International Journal of Pharmaceutical Sciences and Drug Analysis

E-ISSN: 2788-9254
P-ISSN: 2788-9246
www.pharmacyjournal.info
IJPSDA 2022; 2(1): 01-05
Received: 01-11-2021
Accepted: 09-12-2021

Gudisa Bereda
Department of Pharmacy, Negelle Health Science College, Guji, Ethiopia
Email: gudisabareda95@gmail.com

Corresponding Author:
Gudisa Bereda
Department of Pharmacy, Negelle Health Science College, Guji, Ethiopia

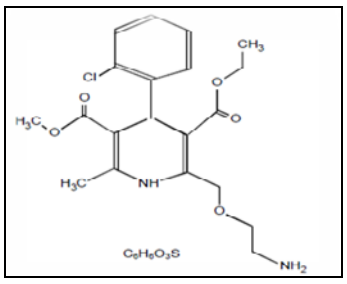
Apothegmatic of amlodipine: Recent and henceforth documentary

Gudisa Bereda

Abstract
Amlodipine's function in alleviating stable angina is owing to the decreasing of afterload secondary to its vasodilatory and antihypertensive properties. Amlodipine suppresses calcium ion influx across cell membranes selectively, with a higher outcome on vascular smooth muscle cells than on cardiac muscle cells. Amlodipine tablets are indicated for the symptomatic treatment of chronic stable angina. They perhaps used alone or in combination with distinctive antianginal agents. Amlodipine is initially administered orally and is available as 2.5 mg, 5 mg, and 10 mg tablets. The eloquent adverse effects of amlodipine involve peripheral edema (swelling of your legs or ankles), heart failure, hypoesthesia, neuropathy peripheral, paresthesia. Amlodipine tablets should be taken with a glass of liquid (e.g. a glass of water) with or without food. Grapefruit juice and grapefruit should not be consumed by people who are taking Amlodipine tablets.

Keywords: Amlodipine, apothegmatic, documentary, henceforth

Introduction
Amlodipine is a long-acting CCBs (dihydropyridine class) used as an anti-hypertensive and in the treatment of angina. For racemic amlodipine, there is lone crystalline figure of the anhydrous material characterized by single crystal X-ray diffraction. Additionally to the anhydrous figure, monohydrate and dihydrate forms have been characterized by single crystal and powder X-ray diffraction, as well as by FT-IR and thermal analysis methods. Amlodipine is chemically demonstrated as 3-Ethyl-5-methyl (±)-2-[(2-aminoethoxy) methyl]-4-(2-chlorophenyl)-1, 4-dihydro-6-methyl-3, 5-pyridinedicarboxylate, mono benzene sulphonate. Its empirical formula is $C_{20}H_{25}CIN_2O_5$ $C_6H_6O_3S$ 1-3], and its structural formula is:



Mechanism of Action: Amlodipine is DCCBs (calcium ion antagonist or slow-channel blocker) that suppresses the transmembrane influx of calcium ions into vascular smooth muscle and cardiac muscle. The contractile procedures of cardiac muscle and vascular smooth muscle are dependent upon the movement of extracellular calcium ions into these cells through specific ion channels. Amlodipine obviates calcium ion influx across cell membranes selectively, with a more consequence on vascular smooth muscle cells than on cardiac muscle cells. Amlodipine is a peripheral arterial vasodilator that acts directly on vascular smooth muscle to cause a reduction in peripheral vascular resistance and reduction in BP [4-6]. Amlodipine's function in relieving stable angina is owing to the de-escalating of afterload secondary to its vasodilatory and antihypertensive properties. Downgrading afterload leads to minimizing myocardial O_2 demand at any level of exertion as the heart does not necessitate functioning as hard to pump blood into the systemic circulation. Amlodipine also ameliorates prinzmetal or variant angina by obviating coronary spasms and renewing blood flow in the coronary arteries [7-9].

Pharmacokinetics: Absorption: Well absorbed after oral administration (64-90%) [10]. Distribution: Probably crosses the placenta. Protein Binding: 95–98%. Metabolism and Excretion: Mostly metabolized [11].

Pharmacodynamics: Hemodynamics; following administration of therapeutic doses to patients with hypertension, amlodipine tablets generate vasodilation sequencing in a reduction of supine and standing BPs. These downgrades in BP are not accompanied by an eloquent revamp in heart rate or plasma catecholamine levels with chronic dosing. Whereas the acute IV administration of amlodipine de-escalates arterial BP and accelerates heart rate in hemodynamic studies of patients with chronic stable angina, chronic oral administration of amlodipine in clinical trials did not lead to clinically eloquent revamp in heart rate or BPs in normotensive patients with angina [12-14].

Indications and usage

1. **Hypertension:** Amlodipine is indicated for the 1st-line treatment of hypertension and can be used as the lone agent to control BP in the preponderance of patients. Amlodipine is indicated for the 1st-line treatment of myocardial ischaemia, whether owing to fixed obstruction (stable angina) and/or vasospasm / vasoconstriction (prinzmetal's or variant angina) of coronary vasculature. Amlodipine tablets are indicated for the treatment of hypertension. They perhaps used alone or in combination with distinctive antihypertensive agents [15-17].
2. **Coronary:** Artery Disease (CAD) [18].
3. **Chronic Stable Angina:** Amlodipine tablets are indicated for the symptomatic treatment of chronic stable angina. They perhaps used alone or in combination with distinctive antianginal agents [19].
4. **Vasospastic Angina (Prinzmetal's or Variant Angina):** Amlodipine tablets are indicated for the treatment of confirmed or rule out vasospastic angina. They perhaps used as monotherapy or in combination with distinctive antianginal drugs [20].
5. **Angiographically Documented CAD:** In patients with currently documented CAD by angiography and without heart failure or an ejection fraction <40%, amlodipine tablets are indicated to de-escalate the peril of hospitalization owing to angina and to de-escalate the peril of a coronary revascularization procedure [21-23].

Dosage: Amlodipine is initially administered orally and is available as 2.5 mg, 5 mg, and 10 mg tablets. Additionally, suspensions created from oral tablets are available for pediatric patients and elderly patients with difficulty swallowing [24-26].

Adults: The ordinary starting dose is 5 mg once daily and it perhaps escalate the dose to 10 mg once daily [27, 28].

Use in children and adolescents (6 -17 years old): The recommended ordinary starting dose is 2.5 mg a day. The maximum recommended dose is 5 mg a day. It is significant to keep taking the tablets. Amlodipine 2.5 mg is not currently available and the 2.5 mg dose cannot be acquired with Amlodipine tablets 5 mg and 10 mg as these tablets are not manufactured to break into two equal halves [29-31].

Elderly patients: There is no special dosage for the elderly; although, care must be taken when the dose is escalated [32].

Renal impairment: Amlodipine is extensively metabolised to inactive metabolites with 10% excreted as unchanged drug in the urine. Revamps' in amlodipine plasma concentrations are not correlated with the degree of renal impairment. Amlodipine perhaps used at normal doses in patients with renal failure. Amlodipine is not dialysable [33-35]. In the patients have kidney challenges, the normal dosage is recommended. Amlodipine cannot be removed from the blood by dialysis (artificial kidney). Amlodipine tablets should be administered with particular heed to patients undergoing dialysis [36, 37]. In the patients have liver knots [38, 39]. The person concerned should be made to lie down with their arms and legs up (resting on a couple of cushions, for example). Symptoms of an overdose are: extreme dizziness and/or feeling very light-headed, faint or weak, challenges with breathing, having to urinate very frequently. If BP drop is solemn enough shock can happen [40, 41]. If you forget to take a tablet, leave out that dose completely. Take your next dose at the right time. Do not take a double dose to make up for a forgotten dose [42, 43]. If you stop taking amlodipine tablets your physician will advise you how long to take this medicine. Your condition may return if you stop using this medicine before you are advised [44].

Adverse drug reactions: The eloquent adverse effects of amlodipine involve peripheral edema (swelling of your legs or ankles), heart failure, hypoesthesia, neuropathy peripheral, paresthesia, peripheral ischemia, syncope, tachycardia, vasculitis, weight gain, weight decrease, pulmonary edema, flushing (hot or warm feeling in your face), dizziness, abnormal vision, conjunctivitis, diplopia, micturition disorder, nocturia, hyperglycemia, headache, gingival hyperplasia, drowsiness, arrhythmia (irregular heartbeat), heart palpitations (very fast heartbeat), sexual dysfunction (male and female), muscle rigidity, tremor and/or abnormal muscle movement, Severe skin reactions including intense skin rash, hives, reddening of the skin over your whole body, severe itching, blistering, peeling and swelling of the skin, inflammation of mucous membranes (Stevens Johnson Syndrome) toxic epidermal necrolysis or other allergic reactions, tiredness, extreme sleepiness, nausea, and Inflamed pancreas which may cause severe abdominal and back pain accompanied with feeling very unwell. Calcium channel blockers, including amlodipine, have been linked to rare instances of idiosyncratic drug-induced liver disease. A mixed hepatocellular-cholestatic pattern is a typical feature of amlodipine-induced liver injury [45-47].

Drug interactions: Coadministration of amlodipine and clarithromycin or erythromycin, diltiazem, ketoconazole, itraconazole, and ritonavir has reportedly escalated the peril of hypotension and acute kidney affliction owing to de-escalated metabolism by CYP3A4 and escalate the concentration of amlodipine in the blood. Furthermore, when amlodipine is used together with great doses of statins, there is an escalated peril for myopathy and rhabdomyolysis. In people who have had a kidney transplant, taking amlodipine and cyclosporine together perhaps escalate the levels of cyclosporine in the body [48-50].

Taking Amlodipine tablets with food and drink: Amlodipine tablets should be taken with a glass of liquid (e.g. a glass of water) with or without food. Grapefruit juice and grapefruit should not be consumed by people who are taking amlodipine tablets. This is because grapefruit and grapefruit juice can lead to escalate in the blood levels of the active ingredient amlodipine, which can cause an unpredictable, escalate in the BP decreasing outcome of amlodipine.

Contraindications: Amlodipine is contraindicated in patients with known hypersensitivity to amlodipine or its dosage form components. Additionally, amlodipine is relatively contraindicated in patients with cardiogenic shock, severe aortic stenosis, unstable angina, severe hypotension, heart failure, and hepatic impairment [50, 51]. In cardiogenic shock, the heart cannot pump effectively, and this situation is exacerbated by suppressing the influx of calcium ions into cardiac cells. In solemn aortic stenosis, amlodipine can cause ventricular collapse and dysfunction. Amlodipine causes a reflexive escalate in cardiac contractility in unstable angina, escalating myocardial oxygen demand and worsening ischemia. Amlodipine can further decrease BP, hypoperfusion to vital organs, and syncope in patients with severe hypotension. Patients who have heart failure perhaps experience pulmonary edema, shortness of breath, and dyspnea with amlodipine [53-55]. Lastly, patients with hepatic impairment perhaps not metabolize amlodipine effectively; leading to a longer half-life with possible escalates in plasma concentrations.

Conclusion

Amlodipine is DCCBs (calcium ion antagonist or slow-channel blocker) that suppresses the transmembrane influx of calcium ions into vascular smooth muscle and cardiac muscle. Hemodynamics; following administration of therapeutic doses to patients with hypertension, amlodipine tablets generate vasodilation sequencing in a reduction of supine and standing BPs. Amlodipine is indicated for the first-line treatment of hypertension and can be used as the lone agent to control BP in the preponderance of patients. The eloquent adverse effects of amlodipine involve peripheral edema (swelling of your legs or ankles), heart failure, hypoesthesia, neuropathy peripheral, paresthesia, peripheral ischemia, syncope, tachycardia, vasculitis, weight gain, weight decrease, pulmonary edema.

Abbreviations

BP: Blood pressure; CAD: Coronary Artery Disease: DHP-CCBs: Dihydropyridine calcium channel blockers.

Acknowledgments: The authors acknowledged Endnote-8, Google scholar, Medscape, Wikipedia, and PubMed.

Data Sources: Sources searched include Google Scholar, Research Gate, PubMed, NCBI, NDSS, PMID, PMCID, and Cochrane database. Search terms included: amlodipine usage.

Funding: None

Declarations

Ethical approval and consent to participate: Not applicable

Consent for publication: Not applicable

Availability of data and materials: The datasets generated during the current study are available with correspondent author.

Competing interests

The author has no financial or proprietary interest in any of material discussed in this article.

Author's contributions

GB contributed to preparing the first draft, review and editing the draft, and finally read and approved the manuscript.

References

1. Wang AL, Iadecola C, Wang G. New generations of dihydropyridines for treatment of hypertension. Journal of geriatric cardiology: JGC 2017;14(1):67.
2. Koshy AG. Cilnidipine-Novel Dual Acting Calcium Channel Blocker. IMA Kerala Medical Journal 2011;4(1):22-5.
3. Ananchenko G, Novakovic J, Lewis J. Amlodipine besylate. Profiles of Drug Substances, Excipients and Related Methodology 2012;37:31-77.
4. Selvam RP, Singh AK, Sivakumar T. Transdermal drug delivery systems for antihypertensive drugs-A review. Int J Pharm Biomed Res 2010;1(1):1-8.
5. Su JB. Cardioprotective effects of the if current inhibition by ivabradine during cardiac dysfunction. Current pharmaceutical biotechnology 2013;14(14):1213-9.
6. Su JB. Acepted for publication in a peer reviewed journal. Curr Pharm Biotechnol 2014;14(14):1213-9.
7. Bulsara KG, Cassagnol M. Amlodipine. Stat Pearls [Internet] 2021.
8. Lv C, Wei C, Wang X, Yao H, Li R, Wang B *et al.* The influence of food on the pharmacokinetics of amlodipine and losartan after single-dose of its compound tablets in healthy Chinese subjects. Drug research 2014;64(05):229-35.
9. Rousan TA, Mathew ST, Thadani U. Drug therapy for stable angina pectoris. Drugs 2017;77(3):265-84.
10. Lee SY, Kim JR, Jung JA, Huh W, Bahng MY, Ko JW. Bioequivalence evaluation of two amlodipine salts, besylate and orotate, each in a fixed-dose combination with olmesartan in healthy subjects. Drug design, development and therapy 2015;9:2811.
11. Clark SM, Dunn HE, Hankins GD. A review of oral labetalol and nifedipine in mild to moderate hypertension in pregnancy. In Seminars in perinatology. WB Saunders 2015;39(7):548-555.
12. Angina CS, Angina V, CAD AD. 1 indications and usage 1.1 Hypertension.
13. Agent AA, Brampton ON. PrTARO-AMLODIPINE.
14. Weir MR, Hanes DS, Klassen DK. Brenner and Rector's The Kidney. Bid 12(50), 12-5.
15. Vukadinovic D, Scholz SS, Messerli FH, Weber MA, Williams B, Böhm M *et al.* Peripheral edema and headache associated with amlodipine treatment: a meta-analysis of randomized, placebo-controlled trials. Journal of hypertension 2019;37(10):2093-103.
16. Zafarullah M, Hameed H, Qasim S, Ahmad MA. Management of hypertension among the patients with diabetes mellitus and heart diseases.

17. Snider ME, Nuzum DS, Veverka A. Long-acting nifedipine in the management of the hypertensive patient. Vascular health and risk management 2008;4(6):1249.
18. Bakris G, Briasoulis A, Dahlof B, Jamerson K, Weber MA, Kelly RY *et al.* Accomplish Investigators. Comparison of benazepril plus amlodipine or hydrochlorothiazide in high-risk patients with hypertension and coronary artery disease. The American Journal of cardiology 2013;112(2):255-9.
19. Agent AA. mN~ rvasc⋯. Cardiovascular medicine 71.
20. Meghashyam D, Hari P, Anant B. The Comparative analysis of different Brands of "Amlodipine".
21. Godfraind T. Calcium channel blockers in cardiovascular pharmacotherapy. Journal of cardiovascular pharmacology and therapeutics 2014;19(6):501-15.
22. Dangas G, Tijssen J, Wohrle J, Sondergaard L, Gilard M, Mollmann H. This review updates you on the international literature on therapeutics. Expert pharmacy practitioners–via SHPA Specialty Practice–scan major peer-reviewed journals in areas relevant to Australian pharmacy practice and present precis on major clinical trials, important pharmacoepidemiology studies and pharmacoeconomic research, and other updates relevant to practice. Interested readers are encouraged to explore the original publications in greater detail.
23. Kovacic JC, Mehran R, Sweeny J, Li JR, Moreno P, Baber U *et al.* Clustering of acute and subacute stent thrombosis related to the introduction of generic clopidogrel. Journal of cardiovascular pharmacology and therapeutics 2014;19(2):201-8.
24. Sheraz MA, Ahsan SF, Khan MF, Ahmed S, Ahmad I. Formulations of amlodipine: a review. Journal of pharmaceutics 2016.
25. Chandrasekaran G, Rajalakshmi AN. Fixed dose combination products as Oro-dispersible tablets: A review. Journal of Drug Delivery and Therapeutics 2019;9(2):563-73.
26. Rouaz K, Chiclana-Rodríguez B, Nardi-Ricart A, Suñé-Pou M, Mercadé-Frutos D, Suñé-Negre JM *et al.* Excipients in the Paediatric Population: A Review. Pharmaceutics 2021;13(3):387.
27. Zaiken K, Cheng JW. Azilsartan medoxomil: a new angiotensin receptor blocker. Clinical therapeutics 2011;33(11):1577-89.
28. Drummond W, Munger MA, Rafique M, Maboudian M, Khan M, Keefe DL. Antihypertensive efficacy of the oral direct renin inhibitor aliskiren as add-on therapy in patients not responding to amlodipine monotherapy. The Journal of Clinical Hypertension 2007;9(10):742-50.
29. Al-Rayess H, Fleissner K, Jaber MT, Brundage RC, Sarafoglou K. Manipulation of hydrocortisone tablets leads to iatrogenic Cushing syndrome in a 6-year-old girl with CAH. Journal of the Endocrine Society 2020;4(8):bvaa091.
30. Poulter NR, Dolan E, Gupta AK, O'Brien E, Whitehouse A, Sever PS. Efficacy and safety of incremental dosing of a new single-pill formulation of perindopril and amlodipine in the management of hypertension. American Journal of Cardiovascular Drugs 2019;19(3):313-23.
31. Ito S, Itoh H, Rakugi H, Okuda Y, Yamakawa S. Efficacy and safety of esaxerenone (CS-3150) for the treatment of essential hypertension: a phase 2 randomized, placebo-controlled, double-blind study. Journal of human hypertension 2019;33(7):542-51.
32. Singh S, Bajorek B. Defining 'elderly' in clinical practice guidelines for pharmacotherapy. Pharmacy practice 2014, 12(4).
33. Prikhodko E. Domestic or imported is better? Comparison of the drug Amlodipine from different manufacturers. S (-) amlodipine: new possibilities of pharmacotherapy of arterial hypertension.
34. Robinson MV. Angiotensin-converting enzyme inhibitors, angiotensin ii receptor blockers, and direct renin inhibitors. Pharmacotherapeutics for advanced practice nurse prescribers 295.
35. Düsing R. Valsartan/amlodipine single pill combination for the treatment of hypertension. Expert review of clinical pharmacology 2010;3(6):739-46.
36. Epoetin A. Chronic renal failure patients not on dialysis.
37. Troendle MM, Cumpston KL, Powell AO, Wills BK, Stromberg PE, Rose SR. Adjunctive use of low dose intralipid associated with hemodynamic improvement in combined amlodipine and labetalol overdose refractory to standard therapy. Clin Toxicol 2013;51(7):650-1.
38. Scully C. Medical Problems in Dentistry E-Book. Elsevier Health Sciences 2010.
39. Consta R. Risperdal CONSTA®.
40. Shetland NH, Council SI. Policy for Reducing and Managing Inpatient Falls.
41. Evans BW, Kravitz L, Walker N, Lefteri K, editors. Pharmacy OSCEs: A revision guide. Pharmaceutical Press 2013.
42. Grov C, D'Angelo AB, Flynn AW, Lopez-Rios J, Pantalone DW, Holloway IW *et al.* How do gay and bisexual men make up for missed prep doses, and what impact does missing a dose have on their subsequent sexual behavior? AIDS Education and Prevention 2018;30(4):275-86.
43. Vrijens B, De Geest S, Hughes DA, Przemyslaw K, Demonceau J, Ruppar T *et al.* A new taxonomy for describing and defining adherence to medications. British journal of clinical pharmacology 2012;73(5):691-705.
44. Watt MH, Maman S, Earp JA, Eng E, Setel PW, Golin CE, Jacobson M. "It's all the time in my mind": facilitators of adherence to antiretroviral therapy in a Tanzanian setting. Social science & medicine 2009;68(10):1793-800.
45. Teixeira MZ. New Homeopathic Medicines. Online: http://www.novosmedicamentoshomeopaticos.com/eng/ presentation. asp [accessed July 12, 2013] 2010.
46. Solomen S, Aaron P. Vascular Rehabilitation. JP Medical Ltd 2017.
47. Jangra K, Samagh N. Antihypertensives. In Pharmacology in Clinical Neurosciences. Springer, Singapore 2020, 769-915.
48. Dy GK, Adjei AA. Understanding, recognizing, and managing toxicities of targeted anticancer therapies. CA: a cancer journal for clinicians 2013;63(4):249-79.
49. M Pereira J, A Paiva J. Antimicrobial drug interactions in the critically ill patients. Current clinical pharmacology 2013;8(1):25-38.
50. Anadón A, Martínez-Larrañaga MR, Ares I, Martínez MA. Interactions between nutraceuticals/nutrients and therapeutic drugs. In Nutraceuticals. Academic Press 2016, 855-874.

51. Manrique Y, Lee D, Islam F, Nissen L, Cichero J, Stokes J *et al.* Crushed tablets: does the administration of food vehicles and thickened fluids to aid medication swallowing alter drug release? Journal of Pharmacy and Pharmaceutical Sciences 2014;17(2):207-19.
52. Koziolek M, Alcaro S, Augustijns P, Basit AW, Grimm M, Hens B *et al.* The mechanisms of pharmacokinetic food-drug interactions–A perspective from the UNGAP group. European Journal of Pharmaceutical Sciences 2019;134:31-59.
53. Gordon S, Kittleson M. Drugs used in the management of heart disease and cardiac arrhythmias. Small animal clinical pharmacology 2008;5:380.
54. Adams J, Khan E. Medications Used for the Cardiovascular System. In Understanding Pharmacology in Nursing Practice. Springer, Cham 2020, 167-217.
55. Burkett DE. Heart rate, rhythm, and contractility. Monitoring and Intervention for the Critically Ill Small Animal: The Rule of 20. 2016, 177-206.
56. Gérard L, Galloy AC, Capron A, Hantson P. Mixed amlodipine/valsartan overdose treated by the molecular adsorbent recirculating system (MARS™). Clinical Toxicology 2015;53(6):573-7.