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Floating Drug Delivery Systems: A Review

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ABSTRACT

Most demanding route of administration is oral. Several times dosing of conventional drug delivery system to achieve effective therapeutic range is always abhorred by the patient. Demanding new approach to reduce the number of intake; leading to introduction of gastric retention concept. As most of drugs are absorbed in upper intestinal tract GI retention was base to it. The floating drug delivery system is an admirable approach to gastric retention. Aim of delineating this review on Floating Drug Delivery System was to stash up the recent literature with special cogitation toward principal mechanism to attain gastric retention, also including details of Floating Drug Delivery System such as Classification, Mechanism of work, Method of preparation, Aspect of characterisation, Different factors to be taken care during process of formulation. This review is loaded with data of previous work performed on Floating Drug Delivery System, which includes desirable point to solve, the queries regarding FDDS.

Keywords: Floating microspheres, Floating Drug Delivery System, Gastro Retention, bioavailability, Hydrodynamically Balanced Systems.

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INTRODUCTION

Many oral controlled drug release system have been developed to improve drug bioavailability. However some of these systems do not work as planned, with respect to release of drug as on occasion they pass unexpectedly through the absorption window[1], therefore the design to sustained release preparation requires both prolongation of gastrointestinal transit of dosage form as well as controlled drug release .This requirement leads to formulation of several oral prolonged release formulation .Decreasing in dosing frequency by controlled release, as well as enhancing the bioavailability of oral system by prolongation of release time [2].

This has promoted researcher to attain drug delivery system in stomach for prolonged and predictable time[3]. Such as prolonged gastric retention not only control the time but also the space in the stomach by maintaining the delivery system position at a steady site and there by properly delivering the drug[4]. Prolonged gastric retention improves bioavailability, reduces drug waste and improves solubility for drug that is less soluble in high pH environment[5]. It has application also for local drug delivery to the stomach and proximal small intestine. Gastric retention helps to provide better availability of new product with new therapeutic possibilities and substantial benefits for patients[6].

WHACKS TO GASTRIC RETENTION

Various approaches towards gastric retention have been focused, bringing in preparation of Gastro retentive drug delivery system. Different researches have led to development of various Gastro retentive drug delivery systems (GRDDs).A major rise to Floating Drug Delivery System (FDDs).

Floating systems[7,8]

Floating Drug Delivery Systems (FDDS) have a bulk density lower than gastric fluids and thus remain buoyant in stomach for a prolonged period of time, without affecting the gastric emptying rate. While the system floats on gastric contents, the drug is released slowly at a desired rate from the system. After the release of drug, the residual system is emptied from the stomach. This results in an increase in gastric retention time and a better control of fluctuations in plasma drug concentrations. Floating systems can be classified into two distinct categories, non-effervescent and effervescent systems

Bio/Muco-adhesive Systems[8, 9]

Bio/muco-adhesive systems are those which bind to the gastric epithelial cell surface or mucin and serve as a potential means of extending gastric residence time of drug delivery system in

stomach, by increasing the intimacy and duration of contact of drug with the biological membrane.

Binding of polymers to mucin/epithelial surface can be divided into three broad categories:–

Hydration-mediated adhesion

Bonding-mediated adhesion

Receptor-mediated adhesion

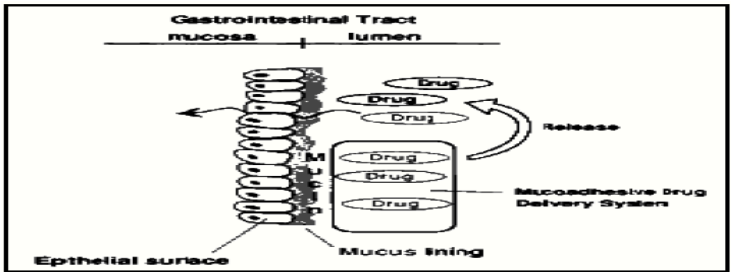

Figure 1: Interaction of a mucoadhesive drug delivery system with the mucus layer on the gastrointestinal surface epithelium

The concept is based on self-protecting mechanism of GIT Mucus secreted continuously by the specialized goblet cells located throughout the GIT plays a cytoprotective role. Bioadhesion is an interfacial phenomenon in which two materials, at least one of which is biological, are held together by means of interfacial forces. The attachment could be between an artificial material and biological substrate, such as adhesion between a polymer and a biological membrane. In the case of polymer attached to the mucin layer of a mucosal tissue, the term "mucoadhesion" is used and is therefore retained on the surface epithelium for extended periods of time. The drug molecules contained in the drug delivery device coated with mucoadhesive polymer are constantly released for absorption. The mucosal layer lines a number of regions of the body including the gastrointestinal tract, the urogenital tract, the airways, the ear, nose and eye.

Swelling and Expanding Systems[10]

These are dosage forms, which after swallowing; swell to an extent that prevents their exit from the pylorus. As a result, the dosage form is retained in stomach for a long period of time. These systems may be named as *"Plug type system"* since they exhibit tendency to remain logged at the pyloric sphincter. On coming in contact with gastric fluid, the polymer imbibes water and swells. The extensive swelling of these polymers is due to the presence of physical/chemical cross-links in the hydrophilic polymer network. These cross-links prevent the dissolution of the polymer and hence maintain the physical integrity of the dosage form.

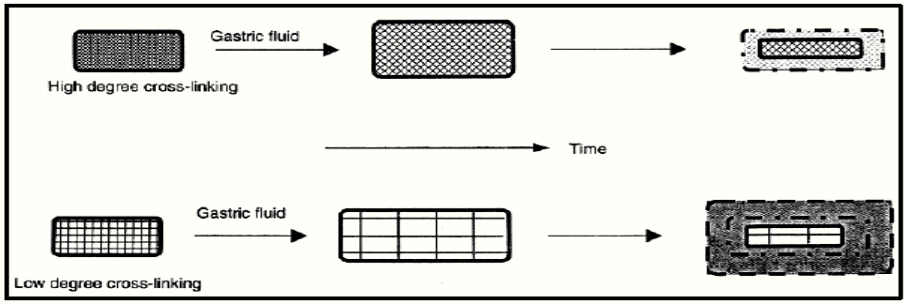

Figure 2: Degree of cross-linking and the swelling behaviour

High Density Systems[11, 8]

These systems with a density of about 3 g/cm^3 are retained in the rogue of stomach and are capable of withstanding its peristaltic movements. A density of 2.6-2.8 g/cm^3 acts as a threshold value after which such systems can be retained in the lower parts of the stomach. High-density formulations include coated pellets. Coating is done by heavy inert material such as barium sulphate, zinc oxide, titanium dioxide, iron powder etc. The weighted pellet can then be covered with a diffusion-controlling polymer membrane.

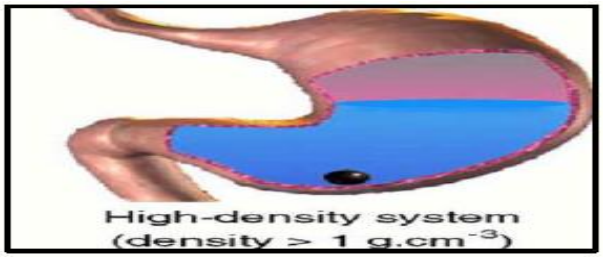

Figure 3: High Density System

Incorporation of Passage Delaying Food Agents[12]

Food excipients like fatty acids e.g. salts of myristic acid change and modify the pattern of stomach to a fed state, thereby decreasing gastric emptying rate and permitting considerable prolongation of release. The delay in gastric emptying after meals rich in fats is largely caused by saturated fatty acids with chain length of C_{10} –C_{14}.

Ion Exchange Resins[13]

Ion exchange resins are loaded with bicarbonate and a negatively charged drug is bound to the resin. The resultant beads are then encapsulated in a semi-permeable membrane to overcome the rapid loss of carbon dioxide. Upon arrival in the acidic environment of the stomach, an exchange of chloride and bicarbonate ions take place. As a result of this reaction carbon dioxide is released and trapped in the membrane thereby carrying beads towards the top of gastric content and producing a floating layer of resin beads in contrast to the uncoated beads, which will sink quickly.

Raft systems[14]

It incorporates alginate gels that have a carbonate component and upon reaction with gastric acid, bubbles form in the gel enabling floating.

Superporous hydrogel[15]

Although these are swellable systems, they differ sufficiently from the conventional types to warrant separate classification. With pore size ranging between10 nm and 100 nm, absorption of water by conventional hydrogel is a very slow process and several hours may be needed premature evacuation of the dosage form may occur. Superporous hydrogels, average pore size >100 , swell to equilibrium size within a minute, due to rapid water uptake by capillary wetting through numerous interconnected open pores. Moreover, they swell to a large size (swelling ratio of approx. 100 or more) and are intended to have sufficient mechanical strength to withstand pressure by gastric contraction.

Floating Drug Delivery System[16]

Floating systems, first described by Davis in 1968 have bulk density lower than that of the gastric fluid and thus remain buoyant in stomach for prolong period. Swelling delivery systems are capable of swelling to a size that prevents their passage through the pylorus. Upon coming in contact with gastric fluid, the polymer imbibes water and swells; as a result the dosage form is retained in the stomach for a longer period of time.

Floating systems are low density systems that have sufficient buoyancy to float over the gastric contents and remain in the stomach for a prolonged period. While the system floats over the gastric contents, the drug is released slowly at the desired rate, which results in increased gastro-retention time and reduces fluctuation in plasma drug concentration. After release of drug, the residual system is emptied from the stomach. This results in an increased GRT and a better control of the fluctuations in plasma drug concentration.

Definition: [17]

Floating Drug Delivery Systems are the drug delivery system which prolongs the retention of the dosage form in the GIT and aid in enhancing the absorption.

FDDS is also considered as “Hydrodynamically Balanced Systems (HBS)”. These systems have more flexibility than the conventional dosage form.

There are certain drugs that can benefit from using gastroretentive devices are:

a. Acting locally in stomach.
b. Primarily absorbed in stomach.
c. Poorly soluble at alkaline pH.

d. Narrow window of absorption.

e. Degrades in the colon.

These buoyant preparations include microsphere, granules, powder, capsule, tablet, pills and laminated films. Most of the floating system are generally single unit system which are unreliable and non-reproducible in prolong residence time in the stomach when administered orally. In contrast to that multiple dosage form (e.g microsphere) has more advantage[2].

Mechanism of floating system[18]

Main working principle of floating system is to remain buoyant over the gastric fluid for extended period of time to increase gastric retention.

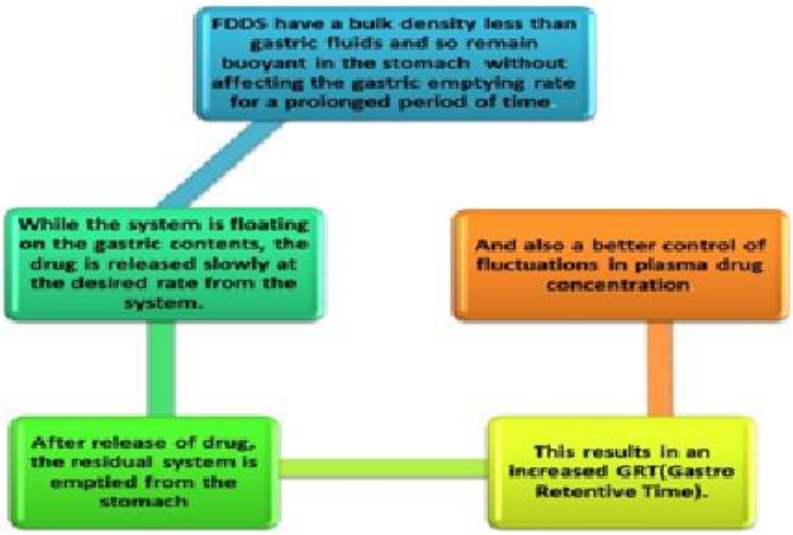

Figure 4: Working principle of FDDS

Mechanicsm behind floating of microsphere[16]

When microspheres come in contact with gastric fluid the gel formers, polysaccharides, and polymers hydrate to form a colloidal gel barrier that controls the rate of fluid penetration into the device and consequent drug release. As the exterior surface of the dosage form dissolves, the gel layer is maintained by the hydration of the adjacent hydrocolloid layer. The air trapped by the swollen polymer lowers the density and confers buoyancy to the microspheres. However a minimal gastric content needed to allow proper achievement of buoyancy.

Types of Floating Drug Delivery System

Based on mechanism to remain buoyant, two distinctly different technologies have been utilized in development of FDDS which are:

A. Effervescent system.

B. Non effervescent system.

Effervescent System: [19]

These buoyant delivery systems are prepared with swellable polymers such as Methocel or polysaccharides e.g., Chitosan and effervescent components, e.g. Sodium bicarbonate and citric or tartaric acid or matrices containing chambers of liquid that gasify at body temperature.

The matrices are fabricated so that upon contact with gastric fluid, carbon dioxide is liberated by the acidity of gastric contents and is entrapped in the gelled hydrocolloid. This produces an upward motion of the dosage form and maintains its buoyancy.

These effervescent systems are further classified into:

Gas generating system

a. Tablets
b. Floating Capsules
c. Multiple Unit Type of Floating Pills
d. Floating system with Ion Exchange Resin.

Volatile liquid / vacuum containing system

a. Intra gastric floating gastro intestinal drug delivery system.
b. Inflatable gastrointestinal drug delivery system
c. Intra gastric osmotically controlled drug delivery system.

Non Effervescent System [20]**:**

Commonly used excipients, here are gel-forming or highly swellable cellulose type hydrocolloids, polysaccharides and matrix forming polymers such as polycarbonate, polyacrylate, polymethacrylate and polystyrene. One of the approaches to the formulation of such floating dosage forms involves intimate mixing of drug with the gel-forming hydrocolloid, which swells in contact with gastric fluid after oral administration and maintains a relative integrity of shape and a bulk density of less than unity within the outer gelatinous barrier. The air entrapped by the swollen polymer confers buoyancy to these dosage forms. The gel structure acts as a reservoir for sustained drug release as the drug is slowly released by controlled diffusion through the gelatinous barrier.

1. Colloidal gel barrier
2. Microporous compartment system
3. Alginate beads
4. Hollow microsphere / microballon
5. Single layer floating tablet
6. Bilayer floating tablet

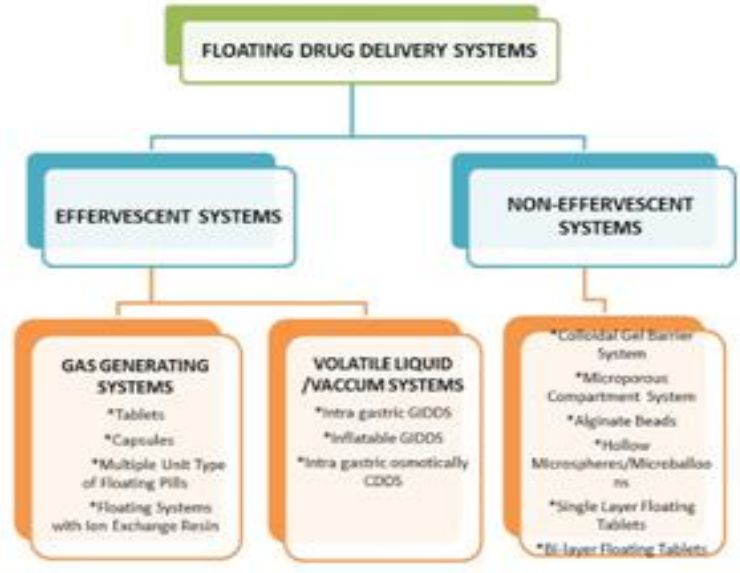

Figure 5: Types of FDDS[18]

Application of floating multiparticulates[21, 22]

Sustained Drug Delivery:

Floating multiparticulates of non-steroidal anti inflammatory drugs are very effective for controlled release as well as it reduces the major side effect of gastric irritation; for example floating microspheres of Indomethacin are quiet beneficial for rheumatic patients.

Solubility Enhancement:

Floating multiparticulates are especially effective in delivery of sparingly soluble and insoluble drugs. It is known that as the solubility of a drug decreases, the time available for drug dissolution becomes less adequate and thus the transit time becomes a significant factor affecting drug absorption. For weakly basic drugs that are poorly soluble at an alkaline pH, hollow microspheres may avoid chance for solubility to become the rate-limiting step in release by restricting such drugs to the stomach. The positioned gastric release is useful for drugs efficiently absorbed through stomach such as Verapamil hydrochloride. The gastro-retentive floating microspheres will alter beneficially the absorption profile of the active agent, thus enhancing its bioavailability.

As carriers:

The floating multiparticulates can be used as carriers for drugs with so-called absorption windows, these substances, for example antiviral, antifungal and antibiotic agents (Sulphonamides, Quinolones, Penici-llin, Cephalosporins, Aminoglycosides and Tetracyclines) are taken up only from very specific sites of the GI mucosa.

Site-Specific Drug Delivery:

Floating multiparticulates can greatly improve the pharmacotherapy of the stomach through local drug release, leading to high drug concentrations at the gastric mucosa, thus eradicating *Helico-bacter pylori* from the sub-mucosal tissue of the stomach and making it possible to treat stomach and duodenal ulcers, gastritis and oesophagitis.

Pharmacokinetic advantages and future potential:

As sustained release systems, floating dosage forms offer various potential advantages evident from several recent publications. Drugs that have poor bioavailability because their absorption is restricted to the upper GI tract can be delivered efficiently there by maximizing their absorption and improving their absolute bioavailabities.

Absorption enhancement:

Drugs which are having poor bioavailability because of site specific absorption from the upper part of the GIT are potential candidates to be formulated as floating drug delivery systems, there by maximizing their absorption.

Minimized adverse activity at the colon:

Retention of the drug in the HBS systems at the stomach minimizes the amount of drug that reaches the colon. Thus, undesirable activities of the drug in colon may be prevented. This Pharmaco-dynamic aspect provides the rationale for GRDF formulation for betalactam antibiotics that are absorbed only from the small intestine, and whose presence in the colon leads to the development of microorganism's resistance.

Reduced fluctuations of drug concentration:

Continuous input of the drug following CRGRDF administration produces blood drug concentrations within a narrower range compared to the immediate release dosage forms. Thus, fluctuations in drug effects are minimized and concentration dependent adverse effects that are associated with peak concentrations can be prevented. This feature is of special importance for drugs with a narrow therapeutic index.

Reduced counter-activity of the body:

In many cases, the pharmacological Response which intervenes with the natural physiologic processes provokes a rebound activity of the body that minimizes drug activity. Slow input of the drug into the body was shown to minimize the counter activity leading to higher drug efficiency.

Extended time over critical (effective) concentration*:*

For certain drugs that have non-concentration dependent pharmacodynamic such as betalactam antibiotics, the clinical response is not associated with peak concentration, but rather with the

duration of time over a critical therapeutic concentration. The sustained mode of administration enables extension of the time over a critical concentration and thus enhances the pharmacological effects and improves the clinical outcome.

Ingredients used for preparation of floating drugs:

A. Polymer

Different varieties of polymer are being used for preparation of floating drug delivery.

- *Hydrophilic polymers*

  These includes gelatin, agar, egg albumin, starch, chitosan, cellulose derivatives; HPMC, DEAE cellulose.

- *Hydrophobic polymers*

  These are include ethyl cellulose, polylactic acid, PMMA, acrylic acid esters etc.

a. Biodegradable polymers

These materials slowly disappear from the site of administration; however it occurs in response to a chemical reaction such as hydrolysis.

Example: Polylactic acid (PLA), polyglycolic acid (PGA), Polycaprolactone (PCL) and several generic classes such as the poly anhydrides and polyorthoesters.

b. Non-Biodegradable

These materials are inert in the environment of use, are eliminated extracted intact from the site of administration.

Example: Polyethylene vinyl acetate (EVA), Polydimethyl siloxane (PDS), Polyether urethane (PEU),Ethyl cellulose (EC), Cellulos acetate (CA), Polyethylene (PE) and Polyvinyl chloride (PVC), Acrycoat, Eudragit S etc.

c. ***Hydrogels***

These polymers swell but do not dissolve when brought in contact with water. As with hydrophobic polymers, hydrogels are inert, removed intact from the site of administration, and function by forming a rate limiting barrier to the transport and release of drugs.

Example: Polyhydroxy ethyl methyl acrylate (PHEMA), cross-linked poly vinyl alcohol (PVA), cross linked polyvinyl pyrrolidone (PVP), poly acryl amide etc.

• *Soluble polymers:*

These are moderate molecular weight(less than 75,000 Daltons) uncross linked polymers that dissolve in water. The rate of dissolution decreases with increasing molecular weight. These materials can be used alone or in combination with hydrophobic polymers to provide devices that slowly erode over time.

Example: polyethylene glycol (PEG), uncross linked poly vinyl alcohol or polyvinyl pyrrolidone, hydroxyl propyl methyl cellulose (Methocel) and copolymers of methacrylic acid and acrylic acid methyl ester (Eudragit L) etc.

B. Inert fatty materials (5%-75%):

Edible, inert fatty materials having a specific gravity of less than one can be used to decrease the hydrophilic property of formulation and hence increase buoyancy. E.g. Beeswax, fatty acids, long chain fatty alcohols, Gelucires® 39/01 and 43/01.

C. *Effervescent agents:*

Sodium bicarbonate, citric acid, tartaric acid, Di-SGC (Di sodium glucine carbonate, CG (Citroglycine).

D. ***Release rate accelerants (5%-60%):*** eg. lactose, mannitol.

E. ***Release rate retardants (5%-60%):*** eg. Dicalcium phosphate, talc, magnesium stearate.

F. ***Buoyancy increasing agents (upto80%):*** eg. Ethyl cellulose.

G. *Low density material:* Polypropylene foam powder.

Factors to be considered during formulation:

1. Addition of polymer solution

High surface tension of water was found caused the solidification and aggregation of polymer on the surface of aqueous phase. To reduce polymer solution contact with the air-water interface and to develop a continuous process for preparing microspheres, a new method developed in result. The method involves the use of a glass tube immersed in an aqueous phase and the polymer solution is introduced through the glass tube without contacting the surface of water. This method improved the yield of microspheres and reduced the extent of aggregate formation.

As the polymer solution is continuously introduced into the main vessel, it will overflow from the top of the vessel together with the prepared microspheres, since most of the formed microspheres will float on the top of the aqueous phase. The microspheres, which overflow from the top of the vessel, can be collected in a container with an appropriate sieve size at the bottom.

2. Effect of rotation speed

The rotation speed of propeller affects yield and size distribution of microspheres. As the rotation speed of propeller is increased, the average particle size decreases, while maintaining its morphology.

3. Effect of temperature

The temperature of the dispersing medium is an important factor in the formation of microspheres as it controls the evaporation rate of the solvents. At lower temperature (10ºC), prepared microsphere crushed and have irregularly shaped morphology. The shell of the microsphere turns translucent during the process, due to the slower diffusion rate of ethanol and dichloromethane. At higher temperatures (40ºC), the shell of the microsphere becomes thin and it might be due to faster diffusion of alcohol in the droplet into aqueous phase and evaporation of dichloromethane immediately after introducing it into the medium

Table 1: Patents on Floated Drug Delivery System for Different Dosage Forms[16]

S.NO	Types of formulation	Patent number
1	Gastric-retentive Dosage Form	U.S- 5,972,389
2	Gastric-retention System	U.S- 5,443,843
3	Bilayer Buoyant Dosage Form	U.S- 5,232,704
4	Powder Formulation	U.S- 5,169,638
5	Floating Drug Delivery Device	U.S- 4,767,627
6	Novel Sustained-release Formulations	U.S- 4,167,558
7	Sustained-release Tablet Formulations	U.S- 4,140,755
8	Novel Floating Dosage Form	U.S- 0013876 A1
9	Gastroretentive Controlled Release	U.S- 6,685,962 B2
10	Microspheres	U.S- 6,207,197 B1
11	Gastro Retentive Dosage Form	U.S-7,413,752
12	Multiple Unit Floating Dosage Form	European patent (EP) 10697
13	Bilayer Tablet	EP-002445
14	Microspheres	U.S-6207197
15	Floating Tablet	U.S-66,352279
16	3-layer Tablet	U.S-5780057
17	Foams (or) Hollow Bodies	U.S-5626876
18	Floating Tablet	U.S-5169639
19	Granule	U.S-4844905
20	Floating Capsule	U.S-4814178,-79
21	Tiny Pills	U.S-4434153
22	Floating Capsule	U.S-4126672
23	Floating Device	U.S-4055178
24	Empty Globular Shells	U.S-3976164

Table 2: List of animal model used for evaluation of FDDS[12]

S.No	Drug	Dosage form	Animal Model	Methodology tested	Results
1.	Repaglinide	Microspheres	Male albino Rabbits	Gamma scintigraphy	Enhanced bioavailability

2.	Repaglinide	Microspheres	Male Sprague-Dawley rats	Organ distribution Study	Enhanced bioavailability about 3.17 times in comparison to the marketed products
3.	Riboflavin	Microballoons	Healthy human Volunteers	Urine excretion Analysis	Prolonged GRT
4.	Ranitidine hydrochloride	Microparticles	Rabbits	Pharmacokinetic Studies	Prolonged GRT >12 hrs and Improve the bioavailability
5.	Orlistat	Microspheres	Albino rabbits	Gamma scintigraphy	The best floating ability (88% ±4% buoyancy) in simulated gastric fluid (SGF) as compared with other formulation Prolonged GRT of over 6 hrs was achieved in all rabbits.

CONCLUSION

Solubility being a major parameter required for the absorption of drug from GIT. To this aspect FDDS come as a revolutionary approach. Gastroretentive property has emerged as an aspect for controlled release, bioavailability enhancement within the absorption window. Floating microsphere with a controlled release property by polymer such as, hydrophilic, hydrophobic polymer, natural gums, biodegradable possess good oral controlled release. This will result in momentous assets for future therapeutic effectiveness.

REFERANCE

1. Yasunori Sato, Yoshiaki Kawashima, Hirofumi Takeuchi, Hiromitsu Yamamoto In vitro and in vivo evaluation of riboflavin-containing microballoons for a floating controlled drug delivery system in healthy humans Int J Pharma 275 (2004) 97–107.
2. Mishra jhansee, dash alok kumar recent advances in gastro retentive drug delivery system: a review. Mintage J Pharma Medical Sci 2013. ISSN 2320-3315.
3. P.dutta, J. Sruti, Ch. Nirajan patra and M.E Bhanoji Rao, Floating microsphere: Recent trend in the development of gastroretentative floating drug delivery system . Int J Pharma Sci Nanotechno
4. Sivannarayana P, Saikishore V, Prameela Rani, Veda Pravallika, Venu Babu Ch. A Review on Novel Approach in Gastro Retentive Floating Drug Delivery: Floating Microspheres. Res J Pharma Biological Chem Sci ISSN: 0975-8585.
5. Abhishek Chandel, Kapil Chauhan, Bharat Parashar, and Hitesh Kumar, Sonia Arora Floating drug delivery systems: A better approach Int Current Pharma J 2012, 1(5): 110-118.
6. Singh BN, Kim KH. Floating drug delivery systems an approach to oral controlled drug

delivery via gastric retention. J Control Rel 2000; 63:235-59.

7. Ponchel G, Irache JM. Specific and nonspecific bioadhesive particulate systems for oral delivery to the gastrointestinal tract. Adv. Drug Del. Rev. 1998; 34: 191-19.
8. Atyabi F, Sharma HL, Mohammad HAH, Fell JT. *In vivo* evaluation of a novel gastroretentive formulation based on ion exchange resins. J. Control. Release, 1996; 42:105-13.
9. Debjit Bhowmik, Chiranjib.B, Margret Chandira, B. Jayakar, K.P.Sampath KumarFloating Drug Delivery System-A Review. Scholars Research Library2009, 1 (2) 199-218ISSN 0975-5071.
10. Rocca JG, Omidian H, Shah K. Progress in gastroretentive drug delivery systems. 2003; [4 screens]. Available,at: URL:http://bbriefings.com/pdf/17/ACF8D8E.pdf Accessed May 20, 2004.
11. Rajkumar K,Sainath Goud R, Sai Sowjanya P, Anusha P,Lavanya Adavi S, E.R Reddy. Floating microsheres: a novel approach in Drug delivery. J Drug Delivery Res. ISSN 2319-1074
12. Bardonnet PL, Faivre V, Pugh WJ, Piffaretti JC, Falson F. Gastroretentive Dosage Forms: Overview and Special case of Helicobacter pylori Journal of Controlled Release 2006; 111: 1-18.
13. YS Tanwar Floating microsphere development, characterization and application, submitted by anonymous on 5-25-2006- Pharma info.net.
14. Vinod K.R., Santhosh Vasa, Anbuazaghan, David Banji, Padmasri , Sandhya approaches for gastro retentive drug delivery systems.2010;1(2).
15. Shakti Dwivedi and Vikash Kumar Floating Drug Delivery Systems- A Concept of Gastro retention Dosages Form In J Res Pharma Biomedical Sci ISSN: 2229-3701.
16. Arunachalam, M. Karthikeyan, Kishore Konam, Pottabathula Hari Prasad, S. Sethuraman, S. Ashutosh kumar, S. Manidipa Floating drug delivery systems: A review ISSN: 0975-7538.
17. Pharma extremes, floating drug delivery system, 2012.
18. Kadam Shasikant M, Kadam S.R, Patil U.S, Ratan G.N, Jamkandi V.G. review of floating drug delivery via gastric retention ISSN2229-3566, 2011.
19. Chanda R, Roy A, Bahadur S, Saha S, Das S, Choudhury A Floating drug delivery: a potential alternative to conventional therapy. Int J Pharmtech Res 2010;2(1):49-59.
20. Punamgaba. Floating microsphere : A Review, Pharmainfo.Net.
21. Patel Ravi, Patel JK. Formulation and development of hydrochlorthiazide. Pharmacy Info Pedia.