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A REVIEW ON BILAYERED FLOATING TABLET OF ANTIHYPERTENSIVE DRUG: THE FUNCTIONAL INSIGHT FOR HYPERTENSION MANAGEMENT

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Abstract

Hypertension is one of the major global risk factors for the cardiovascular disease, stroke and various types of chronic kidney diseases. It is critically important to develop and deploy proven effective interventions and management practices to control blood pressure, reduce the prevalence of heart disease, lower healthcare expenditures, decrease preventable hospitalizations, and improve quality of life. One of the most attractive routes of drug administration is solid oral dosage forms mainly tablets and capsules. The use of flexibility and stability of solid dosage form has made them patient friendly. Conventional oral tablet has frequent dosing and less gastric residence time in stomach, which cause fluctuation of plasma drug concentration, leading to poor therapeutic outcome and sometimes toxicity. Bilayered floating tablets are a better choice than conventional tablets, with improved gastric retention and floating time in the stomach. By facilitating biphasic type delivery, whereby two drugs are released at different rates simultaneously. The bilayered design has advantages such as the ability to formulate incompatible drugs, increase effectiveness and enhance patient compliance. This review put light on various concepts, different advantages, and future prospects of bilayered-floating tablets of antihypertensive drugs for effective management of hypertension.

Keywords: Bilayered tablets, blood pressure, floating tablets, immediate release, antihypertensive drug.

1. Introduction

Hypertension or high blood pressure, is a major ongoing health issue impacting millions of people worldwide. It is the most common but controllable major risk factor for various types of cardiovascular disease includes myocardial infarction, coronary heart disorder, heart failure that leads to stroke, peripheral artery disease and atrial fibrillation. Chronic kidney disease and cognitive impairment is the main single contributor to many deaths and disability around the globe, turning into a significant public health concern [1,2].

Currently, around 874 million mature individuals worldwide have systolic BP of ≥140 mm/Hg, and around 3.5 billion mature individuals have non optimal systolic blood pressure level (i.e., >110–115 mm/Hg). As a result, hypertension affects about one in four adults. Due to population increases and aging a 10% rise in the age-standardized prevalence of hypertension, the sum total of healthy life years lost to non-optimal blood pressure increased by 43% between the years 1990 and 2015 [3,4].

According to data from the Global Burden of Disease study, with 9.4 million deaths and 212 million lost healthy life years, non-optimal blood pressure continues to be the primary risk factor for both the global burden of disease and the global all-cause mortality every year (8.5% of the total) [5].

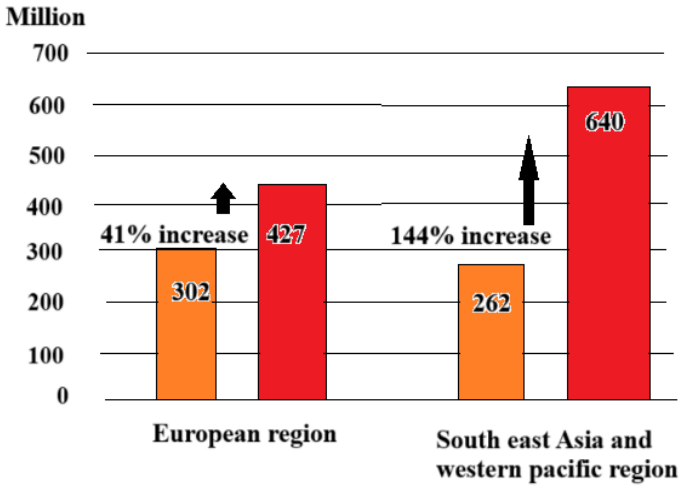

Fig.1- The prevalence of hypertension is rising worldwide, significantly higher in the South east Asia and western Pacific region [6].

Conventional oral treatment for hypertension comes with several challenges, including fluctuating drug levels, frequent dosing, and side effects, which can lead to non-adherence. A major difficulty in the treatment of hypertension is maintaining a consistent drug levels in body for a long period of time. The traditional orally administered drug delivery systems, such as immediate-release tablets, sometimes it results in the change in plasma drug concentrations in body, this leads to a periods of insufficient blood pressure control and increased risk of side effects. [7] This can compromise the efficacy of treatment and impact the therapeutic outcome. To deal with these limitations, innovative drug delivery technologies have been developed, among which bilayered floating tablets have gained notable attention. This kind of oral controlled-release dosage form is intended to increase the drug's duration of gastric residence. One or two medications with varying release rates can be delivered simultaneously. It is possible to control multiple rate-controlling polymers by creating layers of different drugs and polymers, which enables the delivery of different medications [8,9].

The bilayered design allows for the combination to add two different drugs of two different release patterns or different release pattern of the same drug, making it an elegant option for combination therapy in hypertension management [10]. By providing a controlled release layer and sustained release layer mechanism of the drug, it ensures sustained release of active pharmaceutical ingredient (API) over a specified period of time Compared to traditional tablets; this technology has several benefits, such as increased patient compliance, decreased dosing frequency, and improved bioavailability. For the sequential release of two combined medications, bi-layer tablets are suitable [11,12]. It can help maintain consistent blood pressure control throughout the day, reduces risk of heart related events and improve the overall wellness of the patients, Bilayered tablets are widely used for antihypertensive, diabetic, anti-inflammatory, analgesic, and antibiotic medications because these medications often need combination therapy to be effective [13,14]. Bilayereded layers made up of floating systems are designed to help the formulation stay in the stomach. They work especially well for medications that are insoluble or unstable in intestinal fluids. Drug delivery systems that float in the stomach, release the medication over an extended duration at a regulated rate [15, 16].

The creation of bilayered floating tablet for antihypertensive medications presents a viable approach to enhance the results of hypertension patients' treatments. The bilayered floating tablets

offer a novel solution to the challenges comes with hypertension management. Bilayered floating tablets will undoubtedly be important in the treatment of hypertension in the future.

2. Pathophysiology of hypertension

Elevated blood pressure blood in the blood bloodstream is the characteristic of hypertension or high blood pressure. various processes that maintain normal blood pressure, including the SNS, the RAAS system, endothelial function, water & sodium retention, dietary salt, obesity, and insulin resistance been carefully examined to identify the processes that underlie the onset of the illness. Genetics & endothelial dysfunction are also an alternative cause of hypertension. It's a Complex condition affecting several physiological processes [17,18].

2.1. Cardiac output & Peripheral resistance

Pulmonary vascular resistance (PVR) and cardiac output are two essential elements that maintain blood pressure levels within normal ranges. It has been suggested that hypertension results from increased cardiac output caused by sympathetic dysfunction, whereas increases in PVR are essentially the body's response to pressure changes and maintain homeostasis [19,20].

In the pathophysiology of hypertension, peripheral resistance is usually elevated because of higher constriction of the small muscular arterioles. When intracellular calcium levels increase the smooth muscle cells in arteriole walls contract. Long-term Constriction can cause structural reform it leads to permanent resistance. In normal physiology, peripheral resistance rises to shield the capillary bed. Understanding these mechanisms is the key to creating treatments, like calcium channel blockers, that can successfully lower hypertension and prevent harmful complications.

2.2. Renin angiotensin aldosterone system (RAAS):

The renal, cardiovascular system and adrenal are all regulated by the successive peptydergic system known as the renin-angiotensin-aldosterone system Renin-angiotensin-aldosterone system. By influencing arterial constriction and the body's water-sodium retention, primarily controls blood pressure. The pathophysiology of essential hypertension and associated target organ damage has been linked to both circulating Renin-angiotensin-aldosterone system and tissue Renin-angiotensin-aldosterone system, including cardiac Renin-angiotensin-aldosterone system, vascular Renin-angiotensin-aldosterone system, intra-renal Renin-angiotensin-aldosterone system, brain Renin-angiotensin-aldosterone system, and adipose tissue Renin-angiotensin-aldosterone system [13,21].

Renin substrate action on angiotensinogen produces angiotensin I, the angiotensin I is then converted to angiotensin II, a potent substance that constricts blood vessels, elevates blood pressure, and stimulates aldosterone-mediated fluid and sodium retention. Regional blood flow may be modulated by the local Renin-angiotensin-aldosterone system in the kidney, heart, and arterial. By supporting efforts to control hypertension and laying the foundation for more effective therapies, RAS improves patient health and saves lives. The complexity of RAS highlights the need for targeted treatments to address specific mechanisms driving hypertension [22, 23].

2.3. The Autonomic Nervous System (ANS)

The autonomic nervous system's volume, pressure, and chemoreceptor inputs are essential for preserving cardiovascular homeostasis. It does this by regulating cardiac output, peripheral vasculature, & renal function, all of which have an impact on vascular resistance accumulation. An overactive sympathetic nervous system causes hypertension, which raises blood pressure [24, 25].

It controls uncontrollable processes such as breathing, blood pressure, digestion, and heart rate. The parasympathetic nervous system (PNS) and the sympathetic nervous system (CNS) are the two primary components of the ANS. The sympathetic nervous system, also known as the "fight or flight" response, primes the body for hectic or emergency circumstances. On the other hand, the parasympathetic nervous system (PNS) encourages a "rest and digest" state, which aids in energy conservation and recovery. The sympathetic nervous system (SNS) regulates the blood pressure through vasoconstriction and vasodilation by narrowing or widening the blood vessels. It is important in our response to stress and exercise. Inhibiting their effects can reduce blood pressure. Understanding this interplay is critical to our approach to the hypertension therapy.

2.4. Endothelial dysfunction

Vascular endothelial cells control the dilation and constriction of blood vessels through the production of substances such as nitric oxide (vasodilator) and endothelin (vasoconstrictor) [26]. Reduced nitric oxide (NO) availability, a result of elevated oxidative stress in these patients, is the primary underlying process for endothelial dysfunction observed in hypertension. To this extent, endothelium-dependent vasorelaxation remains altered, indicating an irreversible course once hypertension is established, even though efficient anti-hypertensive therapy restores nitric oxide (NO) production. This data suggests endothelial dysfunction as a possible etiological factor in the

onset of hypertension, as do studies showing that suppression of endothelium-derived nitric oxide (NO) synthase causes hypertension in humans (Fig-2) [27]. Hypertension may develop as a result of increased endothelial dysfunction. Therefore, restoring endothelial function holds great potential as a therapeutic strategy.

2.5. Insulin sensitivity

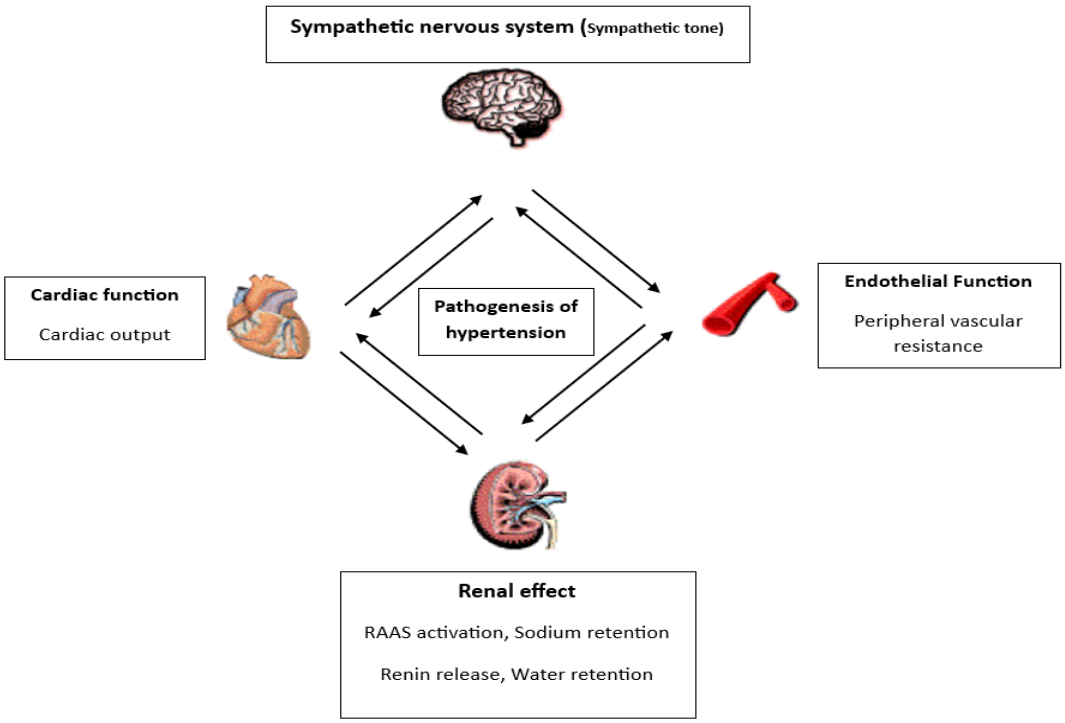

Fig.2 - The systems that contribute to the onset and maintenance of hypertension

Hypertension may result in the development of enhanced endothelial dysfunction. A metabolic syndrome is often indicated by the co-occurrence of several risk factors, including obesity, high blood pressure, diabetes, and high cholesterol [28]. This can increase blood pressure and cause vascular injury. Even non-obese hypertensive patients can present insulin resistance. This hypothesis helps explain how cardiovascular risks can stack, or multiply, increasing overall risk. It reinforces the idea that effective cardiovascular disease prevention must address multiple risk factors.

2.6. Genetic influences

Essential hypertension is probably controlled by many genes. The research show that living with hypertensive parents greatly raises risk of having high blood pressure. Scientific research points to a complicated interaction between inherited risk and sudden environmental changes in high blood pressure. [29]

The variance in blood pressure cannot be explained solely by genetics, indicating the involvement of other risk factors, like epigenetic changes. Recent data suggested that epigenetic mechanisms may play a role in essential hypertension. Human susceptibility to hypertension has been linked to genome-wide DNA methylation. [30,31]

3. Conventional treatment and its drawback

Conventional drug treatment for hypertension typically involves several classes of medications. The main Classes of Antihypertensive Drugs includes

3.1. Diuretics:

Diuretics treat hypertension by increasing the urine production in kidney. The fluid volume reduces in the body and as a result the blood pressure reduces. Diuretics act on the kidneys and it decrease sodium and water reabsorption. It helps to enhance their excretion. This leads to decrease the fluid volume in body. It reduced cardiac burden, lowers the blood pressure and fewer the cardiovascular risks. Effective and widely used [32]. Some examples are Thiazide diuretics (e.g. - Chlorothiazide, Hydrochlorothiazide), Loop diuretics (e.g. - Furosemide) and Potassium-sparing diuretics (e.g. - Eplerenone, Amiloride, Spironolactone).

3.2. Beta blockers:

These beta blockers work very well for treating hypertension as well. It basically works by slowing the heart rate and decreasing cardiac output. Beta blockers generally block the beta receptors and suppress the sympathetic stimulation which results in lowering the blood pressure. As a result the cardiac workload reduces, and oxygen demand minimizes. IT leads to decreasing cardiovascular risks and improving outcomes. This is very much effective in managing hypertension. Examples: metoprolol, atenolol, propranolol

3.3. Angiotensin-converting enzyme inhibitors (ACE): Angiotensin-converting enzyme inhibitors reduce vasoconstriction, which in turn lowers blood pressure, by inhibiting the production of angiotensin II. [33] Vascular relaxation from this causes blood pressure to drop and

fluid retention to decrease. Ultimately it reduced cardiovascular risk, which makes them effective for managing hypertension and heart failure. Examples: lisinopril, captopril, enalapril.

3.4. Angiotensin II receptor blockers (ARB): ARBs treat high blood pressure by blocking Angiotensin II receptors, preventing vasoconstriction and aldosterone-mediated fluid retention. This relaxes the blood vessels, reduces blood pressure results in minimizes cardiovascular stress. ARBs offer similar benefits to ACE inhibitors, including renal protection, with potentially fewer side effects, making them effective for managing hypertension. Examples: valsartan, losartan.

3.5. Calcium Channel Blockers (CCBs): In order to treat hypertension, calcium channel blockers prevent calcium ions from entering cardiac cells and vascular smooth muscle. CCBs cause blood vessel relaxation, reduced vascular resistance, and decreased cardiac workload, lowering blood pressure and oxygen demand effective in managing hypertension, especially in patients with certain comorbidities. Some examples are Dihydropyridine Calcium Channel Blockers (Amlodipine, Nifedipine Felodipine, Isradipine) and Non-dihydropyridine Calcium Channel Blockers (Example - Verapamil, Diltiazem).

4. Drawbacks

The conventional treatment for hypertension management has many drawbacks including gastric emptying time, effects of food, medications, drug interaction. [34]

4.1. Changeable Absorption

4.1.1. Gastric emptying rate: Gastric emptying rate reflects the duration of stomach clearance into the small intestine. Variability in gastric emptying time can significantly impact medication absorption rates.

4.1.2. Food effects: Meals can considerably influence gastric emptying time and drug absorption. Key considerations include:

- Type of food: Fatty meals can slow gastric emptying, while carbohydrates may accelerate it.

- Food-drug interactions: Certain foods can interact with medications, altering their absorption (example-grapefruit juice and certain statins).

- Timing of medication administration: Taking medications with or without food can impact absorption rates and efficacy.

4.2. Impact on Medication Efficacy

Blood pressure variations can result from uneven drug absorption. Loss risk of developing cardiovascular disease blood pressure control may result from this, raising the with signs like drowsiness. To maintain the blood pressure under control Consistent dosing schedules, monitoring the blood pressure, and optimizing medication formulations are used to help Minimize these fluctuations.

4.3. Side Effects:

Many antihypertensive medications are associated with various side effects. For example, ACE inhibitors may result in cough, angioedema, and hyperkalemia as potential side effects. Excessive or over use of Diuretics can lead to electrolyte imbalances in body and beta-blockers may cause bradycardia, fatigue, and sexual dysfunction.

4.4. Drug Interactions:

Antihypertensive medications can interact with other drugs in body. It can potentially reduce their effectiveness also increase the risk of adverse effects.

4.5. Long-Term Management Challenges:

Some medications may require lifelong administration, which can pose challenges for patient compliance due to potential side effects. It also may cause inconvenience to a patient for taking multiple pills.

5. Bilayered floating tablets

It consists of two layers, one for immediate release of drug and the other for sustained release of drug, make up bilayered floating tablets, a kind of oral dosage form intended to deliver drugs in a controlled manner. [35]

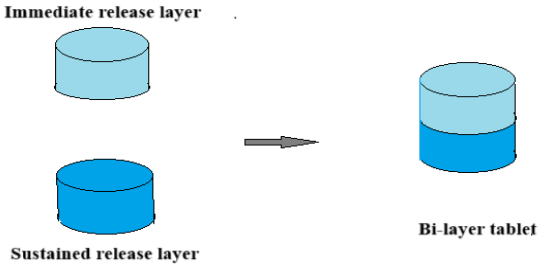

Fig. 3 – Bilayered tablet

5.1. Floating drug delivery system:

The Floating drug delivery systems, or FDDS, are made specifically to remain in the stomach for quite a long time. They float due to incorporated air or gas using effervescent system by slowly releasing from the medicine. This controlled release allows for consistent medicine levels in the body over a extend period of time, which enhance therapeutic efficacy. After releasing the medicine, the empty pill is naturally expelled from the body by various excretion process, provides a convenient and effective treatment approach with improved patient outcomes [36].

5.2. Preparation of bilayered tablet:

Step 1: Formulation

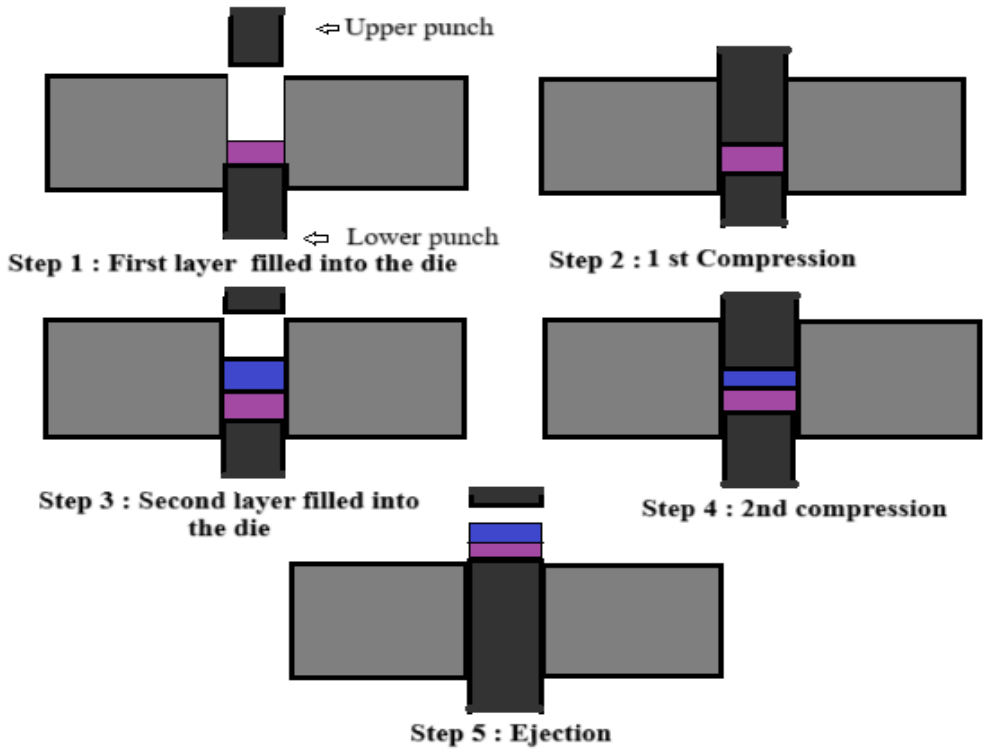

Fig.4-Steps to prepare bilayered tablet [37].

1. Layer 1: first layer blend prepares by mixing the active ingredient including excipients like fillers, binders, disintegrants, and other necessary components. [38]

2. Layer 2: The layer second blend Prepare by mixing the active ingredient, excipients, and other necessary components.

Step 2: Compression of First Layer

1. Tablet press: The first layer compressed by a bilayered tablet press or a standard tablet press with a bilayered attachment.

2. First layer compression: Compress the first blend into a layer in a controlled compression force and specific tablet weight.

Step 3: Layering and Compression of Second Layer

1. Adding second layer: Add the second blend on top of the first layer.

2. Final compression: Compress the two layers together to form a single bilayereded tablet with a higher compression force that ensures a strong bond between the layers.

5.3. Mechanism of floating system:

As floating drug delivery systems [FDDS] have a lower bulk density than gastric fluids, they stay afloat in the stomach for an extended amount of time without influencing the rate at which the stomach empties. The medication is gradually released from the system at the appropriate rate while it is floating on the contents of the stomach. The residual system is drained from the stomach following drug release. As a result, the GRT rises and the variations in the drug concentration in plasma are better managed. However, to maintain the dosage form consistently buoyant on the meal's surface, a minimal level of floating force (F) is also necessary in addition to a minimal gastric content that permits the correct realization of the buoyancy retention principle [39].

A novel apparatus for determining the resultant weight has been reported in the literature to measure the kinetics of the floating force. The device works by continuously measuring the force equal to F (as a function of time) needed to keep the submerged object in place. If F is on the higher positive side, the object floats more easily. In order to avoid the disadvantages of unpredictable intra-gastric buoyancy capability variations, this device aids in optimizing FDDS with regard to stability and durability of floating forces generated. Fig 5 [40]

F = F buoyancy – F gravity = (Df - Ds) gv

Where, F= total vertical force, Df = fluid density,

Ds = Object density, v = Volume, G= acceleration due to gravity

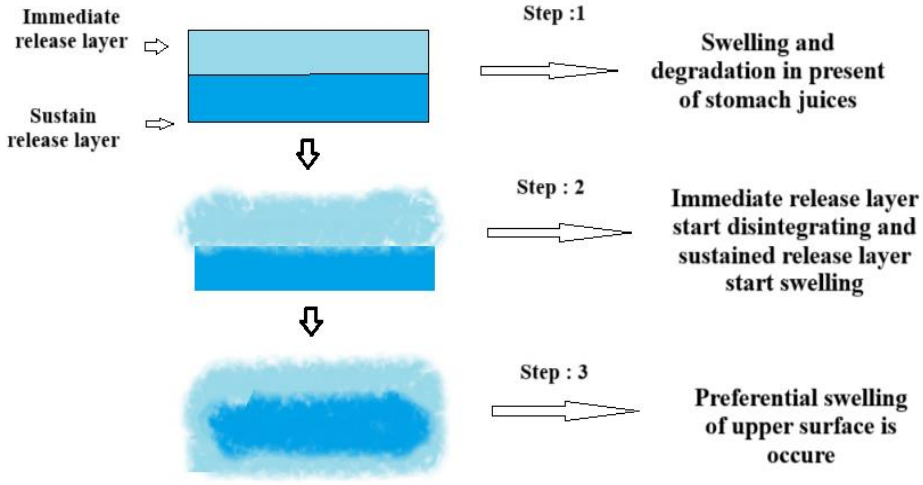

Fig.5- Simple diagram showing the mechanism of floating DDS

5.4. Release pattern of bilayered floating tablets

In order to maintain relative shape integrity and a maximum dry density with less than unity within in the external gelatinous barrier, floating dosage forms entail closely mixing the drug with a gel-forming hydrocolloid that swells when it comes into contact with gastric fluid following oral administration (Fig 6) [41, 42].

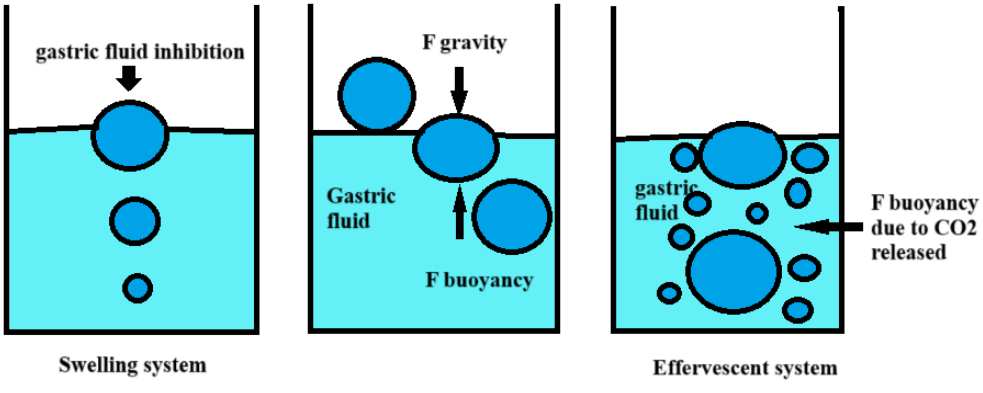

Fig.6 -Release pattern in floating bilayereded tablet

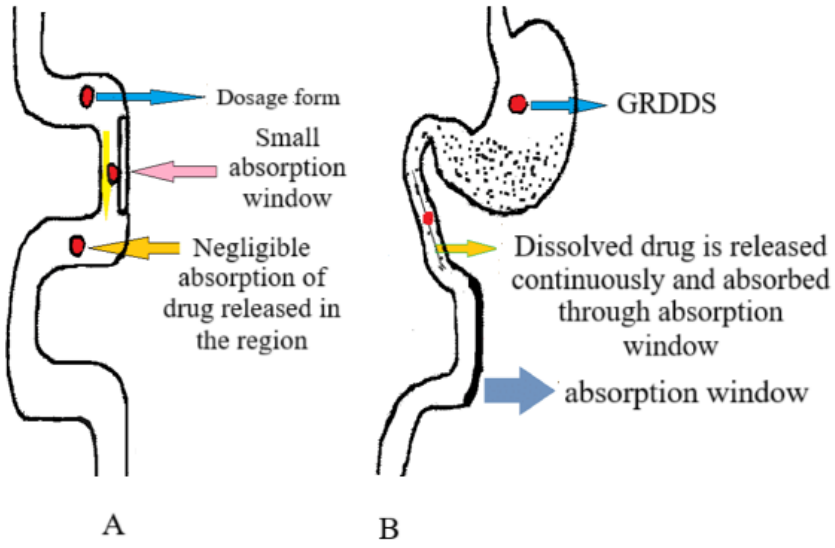

Fig.7: Traditional Dosage i.e. A shows very little absorption While the floating drug (B) is continuously absorbed [44]

5.5. Table 1: Different type polymers generally used in floating drug delivery system [43]

Polymers used in Sustained Release formulation.	Polyethylene Glycol (PEG), Carbopol, Hydroxypropyl Methylcellulose K15M, Hydroxypropyl Methylcellulose K100M, Polycarbonate, Sodium Alginate
Effervescent Generating agent	Sodium Bicarbonate, tartaric Acid and citric acid etc.
Polymers that decrease the release rate.	Magnesium Stearate, talc, Dicalcium Phosphate (DCP)
Buoyancy increaser Polymers.	Ethyl cellulose
Polymers that increase the release rate.	Lactose, mannitol

5.6. Some common natural polymers used in the formulation of floating drug delivery system (FDDS)

Guar gum, Pectin, Chitosan, Xanthum gum, Alginates

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5.7. Various types of floating drug delivery system (FDDS):

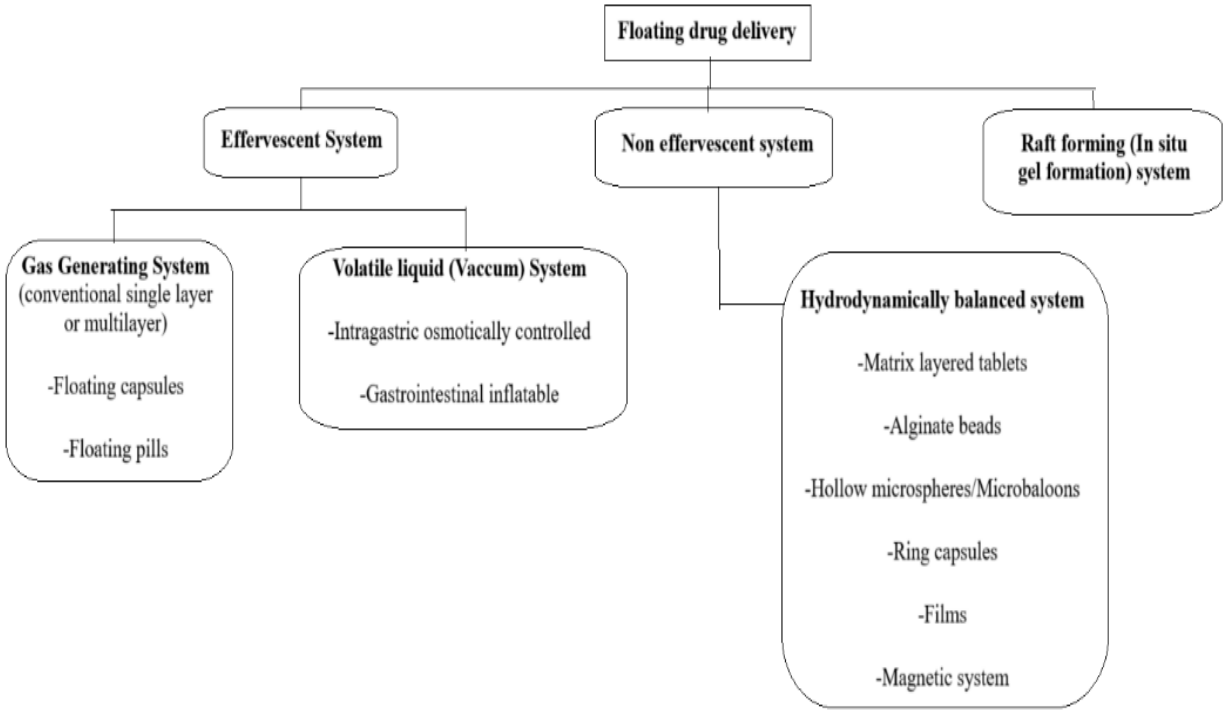

Fig.8 - Types of floating drug delivery system

5.7.1. Effervescent system:

When floating tablets come into contact with gastric juice, they produce carbon dioxide, which is used in effervescent drug delivery systems. By allowing the dosage form to remain afloat in the stomach, this procedure promotes prolonged drug delivery and retention.[45] Advantages include enhanced bioavailability, targeted action, and minimized adverse effects. These formulations usually Include effervescent components, polymers for controlled release, and the active pharmaceutical ingredient (API).

5.7.2. Non-effervescent system:

Non-effervescent systems are completely opposite to effervescent system it floats or remain in the stomach without releasing gas [46]. These systems run by hydrocolloids, polymers, or other materials that swell or gel upon contact with stomach fluids, it allows the dosage form to float or adhere to the gastric mucosa. This approach enables sustained release of the drug leads to improving bioavailability and therapeutic efficacy. Non-effervescent systems are suitable for drugs requiring prolonged gastric retention and can enhance patient compliance by reducing dosing frequency [47].

5.8. Advance techniques used in the preparation of bilayered tablet:

5.8.1. OROS Push Pull Technology: This method primarily consists of two or more than two layers, one of which is a push layer and the other one or more of which must contain the medication [P]. It generally consists of a medication and two or more than two agents, like osmotic and suspending agents, that are used in the drug layer. The tablet's core is surrounded by a semipermeable membrane. [48]

5.8.2. L-OROS Technology: This system is often used to address the drug's solubility issue. The L-OROS system has an osmotic push layer with a semi-permeable membrane, a lipid soft gel product that holds the drug in a dissolved state, and an exit orifice that is drilled. [49]

5.8.3. EN SO TROL Technology: enhanced solubility by a scale factor of or the development of an ideal dosage form Shire's drug delivery lab employs a comprehensive approach, focusing on the identification and incorporation of found enhancers into technologies for controlled release. [50]

5.8.4. DUROS Technology: An inner outer side titanium alloy reservoir and a titanium alloy reservoir makes up the system. This reservoir effectively shields the active molecules from enzymes and is incredibly durable. The DUROS technique is a tiny drug delivery device that looks like a tiny syringe and releases tiny doses of potent medication over the course of months or years.

5.8.5. DUREDAS™ Technology: The double release delivery system from Elan Drug Techniques is another name for this system. With DUREDASTM Technology, a bilayered tablet, two medications can be released either immediately or over time, or the same medication can be released at different rates in a single dosage form. Within a single tablet, the tableting process can

produce two distinct layers: an immediate controlled - release granulates and a hydrophilic matrix complex. A mix of hydrophilic polymers gives the dosage form its modified-release characteristics [51].

5.9. Factors effecting on floating time:

Floating drug delivery systems are influenced by several factors:

1. Caloric content: High-protein and high-fat meals extend floating duration.

2. Meal composition: Indigestible polymers and fatty acids can slow the gastric emptying time.

3. Fed vs. unfed state: Unfed or Fasting state can trigger strong stomach contractions.

4. Frequency of feed: Repeated meals prolong floating time of drug in stomach.

5. Age: Individuals who are over 60, experience extended floating durations of drug.

6. Posture and Concurrent medication administration also impact floating time.

6. Applications

1. A bi-layer tablet can be used to release two medications sequentially. Two incompatible substances should be separated. [52]

2. Sustained release tablet has two layers: a dose maintaining layer, also known as sustain release, another one is immediate release layer, which serves as the initial dose. [53]

3. The improved, useful mechanism of the bi layer tablet addresses the drawbacks of the single-layered tablet. Promoting Patient Convenience and Compliance.

4. The starting dose and prolonged dose of the same or various medications are administered using bilayered tablets. [54]

5. To administer two distinct medications with disparate release profiles, bi layer tablets are utilized.

7. Need for bi layer floating tablets:

1. To regulate the rate at which one or two API are delivered.

2. The Life cycle development and novel delivery methods, like mucoadhesive, buccal, or various chewing devices and floating tablets for GRDDS, can enhance fixed-dose combinations [55].

3. To regulate the production of active pharmaceutical ingredient from one layer by utilizing the functional property of another layer, and to isolate incompatible active pharmaceutical ingredients from one another [56].

4. To achieve a swellable or erodible form for modified release, the active pharmaceutical ingredient layer's total surface area can be altered by sandwiching it between one or two inactive layers [57].

Bilayered floating tablets offer a promising approach for controlled drug delivery, improving patient outcomes and convenience.

8. Advantages of floating bilayereded tablets

1. Patient compliance increases with easy administration. Site-specific delivery is accomplished with floating systems for medications like Furosemide and Riboflavin. [58]

2. Because this system floats in the abdomen for several hours, these tablets offer prolonged drug delivery and longer gastric residence time.

3. Ideal for large-scale manufacturing, Coating can be used to cover up unpleasant odors and bitter tastes. [59]

4. This system is microbiologically and chemically stable.

5. Tablets are inexpensive as compared to other oral drug delivery systems and are simple and convenient to swallow [60].

9. Disadvantages of bilayered floating tablets

1. It is impossible to formulate medications that cause irritation to the gut's gastric mucosa and have issues with solubility and stability [61].

2. The stomach must have a high fluid content in order for the system to function properly.

3. Lack of adequate bonding causes the layer to separate, yield is reduced, and there is a chance that two layers will mix [62].

4. Some medications are amorphous and have low densities, which prevents them from forming compacts because they fight back compression.

5. Swallowing problems of children and patients who are unconscious [63].

10. Advantages of bilayereded tablet over conventional tablets

1. It is possible to maintain a drug's level in blood at steady therapeutic concentrations to enhance drug release, accurateness, protection, and minimize adverse effects. By directing the drug's release to the site of absorption and managing its rate, negative effects can be minimized and the overall drug content can be decreased [64].

2. Compared to conventional delivery methods, fewer daily doses are needed, improving patient comfort. Increased patient compliance results in more effective medication regimens [65].

3. Bilayered tablets are well suited for repeat action products, in which the first dose is delivered by one layer of a layered tablet that quickly dissolves in the stomach. The remaining layers are released into the intestinal environment but remain insoluble in the gastric media.

4. One layer on a blended tablet provides instant release, while another layer behaves as sustained release in bilayered tablets [66].

5. There are various ways to add the loading dose to the maintenance dose in a sustained release drug delivery system, including placing the effective dose in a tablet cover with the maintaining part in the core, as in a compression-coated tablet, and simply adding a sustained dose of a drug to the sustained portion [67].

Table 2: Bilayered Antihypertensive tablets available in the market [68]

Category of drug	Available Drugs	Brand name(proprietary)
diuretic combinations	Hydrochlorothiazide and Amiloride	Moduretic
	spironolactone and hydrochlorothiazide	Aldactazide
ACE inhibitors	Hydrochlorothiazide and Benazepril	Lotensin-HCT
	Captopril and hydrochlorothiazide	Capozide
	Lisinopril and hydro chlorothiazide	zestoretic

Beta blockers and diuretics	Atenolol and chlorthalidone	tenoretic
	Metoprolol and hydrochlorothiazide	Lopressor HCT
	Propranolol and hydrochlorothiazide	inderide
Calcium channel blockers and angiotensin-converting enzyme inhibitors	Amlodipine and	Lotrel
	Diltiazem and enalapril	teczem

12. Conclusion

Bilayered Floating Tablets are an Innovative solution that overcomes the limitations of single-layer tablets. It enables dual drug release features includes sustained and immediate, which lasts up to 24 hours. This innovative system prolongs the gastric retention time, as a result bioavailability enhanced and therapeutic efficacy increases. By allowing Parallel administration of two medications, it improves patient compliance and simplifies treatment Protocols. Bilayered Floating Tablets are particularly beneficial for medications with narrow absorption windows. Antivirals, antibiotics, and antifungals are the type of examples which require precise delivery to achieve favorable effects. Bilayered Floating Tablets offer a versatile and effective drug delivery system. Improves patient outcomes and simplifying pharmaceutical manufacturing, making them an Attractive choice for diverse therapeutic applications.

13. Acknowledgement

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