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A BUOYANT APPROACH FOR RETENTIVE DRUG DELIVERY: FLOATING MICROSPHERES

Soniya Kashyap*, Shikha Yadav, Popin Kumar, Tulsi Bisht

Gyani Inder Singh Institute of Professional Studies, Opp.Malsi Dear Park, Post Sinola, Dehradun, Uttarakhand, 248003, India.

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ABSTRACT

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. Several approaches are currently being used to prolong the GRT, including floating drug delivery systems (FDDS), also known as hydrodynammically balanced systems (HBS), swelling and expanding systems, high density systems, and other delayed gastric emptying devices. The methodologies used in the development of FDDS by formulating effervescent and non-effervescent floating tablet based on buoyancy mechanism. Floating drug delivery systems (FDDS) was to organize the recently focus on the principal mechanism of floatation to achieve gastric retention time. This review article on FDDS includes the different types of FDDS, polymers used in formulation of FDDS, methods for manufacturing of granules, evaluation parameters.

Corresponding author
Soniya Kashyap
Gyani Inder Singh Institute of Professional Studies,
Opp.Malsi Dear Park, Post Sinola, Dehradun,
Uttarakhand, 248003, India.
kashyapsoniya1009@gmail.com
+91 9720095411, 8279719232

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INTRODUCTION

A tablet is a pharmaceutical dosage form. Tablet may be defined as the solid unit dosage form of medicament or medicaments with or without suitable diluents. An ideal tablet should be free of defects such as cracks, chips, discoloration contamination. Tablet may be manufactured by various methods viz.dry granulation, wet granulation, or direct compression depending upon the nature of medicament. It comprises a mixture of active substances and excipients, usually in powder form, pressed or compacted from a powder into solid dose. The Excipients can include diluents, binders or granulating agents, glidants and lubricant.

Gastro retentive Drug Delivery System

Gastro retentive dosage forms (GRDFs) are being used from a very long time to improve therapy with several important drugs. GRDFs greatly improves the pharmacotherapy of stomach by releasing the drug locally and thus results into high concentration of drug at the gastric mucosa which can be sustained over a longer duration of time. Prolonged gastric retention improves bioavailability, reduces drug waste and improves solubility for drugs that are less soluble in a high pH environment. It has application also for local drug delivery to the stomach and proximal small intestine. Gastro retention helps to provide better availability of new products with new therapeutic possibilities and therapeutic are highly benefited. Such retention system (i.e .GRDDS) is important for the drugs that are degraded in intestine or for drugs like antacids or certain enzymes that should act locally in the stomach.

Floating Drug Delivery System

FDDS are also called gastro retentive system. Prolonged time improves bioavailability reduce drug waste, increased solubility for drugs that are less soluble in a high pH environment.That has an absorption window in the stomach or in the upper part of small intestine.

Floating drug delivery systems [FDDS] 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 afecting 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 result is an increased Gastric retention time and a better control of the fluctuations in plasma drug concentration.[(1,2)]

Advantages of FDDS

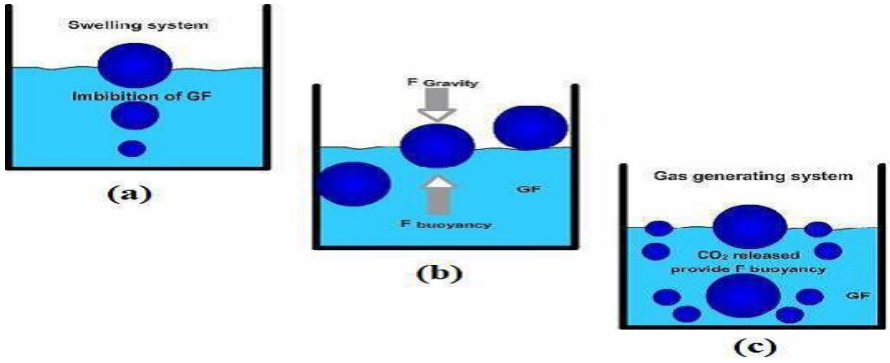
- FDDS are advantageous for drugs meant for local action in the stomach.
- Improved drug absorption.
- Minimizing the mucosal irritation.
- Treatment of gastrointestinal disorders.
- Enhancement of the bioavailability for drugs which can metabolized in the upper GIT.
- Improves patient compliance by decreasing dosing frequency.
- Gastric retention time is increased because of buoyancies can be achieved.
- Better therapeutic effect of short half-life drug.
- Drug release in controlled manner for prolonged period.

Disadvantage of FDDS

- Drug can cause irritation and lesion to gastric mucosa are not suitable to be formulated as floating drug delivery systems.
- These systems also require the presence of food to delay their gastric emptying.
- One of the advantages of floating drug delivery system is that they require a sufficiently high level of fluids in the stomach, so that the drug dosage from float therein and work efficiently.
- Floating system is not suitable for these drugs that have solubility and stability problem in G.I.T.
- These systems require a high level of fluids in the stomach for drug delivery to float and work, efficiently-coat, water.
- Some drugs present in the floating system cause irritation to gastric mucosa.
- Drugs, which are irritant to Gastric mucosa, are also not desirable.

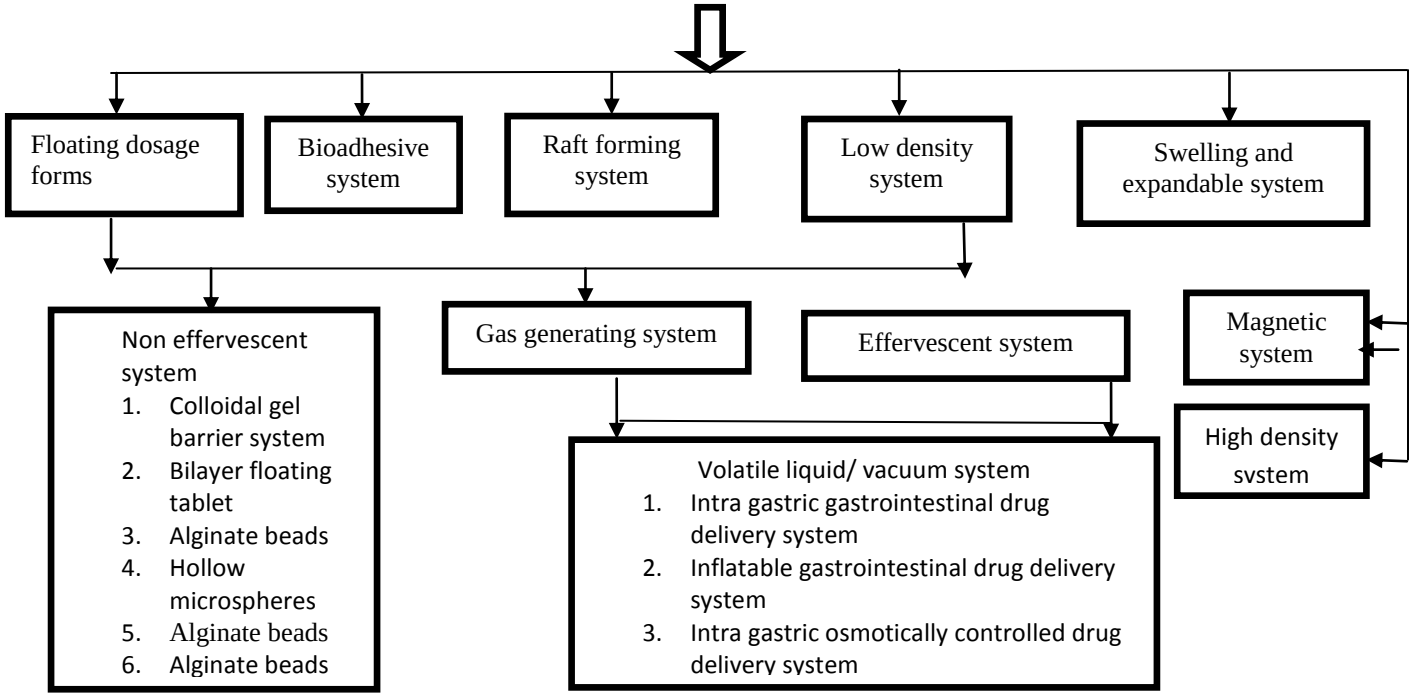
Mechanism of Floating Drug Delivery System-

While the system is floating on the stomach, the drug is released gradually at the desired rate from system.After releasing drug, the residual system is flattened from the stomach besides a minimal gastric content needed to permit suitable attainment of the buoyancy retention principle, a minimal level of floating force (F) is also essential to retain dosage form constantly buoyant on surface of the meal.[(4,6)] If F is on the higher positive side, object floats better. The apparatus helps in optimizing floating drug delivery system with respect to floating forces formed in order to stop the problems of unexpected intragastric buoyancy capability variation.[Fig: 1.].



[Fig: 1.] Mechaism of Floating system.

CLASSIFICATION OF FLOATING DRUG DELIVERY SYSTEM



Floating Dosage Form

The bulk density of this gastric fluids and therfore, remains buoyant in the stomach without causing any effect on the gastric emptying rate for a long time period. The drug release slowly while the system is floating on the gastric stomach. After drug is released, the residual system is emptied from the stomach. This result is an increased GRT and a better control of the fluctuation in plasma drug concentration.

Non-effervescent System

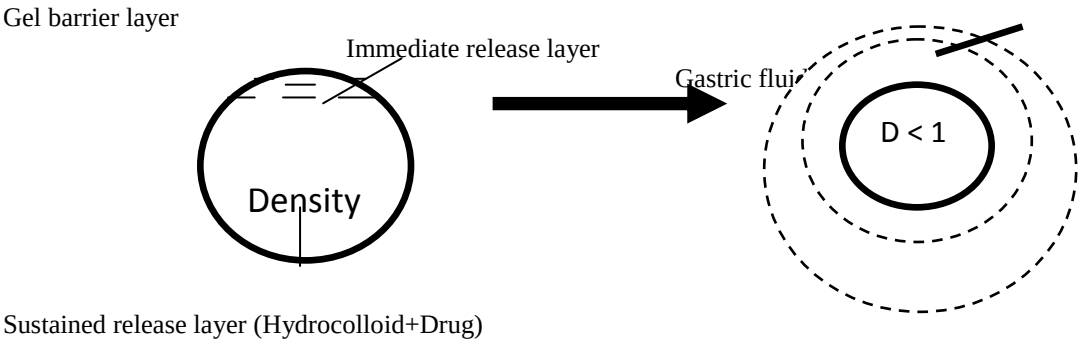
Non-effervescent FDDS use a gel forming [or] swellable cellulose type of hydrocolloids, polysaccharide, matrix forming polymer like polycarbonate, polymethacrylate and polystyrene. One of the formulation methods involves the mixing of the drug with gel forming hydrocolloids which swell in contact with gastric fluid after oral administration and maintains integrity of shape and a bulk density barrier, the air trapped by swollen polymer confer buoyancy to the dosage forms.

Colloidal gel barrier system

These systems incorporate a high level (20-75% w/w) of one or more gel forming, highly swellable, cellulose type hydrocolloids, polysaccharides and matrix forming polymers. Oncoming in contact with gastric fluid, the hydrocolloids in the system hydrate and form a colloidal gel barrier around its surface.[8,12]

Bilayer floating tablet

A bi-layer tablet contain two layer one immediate release layer which release initial dose from system while the another sustained release layer absorbs gastric fluid, forming an impermeable colloidal gel barrier on its surface, and maintain a bulk density of less than unity and thereby it remains buoyant in the stomach.[Fig: 2.].



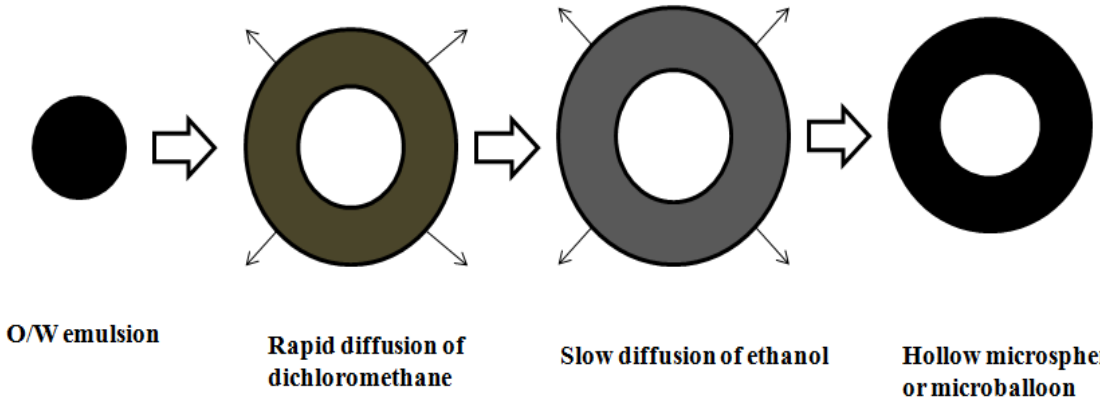
[Fig: 2.] Bilayered HBS Showing the gel barrier layer.

Alginate Beads

Freeze dried calcium alginates have been used to develop multi unit floating dosage froms. By dropping sodium alginate solution into aqueous solution of calcium chloride spherical beads of about 2.5mm diameter can be prepared. These beads are separated and air dried. This results in the formation of aporous system which remains buoyant in the stomach.

Hollow Microspheres

Hollow microspheres are considered as one of the most promising buoyant systems as they possess the unique advantages of multiple-unit system and good flow properties. The general techniques involved in their preparation include simple solvent evaporation or solvent diffusion and evaporation. Polymers such as polycarbonate, cellulose acetate, calcium alginate are used in the preparation of hollow microspheres and buoyancy and drug release from dosage form are dependent on amount of polymers, the plasticizer polymer ratio and the solvent used for formulation.[Fig: 3.]



[Fig:3.] Formulation of Floating hollow microsphere or microballoon.

Effevescent System

A drug delivery system can be made to float in the stomach by incorporating a floating chamber which may be filled with vacuum, air or inert gas.The gas in the floating chamber can be introduced either by the volatilization of an organic solvent or by the effervescent reaction between organic acid and bicarbonate salts. These are matrix types of systems prepared with the help of swellable polymers such as methylcellulose and chitosan and various effervescent compounds, eg, 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 liberate and gas entrapped in swollen hydrocolloids which provides buoyancy to the dosage forms.

Gas generating system

These buoyant delivery systems utilizes effervesce between carbonate/ bicarbonate salts and citric/tartaric acid to liberate CO_2, which gets entrapped in the jellified hydrocolloids layer of the system, thus decreasing its specific gravity and making it float over chime.

Volatile liquid containing system

The GRT of a drug can be sustained by incorporating an inflatable chamber, which contains a liquid e.g. ether, cyclopentane, that gasifies at body temperature to cause the inflation of the chamber in the stomach. These devices are osmotically controlled floating systems containing a hollow deformable that can convert from a collapsed to an expanded position, and returns to the same position after an extended period. The deformable system consists of two chambers separated by an impermeable, pressure-responsive movable bladder. The first chamber contains the drug and the second chamber contains the volatile liquid. The device may also consist of a biodegradable plug made of PVA, polystyrene etc that gradually dissolves causing the inflatable chamber to release gas and collapse a predetermined time to permit the spontaneous ejection of the inflatable system from the stomach.

Bioadhesive System

The term bioadhesion is defined to biological surface i.e. mucus and/or mucosal surface. In instances when the polymeric system interacts with mucus layer only, it is referred as mucoadhesion.In order to develop an ideal oral bioadhesive system, it is important to have a through understanding of mucosa, bioadhesive polymers and mucin-polymers interaction in the physiological environment. Intestinal mucosa is composed of high molecular weight glycoproteins hydrated and covering the mucosa with a continuous adherent blanket.The mucus layer is created biologically to play a number of important functions of protecting the underlaying tissues from various diffusing/corrosive element such as enzymes, acid and other toxic molecules.

Raft Forming System

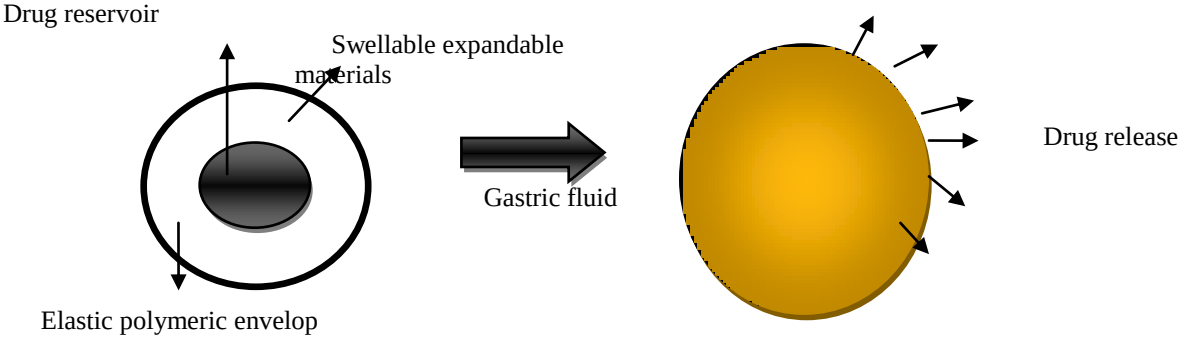
Raft forming systems have received much attention for the delivery of antacids and drug delivery for gastro-intestinal and other disorders. The mechanism involved in the raft formation includes the formation of a viscous cohesive gel in contact with gastric fluids, wherein each portion of the liquid swells forming a continuous layer called a raft. This raft floats on gastric fluid because of the low bulk density created by the formation of CO_2. Usually, the system contains a gel forming agent and alkaline bicarbonates or carbonates responsible for the formation of CO_2 to make the system less dense and able to float on the gastric fluids.

Low Density System

Gas-generating systems inevitably have a lag time before floating on the stomach contents, during which the dosage form may undergo premature evacuation through the pyloric sphincter. Low density systems (<1 g/cm^3) with immediate buoyancy have therefore been developed. They are made of low-density materials, entrapping oil or air. Generally, techniques used to prepare hollow microspheres involve simple solvent evaporation or solvent diffusion methods. Polycarbonate, cellulose acetate, calcium alginate, agar are commonly used as polymers.

Swelling and Expandable System

Swellable systems are also retained in the gastro intestinal tract (GIT) due to their mechanical properties. The swelling is usually results from osmotic absorption of water and the dosage form is small enough to be swallowed by the gastric fluid.[Fig: 4.]



[Fig: 4.] Drug release from swellable system.

Magnetic System:

These systems appear as small gastroretentive capsules containing a magnetic, whose elimination from the stomach is prevented by the interaction with a sufficiently strong magnet applied to the body surface in the region of the stomach.

High Density Systems:

Gastric contents have a density close to water (1.004g/cm^3). When the patient is upright small high-density pellets sink to the bottom of the stomach where they become entrapped in the folds of the antrum and withstand the peristaltic waves of the stomach wall.Excipients used in high-density systems are barium sulphate, zinc oxide, iron, powder, titanium dioxide.[13,16].

Material used mainly

- ✓ Hydroxypropyl methyl cellulose
- ✓ Methyl cellulose
- ✓ Microcrystalline cellulose
- ✓ Sodium bicarbonate
- ✓ Magnesium stearate

Table 1: Marketed products of FDDS.

S.N	Product	Active Ingredients
1	Madopar	Levodopa and benserzide
2	Valrelease	Diazepam
3	Topalkan	Aluminum magnesium Antacid
4	Almagate	Flatcoat Antacid
5	Liquid gavi-son	Alginic acid and sodium bicarbonate

Polymers and other ingredients used in the formulation of gastroretentive dosage forms

Hydrocolloids (20%-75):

They may be anionic, synthesis or non-ionic like modified cellulose derivatives, hydrophilic gums. E.g., Acacia, Agar, Chitosan, Casein, Bentonite, Veegum, Gellan gum, Sodium CMC, Pectin, MC, HPMC K4 M, Calcium alginate, Ethyl cellulose, Polyethylene oxide, Polyethylene glycol, Sodium alginate, PVP.

Inert fatty materials (5%-75%):

Edible, inert fatty materials that have specific gravity <1 can be used to reduce the hydrophilic property of the formulation and therefore increase buoyancy. E.g., Fatty acids, Beeswax, Gelucires 39/01 & 43/01, long chain fatty alcohols, etc.

Effervescent agents:

Citric acid, Sodium bicarbonate, Tartaric acid, Citroglycine, Di-Sodium Glycine Carbonate, etc.

Release rate accelerants (5%-60%):

Lactose, Mnnitol, etc.

Release rate retardants (5%-60%):

Dicalcium phosphate, Talc, Magnesium stearate etc.

Low density material:

Polypropylene foam powder.

Buoyancy increasing agents (up to 80%):

Ethyl cellulose.

METHOD FOR THE MANUFACTURING OF GRANULES

Dry manufacturing methods

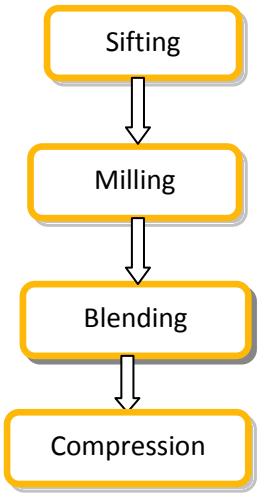
The manufacture of granulations for tablet compression may follow one or a combination of three established methods: the dry methods of direct compression, compression granulation, and wet granulation.

Direct compression

The term “direct compression” is defined as the processs by which tablets are compressed directly from powder mixture of API and suitable excipients.[Fig:5].Some granular chemicals, like potassium chloride, possess free-flowing and cohesive properties that enable them to be compressed directly in a tablet machine without need of granulation. For chemicals lacking this quality, special pharmacceutical excipients may be used to impart the necessary qualities for production of tablets by direct compression. These excipients include fillers, such as spray-dried lactose, microcrystals of alphamonohydrate lactose, sucrose-invert sugarcorn starch mixtures, microcrystalline cellulose, crystalline maltose, and dicalcium phosphate; disintegrating agents, such as direct compression starch, sodium carboxymethylcellulose fibers, and cross-linked polyvinylpyrrolidone; lubricants, such as magnesium stearate and talc; and glidants, such as fumed silicon dioxide.

Merits

- Direct compression is more efficient and economical process as compared to other processes, because it involves only dry blending and compaction of API and necessary excipients.
- The most advantage of direct compression is economical process. Reduced processing time, reduced labor costs, fewer manufacturing steps, and less process validation.
- Particle size uniformity.
- Chemical stability problems for API and excipients would be avoided.



[**Fig: 5.] Processing step of Direct Compression.**

Compression Granulation

- Compression granulation has been used for many years, and is a valuable technique in situations where the effective dose of a drug is too high for direct compaction, and the drug is sensitive to heat, moisture, or both, which precludes wet granulation. Many aspirin and vitamin formulation are prepared for tabletting by compression granulation.
- Compression granulation involves the compaction of the components of a tablet formulation by means of a tablet press or specially designed machinery, followed by milling and screening, prior to final compression into a tablet. When the initial blend of powder is forced into the dies of a large-capacity tablet press and is compacted by means of flat-faced punches, the compacted masses are called slugs, and the process is referred to as "slugging".
- Slugging is just an elaborate method of subjecting a material to increased compression time .The two or more times that the material is subjected to compaction pressures causes a strengthening.
- On a large scale, compression granulation can also be performed on a specially designed machine a roller compactor.

The compaction force of the roller compactor is controlled by three variables:[Fig:6].

- The hydraulic pressure exerted on the compaction rolls.
- The rotational speed of the compaction rolls.
- The rotational speed of the feed screws.
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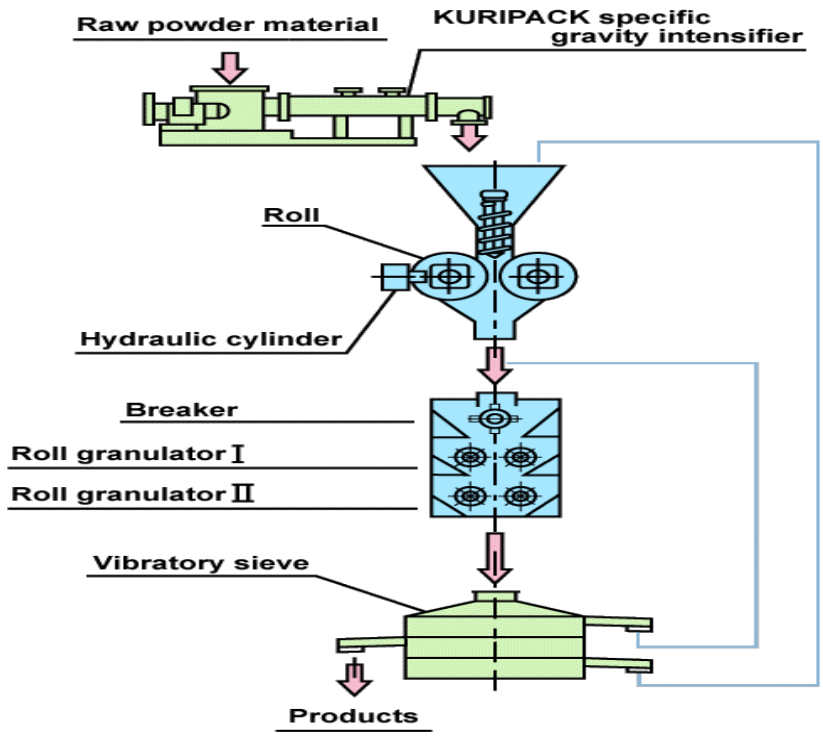


[Fig: 6.] Roller compactor in a granulation production system.

Wet Granulation

The most widely used and most general of method of tablet preparation is the wet –granulation method. Its popularity is due to the greater probability that the granulation will meet all the physical requirements for the compression of good tablets. The steps in the wet method are weighing, mixing, wet massing, screening the damp mass, drying, dry screening, lubrication, and compression. [Fig: 7].

Steps involved in wet granulation

- ✓ Weighing and blending the ingredients,
- ✓ Preparing a damp mass,
- ✓ Screening the damp mass into pellets or granules,
- ✓ Drying the granulation,
- ✓ Sizing the granulation by dry screening,
- ✓ Adding lubricant and blending.

Weighing and blending the ingredients

- Specified quantities of active ingredient, diluents or filler, and disintegrating agent are mixed by mechanical powder blender or mixer until uniform.
- Fillers include lactose, microcrystalline cellulose, starch, powdered sucrose, and calcium phosphate.
- Disintegrating agents include croscarmellose, corn and potato starch glycolate, sodium carboxymethylcellulose, polyvinyl polypyrrolidone (PVP), crospovidone, cation exchange resins, alginic acid, and other material that swell or expand on exposure to moisture and effect the rupture or breakup of the tablet in gastrointestinal tract.
- Croscarmellose (2%) and sodium starch glycolate (5%) are often preferred because of their high water uptake and rapid action.

Preparing a damp mass

- A liquid binder to the powder mixture to facilitate adhesion of the powder particles. A damp mass resembling dough is formed and used to prepare the granulation. A good binder results in appropriate tablet hardness and does not hinder the release of the drug from the tablet.
- Among binding agents are povidone, an aqueous preparation of cornstarch (10-20%), glucose solution (25-50%), molasses, methylcellulose (3%), carboxymethylcellulose, and microcrystalline cellulose.
- When desired, a colorant or flavorant may be added to the binding agent to prepare a granulation with an added feature.

Screening the damp mass into pellets or granules

- The wet mass is pressed through a screen (usually 6 or 8 mesh) to prepare the granules. This may be done by hand or with special equipment that prepares the granules by extrusion through perforations in the apparatus.
- The resultant granules are spread evenly on large pieces of paper in shallow trays and dried.

Drying the Granulation-

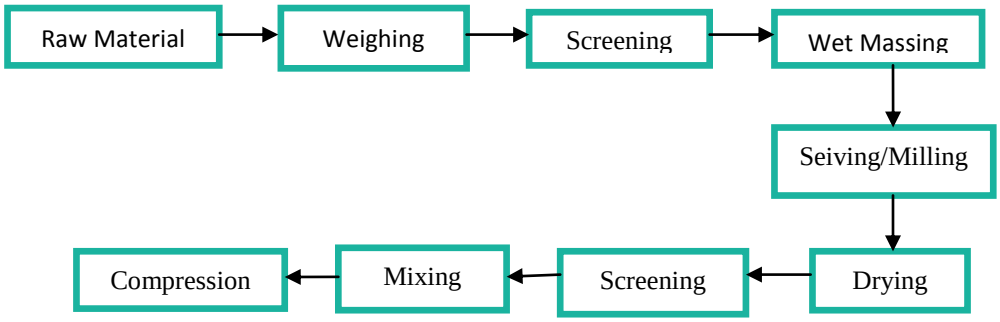
Granules may be dried in thermostatically controlled ovens that constantly record the time, temperature, and humidity.

Sizing the Granulation by Dry Screening

- After drying, the granules are passed through a screen of a smaller mesh than used to prepare the original granulation.
- The degree to which the granules are reduced depends on the size of the punches to be used.
- Screens of 12 to 20 mesh size are generally used for this purpose.
- Sizing of the granules is necessary so that the die cavities for tablet compression may be completely and rapidly filled by the free-flowing granulation.

Adding Lubricant and blending

- ✓ After dry screening, a dry lubricant is dusted over the spread-out granulation through a fine-mesh screen.
- ✓ Lubricant contribute to preparation of compressed tablets in several ways:
- ✓ They improve the flow of the granulation in the hopper to the die cavity.
- ✓ They prevent adhesion of the tablet formulation to the punches and dies during compression.
- ✓ They reduce friction between the tablet and the die wall during the ejection of the tablet from the machine.
- ✓ They give sheen to the finished tablet.
- ✓ Among the more commonly used lubricants are magnesium stearate, calcium stearate, stearic acid, talc, and sodium stearyl fumarate.



[Fig: 7.] Processing step in Wet Granulation.

Evaluation of Tablet

General Appearance:

The general appearance of a tablet, its identity and general elegance is essential for consumer acceptance, for control of lot-to-lot uniformity and tablet-to-tablet uniformity. The control of general appearance involves the measurements of size, shape, color, presence or absence of odor, taste etc.

Size & shape:

It can be dimensionally described & controlled. The thickness of a tablet is only variables. Tablet thickness can be measured by micrometer or by other device. Tablet thickness should be controlled within a ± 5% variation of standard value.

Organoleptic properties:

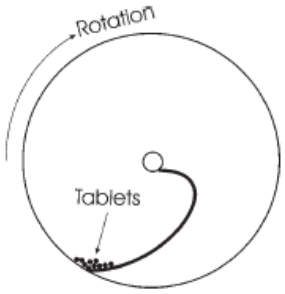
Color distribution must be uniform with no mottling. For visual color comparison compare the color of sample against standard color.

Hardness:

Tablet requires a certain amount of strength or hardness and resistance to friability to withstand mechanical shakes of handling in manufacture, packaging and shipping. Hardness generally measures the tablet crushing strength.

Friability:

Friability of a tablet can determine in laboratory by Roche friabilator. This consist of a plastic chamber that revolves t 25rpm, dropping the tablets through a Distance of six inches in the friabilator, which is then operate for 100 revolution, The tablets are reweighed. Compress tablet that lose than 0.5 to 1.0% the tablet weigh are consider acceptable. [Fig: 8].



[Fig: 8.] Schematic diagram of friability apparatus.

Drug Content and Release:

Weight Variation test (U.S.P):

Take 20 tablet and weighed individually. Calculate average and compare the individual tablet weight to the average. The tablet pass the U.S.P test if no more that 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limit.

Content Uniformity Test:

Randomly select 30 tablets. 10 of these assayed individually. The tablet pass the test if 9 of the 10 tablets must contain not less than 85% and not more than 115% of the labeled drug content and the 10^{th} tablet may not contain less than 75% and more than 125% of the labeled content. If these conditions are not met, remaining 20 tablet assayed individually and none may fall out side of the 85 to 115% range.

Disintegration Test (U.S.P):

The U.S.P. device to test disintegration uses 6 glass tubes that are 3" long; open at the top and 10 mesh screen at the bottom end. To test for disintegration time, one tablet is placed in each tube and the basket rack is positioned in 1-L beaker of water, simulated gastric fluid or simulated intestinal fluid at 37± 2° C such that the tablet remain 2.5 cm below the surface of liquid on their upward movement and not closer than 2.5 cm from the bottom of the beaker in their download movement. Move the basket containing the tablets up and down through a distance of 5-6 cm at a frequency of 28 to 32 cycles per minute. Floating of the tablets can be prevented by placing perforated plastic discs on each tablet.

According to the test of tablet must disintegrate and all particles must pass through the 10 mesh screen in the time specified. If any residue remains, it must have a soft mass.

Dissolution Test (U.S.P.): Two set of apparatus:

Apparatus-1:

A single tablet is placed in a small wire mesh basket attached to the bottom of the shaft connected to a variable speed motor. The basket is immersed in a dissolution medium (as specified in monograph) contained in a 100 ml flask. The flask is cylindrical with a hemispherical bottom. The flask is maintained at 37±0.5° C by a constant temperature bath. The motor is adjusted to turn at the specified speed and sample of the fluid are withdrawn at intervals to determine the amount of drug in solutions.

Apparatus-2:

It is same as apparatus -1, except the basket is replaced by a paddle. The dosage form is allowed to sink to the bottom of the flask before stirring. For dissolution test U.S.P. specifies the dissolution test medium and volume, type of apparatus to be used, rpm of the shaft, time limit of the test and assay procedure for. The test tolerance is expressed as a % of the labeled amount of drug dissolved in the time limit.

Evaluation of floating tablet

Buoyancy/Floating test-

The in vitro buoyancy was determined by floating lag time, as per the method described by a Rosa et al., 1994. Here, the tablets were placed in a 100ml beaker containing 0.1N HCL. The time required for the tablet to rise to the surface and float was determined as floating lag time and total duration of time by which dosage form remain buoyant is called Total Floating Time (TFT).

In vivo confirmation of buoyancy by using radiographic studies:

For this study the tablets were prepared by replacing half of the amount of drug with barium sulphate. After overnight fasting of three healthy volunteers they were fed with low calorie food and allowed to take water after these tablets were administered orally. Radiographs were obtained at specific time intervals, over these periods volunteers were allowed to take water.

Swelling Study-

The swelling behaviour of a dosage form was measured by studying its weight gain or water intake the dimensional changes could be measured in terms of the increase in tablet diameter and/or thickness over time. Water uptake was measured in terms of percent weight gain, as given by the equation.

$$W_U = (W_t - W_0)/W_0 \ X100$$

W_t=Weight of dosage form at time t.
W_0=Initial weight of dosage form

***In-vitro* dissolution study:**

The tablet was placed inside the dissolution vessel. 5ml of sample were withdrawn at time intervals of 1h, 2h, 3h, 4h, 5h, 6h, 7h, 8h, 10h, and 12h. The volume of dissolution fluid adjusted to 900ml by replacing fresh 5ml of dissolution medium after each sampling. The release studies were conducted with 3 tablets, and the mean values were plotted versus time. Each sample was analyzed at maximum wavelength using double beam UV visible spectrophotometer against reagent blank.

X-ray/gamma Scintigraphy:

X-ray/gamma Scintigraphy is a very popular evaluation parameter for floating dosage form nowadays. It helps to locate dosage form in the gastrointestinal tract (GIT), by which one predict and correlate the gastric emptying time and the passage of dosage form in the GIT.

Table 2: List of Abbreviations.

1	FDDS	Floating drug delivery system
2	HBS	Hydrodynammically balanced system
3	$GRDF_S$	Gastro retentive dosage forms
4	g/cm	Gram per centimetre
5	API	Active pharmaceutical ingredient
6	TFT	Total floating time

CONCLUSION

The principle of buoyant preparation offers a simple and practical approach to achieve increased gastric residence time for the controlled release and sustained release dosages form . These systems provide the benefit of better and delay absorption of drugs that are absorbed from upper part of stomach. Local action of drug is increased as the system rests in stomach for longer time. The currently available polymer-mediated Non- effervescent and effervescent FDDS, designed on the basis of delayed gastric emptying and buoyant principles, effective approach to the modulation of controlled oral drug delivery.

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Conflict of intrest

To the designing and development of floating system for retentive drug delivery author thought that this research section carried an excellent development of new formulation and evaluate them. So that author review many research and review articles to obtain a cross section idea to develop the effective buoyant drug delivery. This type of research studies in future should also be design in different area of drug delivery system for better outcome of social of society.

REFERENCES

1. Yadav A.V., Gokhale S.B., 2004. A text book of pharmaceutics, published by Nirali prakashan, Fifth edition, p.9.
2. Badoni A., Ojha A., Ganaranjan G., Kothiyal, Review drug delivery system, www.thepharmajournal.com,2011; 1(.8): p-32.
3. Dhiman Sonia, Singh G.T., Rehni A.K., Sood Surbhi, Arora Sandeep, Gastroretentive: A controlled release drug delivery system, Asian journal of pharmaceutical and clinical research, 2011; 4(1): 5-13.
4. Atmakuri Lakshmana Rao, Vemu Naga Jahnavi, Dasari Santhi Krupa, Advances in Floating Drug Delivery Systems, International Journal of Drug Formulation and Research, 2011; 2(5): 60-72.
5. Dr. S.D.Pande, Ku. Pranita V. Vadiya, Ku Priyanka N. Gulhane, Floating Drug Delivery System (FDDS): A New Way For Oral Drug Delivery System, (2013); 3(1): 1-13.
6. Meenakshi Bharkatiya, Santosh Kitawat, Annapurna Ojha, Floating Drug Delivery System: A Review,Journal of Drug Delivery & Therapeutics; (2014); 4(2): 130-134.
7. Jayvadan Patel, Pundarikakshudu Kilambi, An overview of a gastro-retentive floating drug delivery system, International Journal of Pharmaceutical and Clinical Science, (2013); 3(1): 1-13.
8. Geetha A., Kumar Rajendra J., Mohan Krishna CH., Sateesh V., Raju PN, A Review on Floating Drug Delivery System, International Journal of Pharmaceutical Research and Biomedical Analysis, (2012);1(1): 1-13.
9. www.pharmamirror.com
10. Mansi Sharma, Kumar Ashwini Chaturvedi, Kumar Umesh Singh, Prateek Sehgal, Floating Drug Delivery System: An Approach to Oral Controlled Drug Delivery, 7(1): 1-14.
11. Rathod HJ, Mehta DP, Yadav JS, A review on Gastroretentive Drug Delivery Systems, PharmaTutor, (2016); 4(7): 29-40.
12. Gupta Pooja, Gnanarajan, Kothiyal Preeti, Floating Drug Delivery System: A Review, International Journal of Pharma Research & Review, (2015); 4(8): 37-44.
13. Dixit Nikita, Floating Drug Delivery System, Journal of Current Pharmaceutical Research (2011); 7(1): 6-20.
14. Chhetri H.M., Thapa Panna,An Overview on Gastroretentive Drug Delivery System,Journal of Science, Engineering and Technology, (2014) 10(1): 90-103.
15. Nayak A.K., Maji Ruma, Das Biswarup, Gastroretentive drug delivery system:a review, Asian Journal of Pharmaceutical and Clinical Research, (2010) 3(1): 2-10.
16. Sarawade Anupama, Ratnaparkhi M.P., Chaudhari Shilpa, Floating Drug Delivery System, International Journal of Research and Development in Pharmacy and Life Sciences,(2014); 3(5): 1106-1115.
17. Chaudhary Kamya, Rana A.C., Bala Rajni, Seth Nimrata, Review:Scale up Process of Tablet Production: A Prospective Discussion, International Journal of Pharmacy and Biological Sciences, (2012); 2(3): 223-239.
18. Santanu Roy Chowdhury, Verma Pooja, Floating Drug Delivery System- A New Era in Novel Drug Delivery System, International Journal of Pharmaceutical Research and Bio-Science (2012); 1(5): 91-107.
19. Lachman Leon, Lieberman Herbert A., Kanig Joseph L., The Theory and Practise of Industrial Pharmacy, Varghese Publishing House, Third Edition, p.-318-319.
20. Allen Loyd V.Jr.,Phd, Ansel Howard C.Phd, Ansel's Pharmaceutical Dosage Forms and Drug Delivery System, Published by Wolters Kluwer (India) Pvt.Ltd., New Delhi, Eighth Edition, p.- 240-242.