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Review Article

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A BRIEF NOTE ON GASTRO RETENTIVE DRUG DELIVERY SYSTEM AND THEIR METHODS AND APPROACHES

***[1]Kelli Sankeerthana and [2]M. VaraLakshmi**

[1]PG Student School of Pharmaceutical Sciences and Technologies JNTUK, Kakinada.
[2]Assistant Professor At School of Pharmaceutical Sciences and Technologies, JNTUK, Kakinada.

***Corresponding Author: Kelli Sankeerthana**

PG Student School of Pharmaceutical Sciences and Technologies JNTUK, Kakinada.

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ABSTRACT

Development gastric retentive drug delivery systems were meant for long term controlled release of drugs in order to increase absorption window & to increase the drug bio availability which relates to increase of drug plasma peak concentration leads to two drug wastage by following many mechanisms this review will explain about of the mechanism swellable floating mechanism thus prevent the drug dosage form from early emptying from the gastric system thus implies the therapeutic effects to the targeted region.

KEYWORDS: Gastric retentive systems narrow absorption windows plasma peak concentration, Gastric emptying.

INTRODUCTION

From the past many decades oral controlled released dosage forms play a major role for the treatments.[1] These dosage forms were designed on the bases of patient acceptance and easy formulation etc..,but these formulations were have an difficulties like the small intestine and stomach(major absorption) were the drug was not completely released that leads improper bioavailability chances, gastric motility, gastric transit and also orally controlled released dosage form were not successful release the dosage form to the desired region like GIT and sometimes it's not suitable for gastric juices thus cause improper release rate. In order to prevent this difficulties gastro retentive release dosage forms were formulated to increase the rate of bioavailability, gastro retentive forms can remain in gastric PH for several hours provides gastric residence time, improper solubility of some drug these less soluble in and high PH and reduce dosage wasting and frequency dosing.[1,2,9] By this GRDDS most of the drug were formulated and successfully administered in order to attain good therapeutic levels.

GRDDS were prepared in order to achieve a good therapeutic effect viscosity enhancer (or) low density excipients (or) cross linkers (or) high density excipients (or) swellable (or) muco-adhesive excipients were most recommended in preparation of GRDDS.[2,3,11]

Physiological anatomy of stomach

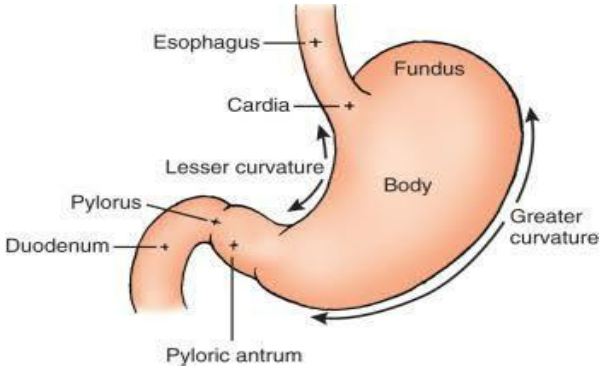
Stomach was the major part which was used for temporary of food, digestion of food and for grinding of food then passes into duodenum.

Stomach was divided in 2 parts

1) pyloric part
2) proximal part

Proximal part consists of funds and body where most of the food undigested was stored.

Pyloric part used for mixing and also acts as a pump which attains propelling actions for gastric emptying.[2,5]



Gastric emptying occurs in both fasting an undigestive phase with a continuous series of electrical events which occurs for 2-3 hrs.[3]

Table: Transit time of various parts of GIT

Organ	Transit time (hr)
Stomach	<1 (fasting) >3 (fed)
Small intestine	3-4
Large intestine	20-30

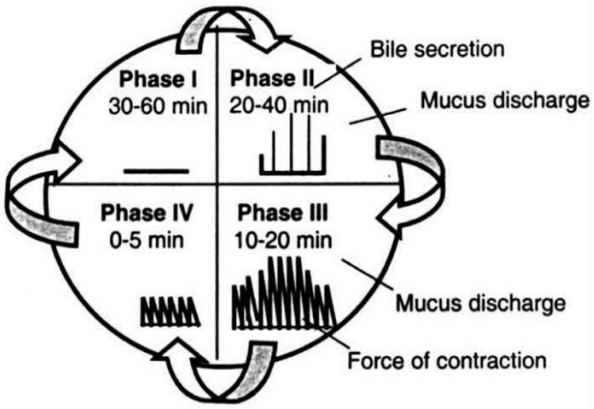
This series of electrical events were called as migrating myoelectrical cycle which contains 4 phases[2,3,4]

Phase-1: Basic phase lasts for 30-60mins.

Phase-2: Prerelease phase lasts for 20-40mints with intermittent potential action and contractions.

Phase-3: Burst phase taste for 10-20 with continues and intense contractions.

Phase-4: 0-5 min and occurs between phase 1 and 2 of consecutive cycle.[2,4,5]



Suitable drug measures for preparing GRDDS

- Selection of drug candidates were probably characterized based on some conditions like
- Drug with narrow therapeutic effect in GIT
- Drug which are insoluble in alkaline PH.[1,10]
- Drug were degraded by the colon targeting by enzymes (or) bacteria
- Drug which are absorbed in stomach and upper part of GIT
- Drug which are primitively disturb the colon bacteria
- Drug with local therapeutic activity
- By preparing of GRDDS was an advantageous from preventing drug adverse effect which are generally occurred by oral by reducing dosage frequency
- GRDDS reaches the maximum contact time with targeted area[6,7]

Factor affecting on GRDDS

Drug absorption mainly depends gastric retention time. Absorption occurs between stomach and duodenum contact time of dug which increase the absorption rate.[1,6] The absorption rate absorption also depends on gastric retention time and it lasts about 2-3hrs.[8]

Gastric empting depends on the factors and those are classified into 3 types[6]

1) Pharmaceutical factors
2) Physiological factors
3) Biological factors

1) Pharmaceutical factors

A) Density

Density of adosage form experiences an diversified use in the gastric emptying time.

Density of used the substances(excipients) should be lesser than the gastric substance (fluids) that is less than (<) 1gm/cm3 in order to float on gastric fluid to prevent from gastric emptying and increase gastric retention time.[2]

Also higher density substances(excipients) were also been used that is greater than (>) 15 to 2.4gm /cm3 than the gastric substances in order to submerge to the lower part of stomach and attach to the mucus layer and thus prevents from gastric emptying.[2,12]

B) Size

Size of drug (or) dosage form largely varies the gastric emptying time.

Generally smaller size of dosage form causes gastric emptying rapidly.

Whereas large particle size causes increase in gastric transit time by preventing itself from emptying because the large sized particle are enable to cross the pyloric sphincters.[2,13]

2) Physiological factors

A) Fed (or) fasting state

In case of fed state presence of food causes delay of gastric emptying time.[1]

In the fed state strong contractions occurs and occurred and swept out the undigested food along with the dosage form. In fasting state gastric retention was longer due to absence of contractions.[1,14]

B) Nature of meal

If meal contents more increases gastric retention time protein causes delay of the gastric emptying. If meals contains fatty acids also causes increases in gastric retention time.[15]

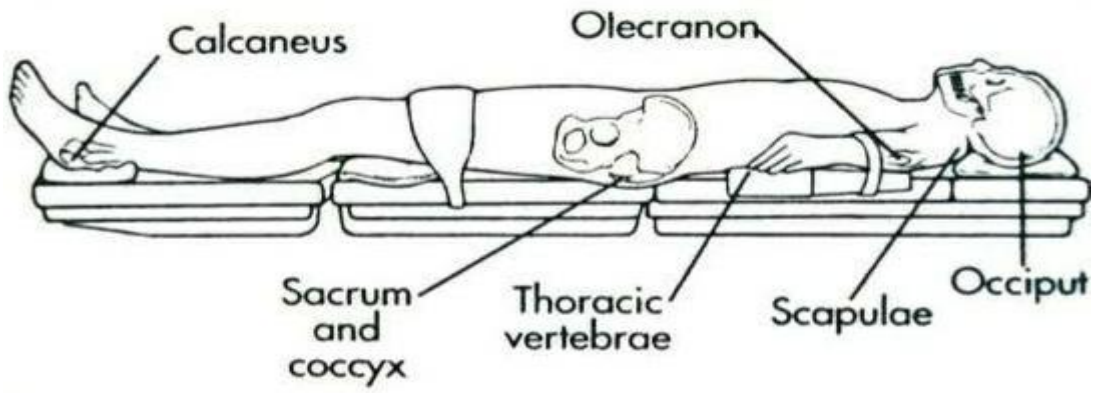
3) Biological factors

A) Sex (or) gender

Generally males have an lower gastric retention time than the females. Because males will heavily participates in the generally activities like walking and work etc.[14,15]

B) Posture

Posture also defines the gastric retention time. After a meal the person in supine posture increases the gastric emptying time.[16]



C) Age

Gastric retention time also depends on age 70 years person have more gastric time than the younger age.[17]

D) Emotion

If a person was depressed, the rate of gastric retention well maintained (more retention time). A person with an anxiety has lesser gastric retention time.[1,18]

Advantages

- GRDDS increase bioavailability of drug dosage form
- By using this sustain drug delivery which reduce the frequency of dosing
- This GRDDS were prolonged onset of action result in reduction of fluctuations of drug concentration.
- It minimizes the colon adverse activities increase the half life of drug. Thus results in flip-flop pharmacokinetics.[2,19]
- Controlled or sustained release of drug provides effective local action at diseased site.
- These are useful for the drugs which are poorly soluble in the alkaline ph.
- Due to increase bioavailability an absorption rate it prevents the dose dumping.[2,20]

Disadvantages

- GRDDS increases the drug bioavailability with certain limitation
- One of the major limitation include floating system requires more fluid in order to float on the gastric fluid to avoid gastric emptying.
- Drug with characteristic gastric irritant on prolong contact causes gastric lessions.

eg: aspirin

- In case of bioadhesive dosage they react with the mucus thus forming hydrogen bonds (or) strong interactions which are not easily dispatchable.
- Present of more turnover of mucus causes some mucus aggregation.
- Drug with insoluble acidic gastric pH environment not suitable for GRDDS.[22]

eg: phenytoin

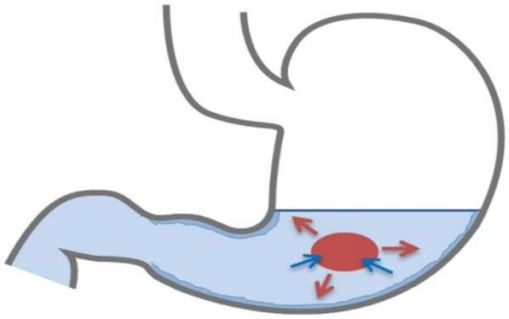
- Dosage form taken (or) administered during the fasting state, as they should resist from the house keeping waves.
- The system requires food present in order to maintain the more gastric retention time.[2,21]

Types of gastro retentive dosage form

A) Expandable system

These expandable type of dosage form were mostly used for veterinary usage and later in human use.[7,23]

These dosage forms expand itself when they reaches in to stomach (or) unfold their intra compressed structure thus attain an effective size and prevent swept out during gastric emptying time by with standing from high peristalsis movement of stomach.[6,24]

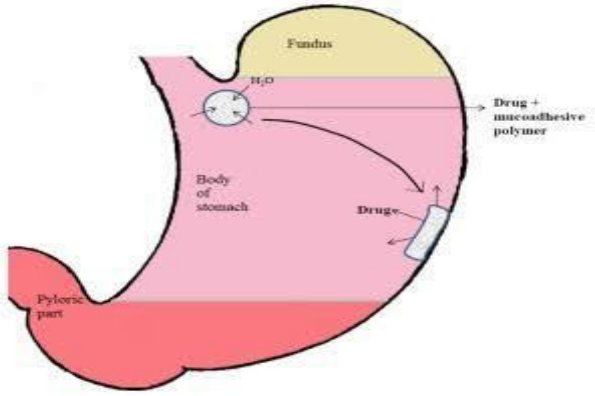


B) Bio/mucoadhesive system

Bio/mucoadhesive systems were intended to link/get attached to the epithelial cell surface of mucus layer for all the time the complete absorption and release of drug. Dosage from up on release into stomach then gets attached to mucus layer.[6,.25]

But the potent does not impact on mucus layer because up on emptying and on peristaltic movement the mucus layer will swept of and by continuous production of mucosa will cause the bioadhesive system.[1,.26]

Bioadhesive materials like carbopol, lectins, chitosin were used.[27]



C) Floating drug delivery systems

Floating drug delivery system were generally GRDDS. These dosage forms were float on surface of gastric fluid and execute an high gastro retentivetime. Thus obtains an complete bioavailability and absorption.[6,28]

1) Effervescent/gas generating system

The title itself explains the nature of the dosage form. This gas generating dosage forms were consists of matrices made up of polymers (swellable) **eg**: polysaccharides (chitosin) and effervescent component **eg**: Na2CO3, citric acid etc these all polymer upon reachingthe gastric/stomach release the co2 gas (or) sometimeseven volatile liquids where also been filled.[2,29]

2) Non-effervescent system

Non-effervescent systems are non gas forming/releasing system. These dosage forms upon swallowing they swells themselves prevents from their exit from the stomach.[2,30]

They swell when come in contact with the gastric fluid as they prepared in a way that drug was mixed with gel up on interaction with gastric fluid it tend to air entrapped by swollen polymer thus made themselves buoyancy. Polymers were HPMC, sodium alginate, CaCl2, polycarbonate, polyvinyl acetate etc.[2,31]

a) Colloidal gel barrier system

These are named as hydro dynamically balanced system firstly by Sheth and Tossounian.

These systems contain 2(or) more gel forming highly soluble cellulose type hydro colloids.[1,7]
Eg: HPLC, HPMC, polyacrylate.
These hydrocolloids upon reaction with gastric juice they start hydrates and form colloidal gel barrier around it surface.

These prolong GRT were readily reaches the target site for complete release of drug to the diseased site (or) target site.[32]

b) Micro porous compartment system

In this system drug was enclose in a micro porous coating layer where upper and the bottom layer but the adjacent layer (or) side walls were completely sealed to prevent the escape of un dissolved drug.[7,33]

Upon interaction of gastric fluid these fluids enter in to through the pores and again this fluid swept by talking some amount of dissolved drug. Thus forms continuous transport across the intestine for complete absorption.[1,33]

c) Alginate beads

This alginate beads were prepared by freeze dried method. Where sodium alginate solution was drop in to calcium chloride solution drop wise these forms alginate beads where drug was immobilized (or) packed in to these beads and these beads where separated and freeze dried and stored in liquid nitrogen[7,.34,35]

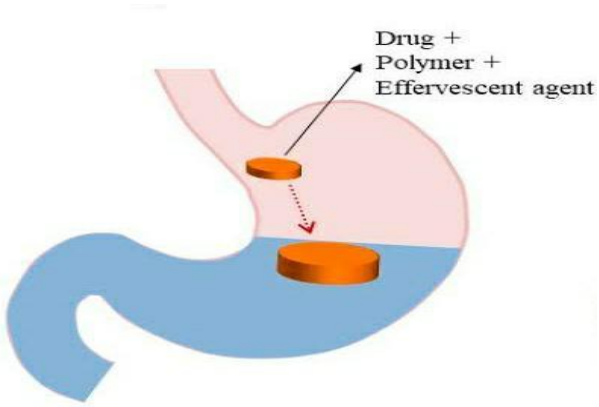
d) Hallow microspheres/ microballons

These hallow microspheres were continuously floated over in acidic medium containing surfactant for >12hrs.[36]

These were prepared by emulsent solvent evaporation method by mixing drug with acrylic polymer and dissolved in ethanol/dichloromethane solution and these were completely stirred in polyvinyl alcohol solution. This forms the internal cavity with drug loaded along with the polymer.[37]

D) Low density system

In these low density system the excipients of low density were used with an 1g/cm3. These low density excipients along with the drug were made them to float on the gastric fluids to prevent them from exit from the stomach during the gastric emptying thus helps to improve bioavailability and release rate.[6]

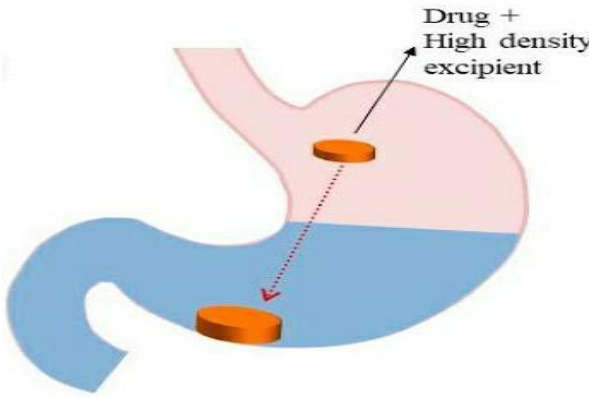


E) High density system

In these low density system excipients of high density <3gm/cm3 were used.

These high density excipients were mixed with drug these settle to bottom of the stomach and these prevent

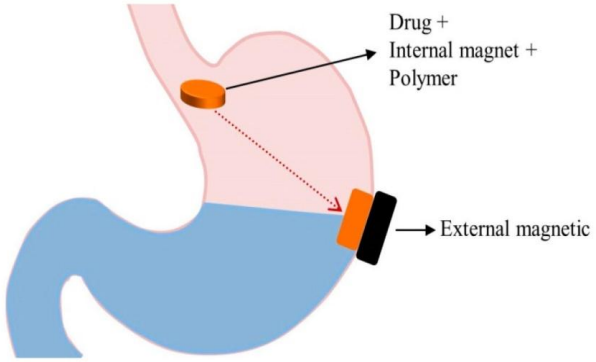
from exit from the stomach thus prevents from strong contractions.[6,24,38]



F) Magnetic system

Magnetic system a small repulsive magnet were fitted inside the cavity along with the drug and an another magnet was placed at outer side of the stomach near the intestine thus the attraction of both the small magnets align them in an strong form from swepting away from the stomach along with the gastric fluid.

These also retain themselves from the strong contraction and peristaltic movement.[39,40]



Evaluation Tests

A. Particle size Morphology: The particle size can be identified by using DSC & Electron microscopy each bead were well enveloped by the polymer materials thus given an outlook as spherical shaped beads.

B. Floating test & Buoyancy test: The GRPDS dosage product should attain their buoyancy property in order to float on the surface of fluids to prevent themselves from gastric emptying thus increases the retention time. So these are tested in artificially prepared gastric juices then accordingly time was noted.

C. Invitro drug release: The dosage were depressed in dissolution medium in a beaker of dissolution apparatus of paddle type in order to detect the drug release in the medium was acquired by collecting the sample in the respective intervals and the samples were tested with U.V Spectrophotometer.[28]

CONCLUSION

The drug therapeutic effect required for the local part of upper GIT can be achieved by gastric retentive dosage forms thus this improves the therapeutic effect by drug to upper GI track by including the floating mechanism which resists themselves from gastric emptying & produces the controlled drug release rate.

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