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Gastro Retentive Drug Delivery Systems: A Review

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ABSTRACT :

In the realm of oral drug delivery, the gastro-retentive drug delivery system (GRDDS) has grown tremendously in popularity lately. It is a commonly used method that can address numerous issues with traditional oral administration, such as poor bioavailability, by keeping the dose form in the stomach for a longer time and releasing the medicine gradually. To create GRDDS, a variety of cutting-edge techniques are being used, including magnetic field-assisted gastro-retention, plug-type swelling system, muco-adhesion technique, and floating system with or without effervescence. In addition to in vitro characterization, a well-planned in vivo investigation is necessary for the successful development of GRDDS to demonstrate extended drug release and improved gastro-retention. MRI and gamma scintigraphy are widely used methods to assess in vivo stomach residence duration[1]. For this type of dose form, determining their overall in vivo efficacy is still a significant problem, particularly in small animals like mice or rats. Despite a great number of promising in vitro outcomes, there are very few reported in vivo investigations using beagle dogs, rabbits, and human beings. Despite the many benefits, the obstacles that restrict the number of GRDDS on the market are the wide range of subject changes in gastrointestinal physiological conditions, the impact of food, and the fluctuating rate of gastric emptying time. This review paper covers the current GRDDS in vivo works, along with the obstacles and constraints[1].

KEYWORD:- Gastroretention, conventional drug delivery, Anatomy of GIT, GIT's physiology[2].

INTRODUCTION:-

The most practical and recommended method of delivering any medication to the systemic circulation is oral administration. The pharmaceutical industry has recently shown a growing interest in oral controlled-release drug delivery due to its potential to improve therapeutic benefits, including patient compliance, formulation flexibility, and ease of dosage administration. Short half-lives and easy absorption from the gastrointestinal tract (GIT) mean that drugs are rapidly removed from the systemic circulation. It takes frequent doses of these medications to attain appropriate therapeutic action [3].

To get around this restriction, oral sustained-controlled release formulations have been developed. These formulations release the medication gradually into the gastrointestinal tract (GIT) and keep an effective concentration of the medication in the systemic circulation for an extended period. Such a drug delivery would be held in the stomach following oral administration and release of the medication in a regulated manner, allowing the medicine to be constantly given to the gastrointestinal tract's absorption sites (GIT) [3].

The two main problems with these drug delivery systems are the short gastric retention time (GRT) and the erratic short gastric emptying time (GET), which can cause the drug to not release completely from the dosage form in the absorption zone (the stomach or upper portion of the small intestine), which reduces the effectiveness of the dose that is administered [3].

To provide a controlled-release dosage form that is specific to a given place, the drug delivery should prolong the gastric residence period. Extended stomach retention enhances the solubility of drugs that are less soluble in high pH environments, prolongs the time of drug release, decreases drug waste, and boosts bioavailability [3]. Additionally, extended gastric retention time (GRT) in the stomach may be beneficial for local action in the upper portion of the small intestine, such as the management of peptic ulcers, among other conditions[3]

Grdds's physicochemical characteristics

The dosage form's size, shape, and density are among its physicochemical characteristics, and these factors are crucial to the formulation of GRDDS. High-density systems sink to the bottom of the stomach, whereas dose forms with a density lower than the contents of the stomach can float to the top.

An optimum formulation will have a density between 1.0 and 2.5 g/cm3. More than 7.5 mm in diameter dosage forms have superior gastric residence time (GRT). Devices with a tetrahedron, spherical, or circular shape have good gastroretentive qualities[4].

GRDDS help these medications by enhancing their:-

- Bioavailability
- The effectiveness of the therapy and the potential for dosage reduction.
- In addition to these benefits, these systems provide several pharmacokinetic benefits, such as the ability to maintain steady therapeutic levels over an extended length of time, which reduces fluctuations in the therapeutic levels.
- Reduce drug waste
- Enhances the solubility of medications that are less soluble in high pH environments (such as weakly basic medicines like papaverine and domperidone).
- Improves local drug distribution to the stomach and proximal small intestine[4].

Physiological elements influencing GRDDS retention in the stomach

The fed or unfed condition, the type of meal, the calorie content, and the frequency of feeding are the main variables influencing the stomach retention time of dose forms. Because of the increased GI motility during fasting, there is a reduction in stomach retention time. Peristalsis is responsible for emptying the contents of the stomach. When the dose form is administered at the same time as peristalsis, the stomach residence is brief. Peristalsis, on the other hand, is delayed after meals and could contribute to the formulation's longer stomach residence[4]. GIT is prolonged by a high-calorie meal rich in proteins, lipids, and fibrous materials. When there are several meals, gastric retention is greater than it would be with only one meal because peristalsis is continuously inhibited[4].

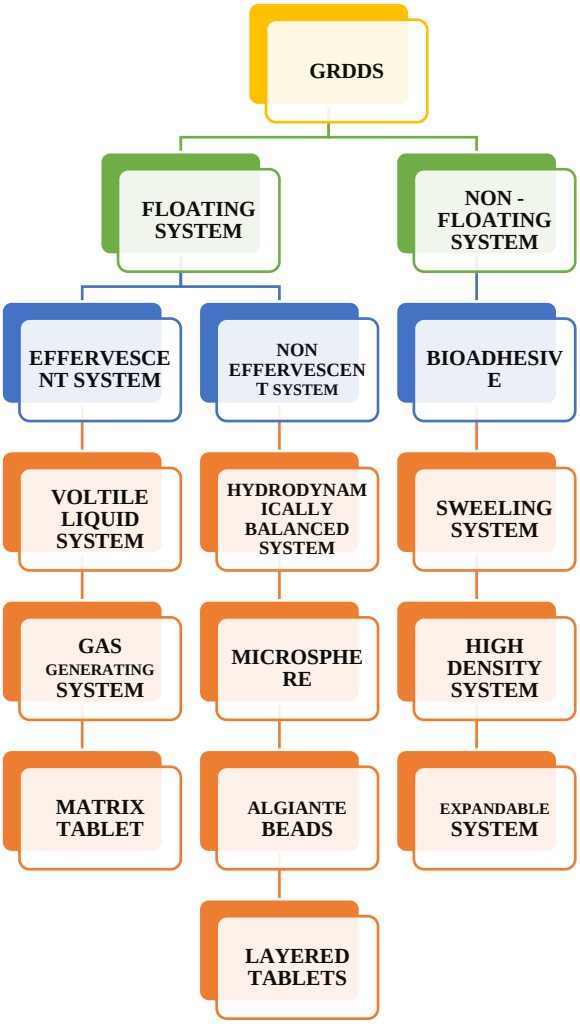
Approaches to gastro retentive dose forms

Gastro retentive approaches are techniques used in pharmaceutical formulation to prolong the residence time of drugs in the stomach[2].
This is particularly beneficial for drugs that have absorption or degradation issues in the lower gastrointestinal tract or require sustained release[2].
Here are some common gastro retentive approaches:

1. **Floating Systems**: These systems contain buoyant components that enable the dosage form to float on the gastric fluid, thereby prolonging gastric residence time. Materials such as gas-generating agents (e.g., effervescent agents), low-density polymers, or hollow microspheres are used to create floating dosage forms.
2. **Bioadhesive Systems:** Bioadhesive polymers are used to adhere the dosage form to the gastric mucosa, prolonging contact time and enhancing drug absorption. Polymers such as chitosan, carpool, and hydroxypropyl methylcellulose (HPMC) are commonly employed for their bioadhesive properties.
3. **Expandable or Swelling Systems**: These systems swell or expand upon contact with gastric fluid, leading to increased size and reduced gastric emptying rate. Hydrocolloid polymers like sodium alginate and methylcellulose are often utilized to achieve controlled swelling.
4. **High-Density Systems:** Dosage forms with high-density sink in the gastric fluid, thus remaining in the stomach for a longer duration. Heavy metals or metal salts can be incorporated into the formulation to increase density.
5. **Mucoadhesive Similar** to bioadhesive systems, mucoadhesive formulations adhere to the gastric mucosa, prolonging contact time and improving drug absorption. Natural polymers such as chitosan and synthetic polymers like polyacrylic acids are used for their mucoadhesive properties.
6. **Magnetic Systems:** Magnetic particles or ferromagnetic materials are incorporated into the formulation, allowing external magnetic fields to control gastric retention. This approach is less common but has potential applications in targeted drug delivery.
7. **Raft-Forming Systems**: These systems form a floating gel layer on top of the gastric content, creating a barrier that delays gastric emptying. Alginate-based formulations are commonly used for their ability to form a viscous gel upon contact with gastric fluid.
8. **Osmotic Systems:-**Osmotic tablets or capsules contain an osmotic core that releases drug solution continuously through a semipermeable membrane. This continuous release helps maintain drug concentration in the stomach, prolonging gastric residence time.

These gastro retentive approaches offer various strategies to enhance the bioavailability and efficacy of drugs that require prolonged gastric retention. The selection of the appropriate approach depends on factors such as drug properties, desired release profile, and patient requirements[6].

GRDDS classification[4]



In vitro evaluation of GRDDS

To ensure optimal in vivo performance in terms of floating lag time and floating duration, as well as a suitable composition, in vitro evaluations of GRDDS are important. General tablet parameters such as hardness, friability, general appearance, drug content, uniformity of content, weight variation, and in vitro drug release are among the routine evaluation tests for tablet dosage forms [1]. The literature has used simulated gastric fluid and deionized water to evaluate floating behavior, including floating lag time and duration for any GRDDS. These two media are used to look for potential variations in the dosage forms' buoyancy capabilities. Furthermore, the polymeric dosage's swelling properties and rate of swelling
Forms dissolved in 0.1N HCl are tested for at least eight hours to make sure the drug releases and the floating mechanism works. This is accomplished by weighing the increased weight or the size of the swollen tablet once the study is complete. The test medium for in vitro drug release tests is simulated gastric fluid[1].

After a predetermined amount of time, samples are taken out of the dissolution baskets and suitably diluted to be examined for drug content[1].

In vivo gastric retention as a surrogate of pharmacokinetic study

To demonstrate the in vivo effectiveness of any GRDDS, a properly executed in vivo study using a suitable animal model or healthy human subjects is vital. However, it can be difficult to deal with smaller animals, such as mice, rats, guinea pigs, or rabbits, to check gastric retention while performing a bioavailability study. This is particularly true for large tablet dosage forms. Because of this, the majority of the literature on the formulation of GRDDS has demonstrated the proof of in vivo gastric retention in animals that are relatively larger, such as dogs or human subjects, along with significant in vitro characterization studies like dissolution studies, floating lag time estimation, and floating duration estimation. The prolonged in vivo stomach retention was proposed as a theory that believed the GRDDS would provide greater therapeutic efficacy in comparison to the traditional dose form[1].

ADVANTAGES OF GASTRO RETENTIVE DRUG DELIVERY SYSTEMS

1. Enhanced bioavailability
2. Enhanced first-pass biotransformation
3. . Sustained drug delivery/reduced frequency of dosing
4. Targeted therapy for local ailments in the upper GIT
5. . Reduced fluctuations of drug concentration
6. . Minimization of fluctuations in drug concentration
7. Site-specific drug delivery
8. Minimized adverse activity in the colon
9. . Extended time over critical (effective) concentration
10. Reduced counter-activity of the body[2]

DISADVANTAGES OF GASTRO RETENTIVE DRUG DELIVERY SYSTEMS

- Not suitable for medications with low acid solubility. For example, phenytoin
- Inappropriate for medications that become unstable in an acidic environment. For example, erythromycin
- Slow-release medications that irritate the stomach or create ulcers. Examples are NSAIDs and aspirin
- Drugs that the intestines more readily absorb. For example, corticosteroid
- Medication that passes through the GIT is equally effective. Such as nifidipine and isosorbide dinitrate
- To float and function efficiently, floating drug delivery systems need a high fluid level in the stomach[2].

CONCLUSION :

The review of the literature leads to the conclusion that GRDDs provide several potential benefits for drugs with low bioavailability.
The process of drug absorption in the gastrointestinal tract is different, and the duration it takes for drug absorption increases when the dosage form remains in the stomach prolonged[2].
However, most of them have demonstrated several benefits of GRDDS in patients. The required dosage and simplicity of manufacturing for each drug candidate or combination of pharmaceuticals must be evaluated on an individual basis[6].
For formulations containing high doses, polymer selection remains essential. The compressibility required to take advantage of the high doses of the APIs depends on this choice.
Nonetheless, the amount of the polymer in the dose form should determine the optimum criteria; a minimum amount that significantly increasesstomach retention should be favored [5].
While several methods, including buoyant, bioadhesive, effervescent, sinking, magnetic, swelling, etc[5].

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