International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 324-338 www.ijprajournal.com ISSN: 2249-7781

Review Article on Floating Drug Delivery System

Dhapate Monali*, Ghodke Dhananjay, Baokar Krushna, Kamble Subodh, Kamble Rohini

Department of pharmaceutics SVPM's college of pharmacy Malegaon(bk), Baramati

Date of Submission: 01-07-2021 Date of Acceptance: 13-07-2021

ABSTRACT: Floating drug delivery systems (FDDS) or hydro dynamically 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. Floating drug delivery systems (FDDS) is to organize the recently focus on the principal mechanism of floatation to achieve gastric retention time. The recent developments of FDDS including the physiological and formulation variables affecting gastric retention, approaches to design floating systems, and their classification and formulation aspects are covered in detail. Gastric emptying of dosage forms is an extremely variable process and ability to prolong and control the gastric emptying time is a valuable asset for dosage forms, which reside in the stomach for a longer period of time than conventional dosage forms. Gastroretentive systems can remain in the gastric region for several hours for significantly prolong residence time of drugs by which improves bioavailability, reduces drug waste, and improves solubility for drugs that are less soluble in a high pH environment.

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 Gastric retention time 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. Many buoyant systems have been developed based on granules, powders, capsules, tablets, laminated films and hollow microspheres.

The current topic is undertaken to know the detail study of Floating Drug Delivery System their Formulation methods & Evaluation parameters.

Keywords: FDDS, Gastroretentive Drug Delivery System, Classification, Applications.

INTRODUCTION TO FLOATING DRUG DELIVERY SYSTEM (FDDS)

Floating drug delivery 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.[1]Floating drug delivery systems (FDDS) is to organize the recently focus on the principal mechanism of floatation to achieve gastric retention time. The recent developments of FDDS including the physiological and formulation variables affecting gastric retention, approaches to design floating systems, their classification and formulation aspects are covered in detail. Gastric emptying of dosage forms is an extremely variable process and ability to prolong and control the gastric emptying time is a valuable asset for dosage forms, which reside in the stomach for a longer period of time than conventional dosage forms. Gastroretentive systems can remain in the gastric region for several hours for significantly prolong residence time of drugs by which improves bioavailability, reduces drug waste, and improves solubility for drugs that are less soluble in a high pH environment.[2]

Factors affecting Floating Drug Delivery System:

1. Density of the Dosage Form

Dosage forms having a density lower than the gastric content can float to the surface, while high density system sink to the bottom of the stomach, both positions may isolate the dosage systems from the pylorus. Density of <1.009 g/cm^3 is required to exhibit floating property. However the floating

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 324-338 www.ijprajournal.com ISSN: 2249-7781

tendency of the dosage from 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.[3]

2. Size of the Dosage Form

Dosage form units with a diameter in the micrometer range 1 µm to 1000 µm are reported to have an increased gastric retention time.[4, 5]

3. Shape of the Dosage Form

Ring shaped and tetrahedron shaped devices have a better gastric residence tie as compared to other shapes. Tetrahedron and ring shaped devices with a flexural modulus of 48 and 22.5 kilo pounds per square inch (KSI) are reported to have better gastric retention time (GRT), 90% to 100% retention at 24 hr compared with other shapes.[4]

4. Fed and Unfed State

Under fasting conditions, the gastroretentive mobility is characterized by periods of strong motor activity or myoelectric cycle (MCC) that occurs every 1.5 to 2 hr. The myoelectric cycle (MCC) sweeps the undigested material from the stomach and if the timing of administration of the formulation coincides with that of the myoelectric cycle (MCC), the gastric retention time (GRT) of the unit can be expected to be very short. However, in the fed state, myoelectric cycle (MCC) is delayed and GRT is considered longer.[6]

5. Food Intake

Gastrointestinal tract (GIT) is longer in fed state.[7]

6. Nature, Caloric Content

The rate of gastric emptying primarily depends on the caloric content of the ingested meal. It does not differ for proteins, fats, carbohydrates as long as their caloric content is the same. Generally increase in acidity, osmolarity and caloric valve shows down gastric emptying. Gastric retention time (GRT) can be increased between 4 and 10 hr with a meal that is high in proteins and fats.[8]

7. Frequency of Meal

The gastric retention time (GRT) can increase by over 400min when successive meals are given compared with a single meal due to the low frequency of myoelectric cycle (MCC).

8. Gender

Gastric emptying rate may differ in male and female, generally the gastric emptying in female was slower than male.

9. Age

Elderly people, especially those over 70 years have a longer gastroretentive time. Thus gastric emptying time is slow down.

10. Posture

The effect of posture on gastric retention time (GRT), found no significant difference in the mean Gastric retention time (GRT) for individuals in the uprights, ambulatory and supine state. In the upright position, the floating system floated to the top the gastric content and remained for a longer time, showing prolonged gastric retention time (GRT). But the non-floating units settled to the lower part of the stomach and underwent faster emptying as a result of peristaltic contractions. The floating unit remained away from the pylorus. However, in supine position, the floating units are emptied faster than the non-floating unit of similar size.[9]

11. Disease State

In gastric ulcer, diabetes and hypothyroidism there is an increase gastric retention time (GRT). In the case of hypothyroidism and duodenal ulcers there is decrease in gastric retention time (GRT).

Approaches for Floating Drug Delivery System:

Floating System

Floating system are low- density systems that have sufficient buoyancy to float over the gastric content and remain in the stomach for a prolong period of time. After the drug is released from the stomach, the delivery system is expelled based on the buoyancy mechanism, floating system is classified as follows:[10]

1. Non- Effervescent System
2. Effervescent System

1. Non- Effervescent System

These are a type of floating gastroretentive drug delivery systems in which gel forming or highly swellable cellulose type hydrocolloids, polysaccharide and matrix forming polymers like polycarbonate, polystyrene, polymethacrylate etc. are used.[11, 12]

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 324-338 www.ijprajournal.com ISSN: 2249-7781

a. Hydrodyanamically Balanced System:

This type of system contain drug with gel forming hydrocolloids formulated into a single unit dosage form. Upon the contact with gastric fluids, the hydrocolloid swells to form a gel barrier which facilitates the system to remains buoyant in the stomach. It is shown in fig. 4.

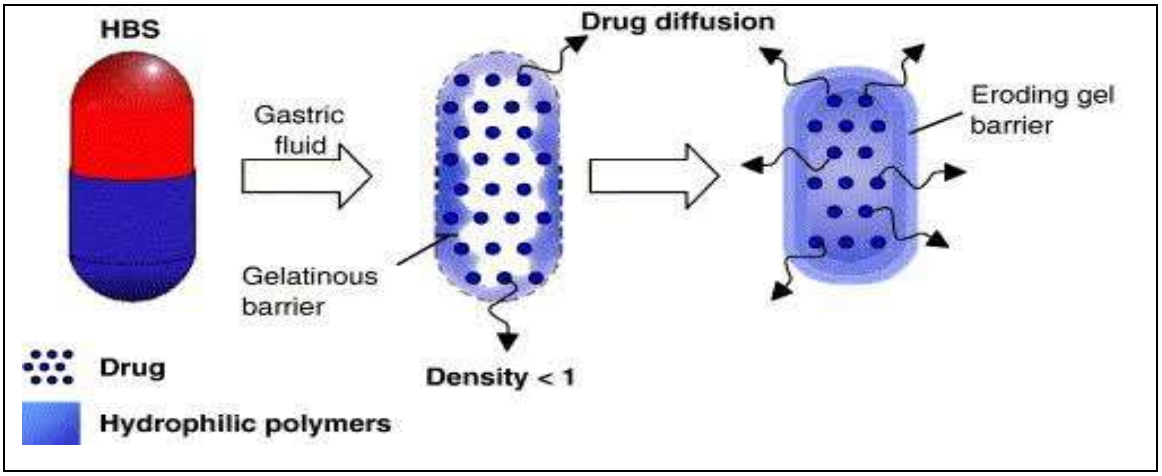

Fig. 4: Hydrodyanamically Balanced System.

b. Single Layer Floating Tablets:

This type of tablets contain drug mixed with gel forming hydrocolloids and other excipient. Which swell in contact with gastric fluid and maintain bulk density of less than one and hence remain buoyant in the stomach. It is shown in fig. 5.

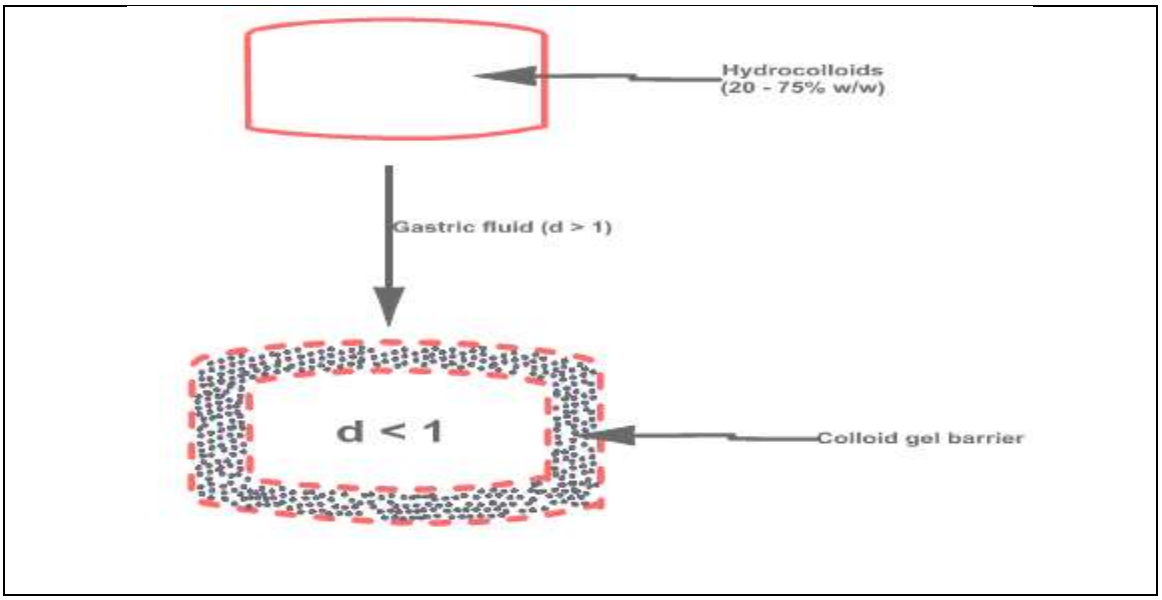

Fig. 5: Formation of Colloidal Gel Barriers.

c. Bi- Layer Floating Tablets:

This type of tablets contains two layers, one is immediate releasing layer and other is sustained release layer containing drug and hydrocolloids which remain in the stomach for a prolonged period. It is shown in fig. 6.

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 324-338 www.ijprajournal.com ISSN: 2249-7781

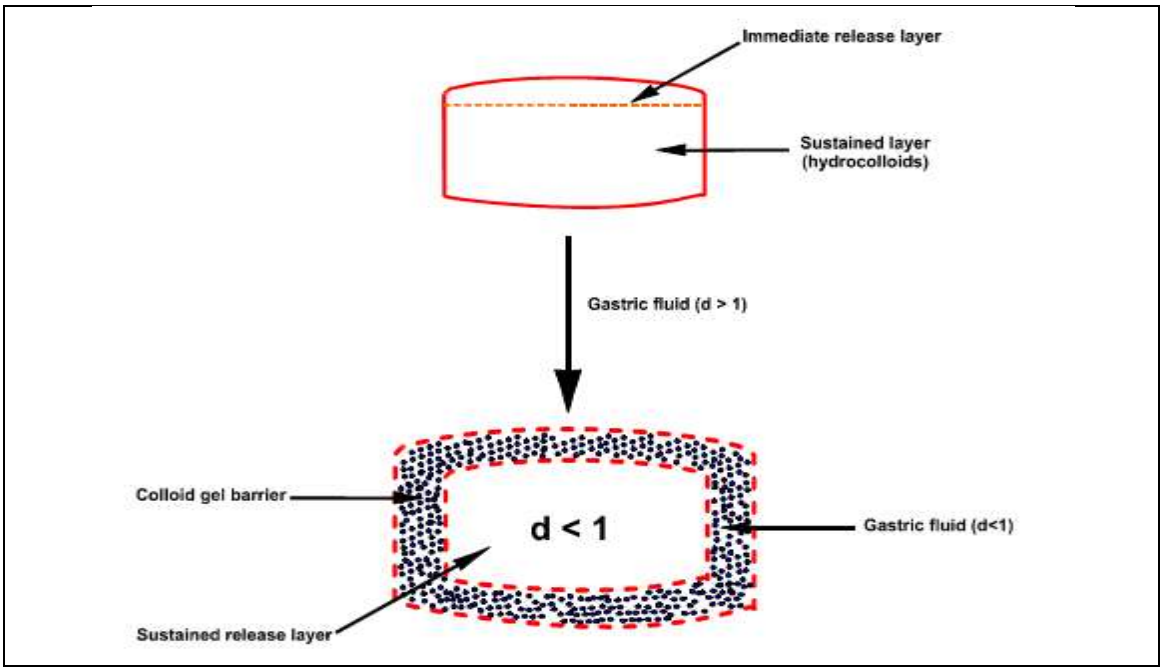

Fig. 6: Bi-Layer Floating Tablets.

d. Alginate Beads:

Talukdar and Fassihi developed multiple unit floating systems based on cross linked beads. These are formulated using calcium and low methoxylated pectin and sodium alginate. In this type sodium alginate solution is added to aqueous solution of calcium chloride which causes precipitation of calcium alginate beads. These are then separated and dried by air convection and freeze dried. This results in the formation of a porous system which remains buoyant in the stomach.

e. Microballons / Hollow Microsphere:

These systems contain outer polymer shells loaded with a drug. Polymer shells are made up of polymers like polycarbonate, cellulose acetate, calcium alginate, eudragit s, agar etc. Buoyancy lag time and drug release from the system is dependent on the quantity of polymers used in the formulations. These are prepared by emulsion solvent diffusion method. The steps are involved in fig. 7.

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 324-338 www.ijprajournal.com ISSN: 2249-7781

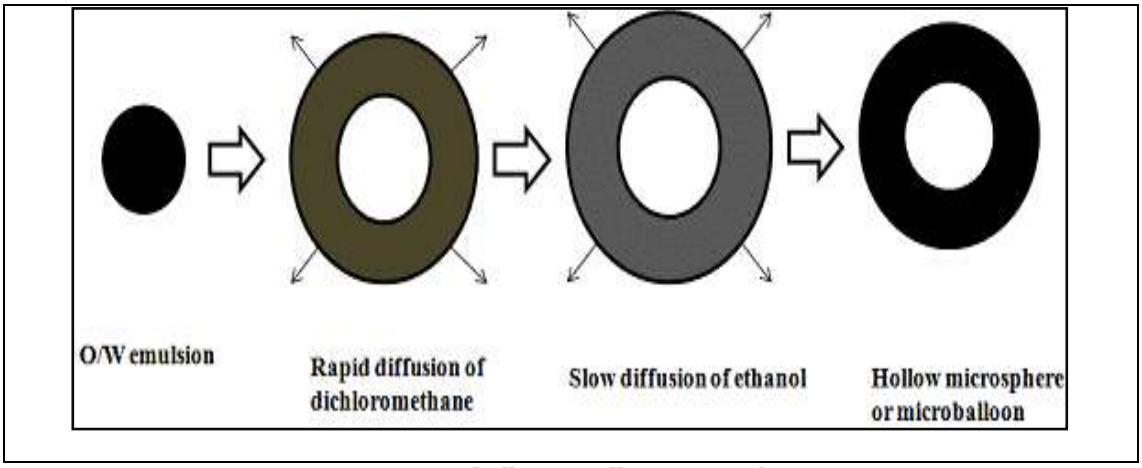

Fig. 7: Microballons / Hollow Microsphere.

2. Effervescent Systems

The main mechanism involved in this system is the production of carbon dioxide gas due to reaction between sodium carbonate, citric acid and tartaric acid. The gas produced results in the reduction of density of the system there by making it to float on the gastric fluid. These systems classified as follows.[13]

a. Gas Generating Systems
b. Volatile Liquid/Vaccume Containing Systems

a. Gas Generating Systems

These are matrix type of systems utilize effervscent compound like sodium bicarbonate, citric acid and tartaric acid. It is further divided as follows:

i. Floating Pills

These are multiple type of floating dosage system composed of effervscent layer and swellable membrane layers coated with sustained release pills. The sustained release pills are surrounded by two layers. The inner layer consists of effervscentagentsand outer layer consists of swellable membrane. The system swells due to swellable membrane and then sinks due to presence of effervscent agents, Co_2 is released and the system floats.[14]

ii. Floating Capsule

These are prepared by formulating mixture of sodium bicarbonate and sodium alginate. On exposure to acidic environment, carbon dioxide gas is generated which is trapped in the hydrating gel network and makes the system to float.

iii. Floating System Based On Ion Exchange Resins

This system involves resin beds loaded with bicarbonates and theophylline. This is then coated with ethyl cellulose which is usually insoluble but permeable to water. These causes carbon dioxide to release and the system to float.

b. Volatile Liquid/Vacuum Containing Systems

i. Intra-gastric Floating Gastrointestinal Drug Delivery Systems

These systems can be made to float in the stomach because of floatation chamber which contains vaccume or filled with air harmless gas and a microporous compartment enclosing drug reservoir. It shown in fig.8.

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 324-338 www.ijprajournal.com ISSN: 2249-7781

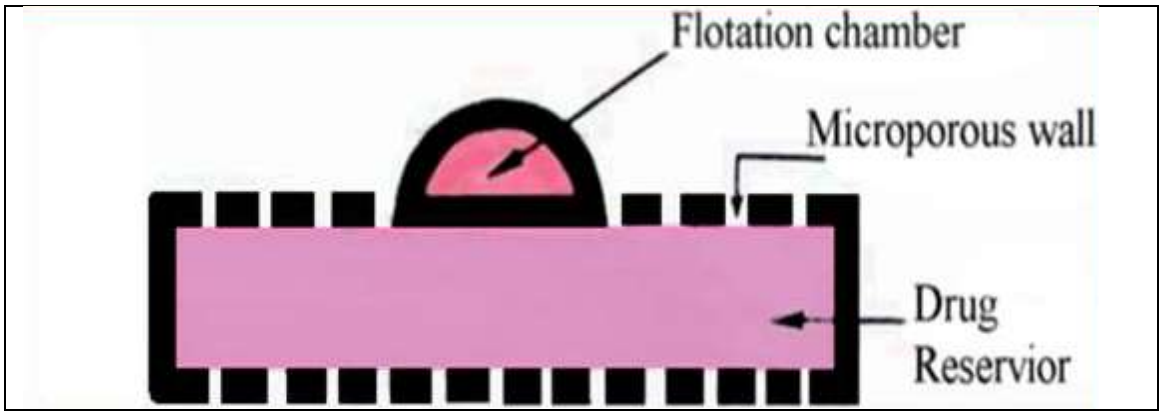

Fig. 8: Intra-gastric Floating Gastrointestinal Drug Delivery Systems.

ii. Inflatable Gastrointestinal Delivery Systems

In these systems an inflatable chamber containing liquid ether that gasifies at body temperature to inflate in the stomach. Inflatable chamber contains bioerodiable polymer filament (e.g. copolymer of polyvinyl alcohol and polyethylene) that gradually dissolves in gastric fluid and finally causes inflatable chamber to release gas and collapse. It shown in fig. 9.

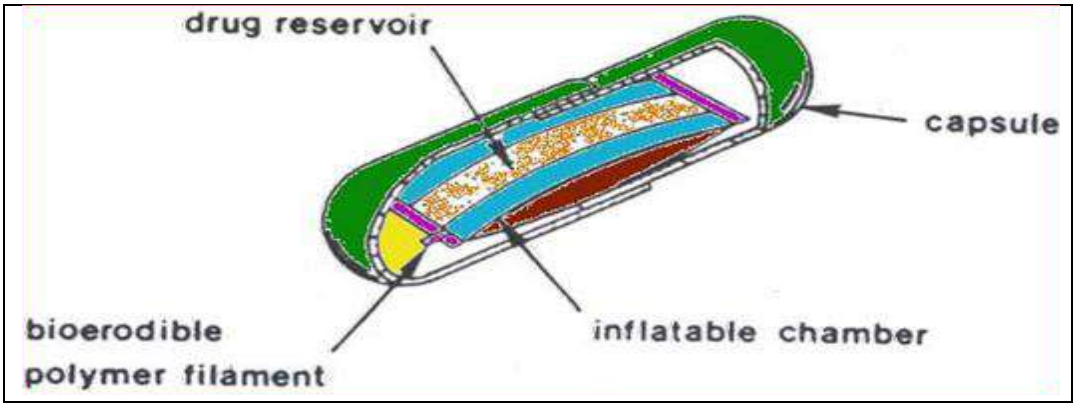

Fig. 9: Inflatable Gastrointestinal Delivery Systems.

iii. Intra-gastric Osmotically Controlled Drug Delivery Systems

It is comprised of an osmotic pressure controlled drug delivery device and an inflatable floating capsule. The osmotic pressure controlled drug delivery device consists of two components; drug reservoir compartment and osmotically active compartment. The drug reservoir compartment is enclosed by a pressure responsive collapsible bag, which is impermeable to vapour and liquid. The osmotically active compartment is enclosed by semipermiable housing. It shown in fig. 10.

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 324-338 www.ijprajournal.com ISSN: 2249-7781

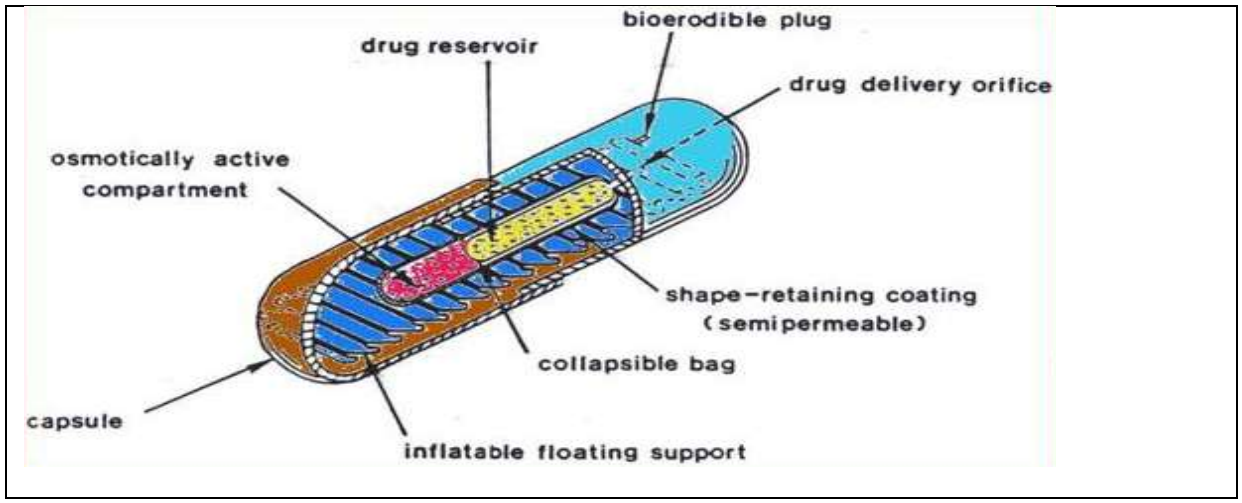

Fig. 10: Intra-gastric Osmotically Controlled Drug Delivery Systems.

ii. Non Floating System:

These are another class of gastroretentive drug delivery system which do not float but remain in the stomach for a prolonged time period. These systems are formulated by any of the following approaches.

1. Bioadhesive Systems

These types of systems adhere to the biological membrane of the stomach and maintain intimate contact with the membrane for a longer time and hence retains in stomach for its prolonged release. These systems are formulated using bioadhesive polymers.

2. Swelling Systems

These are a type of non floatinggastroretentive drug delivery system, which when enters stomach swells (due to presence of swellable polymers) to an extent that cannot pass through the pyloric sphincter leading to its retention in the stomach.

3. High Density System

These systems possess density greater than the gastric fluids due to which the system sinks to the bottom and remains in the stomach. These are formulated by coating drug on heavy inert materials like zinc oxide, titanium dioxide, iron powder, etc. It shown in fig. 11.

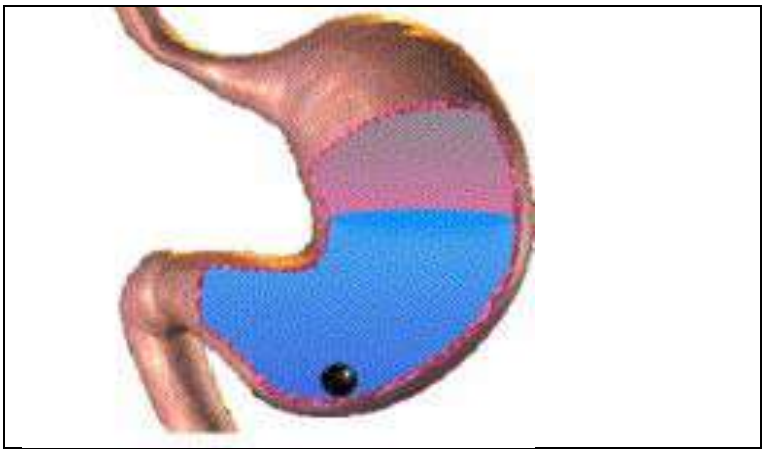

Fig. 11: High Density System.

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 324-338 www.ijprajournal.com ISSN: 2249-7781

4. Expandable Systems

These systems are capable of expanding and retain in the stomach for longer periods. These are usually formulated as a capsule containing dosage form in folded and impact form. After being exposed to stomach environment, capsule shell disintegrates and dosage form expands preventing its exit through the stomach by using suitable polymers, sustained and controlled drug delivery can be achieved.

Introduction of Floating Microsphere

Microspheres are defined as Monolithic sphere or therapeutic agent distributed throughout the matrix either as a molecular dispersion of particles or can be defined as structure made up of continuous phase of one or more miscible polymers in which drug particles are dispersed at the molecular or macroscopic level.[15,16]

Microspheres are small spherical particles, with diameters in the range (typically 1µm to 1000µm). Microspheres can be manufactured from various natural and synthetic materials. Glass microspheres, polymer microspheres and ceramic microspheres are commercially available. Solid and hollow microspheres vary widely in density and are used for different applications. Hollow microspheres are typically used as lower the density of a material. Hollow microspheres, microballoons or floating microparticles are terms used synonymously for floating microspheres. Floating microspheres are, in a strict sense, spherical empty particles without a core. These are free-flowing particles, with size ranging from 1 to 1000µm. This gastrointestinal transit-controlled preparation is designed to float on gastric juice with a specific density of less than one. This property results in delayed transit through the stomach. The drug is released slowly at desired rate, resulting in increased gastric retention with reduced fluctuations in plasma drug concentration. Various attempts have been done to retain the dosage form in the stomach as a way of increasing retention time.[17]

Method of preparation of Floating Microspheres:

The following methods are used for the preparation of floating microspheres.

A. Emulsion solvent evaporation technique
B. Emulsion cross linking technique
C. Emulsion-solvent diffusion technique
D. Emulsification heat stabilizing technique
E. Multiple emulsion method.
F. Coacervation phase separation technique
G. Spray Drying Technique
H. Polymerization technique
a) Normal polymerization
b) Interfacial polymerization
I. Ionic gelation technique

A. Emulsion Solvent Evaporation Technique

The coating polymer is dissolved in organic solvent which is immiscible with the liquid manufacturing vehicle. A core material is dissolved or dispersed in the coating phase with agitation. The above solution is dispersed in the liquid manufacturing vehicle phase to obtain the appropriate size microsphere. The mixture is then heated if necessary to evaporate the solvent, polymer shrink around the core. If the core material is dissolved in the coating polymer solution, matrix type microspheres will be formed.[18]

B. Emulsion Cross Linking Technique

This method, the drug is dissolved in aqueous solution of carrier such as gelatin which is previously heated for 1hr at 40ºC. This solution is added drop wise to oil phase such as liquid paraffin containing a suitable surfactant at a stirring speed of 1500 rpm for 10min at 3ºC. This resultant w/o emulsion is further stirred for 10 min at 15ºC. The microspheres are washed with suitable organic solvent and air dried. The formed microspheres are cross linked by dispersing in 5 ml of aqueous glutaraldehyde saturated toluene solution at room temperature at 3 hr, further treated with 100 ml of 10 mm glycine solution containing 0.1% w/v of tween 80 at 37ºC for 10 min to stop the cross linking. The main disadvantage of this method is excessive exposure of active ingredients to chemicals, when they are added at the time of preparation and then subjected to centrifugation, washing and separation. [19]

C. Emulsion-Solvent Diffusion Technique

In this method, the drug is dissolved in suitable polymer solution in ethanol and dichloromethane. This drug polymer solution is added drop wise to sodium lauryl sulphate (SLS) solution, stirred by propeller type agitator at room temperature at 150 rpm for 1hr, washed and dried in desiccator at room temperature. The floating microspheres prepared by this method have improved residence time in colon.[20]

D. Emulsification Heat Stabilizing Technique

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 324-338 www.ijprajournal.com ISSN: 2249-7781

The aqueous polymer solution is prepared by dissolving polymer (egg albumin) in water in presence of surfactant such as Tween 80 by mechanical stirring for 30min. The oil phase is prepared by mixing 20ml of suitable oil and 5 ml of diethyl ether with 1% span 80 (as a emulsifier) by magnetic stirring. Further oil phase is added to aqueous phase by stirring at 800-1000 rpm for 30 min. The above primary emulsion is added to preheated 65-70ºC oil by passing through the needle and stirred at 800-1200 rpm for 2 hrs till the solidification of microspheres takes place. The resulted microspheres suspension is cooled to room temperature by magnetic stirring, 100 ml of anhydrous ether is added. The above suspension is centrifuged for 15 min, washed with ether to remove oily trace. The obtained microspheres are then dried in desiccators overnight and stored at 4ºC in dark.[21]

E. Multiple Emulsion Method

Multiple emulsion method involves in the formation of the multiple emulsion or double emulsion type of w/o/w and is best suited water soluble drugs, peptides, protein and the vaccines. The contineous phase has generally consisted of the polymer solution that eventually encapsulated the protein contained in dispersed aqueous phase. The primary emulsion is subjected then to the homogenization results in the formation of multiple emulsions.[16]

F. Co-acervation Phase Separation Technique

In this method, the drug particles are dispersed in a solution of the polymer and an incompatible polymer is added to the system which makes the first polymer to phase separate and the drug particles. Addition of non-solvent results in the solidification of a polymer. The agglomeration must be avoided by stirring the suspension using a suitable speed stirror since as the process of microspheres formation beings the formed polymerize globules start to stick and form the agglomerates.[23]

G. Spray Drying Technique

In Spray Drying Technique, the polymer is first dissolved in a suitable volatile organic solvent. The drug in the solid form is then dispersed in the polymer solution with high speed homogenization. This dispersion is then atomized in a stream of hot air. The atomization leads to the formation of the small droplets from which the solvent evaporates instantaneously leading the formation of the microspheres in a size range 1-100µm. Microspheres are collected in cyclone separator.[24,25]

H. Polymerization technique:

1. Normal Polymerization

Normal Polymerization is carried out using different techniques as bulk, suspension, precipitation, emulsion and micellar polymerization processes. Pure polymers are formed by bulk polymerization.

2. Interfacial Polymerization

It involves the reaction of various monomers at the interface between the two immiscible liquid phases to form a film of polymer that essentially envelops the dispersed.[26]

I. Ionic Gelation Technique

In this method cross linking agent and polymers are dispersed in the purified water to form a homogeneous polymer mixture. The drug was added to the polymer dispersed and mixed thoroughly on a magnetic stirrer to form a homogeneous dispersion. The gelation medium was prepared by dissolving calcium chloride in 2% glacial acetic acid. The homogeneous alginate solution was extruded using syringe needle into the gelation medium. Then, microspheres was collected and washed with distilled water, dried at room temperature for 24hr.[13]

Polymer used in formulation FDDS

Hydrochlorides: Hydroxypropyl methylcelluloseK4M,Hydroxypropyl methylcellulose K15M, Hydroxypropyl methylcellulose100, Hydroxypropyl methylcellulose 1000,Hydroxypropyl methylcellulose 4000 , β-Cyclodextrin, Sodium alginate, Carbopol 934P, Hydroxypropyl cellulose,,Eudragit L-100, Eudragit S-100, Poly-vinyl pyrrolidone, Carboxymethyl cellulose, Chitosan, Poly vinyl alcohol,Polyethylene oxide, Polyethylene glycol, Polycarbonate, Acrylic polymer and Carbopol.

Inert fatty materials: Beeswax, fatty acids, long chain fatty alcohols.

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

Non effervescent agent: Polysaccharide, Polycarbonate, Polyacrylate.

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 324-338 www.ijprajournal.com ISSN: 2249-7781

Release rate accelerants (5%-60%): lactose, mannitol.
Release rate retardants (5%-60%): Dicalcium phosphate, talc, magnesium stearate.
Buoyancy increasing agents (upto80%): Ethyl cellulose.
Low density material: Polypropylene foam powder.[27]

Drug studies as floating microspheres

Sr No	Drug	Polymer	Method	Ref
1	Boswellic acid	Ethylcellulose, Hydroxypropylmethylcellulose	Solvent Evaporation Method	28
2	Famotidine	Ethylcellulose, Hydroxypropylmethylcellulose	Solvent Evaporation Method	29
3	Flupirtine maleate	Ethylcellulose, Hydroxypropylmethylcellulose	Solvent Evaporation Method	30
4	Metformin HCL	Eudragit RS 100, Hydroxypropylmethylcellulose	Emulsion Solvent Evaporation Method	31
5	Acebutolol	Acrycoat S100, Cellulose acetate, Eudragit S100	Solvent Diffusion-Evaporation Method	32
6	DextromethophanHcL	Ethylcellulose, Hydroxypropylmethylcellulose	Emulsion Solvent Evaporation Method	33
7	Captopril	Hydroxypropylmethylcellulose K4M	Solvent Evaporation Method	34
8	Nateglinide	Ethylcellulose, Eudragit S100	O/W Emulsion Solvent Evaporation Method	35
9	Cefdinir	Ethylcellulose, Eudragit, Hydroxypropylmethylcellulose	Solvent Evaporation Method	36
10	Curcumin	Ethylcellulose,EudragitS100, Hydroxypropylmethylcellulose	Emulsion Solvent Diffusion Method	37
11	Repaglinide	Ethylcellulose, Hydroxypropylmethylcellulose	Solvent Diffusion-Evaporation Method	38
12	Norfloxacin	Ethylcellulose, Hydroxypropylmethylcellulose	Non Aqueous Solvent Evaporation Method	39
13	Amoxicillin	Ethylcellulose, Hydroxypropylmethylcellulose	Emulsion Solvent Diffusion Method	40
14	Misoprostol	Ethylcellulose, Hydroxypropylmethylcellulose K100M	Emulsion Solvent Evaporation Method	41

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 324-338 www.ijprajournal.com ISSN: 2249-7781

15	Meclizine HCL	Eudragit RL 100, Hydroxypropylmethylcellulose K15M	Emulsion Solvent Evaporation Method	42
16	Lansoprazole	Ethylcellulose, Hydroxypropylmethylcellulose	Non Aqueous Solvent Evaporation Method	43
17	Clarithromycin	Ethylcellulose	Solvent Evaporation Method	44
18	Glipizide	Acrycoat, Ethylcellulose, Eudragit	Emulsion Solvent Diffusion Method	45
19	Stavudine	Eudragit RS 100	Emulsion Solvent Diffusion Method	46
20	Aceclofenac	Ethylcellulose, Hydroxypropylmethylcellulose	Emulsion Solvent Diffusion Method	47
21	Orlistat	Cellulose acetate, Ethylcellulose, Eudragit RL100,	Solvent Diffusion-Evaporation Method	48
22	Ranitidine HCl	Chitosan,Ethylcellulose	Emulsion Solvent Diffusion Method	49
23	Valsartan	Ethylcellulose, Eudragit	Solvent Evaporation Method	50
24	Amlodipine besylate	Ethylcellulose, Hydroxypropyl methylcellulose	Solvent Evaporation Method	51
25	Salbutamol sulfate	Eudragit L 100	Solvent Evaporation Method	52
26	Rosiglitazone	Guargum, Xanthan gum	Ionotropic Gelation Method	53
27	Cimetidine	Ethylcellulose, Hydroxypropylmethylcellulose	Solvent Evaporation Method	54
28	Indometacin	Eudragit RS100, Eudragit S100	Emulsion Solvent Diffusion Method	55
29	Ketoprofen	Ethylcellulose, Hydroxypropylmethylcellulose	Emulsion Solvent Diffusion Method	56
30	Metoprolol succinate	Eudragit S100	Non Aqueous Solvent Evaporation Method	57
31	Dasatinib	Ethylcellulose, Eudragit S100	Emulsion Solvent Diffusion Method	58
32	Glibenclamide	Ethylcellulose, Eudragit RS100, Hydroxypropylmethylcellulose	Solvent Diffusion-Evaporation Method	59
33	Sitagliptin Phosphate	Eudragit RS 100, Hydroxypropylmethylcellulose	Non Aqueous Solvent Evaporation Method	60
34	Tolperisone HcL	Ethyl cellulose,	Non Aqueous Solvent	61

		Hydroxypropylmethylcellulose 15 cPs	Evaporation Method	
35	Clarithromycin	Albumin, chitosan	Heat Stabilization Method	62
36	Lamivudine	Hydroxypropylmethylcellulose, Sodium alginate	Ionotropic Gelation Method	63
37	Ketoprofen	Eudragit L 100, Eudragit S 100	Emulsion Solvent Diffusion Method	64
38	Verapamil HCL	Ethylcellulose, HydroxypropylmethylcelluloseK4M , HydroxypropylmethylcelluloseK15M	Emulsion Solvent Evaporation Method	65
39	Ibuprofen	Ethylcellulose	Solvent Evaporation Method	66
40	Cefuroxime axetil	Carbopol 934, Sodium alginate	Ionic Gelation Method	67
41	Rabeprazole	Ethyl cellulose, Hydroxypropylmethylcellulose	Emulsion Solvent Evaporation Method	68
42	Pioglitazone HCL	Hydroxypropylmethylcellulose	Ionotropic Gelation Method	69
43	Ofloxacin	Ethylcellulose,HydroxypropylmethylcelluloseK4M &K15M	Non Aqueous Solvent Evaporation Method	70

REFERENCES

[1]. Ishwarya M, Ramu S, Kumar S. Floating Microspheres a Promising Drug Delivery. Int J Pharm and Pharma Res 2017; 11(1):375-388.
[2]. Shah S, Patel J, Pate N. Stomach Specific Floating Drug Delivery System. Int J Pharm Tech Res 2009;1(3):623-633.
[3]. Joshi V, Jaimini M. Review On: Floating Multi-Particulate Oral Drug Delivery Systems. Int Res J Pharm. 2012; 3(2): 59-63.
[4]. Kataria S, Middha A. Review On: Floating Drug Delivery System. Int Res J Pharm. 2011; 2(9): 18-24.
[5]. Badoni A, Ojha A, and Kothiyal P. Review on: Gastro Retentive Drug Delivery System. Pharm Innov.2012; 1(8): 32-42.
[6]. Jayanthi C, Joshi H. Buoyant Drug Delivery Systems. World J Pharm and Pharma.2012; 1(3): 1210-1225.
[7]. Dwivedi S, Kumar V. Floating Drug Delivery Systems A Concept of Gastro Retentive Dosage Form. Int J Res Pharma and Biomed Sci. 2011; 2(4): 1413-1426.
[8]. Nayak AK, Maji R, and Das B.Review On: Gastro Retentive Drug Delivery Systems. Asn J Pharma and Clinical Res. 2010; 3(1): 2-10.
[9]. Narang N. Review On: Floating Drug Delivery System. Int J App Pharma. 2011;3(1):1-7.
[10]. Kavitha S, Peeyush KM, Anil B, Akanksha G and Navneet G. Review On: Floating Microsphere as Gastro Retentive Drug Delivery Systems. World J Pharma Res. 2015;4(3):668-684.
[11]. Kristal J, Vreer F, Zorko B. Optimisation of Floating Matrix Tablet and Evaluation of their Gastric Residence Time. Int J Pharm. 2000; 1(95): 125 – 130.
[12]. Chien YW. Rate-controlled Drug Delivery Systems. Ind J Pharm Sci. 1988; 63-65.
[13]. Ishwarya M, Ramu S, Kumar S. Floating Microspheres a Promising Drug Delivery. Int J Pharm and Pharma Res.2017; 11 (1): 375-388.
[14]. Rathor S, Ram A. Porous Microspheres of 5-Fluorouracil for Site Specific Drug Delivery System. Int J Pharma Res. 2011; 3(1): 38-42.

[15]. Shivhare U.D., Tijare P.M. Formulation and characterization of Microspheres of selected Anti-infective agent for Urinary tract Infection. Journal of drug delivery research. 2013;2 (1),16-26.
[16]. Ramteke K.H, Jadhav V.B, Dhole S.N. Microspheres: as carriers used for novel drug delivery system. IOSR Journal of Pharmacy. July 2012; 2(4), 44-48.
[17]. Saxena A, Gaur K, Singh V. Floating Microspheres Drug Delivery System. American J Pharm &Pharma Sci. 2014; 1(2): 27-36.
[18]. Majeed A, Khan MR, Ranjha NM. Microspheres A Potential Carrier for Drug. Pak J Pharma Res. 2015; 1(1):19-24.
[19]. Chakradhari MK, Khinchi MP, Gupta MK. Review On: Colon Targeting Microspheres. Asian J PharmaEduAnd Res. 2012; 1(2): 16-30.
[20]. Sudheer P, Kumar H, Thomas L. Floating Microspheres an Excellent Approach for Gastric Retention. J Pharma Res. 2015; 14(4): 71-80.
[21]. Phalguna Y, Venkateshwarlu BS, Gudas GK. HPMC Microspheres of Zidovudine for Sustained Release. Int J Pharm and Pharma Sci. 2013; 2(4): 41-43.
[22]. Ramteke KH, Jadhav VB, Dhole SN. Microspheres as Carriers Used for Novel Drug Delivery System. J Pharm. 2012; 2(4): 44-48.
[23]. Kapil K, Rai AK.Floating Microspheres an Innovative Approach for Gastro Retention. J Pharm Res. 2012; 5(2): 883-886.
[24]. Bansal H, Kaur SP, Gupta AK. Microsphere Methods of Preparation and Applications A Comparative Study. Int J PharmaSci Rev and Res. 2011; 10(1): 1-18.
[25]. Verma NK, Vishwakarma DK, Mishra JN. Recent Advances in Microspheres Technology for Drug Delivery. Int J Pharm Sci Nanotech. 2015; 8(2): 2799-2813.
[26]. Gayathridevi M, Nesalin A, Mani T. Review On: Floating Microspheres. Int J Res Pharm and Chem. 2016; 6(3): 501- 510.
[27]. Badola A, Kothiyal P. Gastroretentive Drug Delivery System. Int J Res And Rev In Pharm And Life Sci. 2016; 5(4): 2178-2187.
[28]. Fartyal S, Singh M, Gupta R. Formulation and Evaluation of Floating Microspheres of Boswellic acid. Int J Pharm Tech Res 2011;1(3): 76-81.
[29]. Singh B, Kanoujia J, Pandey M. Formulation and Evaluation of Floating Microspheres of Famotidine. Int J Pharm Tech Res 2010;2(2):1415-1420.
[30]. Sony A, Jain S. Formulation & Evaluation of Floating Microspheres of Flupirtine Maleate. Int J Pharm & Life Sci. 2013; 4(4): 2535-2540.
[31]. Dubey M, Kesharwani P, Tiwari A. Formulation and Evaluation of Floating Microsphere Containing Anti Diabetic Drug Int J Pharma and Chem Sci 2012;1(3):1387-1396.
[32]. Kusuma D. Formulation and Evaluation of Floating Microspheres of Acebutolol. Int J Pharm Sci Rev Res 2017;46(1):31-36.
[33]. Perumandla PK. Formulation and In-vitro Evaluation of Floating Microspheres of Dextromethorphan Hydrobromide. Int J Pharm and Pharma Sci 2014;6(4): 206-210.
[34]. Kapoor D, Patel R. Formulation, Optimization and Evaluation of Floating Microspheres of Captopril. Asian J Biomedical and Pharm Sci 2012;2(9): 1-10.
[35]. Pandey N, Sah A, Mahara K.Formulation & Evaluation of Floating Microspheres of Nateglinide Int J Pharma Sci and Res 2016;7(11):453-464.
[36]. Goud AK, Kumar AD Preparation and Evaluation of Floating Microspheres of Cefdinir in Treatment of Otitis Media and Respiratory Tract Infections. J Pharmacovigilance 2016;4(3):1-4.
[37]. Kumar K, Rai AK Development and Evaluation of Floating Microspheres of Curcumin. Tropical J Pharma Res 2012; 11 (5): 713-719.
[38]. Sharma M, Kohli S. Floating Microspheres of Repaglinide Formulation, Optimization, Characterization and In–vitro Evaluation. Int J Chem Sci 2014; 12(4): 1259-1272.
[39]. Ramesh Y, Balachandra P, Chinnaiah S. Formulation and Evaluation of Floating Microspheres of Norfloxacin. Res J Chem Env Sci 2013;1(4): 18-28.
[40]. Goyal MK, Mehta SC. Preparation and Evaluation of Calcium Silicate Based Floating Microspheres of Amoxicillin. J Applied Pharm Sci 2011;1(4):137-141.

[41]. Kondi V, Varma M. Formulation and Evaluation of Floating Microspheres ofMisoprostol Int J Pharm Sci and Nanotech 2017; 1(10):3608-3615.
[42]. Rabab AH, Marwa HA. Formulation and Evaluation of Sustained Release Floating Microspheres. Int J Trend Res and Dev 2017;4(3):356-359.
[43]. David B, Anbazhagan S. Formulation and In vitro Characterization of Lansoprazole Floating Gastroretentive Microspheres by Modified Non Aqueous Solvent Evaporation Method. Der Pharma Chemica 2010; 2(5): 419-425.
[44]. Bathini ST. Formulation and In-vitro Evaluation of Clarithromycin Floating Microspheres for Eradication of Helicobacter Pylori. Der Pharmacia Lettre 2011; 3(6):90-101.
[45]. Sarode SM, Magar RM. Formulation and Evaluation of Floating Microspheres of Glipizide. J Chem Pharm Res 2011; 3(3):775-783.
[46]. Josephine LJ, Wilson B, Shanaz B. Formulation and In-vitro Evaluation of Floating Microspheres of Anti Retroviral Drug as A Gastroretentive Dosage Form. Int J Res Pharm and Chem 2011;1(3):520-527.
[47]. Sivakumar T, Rathi J. Preparation and Evaluation of Aceclofenac Floating Oral Delivery System. Der Pharmacia Sinica 2011;2 (5):43-53.
[48]. Kumar V, Jalwal P. Formulation and Evaluation of Floating Microspheres of Ranitidine Hydrochloride. Int J Pharma Professional Res 2014;2(5):1008-1015.
[49]. Kaushik AK, Tiwari AK. Preparation of Floating Microsphere of Valsartan In-vitro Characterization. Int J Res Ayurveda Pharma 2015;6(1):124-130.
[50]. Mazumder R, Sharma M, Mishra A. Formulation and Evaluation of Floating Microspheres of Amlodipine Besylate . Pharmacophore 2014;5 (4):602-609.
[51]. Bhattacharjee RP, Kausalya J. Formulation and In vitro Evaluation of Salbutamol Sulphate Floating Microspheres. Indo American J Pharm Res 2013;3(2):1178-1184.
[52]. Ramu S, Suresh P, Ramakrishna G. Formulation and Evaluation of Floating Microspheres ofRosiglitazone. Int J Pharm, Chem and Bio Sci. 2015; 5(4): 907-918.
[53]. Kumar A. Floating Microspheres of Cimetidine: Formulation, Characterization and In vitro Evaluation. Acta Pharm. 2005;55:277–285
[54]. Bhardwaj P, Chaurasiya H. Formulation and In vitro Evaluation of Floating Microballons of Indomethacin. Acta Poloniae Pharm Drug Res. 2010;3(67):291-298.
[55]. Hafeez A, Maurya A, Singh J.In-vitroEvaluation of Floating Microspheres of Ketoprofen. J Scientific and Inno Res 2013; 2 (3): 714-722.
[56]. Nadigoti J, Dharani S, Yamsani M. Formulation and Evaluation of Floating Microspheres of Metoprolol Succinate. Asian J Pharm and Clinical Res. 2011;4(1):132-135.
[57]. Kodithyala M, Sudhamani K. Formulation and Evaluation of Dasatinib Floating Microspheres. Int J Inno Pharm Sci and Res. 2014;2(9):2086-2105.
[58]. Taneja R, Kataria MK, Bilandi A. Formulation and Evaluation of Floating Microspheres of Glibenclamide. Int J Pharm Res.2014;3(2):48-57.
[59]. Vadaliya SK, Desai HT. Formulation and In-vitroEvaluation of Floating Microspheres of Anti Diabetic Drug Prepared by Solvent Evaporation Method. Int J Pharm and Chem Sci. 2013;2(1):397-403.
[60]. Jani P, Vadalia K, Dedania R. Formulation and Evaluation of Controlled Release Floating Microspheres of Tolperisone Hydrochloride. Asian J Pharm 2012;190-197.
[61]. Sarojini S, Kumar A. Formulation and Evaluation of Albumin Chitosan Floating Microspheres Containing Clarithromycin and Estimation by Spectrophotometric Method. Res J Pharm, Bio and Chem Sci. 2010;1(2):207-214.
[62]. Reddy RB, Malleswari KP. Preparation and In vitro Evaluation of Lamivudine floating Sodium Alginate Beds. Int J Pharm and Clinical Res. 2012;4(4):81-88.
[63]. Najmuddin M, Shelar S, Ali A. Formulation and In- vitroEvaluation of Floating Microspheres of Ketoprofen Prepared by Emulsion Solvent Diffusion Method. Int J Appl Pharm. 2010;2(1): 13-17.

[64]. Reddy B, Navaneetha G. Formulation Development and In- vitroEvaluation of Gastroretentive Floating Microspheres of Verapamil Hydrochloride. J Pharm and Sci Innov. 2015; 4(3):183-189.
[65]. Verma NK, Mishra JN, Alam J. Formulation and Characterizationof Floating Microspheres of Ibuprofen. Int J Res Pharm Sci 2015; 5(1):18-22.
[66]. Chorghe LS, Deshmukh MT. Formulation and Evaluation of Gastroretentive Cefuroxime Axetil Floating Microspheres.European J Pharm and Med Res. 2017; 4(9):380-385.
[67]. Rao N, Kumar A. Formulation and Evaluation of Rabeprazole Microspheres. Int J Pharma and Bio Sci. 2013;3(2):504-516.
[68]. Pandey A, Bhadoria V. Formulation Development and Optimization of Pioglitazone Hydrochloride Microspheres Using Ionotropic Gelation Technique. Pharmacia. 2011; 1(2):67-72.
[69]. Nethaji R, Pattaratte S, Palanivelu M. Development and Evaluation Gastroretentive Floating Microspheres of Ofloxacin. Asian J Pharm and Hea Sci. 2015;5(1):1193-1202.