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REVIEW ARTICLE

FLOATING TABLET AND IT' S TECHNOLOGY: AN OVERVIEW

V.Priyanka*[1], C. Surya Prakash Reddy[1], Dr. C. Sowmya[1], Ranjit Kumar Singh[2]

1. Raghavendra Institute of Pharmaceutical Education and Research, Ananthapuramu, Andhra Pradesh, India – 515721.
2. Bafna Pharmaceuticals Limited, Grantlyon Village, Chennai-600052.

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Abstract:

Sustained- release system includes any drug delivery system that achieves a slow release of drug over an extended period of time and helps to improve therapy. The delivery system used for sustained action should only produce a sustained action at a predetermined rate by maintaining a constant and effective drug level in the body with undesirable side effects[1].Several approaches are currently utilized in the prolongation of the GRT, including floating drug delivery systems (FDDS), swelling and expanding systems, polymeric bioadhesive systems, high-density systems, modified-shape systems and other delayed gastric emptying devices. In this review, current & recent developments of Stomach Specific FDDS are discussed.

Keywords: Floating drug delivery systems, Sustained action, Swelling, Bioadhesive.

Introduction

Controlled Drug Delivery Systems

Controlled drug delivery systems have been developed to control the rate of drug delivery, sustaining the duration of therapeutic activity or targeting the delivery of drug to a tissue. Controlled drug delivery or modified drug delivery systems are conveniently divided into four categories.

1. Delayed release
2. Sustained release
3. Site-specific targeting
4. Receptor targeting

More precisely, controlled delivery can be defined as

1) A sustained drug action at a predetermined rate by maintaining a relatively constant, effective drug level in the body with concomitant minimization of undesirable side effects.
2) Localized drug action by spatial placement of a controlled release system adjacent to or in the diseased tissue.
3) Targeted drug action by using carriers or chemical derivatives to deliver drug to a particular target cell .
4) Provide a physiologically / therapeutically based drug release system. In other words, the amount and the rate of drug release are determined by the physiological/ therapeutic needs of the body.

A controlled drug delivery system is usually designed to deliver the drug at particular rate. Safe and effective blood levels are maintained for a period as long as the system continues to deliver the drug. This predetermined rate of drug release is based on the desired therapeutic concentration and the drug's pharmacokinetics.

Advantages of Controlled Drug Delivery Systems

1. Overcome patient compliance problems.
2. Employ less drug
   a) Minimize or eliminate local side effects
   b) Minimize or eliminate systemic side effects
   c) Obtain less potentiation or reduction in drug activity with chronic use.
   d) Minimize drug accumulation with chronic dosing.
3. Improve efficiency in treatment
   a) Cures or controls condition more promptly.
   b) Improves control of condition i.e., reduced fluctuation in drug level.
   c) Improves bioavailability of some drugs.
   d) Make use of special effects, e.g. Sustained-release aspirin for morning relief of arthritis by dosing before bedtime.
4. Economy i.e. reduction in health care costs. The average cost of treatment over an extended time period may be less, with lesser frequency of dosing, enhanced therapeutic benefits and reduced side effects. The time required for health care personnel to dispense and administer the drug and monitor patient is also reduced.

Disadvantages

1) Decreased systemic availability in comparison to immediate release conventional dosage forms, which may be due to incomplete release, increased first-pass metabolism, increased instability, insufficient residence time for complete release, site specific absorption, pH dependent stability etc.
2) Poor in vitro – in vivo correlation.
3) Retrieval of drug is difficult in case of toxicity, poisoning or hypersensitivity reactions.
4) Reduced potential for dose adjustment of drugs normally administered in varying strengths.

Gastro Retentive Drug Delivery Devices

These are primarily controlled release drug delivery systems, which gets retained for longer period of time in stomach, thus helping in absorption of drug for the intended duration of time, which in turn improves bioavailability by reducing drug wastage, and improving solubility of drugs that are less soluble at high pH environment . It also helps in achieving local delivery of drug in the stomach and proximal small intestine. G.R.D.D devices can be useful for the spatial and temporal delivery of many drugs. Floating systems are one of the important categories of drug delivery systems with gastric retentive behavior[2]. Drugs which take advantage of gastric retention include: furosemide, allopurinol ciprofloxacin and metformin.

The most commonly used polymers in gastro retentive drug delivery systems include HPMC, polyacrylate polymers, polyvinyl acetate, Carbopol, agar, sodium alginate, calcium chloride, polyethylene oxide and polycarbonates[3].

Many drugs categorized as once a day delivery have demonstrated to have sub optimal absorption due to dependence on transit time of the dosage form. A system designed for longer gastric retention will extend all the time with in which drug absorption can occur in small intestine. So it has been suggested that compounding the drugs with narrow absorption window in a unique dosage form prolongs gastric residence time and would enable an extended absorption phase of these drugs[4].

Ideal candidates for gastro retentive drug delivery systems:

- Drug which act locally in the stomach.
- Drugs which get primarily absorbed in the stomach.
- Drugs which are poorly soluble at alkaline pH.
- Drugs with a narrow therapeutic window of absorption.
- Drugs which are absorbed rapidly from GI tract.
- Drugs that degrade in the colon.

There are certain situations where gastric retention is not advisable. They are

1. Aspirin and other non-steroidal anti-inflammatory drugs are known to cause gastric lesions, and slow release of such drugs in the stomach may irritate the stomach lining

2. Drugs which are unstable in the acidic environment should not be formulated into G.R.D.D.S.

3.Other drugs, such as isosorbide dinitrate, that are absorbed equally well throughout the GI tract will not benefit from using gastric retentive devices[5].

Approaches to Gastric Retention[6]

i) Mucoadhesive or bioadhesive systems

These system permit a given dosage form to be incorporated with bioadhesive agent or mucoadhesive agents making the device to get adhered to the stomach walls, thus resisting gastric emptying.But it may result in unpredictable adherence as the mucus on the walls of the stomach is in a state of constant renewal.

ii) Floating drug delivery systems (FDDS)

The floating drug delivery systems float in the stomach after its administration. These systems are based on the following mechanisms:

➢ Hydrodynamically balanced systems (HBS):-

These are single-unit dosage forms, containing one or more gel-forming hydrophilic polymers such as Hydroxypropyl methylcellulose (HPMC) although hydroxy ethyl cellulose (HEC), hydroxyl propyl cellulose (HPC), sodium carboxy methylcellulose

(NaCMC), agar, or alginic acid . The polymer is being mixed with the drug and usually administered in a gelatin capsule. The capsule gets rapidly dissolved in the gastric fluid, producing a floating mass. Drug release is getting controlled by the formation of a boundary at the surface. Continuous erosion of the surface allows water to get penetrated into the inner layers, maintaining surface hydration and helping in its buoyancy. Incorporation of fatty materials gives low-density formulations and reduced penetration of water thus reducing the erosion quickly.

➢ **Low density systems: -**

They have a bulk density lower than that of G.I fluids and so they remain buoyant in the stomach without affecting the gastric emptying rate for a longer period of time. They are other wise called as micro balloons. While the system is floating on the gastric contents, the drug gets released slowly at a desired rate from the stomach. After the drug release, the residual system is emptied from the stomach. Which results in an increase in the gastric retention and a better control of fluctuations in the plasma drug concentration.

➢ **Raft forming systems: -**

These have a carbonate compound which upon reaction with gastric acid in the stomach form bubbles and make the device to float. Here a gel-forming solution swells forming a viscous cohesive gel that contains entrapped carbon dioxide bubbles when they come in contact with the gastric fluid. Formulations can contain antacids such as aluminium hydroxide or calcium carbonate to reduce gastric acidity. These systems produce a layer on the top of gastric fluids.

➢ **Effervescent system or gas forming systems: -**

Gas generating materials such as sodium bicarbonate, calcium bicarbonate etc are incorporated which upon reaction with G.I fluids evolve $C0_2$ gas which makes them to float. The buoyancy of the tablet is prolonged for 8-10 hours. The most commonly used excipients in the development of effervescent systems are swellable polymers such as HPMC, polysaccharides and effervescent mixtures,(e.g. Sodium bicarbonate or calcium carbonate and tartaric acid or citric acid). The tablets are so prepared that when they come in contact with the stomach, $C0_2$ is liberated by the acidity of the gastric contents in the stomach and is entrapped in the gellified hydrocolloid matrix , which creates an upward movement of the dose and maintains buoyancy. A decrease in the specific gravity makes the dosage form to float on the chyme. The $C0_2$ generating components are mixed within the tablets matrix containing hydrophilic swellable polymer alone or in combination, in each case a single layer tablet may be produced or even a bilayer tablet may be produced .

iii) High density systems

Gastric contents in the G.I.T have density close to that of water. When the patient is upright high-density tablets sink to bottom of the stomach and they get entrapped in the folds of the antrum and able to withstand the peristaltic waves of the stomach .

iv) Magnetic systems

This system is based on a simple idea that the dosage form contains a small internal magnet, and a magnet is placed on the abdomen over the position of the stomach. Although these systems seem to work, the external magnet must be positioned with a degree of precision that might compromise patient compliance.

v) Superporous hydrogels

Although these are swellable systems they differ sufficiently from the conventional types to warrant separate classification, with pore size ranging 10nm-10µm.Absorption of water by conventional hydrogel is a very slow process and several hours may be needed to reach an equilibrium state and during which premature evacuation of the dosage form may occur. Superporous hydrogels having an average pore size of greater than 100µm, swell to equilibrium size with in a minute, due to rapid water uptake by capillary wetting through numerous inter-connected open pores and they swell to a larger size and are intended to have sufficient mechanical strength to withstand pressure by gastric contraction. This is achieved by co-formulation of a hydrophilic particulate material.

Advantages of GRDF's[7]

- Enhanced bioavailability of drugs which are mainly absorbed from the upper part of the gastro Intestinal system.
- Useful for local treatment in case of stomach ulcers and lesions.
- Improving patient compliance by reducing dose.
- Enhanced therapeutic efficacy.
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LIMITATIONS

1. The main disadvantage of floating drug delivery system is requirement of a sufficient level of fluids in the stomach for the drug to float. However this can be overcome by coating the tablet with the help of bioadhesive polymers that easily stick to the mucosal lining of the stomach
2. Floating systems are not feasible for those drugs that have solubility or stability problems in gastric fluids. Drugs such as Nifedipine, which is well absorbed along the entire GI tract
3. Drugs that are unstable and destroyed in the gastric environment are poor candidates for FDDS.
4. Drugs that are irritant to the gastric mucosa or induce gastric lesions are not good candidates for FDDS

5. Drugs that are absorbed throughout the gastro intestinal tract should be discarded for FDDS as prolonging the GRT of such drugs appears to offer no advantage in terms of bioavailability.
6. Poorly acid soluble drugs may show dissolution problem in gastric fluid and consequently may not be released to a sufficient extent. It might, therefore be advisable not to exploit FDDS with these drugs.
7. Finally, for the selective delivery of a few drugs in the colon i.e., Corticosteroids, 5-aminosalicylic acid, prolonging the GRT though FDDS may prove inferior to other specifically designed oral colonic drug delivery

EVALUATION PARAMETERS OF STOMACH SPECIFIC FDDS[8]

Weight variation:

Uniformity of Weight according to Indian pharmacopoeia, 20 tablets were selected at random, weight together and individually for the determination of weight of tablets. The mean and standard deviations were calculated.

Hardness

Hardness or tablet crushing strength (fc), the force required to break a tablet in a diametric

Compression was measured using Monsanto tablet hardness tester. It is expressed in kg/cm2.

Thickness:

Thickness and diameter of ten tablets were measured using vernier calipers.

Friability

Friability The friability test was carried out in Roch Friabilator. Ten tablets were weighted (Wo)

initially and put in a rotating drum. Then the tablets were subjected to 100 falls of 6 in. height.

After completion of rotation, the tablets were again weighted (W).

$$\% \text{ Weight loss or friability (f)} = (1 - w/ w0) \times 100$$

Disintegration time

In vitro disintegration time was determined using disintegration test apparatus. For this, a tablet was placed in each of the six tubes of the apparatus and one disc was added to each tube. The time taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured.

Buoyancy time

A tablet was introduces in to beaker containing 100ml of 0.1N HCL. The time taken by the tablet to come up to the surface and floated was taken as the buoyancy time. An average of threedeterminations from of batch was taken for the floating forms.

Floating time and dissolution:

The test for floating time measurement is usually performed in stimulated gastric fluid or 0.1 mole.lit-1 HCl maintained at 37^0 C. It is determined by using USP dissolution apparatus containing 900 ml of 0.1 mole.lit-1 HCl as the dissolution medium at 37 ⁰C. The time taken by the dosage form to float is termed as floating lag time and the time for which the dosage form floats is termed as the floating or flotation time.[9]

Drug release:

Dissolution tests are performed using the dissolution apparatus. Samples are withdrawn periodically from the dissolution medium with replacement and then analyzed for their drug content after an appropriate dilution.

Content uniformity

The drug content in each formulation was determined by triturating 20 tablets and powder equivalent to average weight was added in 100ml of solvent, followed by stirring for 30 minutes.

The solution was filtered through a 0.45µ membrane filter, diluted suitably and the absorbance of resultant solution was measured spectrophotometrically in UV[10].

CONCLUSION

Drug absorption in the GIT is a highly variable procedure prolonging gastric retention of the drug and thus extends the time for drug absorption. Floating drug delivery system promises to be a potential approach for drug gastro retention. Although there are lot of difficulties to be worked out to achieve prolonged gastric retention, a large number of companies are focusing toward commercializing this technique.

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