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Review Article

A brief review on bilayer floating tablet

Kumari Roshani*, Prabhudutta Panda, D.K. Vishwakarma and Navneet Kumar Verma

Department of Pharmaceutics, Kailash Institute of Pharmacy and Management, GIDA, Gorakhpur, (U.P), India

QR Code



*Correspondence Info:

Kumari Roshani
Department of Pharmaceutics,
Kailash Institute of Pharmacy and Management,
GIDA, Gorakhpur, (U.P), India

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Abstract

Bilayer tablet is innovative period for the successful improvement of controlled release formulation along with a variety of features to provide a technique of successful drug delivery system. Controlled release dosage forms have been comprehensively used to improve therapy with several important drugs. Inclusion of drug in controlled release gastro-retentive dosage forms which can remain in the gastric region for several hours would considerably extend the gastric residence time of drugs and improve bioavailability, reduce drug waste and enhance the solubility of drugs that are less soluble in high pH environment. Numerous approaches are presently utilized in the prolongation of Gastric Retention Time, including floating drug delivery system, swelling and expanding systems, polymeric bio adhesive systems, high-density systems, modified shape systems and other deferred gastric emptying strategy.

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

1. Introduction

Oral ingestion has long been the most convenient and commonly employed route of drug delivery due to its ease of administration. Conventional dosage form produce wide ranging fluctuation in drug concentration in the blood stream and tissues with consequent undesirable toxicity and poor efficiency. The aim in designing sustained or controlled delivery systems is to decrease the frequency of the dosing or to increase effectiveness of the drug by localization at the site of action, reducing the dose required. The main objective of sustained release drug delivery is to make sure safety and to improve effectiveness of drugs as well as 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]

1.1 Advantages of the bi-layer tablets

- 1) Bi-Layer execution with optional single layer conversion kit.
- 2) The cost is lower compared to all other oral dosage forms.
- 3) Greatest chemical and microbial stability over all oral dosage forms.
- 4) Objectionable odor and bitter taste can be masked by coating technique.

1.2 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 provides sustained drug delivery like HBS dosage form, modify gastric residence time as this system remains in stomach for many hours.
- 4) It maintains optimum therapeutic window as a result drug delivery with controlled release 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]

1.3 Disadvantages of floating bi-layer tablets

- 1) Increased fluid levels are required in the stomach so that the system floats properly.
- 2) Drugs with solubility and stability problems 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 layers occurs due to insufficient bonding and reduction in yield occurs.
- 6) Hardness is another 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]

1.4 Ideal properties for bi-layer tablet dosage form

- 1) Drug must be released in a reproducible and expected manner in bi-layer tablet.
- 2) Chemical and physical stability is a must.
- 3) During product shelf life, chemical stability is a 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 withstand 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]

1.5 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.

1.6 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 formulator to achieve these conditions, especially in the bi-layer tablet formulation where double compression technique is involved, because of poor flow and compatibility characteristics of the drug which will result in capping and/or lamination. The compaction of a material involves both the compressibility and consolidation.

1.7 Compression

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

1.8 Consolidation

It is the property of the material in which there is increased mechanical strength due to interparticulate interaction (bonding). The compression force on layer 1 was

found to be a major factor influencing tablets delaminating.[4,8]

2. 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 tableting 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]

3. Preformulation of drug

Particle size distribution:

The particle size distribution was measured using sieving method.

Photo microscope study:

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

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,

$$\tan \theta = h/r$$

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

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 $37 \pm 1^\circ\text{C}$ and 100% relative humidity for 2 days and investigated for the amount of moisture uptake by difference between weights.

Density

The loose bulk density (LBD) and tapped bulk density (TBD) were determined and calculated using the following formulas,

$\text{LBD}^{1/4}$ weight of the powder = volume of the packing

$\text{TBD}^{1/4}$ weight of the powder = tapped volume of the packing

Compressibility index

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

$$C = 100 \times (1 - \text{DB}/\text{PT}) \quad [\text{I.P., 1996; U.S. P., 2000:1944}].$$

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.

$$\text{Compressibility index (\%)} = \frac{\rho_t - \rho_o}{\rho_t} \times 100$$

Where ρ_t = Tapped density g/ml, ρ_o = Bulk density g/ml.

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,

$$D_b = M / V_o$$

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,

$$D_t = M / V_t$$

Tapped density = Weight of powder taken / Tapped Volume

Hausner's ratio

It is calculated by the formula,

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

$$\text{Hausner ratio} = \frac{V_o}{V_f}$$

Where, V_o = Unsettled apparent volume, V_f = Final tapped volume.

OR

$$H = \frac{\rho_T}{\rho_B}$$

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

4. 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.

$$\%F = [1 - (W_t/W)] \times 100$$

Where W – Initial weight of tablet, W_t - 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

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

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 0.45 μm 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 $2.5 \text{ cm} \pm 0.2 \text{ cm}$ 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 $37^\circ\text{C} \pm 0.5^\circ\text{C}$. 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

It 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: $V = \pi r^2 h$, $d = m/v$, 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 37°C . 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 (W_1) and placed in a glass beaker, containing 200 mL of 0.1 N HCl, maintained in a water bath at $37 \pm 0.5^\circ\text{C}$. 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 (W_2). The swelling index (SI) is calculated using the formula

$$SI = \frac{W_t - W_0}{W_0} \times 100$$

W_t = (Weight of swollen tablet), W_0 = (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, BaSO_4 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 ^{99}Tc .

Gastroscopy

Gastroscopy is peroral endoscopy used with fiber optics or video systems. Gastroscopy is used to 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.

^{13}C Octanoic Acid Breath Test

^{13}C Octanoic acid is incorporated into GRDDS. In stomach due to chemical reaction, octanoic acid liberates CO_2 gas which comes out in breath. The important Carbon atom which will come in CO_2 is replaced with ^{13}C isotope. So time up to which $^{13}\text{CO}_2$ 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 CO_2 release. So this method is cheaper than other. [10, 13-15]

5. Recent development in the field of bilayer tablet

Table 1: Various Advancements in the Field of Bilayer Tablets

Drug	Dosage Form	Rationale	Ref. No.
Diclofenac, Cyclobenzaprine	Bi-layer tablets	Synergistic effect in pain	[16]
Granisetron HCl	Bi-layer buccal tablets	To overcome bioavailability problem, reducing side effect	[17]
Metformin HCl, Glimipiride	Bi-layer tablets	Synergistic effect in diabetes	[18]
Indomethacin	Bi-layer floating tablet	Biphasic drug release	[19]
Metformin HCl, Atorvastatin Calcium	Bi-layer tablet	To develop poly therapy for the treatment of NIDDS & hyperlipidemia	[20]
Cefixime Trihydrate Dicloxacilline Sodium	Bi-layer tablet	Synergistic effect in bacterial infections	[21]
Piracetam, Vinpocetin	Bi-layer tablet	Synergistic effect in Alzheimer disease	[22]
Metformin HCl, Pioglitazone	Bilayer tablet	Synergistic effecting diabetes mellitus	[23]
Atenolol	Bilayer buccal tablet	To overcome bioavailability problem, reducing side effects and frequency of administration	[24]
Cefuroxime Axetil Potassium Clavulanate	Bilayer tablets	Synergistic effect against microbial infections and to minimize dose dependent side effects	[25]
Amlodipine Besilate Metoprolol Succinate	Bilayer tablet	Synergistic effect in hypertension	[26]
Diclofenac Sodium, Paracetamol	Bilayer tablet	Synergistic effect in pain	[27]
Ibuprofen, Methocarbamol	Bilayer tablet	Synergistic effect of drugs in back pain	[28]
Atorvastatin, Calcium	Bilayer buccal tablet	To overcome bioavailability problem, reducing side effects and frequency of administration	[29]
Paracetamol, Diclofenac	Bilayer tablet	Synergistic effect of drugs in pain	[30]
Losartan	Bilayer tablet	Biphasic release profile	[31]
Metformin HCl, Pioglitazone	Bilayer tablet	Synergistic effect in diabetes mellitus	[32]
Guaiifenesin	Bilayer tablet	Biphasic release profile	[33]
Tramadol, Acetaminophen	Bilayer tablet	Synergistic effect of drugs in pain	[34]
Atenolol, Lovastatin	bilayer floating tablet	Synergistic effect in hypertension and biphasic release profile	[35]
Montelukast, Levocetirizine	Bilayer tablet	To improve the stability of drugs in combination	[36]
Salbutamol, Theophylline	Bilayer tablet	Synergistic effect of drugs in asthma	[37]
Glipizide, Metformin HCl	Bilayer tablet	To avoid interaction b/w incompatible drugs	[38,39]
Telmisartan Hydrochlorothiazide	Bilayer tablet	To minimize contact b/w hydrochlorothiazide & basic component of telmisartan	[40]
Amlodipine, Atenolol	Bilayer tablet	To improve the stability of drugs in combination	[41]
Ascorbic acid, Cyanocobalamin	Double layer suppositories	To avoid interaction b/w incompatible vitamins	[42]
Rifampicin, Isoniazid	Capsule & tablet in capsule	To avoid interaction b/w incompatible drugs	[43]
Misorostol, Diclofenac	Bilayer tablet	To minimize contact b/w drugs	[44]
Propranolol HCl	Bilayer tablet	Bimodal drug release	[45]
Artesunate, Amlodipine	Tablet in tablet	To minimize contact b/w drugs	[46]
Telmisartan, Simvastatin	Bilayer tablet	To minimize contact b/n Simvastatin & telmisartan	[47]
Cefuroxime Axetil	Bilayer floating tablet	Bimodal drug release	[48]
Metformin, Glipizide	Bilayer tablet	Synergistic effect of drugs in diabetes	[49]
Ranitidine Aspirin	Single layer coated tablets	To minimize the contact of two incompatible drugs	[50]
Aspirin Ranitidine	Single layer tablets	To minimize the contact of two incompatible drugs	[51]
Statin Aspirin	Bilayer tablet	To minimize interaction b/w two drugs and side effects due to aspirin	[52]
Furosemide	Bilayer floating tablets	To enhance bioavailability	[53]

Recent advances

Strübing et al investigated the mechanism of floating and drug release behaviour of poly (vinyl acetate)-based floating tablets with membrane controlled drug delivery. Tablets containing propranolol HCl with Kollidon® SR as an excipient for direct compression and different Kollicoat® SR 30 D/Kollicoat® IR coats, varying from 10 to 20 mg polymer/cm², were investigated with regard to drug release in 0.1 mol/l HCl. Furthermore, the onset of floating, the floating duration and the floating strength of the device were determined. In addition, bench top MRI studies of selected samples were performed. Coated tablets with a 10 mg polymer/cm² SR/IR, and an 8.5: 1.5 coating exhibited the shortest lag-times prior to drug release and the onset of floating, and also the fastest increase in and the highest maximum values of the floating strength. Jang et al prepared a gastro-retentive drug delivery system of DA-6034, a new synthetic Flavonoids derivative, for the treatment of gastritis using an effervescent floating matrix system (EFMS). The therapeutic limitations of DA-6034 caused by its low solubility in acidic conditions were overcome by using the EFMS, which was designed to allow the tablets to float in gastric fluid and release the drug continuously. The release of DA-6034 from the tablets in acidic media was significantly improved by using EFMS, and this was attributed to the effect of the solubilizers and the alkalizing agent such as, sodium bicarbonate, used as gas generating agent. DA-6034 EFMS tablets showed enhanced gastro-protective effects in gastric ulcer induced beagle dogs, indicating the therapeutic potential of EFMS tablets for the treatment of gastritis. [54-56]

Future potential for bilayer floating tablets

Future prospects with respect to herbal drugs Herbal drug delivery is the emerging field in the pharmacy. The use of FBDDS for herbal medicament is the novel approach for the better delivery. The drug release profile has been a major focusing area for the pharmaceutical research scientists for the past two decades. The scientists are finding it a great opportunity to work on GI transit profiles. This has given rise to new products with substantial benefits to the patients. Now with the advent of FBDDS the products have been designed which could release drug for up to 12 or 24 hrs. Using bilayer floating approach combination of two herbal drugs can be also given for more therapeutic effect. Bilayer floating also provides the IR and SR concept for herbal drug as well. Bilayer floating tablets can be beneficial in hypertension and diabetes as immediate response can be achieved by using loading dose as one layer along with sustained release layer which will maintain the concentration of the drug in plasma for prolonged period of time. [57, 58]

6. Conclusion

Bilayer tablet is superior technology to prevail over the deficiency of single layered tablet. Bilayer tablets provide one of the significant intend approaches where incompatible drugs, with different suggestion and same drug with different release rate can be integrated in a single unit. Bilayer tablet is suitable for chronological 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. Many different types of presses are being used to produce bilayer tablets, ranging from simple single-sided press to highly sophisticated machines. The preparation of tablets in the form of bilayers is used to provide systems for the administration of drugs, which are incompatible and to provide controlled release tablet preparations by providing surrounding or multiple swelling layers.

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