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Introduction and Application of Bilayer Floating Tablet: A Brief Review

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ABSTRACT
Bilayer tablet is an innovation period for the successful advancement of controlled release formulation as well as a variety of features to produce a successful drug delivery system technique. Controlled release dose forms have been widely employed to improve treatment with a number of key medications. Inclusion of drugs in controlled release gastro-retentive dosage forms that can remain in the gastric region for several hours would significantly increase drug bioavailability, reduce drug waste, and improve the solubility of drugs that are less soluble in high pH environments. Floating drug delivery systems, swelling and expanding systems, polymeric bio adhesive systems, high-density systems, changed form systems, and other postponed gastric systems are now used in the extension of Gastric Retention Time.

Keywords: *Bilayer tablet, Controlled release, Gastro retentive dosage forms, bioavailability*

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INTRODUCTION

Because of its ease of administration, oral consumption has long been the most convenient and widely used route of medication delivery. Conventional dosage forms provide a wide range of fluctuations in drug concentrations in the bloodstream and tissues, resulting in undesired toxicity and inefficiency. The goal of constructing sustained or controlled delivery systems is to reduce the frequency of dosing or to maximise medication effectiveness by localisation at the site of action, hence lowering the dose necessary. The primary goal of continuous release drug delivery is to ensure drug safety and effectiveness while improving patient compliance. [1] Now a day's various developed & developing countries move towards combination therapy for treatment of various diseases & disorders requiring long term therapy such as hypertension, diabetes and Cardio vascular diseases. Bi-layer tablets are suitable for sequential release of two drugs in combination, separate two incompatible substances and also for sustained release tablet in which one layer is immediate release as initial dose and second layer is maintenance dose. Bi-layer tablets consist of monolithic partially coated or multilayered matrices. In the case of bi-layered tablets drug release can be rendered almost unidirectional if the drug can be incorporated in the upper non-adhesive layer its delivery occurs into the whole oral cavity. The mechanical strength of bi-layered tablets has been observed not to be a controlling factor in drug release. Challenges during development of bi-layer tablets include the order of layer sequence, layer weight ratio, and elastic mismatch of the adjacent layers, first layer tamping force and cross contamination between layers. If these factors are not well controlled in one way then other will affect the bi-layer compression pressure and the quality attributes like mechanical strength and individual layer weight control. Therefore care must be taken to enable design of a vigorous product and process. [2] In the last decade, interest in developing a combination of two or more active pharmaceutical ingredients in a single dosage form has increased in the pharmaceutical industry, promoting patient convenience and compliance. Bi-layer tablets can be a primary option to avoid chemical incompatibilities between APIS by physical separation, and to enable the development of different drug release profiles (immediate release with extended release). [3]

Flexible Concept

1. They are a unit dosage form and offer the greatest capabilities of all oral dosage forms for the greatest dose precision and the least content variability.
2. Suitable for large scale production. [4]
3. This system provide sustained drug delivery like HBS dosage form modify gastric residence time as this system remain in stomach for many hours.

4. It maintains optimum therapeutic window as a result drug delivery with controlled released is achieved.
5. Better patient compliance is achieved due to its ease of administration.
6. It maintains constant blood level.
7. Site specific drug delivery is achieved for the drugs such as furosemide and riboflavin which are formulated as floating system.
8. Due to higher dose precision and lesser content variation they are the most compatible oral dosage form. .
9. Better suited for large scale production.
10. Swallowing of tablets is easy.
11. Lesser cost compared to other oral dosage forms.
12. These are the most lighter and compact.[5]

Disadvantages of floating bi-layer tablets

1. Increased fluid levels are required in the stomach so that the system float properly.
2. Drugs with solubility and stability problem in stomach cannot be formulated as floating dosage form.
3. Irritation producing drugs on gastric mucosa can be formulated as floating dosage form.
4. Capping is the major problem in bilayer tablets.
5. Separation of layer occurs due to insufficient bonding and reduction in yield occurs.
6. Hardness is other problem.
7. There are chances of cross contamination between two layers.
8. Due to low density and amorphous nature of some drugs compacts do not form because they resist compression.
9. There is less control over weight of individual layer.
10. Swallowing problem in case of children and unconscious patients.
11. Bioavailability problem occurs in case of poor wetting and less dissolution properties.
12. Sometimes encapsulation or coating is required for the drugs that are oxygen sensitive, bitter tasting and with bad odor. [5,6]

Ideal properties for bi-layer tablet dosage form

1. Drug must be released in reproducible and expected manner in bi-layer tablet.
2. Chemical and physical stability is must.
3. During product shelf life chemical stability is main concern.
4. They should be free from visual defects.
5. A bi-layer tablet should have elegant product identity while free of defects like chips, cracks, discoloration and contamination.
6. It should have sufficient strength to with stand mechanical shock during its production packaging, shipping and dispensing.
7. It should have the chemical and physical stability to maintain its physical attributes over time.
8. The bi-layer tablet must be able to release the medicinal agents in a predictable and reproducible manner.
9. It must have a chemical stability shelf-life, so as not to follow alteration of the medicinal agents. [7, 8]

Preparation

Bi-layer tablets are prepared with one layer of drug for immediate release with the second layer designed to release drug later, either as a second dose or in an extended release form. The bi-layer tablets with two incompatible drugs can also be prepared by compressing separate layers of each drug so as to minimize the area of contact between two layers.

Compaction

To produce an adequate tablet formulation, certain requirements such as sufficient mechanical strength and desired drug release profile must be met. At times, this may be a difficult task for the for mulator to achieve these conditions, especially in the bi-layer tablet formulation where double compression technique is involved, because of Poor flow and compatibility characteristic of the drug which will result in capping and/or lamination. The compaction of a material involves both the compressibility and consolidation.

Compression

It is defined as reduction in bulk volume by eliminating voids and bringing particles into closer contacts.

Consolidation

It is the property of the material in which there is increased mechanical strength due to inter particulate interaction (bonding). The compression force on layer1 was found to be a major factor influencing tablets delaminating.[4,8]

METHODOLOGY USED FOR BI-LAYER FLOATING TABLET

1. Oros ® Push Pull Technology

2. L-Oros Tm Technology
3. DUROS Technology
4. Elan Drug Technologies' Dual Release Drug Delivery System
5. EN SO TROL Technology
6. Rotab Bilayer
7. Geminex Technology.

1. Oros ® Push Pull Technology

Two or three layer system a drug layer and push layer. Drug layer contain drug with other agents and due to this drug is less soluble. Sometimes suspending agent and osmotic agent are also added. The tablet core is surrounded by semi permeable membrane.

2. L-Oros Tm Technology

Alza developed L-OROS system due to solubility problem. The system contain a drug in dissolved state in a lipid soft gel product which is produced first and then barrier membrane, after which osmotic membrane and semi permeable membrane coat is applied and is then drilled out through external orifice.

3. DUROS Technology

This technology is also known as miniature drug dispensing system which works like a miniature syringe and release small quantity of drug consistently over a period of time .There is an outer cylindrical titanium alloy reservoir which has high impact strength due to which drug molecules inside it are protected from enzymes.

4. Elan Drug Technologies' Dual Release Drug Delivery System

The DUREDASTM Technology provides combination release of drugs together and different release pattern of single drug i.e. it provides sustained release as well as immediate release. This technology provides various advantages i.e. two drug components provide tailored release and it's another benefit is that it consist of bilayer tablet technology in which it contain modified as well as immediate release pattern in one tablet. In these different controlled release formulations are combined together.

5. EN SO TROL Technology

An integrated approach is used by Shire laboratory for drug delivery system which focus on identification and incorporation of enhancer which is identified to form optimized dosage form in controlled release system. By this enhancement in solubility is achieved.

6. RoTab Bilayer

a. Software:

It is modular designed software to which additional functions can be added. PC- system with 15" touch- screens is an advanced system which provides fast graphical evaluations with accurate results.

b. Working:

Ro Tab bi-layer when using is switched to production mode. Dose and compression force is automatically regulated by adjusting filling speed and die table. Hardness is also regulated when required.

c. R and D modified technique:

R and D modified Ro Tab Bi-layer is featured with measuring points on which there are graphical visualization and evaluation are possible. There is an additional alarm function on which punch tightness is controlled. Anytime up gradation is possible which are R and D Plus.

d. R and D Plus:

R and D Plus provides improved standards in tabletting technology with all important functions such as punch tightness control, display of force displacement and tablet scraper force.

7. Geminex Technology

In this drug delivery system at different time more than one drug can be delivered. This technology basically increases the therapeutic efficacy of the drug by decreasing its side effects. It is useful both to industry as well as patient as in single tablet it provides delivery of drug at different rates. [4, 5, 9, 10]

PREFORMULATION OF DRUG

1. Particle size distribution:

The particle size distribution was measured using sieving method.

2. Photo microscope study:
Photo-microscope image of TGG and GG was taken (×450 magnifications) by photomicroscope

3. Angle of repose:
It is defined as the maximum angle possible between the surface of pile of the powder and the horizontal plane. Fixed funnel method was used. A funnel was fixed with its tip at a given height (h), above a flat horizontal surface on which a graph paper was placed. Powder was carefully poured through a funnel till the apex of the conical pile just touches the tip of funnel. The angle of repose was then calculated using the formula,

$$\text{Tan } \theta = h/r$$

Where h and r are the height and radius of the powder cone.

4. Moisture sorption capacity:
All disintegrates have capacity to absorb moisture from atmosphere which affects moisture sensitive drugs. Moisture sorption capacity was performed by taking 1 g of disintegrate uniformly distributed in petri-dish and kept in stability chamber at 37±1oC and 100% relative humidity for 2 days and investigated for the amount of moisture uptake by difference between weights.

5. Density
The loose bulk density (LBD) and tapped bulk density (TBD) were determined and calculated using the following formulas,
$LBD^{1/4}$ weight of the powder = volume of the packing
$TBD^{1/4}$ weight of the powder = tapped volume of the packing

6. Compressibility index
The compressibility index of the disintegrate was determined by Carr's compressibility index.

$$C = 100 \text{ x } (1\text{-ÞB/ÞT})$$ [I.P., 1996; U.S. P., 2000:1944].

The propensity of the powder to be compressed is measured by compressibility index and it also helps in measurement of settling property and inter particulate interaction.

$$\text{Compressibility index (\%)} = \rho t - \rho o^{*} 100 / \rho t$$

Where ρt = Tapped density g/ml, ρo = Bulk density g/ml.

7. Bulk Density (Db)
It is the ratio of powder to bulk volume. The bulk density depends on particle size distribution, shape and cohesiveness of particles. Accurately weighed quantity of powder was carefully poured into graduated measuring cylinder through large funnel and volume was measured which is called initial bulk volume. Bulk density is expressed in gm/cc and is given by,

$$Db = M / Vo$$

8. **Tapped Density (Dt)**
Ten grams of powder was introduced into a clean, dry 100ml measuring cylinder. The cylinder was then tapped 100 times from a constant height and tapped volume was read. It is expressed in gm/cc and is given by,

$$Dt = M / Vt$$

Tapped density= Weight of powder taken/ Tapped Volume

9. **Hausner's ratio**
It is calculated by the formula,

$$\text{Hausner ratio= Tapped density/ Bulk density}$$

$$\text{Hausner ratio= Vo/Vf}$$

Where, Vo= Unsettled apparent volume, Vf= Final tapped volume.

OR

$$H = \rho_T/\rho_B$$

Where ρ_B is the freely settled bulk density of the powder, and ρT is the tapped density of the Powder. [3, 11, 12, 13]

CHARACTERIZATION OF TABLET
General Appearance:
The general appearance of a tablet, its visual identity and overall "elegance" is essential for consumer acceptance. Includes in are tablet's size, shape, color, presence or absence of an odor, taste, surface texture, physical flaws and consistency and legibility of any identifying marking.

Size and Shape:

The size and shape of the tablet can be dimensionally described, monitored and controlled.

Tablet Thickness

In this three tablets are randomly taken and then their thickness and diameter are measured by Vernier caliper or by using calibrated screw gauze.

Hardness

Expressed in kg/cm2 and it is checked using Monsanto hardness tester by randomly picking three tablets. Hardness helps in knowing ability of the tablet to withstand mechanical shock during handling of tablets.

Friability

Ten tablets are selected and weighed and then placed in friabilator apparatus which rotate at 25 rpm speed for 4 minutes. After 4 minutes tablets are weighed again.

$$\%F = [1-(Wt/W)]*100$$

Where W– Initial weight of tablet, Wt - Weight of tablet after revolution.
If % Friability of tablets is less than 1% is considered acceptable.

Weight variation

Weight variation was carried out for both immediate release and sustained release layers. 20 tablets were weighed and the average weight was calculated. Then the tablets were weighed individually. The percentage weight deviation of each tablet from average weight was calculated using the following formula

$$\% \text{ deviation} = \text{Average weight-individual weight/average weight} \times 100$$

Assay/drug content

Ten tablets were selected randomly, weighed and triturated; a quantity of triturate equal to 100mg of Verapamil HCl was transferred to 100ml volumetric flask and was dissolved in 0.1N HCl. It was sonicated for 30 min and filtered through 0.45µm membrane filter. The absorbance after suitable dilutions was measured in a UV Visible Spectrophotometer at 278 nm using 0.1N HCl as blank.

In vitro Buoyancy Studies

The in vitro buoyancy was determined by floating lag time. The tablets were placed in a beaker containing 100mL 0.1N HCl and the time required for the tablet to rise to the surface and float was determined as floating lag time.

In vitro Dissolution Studies

Release rate of all the designed formulations were studied up to 12 hours using USP type II dissolution apparatus (Rotating Paddle method) at 75 rpm. A distance of 2.5 cm± 0.2 cm was maintained between the paddle and bottom of dissolution vessel. The dissolution medium (900 ml) consisted of 0.1N hydrochloric acid (1.2 pH), maintained at 37oC ± 0.5 ^{o}C. Sample of 5 ml was withdrawn at specific time intervals throughout the dissolution study of 12 hours for analysis and replaced with fresh dissolution medium. After appropriate dilution the samples were analyzed for Verapamil HCl using UV-Visible spectrophotometer at 278nm. The release studies were conducted in triplicate.

Stability Studies

The selected formulations were subjected for stability studies based on their drug content and in-vitro drug release characteristics. The formulations were stored in tightly closed amber coloured glass container in stability chamber. The formulations were stored at different storage conditions like 50C/Ambient, 250 C/ 60 % RH and 400C/ 75 % RH for 60 days. The formulations were subjected to different tests namely hardness, drug content and in-vitro drug release study after 60 days and reported.

Tablet Density

t is an important parameter in case of floating tablets. If density is less than (1.004) gastric fluid, than only the tablets will float. It is calculated using formula: $V=\pi r2h$, d = m/v, r = Radius of tablet, h = crown thickness (g/cc), m = Mass of tablet.

Disintegration Time

In this one tablet is placed in disintegration apparatus containing buffer 0.1N HCl or PBS pH 6.8 and test is carried out at 37oC. The time taken by tablet to Disintegrate is noted as disintegration time.

Floating Lag Time

It is the time interval taken by the tablets to start floating. It should be less than one minute. It is measured by dissolution test apparatus containing 0.1 N HCl (900ml).

Floating Time
It is the total time taken by which the tablets remain floating in the media.

Drug Content Uniformity
Ten tablets are taken and powdered equivalent weight of drug dose is taken and is transferred to volumetric flask and then buffer is added and absorbance is determined using U.V spectrophotometer.

Swelling Study
Initially tablet is weighed (W1) and placed in a glass beaker, containing 200 mL of 0.1 N HCl, maintained in a water bath at 37 ± 0.5 _C. At different time intervals, the tablet is removed and the excess of liquid is carefully removed by a filter paper. The swollen tablet is reweighed (W2). The swelling index (SI) is calculated using the formula

SI= Wt -W0/W0*100

Wt= (Weight of swollen tablet), W0= (Initial weight of tablet).
In-vivo evaluation

Radiology
X-ray is widely used for examination of internal body systems. Barium Sulphate is widely used Radio Opaque Marker. So, BaSO4 is incorporated inside dosage form and X-ray images are taken at various intervals to view gastric retention.

Scintigraphy
Similar to X-ray, emitting materials are incorporated into dosage form and then images are taken by scintigraphy. Widely used emitting material is 99Tc.

Gastroscopy
Gastroscopy is peroral endoscopy used with fiber optics or video systems. Gastroscopy is used o inspect visually the effect of prolongation in stomach. It can also give the detailed evaluation of GRDDS.

Magnetic Marker Monitoring
In this technique, dosage form is magnetically marked with incorporating iron powder inside, and images can be taken by very sensitive bio-magnetic measurement equipment. Advantage of this method is that it is radiation less and so not hazardous.

Ultrasonography
Used sometimes, not used generally because it is not traceable at intestine.

13C Octanoic Acid Breath Test
13C Octanoic acid is incorporated into GRDDS. In stomach due to chemical reaction, octanoic acid liberates CO2 gas which comes out in breath. The important Carbon atom which will come in CO2 is replaced with 13C isotope. So time up to which 13CO2 gas is observed in breath can be considered as gastric retention time of dosage form. As the dosage form moves to intestine, there is no reaction and no CO2 release. So this method is cheaper than other. [10, 13-15]

RECENT ADVANCES
Strübing et al studied the floating mechanism and drug release behaviour of poly (vinyl acetate)-based floating tablets with membrane controlled drug delivery. Propranolol HCl tablets with Kollidon® SR as an excipient for direct compression and varied Kollicoat® SR 30 D/Kollicoat® IR coats ranging from 10 to 20 mg polymer/cm2 were tested for drug release in 0.1 mol/l HCl. The commencement of floating, floating duration, and floating strength of the gadget were also determined. Furthermore, bench top MRI investigations on chosen samples were carried out. Coated tablets with a 10 mg polymer/cm2 SR/IR and an 8.5: 1.5 coating had the lowest lag-times between drug release and the commencement of floating, as well as the quickest increase in and highest maximum values of floating strength. Jang et al used an effervescent floating matrix system (EFMS) to create a gastro-retentive drug delivery system of DA-6034, a novel synthetic Flavonoids derivative, for the treatment of gastritis. The EFMS was designed to allow the tablets to float in stomach fluid and release the medicine continually, overcoming the therapeutic limitations of DA-6034 imposed by its limited solubility in acidic circumstances. The use of EFMS considerably improved the release of DA-6034 from tablets in acidic conditions, which was attributed to the action of solubilizers and alkalizing agents such as sodium bicarbonate,

which was utilised as a gas producing agent. In gastric ulcer-induced beagle dogs, DA-6034 EFMS pills shown improved gastro-protective effects, showing the therapeutic potential of EFMS tablets for the treatment of gastritis. [16-18]

FUTURE POTENTIAL FOR BILAYER FLOATING TABLETS

Prospects for Herbal Drugs in the Future Herbal medicine delivery is a new area of study in the pharmacy. The use of FBDDS for herbal medicine delivery is an innovative strategy for improved delivery. For the past two decades, pharmaceutical research professionals have focused on the medication release profile. The experts see it as an excellent opportunity to concentrate on GI transit profiles. This has resulted in the development of novel products that provide significant benefits to patients. With the introduction of FBDDS, items that might release medication for up to 12 or 24 hours have been developed. For a better therapeutic effect, a bilayer floating technique with two herbal medications can be used. The IR and SR concept for natural drugs is also provided by bilayer floating. Bilayer floating tablets can help with hypertension and diabetes because they provide an immediate reaction by combining a loading dosage as one layer with a sustained release layer that keeps the medication concentration in plasma for an extended length of time. [19-20].

APPLICATION OF BILAYER FLOATING TABLET

Bilayer tablets are ideal for the sequential release of two medications that will be administered together. It separates the two incompatible medications. The sustained-release pills have one layer that contains the initial loading dose and the second layer that contains the sustained dose. Bilayer tablets are the most recent technology that can assist overcome the limits of a single-layered tablet. Bilayer tablets aid in the simultaneous administration of two separate medicines with distinct release patterns. Bilayer tablets are used to deliver fix dosages containing several APIs. They are used to expand and change the surface area of active medicinal components for tailored release by using erodible barriers [21,22].

A). Herbal bilayer floating tablets

Bilayer floating tablet is the best option for herbal drug delivery. It could release drug upto 12-24 hours. It improves the therapeutic effect of drug. Some of the herbal drugs that can be delivered as bilayer floating tablets are:

i. Forskolin: It is used as anti-obesity agent reducing fat in body muscles. It may enhance fat loss without loss of muscle mass.
ii. Black myrobalan: It shows uniform anti-bacterial activity against ten clinical strains of H.pylori.
iii. Ginger root: It is used for the treatment of gastrointestinal ailments such as motion sickness, dyspepsia and hyperemesis gravidarum and it also have chemopreventative activity in animal models.
iv. Turmeric: It prevents gastric and colon cancers in rodents.
v. Berberine: It shows variety of activity against bacteria, viruses, fungi, protozoans, and helminthes [23].

B). Treatment of diseases

i. Hypertension and angina pectoris

Nifedipine is a calcium channel blocker of the di-hydropyridine type which is mainly used for the treatment of hypertension and angina pectoris. Nifedipine is a suitable candidate for CR administration due to its short elimination half-life of 2-hrs, its rapid and complete drug absorption over the entire gastrointestinal tract, despite its low water solubility and the relationship between drug plasma concentration and blood pressure reduction [23,24]. Controlled release formulation of nifedipine would be effective in overcoming the dissolution limitation by slowly supplying the drug from the intact matrix base during its sojoum in the gastrointestinal tract and its thus expected to decrease side effect and improve patient compliance. Control release tablet for oral administration designed to deliver the drug at gastric region for treatment of hypertension [25].

ii. Cardiovascular disease:

Atorvastatin immediate release and aspirin pulsatile release for the treatment of cardiovascular diseases. Four formulations were prepared for immediate release layer of atorvastatin using different concentrations of microcrystalline cellulose and talc by different compression method [26-28].

iii. Peptic ulcer:

The major target of bilayer tablet is to decrease the pain and promotes ulcer healing, prevention of complications/relapse.

C). Targeted drug delivery system

It is the method of delivering medications to the patients in the manner that increases the concentration of medication in some part of body related to other. The aim of targeted drug delivery system is to prolong, localize, target and have protected drug interaction with the diseased tissue. It reduces the frequency of dosage taken by patient. There are different types of drug delivery route such as polymeric micelles, liposomes, lipoproteinbased drug carrier, nano-particle drug carrier, dendrimers, etc. It is also used to treat cardiovascular disease and diabetes. The most important application is to treat cancerous tumours [29-31].

D). Controlled drug delivery system

It aims at releasing the dose of therapeutic directly in the desired zone during the required period of time. It allows the maximizing the efficacy of the therapeutic and minimizing e side effects. For floating drug delivery system, the polymers used must be highly swellable in shortest time [32]. The control release matrix tablet containing uniform mixture of drug, polymer and excipients including gas–generating agents. Nifedipine was mixed using variable amount of Carbopol p 934 and HPMC (K4M, K15M) properly in a mortar with weighed number of excipients. The well will mix powder was compressed by direct compression technique and used as controlled release layer [33,34].

CONCLUSION

Bilayer tablets are superior technology that overcomes the shortcomings of single layered tablets. Bilayer tablets are one of the key intend ways for combining incompatible medications with various suggestions and the same drug with variable release rates in a single unit. A bilayer tablet is appropriate for the sequential release of two medications in combination, the separation of two incompatible substances, and the development of a sustained release tablet in which one layer is immediate release as the first dose and the second layer is maintenance dose. It is also useful for enhancing gastric emptying time and bioavailability by promoting gastric retention. Another advantage is that two medications can be administered at the same time, which improves patient compliance. Antiviral, antibiotic, and antifungal drugs with a small absorption window stand out as superior candidates for floating bilayer dosage form. Interest in producing a combination of two or more active pharmaceutical ingredients (API) in a single dose form (bilayer tablet) has grown in the pharmaceutical industry over the last decade, enhancing patient convenience and compliance. Due to the use of different materials and complex geometric boundaries between adjacent layers, the mechanical structures of this drug delivery system have become quite intricate, requiring complicated tablet architectures as well as patient friendly. A gastrointestinal retentive drug delivery system increases the retention period of dose forms in the stomach or upper gastro-intestinal tract, hence improving drug solubility, bioavailability, and therapeutic efficacy. Bilayer tablets are manufactured using a variety of presses, ranging from simple single-sided presses to extremely sophisticated machinery. The manufacture of bilayer tablets is utilised to offer solutions for the administration of incompatible medications as well as controlled release tablet formulations by providing surrounding or multiple swelling layers.

REFERENCES

1. Kotta Kranthi Kumar, Mahesh M, Sasikanth K. Design, Development and Characterization of Sustained Release of Metformin and Gliclazide bi-layered Tablets, International Journal of Biopharmaceutics, 1(2), 2010, 67-71.
2. Mounica rayaprolu, kumar junju mohan, kumar voleti vijaya, bolla sai padmini , pavani M-A new venture in drug delivery: bi-layered table review, international journals of research in pharmaceutical and nano science.2(3),2013,305-316.
3. Ashok morsu, Vishnu P, naveen babu K, Rao v. umamaheshwara, madhu bollarum – An overview on bi-layer tablet; international journals of research and review in pharmacy and applied science,2014,4(1),957-974.
4. Kiran B siva sai, rao P sambasiva, babu raveendra – bilayer tablet : A review ;international journal of pharmaceutical ,chemical and biological sciences .2015 ,5(3),510-516.
5. Kaur parmjit,dhiman Sonia,arora sandeep –floating bilayer tablet technology :A review ; int. j. pharm.sci.rev.res.19(1),mar-apr.2013; n^0 23,112-122.
6. Sowmya C, Suryaprakash CR, Tabasum SG, Varma V. An Overview on Bi-Layer Tablets. International Journal of Pharmacy &Technology 4, 2012, 2143-2156.
7. Pethkar shraddha V, suggala vijay, gholap saket, jain hemant kumar, swain kapileswar- review on :bi-layer floating tablet ;world journal of pharmacy and pharmaceutical science ,volume 5,issue 02,1411-1425.
8. Ghosh rishikes, anwarud haque md, ,paul rani tripti,al-amin, bhuiyan mohiuddin ahmed, dewan irin-bilayer tablet technology :An overview ;world journal of pharmaceutical research volume 3, issue4,150-163.
9. Rameshwar varma ,kishar dever, tushar gangrade, -bilayer tablet for various drugs :A review ;scholar academic journal f pharmacy,2014, 3(3), 271-279.
10. Parsekar sarvesh D,prabhu shruti, shetty amitha, azaharuddhin mahd, and shabaraya A.R-A brief eview on floating bilayer tablet as a convenient gastro retentive drug delivery system :international journal of pharmaceutical and chemical science, vol3(3),apr-jun 2014,420-430.
11. A divay, kavitha.,kumar M rupesh , SD jagadeesh singh- bi-layer tablet technology :AN overview ; journal of applied pharmaceutical science ,01(8),2011,43-47.
12. Atram SC, Udavant YK, Salunke RJ, Neb GB, Shahi SR, Gulecha BS, Padalkar AN. Formulation and evaluation of bilayer tablet containing Metoprolol succinate and Amlodipine besylate as a model drug for anti hypertensive therapy. J Pharm Res 2009;2(8):1335-47.
13. KM. asha spandana,kumar SK senthil, S parthiban-formulation and evaluation of floating bilayer tablet containing verapamil hydrochloride :international journal of pharmaceutical development and technology,3(1),2013,23-27.
14. Dixit N. Floating Drug Delivery System. J Current Pharm Res. 2011;7(1):6-20.
15. Sarma anupam, deb pulak and dash suvakanta-bilayer tablet and upredas technology:A review ;IJPBS,volume 3.issue2,apr-jun,2013,554-563.

16. Kare P, Jain D and Jain V. Floating Drug Delivery Systems: An Overview of Pharmacy Research. 2010;3(6):1274-1279.
17. Hardenia SS. Floating Drug Delivery Systems: A Review Asian J of Pharmacy and Life Sci. 2011;1(3):96-106.
18. Christian V, Ghedia T and Gajjar V. A Review on Floating Drug Delivery System As A Part of GRDDS. Int J Pharm Res Dev. 2011;3(6):233 – 241.
19. Narang N. An updated review on: floating drug delivery system (FDDS). Int J App Pharm. 2011;3(1):1-7.
20. Dantoriya S, Bhandari G, Mahajan SC and Mishra P. The Recent Developments On Gastric Floating Drug Delivery Systems: An Overveiw. World J Pharm Res. 2013;2(6):2034-62.
21. Chawla G, Gupta AP, Bansal K (2004) Gastroretentive Drug Delivery System. In: Progress in Controlled and Novel Drug Delivery System, NK Jain First Edition, pp. 76-97.
22. Rao SV, B Priyanka, K Padmalatha (2019) Bilayer tablet technology: a novel approach, GSC Bio Pharm Sciences 7(2): 022-028.
23. Desai S, Bolton S (1993) A Floating Controlled Release System: In-Vitro – In-Vivo Evaluation. Pharm Res 10: 1321-1325.
24. Parnapalli M, Arshad BK (2012) Recent Apporaches in Bilayered Technology: Review. International Journal of Pharmaceutical Science and Research 3: 4681-4688.
25. Patwekar SL, Baramade MK (2012) Controlled Release Approach to Novel Multiparticulate. Drug Delivery System International Journal of Pharmacy and Pharmaceutical Sciences 4: 757-763.
26. Ahmed SI, Mangamoori LN, Rao YM (2010) Formulation and characterization of matrix and triple-layer matrix tablets for oral controlled drug delivery. International Journal of Pharmaceutical Sciences 2(7): 137-143.
27. Panchal AH (2013) A Novel Approach of Bilayer Tablet: A Review. International Research Journal of Pharmacy 3(5): 44-59.
28. Agyilirah GA, Green M, duCret R, Banker GS (1991) Evaluation of the gastric retention properties of a cross linked polymer coated tablet versus those of a non-disintegrating tablets. Int J Pharm 75: 241-247.
29. Shrikant M, Shah S, Upadhay P (2012) Floating bilayer drug delivery systems- An unconventional approach in conventional form. Am J Pharm Tech Res 2(2): 609-628.
30. Pattanayak DP, Dinda SC (2011) Bilayer tablet formulation of Metformin HCl and Glimepiride: A novel approach to improve therapeutic efficacy. Int J Drug Discovery Herb 1(1): 1-4.
31. Gahiwade HP, Patil MV, Thakare BW, Vinod MT, et al. (2012) Formulation and In-vitro evaluation of Trifluperazine HCl bilayer floating tablets. International Journal of Pharma and BioScience 2: 166-172.
32. Shukla S, PandyaV, Bhardia P, Jonwal N, Bhatt D (2013) Bi-layer Tablet system – An Innovative trend. Asian J Pharm Res 3(2): 49-56.
33. Parnapalli M, Arshad BK (2012) Recent Apporaches in Bilayered Technology: Review. International Journal of Pharmaceutical Science and Research 3: 4681-4688.
34. Karudumpala S, Chetty M, Gnanaprakash K, Venkatesh B, Sankar P (2013) A review on bilayer floating tablets. Int J Res Pharm Sci 4(2): 354-360.