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A Review of Telmisartan and Amlodipine in Hypertensive Treatment



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**Patil Shubham Kailas*¹, Ganesh Ramdas Asabe²,
K.R Biyani, R.H Kale**

*PRMSS Anuradha College of Pharmacy, Chikhli, Dist-
Buldana (M.S) India 443201.*

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ABSTRACT

This product or medication is the combination of Telmisartan and amlodipine which work together to control Blood Pressure in Adults. This combination relaxes the blood vessels and helps the blood to flow more easily through it. The medication is mainly given to the patient who suffers from high blood pressure. It reduces the risk of cardiac arrest or stroke by reducing elevated blood pressure. The combination of the drug has confirmed that once-daily dosing provides 24-Hrs control of blood pressure. This combination is an additive effect with diuretics, beta blockers, and angiotensin-converting enzyme inhibitors. This combination makes a very useful agent for the treatment of hypertension.



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INTRODUCTION

Telmisartan

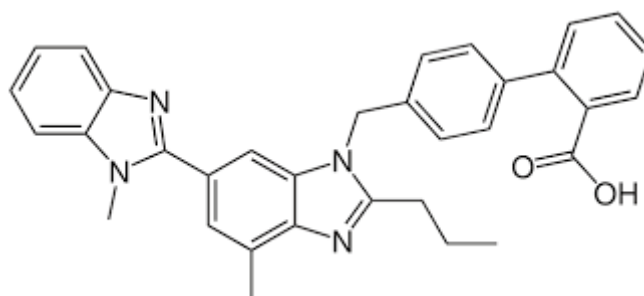


Figure No:- 1 Structure of Telmisartan

The medication used to treat high blood pressure, heart failure, and diabetic kidney disease coronary heart disease(CHD) congestive heart failure (CHF) peripheral arterial disease.[1] It is a reasonable initial treatment for high blood pressure.[1] It is taken by mouth.[1] Versions are available as the combination[2] telmisartan/hydrochlorothiazide and telmisartan/amlodipine[1]. The prevalence of hypertension in India is on the rise with 25% of urban and 10% of the rural population being affected by it.[4] The purpose of antihypertensive treatment is to reduce morbidity and mortality associated with cardiovascular and cerebrovascular events resulting from hypertension.[3] Various classes of drugs are being used in the treatment of hypertension such as diuretics, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers (ARBs), calcium channel blockers, and β -adrenergic blockers.[5] ARBs are one of the first-line drugs for the treatment of hypertension. ARBs are being preferred because they are effective in reducing blood pressure (BP) with a good tolerability profile, and convenient once a day dosing.[6] Losartan was the first marketed ARB and then telmisartan was approved by the Food and Drug Administration (FDA), and it offers the advantage of a long plasma half-life of 24 h and improves insulin sensitivity and lipid profiles.[8]

Various studies have demonstrated the difference in antihypertensive efficacies among ARBs.[9] Although previous studies have compared the antihypertensive efficacy of ARBs based on cuff BP change, such comparisons have largely been against a single member of this group. Hypertension and dyslipidemia often coexist and are well-established risk factors for cardiovascular diseases.[10]

Amlodipine

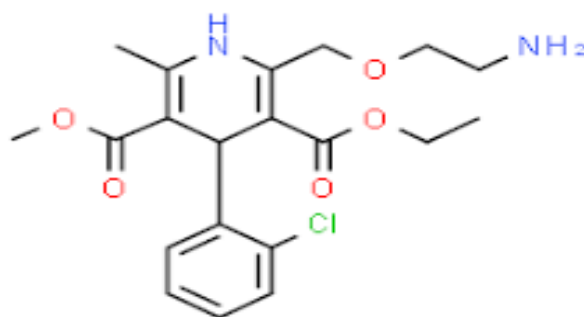


Figure No:- 2 Structure of Amlodipine.

Amlodipine is a dihydropyridine (second generation) calcium channel blocking agent it is also a peripheral arterial vasodilator. Amlodipine is more preferable for arterial vascular smooth muscle as compared to cardiac tissue. pharmacokinetically it is the most distinct DPH. It has a complete but slow oral absorption peak after 6 to 9 hrs the early vasodilator side effect is largely avoided because of less extensive and less variable first-pass metabolism its oral bioavailability is higher and more consistent.[5] The volume of distribution and T1/2 are exceptionally long diurnal fluctuation in blood level is small and action extended over the next morning.[5] Amlodipine can be used as monotherapy or in combination with several different medications to manage hypertension or CAD in patients. Amlodipine has antioxidant properties and an ability to enhance the production of nitric oxide (NO), an important vasodilator that decreases blood pressure. The option for single daily dosing of amlodipine is an attractive feature of this drug.

Amlodipine was patented in 1982 and approved for medical use in 1990.[16] It is on the World Health Organization's List of Essential Medicines.[17] It is available as a generic medication.[15] In 2017, it was the fifth most commonly prescribed medication in the United States, with more than 72 million prescriptions.[18][19]

Why does Telmisartan combine with Amlodipine?

-Telmisartan is an angiotensin receptor blocker (ARB) and amlodipine is a calcium channel blocker. They both work differently to relax the blood vessels so that blood can flow more easily. These medications are used together when one drug is not controlling your blood pressure.

PHARMACOLOGY

Pharmacodynamics

Mechanism of action

Both the drug (telmisartan and amlodipine) have a different mechanism of action as follows.

Telmisartan

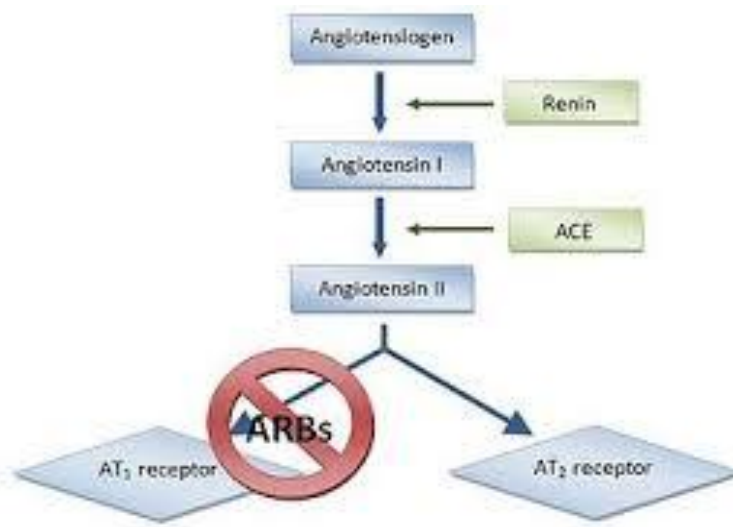


Figure No:- 3 MOA of Telmisartan.

Renin-Angiotensin-Aldosterone System (RAAS)

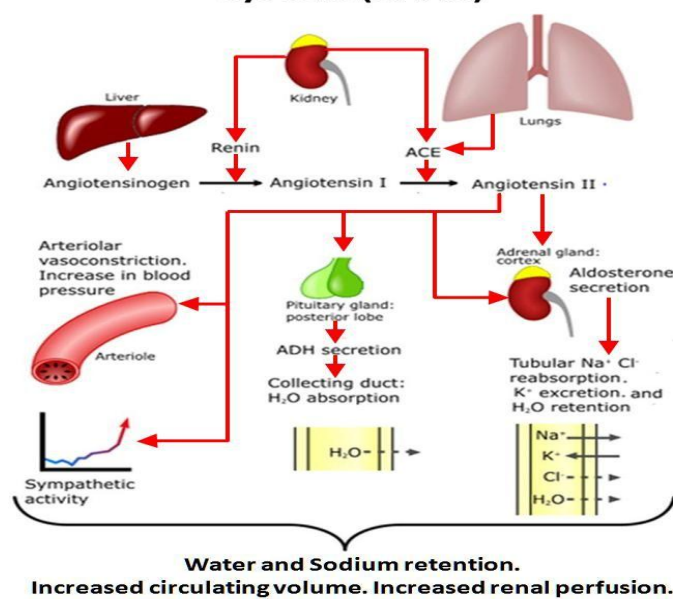


Figure No:- 3.1 MOA of Telmisartan (RAAS).

Telmisartan is an angiotensin II receptor blocker that shows a high affinity for the angiotensin II receptor type 1 (AT1), with a binding affinity 3000 times greater for AT1 than AT2.

Telmisartan's activity at the peroxisome proliferator-activated receptor delta (PPAR- δ) receptor has prompted speculation around its potential as a sports doping agent as an alternative to GW 501516.[11] Telmisartan activates PPAR- δ receptors in several tissues.[13][14][20][21]

Amlodipine

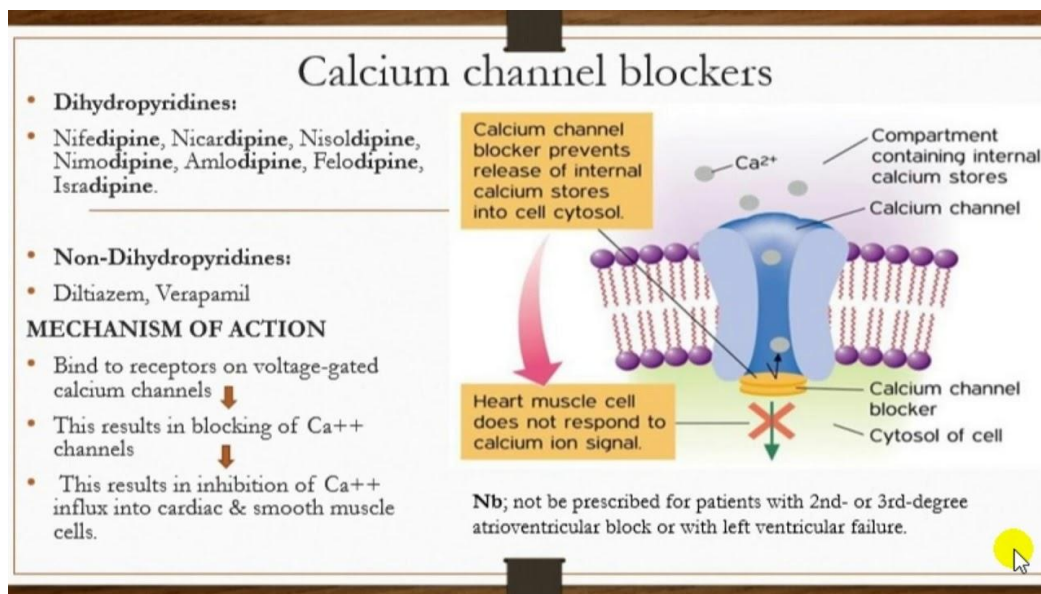


Figure No:- 4 MOA of Amlodipine.

The MOA of amlodipine is similar to the other calcium channel blockers. Amlodipine inhibits the transmembrane influx of calcium ion into vascular smooth muscle and cardiac muscle.[22] Amlodipine binds to both dihydropyridine and nonhydropyridine binding sites. The contractile processes of cardiac muscle and vascular smooth muscle are dependent upon the movement of extracellular calcium ions these cells through specific ion channels. Amlodipine inhibits calcium ion influx across cell membranes selectively, with a greater effect on vascular smooth muscle cells than cardiac muscle cells.[22]

Pharmacokinetics

Telmisartan

Absorption

Absolute bioavailability depends on the dosage. Food slightly decreases the bioavailability (a decrease of about 6% is seen when the 40-mg dose is administered with food).[22][26]

Amlodipine

Absorption

Amlodipine absorbed slowly and almost completely from the gastrointestinal tract. Peak plasma concentrations are achieved 6-12 hours after oral administration. The estimated bioavailability of amlodipine is 64-90%. Steady-state plasma amlodipine levels are achieved after 7-8 days of consecutive daily dosing. Absorption is not affected by food.[26]

Telmisartan

Metabolism

Minimally metabolized by conjugation to form a pharmacologically inactive acyl glucuronide; the glucuronide of the parent compound is the only metabolite that has been identified in human plasma and urine. The cytochrome P450 isoenzymes are not involved in the metabolism of telmisartan.

Amlodipine

Metabolism

Amlodipine is heavily (approximately 90%) converted to inactive metabolites via hepatic breakdown with 10% of the parent compound and 60% of the metabolites found excreted in the urine.[26]

Telmisartan

Route of elimination

Following either intravenous or oral administration of ¹⁴C-labeled telmisartan, most of the administered dose (>97%) was eliminated unchanged in feces via biliary excretion; only

minute amounts were found in the urine (0.91% and 0.49% of total radioactivity, respectively).[26]

Amlodipine

Route of elimination

Elimination from the plasma occurs in a biphasic with a terminal elimination half-life of about 30–50 hours. Steady-state plasma levels of amlodipine are reached after 7-8 days of consecutive daily dosing.[26]

Medical Uses

Telmisartan

Telmisartan is used to treat high blood pressure, heart failure, and diabetic kidney disease.[1] It is a reasonable initial treatment for high blood pressure.[1][12]

Amlodipine

Amlodipine is used in the management of hypertension[24] and coronary artery disease in people with either stable angina (where chest pain occurs mostly after physical or emotional stress)[25] or vasospastic angina (where it occurs in cycles) and without heart failure. It can be used as either monotherapy or combination therapy for the management of hypertension or coronary artery disease.

Amlodipine along with other calcium channel blockers is considered the first choice in the pharmacological management of Raynaud's phenomenon.[23]

contraindications

- prior hypersensitivity to Telmisartan/Amlodipine.
- pregnant and lactating females.
- patient with anuria.etc.[22]

Side effects

- Tingling of the hands or feet.
- fever/headache/runny nose/nasal congestion.

-slow or fast heartbeat.

-pounding in the ears.

-joint pain

-dizziness/nervousness.

SUMMARY

From the above article, it is concluded that the combination of telmisartan and amlodipine helps to reduce the elevated blood pressure in Adults. The telmisartan and amlodipine combination respectively provide 24-Hrs lowering blood pressure in a patient with mild to moderate hypertension.

The combination of these medications (Telmisartan and Amlodipine) give a positive effect on the echocardiographic index of the Heart by reducing LV hypertrophy and improve LV diastolic function.

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