

A REVIEW ON FLOATING DRUG DELIVERY SYSTEM

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ABSTRACT

The objective of our review is to compile the recent advancements and literatures regarding the novel dosage form i.e. the floating drug delivery systems (FDDS) that can be retained in the stomach for a prolonged period of time and gives therapeutic action in a predetermined manner. Floating drug delivery system provides local delivery to specific region like stomach and proximal small intestine and it's also shows better bioavailability and improved therapeutic activity and substantial benefits to patients. Gastric emptying is a complex process and makes in vivo performance of the drug delivery systems uncertain. Gastro retentive dosage forms (GRDF) has

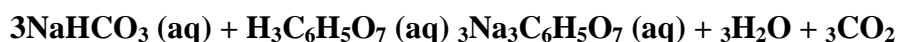
achieved significant interest in the past few years because some limitations encountered with conventional and oral controlled release drug delivery system can be avoided. Effervescent floating drug delivery systems release gas (CO₂), thus reduce the density of the system and remain buoyant in the stomach for a prolonged period of time and released the drug slowly at a desired rate so it can be used to prolong the gastric residence time in order to improve the bioavailability of drug. In the present article we will discuss mechanism of effervescent floating drug delivery system, some marketed product related to this as well as various patents on this.

KEYWORDS: Floating, Prolonged, Gastro retentive, Effervescent.

INTRODUCTION

Purpose is the acid base reaction between sodium The oral route is most preferable route for administration of the drug but it may have some disadvantages like slow onset of action or slow absorption. This problem can be overcome by using alternative dosage form or

administering the drug via other routes. While we are selecting a dosage form or route for administration of drug there are some parameters should be consider like stability and bioavailability of the formulation as well as active pharmaceutical ingredients^[1] The Effervescent floating tablets can be used as alternative dosage form to minimize some problems associated with conventional dosage forms. The Effervescent floating tablets also reduce fluctuations of drug concentration and can be used to increase the bioavailability of drug.^[2] Simply, Effervescence means release of CO₂ gas due to reaction of acids and bicarbonates in presence of H₂O. Some common acids used in this reaction are citric, malic, tartaric, adipic and fumaric acid and bicarbonate used in the effervescent reaction is sodium bicarbonate, potassium bicarbonate, sodium carbonate and potassium carbonate. The most common reaction for pharmaceutical purpose is the acid base reaction between sodium bicarbonate and citric acid.



This reaction occurs in presence of water, even with small amount as catalyzing agent, which increases the rate of reaction. As water act as a catalyzing agent for the reaction so all the moisture sensitive products or effervescent products is stored in moisture free environment.^[3]

Due to development of gas in effervescent floating drug delivery systems the density of the system is reduced and the dosage form remains buoyant in the stomach for a prolonged period of time which released the drug slowly at a desired rate. So it is possible to prolong the gastric residence time of drug using effervescent floating drug delivery systems or hydro dynamically balanced system.^[4] Effervescent floating drug delivery systems requires matrices prepared with swellable polymers such as methocel polysaccharides, e.g., Chitosan and effervescent components such as sodium bicarbonate and citric or tartaric acid or matrices containing chambers of liquid that gasify at body temperature.^[5] Effervescent floating Drugs which cause irritation to gastric mucosa are tablets are prepared by compressing the active ingredients with mixture of sodium bicarbonate and organic acids such as citric and tartaric acid.^[6] The main advantages of effervescent floating tablets are quick production of solution. Thus, it is faster and better to absorb.^[7]

On the other hand floating drug delivery systems (FDDS) is designed in such manner that it has bulk density less than gastric fluids and because of this, these systems remains buoyant for a prolonged period of time (Approx. 3-4 hours) in the stomach without affecting the

gastric emptying rate.^[8, 9] The underlying principle is very simple i.e., to make the dosage form less dense than the gastric fluids so that it can float on them. The drug is released slowly at the desired rate from the system and after release of the drug; the residual system is emptied from the stomach. As a result gastric residence time is increased and fluctuations in plasma drug concentration can be better controlled.^[10] Floating drug delivery system provides local delivery to specific region like stomach and proximal small intestine and it's also shows better bioavailability, improved therapeutic activity and substantial benefits to patients.^[11]

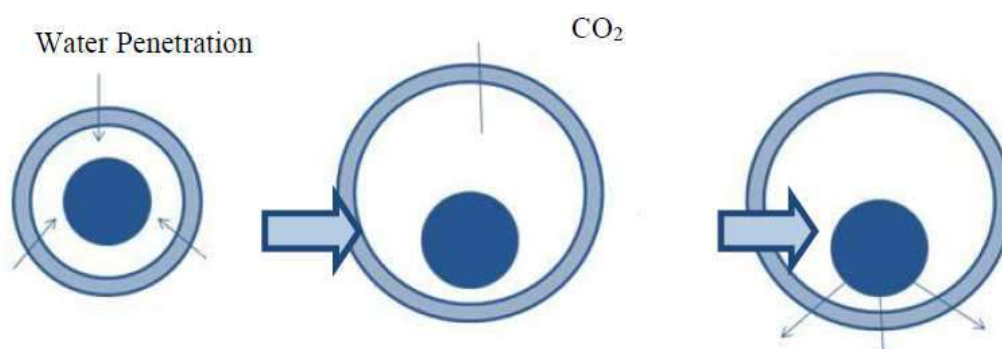


Figure: 1 Working Principle of Effervescent Floating Drug Delivery System

Advantages of Effervescent Floating drug delivery system.^[12, 13]

- Increases the oral bioavailability of drug.
- Enhanced first pass biotransformation.
- Sustained drug delivery/ reduced frequency of dosing.
- Reduced fluctuations of drug concentration.
- Improved receptor activation selectivity.
- Reduced counter-activity of body.
- Extended time over critical (Effective) concentration.
- Minimized adverse activity at the colon.
- Receptor activation selectivity is improved.
- Site specific drug delivery.

Limitation of Effervescent Floating Drug Delivery System^[14]

- Floating drug delivery requires sufficient high level of fluids in the stomach.
- Not suitable for the drug that have solubility or stability problem in GIT.
- Gastric retention is influenced by many factors such as gastric motility, pH and presence of food. These factors are never constant and hence the buoyancy cannot be predicted.

- The dose should be taken with a full glass of water.

Factors Affecting the Gastric Residence Time of Effervescent Floating Drug Delivery System^[15-17]

Nature of Meal: Motility pattern of the stomach can change to fed state when indigestible polymers or fatty acid salts are fed and because of this the gastric emptying rate is decreased and drug release is prolonged.

Frequency of Feed: when successive meals are given, the GRT can increase by over 40 minutes compared with a single meal because of the low frequency of migrating myoelectric complex.

Gender: Mean GRT of a male in meals (3.4 ± 0.4 hours) is less compared to the female of the same age and race (4.6 ± 1.2 hours), regardless of the height, weight and body surface of the two.

Age: Elderly people have a significantly longer GRT, especially those who are over 70 years of age.

Fed and Unfed State: under fasting conditions, the GI motility is characterised by periods of strong motility activity or the migrating myoelectric complex (MMC) that occurs every 1.5 to 2 hours. The MMC sweeps undigested material from the stomach and, if the timing of the administration of the formulation coincides with that of the MMC the GRT of the unit can be expected to be very short. However, in the fed state, MMC is delayed and GRT is considerably longer.

Mechanism of Floating Effervescent Tablets: The concept of floating tablets is mainly based on the matrix type drug delivery system such that the drug remains embedded in the matrix which after coming in contact with the gastric fluid swells up and the slow erosion of the drug without disintegration of the tablet takes place. When the tablet comes in the contact of gastric fluid, it produces effervescence by releasing CO₂ gas. When the fluid penetrates into the tablet, tablet starts floating.^[18] Various types of polymer of different grade provide low density system so give better efficiency in gastric fluid. The system is design to float and shows sustain release for better patient compliance and reduce dose frequency and adverse effect of drug.^[19]

$$F = F(\text{buoyancy}) - F(\text{gravity}) = (D_1 - D_2) g \cdot v$$

Where,

F= total vertical force;

D1 = fluid density;

D2 = object density;

v = volume and are also called as gastro-retentive drug delivery

g = acceleration due to gravity^[20]

METHOD OF PREPARATION OF FLOATING EFFERVESCENT TABLET

- By direct compression
- By wet granulation
- Dry Granulation

Wet Granulation: This technique is most widely used and most general method for preparation of tablets. The acid and carbonate parts of the effervescent formulation can be granulated either separately or as a mixture with water (Crystal water of citric acid, liquid water, or water vapour), ethanol (Possibly diluted with water), isopropanol, or other solvents. When granulating either with solvents containing water or pure water, the effervescent reaction will start. Care must be taken to maintain adequate control of the process. Vacuum processing is often beneficial due to ability to control the effervescent reaction and the drying process.^[22, 23]

Dry Granulation: When ingredients used in tablet formulation is sensitive to moisture then slugging may use. Slugging of the material is done by using heavy-duty tableting equipment or with roller compaction.

Direct Compression: In Direct compression vehicles can be used which are having good free-flowing properties, no segregating and are having compressible mixture. Direct compression technique buoyancy gravity force is mainly used in the formulation of floating effervescent tablet and for all moisture sensitive products.^[24]

Natural and Synthetic Polymer Used in Floating Drug Delivery System: Floating drug delivery system are also called as gastro-retentive drug delivery system that controlled the release of drug and prolong the retention time of drug in comparison to the conventional

drug by the use of various polymeric substances including natural polymer such as Guar gum, Xanthan gum, Gellan gum or synthetic polymer such as-HPMC (K4M, K 15M,K100M), Carbopol 934 p, Polyvinyl alcohol, Polyamides, Polycarbonates, Polymethacrylic acid.

EVALUATION OF FLOATING DRUG DELIVERY SYSTEM:

Various parameters used in evaluation of effervescent floating tablet. Pre-compression parameters: pre-compression parameter include in effervescent floating tablet are-flow properties include, bulk density, tapped density, Hausner and Carr's index.^[30]

Post-Compression Parameter

- Drug release
- Measurement of buoyancy capabilities.
- Swelling index
- Floating lag time
- *In-vitro* dissolution.

Buoyancy / Floating Test: The tablets were placed in a 100ml beaker containing 0.1N HCl. The time required for the tablet to rise to the surface and float was determined as floating lag time and total duration of time.^[31]

It is determined by using USP dissolution apparatus containing 900 ml of 0.1mole/lit HCl as the dissolution medium at 37°C. 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.^[32]

Swelling Study: The floating tablets were weighed individually (Designated as W₀) and placed separately in glass beaker containing 200 ml of 0.1 N HCl and incubated at 37°C ± 1°C at a regular 1hrs intervals till 24 hrs. The floating tablets are removed from beaker and the excess surface liquid is removed carefully using the tissue paper. The swollen floating tablets were then re-weighed (W_t) and % swelling index (SI) was calculated using the following formula.^[33,34]

$$\text{Swelling index \% (SI)} = [(W_t - W_0) / W_0] * 100$$

Where,

S.I. = Swelling index

W_t = Weight of tablet at time t

Wo = Weight of tablet before placing in the beaker.

***In vitro* Dissolution Studies:** The *In vitro* dissolution study was performing by using a United States Pharmacopeia (USP) type II (Paddle) apparatus at a rotational speed of 100 rpm. Exactly 900 ml of 0.1 N HCl is used as the dissolution medium and the temperature was maintained at $37^{\circ}\text{C} \pm 0.5^{\circ}\text{C}$. A sample (10 ml) of the solution was withdrawn from the dissolution apparatus at specified time interval for 24 hrs. and the same volume was replaced with pre-warmed fresh dissolution media. The samples were filtered through a Whatman filter paper and diluted to a suitable concentration of 0.1 N HCl.^[35]

Drug Release: Dissolution test were performed using dissolution test apparatus. Samples are withdrawn periodically from the dissolution medium with replacement and then analysed for their drug content after an appropriate dilution.^[36, 37]

Various Patents on Floating Drug Delivery System for Different Dosage Forms.^[38, 39]

Dudhara *et al.*^[40], develop gastric retention control drug delivery system which shows biphasic release control release system comprise a control release core having drug, swellable polymer and gas generating agent thus it may capable of swelling and floating in gastrointestinal fluid for longer period of time and maintain its physical integrity on other hand a rapidly releasing coat having drug and excipients and the core is surrounded with coating composition which shows biphasic release of drug in the gastrointestinal fluids. Thus the drug used in this technique shows better oral absorption and therapeutic effect. Lohray *et al.*^[41], Work on novel floating dosage form. His invention is based on novel pharmaceutical composition containing active ingredients which may retained in the stomach or upper G.I. tract for controlled release of drug and thus it improve absorption and therapeutic effect of the drug. In his invention he also provide a method for preparation of floating dosage form are in the form of bilayer tablet in which the one layer of tablet is used for spatial control and second one is for temporal control. Friedman *et al.*^[42], Work on gastro retentive controlled release pharmaceutical dosage forms Pharmaceutical gastro retentive drug delivery systems for the controlled release of an active agent in the gastrointestinal tract are disclosed, which comprise: A single- or multi layered matrix comprising a polymer that does not retain in the stomach more than a conventional dosage form selected from.

- Degradable polymers that may be hydrophilic polymers not instantly soluble in gastric fluids enteric polymers substantially insoluble at pH less than 5.5 and/or hydrophobic polymers and mixtures thereof;
- Non degradable polymers; and any mixtures of (1) and (2);
- A continuous or non-continuous membrane comprising at least one polymer having a substantial mechanical strength; and
- a drug; wherein the matrix when affixed or attached to the membrane prevents evacuation from the stomach of the delivery system for a period of time off from about 3 to about 24 hours.

Table 1: Some effervescent tablets and their brand leaders in India^[21]

Name of product	Active ingredient	Manufacturer
Prolyte	fizz Glucose + Potassium Chloride +Sodium Bicarbonate + Sodium Chloride+ Anhydrous Citric Acid	Cipla
Solpado	Paracetamol, Codeine phosphate	Sanofi-aventis
Zantac	Ranitidine	Glaxosmithkline
Tagame	Cimetidine	Glaxosmithkline
Histac	Ranitidine HCl	Ranbaxy
Hangoverz	Aspirin, Caffeine	Pious Pharma. Ltd
Pepfiz-O and L	Papain, Fungal diastase, Simeticone	Ranbaxy

Table 2: Marketed products of floating drug delivery system^[25-27]

S.No	Products	Active Ingredients
1	Madapar	Levodopa and benserzide
2	Valrelease	Diazepam
3	Topalkan	Aluminum magnesium Antacid
4	Almagateflatcoat	Antacid
5	Liquid gavison	Alginic acid and sodium Bicarbonate
6	Cytotec	Misoprostol
7	Convion	Ferrous sulphate

Table 3: List of some common natural polymers used in floating drug delivery system and their sources.^[28-29]

S.No.	Natural	Polymer Source
1	Guar gum	Endosperm of the seed of <i>Cyamopsistetragonolobis</i>
2	Pectin	Citrus peel, apple pomace, sugar beet pulp etc.
3	Chitosan	Shell of marine invertebrate's
4	Xanthum gum	Fermentation of glucose by <i>xanthomonascampestris</i>
5	Psyllium husk starch	Seed coat of plant ago ovate storage polysaccharides in plants
6	Gellan gum	<i>Pseudomonas elodea</i>
7	Alginates	<i>Laminaeiahyperboria</i> , <i>Ascophyllumnodosum</i>

CONCLUSION

Recently many drugs have been formulated as floating drug delivery systems with an objective of sustained release and restricting the region of drug release to stomach. The principle of buoyant preparation offers a simple and practical approach to achieve increased gastric residence time for the dosage form and sustained drug release. The currently available polymer-mediated non effervescent and effervescent FDDS, designed on the basis of delayed gastric emptying and buoyancy principles, appear to be a very much effective approach to the modulation of controlled oral drug delivery. The most important criteria which has to be looked into for the productions of a floating drug delivery system is that the density of the dosage form should be less than that of gastric fluid. And hence, it can be concluded that these dosage forms serve the best in the treatment of diseases related to the GIT and for extracting a prolonged action from a drug with a short half life.

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