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A REVIEW OF SIMULTANEOUS DETERMINATION OF TWO DRUGS ATENOLOL AND AMLODIPINE

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Abstract

The combination of Atenolol-Amlodipine is a fixed dose combination is introduced in India, having better therapeutic profile. Atenolol is a β adrenoceptor blocking agents and competitively inhibit the actions of adrenergic agonist on β-receptors. Amlodipine is a prototype second generation dihydropyridine calcium channel blocker. It produces less reduction of myocardial contractility. It was found that both the drugs are estimated by various analytical methods individually. Spectrophotometry, Spectroflourimetry, Spectrocolormetric and Chromatographic methods are required for their stability studies. There is only one chromatographic method was reported for their simultaneous estimation by HPTLC in its combined dosage forms. So it was felt that there is a need to develop a simple, accurate and precise analytical method for the simultaneous estimation of Atenolol-amlodipine by RP-HPLC in its combined tablet dosage forms.

Key Words: RP HPLC, Validation, Atenolol, Amlodipine.

Drug Profile

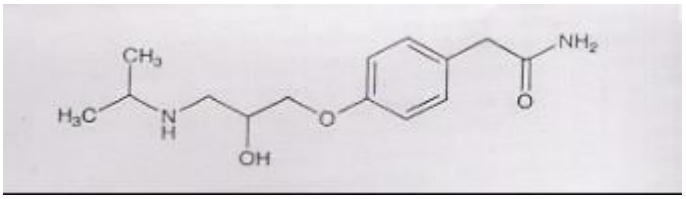
Introduction

The combination of Atenolol-Amlodipine is a fixed dose combination is introduced in India, having better therapeutic profile.

Composition: Each tablet contains

Atenolol	:	50 mg
Amlodipine	:	5 mg

Atenolol Chemical Structure[1]:



Molecular formula : $C_{14}H_{22}N_2O_3$

Molecular weight : 266.34

Chemical name : 4-[2-Hydroxy-3-[(1-methyl ethyl) amino]propoxy] benzeneacetamide

Melting range : 146.0-148.0

Description[2,3]:

Appearance : White or almost white powder

Solubility:

Freely soluble in methanol, DMF, Soluble in acetic acid , DMSO, Sparingly soluble in 96% ethanol. Slightly soluble in water, isopropanol, very slightly soluble in acetone, Dioxane, Insoluble in acetonitrile, ethyl acetate, chloroform.

Therapeutic Category:

Cardio vascular drug- β-adrenergic blocker, antihypertensive

Mechanism of Action[4]:

All β adrenoceptor blocking agents are synthetic compounds and competitively inhibit the actions of adrenergic agonist on β-receptors. β-adrenoceptors are located predominantely in heart (beta-1), in the arteries and arterioles of skeletol muscle (beta-2), where their stimulation induces cardiac excitation, peripheral vasodilation, and bronchial relaxation respectively. β-blockers combines reversily with these receptors to block the responses to sympathetic nerve stimulation or circulating catecholamines.

Pharmacokinetics[5]: A relatively selective β_1-blocker having low lipid solubility. It is incompletely absorbed orally, but first pass metabolism is not significant. Because of longer duration of action, once daily dose is often sufficient. It is excreted in urine, mostly as glucuronides.

Therapeutic Indications:[6]

It is indicated for the treatment of

- ❖ Hypertension
- ❖ Angina pectoris
- ❖ Cardiac arrhythmias
- ❖ Myocardial infraction
- ❖ CHf
- ❖ Thyrotoxicos
- ❖ Migrane
- ❖ Anxiety
- ❖ Glaucoma
- ❖ Hypertrophic cardiomyopathy

Adverse Effects:

1. Accentuates myocardial insufficiency
2. Bradycardia
3. Worsens chronic obstructive lungs disease
4. Exacerbates variant (prinzmental's) angina
5. Plasma lipid profile may be altered on long term use
6. Tiredness and reduce exercise capacity

Contraindications[7]:

Beta-blockers are contraindicated in sinus bradycardia; greater than first degree heart block; congestive heart failure; Cardiogenic heart shock; Overt cardiac failure and hypersensitivity to beta-blockers. Beta-blockers are contraindicated in the management of myocardial infraction patients with a heart rate below 45 beats/min heart block greater than first degree (PR interval more than 0.24 sec); systolic blood pressure less than 100mmHg; or moderate to severe heart failure.

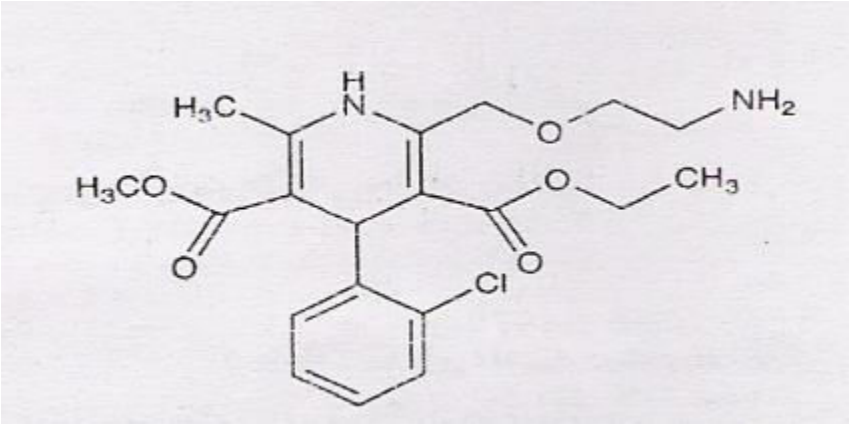
Dosage And Administration[8]: Once daily dose is sufficient. Available as

Betacard - 25 mg tab

Aten - 50 mg tab

AMLODIPINE

Chemical Structure[9]:



Chemical Name:

2-[(2-Aminoethoxy)methyl]-4-(2-chloro phenyl)-1, 4-dihydro-6-methyl -3,

5-pyridinedicarboxylic acid, 3-ethyl, 5-methyl ester;

Molecular formula : C20H25ClN2O5

Molecular weight : 408.88

Melting range : 1780-1790C

Description[10,11] : Crystal white powder

Solubility:

Freely soluble in methanol, DMF, Soluble in acetic acid DMSO, Sparingly soluble in 96% ethanol. Slightly soluble in water, isopropanol, very slightly soluble in acetone, Dioxane, Insoluble in acetonitrile, ethyl acetate, chloroform.

Therapeutic category : Antianginal, Antihypertensive

Mechanism of Action[12]: Amlodipine is a prototype second generation dihydropyridine calcium channel blocker. It produces less reduction of myocardial contractility.It can be safely combined with thiazides, beta-blocker, ACE inhibitors and nitrates.

Pharmacokinetics: Pharmacokinetically it is the most distinct DHP(dihydropyridine). It has complete but slow oral absorption: peak reaches after 6 to 9 hours-the early vasodilator side effects (palpitation, flushing, headache,

postural dizziness) are largely avoided. Because of less extensive and less variable first pass metabolism, its oral bioavailability is higher and more consistent. Volume of distribution and $t^{1/2}$ are exceptionally long: diurnal fluctuation in blood level is small and action extends over the next morning.

Therapeutic Indications[13]:

- ❖ Anginapectoris
- ❖ Hypertension
- ❖ Arrhythmias
- ❖ Hypertrophic cardio myopathy

Adverse Effects:

Incidence of side effects is low, but the profile is similar to verapamil. It also increases plasma digoxin, like verapamil.

Diltizem should not be given to the patients with pre existing sinus, A-V nodal or myocardial disease. Only low doses should be given to the patients on β- blockers.

Contraindications[14]: Amlodipine is contraindicatedb in left ventricular dysfunction, cardiogenic shock, sick sinus syndrome, and II and III degree A-V block.

Dosage And Administration[15]**:** 5-10 mg OD

Marketed Brands Available:

Amcard	-	2.5 mg tab
Amlopin	-	5 mg tab

Conclusion

It is clear from the present study that if Atenolol-Amlodipine are simultaneously estimated by RP-HPLC and more advanced methods than their formulations are simple, accurate, specific and precise in operation and can be employed for estimation of Atenolol-Amlodipine in its combined tablet dosage forms. This is also helpful to standardise the developed method, to analyse the marketed formulation for their reliability and accuracy, to perform the recovery studies and to validate the method for their accuracy, precision and reproducibility. So more analytical research are needed for making their formulations more potent.

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