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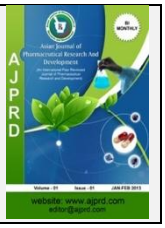

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Review Article

An Overview of Floating Tablet

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A B S T R A C T

Flash nanoprecipitation (FNP) is a widely used technique for preparing particulate carriers based on various polymers that has been shown to be a promising technology for the industrial production of drug-loaded nanoparticles. The use of amphiphilic block copolymers as a stabilizer to protect the nanoparticles from aggregation makes flash nanoprecipitation (FNP) an ideal method for rapidly preparing nanosized drug particles with high drug-loading efficiency. Flash nanoprecipitation (FNP) is a controlled antisolvent precipitation process that has been shown to be effective for producing drug nanoparticles with a defined mean particle size and narrow particle size distribution. However, the physical instability of the generated nanoparticles remains a significant barrier to the use of this technology in pharmaceutical formulation. This review discusses the use of FNP to create poorly water-soluble drug nanoparticles using controllable mixing devices such as confined impinging jets mixers (CIJM), multi-inlet vortex mixers (MIVM), and a variety of other microfluidic mixer systems. The mechanisms and processes of drug nanoparticle formation by FNP are described in detail. Then, during the FNP process, the supersaturation level and mixing rate are controlled to tailor the ultrafine drug nanoparticles, as well as the influence of drugs, solvent, anti-solvent, and stabilizers. The control of supersaturation level and mixing rate during the FNP process to tailor ultrafine drug nanoparticles is discussed, as well as the influence of drugs, solvent, anti-solvent, stabilizers, and temperature on fabrication.

Keyword: Flash Nanoprecipitation, Multi-Inlet Vortex Mixers, Nanoparticles

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INTRODUCTION

Floating drug delivery systems or hydrodynamically controlled systems are low-density systems that remain buoyant over the gastric contents without disturbing the gastric emptying rate for a prolonged period.[1] These are useful for drugs that are poorly soluble or unstable in intestinal fluids. When the system is floating on the gastric contents, the drug is released at a controlled rate from the system and is emptied from the stomach after the release of the drug results in an improved gastric retention time had control of the fluctuations in plasma drug concentration, achieve greater therapeutic benefit of the drug substance. For example, drugs that are absorbed in the proximal part of the GIT and drugs that are poorly soluble in or degraded by the alkaline pH may benefit from prolonged gastric retention. In addition, for local and sustained delivery of drug to the stomach and proximal small intestine is used to treat certain conditions, prolonged gastric retention of the therapeutic moiety may offer numerous advantages including improved bioavailability and therapeutic efficacy and possible reduction of dose size.[2] Minimum gastric content is needed for proper attainment of the floating. A minimum floating force (F) is also required to keep the dosage form buoyant on the surface of the meal. To measure the floating force, a novel apparatus for the determination of resultant weight was used which operates by measuring continuously the force equivalent to F (as a function of time required) required to maintain the submerged object. The object floats better if F is on the higher positive side. Oral controlled-release dosage forms have been developed over the past three decades due to their considerable therapeutic advantages such as:

1. Easily administrations.
2. Low cost of therapy.
3. Patient compliance and flexibility in formulation

The ultimate goal of any drug delivery is Effective disease disorder management, minimum side effects, and greater patient compliance in acost-effective manner. More than 50% of the drug delivery systems available in the market are oral drug delivery systems.[3] Controlled release drug delivery Systems (CRDDS) provide drug release at a predetermined, predictable and controlled rate. Controlled release drug delivery system is capable of achieving benefits like maintenance of optimum Therapeutic drug concentration in blood with predictable and reproducible release rates for an extended period, enhancement of the activity of duration for short half-life drugs, elimination of side effects, reduction frequency of dosing and wastage of drugs, optimized therapy and better patient compliances. The controlled gastric retention of solid dosage forms may be achieved by mucoadhesive systems that causebio-adhesion to stomach mucosa, floating systems, swelling and expanding systems, modified-shape systems, high-density systems, and other delayed gastric emptying devices. Gastro retentive dosage form can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs. Prolonged gastric retention improves bioavailability, reduces drug waste, and improves the solubility of drugs that are less soluble in a high pH environment. Gastro retention helps to provide better availability of new products with suitable therapeutic activity and substantial benefits for patients.[4]

Advantages of Floating Drug Delivery System: [5]

- It is very useful for drugs that are particularly absorbed from the stomach or the proximal part of the small intestine, e.g., Riboflavin and Furosemide
- It minimizes the fluctuations in plasma drug concentration and prevents concentration-dependent adverse effects associated with peak concentrations of drugs found useful for drugs with a narrow therapeutic index
- It is advantageous for drugs with poor bioavailability because of site-specific absorption from the upper part of the GIT thereby maximizing their absorption.
- It is useful for drugs with short half-life to get an appreciable therapeutic activity
- Enhancement of the bioavailability for drugs that can metabolized in the upper GIT
- It is used to overcome the adversities of gastric retention time as well as the gastric emptying time The duration of treatment through a single dose is efficient and releases the drug over an extended period.

A disadvantage of floating tablet:[6]

- It is not feasible for those drugs that suffer from solubility or stability problems in the GI tract.
- It requires a high level of gastric fluid in the stomach for drug delivery to float and work efficiently in fluid. However, this limitation can be overcome by coating the dosage form with the help of bioadhesive polymers that easily adhere to the mucosal lining of the stomach
- GRT is influenced by many factors like gastric motility, pH, and the presence of food which are never constant and could not predict the buoyancy
- It offers high variability in gastric emptying time
- The dosage form should be administered with a minimum of glass full of water (200-250 ml)
- The drugs, which are absorbed throughout GIT, undergo first-pass metabolism (Nifedipine, Propranolol, etc.), are not a desirable candidate
- The ability of a drug to remain in the stomach depends upon the subject being positioned upright.

CLASSIFICATION OF FLOATING TABLET:[9]

Non-effervescent system: The non-effervescent FDDS is based on the polymer's swelling mechanism or bioadhesion to the GI tract's mucosal layer. In non-effervescent FDDS, gel-forming or highly swellable cellulose-type hydrocolloids, polysaccharides, matrix-forming materials including polycarbonate, polyacrylate, polymethacrylate, and polystyrene, as well as bio-adhesive polymers like chitosan and carbopol, are the most often employed excipients.

Effervescent system: Gas-producing agents, such as sodium bicarbonate, and other organic acids, such as citric and tartaric acid, included in the formulation, are used in effervescent systems to create carbon dioxide (CO2) gas, which lowers the system's density and causes it to float on the stomach contents. Alternatively, a matrix containing a percentage of liquid can be included to generate gas that evaporates at body temperature.

Colloidal Gel Barrier System: Sheth and Tossounian were the ones who initially created a hydrodynamically balanced system. Gel-forming hydrocolloids help them stay buoyant in the stomach, which improves GRT and increases the quantity of medication at the absorption site. This technique uses a variety of gel-forming agents, including matrix-forming polymers like polystyrene and polycarbophil, as well as highly soluble cellulose-type hydrocolloids like hydroxyethyl, hydroxypropyl, and hydroxypropyl methylcellulose**.**

Bilayer floating tablet: A bilayer tablet contains two layers immediate release layer which releasesthe initial dose from the system while the other sustained release layer absorbs gastric fluid, forming an impermeable colloidal gel barrier on its surface, and maintaining a bulk density of less than unity and thereby it remains buoyant in the stomach.

Micro porous Compartment System: In this inside the micro porous compartment which has pores in the top and bottom walls contains an encapsulated drug reservoir. In the drug reservoir peripheral walls are completely sealed due to this sealing direct contact of the undissolved drug with the gastric surface is prevented. Entrapped air in the floating chamber stimulates the system to float over gastric content. Through an aperture, the gastric fluid enters which dissolves the drug for absorption across the intestine.

Volatile liquid-containing systems:It is possible to include an inflatable chamber filled with fluids to offer a medication delivery device with sustained gastric retention. This system contains liquids like cyclopentane and ether, which gasify at body temperature and cause the stomach chamber to expand. They are made up of osmotically regulated floating structures called hollow deformable units. The system is split into two halves. There is a

medicine in the first compartment and a volatile liquid in the second.

Raft forming systems: Raft forming systems have received much attention for the delivery of antacids and drug delivery for gastrointestinal infections and disorders. The basic mechanism involved in the raft formation includes the formation of viscous cohesive gel in contact with gastric fluids, wherein each portion of the liquid swells forming a continuous layer called a raft. The raft floats. because the buoyancy created by the formation of CO_2acts as a barrier to prevent the reflux of gastric contents like HCl and enzymes into the esophagus. Usually, the system contains a gel-forming agent and alkaline bicarbonates or carbonates responsible for the formation to make the system less dense and float on the gastric fluid.

METHODS OF PREPARATION

Methodology for single-layer floating tablets: Basically, single-layer floating tablets are prepared by compression methods. For this normally three basic compression methods are used. They are as follows: -

- Direct compression,
- Dry granulation,
- Wet granulation

Direct compression: The practice of compressing tablets straight from powdered ingredients without changing the materials' physical composition is known as direct compression. This technique is applied to crystalline substances with good compressibility and flow characteristics, such as ammonium chloride, sodium chloride, methenamine, and potassium salts (chloride, chlorate, and bromide). Tablet computers are used to create compressed tablets using a single compression process. The tablet machine's upper and lower punches crush the material under high pressure when a certain amount of powdered tablet material flows into a die.

Dry granulation method: It is defined as the formation of granules by slugging if the tablet ingredients are sensitive to moisture and/or unable to withstand elevated temperature during drying.

Wet granulation method: In wet granulation, the active ingredient, diluents, and disintegrants are mixed or blended well in a rapid mixer granulator (RMG). The RMG is a multi-purpose chopper that consists of an impeller and a chopper and is used for high-speed dispersion of dry powders and aqueous or solvent granulations. Moist materials from wet milling steps are placed on large trays and placed in drying chambers with a circulating air current and thermo-stable heat controller. Commonly used dryers are tray dryersand fluidized bed dryers. After drying, the granules are reduced in particle size by passing through the smaller mesh screen. After this, the lubricant or glidant is added as a fine powder to promote the flow of granules. These granules are then compressed to get a tablet. Dry granulation when compared with wet granulation has a shorter, more cost-effective manufacturing process. Because it does not entail heat or moisture, dry granulation is especially suitable for active ingredients that are sensitive to solvents, or labile to moisture and elevated temperatures.

METHOD OF EVALUATION

Pre compression parameter

Drug-excipientinteractions: This is done using FTIR. Appearance of a new peak, and/or disappearance of the original drug or excipient peak indicate the DE interaction. Apart from the above-mentioned evaluation parameters, for the effect of aging with the help of Differential Scanning Calorimeter or Hot stage polarizing microscopy.[10]

Bulk density: It is the ratio of total mass of powder to the bulk volume of powder. Accurately weighed batch (F1–F9) powder was placed in a 10 mL graduated measuring cylinder. The initial volume was observed. The Db was calculated in gm/mL using the following formulae,

$$Db = M/Vb$$

Where, Db =Bulk density, M=Mass of the powder, Vb =Bulk volume of powder

Tapped density: Accurately weighed batch (F1-F10) powder was placed in 10 mL graduated measuring cylinder. The cylinder was tapped initially 100 times from a distance of 14+2 mm. The tapped volume was measured to the nearest graduated unit. Again the tap volume was measured to the nearest graduated unit. The Dt was calculated in g/mL using the following formulae, [11]

$$Dt = M/Vt$$

Where, Dt =Tapped density, Vt =Tapped volume of the powder, Dt =Tapped density, M=Mass of the powder

Angle of repose: Good flow properties are critical for the development of any pharmaceutical tablets, capsules, or powder formulations. The angle of repose is defined as the maximum angle possible between the surface of the pie of powder and the horizontal plane. It is performed to determine the flow property of powder done by the funnel method. The powder mass was allowed to flow through the funnel orifice, kept vertically to a plane paper kept on a horizontal surface, giving a heap angle of powder on a paper. The diameter of the powder cone was measured and the angle of repose was calculated using the following equation [12]

$$\tan\theta = h/r$$

Where, h and r are the height and radius of the powder cone, respectively.

Hasusner's ratio: Hasusner's ratio is carried out by tapped density divided by bulk density.

$$\text{Hasusner's ratio} = Tappeddensity/Bulkdensity$$

Carr's consolidation index: Carr developed an indirect method of measuring powder flow from bulk densities. The % compressibility of the powder was a direct measure of the potential powder arch or bridge strength and stability. Carr's index of each formulation was calculated using the given formula.

$$\text{Carr's index } (\%) = [(Dt - Db) \times 100]/Dt$$

Post compression parameter

Appearance: The tablets were checked for the presence of cracks, pinholes, etc. There should be uniformity in the color and the dimensions of the tablets.

Hardness: A tablet's hardness reveals its capacity to tolerate managing mechanical shocks. The hardness of the tablet was assessed using the Monsanto hardness tester. The unit of measurement is kg/cm^2. Five tablets were chosen at random, and their hardness was assessed.

Friability: Roche Friabilator was used to gauge tablet strength. 20 tablets were weighed, put into the friabilator, turned 100 times, then removed and dusted. Reweighing the tablets allowed for the calculation of the weight reduction percentage. The % friability was calculated by:

$F= [(W_{initial}- W_{final}) \times 100]/ W_{initial})$

Weight variation: From each batch, 20 tablets were chosen at random, and they were all weighed separately and collectively using an electronic balance. The typical weight was recorded.[13]

PD= [(WH-WL) × 100]/ WH

Where, PD= percentage deviation

WH= highest weight (mg)

WL= lowest weight (mg)

Drug content:Ten tablets from each batch were weighed and powdered. Powder equivalent to the average weight of the tablet was accurately weighed in a 100 ml volumetric flask and dissolved in a suitable quantity of 0.1 N HCl. Then the volume was made up to 100ml with 0.1 N HCl and filtered. 2 ml of filtrate was transferred to a 100 ml volumetric flask and the volume was made with 0.1 N HCl. The absorbance of the resulting solution is measured by UV spectrophotometer at drug-specificnm range.[14]

FloatingTest: The tablets were placed in a 100 ml beaker containing 0.1 N HCl. The time between the introduction of the dosage form and its buoyancy on 0.1 N HCl, and the time during which the dosage form remains buoyant were measured. The time taken for the dosage form to emerge on the surface of the medium is called Floating Lag Time(FLT) or Buoyancy Lag Time (BLT) and the total duration of time during which the dosage form remains buoyant is called Total Floating Time (TFT).[15]

Swelling Study: The swelling behavior of a dosage form is measured by studying its weight gain or water uptake (WU). The study was done by immersing the dosage form in 0.1 N HCl at 37^oC and determining these factors at regular intervals up to a period of 12 hours. Water uptake was measured in terms of percent weight gain, as given by the equation. [15]

WU = (Wt –Wo) x 100 / Wo

Wt = Weight of the dosage form at time t.

Wo = Initial weight of the dosage form.

In-vitro drug release study:

The USP basket technique was used for the release testing. 900ml of 0.1N HCL was added to the jar, and the medium was allowed to acclimate to a temperature of 37^0C while rotating at 50 rpm. The tablet was placed inside the container and basket, and the machine ran for twelve hours at a speed of fifty rotations per minute. At regular intervals, 10 ml of the fluid was withdrawn, filtered, and then reintroduced. With the use of the dissolving solution, the samples were properly diluted [16]

Stability Studies:

The success of an effective formulation can be evaluated only through stability studies. The purpose of stability testing is to obtain a stable product that assures its safety and efficacy up to the end of shelf life at defined storage conditions and pack profile. The prepared floating tablets of glimepiride were placed in plastic tubes containing desiccant and stored at ambient humidity conditions, at room temperature, oven temperature (40 ± 2^0c), and in the refrigerator ($2\text{-}8^0c$) for a period of one month after storing them at $40^0C\pm2^0C/75\%RH\pm5\%RH$ for 28 days.[17]

Conclusion: Floating tablets have emerged as apowerful means of improving bioavailability providing sustained release and avoiding the adverse effects of many drugs. Drugs that have poor bioavailability because of their limited absorption to the upper gastrointestinal tract can be delivered efficiently thereby maximizing their absorption and improving their absolute bioavailability Floating tablets have proved to be a potential approach for gastric retention.

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CONFLICT OF INTEREST

The authors have no conflicts of interest.

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