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FLOATING DRUG DELIVERY SYSTEMS - A REVIEW

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ABSTRACT

Floating drug delivery systems (FDDS) mainly depends on the principle of floatation. The recent developments of FDDS including physicochemical properties and mechanism are explained in detail. When compared with the other conventional dosage forms, floating drug delivery system shows effective therapeutic activities. The different methodologies such as effervescent and non-effervescent systems are introduced based on the parameter density. The novel methodologies in FDDS includes such as single dose and multi dosing system. This review also involves in giving information about in-vitro and in-vivo dissolution studies. Floating dosage forms can be delivered in conventional forms like tablets, capsules with the addition of suitable ingredients along with the gas generating agent. Floating drug delivery system improves the drug bio-availability and patient compliance by enhancing the gastric retention time and controlling drug release. In recent years there are several technologies were to develop to overcome the barriers like short gastric retention time and unpredictable gastric emptying time. In this review, we discussed about novel technologies and developments regarding floating drug delivery system.

INTRODUCTION

Floating drug delivery systems elucidate that the systems have less density, have a high property of buoyancy to float the drug on the gastric fluids present in stomach and help in maintain the drug for longer duration of action.[1] The system was first introduced by DAVIS in 1968. They are less-density systems with Floating buoyancy to float on the gastric fluids for longer period of time.[2] The drugs which shows shorter biological half-life, they can be

sustained by floating drug delivery system and their efficacy can be increased and help in decreasing the dosing frequency. This system was used to improve patient compliance nature and to shows effective.

This system is measured to increase the duration of the dosage form. Drugs that having effective solubility in the acidic media shows poor bioavailability pharmacological activity.

Gastric motility[3,4]

It is controlled by a set of neural and hormonal signals. Nerve control originates from the parasympathetic and sympathetic systems. The bottom line is that the patterns of gastric motility Gastric emptying task. It is controlled by a complex set of neural and hormonal signals. Nervous control likely are a result from smooth muscle cells integrating a large number of inhibitory and stimulatory signals. Liquid readily passes through the pylorus in spurts, but solids must be reduced to a diameter of less than 1-2 mm before passing pyloric gatekeeper.

Gastric empty rate

It takes place at the time of fasting and fed states. This occurs at 2 phases. During fasting state an inter-digestive phase of electrical events take occurs, which cycle both through stomach and intestine every 2 to 3 hours. This is known as inter-digestive myo-electric cycle or migrating myo-electric cycle (MMC).

Phase I (Basal phase): takes place from 40-60 minutes with less number of contractions.

Phase II (Pre-burst phase): takes place from 40 - 60 minutes with some contractions. At this phase the intensity and frequency also gradually increases.

Phase III (burst phase): takes place from 4 -6 minutes. It involves regular contractions for shorter period of time. It is also called as the housekeeper wave.

Phase IV: It takes place from 0 -5 minutes and happens between phases III and I of 2 consecutive cycles.[4]

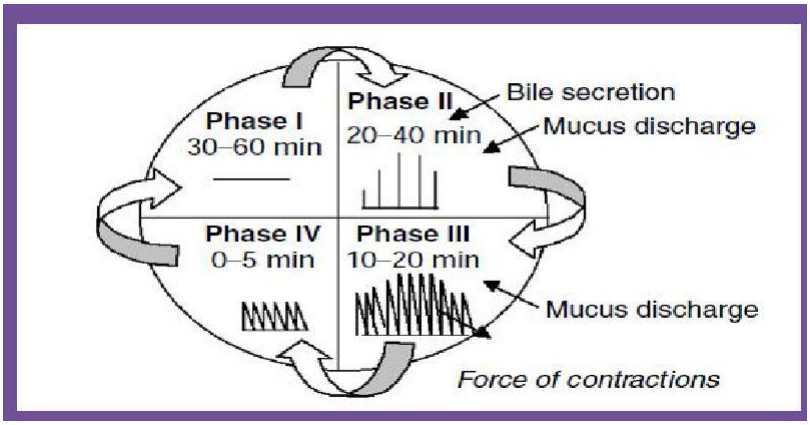

Fig 1: Motility pattern in GI.

Advantages[5]

- Increased bioavailability
- Less dosing frequency
- Target drug delivery
- Proper receptor activation
- Less side effects

Disadvantages[5]

- Un-stability of drug in acidic media
- Require high amount of gastric fluid in the stomach to float drug
- Irritation of mucous membrane

Factors affecting gastric retention[6,7,8,9]

There several factors effecting the gastric retention time of dosage form. They effects the efficacy of gastric retention time. They are

- **Density** –The buoyancy of the dosage form is mainly depend on the density
- **Size** –The diameter of the dosage form not more then 9.55mm.
- **Shape of dosage form** – Tetrahedron and ring-shaped devices are showing better GRT.
- **Fed or unfed state** – The GI motility shows motor activity under fasting conditions takes place at 1.5-2 hrs.
- **Nature of meal** – The indigestible polymers or fatty acids decreases the gastric emptying rate.
- **Caloric content** -The proteins and fats increased with meal for 4-10 hrs by increasing the GRT.

- **Frequency of feed** – Due to the low frequency of MMC by successive meals over 400 mins the GRT increases.
- **Gender** –Based on the weight, height and body surface the GRT in males is less when compared with females.
- **Age** –The age over 70 years people has higher GRT.
- **Posture**-Based on the posture the GRT varies between one patient to another.
- **Concomitant drug administration**– Anti-cholinergics, opioids and pro-kinetic agents can decrease the gastric emptying time.
- **Biological factors** – The patients suffering with diabetes and Crohn's disease will have lesser GRT.

Need for controlled release gastro retentive drug delivery

The GRDF dosage form will show a novel and important therapeutic actions such as-

1. It shows effective action on slightly soluble and insoluble drugs. It is also termed as the solubility of the drug decreases, then the drug dissolution time becomes less and thus, the transit time becomes a factor of drug absorption.
2. To control this problem, effective, gastro-retentive dosage forms have been identified that provide continuous, controlled administration of slightly soluble drugs at the absorption site.

- The GRDFs improves the pharmacotherapy of the stomach through drug release, it leads to enhance the drug concentration at gastric mucosa.
- GRDFs can also be used as carriers for drugs are known as absorption windows.

CLASSIFICATION OF FLOATING DRUG DELIVERY SYSTEM[11,12, 13]

A. Single Unit Floating Dosage Systems

a) Effervescent Systems (Gas-generating Systems)

b) Non-effervescent Systems

B. Multiple Unit Floating Dosage System

a) Effervescent Systems (Gas-generating Systems)

b) Non-effervescent Systems

c) Hollow Microspheres

C. Raft Forming System

A. Single Unit Floating Dosage Systems: Single unit dosage forms are easy to produce, due to their smaller size they are easily float on the surface. Larger volume dosage forms are causing discomfort and decreases the bioavailability.

a) Effervescent Systems (Gas-generating Systems)

These systems are prepared by using polymers such as chitosan and methylcellulose, as well as several effervescent components such as sodium bicarbonate, citric acid and tartaric acid. Then CO2 is produced when it comes into contact with acidic gastric contents and becomes swollen hydrocolloids, giving dose buoyancy.

b) Non-effervescent System

Polysaccharides, hydrocolloids, matrix forming agents are used to form gel forming or swelling cellulose type in non-effervescent system. This method of preparation is a simple approach to mixing the drug and the hydrocolloid-forming gel. This dosage form swells in contact with gastric fluids following oral administration and attains a bulk density of < 1. Then swollen gel-like structure formed and it acts as a reservoir and allows the gelatinous mass to sustain release of the drug.

B. Multiple Unit Floating Dosage Systems

This is an alternative system. It shows that inter and intra subject differences in drug absorption rate as well as dose dumping.

a) Effervescent Systems

A multi dose system was created, consisting of a calcium alginate core and a calcium alginate/PVA membrane discrete by an air compartment. The PVA filter out in the presence of water and enhance the membrane permeability, by preserving the air compartment integrity. The molecular weight and PVA concentration increases results in better floating properties. Due to the formation of calcium alginate, sodium alginate solution introduced drop by drop into calcium chloride solution, allows the drop surface to gel instantly. The obtained beads are freeze dried, creates a porous structure in floating.

b) Non-effervescent Systems

By the process of extrusion, a multiple dose containing indomethacin is noted as a reference drug. The acetic acid and chitosan are extruded through a blade, the extruded is cut dried the

chitosan hydrates floats on the acidic media then the drug release can be achieved by changing the drug polymer ratio.

c) Hollow Micro spheres

The hallow microspheres filled with drugs are present in the outer polymer shelf and they are prepared by using emulsion solvent diffusion method. The drug solution and polymer were poured into PVA solution at 40^0 C. The creation of the dispersed polymer droplight by evaporation of dichloromethane. The gas waves was produced by drug polymer microsphere. More than 12 hours the microspheres were floats on the surfactant of acidic solution.

C. Raft Forming System

Whenever gel forming solution and gastric fluid comes into contact with each other, it swells, forming viscous cohesive gels and bubbles of CO_2.The gastric acidity was minimised by using calcium carbonate or aluminium hydroxide in the formulation. The prepared viscous cohesive gel comes to contact with the gastric fluid, the liquid swells, forms a layer is known as raft. This raft floats on stomach environment by its less density and produces CO_2.

METHOD OF PREPARATION[15]

Solvent evaporation method

The creation of hallow inner core by solvent diffusion and evaporation methods. The polymer was dissolved in an organic solution.

The drug solution is emulsified PVA to form O/W emulsion by enhancing the temperature or continuous stirring, then the organic solvent was evaporated.

Then the solvent was removed and causes polymer to precipitate at the oil in water interface and making them hallow which allows to float.

1) Ionotropic Gelation Method

The ability of polyelectrolytes comes to contact with the counter ion causes ionotropic gelation, which forms beads. This technique was commonly used in the preparation of beads. Polyvalent cations combine with anions to form mesh like structures. The drug solution was poured into polyvalent cationic solution to form hydrogen beads.

2) Emulsion solvent diffusion method

The new emulsion was prepared by using emulsion solvent diffusion process by drug and micro-balloon.

Polymer along with the drug solution was poured into the methylene chloride solution as drop by drop, methylene chloride evaporates and creates micro particles.

Evaluations of floating drug delivery system[16-19]

Shape of tablets: Size, shape of the tablet can be dimensionally described, monitored and controlled.

Tablet dimensions and Thickness: The Thickness, diameter of the tablet is expressed in mm by using a micro-meter screw gauge or vernier calliper.

Weight variation test: 20 tablets are randomly selected from the batch and to calculate the average weight of total 20 tablets and compare with each individual tablet weight to the average weight and expressed in %. To calculate weight variation by using the formula as follows.

$$weight\ variation = \frac{Individual\ weight - Average\ weight}{Average\ weight} \times 100$$

Hardness/Crushing strength: The Force required to break a tablet called hardness (crushing strength). The resistance of the tablet chipping, abrasion or breakage under condition of storage transformation and handling before usage depends on its hardness. The Hardness test is performed by using a Monsanto or Pfizer Hardness Tester.

In-vitro dissolution study: Dissolution study is carried out by using USP type-II apparatus. The dissolution test is performed using 900 ml of the dissolution medium at 50 rpm and 37±0.5°C. A sample of 05 ml were periodically withdrawn and the sample volume was replaced with an equal volume of fresh dissolution medium to maintain sink conditions. The collected samples are analysed spectrophotometrically at the specific wavelength.

Determination of drug content in tablets:10 tablets from each batch are selected randomly and transferred to a 100 ml volumetric flask filled up with 0.1(N) HCL. Stir and keep it aside for 2 h then take 1 ml from the volumetric flask and transfer it to the test tube. Samples are then filtered, suitably diluted and analysed spectrophotometrically at a suitable wavelength.

Friability: It is used to measure the mechanical strength of tablets. Roche friabilator was used to determine the friability of the tablet. A pre weighed tablets were placed in the friabilator. Fibrillatory consist of a plastic-chamber that revolves at 25 rpm, dropping those tablets at a distance of 6 inches in each revolution. The tablets were rotated in the friabilator for at least 4 minutes. At the end of test, tablets were dusted and reweighed, the loss in the weight of tablet is the measure of friability and is expressed in percentage as.

%Friability = loss in weight / Initial weight x 100

Measurement of the density of the formulation: The apparent densities of the tablets are calculated from their volumes and masses in triplicate. volume V of the cylindrical tablets are calculated from their height h and radius r (both determined with a micrometer gauge) using the mathematical equation for a cylinder.

$$V = A \times r^2 \times h$$

Buoyancy/Floating test: The time between introduction of the dosage form and its buoyancy on the simulated gastric fluid and the time during which the dosage form remain buoyant are measured. The time taken for the dosage form to emerge on the surface of a medium called floating lag time (FLT) or buoyancy lag time (BLT) and total duration of time by which dosage form remain buoyant is called total floating time (TFT).

Swelling behaviour: The swelling behaviour of a dosage form is measured by studying its weight gain or water uptake. The dimensional changes could be measured in terms of the increase in tablet diameter and/or thickness over time. Water uptake can be measured in terms of percent weight gain, as given by the equation.

$$WU = (W_t - W_o) \times 100$$

Where, WU= Water uptake

W_t = Weight of dosage form at time t

W_o = Initial weight of dosage form

CONCLUSION

Now a days, numerous drugs have been formulated as floating drug delivery systems with the scope of sustained release, restricting the region of drug release in the stomach due to buoyant nature which achieves increased gastric residence time for the dosage form. The currently available polymer-mediated, non-effervescent and effervescent FDDS, designed on the basis of delayed gastric emptying and buoyancy principles. The floating of the system is

due to density of the dosage form that should be less than that of gastric fluid. There are several evidences are involved to prove it and the main objective of this system is to improve the bioavailability of the dosage form. So, it causes prolonged action from a drug with a short half-life.

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