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Review Article

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A Review on Gastroretentive Drug Delivery System of Antihypertensive Drugs

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Abstract Oral drug administration is also the favored method of drug administration. GRDDSs are a novel approach in the Pharmaceutical Industry (Gastroretentive Drug Delivery System). Dosage forms that can be retained in the stomach are called GRDDs. By continually releasing the drug for a long period of time until it reaches its absorption site, GRDDSs can enhance the regulated release of drugs with an absorption window. GRDDS are thus favourable for such drugs by improving their bioavailability, therapeutic effectiveness, and the possibility of dose reduction, as well as improving drug solubility, which is less soluble in a high pH setting. In this review, Gastroretentive Drug Delivery System of antihypertensive is discussed.

Keywords Gastroretentive Drug Delivery System, Floating, Antihypertensive, GRDDS, FDDS

Introduction

Drug delivery systems are a competitive mechanism for diversifying markets and indications, improving product life cycles, and creating new opportunities [1-2]. Oral drug administration is also the favored method of drug administration [3]. Because of its ease of ingestion, pain avoidance, versatility, and most notably, patient enforcement, oral administration is the most common route for systemic impact. Furthermore, since strong oral delivery systems do not need sterile conditions, they are less costly to produce [1-3]. Solid drug formulations are widely used due to their low cost, ease of administration, effective dosage self-medication, pain avoidance, and, most notably, patient compliance. Tablets and capsules are the most popular solid dosage types [3-4]. A tablet that dissolves or disintrigrants in the oral cavity without the need for water or chewing is a fast-dissolving drug delivery device in most situations. To obscure the taste of the active agent, most fast-dissolving delivery system films must contain substances [4-5]. GRDDSs are a novel approach in the Pharmaceutical Industry (Gastroretentive Drug Delivery System). Dosage forms that can be retained in the stomach are called GRDDs. By continually releasing the drug for a long period of time until it reaches its absorption site, GRDDSs can enhance the regulated release of drugs with an absorption window [6]. Gastroretentive dosage forms are intended to be stored in the gastric region for an extended period of time and release inserted drug candidates, allowing for continuous and prolonged drug input to the upper part of the GIT and thereby maintaining optimum bioavailability [7]. As a result, they not only extend dosing cycles but also improve patient consistency above that of currently available controlled release dosage formulations [7-9]. GRDDS are thus favourable for such drugs by improving their bioavailability, therapeutic effectiveness, and the possibility of dose reduction, as well as improving drug solubility, which is less soluble in a high pH setting [10]. Apart from these benefits, these devices have pharmacokinetic benefits such as the

continuation of steady therapeutic levels for a long period of time and hence a decrease in therapeutic level fluctuation. Gastric preservation would have benefits such as allowing products with short absorption windows to be delivered to the small intestine. Additionally, a longer gastric retention period in the stomach can be beneficial for local action in the upper small intestine [8-10].

Stomach's Physiology

The functions of stomach are to store and macerate food, and begin early phases of food digestion [11]. The stomach is an organ that has the ability to store and combine food. The stomach is divided into three areas anatomically: fundus, body, and antrum (pylorus). There are members of certain mammalian orders with extremely sacculated forestomachs (e.g., some artiodactyls and some primates). This division is permanent, and it assists in the digestion of meals [11]. Between the oesophagus and the first portion of the small intestine is the stomach, a thickly walled organ (the duodenum). The fundus of the stomach lies against the diaphragm on the left side of the abdominal cavity. The pancreas is located beneath the stomach. The larger curvature drapes the bigger omentum. The stomach is lined with a mucous membrane that includes glands (with main cells) that produce gastric fluids. This digestive fluid can create up to three quarts each day. Due to the parasympathetic signals of the vagus nerve, the gastric glands begin secreting before food enters the stomach, making the stomach a storage tank for that acid.

Each of the region of the stomach has its own set of cells and activities. The sections are as follows:

- Where the contents of the oesophagus drain into the stomach is the cardiac area.
- The fundus, which is created by the organ's top curvature.
- The major core portion is the body.
- The bottom part of the organ, known as the pylorus or atrium, aids in the emptying of the contents into the small intestine.

The contents of the stomach are kept confined by two smooth muscular valves, or sphincters. They are the following:

- The sphincter that separates the oesophagus and the heart.
- The pyloric sphincter, also known as the pyloric aperture, separates the stomach from the small intestine.

The hepatic left gastric, right gastric, and right gastroepiploic branches, as well as the lineal left gastroepiploic and short gastric branches, all nourish the stomach. They feed the muscular coat, then ramify in the submucous coat before reaching the mucous membrane. At the base of the stomach tubules, the arteries split into a plexus of tiny capillaries that flow upward between the tubules. They merge with one another to produce a plexus of bigger capillaries that surround the tube openings and form hexagonal meshes surrounding the ducts. The veins emerge from these and follow a straight path downhill, between the tubules, to the submucous tissue, where they terminate in the lineal and superior mesenteric veins or the portal vein directly. There are a lot of lymphatics. They are made up of a superficial and a deep set, and they go along the organ's two curvatures to the lymph glands. The nerves are the terminal branches of the right and left urethras, as well as other sections of the organ, with the former dispersed on the back and the latter on the front. It also receives a large number of sympathetic plexus branches from the celiac plexus. In the gut, nerve plexuses are located in the submucous coat and between the layers of the muscular coat. The muscle tissue and the mucous membrane get fibrils from these plexuses [11-13].

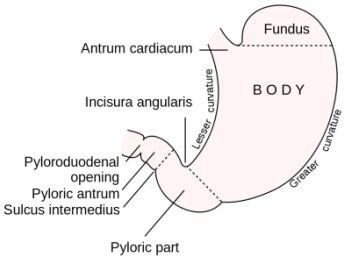


Figure 1: Diagram of Stocmach [11]

An ideal Properties of Gastroretentive Drug Delivery System

- Drugs acting locally in the upper part of GIT.
- Drugs are mainly absorbed in the upper part of GIT.
- Drugs are less soluble at basic pH.
- Drugs having narrow absorption window.
- Drugs are quickly absorbed from GIT.
- Drugs are unstable or degraded at basic pH [5-10].

Requirements for Gastroretentive Drug Delivery System

- Drugs that are absorbed from the gastrointestinal tract's proximal portion
- Drugs that are less soluble or are destroyed by the basic pH at the GIT's lower region
- Drugs that are absorbed despite the fact that the stomach emptying time varies.
- To treat some diseases, local or sustained medication administration to the stomach and proximal small intestine is used.
- Very usefull for treating peptic ulcers caused by *H. Pylori* infections [8-11].

Approaches of Gastroretentive Drug Delivery System

The possible approaches of Gastroretentive Drug Delivery System are as follows:

- Low-density systems/ floating systems
- High density systems
- Expandable systems
- Bioadhesive systems
- Raft forming systems
- Bioadhesive systems
- Raft forming systems
- Super-porous hydrogel systems
- Magnetic systems
- Ion-exchange resin systems [14-25]

Advantages of Gastroretentive Drug Delivery System

- Enhanced bioavailability
- Sustained drug delivery
- Site specific drug delivery
- Reduced fluctuation of drug concentrations
- Improved selectivity in receptor activation [7-9]

Limitations of Gastroretentive Drug Delivery System

Gastroretentive Drug Delivery System has the ability to improve the bioavailability of medicines with narrow absorption window. They do, however, have certain limits.

- GRDDS require high fluid level in stomach to float and work effectively.
- Ulcerogenic drugs are not suitable
- Drugs that absorbed from colon.
- Patients with achlorhydria
- GRDDS are not suitable drugs that are not stable and solubility issues in stomach.
- Drugs having irritant effect on gastric mucosa are not suitable for GRDDS.
- Drugs which undergo first pass metabolism are not suitable candidate e.g. Nifedipine [25].

Factors Effecting Gastric Retention of Dosage Forms

- Density
- Size
- Shape of dosage forms
- Single or multiple unit formulation
- Fed or unfedstate- under fasting conditions
- Nature of meal
- Caloric content
- Frequency of feed
- Gender
- Age
- Posture
- Disease State
- Concomitant Intake of Drug
- Gastric motility enhancers or depressants

Mechanism of Floating Drug Delivery Systems

The slow drug release is accompanied with requisite rate during the system flow on the gastric contents. Based on the buoyancy mechanism, floating systems are classified as follows

- Low density systems
- Hydrodynamically balanced system
- Microporous compartment systems
- Alginate beads
- Hollow microspheres
- Gas generating systems
- Volatile Liquid/Vacuum Containing Systems [17-26].

Evaluation of Gastroretentive Drug Delivery System

Pre compression parameters:

- Bulk density
- Tapped density
- Hausner's ratio (HR)
- Carr's compressibility index
- Angle of repose

Post Compression Parameters:

- Weight variation test
- Hardness test
- Friability test
- Floatation studies
- Drug content uniformity
- Drug release study [17-26]

Hypertension

"High blood pressure (hypertension) is a common condition in which the long-term force of the blood against your artery walls is high enough that it may eventually cause health problems, such as heart disease" [27].

The amount of blood your heart pumps, as well as the amount of resistance to blood flow in your arteries, influence your blood pressure. The greater your blood pressure, the more blood your heart pumps and the narrower your arteries become. The measurement of blood pressure is in millimetres of mercury (mm Hg). Both the systolic and diastolic pressures are essential. Hypertension may be present if the values are excessively high. There may be inadequate blood flow to important organs, such as the brain, if blood pressure levels are too low [27-29].

Systolic Blood Pressure: The pressure exerted by your blood flowing through your arteries is not constant but is dynamic, and constantly reflects what the heart is doing at a given moment. When the heart is actively beating (an event called "systole"), it is ejecting blood out into the arteries. This dynamic ejection of blood into the arteries causes the pressure within the arteries to rise. The peak blood pressure reached during active cardiac contraction is called the systolic blood pressure. A "normal" systolic blood pressure when a person is sitting quietly is 120 mmHg or below [27-29].

Diastolic Blood Pressure: The diastolic blood pressure is the pressure the blood exerts within the arteries in between heartbeats, that is, when the heart is not actively ejecting blood into the arteries [27-29].

Sign and Symptoms: Hypertension is usually a quiet illness. Many people will not show any signs or symptoms. It may take years, if not decades, for the disease to progress to the point where symptoms are visible. Even yet, these symptoms might be due to anything else. Even then, these symptoms may be attributed to other issues.

Symptoms of severe hypertension may include:

- blood in the urine
- chest pain
- dizziness
- Fatigue or confusion
- flushing
- headaches
- nosebleeds
- Pounding in your chest, neck, or ears
- shortness of breath
- visual changes [30-31]

Causes of Hypertension

There are two types of hypertension. Each type has a different cause.

Primary Hypertension

Primary hypertension is also called essential hypertension. This kind of hypertension develops gradually and has no known aetiology. This is the most common kind of high blood pressure. The processes that cause blood pressure to gradually rise are yet unknown to researchers. A number of things might be at play. These may include:

Environment: Unhealthy lifestyle choices, such as a lack of physical exercise and a bad diet, can take a toll on your body over time. Weight issues can be caused by lifestyle decisions. Hypertension is more likely if you are overweight or obese.

Physical changes: If anything in your body changes, you may start to have problems all over your body. One of these concerns might be high blood pressure. Changes in kidney function related to age, for example, are considered to disturb the body's normal salt and fluid balance. Your blood pressure may rise as a result of this shift.

Genes: Hypertension is a condition that some people are genetically susceptible to. This might be due to inherited genetic abnormalities or gene mutations from your parents [28-31].

Secondary Hypertension

Secondary hypertension develops more quickly than primary hypertension and might be more severe. Secondary hypertension can be caused by a number of factors, including:

- adrenal gland problems

- alcohol abuse or chronic use
- certain endocrine tumors
- congenital heart defects
- kidney disease
- obstructive sleep apnea
- problems with your thyroid
- side effects of medications
- use of illegal drugs [28-31]

Table 1: Diagnosis of Hypertension [32-35]

Category	Systolic (mmHg)	Diastolic (mmHg)
Optimal	<120	<80
Normal	120-129	80-84
High Normal	130-139	85-89
Grade 1 Hypertension	140-159	90-99
Grade 2 Hypertension	160-179	100-109
Hypertension Crisis	≥180	≥110

Pathophysiology of Hypertension

Essential hypertension has a complicated and complex aetiology. Hypertensive processes include the interplay of several organ systems and numerous mechanisms of independent or interdependent pathways, and the kidney is both a contributing and a target organ. Genetics, activation of neurohormonal systems such as the sympathetic nervous system and the renin-angiotensin-aldosterone system, obesity, and increased dietary salt consumption are all key factors in the aetiology of hypertension. The condition of persistently elevated systemic blood pressure is known as arterial hypertension (BP). The product of cardiac output and total peripheral vascular resistance is blood pressure (BP) [36-39].

Secondary hypertension accounts for around 5-10% of all cases of hypertension, with primary hypertension accounting for the rest. The aetiology of secondary hypertension is recognised, but the cause of initial hypertension is unknown (i.e., idiopathic). Secondary hypertension can be caused by a variety of causes. Regardless of the reason, arterial pressure rises as a result of a rise in cardiac output, a rise in systemic vascular resistance, or a combination of the two. Higher neurohumoral stimulation of the heart or increased blood volume are the two most common causes of increased cardiac output. Increased sympathetic activity or the effects of circulating vasoconstrictors are the most prevalent causes of increased systemic vascular resistance. Secondary hypertension is best treated by treating or eliminating the underlying illness or pathology, however antihypertensive medications may still be required.

Some causes for secondary hypertension are listed below:

- Aortic coarctation
- Chronic renal disease
- Hyper- or hypothyroidism
- Pheochromocytoma
- Preeclampsia
- Primary hyperaldosteronism
- Renal artery stenosis
- Sleep apnea
- Stress [40-47]

Management of Hypertension

The hypertension can be managed by Lifestyle modifications and drugs. In lifestyle, it usually restricted by “dietary changes, physical exercise, weight loss, yoga, meditation etc.” [48-50].

"Several fitness regimes can be effective in lowering the blood pressure, including isometric resistance exercise, cardiovascular exercise, resistance exercise and breathing related exercise" [48-49].

Medications

Hypertension is treated by many types of medicines, are known as antihypertensive drugs, are currently available e.g. Calcium channel blockers, Adrenergic receptor antagonists (beta and alpha blockers), Vasodilators, Aldosterone receptor antagonist, ACE inhibitors, Renin inhibitors, Diuretics, AT_2 receptor antagonists, Endothelium receptor blockers etc [51-53].

Classification of Antihypertensive Drugs [54-57]

Table 2: Classification of Antihypertensive Drugs

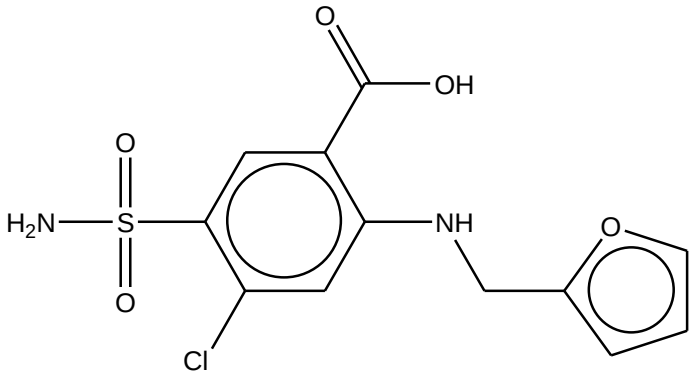
Diuretics	
Loop diuretics	
"Bumetanide"	"Ethacrynic acid"
"Furosemide"	"Torsemide"
Thiazide diuretics	
"Epitizide"	"Chlorothiazide"
"Bendroflumethiazide"	"Methyclothiazide"
"Polythiazide"	
Thiazide-like diuretics	
"Indapamide"	"Chlorthalidone"
"Metalozone"	"Xipamide"
"Clopamide"	
Potassium-sparing diuretics	
"Amiloride"	"Triamterene"
"Spironolactone"	"Eplerenone"
Calcium channel blockers	
Dihydropyridines	
"Amlodipine"	"Cilnidipine"
"Clevidipine"	"Felodipine"
"Isradipine"	"Lercanidipine"
"Levamlodipine"	"Nicardipine"
"Nifedipine"	"Nimodipine"
"Nisoldipine"	"Nitrendipine"
Non-dihydropyridines	
"Diltiazem"	"Verapamil"
ACE inhibitors	
"Captopril"	"Enalapril"
"Fosinopril"	"Lisinopril"
"Moexipril"	"Perindopril"

"Quinapril"	"Ramipril"
"Trandolapril"	"Benazepril"
Angiotensin II receptor antagonists	
"Azilsartan"	"Candesartan"
"Eprosartan"	"Irbesartan"
"Losartan"	"Olmesartan"
"Telmisartan"	"Valsartan"
"Fimasartan"	
Adrenergic receptor antagonists	
Beta blockers	
"Acebutolol"	"Atenolol"
"Bisoprolol"	"Betaxolol"
"Carteolol"	"Carvedilol"
"Labetalol"	"Metoprolol"
"Nadolol"	"Nebivolol"
"Oxprenolol"	"Penbutolol"
"Pindolol"	"Propranolol"
"Timolol"	
Alpha blockers	
"Doxazosin"	"Phentolamine"
"Indoramin"	"Phenoxybenamine"
"Prazosin"	"Terazosin"
"Tolazoline"	
Mixed Alpha + Beta blockers	
"Bucindolol"	"Carvedilol"
"Labetalol"	
Vasodilators	
"Sodium nitroprusside"	"Hydralazine"
Renin inhibitors	
"Aliskiren"	
Aldosterone receptor antagonist	
"Eplerenone"	"Spironolactone"
Alpha-2 adrenergic receptor agonists	
"Clonidine"	"Guanabenz"
"Guanfacine"	"Methyldopa"
"Moxonidine"	
Endothelium receptor blockers	
"Bosentan"	

Gastroretentive Drug Delivery System of Antihypertensive Drugs

Furosemide

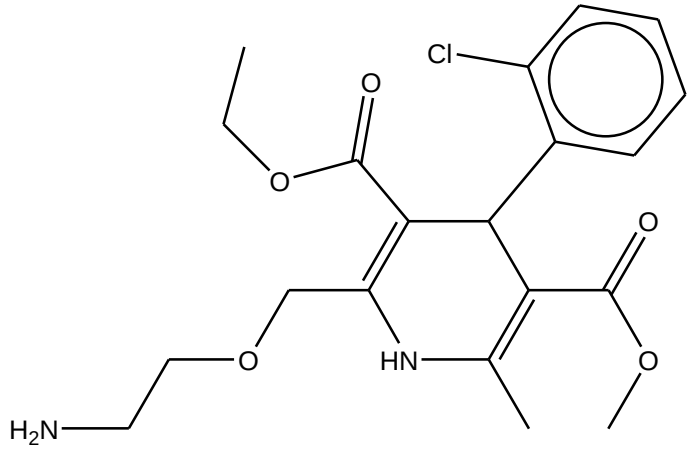
Furosemide is used to reduce extra fluid in the body (edema) caused by conditions such as heart failure, liver disease, and kidney disease. Bioavailability of Furosemide is 43–69%. It may also be used for the treatment of high blood pressure [58].



Floating drug delivery systems of furosemide were formulated using various concentrations of polymers such as HPMC K4M, HPMC K15M, HPMC K100M, ethyl cellulose and effervescing agents sodium bicarbonate and citric acid. The release of the medication from the floating tablets was discovered to be non fickian diffusion with zero order kinetics [59].

Amlodipine

Amlodipine is used with or without other medications to treat high blood pressure [60].

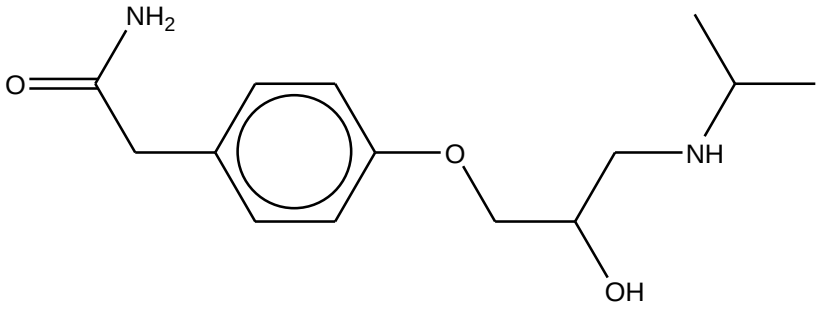


Porwal, A. *et al* (2020) optimized capsulated unfolding type gastroretentive bilayer film constituting immediate release (IR) layer of amlodipine besylate and sustained release (SR) layer of atorvastatin calcium [61].

Amlodipine besylate has maximum solubility in acidic pH and thus most suitable to prolong release of drug in stomach and a novel gastro retentive floating microsphere was developed of Amlodipine Besylate [62].

Atenolol

Atenolol (Tenormin) is a beta-blocker that affects the heart and circulation (blood flow through arteries and veins). Atenolol is used to treat angina and hypertension [63].



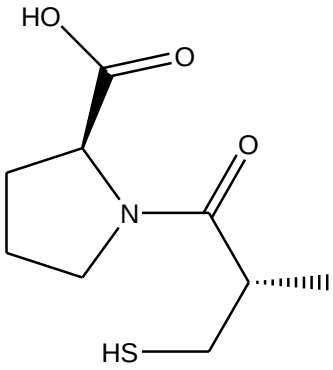
Kumar *et al* (2021) formulated, characterized, and evaluated to establish the bioavailability of gastroretentive mucoadhesive dosage of atenolol in human subjects with possible *in-vitro-in-vivo* correlation [64].

Gastroretentive floating drug delivery systems (GFDDS) of atenolol, an antihypertensive drug, with an oral bioavailability of only 50% (because of its poor absorption from lower gastrointestinal tract) [65].

Eswer and Saritha (2011) prepared Floating tablets of Atenolol with different polymers [66].

Captopril

Captopril is an ACE inhibitor used for the management of essential or renovascular hypertension, congestive heart failure, left ventricular dysfunction following myocardial infarction, and nephropathy [67].



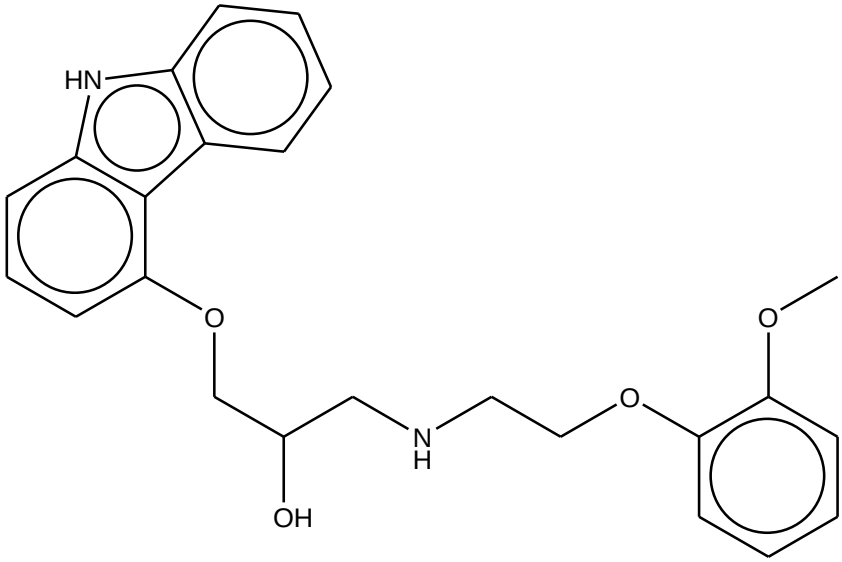
A gastro retentive floating drug delivery system with multiple-unit minitab's based on gas formation technique was developed [68].

FDDS is desirable for drugs with an absorption window in the stomach or in the upper small intestine like as Captopril that is an angiotensin-converting enzyme inhibitor and has been widely used for the treatment of hypertension and congestive heart failure. *In vitro* release of captopril (12 hrs) floating tablets was studied [69].

Kapoor *et al* (2014) developed floating microspheres of Captopril in order to achieve an extended retention in the upper GIT which may enhance the absorption and improve the bioavailability [70].

Carvedilol

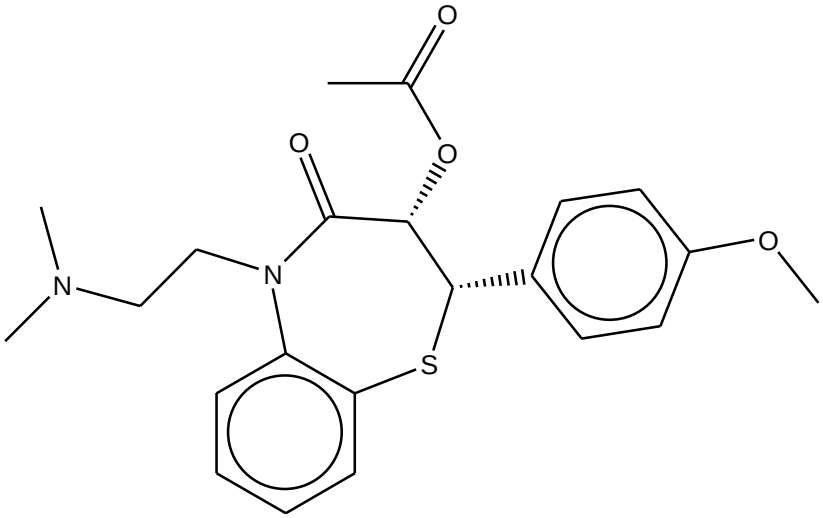
Carvedilol is used to treat high blood pressure and heart failure [71].



Carvedilol (CVD) is an antihypertensive agent with a short half-life, pH-dependent solubility, and narrow absorption window. The floating-drug delivery-system of carvedilol was prepared to increase its half-life [72]. Several researchers have reported FDDS and GRDDS of carvedilol [73-78].

Diltiazem

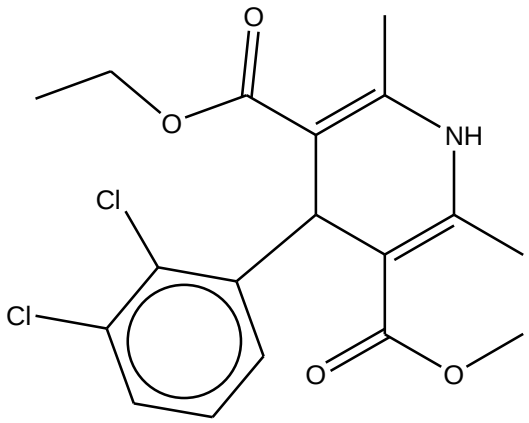
Diltiazem is a calcium channel blocker. It works by relaxing the muscles of your heart and blood vessels. Diltiazem is used to treat hypertension (high blood pressure), angina (chest pain), and certain heart rhythm disorders [79].



Tavakoli *et al* (2007) prepared and evaluated a floating drug delivery system for Diltiazem HCl [80]. Saxena *et al* (2016) formulated and characterized of floating beads of diltiazem hydrochloride [81]. Several other GRDDS and FDDS of Diltiazem were developed [82-88].

Felodipine

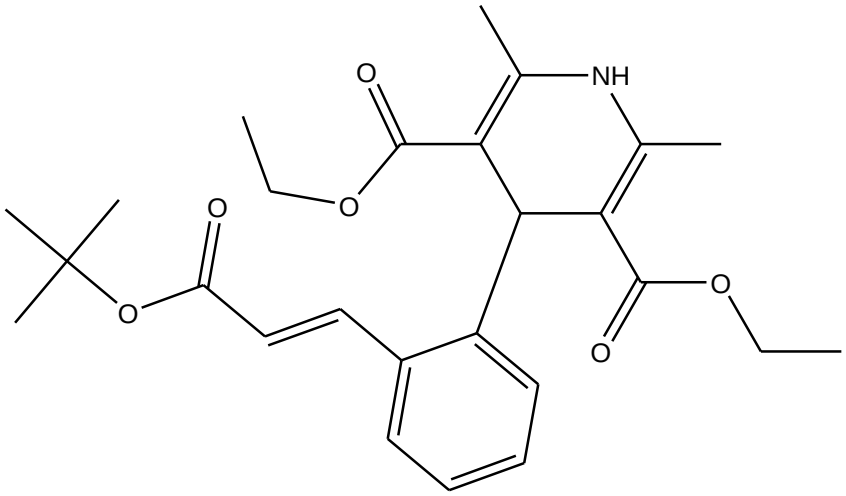
Felodipine is a second generation calcium channel blocker and commonly used antihypertensive agent [89].



Rathod *et al* (2020) developed fibroin-sodium alginate floating microspheres of felodipine (FD) showing modified release [90]. Several other formulations are reported in literature [91-94].

Lacidipine

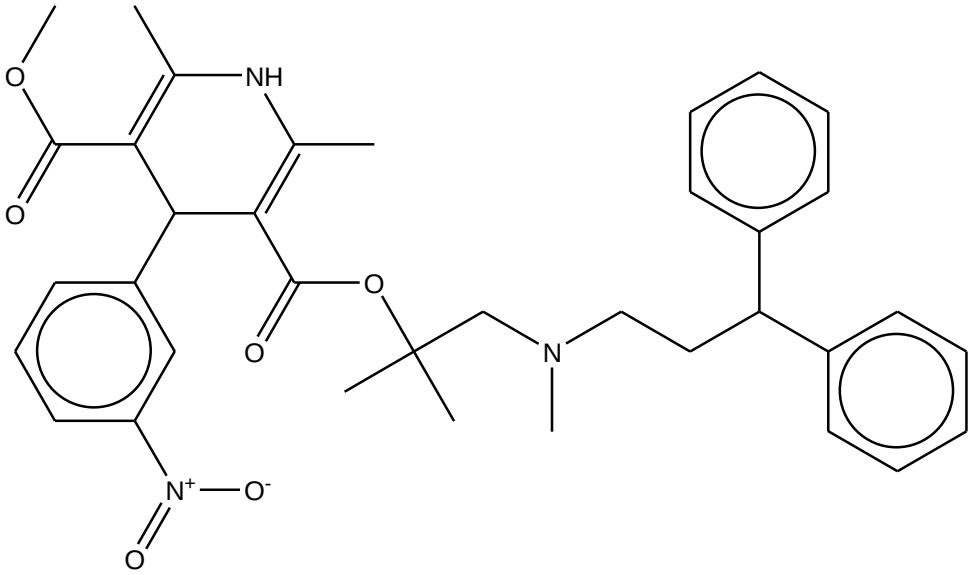
Lacidipine (tradenames Lacipil or Motens) is a calcium channel blocker. It is available as tablets containing 2 or 4 mg [95].



Sultana *et al* (2009) formulated and systematically evaluated *in vitro* performance of mucoadhesive microspheres of lacidipine for treatment of pylorospasm. Lacidipine microspheres containing chitosan were prepared by chemical denaturation using glutaraldehyde as a cross-linking agent. The release followed Higuchi kinetics via a Fickian diffusion [96].

Lercanidipine

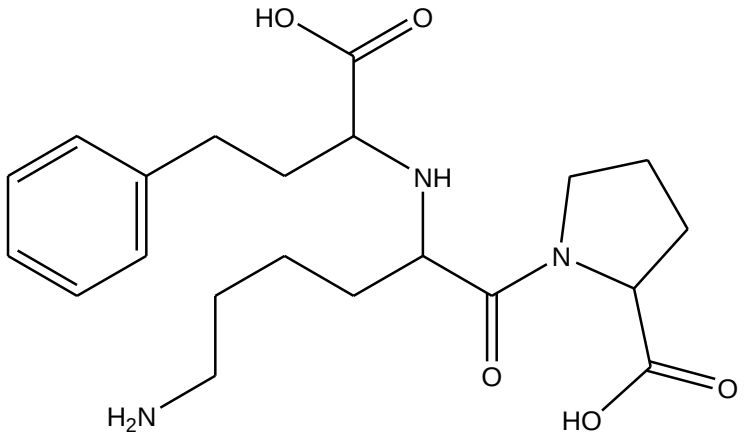
Lercanidipine is used to treat high blood pressure. Lercanidipine is a calcium antagonist of the dihydropyridine group and inhibits the transmembrane influx of calcium into cardiac and smooth muscle [97-98].



Parmar *et al* (2011) developed and characterized of self-nanoemulsifying drug delivery system (SNEDDS) to improve the oral bioavailability of poorly soluble third generation calcium channel blocker lercanidipine (LER) [99].

Lisinopril

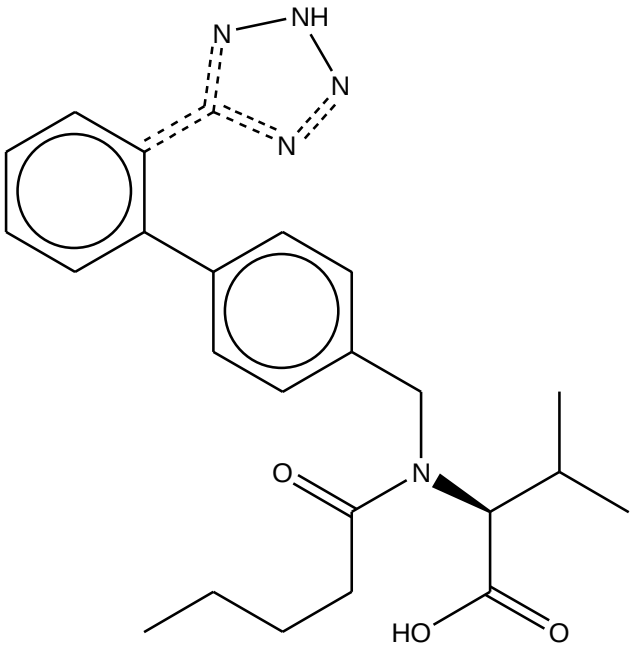
Lisinopril is an oral long-acting angiotensin converting enzyme inhibitor and it is a peptide derivative [100].



Rathod Sayali (2021) designed multiple unit floating drug delivery system for prolong release of Lisinopril by using different amount of waxes, and to study effect of pectin on buoyancy of the system. Increasing the amount of wax in the formulation significantly prolonged the drug release but was insufficient for sustaining the release of highly water-soluble drug [101].

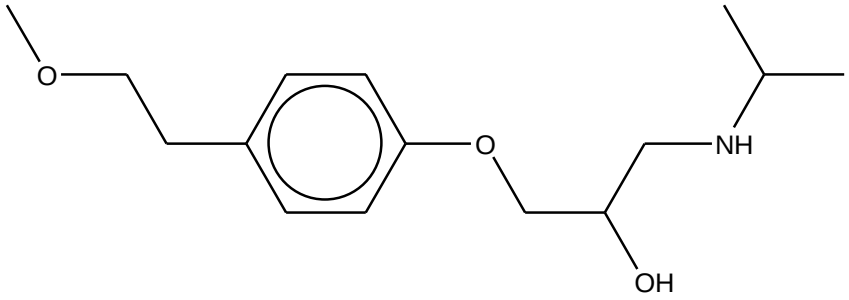
Losartan

Losartan is used to treat high blood pressure and to help protect the kidneys from damage due to diabetes. It is also used to lower the risk of strokes in patients with high blood pressure and an enlarged heart [102]. There are lots of formulations are reported by several researchers [103-118].



Metoprolol

Metoprolol is a beta-blocker that affects the heart and circulation (blood flow through arteries and veins). Metoprolol is used to treat angina and hypertension. Metoprolol is also used to lower your risk of death or needing to be hospitalized for heart failure [119]. There are several GRDDS and FDDS are reported [120-123].

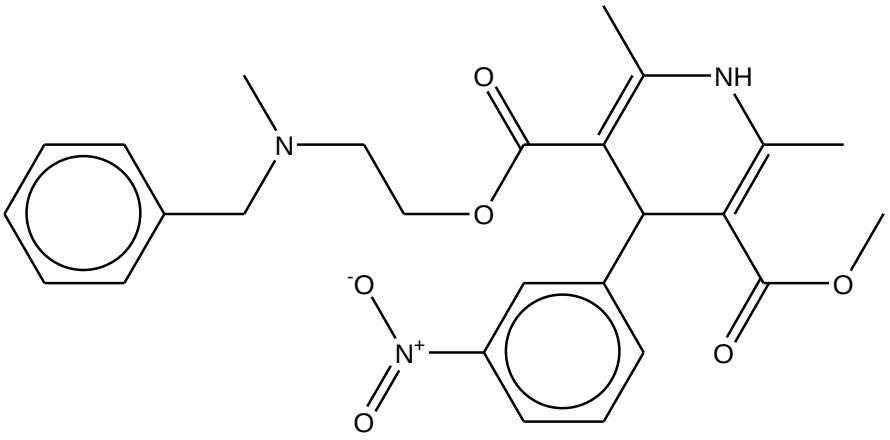


Nicardipine

Nicardipine is a calcium channel blocker used for the short-term treatment of hypertension and chronic stable angina [124-125].

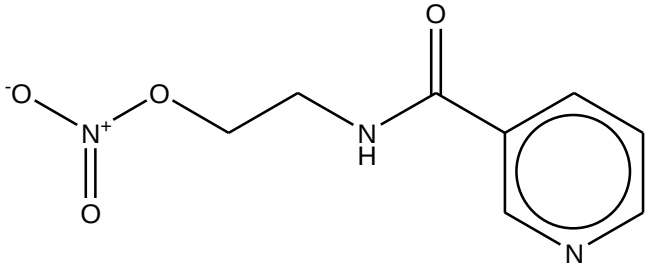
Vamsikrishna *et al* (2021) formulated, developed and evaluated bilayer tablets of Nicardipine [126].

Chabria and Narayanan (2014) formulated and evaluated of oral floating nicardipine hydrochloride tablets using polyethylene glycol 6000 and various HPMC grades [127].



Nicorandil

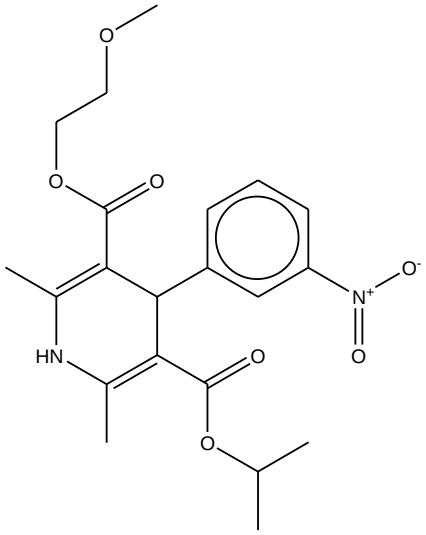
Nicorandil is a type of medicine called a potassium-channel activator. It works by relaxing and widening your blood vessels, which increases the supply of blood and oxygen to your heart. This helps reduce the chest pain angina causes [128].



Ahmed and Nath (2011) formulated and optimized a floating drug delivery system of Nicorandil using full factorial design [129].

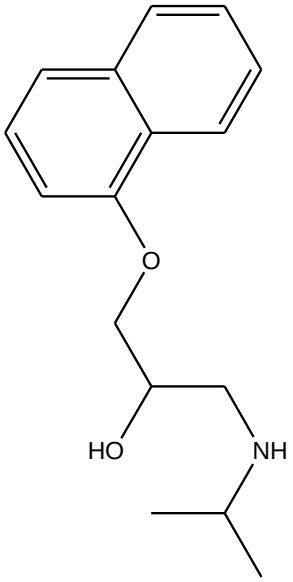
Nimodipine

Nimodipine is a calcium channel blocker used to improve neurological outcomes in patients with subarachnoid hemorrhage due to a ruptured intracranial aneurysm [130]. Bakshi (2016) formulated and evaluated of Gastro Retentive Floating Microspheres of Nimodipine [131].



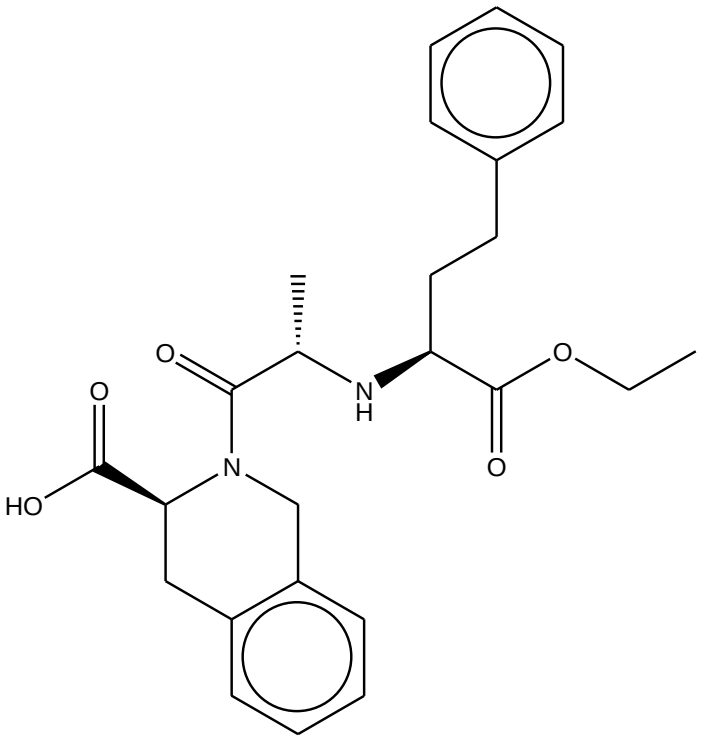
Propranolol

Propranolol is a non-selective beta adrenergic antagonist used to treat hypertension and several GRDDS and FDDS are reported [132-141].



Quinapril

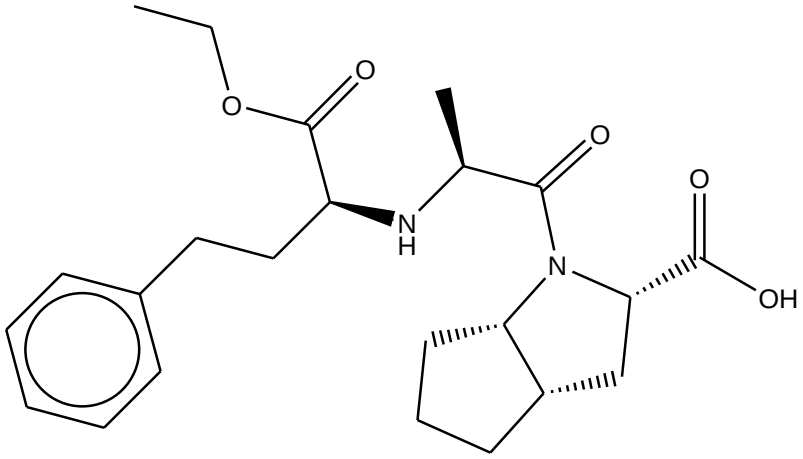
Quinapril is a prodrug of an angiotensin converting enzyme (ACE) inhibitor used in the treatment of hypertension or adjunct in the treatment of heart failure [141].



Mali and Bathe developed and evaluated gastroretentive floating tablets of a quinapril HCl by direct compression technique [143].

Ramipril

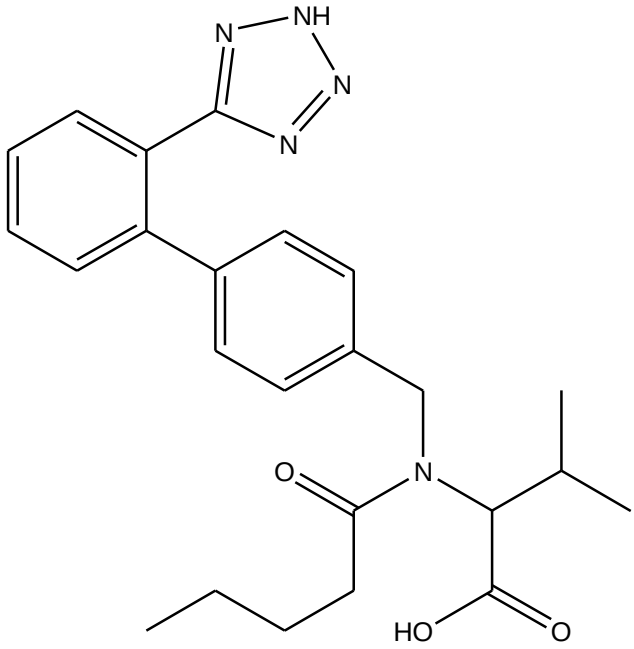
Ramipril belongs to a class of drugs called angiotensin converting enzyme (ACE) inhibitors that are used for treating high blood pressure, heart failure [144].



Gatum *et al* (2018) developed floating Gelucire beads of Ramipril. Ramipril is slightly soluble in water and 2-4 hour half life [145].

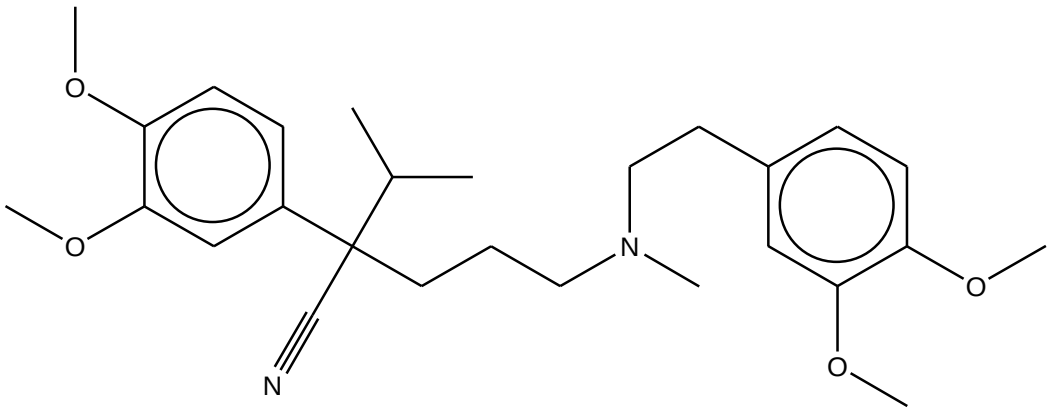
Valsartan

Valsartan is a nonpeptide angiotensin receptor antagonist that selectively blocks the binding of angiotensin II to the angiotensin II type 1 receptor [146-147] and several GRDDS and FDDS are reported [148-154].



Verapamil

Verapamil is a calcium channel blocker. It works by affecting the movement of calcium into the cells of the heart and blood vessels [156].



Saravanakumar *et al* (2019) studied the effect of Sodium Alginate in Combination with Natural and Synthetic Polymers on the Release of Verapamil HCL from its Floating Microspheres [157].

Several brands are listed below [158-163]:

Brand name	**Drug**
Prazopress XL	Prazosin HCl
Coreg CR	Carvedilol
Covera HS	Verapamil HCl
Sular	Nisoldipine

Conclusion

Gastroretentive Drug Delivery System's popularity will undoubtedly grow in the near future due to the availability of diverse innovations and numerous benefits.

Future Scope for GRDDS

In respect of Antihpertensive drugs, while controlling drug release profiles has been a major goal of pharmaceutical research and development for the past two decades, controlling GI transit profiles could be the focus of the next two decades, resulting in the availability of new products with novel therapeutic possibilities and significant patient benefits. Novel gastroretentive products with release and absorption periods of about 24 hours may soon replace so-called "once-a-day" formulations.

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