A REVIEW ON: GASTRORETENTIVE DRUG DELIVERY SYSTEM

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ABSTRACT

Gastric emptying is a complicated and extraordinarily variable process. This reasons the unpredictability of the bioavailability of drug shipping systems. Gastro retentive drug transport structures (GRDDS) have obtained tremendous attention inside the past many years in general because of the reality that they are able to overcome the hindrance of traditional oral controlled launch drug transport structures associated with speedy gastric emptying time. This considerably extends the period of drug release, prolongs dosing c language and will increase bioavailability of drugs and consequently improves compliance of the patients and effectiveness of pharmacotherapy. The principle emphasis is at the complete type and unique varieties of GRDDSs. Finally evaluation strategies of these systems were summarized.

KEYWORDS: Gastro retentive drug delivery system, Floating drug delivery system.

INTRODUCTION[1-2]

diverse drug delivery systems (DDS) have been advanced for maximizing bioavailability, lowering drug waste, expanding healing index and decreasing the side effects of the drug .manufacturing of oral controlled launch (CR) formulations is an attempt to launch the drug slowly into the gastrointestinal tract (GIT) and keep an powerful drug awareness in the systemic circulate for a protracted period of time. Despite essential breakthroughs of the ultimate many years in manufacturing of oral controlled drug shipping systems, there was constrained success inside the case of medication with poor absorption in the GIT. The scintigraphic studies involving measurements of gastric emptying charges in healthy human subjects have found out that several physiological issues which include lack of ability to restrain and discover the drug delivery structures within the favored area of the GIT and the
unpredictable gastric emptying time (approximately 8–12 hrs) variable gastric motility reasons the principal quantity of drug to be unabsorbed And it also reduces the efficacy of the administered dose due to the incomplete drug release from the dosage shape. GRDDS is an method to extend gastric residence time, by targeting website online-specific drug release inside the higher gastrointestinal tract for nearby or systemic effects.

**Merits of Grdds**[^3]

- Affected person compliance through creating a as soon as an afternoon therapy.
- Shipping of medicine with slim absorption window within the small gut region.
- Improved therapeutic efficacy.
- Stepped forward bio-availability is anticipated for tablets which can be absorbed quite simply upon release in the GI tract consisting of cyclosporine, ciprofloxacin, ranitidine, amoxycillin, captopril, etc.
- Longer house time within the stomach might be advantageous for nearby motion in the top a part of the small intestine, for instance remedy of peptic ulcer disease.

**Demerits of Grdds**[^4]

- The drug substance which might be risky at acidic envirment of belly.
- Those device are require high degree of fluid inside the belly for drug delivery to flow and paintings correctly.
- No longer appropriate for drug that have solubility or balance hassle in GIT.

**Drugs Which Require Gastric Retention**[^5]

1. Drugs appearing locally in the stomach E.g. and tablets for H. Pylori viz., Misoprostol
2. Tablets that are broadly speaking absorbed in the stomach E.g. Amoxycillin
3. Tablets those are poorly soluble at alkaline pH E.g. Furosemide, Diazepam, Verapamil, and many others.
4. Tablets with a slender window of absorption E.g. Cyclosporin, Methotrexate, Levodopa, and so forth.
5. Tablets which can be absorbed unexpectedly from the GI tract. E.g. Metonidazole, Tetracycline.
6. Tablets that degrade within the colon. E.g. Ranitidine, Metformin HCl.
Limitations of The Techniques of Gastroretention\textsuperscript{[6]}

1. The floating structures in patients with achlorhydria may be questionable in case of swellable structures, faster swelling homes are required and entire swelling of the gadget should be finished properly before the gastric emptying time.

2. Bioadhesion inside the acidic surroundings and high turnover of mucus may increase questions on the effectiveness of this method, further retention of high-density systems in the antrum element beneath the migrating waves of the belly is questionable.

3. The mucus on the walls of the belly is in a kingdom of regular renewal, resulting in unpredictable adherence.

4. In all the above structures the physical integrity of the device may be very crucial and number one requirement for the success of these structures.

5. No longer suitable for capsules that could reason gastric lesions e.g. Non-steroidal pills. Tablets which might be unstable inside the robust Acidic surroundings, those systems do no longer offer sizable benefits over the conventional dosage paperwork for capsules that are absorbed all through the gastrointestinal tract.

Ingredients used for the preparations of GRDDS\textsuperscript{[7]}

Various ingredients are used in GRDDS. The following polymers have been frequently used for preparation of floating drugs: HPMC K4 M, HPMC K15, HPMC K4, HPMC 4000, HPMC 100, calcium alginate, sodium alginate, Eudragit S100 Eudragit RL, Eudragit S, Eudragit RS, propylene foam, ethyl cellulose, poly methyl methacrylate, methocel K4M, polyethylene oxide, cyclodextrin, CMC, HPC, metolose, PVP, PVA, HPCH, HPC-M, acrylic polymer E4 M, polyethylene glycol, polycarbonate, and carbopol. Suitable hydrocolloids that are used in GRDDS include: synthetics, anionic or nonionic like hydrophilic gums, acacia, pectin, agar, alginates, gelatin, casein, bentonite, veegum, as well as modified cellulose derivatives, such as MC, HPC, HEC and NaCMC.

Other used ingredients in GRDDS are

Effervescent agents like sodium bicarbonate, citric acid, tartaric acid, di-sodium glycine carbonate (DiSGC) and citroglycine (CG).

Release rate accelerants like lactose and mannitol. Release rate retardants such as dicalcium phosphate, talc and magnesium stearate.
Low density materials like polypropylene foam powder (Accurel MP 1000). Surfactants which are used as stabilizers or emulsifiers, play the role of hardening the microspheres as well, e.g. tween 80, span 80 and SLS.

Solvent systems such as: Water, ethanol, dichloromethane, acetonitrile, acetone, isopropyl alcohol and dimethylformamide.

Factors affecting gastric retention time of the dosage form [8-9]

**Density:** The density of the dosage form should be less than that of the gastric contents (1.004g/ml).

**Shape of The Dosage Shape:** A diameter resided within the belly for a longer length than other devices of similar length. The unmarried or a couple of unit system -a couple of unit components display a extra predictable launch profile and insignificant impairing of the overall performance due to failure of the gadgets. permit co administration of devices with distinctive launch profile or containing incompatible materials and allow large margin of protection towards dosage shape failure in comparison with single unit dosage form.

**Size:** Dosage shape having diameter of greater than 7.5mm have extra gastric residence time than that of nine.9mm diameter dosage form.
Nature of meal- feeding of undigestible polymers or fatty acids can change the motility sample of the belly to a fed state, as a consequence reducing gastric emptying charge and prolonging drug release.

Caloric content-GRT can be expanded with the aid of 4-10 with a meal this is excessive in protein and fats.

Frequency the meal – feeding growth over 400 min whilst successive food given are in comparison with the single meal due to low frequency of MMC.

Gender- Suggest ambulatory GRT in male (three.4hrs) is much less in comparison with the age and race matched woman opposite numbers (4.6hrs) regardless of peak, weight and body floor.

Age- people with age greater than 70 have a huge longer GRT.

Concomitant drug administration- tocholinergic like atropine and propetheline, opiates like codeine can prolong GRT.

Types of Gastroretentive Dosage Form[10-11]
Gastroretentive drug delivery system can be divided into

Non Floating System
a. High Density (Sinking) Drug Delivery System.
b. Bioadhesive or mucoadhesive system.
c. Magnetic system.
d. Expandable system.

Floating Drug Delivery System
a. Effervescent System.
i. Gas generating.
ii. Volatile liquid containing System.
a. Intra gastric floating Gastrointestinal drug Delivery System.
b Intra-gastric osmotically controlled drug delivery system.
c. Inflatable gastrointestinal drug delivery system.
b. Non effervescent system
i. Hydrodynamically balanced system
ii. Microballoons or hollow microspheres
iv. Microporous compartment
iii. Alginate beads

**Rationale for The Use of GRDDS**\[12-13\]

A. Effervescent System: These systems are further classified as below-

1. Gas generating system
   The primary mechanism is worried in this device is the production of CO2 gasoline due to reaction among sodium bicarbonate, citric acid and tartaric acid. The gas produced effects in the discount of density. The system consist double layers. The inner layer is and bubbling layer containing sodium bicarbonate and tartaric acid. The outer layer is of a swellable membrane layer containing PVA shellac.

2. Volatile liquid containing system
   Those have an inflatable chamber which includes a liquid e.g. ether, cyclopentane, that gasify at body temperature to cause the inflation of the chamber in the stomach. Those structures osmotically control floating gadget containing a hollow definable unit.

a. Intra gastric floating gastrointestinal drug
   Shipping gadget this system consists of a floatation chamber which incorporates vaccum or an inert, innocent gasoline and a micro porous compartment enclosing drug reservoir.
b. Inflatable gastrointestinal drug transport system
Those systems possess inflatable chamber containing liquid ether (discern 6) which gasifiers at body temperature to inflate the stomach. Inflatable chamber incorporates bio erodible polymer filament (e.g. Copolymer of poly vinyl alcohol and poly ethylene) that progressively dissolves in gastric fluid and finally purpose an inflatable chamber to launch gas and crumble.

c. Intra-gastric osmotically managed drug transport machine\[^{[14]}\]
It is composed of osmotic stress controlled drug transport device and an inflatable floating capsule. In the stomach, inflatable capsule disintegrates and release the osmotically managed drug transport gadget which contains components: drug reservoir compartment and osmotically active compartment.

i. Hydrodynamically balanced machine: it is a technique of a drug with gel forming it's far a formulation of a drug with gel forming hydrocolloids meant to remain buoyant inside the belly contents. Drug transport systems have a bulk density lower than gastric fluids and thus continue to be buoyant within the belly for a extended time frame, without affecting the gastric. After the discharge of the drug, the residual gadget is emptied from the stomach. This effects in an growth within the GRT and a better control of fluctuations within the plasma drug concentrations.

ii. Microballoons\[^{[16]}\]: Microballoons (hole microsphere) are inside the strict feel, empty debris of round form without core. These microspheres are characteristically free flowing powders comprising of proteins or synthetic polymers, ideally having a size less than 200 micrometers.

iii. Microporous compartment: on this system, drug reservoir is encapsulated inside a microporous compartment having pores alongside its pinnacle and backside partitions. The floatation chamber containing entrapped air causes the delivery system to float over the gastric content.

iv Alginate beads: Freeze dried calcium alginates had been used to broaden multi unit floating dosage bureaucracy\[^{[17]}\] by means of losing sodium alginate answer into aqueous solution of calcium chloride round beads of approximately 2-5 mm diameter may be organized. it's far performed by means of the usage of FTIR and HPLC. the arrival of a new
height and/or disappearance of authentic drug or excipient peaks suggest the drug excipients interaction

**Evaluation Parameters of GRDDS**\(^{[18-20]}\)
Assessment parameters of GRDDS commonly encompass.

**Drug-excipient interplay**
It is achieved with the aid of using FTIR and HPLC. The arrival of a brand new peak and/or disappearance of authentic drug or excipient peaks imply the drug excipients interaction.

**Floating lag time**
It's miles the time taken to emerge pill onto the surface after it's far kept in to the dissolution medium. It is measured in mins or seconds. In vitro drug launch and duration of floating
It's miles determined by way of the use of USP II apparatus (paddle) stirring at a speed of 50 or one hundred rpm at 37±2°C in simulated gastric fluid of pH 1.2. Aliquots of the samples are gathered and analyzed for the drug content material. The time for which the drug remains floating on the surface of the medium is the duration of the.

**Floating time**
In vivo evaluation of gastric retention evaluation of the placement of the dosage form within the GIT includes an imaging approach together with γ- scintigraphy and X-ray. In γ-scintigraphy, a small quantity of solid isotope is compounded within the dosage bureaucracy all through its guidance. The inclusion of a γ-emitting radionuclide in a system allows oblique outside statement the use of a γ-digicam or scinti scanner. For x-ray, barium sulfate is used as a evaluation medium. It facilitates to find a dosage shape within the GIT through which one could are expecting and correlate the gastric emptying time and the passage of the dosage shape. In ddition, gastroscopy and ultrasonography studies can be protected in the in vivo evaluation of GRDDS. Gastroscopy incorporates of in keeping with-oral endoscopy, used with a fiberoptic and video machine. Ultrasonograpohy isn't robotically used in the evaluation of GRDDS. In vivo plasma profile also can be acquired by performing the study in a appropriate animal model.

**Water uptake**
have a look at it's far executed through immersing the dosage form in simulated gastric fluid at 37°C and figuring out the dimensional adjustments, along with diameter and thickness, at
everyday c program language period of time. After the stipulated time the swollen drugs are weighed and water uptake is measured inside the phrases of percent weight advantage, as given:

\[(Wt-Wo) \times 100/Wo\]

wherein, Wt and Wo are the weight of the tablet after time t and first of all, respectively. The pills also are evaluated for hardness, friability, weight variant and so on, which can be relevant for conventional instantaneous launch drugs. For the more than one unit dosage bureaucracy like microsphere following assessments also are important aside from the above exams.

- Morphological and dimensional assessment: it's far accomplished with the aid of scanning electron microscopy and optical microscope.
- Percentage yield of microsphere.
- Entrapment overall performance: The drug is extracted through appropriate method and analyzed to discover the quantity of drug gift.

CONCLUSION

Gastroretentive drug transport structures have emerged as present day strategies of improving bioavailability and controlled delivery of drugs that exhibit an absorption window. Gastroretentive drug shipping techniques comprised mainly of floating, bioadhesive, swelling, magnets, and excessive density. Primarily based on the literature, it is able to be concluded that drug absorption within the gastrointestinal tract is a incredibly variable manner and prolonging gastric retention of the dosage form extends the time for drug absorption. Gastro retentive drug shipping structures are able to extend the continuous input of the drug to the upper components of the GIT and improve the bioavailability of many drugs. GRDDS have more than one advantages that consist of extra flexibility and adaptableness of dosage forms which offer clinicians and pharmacists powerful tools to optimize pharmacotherapy.

REFERENCES


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