Review Article

REVIEW ARTICLE ON MULTIPARTICULATE DRUG DELIVERY SYSTEM

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ABSTRACT

Multiparticulate drug delivery system are the drug delivery system which delivery the drug in a oral route. Multiparticulate drug delivery system consisting of descrete units of small particles and each exhibit different characteristic. Multiparticulate drug delivery systems are especially suitable for achieving controlled and delayed release oral formulations with minimize the dose dumping. Oral multiparticulate drug delivery systems shows biopharmaceutical advantages because it shows predictable distribution and transportation in the gastro-intestinal tract. Multiparticulate drug delivery system usefull in order to delivery a drug at a particular site.

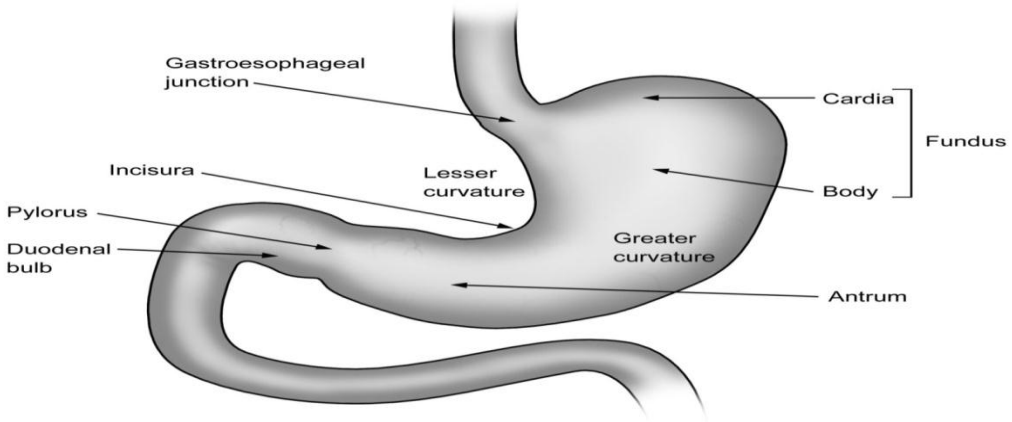
Key Words: Multiparticulate drug delivery, Dose dumping.

INTRODUCTION

Orally controlled drug delivery systems can be classified in to two extensive group, single unit dosage forms & multiple unit dosage forms. Novel drug delivery system have a lot of advantantages it improve the safety and efficacy of the drug by formulating a particular dosage form, for a particular route of administration . Oral route is one of the best route for a drug administration. In oral route the self administration of drug is possible, in this route drug is directly reaches the systemic circulation. There are lot of advancements have been observed in oral controlled drug delivery system.The modification of the GIT transit time is one of the high challenges in the delivery of drug by oral controlled delivery system.[3] Current process explaining that single and multiparticulate drug delivery systems they are actualy suitable for achieving controlled or delayed release oral formulations with risk of low dose dumping, Releasing of drug at a different pattern and it shows different gastric emptying time. Although floating drug delivery contains single unit floating dosage as well as multiple unit dosage forms[1, 2].

These single unit dosage release all drugs at a time or it shows gastric emptying process so it explains the disadvantage of single unit dosage forms.While the multiparticulate system the drug passes through the GIT and it avaids the gastric emptying process, release of drug shows uniformity. The uniform distribution of drug in a multiple unit dosage form along with GIT it shows reproducible in a drug absorption and explain less risk in a local irritation.[4]

PHYSIOLOGY OF STOMACH



Stomach is a J-shaped structure. Stomach receives food from the esophagus, the stomach secretes acid and enzymes that digest food.
Stomach secretes 3 substances like

1. Hydrochloric acid (HCl): It provides acidic medium in the stomach as well as helps to kill pathogens and digestion of proteins. Protien breakdown by the pepsin etc.
2. Mucus: protects stomach from its own digestive secretions.
3. Pepsin: protein digestive enzyme.

The structure of stomach anatomically the divided into 3 main parts

a. Fundus,
b. Body,
c. Antrum (pylorus).
    - Stomach contains proximal part these part made up of fundus and body it helps store undigested material.
    - Antrum is the important site for digestion and act as a pump for gastric emptying by propelling actions.[5]

Drug Release Mechanism from Multiparticulate DDS

1. Diffusion: Diffusion is a process in which they contact with aqueous fluids in the gastrointestinal tract (GIT), water diffuses into the inner side of the particle. In the Drug dissolution process occurs and the drug solutions disperse and release the content across the release coat to the external surface.

2. Erosion: Erosion process the coating of the drug required to erode the particle gradually at a time.

3. Osmosis: Osmosis is allowing water molecule to enter under the proper circumstances, an osmotic pressure is produces it can be built up within the inside of the particle. The drug is forced out of the particle into the external surface through the coating.[6]

Advantages of floating multiparticulate drug delivery system.

1. Better patient compliance by lesser dosing frequency.
2. Bioavailability increases without effected by first pass effect because change in plasma drug concentration is avoided, a necessary plasma drug concentration is maintained by continuous drug release.
3. Gastric retention time is increased because of buoyancy.
4. Absorption of drugs which solubilise only in stomach
5. Release of drug in a controlled manner for long period.
6. Particular Site-specific drug delivery to stomach can be achieved.
7. Avoidance of gastric irritation, because of sustained release effect.
8. Better therapeutic effect of short half-life drugs can be achieved.

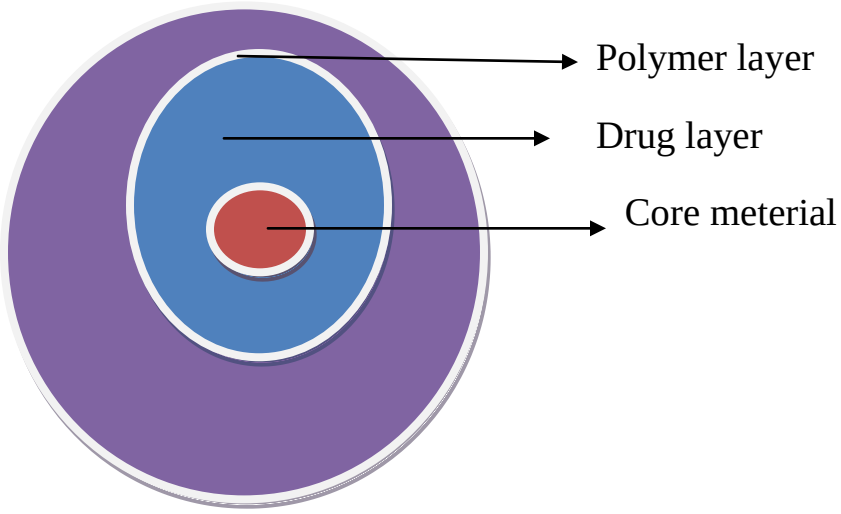
Limitations of floating multiparticulate drug delivery systems.

1. The residence time in the stomach depends upon the digestive state. Hence, floating multiparticulate drug delivery systems should be administered after the meal.
2. The ability to float relies in the hydration state of the dosage form. In order to keep this microsphere floating in-vivo, intermittent administration of water (a tumbler full, every 2 hours) is beneficial.
3. The ability of drug to remain in the stomach depends upon the subject being positioned upright.
4. Floating multiparticulate drug delivery systems are not suitable for the drugs that have solubility or stability problems in the gastric fluid.
5. Drug like Nifedipine, which is well absorbed along the entire GIT and which undergoes significant first pass metabolism, may not be a desirable candidate for floating multiparticulates drug delivery systems since the slow gastric emptying may lead to the reduced systemic bioavailability.[7]

Floating multiparticulate drug delivery system having two approach

1. Noneffervescent Approach
2. Effervescent approach.

Hollow microspheres are spherical empty particles, they donot having any core. This type of microspheres are likely free flowing powders contains proteins or synthetic polymers. These drug delivery systems are mainly oral dosage forms. In these systems, the dosage of the drug substances is divided on a plurality of subunit, typically consisting of number of spherical particles with diameter of 0.05-2.00mm.[4]



1. Effervescent Systems

A. Volatile liquid containing systems

This type of drug delivery system can be sustained because of it absorb an inflatable chamber, which contains a liquid e.g. ether or cyclopentane, these cyclopentane or ether gasifies at body temperature to form a inflatation chamber in the stomach. The device also contain of a bioerodible plug made up of PVA, Polyethylene, etc. It can gradually dissolves and form a inflatable chamber to release gas and collapse after a particular time to permit the spontaneous ejection of the inflatable systems from the stomach.8

B. Gas-generating Systems

These floating drug delivery systems shows effervescent reactions between carbonate/bicarbonate salts and citric/tartaric acid to liberate CO2, which gets entrapped the hydrocolloid layer of the systems so that's why it decreasing its specific gravity and so it making float over chyme. These systems are the matrix types of drug delivery systems formulated with a swellable polymer like ethylcellulose, methylcellulose and various effervescent compounds .Eg tartaric acid,sodium bicarbonate, citric acid. These effervescent type drug delivery systems formulated in a drug when it contact with the acidic gastric contents, CO2 is gets liberated and it will entrapped in swollen hydrocolloids, which provides buoyancy to the dosage forms. 8

2. NON-EFFERVESCENT SYSTEMS

Hollow microspheres are most popular methods of floating drug delivery systems. They are having lot of advantages like multiple unit system as well as better floating properties, because of central hollow space inside the microspheres. The some techniques involved in their preparation include simple solvent evaporation, solvent diffusion and evaporation. In this method the drug release and better floating properties mainly depends on the type of polymer, plasticizer and the solvents used in a preparation. Polymers such as HPMC K4M, HPMCK15, Ethylcellulose methylcellulose etc.9

1. **Alginate beads**:
   Floating alginate beads are formulated by using drug and different polymers. Spherical beads are formed of approximately 2.5 mm in diameter can be prepared by dropping sodium alginate solution

in to aqueous solutions of anhydrous calcium chloride, causing precipitation of calcium alginate. The beads are then separated by filtering a beads and kept for drying.10

2. **Colloidal gel barrier systems :**
This system contains drug with gel-forming agents so that's why they remain buoyant on the stomach content. This results prolong GRT and increasing amount of drug that reaches its absorbtion sites in the solution and it will be ready for absorption. In this system they incorporate highly gel forming agents like hydroxyl propyl cellulose, hydroxyl propyl methyl cellulose(HPMC), hydroxyl ethylcellulose, polysacharides and matrix-forming polymer such as polycarbophil, polyacrylate and polystyrene. they come in contact with coming in gastric fluid, the hydrocolloid in the system hydrates and forms a colloid gel barrier around its surface.11

3. **Microporous compartment system :**
In microporous compartment system it is based on the enclosing of drug reservoir inside a microporous compartment with opening its top and bottom. The contents of the drug Flotation chamber containing accidental air that causes the delivery drug and contents float in the gastric fluid. Gastric fluid enters through the hole, dissolves the drug particles continuous transport across the intestine for drug absorption wall. The surrounding walls of the drug reservoir compartment are completely sealed and it prevent direct contact of the gastric mucosal surface with the undissolved drug. In stomach floating chamber containing entrappedaor that helps content float over in a chamber.**12**

4. **Hollow microsphers:**
Hollow microspheres (microballoons), they loaded with drug in their outer most shells, they are the spherical empty particles without core. They prepared by protiens and synthetic polymer were prepared by solvent diffusion method. The ethanol:dichloromethane solution of the drug and an enteric acrylic polymer these are poured into an agitated aqueous solution of PVA that was maintained temp at 40°C. The gas phase generated droplet by the evaporation of dichloromethane formed microspherical particles containing drug.**13.**

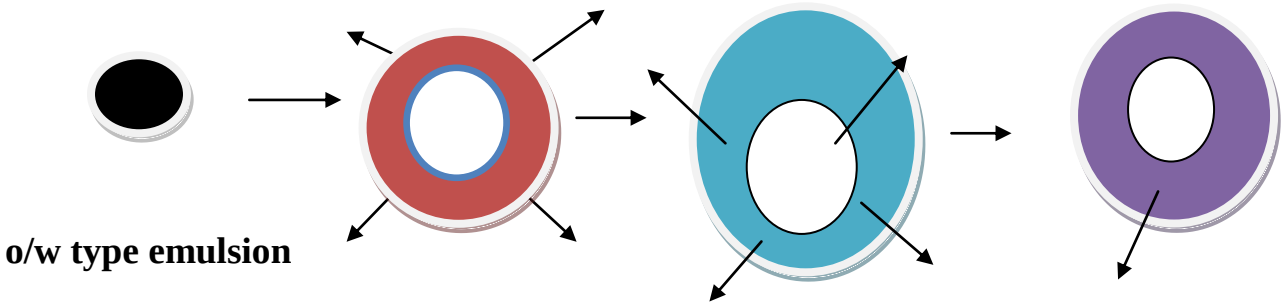


Diagram of hollow microspheres

METHODS OF PREPARATION

1. **Solvent Evaporation Method :**
Floating multiparticulate dosage form can be prepared by solvent evapouration or solvent diffusion methods. It creates the hollow space in a inner core. The polymer is dissolved in an organic solvent. Then drug is either dissolved or dispersed in the polymer solution. The solution containing the drug is then emulsified into an aqueous phase containing suitable additive (surfactants / polymer) to form oil in water emulsion. After the formation of a stable emulsion, the

organic solvent is evaporated either by increasing the temperature under pressure or by continuous stirring. The solvent removal leads to polymer precipitation at the oil/water interface of droplets, forming cavity and thus making them hollow to impart the floating properties. The polymers studied for the development of such systems include cellulose acetate, chitosan, eudragit, Acrycoat, Methocil, polyacrylates, polyvinyl acetate, carbopol, agar, polyethylene oxide and polycarbonate. [14]

2. **Ionotropic gelation method :**
Ionotropic gelation method the cross linking of presence polyelectrolyte in a counterions takes place. The use of polymers like alginates, gellan gum, chitosan, helps to enclose of drugs. This method widely used for the multiparticulate drug delivery system. Coating of drugs also helps to release of drug because of it contain an ions in their structure. acts as release rate retardants contains certain anions on their chemical structure. Anions helps to form a meshwork like strucute. These anions combing with cations and forms a geltation by being a anion blocks.The prepared solution loaded with drug and polymer into the aqueous solution the cations produces hydrogel beads. The ions containg cat ions also, these cations diffuses into the drug-loaded polymeric drops, forms a structure like three dimensional moiety. [15]

CONCLUSION

Multiparticulate drug delivery having several advantages including greater Plasticity and adaptability. These systems are also useful for drugs, which are poorly soluble or unstable in intestinal fluids.Floating systems also helps for the drug retain in a stomach for longer period of time. Floating microspheres have been showing high potential for gastroretention and provide an efficient means of enhancing bioavailability and controlling the release of many drugs in GIT.

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