTROINTESTINAL TRACT PHYSIOLOGY-

Understanding the fundamental principles of physics as well as the workings of the gastrointestinal tract is crucial when researching floating medicine delivery devices. Anatomically, the stomach is separated into three parts: the fundus, body, and pylorus. While the bottom and proximal areas of the body serve as repositories for undigested material, the sinuses are the principal source of mixed motility and serve as pumps for propulsive stomach emptying. The act of eating causes the stomach's contents to be emptied due to fasting and other factors. The two states' training regimens, however, are different. Every two to three hours during fasting, the gastrointestinal tract experiences a sequence of electrical impulses that pass through the stomach and intestines, according to Wilson and Washington. [11, 12].

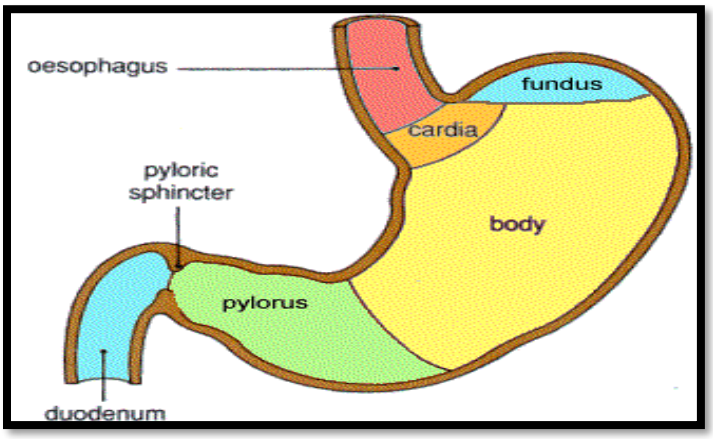

Figure Number 02 - Anatomy of the gastrointestinal tract

Phase I (basal phase) –

It lasts between 40 and 60 minutes, with only a few contractions [13].

Phase II (pre-burst phase) –

With intermittent action potentials and contractions, it lasts 40 to 60 minutes. Attacks gradually increase in intensity and frequency as the phase progresses [14].

Phase III (burst phase)-

Duration is 4-6 minutes. It consists of short, strong, regular contractions. Because of this surge, all undigested stomach material flows into the small intestine. Housekeeping Wave is another name for it [15].

Phase IV-

This occurs between Phase III and Phase I of two consecutive cycles and lasts 0-5 minutes [16].

Mechanism of Floating tablet-

To extend the period that dose forms are retained in the stomach, numerous efforts have been undertaken. These initiatives include floating dosage forms, mucoadhesiveness systems, high-density systems, enhanced moulding techniques, devices to delay gastric emptying, and medications to delay gastric emptying. The most popular among these, taking into account the addition of co-administration, are floating dosage forms. [17].

Because floating drug delivery systems (FDDS) are buoyant in the stomach for longer periods of time without impacting gastric emptying rates, they have a lower bulk density than gastric juice. The medicine is gradually removed from the system at the proper rate while the system floats on the contents of the stomach. The remainder of the system is drained from the stomach after the medicine has been released. [18].

As a result, GRT is improved, and fluctuations in plasma medication concentrations are better managed. To ensure that the dosage form stays buoyant on the surface of the meal, however, a minimum level of buoyancy (F) is also necessary in addition to the minimum gastric contents needed to correctly implement the buoyancy retention principle. [19].

In order to assess the dynamics of the swimming force, a novel device for calculating the weight of the outcome has been documented in the literature. In order to maintain an object in the water, the device measures the force equal to F (as a function of time) continually. The better the floating, the larger F is on the positive side. [20].

THE NEED FOR A FLOATING DRUG DELIVERY SYSTEM IN HYPERTENSION-

In mild conditions, fast-acting therapy is essential, but with the help of conventional therapy, drug bioavailability is insufficient to produce the desired effect. We attempted to arrive at an FDD that is less and more therapeutically effective. From this point of view, we must perform this verification. Hypertension (HTN or HT), also known as hypertension (HBP), is a chronic condition characterized by persistently elevated arterial blood pressure [21].

In most cases, high blood pressure goes unnoticed. The risk of stroke, coronary heart disease, heart failure, atrial fibrillation, peripheral artery disease, blindness, chronic kidney disease, and dementia are all significantly increased by long-term hypertension. One of the biggest causes of death in the globe is hypertension. Primary (essential) or secondary hypertension are the two categories of hypertension. In 90–95% of instances, primary hypertension is characterised as hypertension brought on by non-specific lifestyle or hereditary causes. [22].

Risk factors include salt in the diet, obesity, smoking, and alcohol use. Secondary hypertension is characterised as hypertension with observable causes, including B. Endocrine issues, chronic kidney disease, renal artery stenosis, or oral contraceptive use [23].

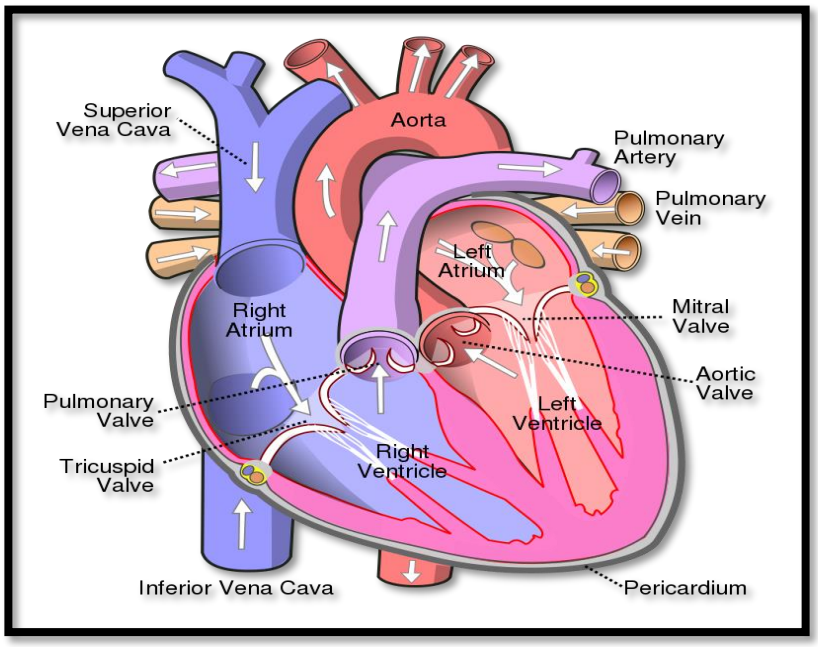

Figure Number 03 - The diagrammatic view of the heart

SIGNS AND SYMPTOMS OF HYPERTENSION-

Rarely does high blood pressure have symptoms; instead, it is frequently found through screening or when a patient visits a doctor for a different issue. Some persons with high blood pressure may experience tinnitus, which is a buzzing or hissing sound in the ears, lightheadedness, dizziness, headaches (particularly in the back of the head and in the morning), blurred vision, and fainting. However, rather than being caused by hypertension itself, these symptoms might be linked to the anxiety that goes along with it. It exists. There are four levels of severity for the alterations that are typical with hypertensive retinopathy. It can be challenging to distinguish between grades II and I. The length and severity of hypertension closely correlate with the degree of retinopathy. [24, 25].

PATHOPHYSIOLOGY OF HYPERTENSION-

Most persons with established essential hypertension experience hypertension despite normal cardiac output due to increased blood flow resistance (total peripheral resistance). There is proof that some young patients with borderline hypertension, often known as prehypertension, also have high cardiac output, an elevated heart rate, and normal peripheral resistance. As their cardiac output declines and their peripheral resistance rises with age, these people later in life develop the usual symptoms of established essential hypertension. It is controversial if this trend is common for all people who later acquire hypertension. Decreased capillary number or density is also a result of increased peripheral resistance in established hypertension. It's possible, but mostly because tiny arteries and arterioles are structurally narrowing. It is unclear if artery vasoconstriction contributes to hypertension. [26].

Decreased peripheral venous compliance, which can raise cardiac preload and venous return and ultimately cause diastolic dysfunction, is also linked to hypertension. High pulse pressure is frequently seen in elderly adults with hypertension (the difference between systolic and diastolic pressure). This can refer to a condition known as isolated systolic hypertension, which is characterised by unusually high systolic blood pressure but normal or low diastolic blood pressure. [27].

Increased arteriosclerosis, which is linked to ageing and can be made worse by hypertension, is typically the explanation for high pulse pressure in older persons with hypertension or isolated systolic hypertension. There are several suggested mechanisms to account for the elevated peripheral resistance in hypertension. The majority of the available research points to anomalies in the sympathetic nervous system or the renal salt and water balance, particularly in the intracranial renin-angiotensin system. Both of these mechanisms may play a role in the majority of cases of essential hypertension; they are not mutually exclusive. Increased peripheral resistance and vascular damage in hypertension may also be caused by endothelial dysfunction and vascular inflammation. [28].

Interleukin-17 may be of importance due to its role in boosting the production of a number of other immune system chemical signals, such as tumour necrosis factor-alpha, interleukin-1, interleukin-6, and interleukin-8, which are known to be related to hypertension. Collecting. Insufficient potassium or too much sodium cause excess intracellular sodium, which constricts vascular smooth muscle, reduces blood flow, and raises blood pressure. [29, 30].

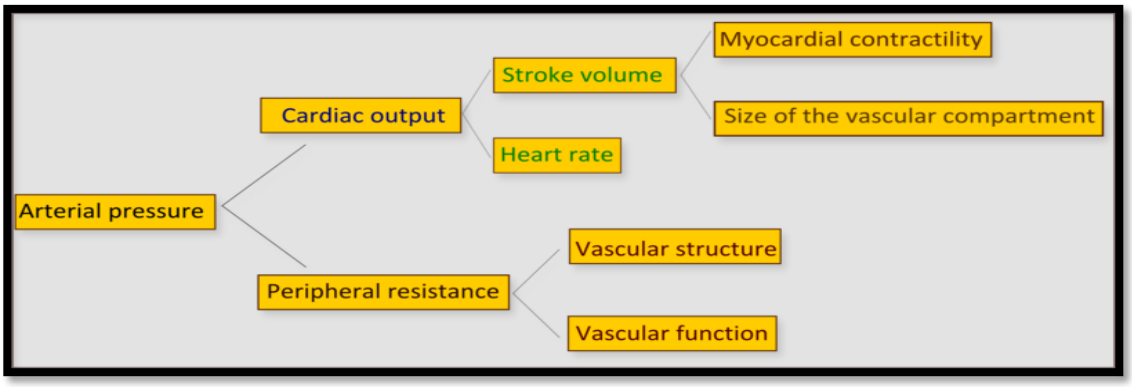

Figure Number 04 - Hypertension Pathophysiology Diagrammatic presentation

FACTORS AFFECTING GASTRIC RESIDENCE TIME OF FLOATING DRUG DELIVERY SYSTEM-

The density of tablets-

The buoyancy and density of the dose form affect the gastric retention time (GRT). The dose form for FDDS should have a lower density than the contents of the stomach. (1.004 g/mL) [31].

Size and Shape-

Due to higher GRT, dosage forms with a diameter greater than 7.5 mm are preferable to those with a diameter of 9.9 mm. Similar to this, it has been found that tetrahedral-shaped dosage forms and annular devices with flexural moduli of 48 and 22.5 KSI had superior GIT with 90–100% retention, making them more appropriate for FDDS than other shapes. [32].

The viscosity of polymer-

The drug release and buoyant characteristics of FDDS are significantly influenced by the viscosities of polymers and their interactions. Due to their superior buoyancy qualities, low-viscosity polymers (such HPMC K100 LV) have shown out to be better FDDS candidates than high-viscosity polymers (like HPMC K4M). Additionally, it was found that when polymer viscosity increased, the release rate decreased. [33]**.**

Fed or Unfed State-

Due to periods of vigorous motor activity or moving myoelectric complexes (MMC) every 1.5–2 hours, unit GRT under fasting settings is anticipated to be very brief. MMC clears the stomach of undigested matter, therefore if the formulation's administration time corresponds with that of MMC, the dosage form's GRT is obviously anticipated to be very brief. However, because of a delayed MMC, feeding dramatically extends GRT. [34].

Nature of meal-

The gastric motility pattern shifts to a fed state when indigestible polymers or fatty acid salts are administered, decreasing the pace of stomach emptying and extending medication release. [35].

Frequency of feed-

Due to reduced MMC frequency, continuous meals may extend GRT by more than 40 minutes compared to single meals. [36].

Gender-

Regardless of height, weight, or body surface area, the mean meal time GRT for men (3.4 ± 0.4 hours) is shorter than that for women of the same age and race (4.6 ± 1.2 hours). [37].

Age-

Older persons have much longer GRT, especially those above 70. [38].

Table Number 01 - Some of the Marketed Formulations of GRDDS

Brand Name	Type/Drug	Manufacturer	Uses	Remarks	References
Madopar	Floating capsule, Levodopa and benserazide	Roche, USA	Peripheral dopa decarboxylase inhibitor Floating	Floating, CR Capsule	[39]
Valrelease	Floating capsule, Diazepam	Hoffmann-LaRoche, USA	Tranquilizer	Floating capsule	[40]
Topalian	Floating Antacid, Aluminum Magnesium Antacid	Pierre Fabre Drug, France	Antacid, antiseptic, and protective	Floating liquid alginate preparation	[41]
Liquid Gaviscon	Floating Gel, Alginic acid and sodium bicarbonate	Glaxo Smith Kline, India	Suppress gastroesophageal reflux and alleviate the heartburn	Effervescent floating liquid alginate preparation	[42]

EVALUATION OF FLOATING DRUG DELIVERY SYSTEM-

In-vitro dissolution study-

Tests for in vitro drug release investigations are normally carried out in fluids that mimic the stomach and intestines and are kept at a temperature of 370°C. A USP Dissolution Apparatus is used for dissolution testing. Periodically, samples were taken out of the dissolution medium, replaced with an equivalent volume of fresh medium, adequately diluted, and then tested for drug content. [43].

Using a novel technique, the dose unit can sink to the bottom of the container before blade rotation starts, as defined in USP XXIII. The dosing device can be equipped with a little loose piece of non-reactive material, such as a few twists of coil wire. To forecast the in vitro performance of floating dosage forms, typical USP or British Pharmacopoeia (BP) based dissolution methodologies have been demonstrated to be insufficient. [44].

Buoyancy / Floating Test-

The floating lag time and the floating or flotation time refer to the interval of time between the introduction of the tablet into the medium and its rise to the upper third of the dissolution vessel. These experiments are typically carried out in simulated stomach fluid or 0.1 mol. lit. 1 HCl maintained at 37 °C, with the dissolution medium being a USP dissolution apparatus with 900 ml of 0.1 mol. HCl. [45].

Determination of floating lag time and total floating time-

Following introduction into the medium, the floating lag time is the amount of time it takes the tablet to rise to the upper third of the dissolution vessel, and the floating time is the amount of time the dosage form is floating. Swim delay time and total swim time are calculated using a USP dissolving apparatus with simulated gastric fluid or 0.1 molar HCl maintained at 370° C and 900 cc of 0.1 molar HCl as the dissolve medium. [46].

Swelling Study-

By observing a dose form's weight rise or water intake, swelling behaviour was determined. The growth in tablet diameter and/or thickness over time could be used to quantify the dimensional changes. The equation used to quantify water uptake expressed it in terms of percent weight increase. [47].

WU = (W1 – W0)/ W0 x 100

Where,

Wt= Weight of dosage form at time t

W0=Initial weight of dosage form

In-vivo study-

For buoyant dose forms, X-ray/gamma scintigraphy is the most crucial evaluation criterion in in vivo research. The animal is fasted for the whole experiment, given free access to water, and X-rayed soon before receiving the floating pill to verify there is no radiopaque substance. The presence of radiopaque elements is necessary for the X-ray viewing of dosage forms. He naturally swallows the formulation and is then dosed with 50 cc of water. [48].

In order to clearly show tablet movement, radiographs of each animal should be taken while they are standing up straight and at a constant distance from the X-ray source. Using an X-ray machine, stomach X-rays were taken every 30 minutes for five hours. [49].

Gamma scintigraphy is a method that, with the right introduction of suitable short-lived gamma-ray radioactive isotopes, enables in vivo non-invasive imaging of dosage forms passing through the target site of administration. The formulation enables for indirect external observation using a gamma-ray camera or scintiscanner due to the presence of a gamma-ray radionuclide. The main downsides of -scintigraphy, however, include the patient-related ionising radiation, the lack of topographical information, the inherent low resolution of the technology, and the time-consuming and expensive production of radiopharmaceuticals. [50].

Specific Gravity-

The displacement method is employed to calculate the floating system's specific gravity, and benzene is utilised as the displacing medium. [51].

APPLICATION OF FLOATING DRUG DELIVERY SYSTEM-

Sustained Drug Delivery-

There are issues with oral CR formulations, such as gastric residence duration in the GIT. The HBS system can be used to solve these issues. The HBS system can float atop the stomach contents since it can stay in the stomach for a long time and has a bulk density lower than 1. The system's relatively big size makes passing through the pyloric aperture illegal. [52].

Enhanced Bioavailability-

Riboflavin CR-GRDF has a much higher bioavailability than non-GRDF CR polymer formulations as compared to their administration. The rate of drug absorption is influenced by a number of interconnected gastrointestinal tract mechanisms related to drug uptake and transport. [53].

Site-Specific Drug Delivery Systems-

These systems are especially useful for medications like riboflavin and furosemide that are primarily absorbed from the stomach or proximal small intestine. The stomach is where furosemide is absorbed the most, followed by the duodenum. [54].

A monolithic floating dose form with enhanced bioavailability and gastrointestinal retention duration has reportedly been created. Comparing floating tablets to traditional furosemide tablets, the AUC obtained with floating tablets was almost 1.8 times higher. 84 A bilayer floating capsule was created to deliver misoprostol topically. NSAID administration. Misoprostol can be delivered slowly to the stomach in order to reach therapeutic levels and lessen medication waste. [55].

Absorption Enhancement-

Because they are absorbed from the top of the GIT site-specifically, drugs with low bioavailability are attractive candidates for formulation as buoyant drug delivery systems, enhancing absorption. [56].

Table 2: The following table compares the conventional drug delivery system with the gastric retention type drug delivery system

Specification	Conventional Dosage Form	Gastro-Retentive Dosage Form	References
Chances of adverse effects	High risk	Low risk	[57]
Patient compliance	Less	Improved	[58]
Narrow absorption window in the small intestine	Not useful	Useful	[59]
Drugs with rapid absorption throughout GIT	Not beneficial	Beneficial	[60]
Colon degrading drugs	Not beneficial	Beneficial	[61]
Locally acting drugs in the stomach	Not beneficial	Beneficial	[62]
Poorly soluble drugs in alkaline pH	Not beneficial	Beneficial	[63]
Dose-dumping risk	High risk	No risk	[64]

CONCLUSION-

The easiest and most popular medicine administration system is the oral drug delivery system. Oral administration is used for more than half of OTC medications. The therapeutic efficacy and toxicity of conventional medication therapy can change as a result of variations in drug concentrations. New techniques, however, have lately been created as a result of recent study. The creation of floating drug delivery devices is the result of these cutting-edge technology. The active component is released through a swelling matrix. These contours are anticipated to maintain the gastric contents' buoyancy without compromising the natural rate of emptying. Drugs with absorption windows can have their bioavailability and regulated delivery increased by using gastric-retentive drug delivery devices.. Approaches to gastric-restricted drug delivery, primarily using buoyancy, bioadhesion, expansion, magnetism, and high-density systems. Each of these drug delivery systems has advantages and disadvantages. This should be taken into account when designing a successful GRDDS.

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CONFLICT OF INTERESTS

Nil

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