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A REVIEW ON SUSTAINED RELEASE TABLET FOR HYPERTENSION

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ABSTRACT :

One of the main factors contributing to a rise in cardiovascular disease is thought to be hypertension (HTN). Maintaining a systolic blood pressure of less than 130 mm Hg is proven to prevent complications in individuals with heart failure, coronary artery disease, stroke, and other cardiovascular disorders. Lowering blood pressure does lessen the risk of cardiovascular disease. For persons with an estimated 10-year risk of atherosclerotic cardiovascular disease of ≥10%, the blood pressure should be lowered to 130/80 mmHg as a main preventive measure against cardiovascular disease (4,5). In South Africa, hypertension is still a rather frequent ailment to see. The management of hypertension involves making the required lifestyle adjustments. Most guidelines still recommend thiazide diuretics as the first-line (or initial) medication of choice. The purpose of this review is to examine how new medications intended to treat heart failure (HF) and diabetic kidney disease (DKD) affect blood pressure (BP).

Keywords: Hypertension, Diabetes, Cardiovascular disease, Diuretics, etc.

Introduction :

A medical disease known as hypertension, or high blood pressure, is characterized by a persistently high blood pressure against the arterial walls. Serious health problems including heart disease and stroke may result from it. ACE inhibitors, including captopril, and alterations in lifestyle are frequently employed to treat hypertension. High blood pressure in the systemic arteries is the hallmark of systemic arterial hypertension. systolic Diastolic blood pressure is the pressure that occurs when the heart relaxes, and blood pressure is the force that the blood applies to the artery walls during cardiac contraction. Another term for high blood pressure is hypertension. The force a person's blood exerts on their blood vessel wall is known as their blood pressure. One of the main risk factors for cardiovascular conditions such as aneurysms, heart attacks, strokes, and heart failure is hypertension. An enlarged and weak spot in the artery is called an aneurysm.

Systolic blood pressure rises by 20 mmHg in people between the ages of 40 and 70, while the relative risk of hypertension decreases slightly in those over 80. For instance, a 20 mmHg variation in systolic blood pressure between 120 and 140 is linked to a yearly variation in absolute risk that is over ten times greater between the ages of 80-89 and 50-59.

The intricate interplay of multiple factors involving the autonomic nervous system and renin is linked to the mechanism of hypertension. A fast rise in blood pressure accompanied by little to no acute harm to critical organs is known as hypertensive urgency. including the brain, kidney, heart, and eyes. Numerous medications have been used to treat hypertensive urgency, such as labetol, clonidine, and captopril. Based on the chemical structure of their active moiety, ACE inhibitors are divided into three classes. Unlike other ACE inhibitors, captopril is given as a prodrug. The medicine captopril is active. Peripheral vascular resistance is decreased by captopril without raising heart rate in response.In emergency rooms, some ACE inhibitor medications are thought to be first-line treatments for hypertensive urgency. The majority of participants were illiterate, which could account for the patients general lack of compliance. It seemed that noncompliance was the primary source of research participants' hypertension urgency.

Renin angiotensin aldosterone system (RAAS) involves the angiotensin converting enzyme (ACE). ACE inhibitors are powerful vasoconstrictors that, when inhibited, can lower blood pressure by dilating and lowering aldosterone secretion. They work by competitively inhibiting the conversion of angiotensin I to angiotensin II. Renin then cleaves the angiotensin that is produced by the liver, converting it from angiotensin I to angiotensin II. Investigators looked into the long-term effects of the angiotensin converting enzyme inhibitor captopril in 76 patients who had different types of hypertension. Systolic and diastolic blood pressure were immediately and significantly reduced while using captopril. Skin manifestations, taste disturbances, dizziness, and productive coughs are the most common side effects; leucopenia and nephrotic syndrome are uncommon but dangerous side effects. Although the use of beta blocking medications is the major treatment, antihypertensive therapy has typically taken the form of graded care regimens with tiny doses of diuretic agents, typically thiazide congeners. The most potent oral ACE inhibitors are beta blockers; centrally acting drugs, such as methyldopa and clonidine hydrochloride; alpha blockers, such as prazocin hydrochloride and reserpine; and, more recently, captopril. The most significant, albeit uncommon, adverse effect of captopril is neutropenia. The development of collagen vascular disorders and renal insufficiency were closely correlated with one other. (For instance, systemic lupus erythematosus and scleroderma. (SLE)

Globally, cardiovascular illnesses account for the majority of deaths. Cardiovascular disorders are closely linked to high blood pressure levels. Terms related to hypertension are helpful in clinical decision-making and are based on blood pressure risk levels for cardiovascular diseases. The WHO

released guidelines for managing hypertension in 2007. ACE (Angiotensin converting enzyme) inhibitors, calcium channel blockers, and thiazide diuretics are on the list of necessary medications for managing hypertension. Antihypertensive single-pill combinations were added to the essential list in 2019. Risk factors for cardiovascular disease include sex, blood pressure, BMI, smoking, diabetes, past hypertensive medication, and a history of cardiovascular disease. Patients who have a diastolic blood pressure of more than 90 mmHg or a systolic blood pressure of less than 140 mmHg are at high risk for cardiovascular illnesses. In 69% of adults with a first myocardial infarction, 77% of adults with a first stroke, and 74% of adults with heart failure, hypertension is present. the elevated risk linked to elevated blood pressure.

ACE inhibitors are prescription drugs used to treat high blood pressure. The activity goes over the indications, contraindications, activity, side effects, and other important aspects of ACE inhibitor medication as it relates to clinical research. In hypertensive patients, angiotensin converting enzyme inhibitors successfully reduce mean arterial blood pressure in addition to both systolic and diastolic blood pressure. ACE inhibitors have been studied as potential antihypertensive medications. Angiotensin receptor blockers, thiazide diuretics, and calcium channel blockers make up the other three medication classes. ACE inhibitors are strongly advised as first choice therapy for individuals with heart failure since they also improve heart failure by lowering afterload, preload, and systolic wall stress, which increases cardiac output without raising heart rate.

The most common chronic illness in the world and the main modifiable risk factor for a number of cardiovascular diseases is hypertension. Captopril has long been utilized in the treatment of hypertension and cardiovascular disease since it is a pril that inhibits the angiotensin converting enzyme. Previous research have demonstrated the anti-hypertensive efficacy of Gedan Tiangya Decoctioon (GJD). One of the primary avoidable risk factors for morbidity and mortality in humans is hypertension. Vascular damage is the primary indicator of hypertension, and oxidative stress and decreased vascular nitric oxide are the causes of hypertension-related target organ damage. .. Numerous factors, such as obesity, insulin resistance, high sodium intake, family history, and sedentary lifestyle, have a significant impact on the development of hypertension.

To find out what your blood pressure is, use our blood pressure chart:

Blood pressure category	Systolic mmHg (upper number)	Diastolic mmHg (lower number)
Normal	Less than 120	Less than 80
Elevated	120-129	Less than 80
High blood pressure (Hypertension) Stage I	130-139	80-89
High blood pressure Stage II	140 or Higher	90 or High
Hypertensive crisis	Higher than 180	Higher than 120

The third most significant risk factor for the attributable burden of illness in South Asia is high blood pressure (BP). Hypertension has a significant negative impact on the state of cardiovascular health, the healthcare system in India, and public health. In India, hypertension is the cause of 57% of all stroke deaths. In a systematic analysis of population health data for attribute mortality, the global and regional burden of illness and risk factor analysis of disease and risk factor research (2001) was conducted. An increasing number of underlying pathophysiological conditions, including hypertrophy, endothelial dysfunction, metabolic syndrome, oxidative stress, and inflammation, are linked to hypertension, a growing global issue.

Blood pressure management

Modifications to lifestyle - Evaluate overall risk - Identify target organ for preferred or competing indications

1) Left ventricular Hypertrophy (LVH)
2) Infarction after myocardium
3) Elevated risk of coronary heart disease
4) Heart attack
5) HeartAttack

With so many antihypertensive classes available, treating hypertension can be done with little adverse effects. Research into pharmaceuticals for the treatment of hypertension has been ongoing. Spironolactone (1957), beta blocker Propranolol (1973), alpha-1 adrenergic receptor blocker Prazosin (1975), centrally acting agonist for the alpha-2 adrenergic receptor Clonidine (1970), angiotensin converting enzyme inhibitor Captopril (1977), calcium channel blocker Verapamil (1977), and angiotensin II receptor blocker losartan (1973) are some of the medications used in between. In order to better understand which type of hypertension a specific pharmacological class of antihypertensive treatment is best advised for, this review aims to characterize the pharmacological classes of antihypertensive drug to the various sites along the arterial site of action.To better understand the mechanism of occurrence of side effects, their pharmacological mechanism is elucidated and explained.

Antihypertensives can be categorized into two main categories. the first category consists of drugs that either directly or indirectly block the renin-angiotensin converting enzyme inhibitors (RENIN-DRIs), beta blockers, and to a lesser extent, DRIs. These drugs work through a variety of mechanisms, however vasodilation is their main side effect. The medications in the second group either cause vasodilation via a non-RAS mechanism or increase intravascular volume by excreting more water and sodium. similar to calcium channel blockers and diuretics (CCB). The second group's action increases RAS activity through negative feedback, which can enhance the effects of medications that target and inhibit RAS. The most preferred

method of drug delivery is oral administration because of its formulation versatility and ease of use. There are numerous drug delivery systems on the market. About half of the medication delivery system. The most common method of delivering drugs has been orally.

Design and formulation of sustained release drug delivery system

Because the oral route of administration allows for greater design flexibility, patient compliance, and handling of different pH levels during the dosage form's transit through the gastrointestinal tract, as well as the influence of the enzyme system on both the medication and the dosage form, it is the preferred method of administration. To produce a gradual release of medication to the gastrointestinal tract, most oral sustained release systems rely on diffusion, dissolution, or a combination of these mechanisms. A zero order sustained release formulation and a sustained release formulation, both theoretically and undesirable. Angiotensin converting enzyme inhibitors have been utilized in the management of chronic heart failure and hypertension. A single oral dosage of 25–150 mg per day is used to treat heart disease; the highest hemodynamic effect is shown 45–90 minutes after the dose is taken. Additionally, the medication is easily soluble in water, has a 1.7-hour elimination half-life, and is stable at higher pH levels, where it degrades and becomes unstable. One of the most popular medications for treating hypertension is captopril. The goal of the sustained release drug delivery system is to introduce a medication into the body at a steady, predictable rate (zero order dissolution).

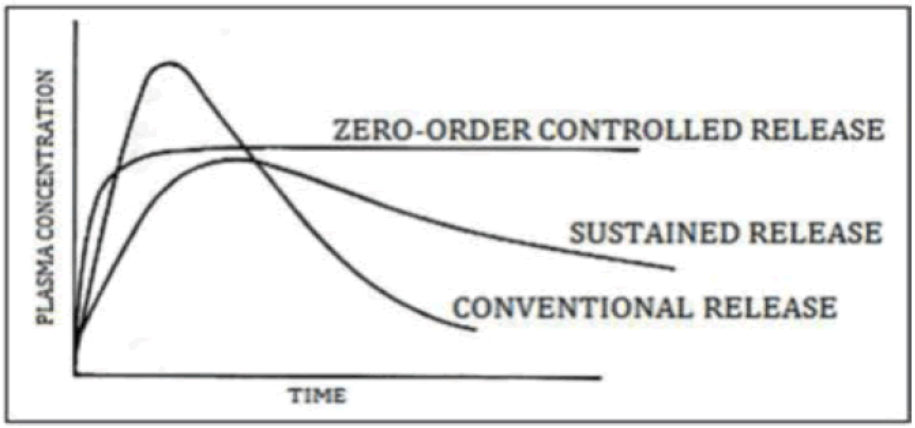

Figure 1. Plasma drug concentration vs. time profile for oral conventional dosing and single oral dose of sustained and controlled release formulation

Medication for hypertension:

Diuretics:

Diuretics come in three different groups and are used to treat hypertension. The most often utilized diuretics are thiazide ones. After taking these drugs for the first one or two days, there is typically no increase in the flow of urine. Most patients see a significant reduction in blood pressure with them, particularly those who are African American, over 60, and diabetic. There are various kinds of diuretics, such as:

thiazide diuretics, loop diuretics, and potassium sparing diuretics.

Thiazide Diuretics: Thiazides encourage both diuresis, or increased urination, and natriuresis, or the release of salt in the urine. Additionally, they relax a person's blood vessels.

Thiazides are prescribed by medical practitioners to treat excessive blood pressure, edema (fluid accumulation), and congestive heart failure.

Angiotensin converting enzyme inhibitor (ACEs):

Since ACEIs are efficient, seldom cause side effects, and lessen the risk of heart attacks and strokes, they are frequently used to treat hypertension. Patients with diabetes mellitus who have protein in their urine and those with chronic kidney disease, in whom they appear to have favorable effects in delaying the loss of kidney function, are the two populations for which they are especially useful. Renin is released from the kidney when low blood pressure, low salt consumption, or use of diuretics. Renin generates AT-II, which constricts blood vessels, retains salt and water by the kidney, and raises blood pressure. ACE blocks the effects of the renin angiotensin system (RAS). The balance between the vasoconstrictive and salt-retentive characteristics of Angiotensin II and the vasodilatory and natriuretic features of Bradykinin is regulated by the angiotensin-converting enzyme. By reducing the synthesis of angiotensin II and the breakdown of bradykinin, ACE inhibitors upset this equilibrium. ACE inhibitors also affect the synthesis and breakdown of a number of other vasoactive molecules, including substance P, though it is unclear how much of these chemicals contribute to the beneficial or harmful effects of ACE inhibitors.

Angiotensin receptor blocker (ARBs):

ARBs also inhibit the RAS, or renin-angiotensin system. Like ACEIs, however their mode of action is different: instead of preventing the synthesis of AT-II in the tissue, they impede its action. These medications preserve life quality. They don't produce a bothersome cough. The main vasoactive peptide in the RAAS, AT II, acts on two receptors: AT I and AT II. Activation of AT I receptors raises blood pressure because it causes the smooth muscle in the blood vessels to contract, increasing systemic vascular resistance, sympathetic activity, and sodium (Na) water retention as a result of increased Na reabsorption in the proximal convoluted tubule, elevated sympathetic activity, elevated systemic vascular resistance, and so forth. The indications for using ARBs and ACEIs are comparable. However, ARB medication is appropriate and recommended as a backup for individuals who cannot take ACEI therapy because of angioneurotic edema or a cough brought on by ACEIs. Beta blockers, alpha blocker and symphotholytic drug.

Pre Formulation Study:

Angle of Repose

Angle of Repose is defined as the maximum angle possible between surface of a pile of the powder and horizontal plane. The frictional force in a loose powder or granules can be measured by the angle of Repose.

Carr's compressibility index

The compressibility index of the granules was determined by the carr's compressibility index. Carr's index can be calculated by using the following formula

Carr's index (%) = TBD – LBD× TBD × 100

Post-Compression Parameters

Physical characteristics of the produced matrix tablet, such as hardness and friability, swelling index, and drug content, were assessed.

Hardness test

A specific level of strength or hardness and resistance to friability is needed for tablets to endure mechanical shocks during manufacturing, packaging, and delivery. A digital hardness tester was used to assess the tablet's hardness. From each formulation, three tablets were chosen at random, and the mean and standard deviation were computed.

Friability test

It is the phenomenon whereby tablet surfaces are damaged and show evidence of lamination.
The friability of tablets was determined by using Electro lab, USP EF 2 friabilator. It is expressed in percentage (%). Friabilator was operated at 25 RPM for 4 minutes. The percentage friability was then calculated by,
F= W initial -W final × W initial × 100

Swelling index

Tablet swelling is caused by the absorption of liquid, which increases the tablet's weight and volume. The particle's ability to absorb liquid may be caused by the hydration of macromolecules or by the saturation of internal capillary spaces. Through the pores in the particles, the liquid enters and binds to the big molecules, breaking the hydrogen bond and causing the particle to inflate. The pill can quantify the degree of edema in terms of percentage weight gain. The swelling index can be calculated by the following equation:
Swelling index (SI) = { Wt- Wo } / Wo ×100
Where, Wt = weight of tablet at time t
Wo = Initial weight of tablet
In Vitro drug release kinetic study

Zero order Kinetic:

A zero order release wound be predicted by the following equation

Qt – Qo = Kot

Where,
Qt= amount of drug release dissolved in time 't'
Co = Initial amount of drug concentration in solution.
Kot = Zero order rate constant.
Zero-Order kinetics describe reactions and processes where the rate and half-life are independent of the reactants' concentrations.

First order Kinetics:

A first order release would be predicted by following equation
Log Qt = Log Qo – Kit / 2.303
Where
Qt = Amount of drug released in time 't'
Co = Initial Amount of drug concentration in solution
Kit = first order rate constant
A first-order reaction is a reaction that proceeds at a rate that depends linearly on only one reactant concentration.

Approaches of oral sustained or controlled release formulation:

Many pharmaceutical techniques have been used to create long-acting devices that can deliver a medicine in a regulated and sustained release manner using a once-daily formulation. The various approaches used and their drawbacks are explained as follows.

Matrix tablet:

By slowing down the rate of breakdown, a variety of techniques can be used to manufacture water-soluble drugs into sustained release dosage forms. Hydrophilic polymers have received a lot of interest lately in the design of oral controlled drug delivery systems due to their adaptability in achieving a desired drug release profile, cost-effectiveness, and widespread regulatory acceptability. Cellulose derivatives, including sodium carboxymethyl cellulose, hydroxyl propyl methyl cellulose, and methyl cellulose, are among the hydrophilic polymers that are thought to be stable and safe to use as retardant excipients in the creation of controlled release dosage forms. The polymers derived from cellulose can be used to make formulations with both soluble and insoluble drugs at either a high or low dosage. Polymer hydration leading to gel formation. layer that regulates the drug's rate of release. The outcomes also demonstrate that the surfactants have the power to alter the captopril release mechanism from the matrices. The drug surfactant ionic interaction is the main mechanism via which surfactants delay drug release from HPMC-EC matrices.

Coated Tablets:

This is a traditional method of managing medication release. After passing through the barriers, the medication enters the physiological fluids. The first step in calculating release is determining the kind and makeup of the obstacles. Hydrophilic and hydrophobic polymers make up the majority of barriers, and this is because they are compatible and safe to employ in vivo even at high concentrations.

Floating Tablets:

The purpose of these systems is to increase the medication delivery system's stomach residence time. An extended duration of residence in the stomach for a modified release drug delivery system is especially desirable for drugs that act locally in the stomach, have an absorption window in the stomach or upper part of the small intestine, are unstable in the intestinal or colonic environments, or are poorly soluble at high pH levels. Rahman et al. used direct compression technology to create bilayer tablets containing captopril. PVP-K30, carbopol 934p, and HPMC-K15M either by themselves or in conjunction with the medication. The final formulation had a floating lag time of 10 minutes and released about 95% of the medication in 24 hours in vitro. The tablet remained floatable for the whole study.

Advantages of sustained release dosage form:

1. Reduction in frequency of intake
2. Reduce side effects
3. Uniform release of drug over time
4. Better patient compliance

Disadvantage of sustained release dosage form

1. Toxicity due to dose dumping
2. Increased cost
3. Unpredictable and often poor in vitro-in-vivo correlation.
4. Risk of side effect or toxicity upon fast release of contained drug.
5. Increased potential for first pass clearance.

Conclusion:

Finally, the different ways that the pharmacological types of antihypertensive medications covered in this review work Particular consideration is still required for the ongoing difficulties in managing hypertension. The first medicine of choice for treating hypertension has changed significantly over

time, from diuretics to ACEIs, ARBs, and CCBs, and from monotherapy to low-dose combination single-pill therapy. Numerous clinical studies have examined the assessment pattern, patient adherence to therapy, physician adherence to hypertension management recommendations, cost implications, and other information regarding concomitant diseases.

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