

Combination of Amlodipine and Atenolol: An Overview

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Abstract

Risk of cardiovascular diseases is increasing rapidly. Various classes of cardiovascular drug are available to control hypertension, arrhythmia and angina. Here we summarize various combination of amlodipine and atenolol available in market.

Keywords: Amlodipine; Atenolol; Cardiovascular System

Introduction

The essential components of the human cardiovascular system are the heart, blood and blood vessels [1]. Blood is oxygenated through pulmonary circulation, systemic circulation provide oxygenated blood to rest of the body. Average adult contain 4.7 to 5.7 liters of blood, which include 7% of total body weight. Digestive system supplies nutrients to the body through circulation system by blood which consist of plasma, red blood cells, white blood cells, and platelets.

Oxygen and nutrients diffuse across the blood vessel and enter interstitial fluid, which carries oxygen and nutrients to the target cells, and carbon dioxide and wastes in the opposite direction, other component of the circulatory system, the lymphatic system open.

Arteries

Deliver oxygenated blood to the body by leaving left ventricle, through semilunar valve.

Capillaries

Arteries branch into small passages called arterioles and then into the capillaries [2,3]. The capillaries merge to bring blood into the venous system [4].

Veins

Capillaries merge into venules, which merge into veins.

Venous system feeds into the two major veins:

- Superior vena cava - drains tissues above the heart
- Inferior vena cava - drains tissues below the heart.

These two large veins empty into the right atrium of the heart.

Heart

Human heart consist two atrium and two ventricle for circulation. Four chambers in total: left atrium, left ventricle, right atrium and right ventricle. Right atrium is the upper chamber of the right side of the heart, blood that is returned to the right atrium is deoxygenated and passed into the right ventricle to be pumped through the pulmonary artery to the lungs for re-oxygenation and removal of carbon dioxide. Left atrium receives newly oxygenated blood from lungs as well as the pulmonary vein which is passed into strong left ventricle to be pumped through aorta to the different organs of the body.

Cardiovascular system

Hemoglobin molecules combine 98.5% of oxygenated blood and remain 1.5% physically dissolved in other blood liquids which are not connected to hemoglobin. The hemoglobin molecule is the primary transporter of oxygen in mammals and many other species.

Cardiac output

Volume of blood being pumped by the heart, in particular by the left or right ventricle, per unit time used in cardiac physiology is termed as Cardiac output (CO, also denoted by the symbols Q). Q is the product of the heart rate (HR), or the number of heart beats

Figure 1: Cardiovascular system.

per minute (bpm), and the stroke volume (SV), which is the volume of blood pumped from the ventricle per beat ($CO = HR \times SV$). Unit is L/min. Healthy person weighing 70 kg, the cardiac output at rest averages about 5 L/min; assuming a heart rate of 70 beats/min, the stroke volume would be approximately 70 mL [5].

Classification of cardiovascular drugs

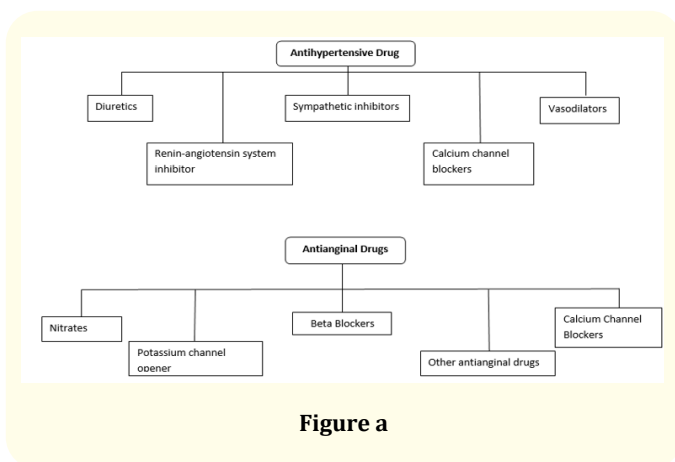


Figure a

Diuretics [6]

- Thiazide: Hydrochlorothiazide, Chlorthalidone, Indapamide
- High ceiling: Furosemide
- Potassium sparing: Spironolactone, Eplerenone, Amiloride
- Renin-angiotensin system inhibitors
- Ace inhibitors: Catopril, Enalapril, Lisinopril, Perindopril, Ramipril, Fosinopril, Quinapril, Trandolapril
- Angiotensin (AT1) receptors blockers: Lorsartan, Candesartan, Valsartan, Telmisartan, Irbesartan,
- Direct rennin inhibitor: Aliskiren.

Sympathetic inhibitors

- Beta-adrenergic blockers: Propranolol, Metoprolol, Atenolol (others)
- Alpha-adrenergic: Parazosin, terazosin, Doxazosin, Phenotolamine, phenoxybenzamine
- Alpha+Beta adrenergic blockers: Labetalol, Carvedilol
- Central sympatholytics: Clonidine, Methyldopa.

Calcium channel blockers

- Phenylalkylamine: Verapamil
- Benzothiazepine: Diltiazem
- Dihydropyridines: Nifedipine, Felodipine, Amlodipine, Nitrendipine, Lacidipine, Lercanidipine, Benidipine.

Vasodialotors

- Arteriolar dilator: Hydralazine, Minoxidil, Diazoxide
- Arteriolar+Venodilator: Nitroprusside Sodium.

Non-steroidal anti-inflammatory drugs

- Short acting: Glyceryl trinitrate, Isosorbide dinitrate(Sublingual)
- Long acting: Isosorbide dinitrate (Oral), isosorbide mononitrate, Erythritol tetranitrate, Pentaerythritol tetranitrate
- Potassium Channel Opener: Nicorandil.

Inotropic drugs

- Cardiac glycosides: Digoxin, Ouabain
- Sympathomimetics: Dobutamine, Dopamine
- PDE 3 inhibitors: Inamrinone, Milrinone
- Aldosterone antagonists: Spironolactone, Eplerenone.

Beta blocker

Beta blockers, also written β -blockers, are a class of medications that are predominantly used to manage abnormal heart rhythms, and to protect the heart from a second heart attack (myocardial infarction) after a first heart attack (secondary prevention) [1]. They are also widely used to treat high blood pressure (hypertension), although they are no longer the first choice for initial treatment of most patients.

β_1 receptor

Actions of the β_1 receptor include:

- Increase cardiac output by increasing heart rate (positive chronotropic effect), conduction velocity (positive dromotropic effect), stroke volume (by enhancing contractility – positive inotropic effect), and rate of relaxation of the myocardium, increasing calcium ion sequestration rate (positive lusitropic effect), which aids in increasing heart rate

- Increase renin secretion from juxtaglomerular cells of the kidney
- Increase ghrelin secretion from the stomach.

β_2 receptor

β_2 stimulates cells to increase energy production and utilization. Receptor is bound to cell membrane.

Actions of the β_2 receptor include:

- Smooth muscle relaxation throughout many areas the body, e.g. in bronchi (bronchodilation, see salbutamol), GI tract (decreased motility), veins (vasodilation of blood vessels), especially those to skeletal muscle (although this vasodilator effect of norepinephrine is relatively minor and overwhelmed by α adrenoceptor-mediated vasoconstriction)
- Lipolysis in adipose tissue
- anabolism in skeletal muscle
- Relax non-pregnant uterus
- Relax detrusor urinae muscle of bladder wall
- Dilate arteries to skeletal muscle
- glycogenolysis and gluconeogenesis
- Stimulates insulin secretion
- Contract sphincters of GI tract
- Thickened secretions from salivary glands
- Inhibit histamine-release from mast cells
- Increase renin secretion from kidney
- Involved in brain - immune communication.

β_2 agonists can be used to treat

- Asthma and COPD – reduce bronchial smooth muscle contraction thus dilating the bronchus
- Hyperkalemia – increase cellular potassium intake
- preterm birth – reduce uterine smooth muscle contractions.

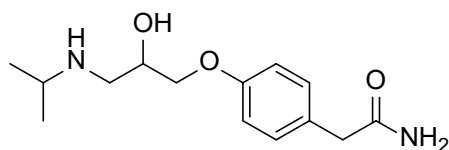
β_3 receptor

Actions of the β_3 receptor include:

- Increase of lipolysis in adipose tissue.

β_3 agonists used as weight-loss drugs, but are limited due to side effect of tremors.

Atenolol



Atenolol is (RS)-4-(2-hydroxy-3-isopropylaminopropoxy)phenylacetamide. Atenolol contains not less than 99.0 per cent and not more than 101.0 per cent of $C_{14}H_{22}N_2O_3$, calculated on the dried basis [7].

Description

A white or almost white powder.

Solubility

Soluble in ethanol; sparingly soluble in water; slightly soluble in dichloromethane; practically insoluble in ether.

Amlodipine Besilate: Slightly soluble in water; freely soluble in methanol; sparingly soluble in ethanol (95 per cent); slightly soluble in 2-propanol.

Atenolol tablets

Atenolol Tablets contain not less than 92.5 per cent and not more than 107.5 percent of the stated amount of atenolol, $C_{14}H_{22}N_2O_3$ in unit dosage form. The tablets may be coated.

Identification

Heat a quantity of the powdered tablets containing about 0.1 g of Atenolol with 15 ml of methanol to 50°, shake for 5 minutes, filter (Whatman No. 42 paper is suitable) and evaporate solvent and filtrate to dryness on water bath. Warm the residue with 10 ml of 0.1 M hydrochloric acid, shake and filter. Add to the filtrate sufficient 1 M sodium hydroxide to make it alkaline, extract with 10 ml of chloroform, dry by shaking with anhydrous sodium sulphate, filter, evaporate the filtrate to dryness on a water-bath and dry the residue at 105° for 1hour. The residue complies with the following test. Determine by infrared absorption spectrophotometry (2.4.6). Compare the spectrum with that obtained with atenolol RS or with the reference spectrum of atenolol.

When examined in the range 230 nm to 360 nm (2.4.7), the solution obtained in the Assay shows absorption maxima at about 275 nm and 282 nm.

Calcium channel blocker

Calcium-channel blockers inhibit Ca^{2+} entry into excitable cells. In coronary and peripheral arterial smooth muscle and the heart, inhibition of Ca^{2+} entry blunts the ability of Ca^{2+} to serve as an intracellular messenger. It is a smooth-muscle dilators and have a negative inotropic effect on the working myocardial cells of the atria and ventricles. It also have effects on impulse formation and conduction in some regions of the heart. It do not inhibit conduction in cell of the His-Purkinje system by a fast Na^{+} -dependent ionic current is responsible for the upstroke of the action potential in the working cells of the atria and ventricles and in the rapidly conducting cells. Sinoatrial and atrioventricular nodes, where depolarization is due primarily to a Ca^{2+} -dependent slow inward current, it slow the sinus pacemaker and inhibit atrioventricular conduction. Nifedipine is much more potent as an inhibitor of calcium channels in smooth muscle than in the heart, whereas verapamil and diltiazem are approximately equipotent in heart and vascular smooth

muscle. Calcium-channel blockers reach their specific binding sites in membranes by first dissolving in the phospholipid bilayer, after which they may interact with hydrophobic regions of proteins that make up, or regulate, these channels.

General pharmacology

Calcium-channel blockers (CCBs) bind to L-type calcium channels located on the vascular smooth muscle, cardiac myocytes, and cardiac nodal tissue (sinoatrial and atrioventricular nodes). These channels are responsible for regulating the influx of calcium into muscle cells, which in turn stimulates smooth muscle contraction and cardiac myocyte contraction.

In cardiac nodal tissue, L-type calcium channels in pacemaker currents and in phase 0 of the action potentials by blocking calcium entry into the cell, CCBs cause vascular smooth muscle relaxation (vasodilation), decreased myocardial force generation (negative inotropy), decreased heart rate (negative chronotropy), and decreased conduction velocity within the heart (negative dromotropy), particularly at the atrioventricular node.

Therapeutic indications

Calcium-channel blockers used to treat hypertension, angina and arrhythmias.

Hypertension

Calcium-channel blockers preferred first-line agents are contraindicated or ineffective, effective in treating hypertension in patients with angina or diabetes. High doses of short-acting calcium-channel blockers should be avoided because of increased risk of myocardial infarction due to excessive vasodilation and marked reflex cardiac stimulation.

Angina

Calcium is essential for muscular contraction. Calcium influx is increased in ischemia because of the membrane depolarization that hypoxia produces. This promotes the activity of several adenosine triphosphate consuming enzymes, thereby depleting energy stores and worsening the ischemia. The calcium-channel blockers protect the tissue by inhibiting the entrance of calcium into cardiac and smooth muscle cells of the coronary and systemic arterial beds. All calcium-channel blockers are therefore arteriolar vasodilators that cause a decrease in smooth muscle tone and vascular resistance. At clinical doses, these agents affect primarily the resistance of vascular smooth muscle and the myocardium. Verapamil mainly affects the myocardium, whereas nifedipine exerts a greater effect on smooth muscle in the peripheral vasculature. Diltiazem is intermediate in its actions. All calcium-channel block-

ers lower blood pressure. They may worsen heart failure due to their negative inotropic effect. Variant angina caused by spontaneous coronary spasm rather than by increased myocardial oxygen requirement is controlled by organic nitrates or calcium-channel blockers; β^2 -blockers are contraindicated.

Arrhythmias

Class IV drugs are calcium-channel blockers, decrease the inward current carried by calcium, resulting in a decreased rate of Phase 4 spontaneous depolarization. They also slow conduction in tissues that are dependent on calcium currents, such as the AV node. Although voltage-sensitive calcium channels occur in many different tissues, the major effect of calcium-channel blockers is on vascular smooth muscle and the heart.

Different classes of calcium-channel blockers

There are three chemical classes of CCBs. Basic of chemical structure and their relative selectivity toward cardiac versus vascular L-type calcium channels. The smoothest muscle selective class are the dihydropyridines, because of their high vascular selectivity, used to reduce systemic vascular resistance and arterial pressure to treat hypertension. Extended release formulations or long-acting compounds are used to treat angina and are particularly effecting for vasospastic angina and their powerful systemic vasodilator and pressure lowering effects can lead to reflex cardiac stimulation (tachycardia and increased inotropy), which offset the beneficial effects of afterload reduction on myocardial oxygen demand.

Dihydropyridines include the following specific drugs

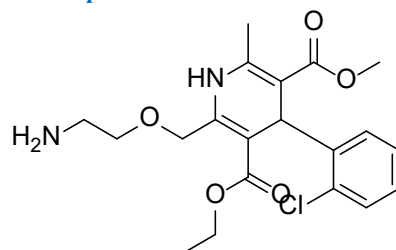
- Amlodipine
- Felodipine
- Isradipine
- Nicardipine
- Nifedipine
- Nimodipine
- Nitrendipine.

Non-dihydropyridines, of which there are only two currently used clinically, comprise the other two classes of CCBs. Verapamil (phenylalkylamine class), is relatively selective for the myocardium, and is less effective as a systemic vasodilator drug, used in treating angina (by reducing myocardial oxygen demand and reversing coronary vasospasm) and arrhythmias. Diltiazem (benzothiazepine class) is intermediate between verapamil and dihydropyridines in its selectivity for vascular calcium channels, having both cardiac depressant and vasodilator actions, it is able to reduce arterial pressure without producing the same degree of reflex cardiac stimulation caused by dihydropyridines.

Side Effects and Contraindications

- Dihydropyridines CCBs - flushing, headache, excessive hypotension, edema and reflex tachycardia.
- Baroreceptor reflex activation of sympathetic nerves and lack of direct negative cardiac effects can make dihydropyridines a less desirable choice for stable angina than diltiazem, verapamil or beta-blockers.
- Long-acting dihydropyridines (e.g., extended release nifedipine, amlodipine) - safer anti-hypertensive drugs, in part, because of reduced reflex responses. This characteristic also makes them more suitable for angina than short-acting dihydropyridines.
- The cardiac selective, non-dihydropyridine CCBs can cause excessive bradycardia, impaired electrical conduction (e.g., atrioventricular nodal block), and depressed contractility. Patients having preexistent bradycardia, conduction defects, or heart failure caused by systolic dysfunction should not be given CCBs, especially the cardiac selective, non-dihydropyridines. CCBs, especially non-dihydropyridines, should not be administered to patients being treated with a beta-blocker because beta-blockers also depress cardiac electrical and mechanical activity and therefore the addition of a CCB augments the effects of beta-blockade.

Amlodipine



Amlodipine Besilate is 3-ethyl 5-methyl (4RS)-2-[(2-aminoethoxy)methyl]-4-(2-chlorophenyl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate benzene sulphonate.

Amlodipine Besilate contains not less than 97.0 percent and not more than 102.0 percent of C₂₆H₃₁ClN₂O₈S, in unit dosage form calculated on the anhydrous basis.

Description - A white or almost white powder.

Amlodipine tablets

Amlodipine Tablets contain Amlodipine Besilate. Amlodipine Tablets contain not less than 90.0 percent and not more than 110.0 percent of the stated amount of amlodipine, C₂₀H₂₅ClN₂O₅.

Marketed formulation of Amlodipine and atenolol are summarized in table 1 [8-10].

S. No.	Brand Name	Combination	Manufacturing Brand
1.	Aamin A	Amlodipine 50 mg and Atenolol 5 mg	Medisys Biotech Pvt.Ltd.
2.	Acord A	Amlodipine 50 mg and Atenolol 5 mg	Invision Medi Sciences Pvt. Ltd
3.	Acord A	Amlodipine 50 mg and Atenolol 5 mg	Invision Medi Sciences Pvt. Ltd
4.	Adipin Plus	Amlodipine 50 mg and Atenolol 5 mg	Sani Medicaments Pvt. Ltd
5.	Adopin AT	Amlodipine 50 mg and Atenolol 5 mg	Indamed Pharmaceuticals PVT. LTD
6.	Adopin AT	Amlodipine 50 mg and Atenolol 5 mg	Purewi Labs Pvt. Ltd
7.	Aglodepin AT	Amlodipine 50 mg and Atenolol 5 mg	Aglowmed Ltd.
8.	Altas AT	Amlodipine 50 mg and Atenolol 5 mg	Anvik Biotech
9.	Altoma	Amlodipine 50 mg and Atenolol 5 mg	Q Check speciality Care
10.	AM-AT	Amlodipine 50 mg and Atenolol 5 mg	Dial Pharmaceuticals pvt.Ltd
11.	AM -T	Amlodipine 50 mg and Atenolol 5 mg	Tas Med India Pvt. Ltd
12.	Amcard-AT	Amlodipine 50 mg and Atenolol 5 mg	Systopic Laboratories Pvt.Ltd
13.	Amedepin AT	Amlodipine 50 mg and Atenolol 5 mg	Cadila Pharmaceutical Ltd. (IRM Pharma)
14.	Amcheck- AT	Amlodipine 50 mg and Atenolol 5 mg	Surge-Radius (Indoco Remedies Ltd)
15.	Amdinx AT	Amlodipine 50 mg and Atenolol 5 mg	BMW Pharmaco India Pvt. Ltd
16.	Amdip AT	Amlodipine 50 mg and Atenolol 5 mg	Dallas Pharmaceuticals
17.	Amdonex AT	Amlodipine 50 mg and Atenolol 5 mg	Aronex lifesciences pvt.Ltd
18.	Amfast AT	Amlodipine 50 mg and Atenolol 5 mg	Oversea Healthcare Pvt. Ltd
19.	Amin A	Amlodipine 50 mg and Atenolol 5 mg	Techyon Biotech Pvt. Ltd
20.	Aminol	Amlodipine 50 mg and Atenolol 5 mg	Alka Pharmaceuticals
21.	Amil AT	Amlodipine 50 mg and Atenolol 5 mg	Sabhali Formulation
22.	Amlibon AT	Amlodipine 50 mg and Atenolol 5 mg	Novartis India Pvt (Sandox)

23.	Amlica AT	Amlodipine 50 mg and Atenolol 5 mg	Cadex Laboratories
24.	Amlip Beta	Amlodipine 50 mg and Atenolol 5 mg	Cipla Limited
25.	Amloact AT	Amlodipine 50 mg and Atenolol 5 mg	Active Healthcare
26.	Amloapt AT	Amlodipine 50 mg and Atenolol 5 mg	APT Cure laboratories
27.	Amloat AT	Amlodipine 50 mg and Atenolol 5 mg	ATOZ pharmaceutical Pvt. Ltd
28.	Amobeta AT	Amlodipine 50 mg and Atenolol 5 mg	Medihealthcare Life sciences (India Pvt. Ltd)
29.	Amlobet	Amlodipine 50 mg and Atenolol 5 mg	Sun Pharmaceuticals Industries Ltd.
30.	Amlobid	Amlodipine 50 mg and Atenolol 5 mg	Ortin Phrmaceutical Laboratories
31.	Amlobin AT	Amlodipine 50 mg and Atenolol 5 mg	Bindlysh Biotech Ltd.
32.	Amlocal AT	Amlodipine 50 mg and Atenolol 5 mg	Acto Pharmaceuticals laboratories
33.	Amlocard Forte	Amlodipine 50 mg and Atenolol 5 mg	Intra Labs India Pvt. ltd
34.	Amlocas AT	Amlodipine 50 mg and Atenolol 5 mg	Casca remedies Pvt. Ltd
35.	Amlocom AT	Amlodipine 50 mg and Atenolol 5 mg	Comed chemicals Ltd.
36.	Amlodac AT	Amlodipine 50 mg and Atenolol 5 mg	Zydus Cadila Healthcare Ltd. (Medica)
37.	Amlogem AT	Amlodipine 50 mg and Atenolol 5 mg	Alkem Laboratories Ltd. (Bergen)
38.	Amlogla Plus	Amlodipine 50 mg and Atenolol 5 mg	Gladcare Formulations Pvt. Ldt
39.	Amloheart AT	Amlodipine 50 mg and Atenolol 5 mg	Lividus pharmaceuticals Pvt. Ltd
40.	Amlokath A	Amlodipine 50 mg and Atenolol 5 mg	Life Medicare & Biotech Pvt.
41.	Amlokind AT	Amlodipine 50 mg and Atenolol 5 mg	Mankind Pharma Pvt. Ltd
42.	Amlokos AT	Amlodipine 50 mg and Atenolol 5 mg	Raptakos Brett & Co. Ltd.
43.	Amlom	Amlodipine 50 mg and Atenolol 5 mg	Acinom Healthcare
44.	Amloman At	Amlodipine 50 mg and Atenolol 5 mg	Mancare Labororatries
45.	Amlong A	Amlodipine 50 mg and Atenolol 5 mg	Micro labs Ltd (Carsyon)
46.	Amlonol	Amlodipine 50 mg and Atenolol 5 mg	Terrace Pharmaceuticals pvt. Ltd
47.	Amlonorm At	Amlodipine 50 mg and Atenolol 5 mg	Acme Pharmaceuticals
48.	Amlonova	Amlodipine 50 mg and Atenolol 5 mg	Haledew Remedies
49.	Amlop AT	Amlodipine 50 mg and Atenolol 5 mg	Allied Chemical & Pharmaceutical Pvt. Ltd
50.	Amlopin AT	Amlodipine 50 mg and Atenolol 5 mg	US Vitamins Ltd. (Corvette)
51.	Amlopres AT	Amlodipine 50 mg and Atenolol 5 mg	Cipla limited
52.	Amloray AT	Amlodipine 50 mg and Atenolol 5 mg	Raymed Pharmaceutical Ltd
53.	Amlorld AT	Amlodipine 50 mg and Atenolol 5 mg	Nitro Cadineur
54.	Amlosac AT	Amlodipine 50 mg and Atenolol 5 mg	Parex Pharmaceuticals Pvt.Ltd
55.	Amlosafe AT	Amlodipine 50 mg and Atenolol 5 mg	Aristo Pharmaceutical Pvt. Ltd
56.	Amlostar A	Amlodipine 50 mg and Atenolol 5 mg	Captab Biotec
57.	Amlostat AT	Amlodipine 50 mg and Atenolol 5 mg	Biochem Pharmaceutical Industries Ltd
58.	Amlosure AT	Amlodipine 50 mg and Atenolol 5 mg	Cadell Healthcare Pvt.Ltd
59.	Amlotec AT	Amlodipine 50 mg and Atenolol 5 mg	Technica Labs & Pharma Pvt.Ltd
60.	Amloten	Amlodipine 50 mg and Atenolol 5 mg	Grandix Pharmaceuticals
61.	Amlotest AT	Amlodipine 50 mg and Atenolol 5 mg	Technica Labs & Pharma Pvt. Ltd
62.	Amlotest AT	Amlodipine 50 mg and Atenolol 5 mg	Tested & Trusted Pharma Pvt.Ltd
63.	Amlothens AT	Amlodipine 50 mg and Atenolol 5 mg	Athens Labs Ltd.
64.	Amlotin	Amlodipine 50 mg and Atenolol 5 mg	Biocare Remedies Pvt.Ltd
65.	Amlovas AT	Amlodipine 50 mg and Atenolol 5 mg	Macleods Pharmaceutical Ltd.
66.	Amlovik AT	Amlodipine 50 mg and Atenolol 5 mg	Cardia Labs (A Division of Anvik Biotech)
67.	Amlowin AT	Amlodipine 50 mg and Atenolol 5 mg	Vintage Labs Pvt. Ltd
68.	Amloz AT	Amlodipine 50 mg and Atenolol 5 mg	Shreya Life Sciences Pvt.Ltd

69.	Amlozed AT	Amlodipine 50 mg and Atenolol 5 mg	Zota Pharmaceutical Pvt.Ltd
70.	Amnest AT	Amlodipine 50 mg and Atenolol 5 mg	Welcure Drugs Pharmaceuticals Ltd.
71.	Amnol	Amlodipine 50 mg and Atenolol 5 mg	Jpee Drugs
72.	Amnorm A	Amlodipine 50 mg and Atenolol 5 mg	Varun Life Sciences Pvt.Ltd.
73.	Amodep At	Amlodipine 50 mg and Atenolol 5 mg	FDC Limited (Spectra)/(Vista)
74.	Amodin AT	Amlodipine 50 mg and Atenolol 5 mg	Biochemix Healthcare Pvt.Ltd
75.	Amone AT	Amlodipine 50 mg and Atenolol 5 mg	Talent Healthcare
76.	Amopine AT	Amlodipine 50 mg and Atenolol 5 mg	Shinto Organics (P) Ltd.
77.	Amozn AT	Amlodipine 50 mg and Atenolol 5 mg	Zenon Healthcare Ltd.
78.	Amplife AT	Amlodipine 50 mg and Atenolol 5 mg	Intra Labs India Pvt. Ltd (Intra Life)
79.	Ampin AT	Amlodipine 50 mg and Atenolol 5 mg	Swabhumi Drug ad Pharmaceutical India LTD.
80.	Ampine AT	Amlodipine 50 mg and Atenolol 5 mg	Sunij Pharma Pvt. Ltd
81.	AmrabAT	Amlodipine 50 mg and Atenolol 5 mg	Rapross Pharmaceuticals Pvt.Ltd
82.	Amsar AT	Amlodipine 50 mg and Atenolol 5 mg	Sarthak Biotech Pvt.Ltd
83.	Amsrten	Amlodipine 50 mg and Atenolol 5 mg	Stadmed Pvt.Ltd
84.	Amtas AT	Amlodipine 50 mg and Atenolol 5 mg	Intas Pharmaceutical s Pvt.ltd
85.	Amvik AT	Amlodipine 50 mg and Atenolol 5 mg	Panvik Pharmaceuticals
86.	Amwa AT	Amlodipine 50 mg and Atenolol 5 mg	Kaytross Healthcare Ltd.
87.	Amzen A	Amlodipine 50 mg and Atenolol 5 mg	Welbe Life sciences
89.	Andinx AT	Amlodipine 50 mg and Atenolol 5 mg	BMW PHARMACO INDIA pvt.Ltd
90.	Angi AT	Amlodipine 50 mg and Atenolol 5 mg	Trends Pharma Pvt.Ltd
91.	Angicam Beta	Amlodipine 50 mg and Atenolol 5 mg	Blue Cross Laboratories
92.	Angil AT	Amlodipine 50 mg and Atenolol 5 mg	Anikem laboratories
93.	Amset XT	Amlodipine 50 mg and Atenolol 5 mg	Pulse Pharmaceuticals Pvt.Ltd
94.	Angipres	Amlodipine 50 mg and Atenolol 5 mg	Sirius Healthcare
95.	Angitol Plus	Amlodipine 50 mg and Atenolol 5 mg	Ind-Swift Ltd.
96.	Angizaar AT	Amlodipine 50 mg and Atenolol 5 mg	Micro Labs Ltd.
97.	Anol Ad	Amlodipine 50 mg and Atenolol 5 mg	Payee Remedies
98.	Apin At	Amlodipine 50 mg and Atenolol 5 mg	G R Labotatories Pvt.Ltd
99.	Apine AT	Amlodipine 50 mg and Atenolol 5 mg	Saviour speciality
100.	Asomex AT	Amlodipine 50 mg and Atenolol 5 mg	Emcure Pharmaceuticals Ltd.
101.	Atal	Amlodipine 50 mg and Atenolol 5 mg	Finecure Pharmaceuticals Ltd.
102.	Atam	Amlodipine 50 mg and Atenolol 5 mg	Medinova labs
103.	Atecard AM	Amlodipine 50 mg and Atenolol 5 mg	Dabus pharma Limited
104.	Atedine	Amlodipine 50 mg and Atenolol 5 mg	Lonark Pjpharmaceuticals Pvt.Ltd
105.	Atekind D	Amlodipine 50 mg and Atenolol 5 mg	Mankind Pharma Limited
106.	Atemide	Amlodipine 50 mg and Atenolol 5 mg	Themis Pharmaceutical Ltd.
107.	Atemos AT	Amlodipine 50 mg and Atenolol 5 mg	Alkem Laboratories Ltd (Bergen)
108.	Anol Plus	Amlodipine 50 mg and Atenolol 5 mg	Lincoal Pharmaceutical Ltd.
109.	Anol AD	Amlodipine 50 mg and Atenolol 5 mg	Paycoremedies
110.	Aten AM	Amlodipine 50 mg and Atenolol 5 mg	Zydus Cadila Healthcare Ltd.
111.	Atenex AM	Amlodipine 50 mg and Atenolol 5 mg	Recon Healthcare Ltd.
112.	Atenodip	Amlodipine 50 mg and Atenolol 5 mg	Admac Pharma Ltd.
113.	Atenova SA	Amlodipine 50 mg and Atenolol 5 mg	Lupin Laboratories Ltd.
114.	Atloma	Amlodipine 50 mg and Atenolol 5 mg	Q Check Speciality Care
115.	Atol AM	Amlodipine 50 mg and Atenolol 5 mg	East West Pharma
116.	Atwin AM	Amlodipine 50 mg and Atenolol 5 mg	Embiotic Laborotories (P) Ltd.

Table 1: Marketed Preparation of Amlodipine 50 mg and Atenolol 5 mg.

Drug-drug interaction and side effects

People taking Amlodipine besylate and Atenolol are studied and side effects were observed and divided on the basis of age [11].

< 1 month

- Insomnia (sleeplessness)
- Atrial fibrillation - fibrillation of the muscles of the atria of the heart
- Cardiac failure
- Dermatitis bullous (inflammation of the skin characterized by the presence of bullae which are filled with fluid)
- Febrile neutropenia - fever with reduced white blood cells
- Hyperglycaemia (high blood sugar)
- Hypoalbuminaemia (levels of albumin in blood serum are abnormally low)
- Hypomagnesaemia (electrolyte disturbance in which there is an abnormally low level of magnesium in the blood)
- Mucous membrane disorder (disease of mucous membrane)
- Renal failure (kidney dysfunction).

1 - 6 months

- Fatigue (feeling of tiredness)
- Myalgia (muscle pain)
- Overdose
- Swollen tongue (swelling of tongue)
- Constipation
- Blood calcium decreased
- Blood potassium decreased
- Diplopia (double vision)
- Dizziness
- Dyspnoea (difficult or laboured respiration).

6 - 12 months

- Dizziness
- Dyspnoea (difficult or laboured respiration)
- Asthma
- Asthmatic crisis
- Erythema nodosum (skin inflammation that results in reddish, painful, tender lumps most commonly located in the front of the legs below)
- Ocular hyperaemia (an abnormally large amount of blood in eye)
- Psoriasis (immune-mediated disease that affects the skin)
- Weight decreased
- Affective disorder (mental disorder)
- Anaemia (lack of blood).

1 - 2 years

- Cardiac arrest
- Cellulitis (infection under the skin)
- Diabetic foot infection
- Gastrointestinal haemorrhage (bleeding gastrointestinal tract)
- Hip fracture
- Osteomyelitis (infection of bone)
- Skin ulcer
- Abnormal faeces (abnormal stool)
- Colon adenoma (non-cancerous epithelial colon tumor having a glandular origin and structure)
- Fatigue (feeling of tiredness).

2 - 5 years

- Tooth disorder (tooth disease)
- Transaminases increased
- Chronic kidney disease
- Abnormal faeces (abnormal stool)
- Colon adenoma (non-cancerous epithelial colon tumor having a glandular origin and structure)
- Gastroesophageal reflux disease
- Rectal haemorrhage (bleeding from anus)
- Thrombocytopenia (decrease of platelets in blood)
- Adenoma benign (non-cancerous tumour -secreting)
- Cerebral haemorrhage (bleeding within the brain).

5 - 10 years

- Balance disorder
- Drooling (drop saliva uncontrollably from the mouth)
- Dysphagia
- Gait disturbance
- General physical health deterioration (weak health status)
- Joint swelling
- Parkinson's disease
- Renal failure acute (rapid kidney dysfunction)
- Tremor (trembling or shaking movements in one or more parts of your body)
- Urinary incontinence
- 10+ years
- Burning sensation
- Cough
- Erythema (redness of the skin)
- Pruritus (severe itching of the skin)
- Pulmonary embolism -blockage of the main artery of the lung
- Rash

- Subdural haematoma (blood collects between the skull and the surface of the brain)
- Swelling
- Tinnitus (a ringing in the ears): Not specified
- Fatigue (feeling of tiredness)
- Drug ineffective
- Nausea (feeling of having an urge to vomit)
- Diarrhoea
- Dyspnoea (difficult or laboured respiration)
- Dizziness
- Vomiting
- Headache (pain in head)
- Pain
- Asthenia (weakness)
- Most common drug interactions by gender*: Female
- Arthralgia (joint pain)
- Dizziness
- Fall
- Weight decreased
- Cough
- Pruritus (severe itching of the skin)
- Asthenia (weakness)
- Oedema peripheral (superficial swelling)
- Rash: Male
- Fatigue (feeling of tiredness)
- Dyspnoea (difficult or laboured respiration)
- Headache (pain in head)
- Pneumonia
- Blood glucose increased
- Hypotension (abnormally low blood pressure)
- Rash
- Pyrexia (fever)
- Renal failure (kidney dysfunction)
- Weight decreased.

10 - 19 years

- Completed suicide (act of taking one's own life)
- Cardiac arrest
- Respiratory arrest - cessation of normal respiration due to failure of the lungs to function effectively
- Ascites - accumulation of fluid in the abdominal cavity
- Generalized Oedema (swelling all over the body)
- Hypotension (abnormally low blood pressure)
- Metabolic acidosis (body produces too much acid, or when the kidneys are not removing enough acid from the body)
- Overdose
- Peripheral swelling
- Pleural effusion (water on the lungs).

20 - 29 years

- Blood potassium decreased
- Chronic obstructive pulmonary disease (a progressive disease that makes it hard to breathe)
- Completed suicide (act of taking one's own life)
- Dehydration
- Erectile dysfunction
- Gastrooesophageal reflux disease (stomach contents (food or liquid) leak backwards from the stomach into the oesophagus)
- General physical health deterioration (weak health status)
- Glycosylated haemoglobin increased
- Hernia (hernia happens when part of an internal organ or tissue bulges through a weak area of muscle)
- Hypoaesthesia (reduced sense of touch or sensation).

30 - 39 years

- Blood creatinine increased
- Aplastic anaemia (blood disorder in which the body's bone marrow doesn't make enough new blood cells)
- Abdominal pain upper
- Anaemia (lack of blood)
- Bronchitis
- Cytomegalovirus infection
- Dizziness
- Leukopenia
- Malaise
- Nausea (feeling of having an urge to vomit).

40 - 49 years

- Nausea (feeling of having an urge to vomit)
- Completed suicide (act of taking one's own life)
- Diarrhoea
- Drug ineffective
- Vomiting
- Arthralgia (joint pain)
- Dyspnoea (difficult or laboured respiration)
- Overdose
- Pain
- Back pain.

50 - 59 years

- Vomiting
- Completed suicide (act of taking one's own life)
- Drug ineffective
- Malaise
- Nausea (feeling of having an urge to vomit)
- Pyrexia (fever)

- Hypotension (abnormally low blood pressure)
- Headache (pain in head)
- Anxiety
- Arthralgia (joint pain).

60+ years

- Fatigue (feeling of tiredness)
- Dyspnoea (difficult or laboured respiration)
- Pruritus (severe itching of the skin)
- Arthralgia (joint pain)
- Asthenia (weakness)
- Rash
- Pain in extremity
- Anaemia (lack of blood)
- Cough
- Pain.

Conclusion

Based on our interest in medicinal chemistry and pharmacology we compile the marketed brand of atenolol and amlodipine [12,13-30]. Cardiovascular system is integrating part of our body which include blood vessel, heart and artery. Various complications like hypertension, arrhythmia and angina are the result of abnormal functioning of cardiovascular system. Most commonly used combination for hypertension is amlodipine and atenolol. Amlodipine is a drug of CCBs type and atenolol is a β -blocker.

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Conflict of Interest

The author confirms that there is no conflict of interest for this publication.

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