VOLUME-8, ISSUE-1, JANUARY-2019 • PRINT ISSN No 2277 - 8160

Original Research Paper

Pharma

A COMPREHENSIVE REVIEW ON FLOATING DRUG DELIVERY SYSTEM: A NOVEL DRUG DELIVERY SYSTEM

Dipti Khairiya — Global Institute of Pharmaceutical Education and Research , Kashipur , Uttarakhand, India

Kapil Kumar* — Global Institute of Pharmaceutical Education and Research, Kashipur , Uttrakhand, India*Corresponding Author

ABSTRACT The purpose of writing this review on floating drug delivery system which is also known as hydrodynamically controlled systems (FDDS) was to compile the recent literature with special focus on Classification, Mechanism of Action and Evaluation of floating drug delivery system. Floating Drug delivery systems are those that float immediately upon contact with gastric fluids present promising approaches for increasing the bioavailability of drugs. Floating drug delivery system are low-density systems that have sufficient buoyancy to float over the gastric contents and remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time.

KEYWORDS : Floating Drug delivery systems, factors affecting, mechanism of action, advantage, disadvantage, evaluation parameters, applications

INTRODUCTION

The oral route of drug administration is most commonly used for the therapeutic drugs because of its cost efficiency and easy administration leads to good patients compliance 1. More than 50% of the drug delivery systems available in the market are oral drug delivery system[2].

Oral administration has only limited use for important drugs, from various pharmacological categories, that have poor oral bioavailability due to incomplete absorption and/or degradation in the gastrointestinal (GI) tract. Some of these drugs are characterized by a narrow absorption window (NAW) at the upper part of the gastrointestinal tract. This is because of proximal part of the small intestine exhibits extended absorption properties (including larger gaps between the tight junctions, and dense active transporters). Despite the extensive absorption properties of the duodenum and jejunum, the extent of absorption at these sites is limited because the passage through this region is rapid. Enhancing the gastric residence time (GRT) of a NAW the drug may significantly improve the net extent of its absorption.

Floating Drug Delivery System

Floating drug delivery system is also known as hydrodynamically controlled system. It has low density which gives the drug highest buoyancy to float in gastric content in the stomach and remain buoyant in the stomach without affecting the gastric emptying rate for prolonged period of time. It floats over the gastric contents, the drug is released slowly at the desired rate, prolonging the gastric retention time in the stomach and reducing the variations of drug concentration in plasma3. Usually these types of drugs have very less adverse side effects and have good bioavailability with Long action[1].

The average gastric emptying time in humans which is normally 2-3 hrs through the major absorption zone (stomach and upper part of intestine) can result in incomplete drug release from the drug delivery system leading to reduce the efficacy of administered dose. Lower dosing and less side effects beneficial in the treatment of gastric diseases. Suitable dosage forms for the drugs those are primarily absorbed in the stomach.

Normal gastric time usually ranges between 5 minutes to 2 hours. Depending on the fasted and fed state of the stomach, two distinct patterns of gastrointestinal motility and secretions have been observed. In fasted state the electrical activity of the stomach is governed by some cyclic contractile events commonly known as inter-digestive myloelectric cycle migrating myoelectric complexes (MMC) 4,5,6.

There are four consecutive phases of activity in the MMC.

Phase I – (Basal phase) period of no contraction (30 to 60 minutes)

Phase II – (Pre-burst Phase) period of intermittent contractions (20 – 40 minutes)

Phase III – (Burst Phase) period of regular contractions at the maximal frequency that travel distally also known as housekeeper wave (10 to 20 minutes)

Phase IV – period of transition between phase III and phase I (0 to 5 minutes).

Advantage of Floating Drug Delivery System

1. The floating drug delivery systems are advantageous for drugs absorbed through the stomach. E.g. antacids.
2. Enhanced Bioavailability
3. Enhanced First-Pass Biotransformation
4. Improved drug delivery
5. Reduced frequency/fluctuations of Dosing
6. Control in the amount of drug to be delivered
7. Have a local action on stomach
8. Reduced counter-activity
9. Minimize mucosal irritation
10. Easy administration
11. Convenient equipment for manufacturing
12. Target/site specific drug delivery.
13. Easily metabolized in liver
14. Some drugs are teratogenic which is harmful in pregnancy
15. We can take more then one drug at a time which can cure for more then one disease
16. In Floating Drug Delivery System the half life of drug is more then any Drug Delivery System
17. FDDS is more efficient and less irritant in stomach
18. FDDS improves patient compliance by decreasing dosing frequency.
19. Easily excreated by the body

Disadvantage of Floating Drug Delivery System

1. Not suitable for drugs that have solubility or stability problem in GIT.

2. Drugs which are irritant to gastric mucosa are also not desirable or suitable.

3. Drugs which are well absorbed along the entire GIT and which undergoes first pass metabolism, may not be desirable eg. Nifedipin , Dipin

4. In FDDS require a high level of fluid in the stomach for drug delivery to float and work efficiently

5. Those drugs which are unstable in acidic medium of stomach are not suitable for candidates FDDS

6. The dosage form should be administered with a full glass of water (200-250 ml).

7. High variability in gastric emptying time due to its all or non-emptying process

8. 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 assured.

Classification Of Floating Drug Delivery System

1) Single Unit Floating Dosage Systems

I) Effervescent Systems (Gas-generating Systems)

ii) Non-effervescent Systems (Hydro dynamically balanced systems)

2) Multiple Unit Floating Dosage Systems

I) Effervescent Systems (Gas-generating Systems)

ii) Non-effervescent Systems (Hydro dynamically balanced systems)

iii) Hollow Microspheres

3) Raft Forming Systems

1) Single Unit Floating Dosage System

Single unit dosage forms are easiest to develop but suffers from the risk of losing their effects too early due to their all-or-none emptying from the stomach and, thus they may cause high variability in bioavailability and local irritation due to large amount of drug delivered at a particular site of the gastro intestinal tract7.

I) Effervescent Systems (Gas-generating Systems)

These are matrix types of systems prepared with the help of swellable polymers such as methylcellulose, hydroxypropyl methyl-cellulose or polysaccharides and chitosan and various effervescent compounds, e.g. sodium bicarbonate, calcium carbonate, tartaric acid, and citric acid. They are formulated in such a way that when in contact with the acidic gastric contents, CO2 is liberated and gets entrapped in swollen hydrocolloids, which provides buoyancy to the dosage forms8. In case of single layered tablet (Shweta Arora et al, 2005, Gangadha-rappa H.V, 2007) the liberated carbon dioxide may intimately get mixed within the tablet matrix[22].

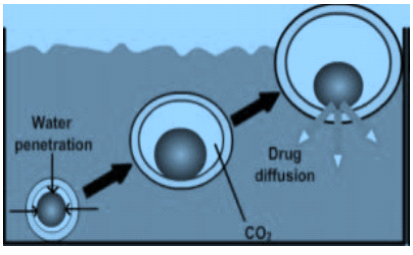

Figure 1: Mechanism of floatation via CO2 generation

1. Non-effervescent System (Hydro dynamically balanced systems)

One or more gel forming, highly swellable, cellulosic hydrocolloids(e.g. hydroxyl ethyl cellulose, hydroxyl propyl cellulose, hydroxypropyl methyl cellulose [HPMC] and sodium carboxy methyl cellulose), polysaccharides, or matrix forming polymers (e.g. polycarbophil, polyacrylates, and polystyrene) are incorporated in high level (20-75% w/w) to tablets or capsules9,10.

For the preparation of these types of systems, the drug and the gelforming hydrocolloid are mixed thoroughly. After oral administration this dosage form swells in contact with gastric fluids and attains a bulk density of < 1. The air entrapped within the swollen matrix imparts buoyancy to the dosage form. The so formed swollen gel-like structure acts as a reservoir and allows sustained release of drug through the gelatinous mass8.

2) Multiple Unit Floating Dosage Systems

Single unit formulations are associated with problems such as sticking together or being obstructed in gastrointestinal tract, which may have a potential danger of producing irritation. Multiple unit systems avoid the 'all-or-none' gastric emptying nature of single unit systems. It reduces the intersubject variability in absorption and the probability for dose dumping is lower[8,11].

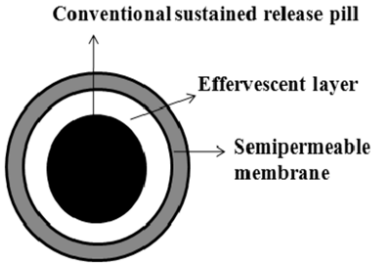

Figure 2: Multiple unit of FDDS

In spite of extensive research and development in the area of HBS and other floating tablets, these systems suffer from an important drawback of high variability of gastrointestinal transit time, when orally administered, because oftheir all-or-nothing gastric emptying nature. Inorder to overcome the above problem, multiple unitfloating systems were developed, which reduce the intersubject variability in absorption and lower the probability of dose-dumping. Reports have been found on the development of both non-effervescent and effervescent multiple unit systems. Much research has been focussed and the scientists are still exploring the field of hollow microspheres, capable of floating on the gastric fluid and having improved gastric retention properties9,10.

I) Effervescent Systems (Gas-generating Systems)

A multiple unit system comprises of calcium alginate core and calcium alginate/PVA membrane, both separated by an air compartment was prepared. In presence of water, the PVA leaches out and increases the membrane permeability, maintaining the integrity of the air compartment. Increase in molecular weight and concentration of PVA, resulted in enhancement of the floating properties of the system. Freeze-drying technique is also reported for the preparation of floating calcium alginate beads. Sodium alginate solution is added drop wise into the aqueous solution of calcium chloride, causing the instant gelation of the droplet surface, due to the formation of calcium alginate. The obtained beads are freeze-dried resulting in a porous structure, which aid in floating. The authors studied the behavior of radiolabeled floating beads and compared with nonfloating beads in human volunteers using gamma scintigraphy. Prolonged gastric residence time of more than 5.5 h was observed for floating beads. The nonfloating beads had a shorter residence time with a mean onset emptying time of 1 hr8,11.

ii) Non-effervescent Systems (Hydro dynamically balanced systems)

A little or no much report was found in the literature on non-effervescent multiple unit systems, as compared to the effervescent systems. However, few workers have reported the possibility of developing such system containing indomethacin, using chitosan as the polymeric excipient. A multiple unit HBS containing indomethacin as a model drug prepared by extrusion process is reported. A mixture of drug, chitosan and acetic acid is extruded through a needle, and the extrudate is cut and dried. Chitosan hydrates float in the acidic media, and the required drug release could be obtained by modifying the drug-polymer ratio8,12.

iii) Hollow Microspheres

These are considered as one of the most promising buoyant systems, as they possess the unique advantages of multiple unit systems as well as better floating properties, because of the central hollow space inside the microsphere. The general techniques involved in their preparation include simple solvent evaporation method and solvent diffusion and evaporation method . The drug release and better floating properties mainly depends upon the type of polymer, plasticizer and the solvents employed for the formulation. Polymers such as Polycarbonate, Eudragit®, and Cellulose acetate were used in the preparation of hollow microspheres, and the drug release can be modulated by optimizing the polymer-plasticizer ratio and the polymer quantity. Sustained release floating microspheres using polycarbonate were developed, using solvent evaporation technique. Aspirin, Griseofulvin and p-nitroaniline were used as model drugs13,14,15.

3) Raft Forming Systems

Raft forming systems have received much attention for the delivery of antacids and drug delivery for gastrointestinal infections and disorders. The mechanism involved in the raft formation includes the formation of viscous cohesive gel in contact with gastric fluids, where in each portion of the liquid swells forming a continuous layer called a raft16,17,18,19. This raft floats on gastric fluids because of low bulk density created by the formation of CO2.

Usually, the system contains a gel forming agent and alkaline bicarbonates or carbonates responsible for the formation of CO2 to make the system less dense and float on the gastric fluids20 an antacid raft forming floating system. The system contains a gel forming agent (e.g. alginic bicarbonate, calcium carbonate, mannitol and a sweetener. These ingredients were granulated, and citric acid was added to the granules. The formulation produces effervescence and aerates the raft formed, making it float acid), sodium bicarbonate and acid neutralizer, which forms a foaming sodium alginate gel (raft) when in contact with gastric fluids. The raft thus formed floats on the gastric fluids and prevents the reflux of the gastric contents (i.e. gastric acid) into the esophagus by acting as a barrier between the stomach and esophagus. A patent assigned to Reckitt and Colman Products Ltd., describes a raft forming formulation for the treatment of helicobacter pylori (H. Pylori) infections in the GIT21.

Factors Affecting Of Floating Drug Delivery System

1. Density of dosage form

Floating is a function of dosage form buoyancy that is dependent on the density. Dosage forms having a density lower than that of gastric fluid experience floating behavior and hence gastric retention. A density of <1.0 gm/cm3 is required to exhibit floating property. However, the floating tendency of the dosage form usually decreases as a function of time, as the dosage form gets immersed into the fluid, as a result of the development of hydrodynamic equilibrium (Tim-mermans and Moes, 1990) 17,22.

2. Fed or unfed state

Under fasting conditions, the GI motility is characterized by periods of strong motor activity or the Migrating Myoelectric Complex (MMC) that occurs every 1.5 to 2 hours 22, 23.

3. Nature of meal

Feeding of indigestible polymers or fatty acid salts can change the motility pattern of the stomach to a fed state, thus decreasing the gastric emptying rate and prolonging drug release 22, 24.

4. Caloric content and feeding frequency

Floating can be increased by four to 10 hours with a meal that is high in proteins and fats. The floating can increase by over 400 minutes when successive meals are given compared with a single meal due to the low frequency of MMC22.

5. Age

Elderly people, especially those over 70, have a significantly longer; floating25. Disease condition such as diabetes and crohn's disease etc also affect drug delivery.

6. Posture

Floating can vary between supine and upright ambulatory states of the patient26.

7. Shape of dosage form

Tetrahedron and ring shaped devices with flexural modules of 48 and 22.5 kilo pounds per square inch (KSI) are reported to have better floating, 90% to 100% retention at 24 hours compared with other shapes27.

Mechanism of Action of Floating Drug Delivery System

Floating drug delivery systems (FDDS) have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents the drug is released slowly at the desired rate from the system. 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.

However, besides a minimal gastric content needed to allow the proper achievement of the buoyancy retention principle, a minimal level of floating force (F) is also required to keep the dosage form reliably buoyant on the surface of the meal. To measure the floating force kinetics, a novel apparatus for determination of resultant weight has been reported in the literature. The apparatus operates by measuring continuously the force equivalent to F (as a function of time) that is required to maintain the submerged object.

The object floats better if F is on the higher positive side. This apparatus helps in optimizing FDDS with respect to stability and durability of floating forces produced in order to prevent the drawbacks of unforeseeable intra-gastric buoyancy capability variations[15,16].

$$F = F_{buoyancy} - F_{gravity} = (Df - Ds)\,gV$$

Where,

F = total vertical force,
Df = fluid density,
Ds = object density,
V = volume and
g = acceleration due to gravity

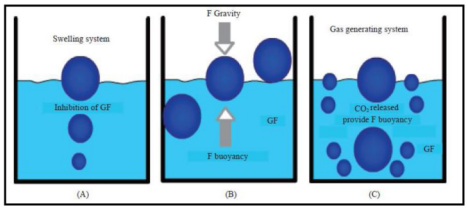

Figure 3: Mechanism of floating of beads (GF=gastric fluid)

Evaluation Parameters

Various parameters that need to be evaluated in gastroretentive formulations include floating duration, dissolution profiles, specific gravity, content uniformity, hardness, and friability in case of solid dosage forms. In the case of multiparticulate drug delivery systems, differential scanning calorimetry (DSC), particle size analysis, flow properties, surface morphology, and mechanical properties are also performed.

1. Size and Shape Evaluation:

The particle size and shape plays a major role in determining solubility rate of the drugs and thus potentially its bioavailability. The particle size of the formulation was determined using Sieve analysis, Photo analysis, Optical microscope, Sedimentation

techniques, Laser diffraction methods, ultrasound attenuation spectroscopy, Air Pollution Emissions Measurements etc[16].

2. Floating Properties:
Effect of formulation variables on the floating properties of gastric floating drug delivery system was determined by using continuous floating monitoring system and statistical experimental design[16].

3. Measurement of buoyancy capabilities of FDDS
The floating behaviour was evaluated with resultant weight measurements. The experiment was carried out in two different media, deionised water in order to monitor possible difference. The higher molecular weight polymers with slower rate of hydration had en-hanced floating behaviour and it was observed more in simulated meal medium compared to de-ionized water17.

4. Hardness, friability, content uniformity (Tablets)
These tests are performed as per described in specified monographs[8].

5. Floating lag time and total floating time determination
The time between the introduction of the tablet into the medium and its rise to upper one third of the dissolution vessel is termed as floating lag time and the time for which the dosage form floats is termed as the floating or flotation time. These tests are usually performed in simulated gastric fluid or 0.1 mole. lit-1 HCl maintained at 37o C, by using USP dissolution apparatus containing 900 ml of 0.1 molar HCl as the dissolution medium[28].

6. Drug release
Dissolution tests are performed using the dissolu-tion apparatus. Samples are withdrawn periodically from the dissolution medium with replacement and then analyzed for their drug content after an appropriate dilution[17].

The test for in vitro drug release studies are usually carried out in simulated gastric and intestinal fluids maintained at 370 C. Dissolution tests are performed using the USP dissolution apparatus. Samples are withdrawn periodically from the dissolution medium, replaced with the same volume of fresh medium each time, and then analyzed for their drug contents after an appropriate dilution. Recent methodology as described in USP XXIII states that the dosage
unit is allowed to sink to the bottom of the vessel before rotation of blade is started. A small, loose piece of non reactive material such as not more than a few turns of wire helix may be attached to the dosage units that would otherwise float. However, standard dissolution methods based on the USP or British Pharmacopoeia (BP) have been shown to be poor predictors of in vitro performance for floating dosage forms8.

7. X-Ray/Gamma scintigraphy
For in vivo studies, X-Ray/Gamma Scintigraphy is the main evaluation parameter for floating dosage form. In each experiment, the animals are allowed to fast overnight with free access to water, and a radiograph is made just before the administration of the floating tablet to ensure the absence of radio-opaque material. Visualization of dosage form by X-ray is due to the inclusion of a radio-opaque material. The formulation is administered by natural swallowing followed by 50 mL of water. The radiographic imaging is taken from each animal in a standing position, and the distance between the source of X-rays and the animal should kept constant for all imaging, so that the tablet movement could be easily noticed. Gastric radiography was done at 30-min time intervals for a period of 5 h using an X-ray machine9-19.

8. Specific Gravity
Displacement method is used to determine the specific gravity of floating system using benzene as a displacing medium8.

9. Pharmacokinetic studies
Pharmacokinetic studies include AUC (Area under Curve), Cmax, and time to reach maximum plasma concentration (Tmax) were estimated using a computer. Statistical analyses were performed using a Student t test with p, 0.05 as the minimal level of significance8,[18].

Applications of Floating Drug Delivery Systems
Floating drug delivery offers several applications for drugs having poor bioavailability because of the narrow absorption window in the upper part of the gastrointestinal tract. It retains the dosage form at the site of absorption and thus enhances the bioavailability 29 , 30 .

1. Sustained Release Drug Delivery System
HBS systems can remain in the stomach for long periods and, hence can release the drug over a prolonged period of time. The problem of short gastric residence time encountered with an oral CR formulation hence can be overcome with these systems. These systems have a bulk density of <1 as a result of which they can float on the gastric contents. These systems are relatively large in size and passing from the pyloric opening is prohibited e.g. Sustained release floating capsules of nicardipine hydrochloride were developed and were evaluated in vivo.

The formulation compared with commercially available MICARD capsules using rabbits. Plasma concentration time curves showed a longer duration for administration (16 hours) in the sustained release floating capsules as compared with conventional MICARD capsules (8 hours) 31.

2. Site-Specific Drug Delivery
These systems are particularly advantageous for drugs that are specifically absorbed from stomach or the proximal part of the small intestine, eg, riboflavin and furosemide. Furosemide is primarily absorbed from the stomach followed by the duodenum. It has been reported that a monolithic floating dosage form with prolonged gastric residence time was developed and the bioavailability was increased17. AUC obtained with the floating tablets was approximately 1.8 times those of conventional furosemide tablets32.

3. Absorption Enhancement
Drugs that have poor bioavailability because of site specific absorption from the upper part of the gastrointestinal tract are potential candidates to be formulated as floating drug delivery systems, thereby maximizing their absorption e.g. a significant increase in the bioavailability of floating dosage forms (42.9%) could be achieved as compared with commercially available LASIX tablets (33.4%) and enteric coated LASIX-long product (29.5%) 16 , 33 , 34 .

4. Enhanced Bioavailability
The bioavailability of riboflavin CR-GRDF is significantly enhanced in comparison to the administration of non-GRDF CR polymeric formulations. There are several different processes, related to absorption and transit of the drug in the gastrointestinal tract, that act con-comitantly to influence the magnitude of drug absorp-tion37.

5. Minimized Adverse Activity at the Colon
Retention of the drug in the HBS systems at the sto-mach minimizes the amount of drug that reaches the colon. Thus, undesirable activities of the drug in colon may be prevented. This Pharmacodynamic aspect pro-vides the rationale for GRDF formulation for betalac-tam antibiotics that are absorbed only from the small intestine, and whose presence in the colon leads to the development of microorganism's resistance37,38,39.

6. Reduced Fluctuation Drug concentration
Continuous input of the drug following CRGRDF admin-istration 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 ef-fects that are associated with peak concentrations can be prevented. This feature is of special importance for drugs with a narrow therapeutic index (Yie W. Chein et al, 1992, Sanjay Garg et al, 2003, Vedha hari b.n.et al, 2010)37,40.

Table 1: Market available product

S.N.	Brand Name	Drug	Dosage form	Polymer Used	Manufacturers
1.	Cifran O.D	Ciprofloxacin	Tablet	Xanthan gum and sodium alginate	Ranbaxy
2.	Conviron	Ferrous Sulphate	Gel	--	Ranbaxy
3.	Liquid Gavison	Mixture of Alginates	Liquid	Alginates	GlaxoSmith Kline
4.	Madopar HBS	Levodopa and Benserazide	Capsule	HPMC	Roche
5.	Glumetza	Metformin Hydrochloride	Tablet	HPMC	Depomed
6.	Topalkan	Al-MG antacid	Liquid	--	Pierre farbe drug, France
7.	Almagate float coat	Al-MG antacid	Liquid	--	Pierre farbe drug, France
8.	Valrelease	Diazapam	capsule	--	Hoffmann La Roche, USA

CONCLUSION

Floating systems or hydrodynamically controlled systems are low-density systems that have sufficient buoyancy to float over the gastric contents and remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time.The floating drug delivery system was prepared in an effort increase the gastric retention time of the dosage form and to control drug release.

Drug absorption in the gastrointestinal tract is a highly variable procedure and prolonging gastric retention of the dosage form extends the time for drug absorption. FDDS promises to be a potential approach for gastric retention. Although there are number of difficulties to be worked out to achieve prolonged gastric retention, a large number of companies are focusing toward commercializing this technique.

REFERENCES

1. Katariya Chanchal, Roy Anitha, Floating Drug Delivery System for Analgesic - A Review, Bachelor of Dental Surgery, Faculty of Pharmacology, Saveetha Dental College and Hospital, Chennai, India. 12-02-2017
2. Chandel Abhishek, Chauhan Kapil, Parashar Bharat, Kumar Hitesh, Arora Sonia Floating drug delivery systems: A better approach, Department of Pharmacy, Manav Bharti University, Solan -173229, Himachal Pradesh, India, Chandel et al., International Current Pharmaceutical Journal 2012.
3. Ikechukwu UR, John Francis DE, Ambi AA. Development and evaluation of Ritonavir hollow microballoons for floating drug delivery. Universal Journal of Pharmaceutical Research. 2017; 2(2): 30-34.
4. Peng-Ju Ma, Guo-JunGao, Hai-Gang Chang, Fa-ZhengShen,Lei Hui and Bao-Zhe Jin-Prolonged and Floating Drug Delivery System of Gabapentin for Effective Management of Pain in Spinal Cord Injury -International Journal of Pharmacology-2016, 435-43.
5. Radwan MA, Abou el Ela AE, Hassan MA, El-Maraghy DA. Pharmacokinetics and analgesic effect of ketorolac floating delivery system. Drug delivery. 22(3), 2015 Apr 3, 320-7.
6. Avinash K, Abha D, Praween K, Abhinav G. 11. Floating Drug Delivery System a Significant Tool for Stomach Specific Release of Cardiovascular Drugs. International Journal of Drug Development and Research. 2012.
7. Sharma N, Agarwal D, Gupta M and Khinchi M. Acomprehensive Review on Floating Drug Delivery System. Int J Res Pharm Biomed Sci. 2011;2:428-441.
8. Siswanto A, Fudholi A, Nugroho AK, Martono S. In Vitro Release Modeling of Aspirin Floating Tablets Using DD Solver Indonesian Journal of Pharmacy, 26(2), 2015 Apr 4, 94.
9. Agnihotri, S.A., Jawalkar, S.S., Aminabhavi, T.M. (2006). Controlled release of cephalexin through gellan gum beads: Effect of formula-tion parameters on entrapment efficiency, size, and drug release, Eur. J. Pharm. Biopharm. 63:249-261. DOI PMid:16621483
10. Babu, V.B.M., Khar, R.K. (1990). In vitro and In vivo studies of sustained release floating dosage forms containing salbutamol sulphate. Pharmazie.; 45: 268-270. PMid:2381979
11. Desai, S., Bolton, S. (1993). A floating controlled release drug delivery system: in vitro-in vivo evaluation. Pharm Res; 10(9): 1321-1325. DOI PMid:8234170
12. Anyanwu NCJ, Adogo LY, Ajide B. Development and evaluation of in situ gelling gastroretentive formulations of Meloxicam. Universal Journal of Pharmaceutical Research. 2017; 2(3): 11-14.
13. Chikhalikar SS and Wakade RB: Floating Drug Delivery System – An Approach To Oral Controlled Drug Delivery. International Journal of PharmTech Research 2012; 4(4) 1812-26.
14. Tripathi GK and Singh S: Formulation and In vitro evaluation of pH sensitive oil entrapped polymeric blended buoyant beads of Amoxicillin. Scholars Research Library 2010; 2 (2): 131-38.
15. Lokendra Singh Arya, Kapil Kumar, Sai Krushna Padhy. Formulation and evaluation of floating microspheres of prazosin hydrochloride as a gastro retentive dosage form. International Journal of Research and Development in Pharmacy and Life Sciences. 2016; 5 (5): 2159-2165.
16. Kharia AA, Hiremath SN, Singhai AK and Jain SK: Design and optimization of floating drug delivery system of acyclovir. Indian Journal of Pharmaceutical Sciences 2010; 72(5): 599-06.
17. 6. Bhowmik D, Chiranjib B, Margret C, Jayakar B and Kumar KPS: Floating Drug Delivery System-A Review. Scholars Research Library 2009; 1(2): 199-18.
18. Vedha H, Chaudhary J: The recent developments on gastric floating drug delivery system: An overview. Journal of Pharmaceutical Technology and Research 2010; 2(1); 524-34.
19. Kapil Kumar, AK Rai. Development and evaluation of floating microspheres of herbal drugs. Tropical Journal of Pharmaceutical Research. 2012; 11(5), 713-719.
20. Geetha A, Rajendra K, Mohan CHK, Sateesh V and Raju PN: A Review on Floating Drug Delivery Systems. International Journal of Pharmaceutical Research and Biomedical Analysis 2012; 1(1): 1-13.
21. Monika Setia, Kapil Kumar, Deepak Teotia. Development and evaluation of gastro-retentive floating beads of dicycloverine hydrochloride, Journal of Drug Delivery and Therapeutics. 2018; 8(4):346-355.
22. Kaza R, Usharani E, Nagaraju R, Haribabu R and Reddy PVS: Design and Evaluation of Sustained release Floating tablets for the treatment of Gastric Ulcers. Journal of Pharmaceutical. Sciences and Research 2009; 1(4): 81-87.
23. Mantry S, Thilothama LR and Shashanka D: Formulation and in vitro evaluation of Metoprolol Succinate Floating Tablets by using two viscosity grade of HPMC. International Journal of Pharmaceutical Sciences and Research 2012; 3(9): 3507-13.
24. Raju DB, Sreenivas R and Varma MM: Formulation and evaluation of floating drug delivery system of Metformin Hydrochloride. Journal of Chemical and Pharmaceutical Research 2010; 2(2): 274-78.
25. Narang Neha, An Updated Review on: Floating Drug Delivery System (FDDS) Research Article, Shri Baba Mastnath Institute of Pharmaceutical Sciences and Research, Asthal Bohar, Rohtak, (Haryana), 05 Oct 2010
26. Singh BN, Kim KH. Floating drug delivery system: An approach to the controlled drug delivery via gastric retention. J Control Release 2000; 63: 235-259.
27. Shah SH, Patel JK, Patel NV. Stomach specific floating drug delivery system: A review. Int J Pharm Res 2009; 1(3): 623-633.
28. Arora S, Ali A, Ahuja A, Khar RK, Baboota S. Floating drug delivery systems: A review. AAPS PharmSciTech 2005; 6(3): E372- E390.
29. Tanwar YS, Naruka PS, Ojha GR. Development and evaluation of floating microspheres of verapamil hydrochloride. Brazilian J of Pharm Sci 2007; 43: 529-534.
30. Chudiwal P., Pawar P.L., Nagaras M.A., Mandlik S.K., Pandya S.V., Wakte P.: Int. J. Pharm. Tech. Res. 1, 1366 (2006).
31. Saddam C Shaikh, Dnyaneshwar Sanap, Dipak V Bhusari, Shirish Jain, Pooja P Kochar, Vikram N Sanchati. Formulation and evaluation of Ibuprofen gastro-retentive floating tablets. Universal Journal of Pharmaceutical Research. 2018; 3(4): 20-25.
32. Monika Setia, Kapil Kumar, Deepak Teotia. Gastro-retentive floating beads a new trend of drug delivery system. Journal of Drug Delivery andTherapeutics. 2018; 8(3): 169-180.
33. Kapil Kumar, AK Rai. Evaluation of anti-inflammatory and anti-arthritic activities of floating microspheres of herbal drug, International research journal of pharmacy. 2012; 3(1):186-193.
34. T L Russell, R R Berardi, J L Bernett, L L Dermentzoglou, K M Jarvenpaa, S P Schmaltz, J B Dressman, Upper gastrointestinal pH in seventy nine healthy elderly North American men and women. Pharm Res; 1993; 10(2); 187-196.
35. Felix Sunday Yusuf. Formulation and in-vitro evaluation of floating microballoons ofstavudine. Universal Journal of Pharmaceutical Research. 2016; 1(1): 13-19.
36. W Sawicki, Pharmacokinetics of verapamil and nor verapamil from controlled release floating pellets in humans. Eur J Pharm Biopharm; 2002; 53; 29-35.
37. B M Singh and K H Kim, Floating drug delivery systems: an approach to oral controlled drug delivery via gastric retention. J Control Release 2000; 63:235-259.
38. S K Jain, G P Agarwal, N K Jain, Evaluation of porous carrier based floating orlistat microspheres for gastric delivery. AAPS PharmSciTech; 2006:7(4)
39. Baumgartner S, Kristl J, Vrecer F. Optimization of floating matrix tablets and evaluation of their gastric residence time. Int J Pharm 2000; 195: 125-135.
40. Kapil Kumar, AK Rai. Floating Microsphere: An innovative Approach for Gastro retention. Journal of Pharmacy Research. 2012; 5(2):883-886.