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GRDDS: An approach for systemic delivery of dosage forms

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ABSTRACT

From the past few decades various advancement are made in the felid of research and development of various controlled and sustained release dosage forms. There were various incompatibility and problems with the delivery of these dosage forms in the systemic circulation and enhance the retention time of there dosage forms. To overcome the obstacles and to enhance the effect of the dosage forms various approaches of GRDDS have been developed like Raft forming system, Floating system, Modified shape, Magnetic system etc. different types of polymers support these systems to enhance the floating and improve the gastric retention time of the dosage forms.

Key words: GRDDS, Raft forming system, low-density system

1. INTRODUCTION

GRDDS is one of the most commonly used route used for the delivery of drug to the systemic circulation in the body because it is easy to formulate the drug used for the oral route and can also be easily administered to the patient's body. Many drugs which have higher absorptivity and very short half life in GIT tract have much higher rate of elimination from the systemic circulation of body. To achive the therapeutic efficacy frequent dosing of such drugs is needed. To eliminate this defect oral sustained controlled release formulation is a substitute for the release of drug at a predetermined rate and contain effective drug concentration in systemic circulation. Afterwards, administration from the oral route it is required to position the drug into the stomach for its release at the rate determined previously in controlled way for its absorption and availability into the systemic circulation.

GRDDS is a method to retain the drug into the stomach region resulting into the extension of gastric residence time of drug. There were several gastro-retentive drug delivery methods is been designed and developed for the purpose of retaining the drug in the gastric region to withstand the peristaltic movement of stomach for the purpose of gastric emptying. This GRDDS extends the dosing frequency and improves patient compliance by eliminating the concept of multiple dosing of particular drug. [1]

2. ADVANTAGES

- It maintains a therapeutic level which is constant over longer period of time. E.g. Beta lactams antibiotics.
- Bioavailability of drugs is enhanced.
- Patient compliance is improved by decreasing dosing frequency.
- Treatment of GI disorders like GERD (Gastroesophageal reflux disease), Helicobacter pylori infection, etc.
- Floating drug delivery system provides a feasible approach for the drugs that have limited absorption in the intestine.
- Beneficial for drugs that are absorbed through stomach. [2]

3. DISADVANTAGES

- Drugs which undergo significant first pass metabolism, are not desirable candidate.
- Drugs showing various solubility or stability problems in the highly acidic environment of GIT cannot be formulated as GRDDS.
- Adherence of drugs with the mucus cannot be predicted because of continuous renewal of mucus wall of stomach.
- Some drugs may lead to various irritation to the gastric mucosa.
- Patient requires high level of fluids in stomach for floating and working efficiently so more water intake is prescribed with the intake of such dosage form.
- In supine posture (like sleeping), floating dosage form may be swept away (if not of larger size) by contractile waves which occurs in GIT. So, patient should not take floating dosage form just before going to bed.

- Gastric retention may be affected by many factors such as gastric motility, pH and presence of food. These factors are never constant and hence the buoyancy cannot be predicted accurately.[2,3]

4. Approaches to achieve gastric retention [3,4]

4.1. Floating or Low-density drug delivery system

Floating can be achieved by using-

4.1.1.Effervescent system

4.1.1.1.Gas generating system

4.1.1.2.Volatile-liquid containing system

4.1.2. Non- effervescent system

4.1.2.1.Expandable or swellable system

4.1.2.2.Inherently low-density system

4.2. High density sinking system

4.3. Modified shape or unfolding system

4.4. Muco-adhesive drug delivery system

4.5. Super porous hydrogel system

4.6. Magnetic system

4.7. Raft forming system

4.8. Colloidal gel barrier system

4.1.Floating or Low-density drug delivery system

This system is used for the drugs which mostly get absorbed or made to be absorbed in stomach or duodenum of GIT. This method is unaffected by the rate of gastric emptying over a prolonged period of time as the density of the floating drug delivery system is lower than then gastric fluid so the drug remains buoyant in the stomach and its content get released slowly.

4.1.1. Effervescent system

In this system gas is generated with help of various gas generating agent like NaHCO3 and other organic acids. This generated gas decreases the density of the system and make the drug float over the gastric fluid. [5]

4.1.1.1.Gas Generating system

Reaction takes place between citric acid, tartaric acid and sodium bicarbonate which leads to generation of CO_2. This generated gas get entrapped in the hydrocolloid layer which decreases the density of the system due to which the system starts to float over the gastric fluid. This system is generally double layered in which outer layer is a swellable polymer matrix and inner layer is effervescent layer.

4.1.1.2.Volatile liquid containing system

At body temperature various fluid get vaporized like ether, cyclopentane such fluids are filled in inflatable chamber. When we intake such dosage forms than these fluids get vaporized and lead to floatation of dosage form.

4.1.2. Non-effervescent system

The non-effervescent, floating drug delivery system basically works on mechanism of polymer swelling or bio-adhesion of polymer to mucosal membrane of GIT. It is of two types i.e.,

4.1.2.1. Expandable or swellable system

In this system the dosage form is larger enough than the size of pyloric sphincter, so it withstands the gastric transit in stomach, but the dosage form should be of sufficient size as it can be easily administered and won't cause any gastric obstruction.

4.1.2.2. Inherently low-density system

This system gives us the solution of previous system in which the dosage form gets settled down initially before floating. Inherently low-density system may be formulated by one of the two ways:

- Air entrapment.
- Incorporation of low-density material.

4.2.High-density or non-floating drug delivery system

In this system, the dosage form was formulated having density higher than that of normal gastric fluid i.e., 1.004gm/cm^3. These formulations are being prepared by coating the drug with a heavy core or mixing with the material like barium sulphate, zinc oxide, iron powder, etc. which leads to increase in density up to 1.5-2.4 gm/cm^3.[3]

4.3.Modified shape or unfolding system

In this system, the drug is incorporated into various different geometric shape like ring, disc, spiral, tetrahedron, etc. these systems are fitted tightly and packed into a gelatin shell of capsule and unfold into stomach after dissolution of capsule shell. The unfolding system unfolds to a larger size causing limit pressure to pyloric sphincter and leads to increase in gastric retention time of dosage form.

4.4. Muco-adhesive or Gastro-adhesive drug delivery system

In this system, a muco-adhesive polymer is used that gets adhered to the gastric mucosal surface which causes increase in GRT in GIT. Muco-adhesive polymer may be of different origin like Natural origin (guar gum, gelatin, etc.), Semi-synthetic origin (Carbopol, HPMC, etc.).

4.5.Super- porous hydrogel system

Polymer which are highly soluble in nature such as sodium alginate and croscarmellose sodium are mostly used in this system. The gastric retention time of dosage forms is improved by super-porous hydrogel system of avg. size of pore i.e., 100µm or greater. These polymers swell to a specific size due to uptake of water by capillary wetting by various inter-connected pores. This result in swelling of polymer to large size i.e., 100µm or more. Such formulations have high elasticity because of higher mechanical strength. [2]

4.6.Magnetically controlled system

During the formulation of dosage form various small size magnets are incorporated in the formulation. An external magnet is placed over the abdomen which controls the position of the dosage forms and enhances the gastric retention time. Patient compliance should also be considered during the placement of external magnet. [2]

4.7.Raft forming system

These systems are very much effective in obtaining local effect as a blockage is formed in between esophagus and stomach through it. This system is very much useful in treatment of gastro-esophageal reflux disease and peptic ulcer. A continuous layer known as raft is formed after contact with the gastric fluid, as the system becomes swelled and forms a viscous cohesive gel. With the use of sodium alginate as the gel forming polymer, sodium bicarbonate and gas generating agent the antacid raft forming system is developed. The generation of CO_2 reduces the bulk density of system due to which the raft floats on the gastric fluid. Drug gets released in sustained manner from the raft as it keeps floating for few hours over gastric fluid. This system is useful for delivery of drugs having antacid nature. [2]

4.8.Colloidal gel barrier system

In this system the formulation is made up of one or more gel forming highly soluble hydrocolloids such as hydroxypropyl methyl cellulose (HPMC), polysaccharides, hydroxyethyl cellulose, hydroxypropyl cellulose and matrix forming polymer like polystyrene and polyacrylate. When these polymers come in contact with gastric fluid the hydration of hydrocolloids present in the system is done which causes the formation of a colloidal gel barrier around their surface. [6]

5. CONCLUSION

Gastroretentive drug delivery system is explored deeply from the past few decades due to its various advantages and uses. GRDDS can be used for the delivery of the controlled released formulations and well as sustained release dosage form. In can also be used for the drugs showing local responses used to treat various gastric infections and disorders. Various approaches have been developed for increasing the gastric retention time of dosage forms and researchers are kept on searching various technique's and polymers to make these approaches more effective and affordable to patients.

6. REFERENCES

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