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Review Article

FLOATING DRUG DELIVERY SYSTEMS- A REVIEW OF RECENT RESEARCH

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Abstract: Formulation of floating drug delivery system (FDDS) is a topic of current interest in pharmaceutical product development. Floating drug delivery systems are low-density systems that float over the gastric content and remain buoyant in the stomach for a prolonged period of time. They enhance drug bioavailability, reduce drug wastage and provide controlled drug delivery and better patient compliance. Literature on FDDS types, advantages, disadvantages, factors, evaluation and applications along with recent research in this area are reviewed in this article.
Key words: Floating drug delivery systems, Formulation approaches, Evaluation methods, Recent Research, Review

INTRODUCTION

Oral drug delivery is the most desirable and preferred method of administering therapeutic agents for their systemic effects. The high level of patient compliance in taking oral dosage forms is due to the ease of administration, patient compliance, flexibility in formulation and handling of these forms[1]. However the oral route of administration suffers with certain drawbacks mainly short residence time of the dosage form in the GI tract, unpredictable gastric emptying and degradation of the drug due to highly reactive nature of GI contents. Gastric emptying is a complex process and makes *in vivo* performance of the drug delivery system uncertain. Formulation of floating drug delivery systems is an useful approach to avoid this variability with increased gastric retention time of the drug delivery system[2,3]. 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[4].After release of drug, the residual system is emptied from the stomach. Floatation of a drug delivery system in the stomach can be achieved by incorporating floating chamber filled with vacuum, air, or inert gas.

CLASSIFICATION OF FDDS:

A) Single Unit Systems:

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 tract[5].

Noneffervescent 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 capsules[6,7].

For the preparation of these types of systems, the drug and the gel forming 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 mass.

Effervescent systems or gas generating systems:

These are matrix types of systems prepared with the help of swellable polymers such as methylcellulose and chitosan and various effervescent compounds, e.g. sodium bicarbonate, tartaric acid, and citric acid. They are formulated in such a way that when in contact with the acidic gastric contents, CO_2 is liberated and gets entrapped in swollen hydrocolloids, which provides buoyancy to the dosage forms. The optimal stoichiometric ratio of citric acid and sodium bicarbonate for gas generation is reported to be 0.76:1.

B) Multiple Unit 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 inter subject variability in absorption and the probability for dose dumping is lower[8].

Noneffervescent systems:

A little or no much report was found in the literature on noneffervescent 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 ratio.

Effervescent 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 behaviour 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 hr[9].

Floating microspheres:
A controlled release system designed to increase its residence time in the stomach without contact with the mucosa was achieved through the preparation of floating microspheres. Techniques involved in their preparation include simple solvent evaporation, and solvent diffusion and evaporation. The drug release and better floating properties mainly depend on the type of polymer, plasticizer and the solvents employed for the preparation. Polymers, such as polycarbonate, Eudragit® S and cellulose acetate, are used in the preparation of hollow microspheres, and the drug release can be modified by optimizing the amount of polymer and the polymer plasticizer ratio[10].

C) Raft Forming Systems:
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 of the buoyancy created by the formation of CO_2 and act as a barrier to prevent the reflux of gastric Contents like HCl and enzymes into the oesophagus. Usually, the system contains a gel forming agent and alkaline bicarbonates or carbonates responsible for the formation of to make the system less dense and float on the gastric fluids[11]. Reckitt and Colman Products Ltd. have come out with such formulation in the treatment of H.pylori infections of GIT.

Advantages of FDDS[12]
Floating dosage systems form important technological drug delivery systems with gastric retentive behaviour and offer several advantages in drug delivery. These advantages include:

1. Improved drug absorption, because of increased gastric residence time and more time spent by the dosage form at its absorption site
2. Controlled delivery of drugs.
3. Delivery of drugs for local action in the stomach.
4. Minimizing the mucosal irritation due to drugs, by drug releasing slowly at controlled rate.
5. Treatment of gastrointestinal disorders such as gastro-oesophageal reflux.
6. Simple and conventional equipment for manufacture.
7. Ease of administration and better patient compliance.
8. Site-specific drug delivery.

Disadvantages of FDDS[13,14,15]

1. Floating systems are not feasible for those drugs that have solubility or stability problems in gastric fluids.
2. Drugs such as Nifedipine, which is well absorbed along the entire GI tract and which undergo significant first-pass metabolism, may not be suitable candidates for FDDS since the slow gastric emptying may lead to reduced systemic bioavailability. Also there are limitations to the applicability of FDDS for drugs that are irritant to gastric mucosa.
3. 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.
4. Drugs that cause irritation and lesion to gastric mucosa are not suitable to be formulated as floating drug delivery systems.

FORMULATION OF FDDS:
Suitable Drug Candidates for FDDS:
Various drugs have their greatest therapeutic effect when released in the stomach, particularly when the release is prolonged in a continuous, controlled manner. In general, appropriate candidates for FDDS are molecules that have poor colonic absorption but are characterized by better absorption properties at the upper parts of the GIT[16-20].

1. Drugs with narrow absorption window in GIT, e.g., Riboflavin and Levodopa
2. Drugs that primarily absorbed from stomach and upper part of GIT, e.g., Calcium supplements, chlordiazepoxide and cinnarazine.
3. Drugs that act locally in the stomach, e.g., Antacids and Misoprostol.
4. Drugs that degrade in the colon, e.g., Ranitidine HCl and Metronidazole.
5. Drugs that disturb normal colonic bacteria, e.g., Amoxicillin Trihydrate.

Excipients Used in FDDS[21]
1. Polymers: The following polymers used in preparations of FDDS -HPMC K4 M, Calcium alginate, Eudragit S100, Eudragit RL, Propylene foam, Eudragit RS, ethyl cellulose, poly methyl methacrylate, Methocel K4M, Polyethylene oxide, β Cyclodextrin,HPMC 4000, HPMC 100, CMC, Polyethylene glycol,polycarbonate, PVA, Polycarbonate, Sodium alginate, HPC-L, CP 934P, HPC, Eudragit S, HPMC, Metolose S.M. 100, PVP, HPC-H, HPC-M, HPMC K15, Polyox, HPMC K4, Acrylic polymer, E4M and Carbopol.

2. Inert fatty materials (5%-75%): Edible, inert fatty material 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.

3. Effervescent agents: Sodium bicarbonate, citric acid, tartaric acid, Di-SGC (Di-Sodium Glycine Carbonate, CG (Citroglycine).

4. Release rate accelerants (5%-60%): eg. Lactose, mannitol.

5. Release rate retardants (5%-60%): eg.Dicalciumphosphate, talc, magnesium stearate.

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

7. Low density material: Polypropylene foam powder (AccurelMP 1000).

Factors Affecting the Floating and Floating Time:

1. **Density: -** Floating is a function of dosage form buoyancy that is dependent on the density.
2. **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 shapes[22].
3. **Concomitant drug administration: -** Anticholinergics like atropine and propantheline, opiates like codeine and prokinetic agents like metoclopramide and cisapride; can affect floating time.
4. **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[23].
5. **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[24].
6. **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 MMC.

7. **Age: -** Elderly people, especially those over 70, have a significantly longer; floating[25].

Disease condition such as diabetes and crohn's disease etc also affect drug delivery.

8. **Posture: -** Floating can vary between supine and upright ambulatory states of the patient[26].

EVALUTION OF FDDS:

Different studies reported in the literature indicate that pharmaceutical dosage forms exhibiting gastric residence invitro floating behavior show prolonged gastric residence invivo. Although, in vitro floating behavior alone is not sufficient proof for efficient gastric retention so *in vivo* studies can provide definite proof that prolonged gastric residence is obtained.

1) Hardness, Friability, Assay, Content Uniformity:

These tests are performed as per described in specified monographs.

2) Floating lag time and 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 37^0 C, by using USP dissolution apparatus containing 900 ml of 0.1 molar HCl as the dissolution medium[27].

3) Drug release:

The test for in vitro drug release studies are usually carried out in simulated gastric and intestinal fluids maintained at 37^0C.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 forms.

4) Drug loading, drug entrapment efficiency, particle size, analysis, surface characterization, micromeritics studies and percentage yield (for floating microspheres and beads):

Drug loading is assessed by crushing accurately weighed sample of beads or microspheres in a mortar and added to the appropriate dissolution medium which is then centrifuged, filtered and analyzed by various analytical methods like spectrophotometry. The percentage drug loading is calculated by dividing the amount of drug in the sample by the weight of total beads or microspheres. The particle size and the size distribution of beads or microspheres are determined in the dry state using the optical microscopy method. The external and cross-sectional morphology (surface characterization) is done by scanning electron microscope (SEM). The measured weight of prepared microspheres was divided by total amount of all non-volatile components used for the preparation of microspheres, which will give the total percentage yield of floating microspheres[28,29].

5) Specific Gravity:

Displacement method is used to determine the specific gravity of floating system using benzene as a displacing medium[30].

6) Weight gain and water uptake (WU):

Weight gain or water uptake can be studied by considering the swelling behaviour of Floating dosage form. The study is done by immersing the dosage form in simulated gastric fluid at 37^0 C and determining the dimensional changes like tablet diameter and/ or thickness at regular 1-h time intervals until 24 h, the tablets were removed from beaker, and the excess surface liquid was removed carefully using the paper. The swollen tablets were then reweighed and WU is measured in the terms of percent weight gain, as given by equation

$WU = (Wt - W_O) X 100 / Wo$

In which Wt and Wo are the weights of the dosage form at time t and initially, respectively[31].

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 50ml 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 machine. Gamma scintigraphy is a technique whereby the transit of a dosage form through its intended site of delivery can be non-invasively imaged *in vivo* via the judicious introduction of an appropriate short lived gamma emitting radioisotope. The inclusion of a γ-emitting radionucleide in a formulation allows indirect external observation using a γ-camera or scintiscanner. But the main drawback of γ- scintigraphy are the associated ionizing radiation for the patient, the limited topographic information, low resolution inherent to the technique and the complicated and expensive preparation of radiopharmaceutical[32,33].

8) 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 Significance[34].

APPLICATIONS OF FDDS:

1. Enhanced Bioavailability:

The bioavailability of riboflavin CR-GRDF is significantly enhanced in comparison to the administration of non-GRDFCR polymeric formulations. There are several different processes, related to absorption and transit of the drug in the gastrointestinal tract, that act Concomitantly to influence the magnitude of drug absorption[35].

2. Sustained drug delivery:

Oral CR formulations are encountered with problems such as gastric residence time in the GIT. These problems can be overcome with the HBS systems which can remain in the stomach for long periods and have a bulk density <1 as a result of which they can float on the gastric contents. These systems are relatively larger in size and passing from the pyloric opening is prohibited[36].

3. Site specific drug delivery systems:

These systems are particularly advantageous for drugs that are specifically absorbed from the stomach or the proximal part of the small intestine .The controlled, slow delivery of drug to the stomach provides sufficient local therapeutic levels and limits the systemic exposure to the drug. This reduces side effects that are caused by the drug in the blood circulation. In addition, the prolonged gastric availability from a site directed delivery system may also reduce the dosing frequency. Eg: Furosemide and Riboflavin[37].

4. 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[38].

5. 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 Pharmacodynamic 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.

6. 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[39].

Recent Research on Floating Drug Delivery Systems:

Several studies reported the formulation and evaluation of floating drug delivery systems of various drugs for enhancing their bioavailability and for obtaining controlled release.A summary of recent research on floating drug delivery systems is given in Table 1

CONCLUSION

Formulation of floating drug delivery systems is an efficient and potential approach for gastric retention of dosage forms to improve bioavailability and also to achieve controlled release. Though several approaches and techniques are developed for FDDS, research in this area is needed until an ideal system with applicability and industrial feasibility is developed.

Table 1 : Summary of Recent Research on Floating Drug Delivery Systems[40-83]

S. NO	Drugs (Category)	Type of dosage form	Excipients/ Polymers Used	Method	Reason/Result	Ref. No
1	Diltiazem Hydrochloride (Anti-Hyper	Tablet	HPMC K100M, Sodium CMC, Sodium alginate, Sodium	Melt granulation method	The results of the study indicated that the platform technology based on the use	40

	tensive)		bicarbonate, Ethyl Cellulose, White Beeswax		of 50 % matrix forming polymer, 5% bees wax and 5% ethyl cellulose was suitable for the design of floating tablets of water soluble drug.	
2	Atenolol (Anti Hypertensive)	Tablet	HPMC K4M, K15M,Hydrogenated Cotton Seed Oil, Sodium bicarbonate	Direct compression	Extended drug release and bioavailability, increased gastric retention	41
3	Lasartan Potassium (Anti Hypertensive)	Matrix Tablet	HPMC K15M, Xanthan Gum, Sodium Bicarbonate	Direct compression	Effective site of absorption for longer period of time and releases the drug in sustained manner	42
4	Itropride (Anti Ulcer)	Tablets	Sodium bicarbonate, Citric Acid, Xanthan Gum, HPMC K4M	Direct compression	HPMC K4M,xanthan gum, in combination were found to be promising for gastro retentive drug delivery system	43
5	Sitagliptin (Anti Diabetic)	Microspheres	HPMC, Eudragit Rs100	Emulsion Solvent evaporation technique	Microspheres show excellent physico-chemical properties in control release pattern include bioavailability and patient compliance	44
6	Verapamil Hydrochloride (Anti Hypertensive)	Tablet	HPMC K4M, K15M, Micro Crystalline Cellulose 102,Sodium bicarbonate	Direct compression	Increase sustained release with lesser floating lag time	45
7	Tapentadol Hydrochloride (Nor Epinephrine Reuptake Receptor)	Matrix Tablet	Xanthan Gum, Chitosan, Sodium bicarbonate	Direct compression	Good Invitro as well as Invivo gastro rentive Floating Drug Delivery of Tapentadol Hcl	46
8	Montelukast Sodium (Anti Asthma)	Tablet	HPMC K4M,K15M, Xanthan Gum, Sodium bicarbonate	Direct compression	Prolonged release for a period of 24hrs and the release was dependent on ratio and type of polymer used	47
9	Lamotrigine (Anti Convulsant)	matrix tablets	Citric Acid Anhydrous, Sodium bicarbonate, HPMC K100M, Ethyl Cellulose	direct compression	matrix tablets with sufficient floating time and sustained release upto 24 hrs	48
10	Famotidine (Histamine H_2 Receptor Antagonist)	Tablet	Methocel K100,K15M, Sodium bicarbonate, Citric Acid	Direct compression	Improved bioavailability and gastric residence time	49
11	Ciprofloxacin (Anti Biotic)	Tablet	Methocel K4M, K15M,K100M, Sodium bicarbonate	Direct compression	Increased G.I absorption and controlled release of drug	50
12	Gabapentin (Anti Convulsant)	Tablet	HPMC K100,K15M, Polyox WSR303, Sodium bicarbonate	Direct compression	Increased bioavailability and prolonged drug release	51
13	Itropride (Anti Ulcer)	Tablet	Sodium bicarbonate, HPMC K4M,	Direct compression	Drug release from the floating tablets was slow	52

			K100M,K15M		and spread over 24hr	
14	Tizanidine Hydrochloride (Centrally Acting Muscle Relaxant)	Matrix Tablet	HPMC K4M, K100M,K15M, Dicalcium Phosphate	Wet granulation	Sustained release over 24hr	53
15	Cefpodoxime Proxetil (Cephalosporin Prodrug)	Matrix Tablet	HPMC K4M, Sodium CMC, Carbopol 943P, Sodium bicarbonate, Lactose	Direct compression	Prolonged gastric residence time and increased drug absorption and bioavailability	54
16	Salbutamol Sulphate (Anti Asthma)	Matrix Tablet	Ethyl Cellulose, Acrycoal S100,Sodium bicarbonate, Citric Acid, Tartaric Acid	Wet granulation	Increased floating duration with less lag time	55
17	Foscarnet Sodium (Antiviral Drug)	Alginate Beads	HPMC K15m,Guar Gum, Tamarind Gum.	Ionic gelation method	Prolong gastric residence time and increased bioavailability	56
18	Ritonavir (Anti Viral Drug)	Microspheres	HPMC, Sodium Bicarbonate, Acetic Acid, Calcium Chloride Solution, Sodium alginate	Simple dripping method	Buoyancy and controlled release of drug was depended upon amount concentration of sodium bicarbonate	57
19	Aceclofenac (NSAID)	Pulsatile microspheres	Eudragit L100,S100	Emulsion Solvent diffusion technique	A two phase release pattern with initial lag time during floating in acidic medium was followed by rapid releasing phosphate buffer	58
20	Baclofen (Anti spamotic)	Matrix tablets	HPMC K4M, Carbopol 934, Sodium bicarbonate, Citric Acid, Sodium CMC	Direct compression	Increased gastric residence time and bioavailability	59
21	Labetalol Hydrochloride (Anti Hypertensive)	Tablet	HPMC K4M,Carbopal 934P, Sodium CMC, Citric Acid, Sodium bicarbonate	Direct compression using simplex centroid design	Improved bioavailability and controlled release over 12hr	60
22	Ofloxacin (Anti Bacterial)	Tablet	HPMC K4M,K100M,K15M,Sodiumbicarbonate, PVP K90	Wet granulation	Prolonged gastric residence time, controlled and uniform release	61
23	Levofloxacin (Anti Bacterial)	Tablet	HPMC, EC, PVP K30, Citric Acid Sodium Bicarbonate	Direct compression	Drug release with prolonged Period.	62
24	Rifabutine (Anti Mycobacterial)	Gellan gum beads	Deacetylated Gellan Gum	Ionotropic gelation in acidic medium	Sustained pharmacological action and improved bioavailability	63
25	Cephalexin (B-Lactum Anti Biotic)	Microspheres	Ethyl Cellulose	Emulsion solvent evapouration technique	Improved bioavailability and prolonged drug release upto 12hrs	64
26	Glipizide (Anti Diabetic)	Microspheres	Acrycoat S100, Eudragit RS100, Ethyl Cellulose	Solvent evapouration technique	Polymer ratio effected the size, entrapment efficiency, % buoyancy and drug release	65
27	Metoprolol Tartrate (CardioSelective β Blocker)	Core mini tablets	HPMC K15m, PVPK30, MCC.	Wet granulation	Increased gastric residence time.	66

28	Lornoxicam (NSAID)	Matrix tablets	HPMC K15M, Calcium Carbonate (13%).	Direct compression	Prolonged gastric residence time and improved Bioavailability.	67
29	Famotidine (Histamine H_2 Receptor Antagonist)	Gel beads	Sodium alginate, HPMC K15M, Carbopal 943P	Emulsion gelation method	Prolonged the gastric residence time upto 8hr and improved bioavailability	68
30	Cephalexin (B-Lactum Anti Biotic)	Tablet	HPMC K100M, Citric Acid, Sodium bicarbonate	Wet granulation	Drug release over 12hr	69
31	Acyclovir (Anti Viral Drug)	Tablet	Psyllium Husk, HPMC K4M, Sodium bicarbonate	Wet granulation	Increased gastric residence time and bioavailability	70
32	Ofloxacin Hydrochloride (Anti Bacterial)	Microspheres	Ethyl Cellulose, PVP K90, Poly Vinyl Alcohol	Solvent diffusion technique	Floating microspheres of can be selected for the development of GDDS of ofloxacin hydrochloride for potential therapeutic uses	71
33	Propranolol Hydrochloride (Anti Hypertensive)	Tablet	HPMC K4M, E15LV,Hydroxypropyl Cellulose, Xanthan Gum, Sodium alginate	Direct compression	Increase bioavailability and gastric residence time	72
34	Salbutamol Sulphate (Anti Asthma)	Matrix Tablet	Hpmc, Sodium bicarbonate	Wet granulation	Increased gastric residence time upto 12hrs	73
35	Cephalexin (B-Lactum Anti Biotic)	Tablet	Hpmc K4M,Xanthan Gum, Guar Gum, Tartaricacid,Na_2CO_3	Direct compression	Drug release over 12hr	74
36	Rosiglitazone Maleate (Anti Diabetic)	Micro Sphere	Eudragit RS100, Tributylcitrate, Heavy Liquid Paraffin, Petroleum Ether	Emulsification solvent evaporation method	Control release and improved Bioavailability.	75
37	Silymarin (Anti-Oxidant)	Tablet	Psyllium Husk, HPMC K4M, K15m, Sodium bicarbonate, Crosprovidone, MCC.	Direct compression	Prolonged drug release and improved the bioavailability and patient compliance.	76
38	Metformin Hydrochloride (Anti Diabetic)	Microcapsule	Cellulose Acetate Butyrate , Eudragit	Solvent evaporation method	Enhanced absorption and improved bioavailability	77
39	Captopril (Anti Hypertensive)	Mini tablets	Sodiumbicarbonate,Eudragit RSl30D,RS30D	Direct compression	Buoyancy over a period of 12hr and controlled release properties are achieved	78
40	Atorvastatin Calcium (HMG COA Reductase Inhibitor)	Tablet	HPMC K4M, Sodium bicarbonate, Ethyl Cellulose, Bees Wax	Melt granulation technique	Drug release is over more than 8hrs	79
41	Ranitidine Hydrochloride (Histamine H_2 Receptor Antagonist)	Granules	Compritol, Gelucire 50/13,43/01,Ethyl Cellulose	Melt granulation technique	Increased Gastric residence time and better sustained effect	80
42	Carbamazepine (Anti-Convulsant)	Matrix tablet	HPMC, Sodium Bicarbonate, Ethyl cellulose	Melt granulation	Improved drug absorption and Bioavailability.	81
43	Clarithromycin	Matrix	HPMC K4M,K15M,	Wet	Increased gastric residence	82

	(Anti Biotic)	tablet	Sodium bicarbonate	granulation	time and improved bioavailability	
44	Diltiazem Hcl (Anti-Hypertensive)	Matrix Tablet	HPMC, Methocel K100MCR, Compritol 888 ATO, Sodium bicarbonate	Direct compression method	Drug release from the optimized formulation full filled official USP dissolution criteria for extended release capsule for diltiazem and marketed product	83

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