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A Review on Amlodipine: Pharmacology; Demand and Scope in Global Pharmaceutical Industry

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ABSTRACT

Hypertension is a cardiovascular disease where the systolic blood pressure is greater or equal to 140mmHg or diastolic blood pressure is equal or greater than 90mmHg recorded in a patient in three properly measured tests and is the second most common disease around the globe after diabetes mellitus. There are different classes of antihypertension drugs available in the market namely: CCBs; ARBs; Diuretics; ACEs and Beta blockers. In India and America, one of the most prescribed antihypertension drugs is Amlodipine. Amlodipine is a calcium channel blocker drug that is available in the market under many brand names like Norvasc and Katerzia. It is prescribed as an antihypertensive and antiarrhythmic. Besides this amlodipine also reduces the excessive Ca^{2+} entry in the cardiovascular system thus preventing the subsequent damage to the cell. Amlodipine is a white powder of a molar mass as 567.05 $gmol^{-1}$. Looking into the finances and market value of amlodipine, the global Amlodipine Market value in the year 2019 was evaluated as US$ 1049.6 Mn which increased to US$ 1,083 million in the subsequent year 2020. It's been predicted that Amlodipine market value should grow at a significant CAGR of 3.4% during the forecast period 2021 to 2027. According to the financial analysis of 2020-2021 (April to November), India exported Amlodipine tablets to over 154 countries across the globe reaching the mark of trade value of US$ 77.029 million with the export volume of amlodipine as 2259819 approx. The USA is the largest importer of Amlodipine from India.

INTRODUCTION

Cardiovascular diseases are a group of disorders related to heart and blood vessels. Acc. to WHO survey of 2017, estimates show that cardiovascular diseases take the lives of around 17.7 million people, i.e., 31% of global deaths. More than 75% of death due to cardiovascular deaths occur in low-income and middle-income countries1. Most common among these is hypertension. The product of systemic vascular resistance and the cardiac output gives measurable blood pressure. In order to maintain the blood pressure in the body, our system may either decrease or increase these two factors, i.e., cardiac output or systemic vascular resistance. And if the body is unable to maintain the blood pressure at a normal level it leads to the condition i.e., hypertension.2 Hypertension can be defined as a condition in which the systolic blood pressure is greater or equal to 140mmHg or diastolic blood pressure is equal or greater than 90mmHg recorded in a patient in three properly measured tests. It is the leading cause of various cardiovascular diseases with 57% of all stroke deaths and 24% of all coronary heart diseases deaths in India 3. Also according to the WHO report in 2008, it is estimated that about 40% of total people aged above 25 years suffer hypertension and this is predicted to increase by 30% in 2025 with higher rates in developing than in developed countries 3,4. It is idiopathic in most cases but it is believed that the genetic and environmental factors play a major role in the occurrence of hypertension in a patient. The lifestyle factors causing risk of hypertension may include high intake of fatty food which cause hyperlipidaemia, spicy food, alcohol and tobacco; physical inactivity; low intake of calcium and potassium in food and some psychological stress. The hypertension condition in mostly asymptomatic but the common symptoms include excessive sweating, insomnia, headache, palpitations and giddiness.3 This is the main reason for making the antihypertension market among the biggest global markets of all time.

The main goal for hypertension treatment in a patient is to control and maintain the blood pressure at a normal level. The hypertension treatment approach is dependent upon the condition of the patient and the response of the patient towards the treatment. The different classes of antihypertensive drugs include:

Angiotensin receptor blocker:- They are the orally active antihypertensives drugs that controls the blood pressure by selectively blocking the angiotensin II receptor (AT_1 subtype) which in turn inhibits the renin-angiotensin system. This blockade of AT_1 subtype angiotensin receptor causes physiological effects decreasing the peripheral vascular

resistance by dilating the smooth muscles, decreasing the plasma volume while increasing the excretion of water thus decreasing the blood pressure.5

1. Angiotensin-converting enzyme blocker:- These antihypertensive drugs have same action like ARB, i.e., angiotensin II receptor. But have different mode of action. Besides blocking the angiotensin II receptor, the ACE inhibitors increases the conc. of bradykinin by decreasing its degradation resulting in release of nitric oxide and prostaglandins thereby causing additional vasodilation. the ACE class drugs have relatively better reduction in mortality rate then ARB antihypertensives making patients reliable to this treatment.6

2. Beta blockers:- They are antihypertension drugs which act as a competitive antagonist for beta adrenergic receptors by preventing the receptor interaction with adrenaline hormone. Due to this, force of heart contractility and cardiac output decreases. It is given in combination with other antihypertensive drugs like diuretics, ACE inhibitors, etc., for effective action. Mostly they are prescribed to the patient for treatment of cardiac arrhythmias. 7

3. Diuretics:- Diuretics, also known as water pills which in recent era has become preferred antihypertensive leaving beta blockers behind. They are mostly used to treat salt-sensitive hypertension but in recent studies its been shown that in small doses they are as effective in treating all hypertension as other antihypertensives. Diuretics removes excess of electrolytes and even water thus reducing the blood pressure. It has different subclasses as Thiazide; Loop diuretics (e.g., furosemide, torsemide); Potassium sparing pteridines (e.g., amiloride); Thiazide-like diuretics (e.g., chlorthalidone, indapamide). Thiazides and thiazide-like agents are considered as first line treatment for hypertension patients. 8

4. Calcium channel blockers:- This class of antihypertensives involves the agents which blocks the calcium sensitive channels, especially L-type or long-acting voltage sensitive calcium channels, present in the body. These L-type channels are distributed predominantly in myocardium and is involved in the muscle contraction. These CCBs alter the vascular smooth muscle calcium homeostasis by interfering with the calcium influx. The classification of CCBs can be acc. to the chemical structures as benzothia-zapines (e.g., diltiazem); phenylalkamines (e.g., verapamil) and dihydropyridines (e.g., amlodipine, nifedipine) and acc. to the generations which is based on parameters like pharmacokinetic profiles, receptor binding properties as first generation (e.g., nifedipine, diltiazem, verapamil); second generation (e.g., isradipine, felodipine); third generation (e.g., amlodipine, azelnidipine).

Second-generation drugs have longer duration of action and better vascular selectivity than first generation drugs. Furthermore, these 2nd generation drugs are further classified as slow-release formula (e.g., felodipine) and newer chemical formula (e.g., benidipine, manidipine). On the other hand, third generation drugs are known for their slow onset and prolonged action due to high lipophilic nature and better binding affinity for the calcium channel receptors. 9,10

Data from a meta-analysis showed that in an American population mean persistence was found to be 65% of ARBs vs. 51% diuretics and 28% β-blockers as an antihypertensives. 11

LITERATURE REVIEW

AMLODIPINE

Amlodipine besylate, sold under the brand name Norvasc, is a third-generation calcium channel blocker that is prescribed as an antihypertensive and antiarrhythmic. Besides this amlodipine also reduces the excessive Ca^{2+} entry in the cardiovascular system thus preventing the subsequent damage to the cell. 12,13 Chemically, it is known as 3-Ethyl-5-methyl-(4RS)-2-((2-aminoethoxy)methyl)-4-(2-chlorophenyl)-1,4-dihydro-6-methyl-3,5-pyridinedicarboxylate monobenzenesulphonate.13

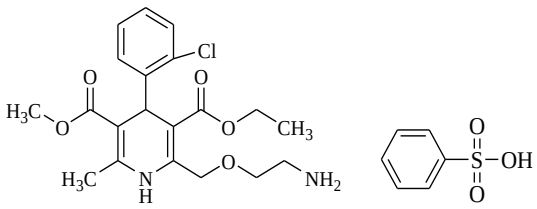


Fig. 1- Chemical str. of Amlodipine besylate

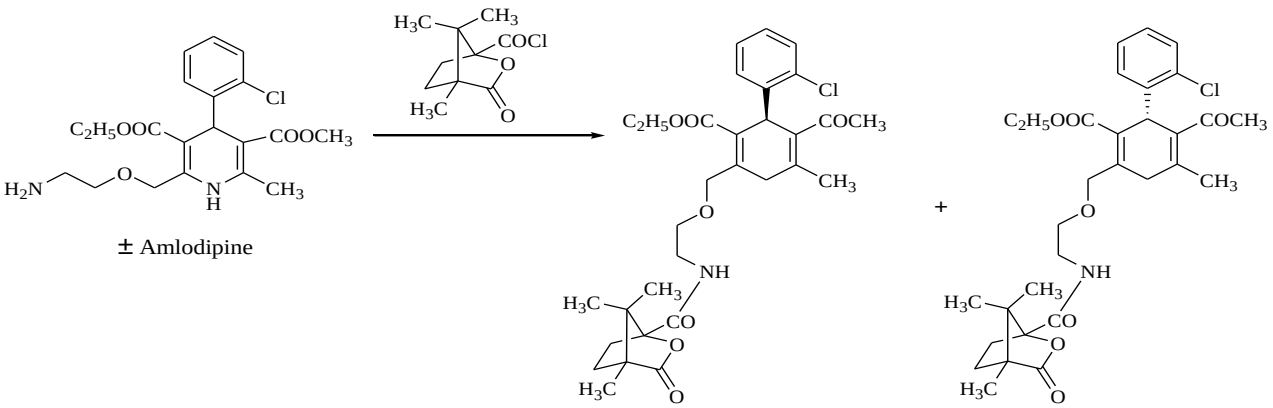
Amlodipine is a white powder of a molar mass as 567.05 $gmol^{-1}$. Given orally, its bioavailability is found to be 64-90% and the duration of action is nearly 24hours. This powder is slightly soluble in water, i.e., about 0.0052$molL^{-1}$ at 37^0C. In the mixture of solvents, it was found that at different temperatures and atmospheric press., the mole fraction solubility of amlodipine in a binary mixture of ethanol and water and propylene glycol and water was found to be maximum at the temp. 313.2K in mass fraction of ethanol and propylene glycol of 0.65 and 0.80 respectively. 13 Also, the spectroscopic study of amlodipine besylate, gave the value of energy of interaction as ΔE= -466.7 kJ/mol which shows a very strong interaction between the amlodipine base and benzenesulphonate which is equivalent to ionic interactions.24

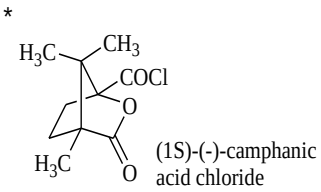
It is a long acting 1,4-dihydropyridine-based drug molecule possessing one chiral centre. Mostly available in its racemic mixture, its two enantiomers, S-(-)- isomer and the R-(+)-isomer differ from each other in the pharmacological action. It is been found that the S-(-)-isomeric form of amlodipine was found to be more potent calcium channel blocker with better therapeutic profile than the R-(+)-isomer. 12,14

Confirmation of S-(-)-isomer as an active enantiomer

S-(-)-isomer was proved as the active confirmation with greater calcium channel blocker activity using the X-ray structural analysis with the help of (1S)-camphoric acid chloride used as a chiral probe.14

1. The racemic amlodipine was converted to diastereomeric amide on reacting with (1S)-camphanic acid chloride.





The X-ray structural analysis was done after crystallizing the product obtained in above equation with water/DMF which gave the configuration at dihydropyridine carbon as S or R.

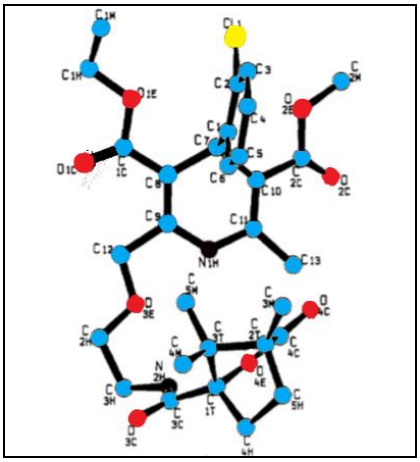
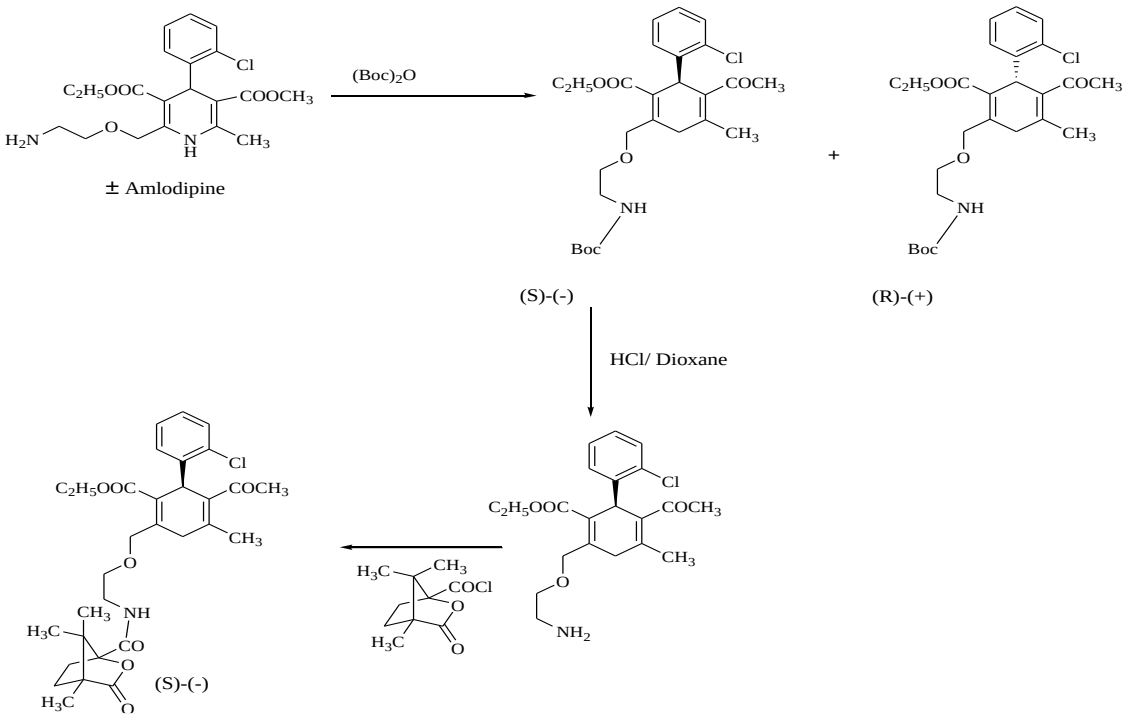


Fig.2:- X-ray structural analysis giving S- configuration

2. Amlodipine was converted to (3^0-butyloxy)carbonyl derivative. After this an enantiomerically pure form is extracted via chromatography on chiral columns. Cleavage of 3^0-butyl group and finally reacting with the (1S)-camphanic acid yielded (S)-(-)- isomer giving a confirmation that the (S)- form is the more potent and active form of amlodipine.



Enantioseparation of Amlodipine besylate

The (S)-(-)-enantiomer of amlodipine has a 2000 times stronger therapeutic profile as the calcium channel blocker for the treatment of hypertension than (R)-(+)-enantiomer, attempts

are being made to separate the (S)-enantiomer so as to increase the efficiency of amlodipine treatment as well as to decrease the toxic effects.17

Prior processes for the separation of (S)- and (R)-isomers include with promising results:- 1. resolution of racemic amlodipine with camphanic acid which is optically active; 2. salt crystallization method of racemic amlodipine with L- and D-tartaric acid in the presence of DMSO; 3. using optically active 2-methoxy-2-phenylethanol (S) and (R)- isomers can be separated; 4. or by intermediate racemic azido acid cinchonidine salts which on conversion yield pure S and R enantiomers of amlodipine. Above all the techniques, the most efficient method is the second method of using DMSO (dimethyl sulphoxide) as a solvent was given by Spargo. This technique involves firstly utilisation of L-tartaric acid which leads to the crystallisation of (R)-isomer and the (S)-isomer remains in the mother liquor. This (S)-isomer is separated out by adding D-tartaric acid. This popular method has disadvantages, i.e., D-tartaric acid is very costly; involves too many steps; also, DMSO used in above procedure may produce rotten cabbage odor in the presence of dimethyl sulphide in municipal wastewater treatment; due to high boiling point causes problem in solvent recovery. 13,15 As per the literature, the L-tartrate salt of amlodipine produced (S)- isomer of amlodipine in DMF (dimethylformamide) when used as a solvent unlike producing (R)- isomer in DMSO solvent.13

Another technique for enantio-separation of Amlodipine besylate which can be used as a promising technique on industrial level is an electrochemical immunosensor based upon magnetism property. This technique combines the function of the magnetic bead (coupled with antibody against S-amlodipine) and the magnetic electrode forming a highly enantioselective capture probe. Besides the enantio-separation, this immunosensor can also detect the concentration of S-amlodipine separated. Moreover, this immunosensor has other advantages like low cost, high sensitivity, perfect stability, and reproducibility. The S-amlodipine isomer gets attached to the S-amlodipine antibody forming the immunocomplex and leaving the R-amlodipine isomer in the supernatant liquid. The S-isomer of amlodipine can be detected by cyclic voltammetry and was eluted from the antibody by treating it with 10mM NaOH solution. The purity of the S-amlodipine so collected can be determined using HPLC technique. 16

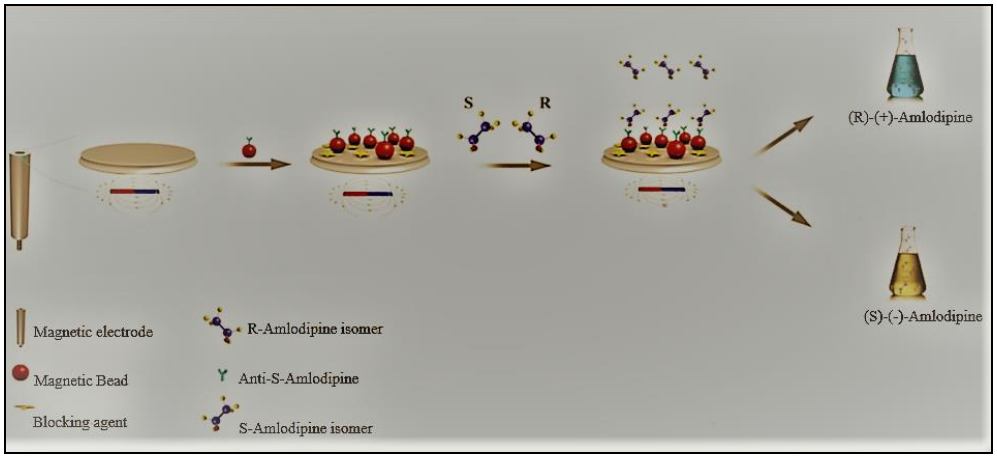
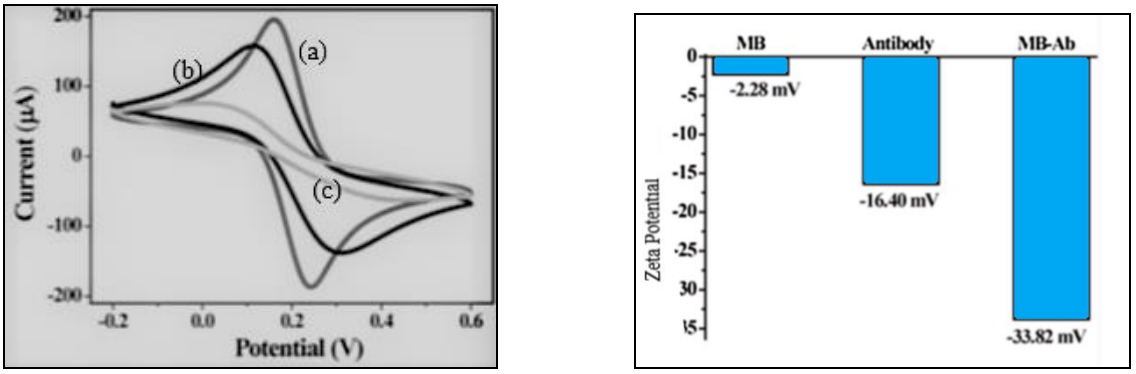


Fig.3:- Schematic view of the process of separation of S-amlodipine from racemic amlodipine.



(i) (ii)

Fig.4:- (i) The cyclic voltammograms of:- (a) bare electrode; (b) capture probe (magnetic beads conjugated with antibody); (c) magnetic electrode with formation of immunoconjugate (S-amlodipine bound to antibody).

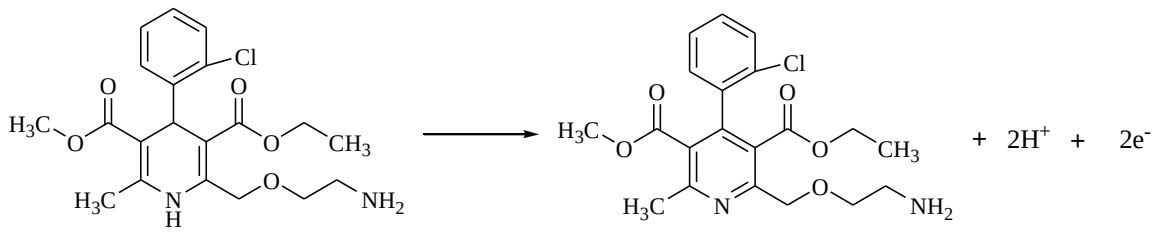
(ii) Zeta potential of magnetic beads (MB), antibody and the conjugate of magnetic bead and antibody.

The magnetic beads were found to be advantageous in using in the capture probe as it increased the binding capacity and also eased the electrode modification process. The proof for the perfect binding of the s-amlodipine with the antibody came from the values of optical rotation which when measured under the same conditions for S-amlodipine, KLH and the immunoconjugate were well maintained. the values of specific rotations of KLH, S-amlodipine and immunoconjugate were found as +58.0; -48.4 and -297.6 respectively. Furthermore, the HPLC values for the separated enantiomers of amlodipine showed positive results for this method of separation. Precisely, this method of separation of enantiomers was

found to beneficiary as this method can firstly, specifically recognise and separate the S-enantiomer from the racemic mixture of amlodipine with high purity and secondly, can accurately determine the amount of separated S-amlodipine. 16

Pharmacokinetics

Amlodipine, which is a third-generation calcium channel blocker drug, is known for its prolonged action. The main reason for its longer duration of action is attributed to the lipophilic character. Being lipophilic in nature, the drug concentration increases in cell membrane on administration gives a depot effect due to which there is a sustained release of the drug and also increases the elimination half-life, which is found to be 36-46 hours enabling the once daily dose. On oxidation, it is converted to pyridine analogs with subsequent de-esterification of 5-methoxycarbonyl group or oxidative deamination of 2-amino-ethoxymethyl side chain leading to the formation of pharmaceutically inactive amlodipine metabolites. The main site for the oxidation of amlodipine is 1,4-dihydropyridine ring.19 Furthermore, amlodipine besylate undergoes first-pass metabolism but less extensively as compared to other calcium channel blockers.9 Acc. to the data in the literature, the electrochemical analysis of amlodipine gave the value of 99.5% as percentage recovery of amlodipine in human serum. 25 Also, as per the findings ,18 the amlodipine if given to treat hypertension during pregnancy or the postpartum period, have found to cross the placenta in measurable quantity but in infant's blood and breast milk (after 24-48 hours prior to delivery) amlodipine is detected in a very low quantity. The amlodipine is excreted from the body via urine and feces. About 60% of amlodipine is excreted through urine out of which 5-10% amlodipine excreted in unchanged form. Furthermore, about 20-25% of amlodipine is excreted through faecal matter. Also, the pharmacokinetics of amlodipine besylate differ in both pregnant and non-pregnant females. 9,18



Amlodipine Pyridine analogue

Fig. 5:- Reaction scheme showing amlodipine undergoing oxidation at 1,4-dihydropyridine ring forming a pyridine analogue.

Photochemical degradation

Photostability of any drug is an important aspect for the drug stability as light can bring about physical or chemical changes in the drug and its derivatives. Amlodipine, which is a 1,4-dihydropyridine antihypertensive drug, is a photolabile, and absorbs intensively in UV-A. As per the literature,20 the quantum yield value of reaction of amlodipine reaches to about 0.001 in UV-A which is low value but this low value of quantum yield value along with the strong absorptive ability of amlodipine in UV spectra is considered to be the main causes of the photo-degradation of amlodipine besylate. Amlodipine, on the absorption of UV rays in UV-A range, releases the H-atom from the forth position resulting in the formation of the free radicle and further aromatisation of the dihydropyridine ring. 20,21 The reaction for photodegradation of Amlodipine:- 22

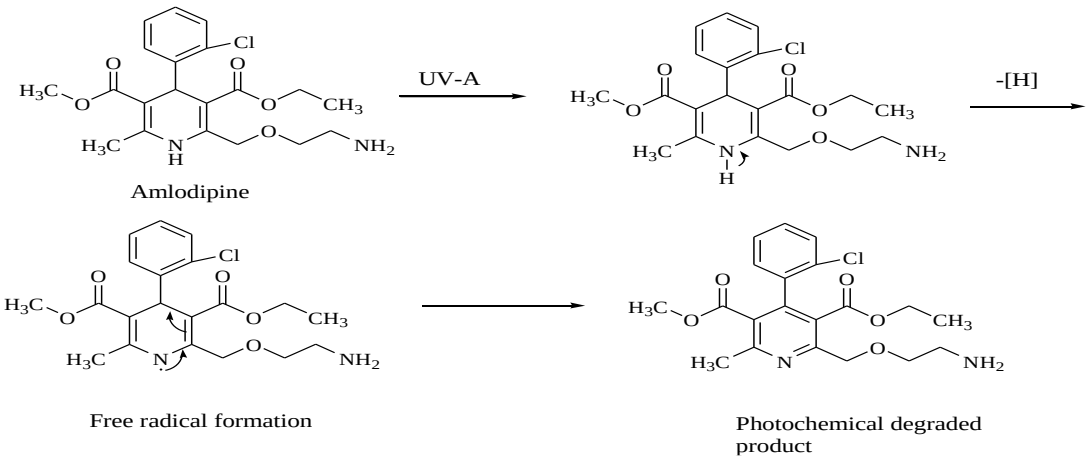


Fig. 6:- Photochemical degradation of Amlodipine.

The photochemical degradation of Amlodipine, can cause toxic effects and may damage surrounding tissues. Thus, in order to increase the photostability different approaches are adopted. The addition of Amlodipine in the liposomes and cyclodextrin have found to increase the photostability of Amlodipine with residual drug conc. as 77% and 90% respectively.22 In liposomes, the drug van be incorporated in the aqueous volume enclosed by lipid molecules or in between the lipid molecules forming phospholipid bilayer. Sometimes, the drug molecule partially gets embedded in the cyclodextrin cavity which causes light-sensitive part exposed outside leading to increase in photodegradation.22 Besides this method, preparation of microspheres containing drug has found to give excellent results by providing better protection to drug from light with residual drug conc. 97%.22,21 Moreover, preparation of oil-in -water dry emulsions of drug has proved not only in

improving the photostability but also the bioavailability of amlodipine.21 Nowadays, microcapsules have attracted researchers as microcapsules not only increases photostability of amlodipine but also as per the literature,23 amlodipine loaded dextrin coated microcapsules have shorter disintegrating time (29.8sec) due to amorphous dispersion and significantly higher plasma conc. as compared to free-base amlodipine. The microcapsules, coated with Eudragit® EPO have smooth surfaces and can be given to geriatric patients as EPO layer is soluble in gastric pH but insoluble in mouth. So, above all methods are somehow successful in preventing amlodipine from any photochemical degradations.23

Comparison of effectiveness of Amlodipine with other antihypertensive drugs

According to the result obtained from the research performed by Furukuwa, the comparison between the different calcium channel blockers, namely, Nifedipine, Nicardipine, Amlodipine, Benidipine and Cilnidipine it has been evidently proven that Amlodipine has the maximum effectiveness in the patients. 27

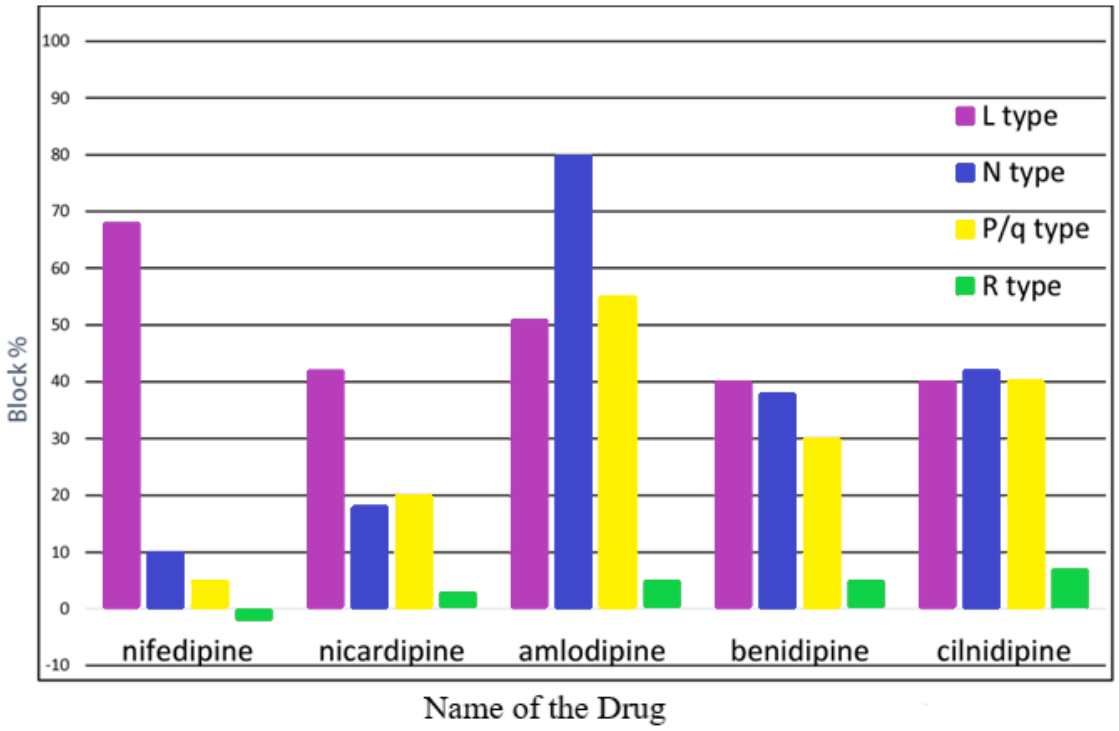


Fig. 7:- Comparison between the effectiveness of different Calcium Channel Blockers.

Moreover, it's been detected that treatment with amlodipine has a positive effect in the prevention of the aortal morphometric alterations and also shown the maximum value of inhibition of deposition of the collagen fibres on the ventricular walls. 28

Possible Side-effects of Amlodipine

The possible side-effects reported by the patients undergoing Amlodipine therapy have reported stomach ache, mild inflammation in the lower parts of hindlimbs (ankles, feet), nauseous feeling, dizziness, headache. In very rare cases, patients have reported appearance of the telangiectasias on the skin. 30

Also in some patients, the treatment using amlodipine besylate has caused the occurrence of gingival hypertrophy and redness, a condition that is characterized by the enlargement of the interdental papillae i.e., inflammation and redness of the gums. The gingival hypertrophy is generally limited to the anterior side of the mouth with the attached and marginal gums or gingivae. Acc. to the collected data, the chances of occurrence of this condition while on amlodipine treatment is found to be around 3.3% which is far less percentage as compared to the chances when on treatment with nifedipine which is approx. 47.8%. 31,32

Amlodipine Besylate Market and Scope

Today the Antihypertensive Drug Market is ranked as the 2nd largest market and all credit goes to the poor health of the people around the globe with the majority in the developing countries. Acc. to the current scenario, the financial experts estimate that the worth of antihypertensives drug market will reach to the market value mark of **"approx. US$ 33.9 Bn"** by the last of 2027. The major companies involved in antihypertensive drug market are shortlisted as:

Pfizer; Novartis; Sanofi; Boehringer Ingelheim, AstraZeneca. 33

As per 2019 survey, Amlodipine besylate has been reported at the 6th position of the best and most prescribed drug in U.S. with the estimated number of prescriptions of amlodipine be 73,542,114 while the total patients in 2019 as 16,419,181 with the cost of dose per day as $0.37. 34

Looking at the total prescription and total hypertension patients prescribed amlodipine has shown a steady increase in the mark from the year 2013-2020 which can be shown in the following table.

YEAR	NO. OF PATIENTS	NO. OF PRESCRIPTIONS
2013	11,513,217	62,816,160
2014	11,986,299	63,722,510
2015	13,717,742	70,986,227
2016	14,177,857	75,201,622
2017	17,624,367	72,508,878
2018	15,858,849	75,902,784
2019	16,419,181	73,542,114

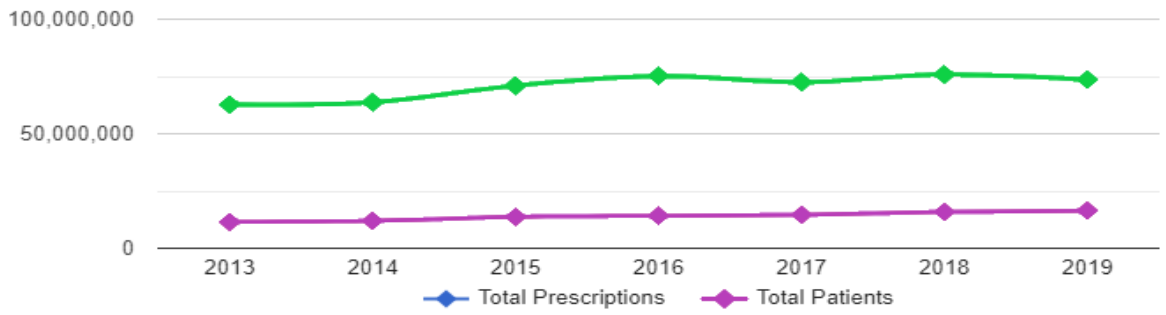


Fig 8:- The graph showing Amlodipine besylate prescription over patients in US from 2013-2019.

The global Amlodipine Market value in the year **2019 was evaluated as US$ 1049.6 Mn** which increased to **US$ 1,083 million in the year 2020**. It's been predicted that Amlodipine market value should grow at the significant **CAGR of 3.4%** during the forecast period 2021 to 2027 and estimated to reach over **US$ 1300 million by the end of 2027** giving the great scope of profit in this sector with a lucrative area of growth being North America and India thus increasing the share value of the concerned pharmaceutical companies. The sole reason of the such a remarkable growth in this market is the increase in the hypertension patients and also there has been found that treatment of hypertension patients suffering from the SARS-COVID-19 with amlodipine besylate has been liked with the depreciation in the fatality rate in such patients thus giving a prominent boast in the amlodipine market even during the corona phase where other industries have been affected in the negative terms but the global amlodipine market have the positive effect in the current scene but also in the future. 35,36

Though the industries had their focus on the mono-dose dosage forms but now there is a shift in the attention of the pharmaceutical companies towards the combination dose and the main reason for that is that these combination doses are found to be more effective in the condition. For example, the combination drug of Benazepril and Amlodipine has elucidated a positive effect in the depreciation in the chances of occurrence of nephropathy in the patients and this drug combination has found to be more effective in comparison to the Benazepril-Hydrochlorothiazide in controlling the elevation of cardiovascular symptoms in high-risk patients. 34

The whole amlodipine market is segmented in three sectors for the proper study namely: -

- Clinical Application
- Distribution Channel (Retail pharmacies; hospital pharmacies; online pharmacies)
- Geographical Area (North America; Asia; Europe; Latin America; Middle East and Africa)

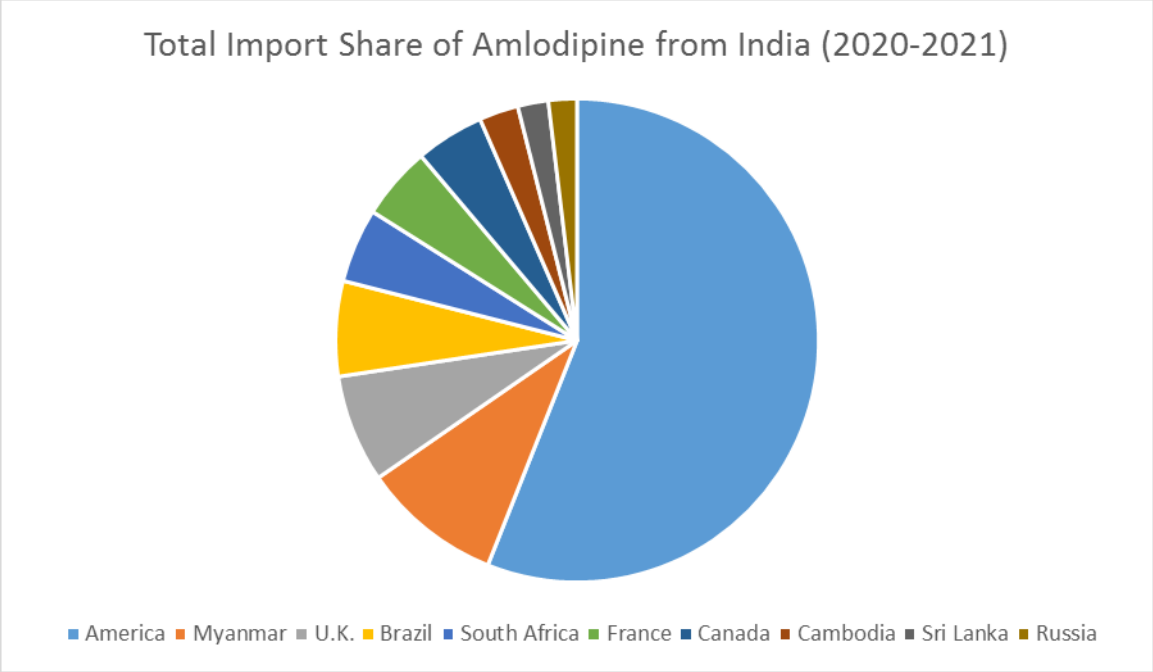
Though many antihypertension drugs have been prevailing in the global market but still Amlodipine has been able to survive in the top 20 antihypertension drugs list and in India it's one of the most commonly prescribed drugs.

Analysis of India's total export of Amlodipine in the Financial Year of 2020-2021

According to the financial analysis of 2020-2021 (April to November), India exported Amlodipine tablets to over 154 countries across the globe reaching the mark of trade value of US$ 77.029 million with the export volume of amlodipine as 2259819 approx. The USA is the largest importer of Amlodipine from India with a total Amlodipine import value of US$ 32.279 million which accounts for a share of approx. 41.9% of India's total Amlodipine export shipment while Zambia sharing the least import shipment value of Amlodipine from India. 36

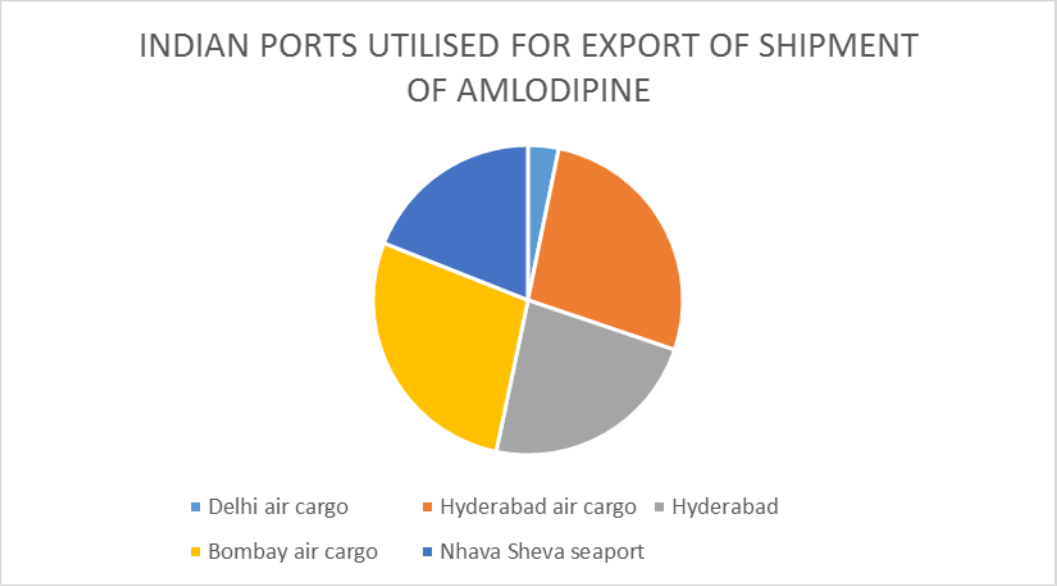
The following table shows the name of the top 10 countries along with their total import of Amlodipine from India from April to November in the financial year 2020-2021 in the ascending order:

NAME OF THE COUNTRY	TOTAL IMPORT VALUE (US$ Million)
Russia	1.1
Sri Lanka	1.18
Cambodia	1.51
Canada	2.65
France	2.81
South Africa	2.86
Brazil	3.67
U.K.	4.16
Myanmar	5.39
United States of America	32.279



India's total export revenue in the top 5 countries namely, United States of America; Myanmar; U.K.; Brazil and South Africa alone accounts for total financial value of US$ 48.36 million i.e., more than 62.78% of India's total export of Amlodipine. India is the exporter of Amlodipine shipments to almost all the major countries of the world thus giving its little contribution in providing boast to the Indian economy. India's total Amlodipine export share value accounts for around 0.04% of total market share of India.

With such a huge value of Amlodipine export market value of India motivates the manufacturer to engage more in this platform.



All in all, there are around 24 top Indian ports that are involved in the export of Amlodipine shipments from India but among them all, Bombay Air Cargo and Hyderabad Air cargo are the major ports used in the Amlodipine export with the share value percentage of 27.7% and 27% respectively.

Export duty is the fees that the exporter has to pay to the government in order to get permission to export the product. The export duty is different for every product and is decided and levied by the government of that country. The export duty on the product is decided as per the HS Codes of the product. The HS code is the special standardised number code assigned to the product and this helps in classification of the products into different categories.

Amlodipine has the HS Code of 30049072 and is categorized under the medicaments in packaged forms for retail sales along with other drugs namely, Nifedipine; Lacidipine and Verapamil. The MEIS rate for Amlodipine is set for 3% and DBK rate is 1.9% along with IGST of 12%. 38

CONCLUSION

Hypertension, also known as silent killer is the most prevailing disease around the globe. As per WHO estimates of the year 2015, one out of every four men and one out of every five women are diagnosed with hypertension. The steady increase in the number of patients diagnosed with hypertension, especially in developing countries is the solemn reason of the boost in the production and sales of the antihypertensive group of drugs. Though there are many antihypertensive drugs available in the market with ARBs and diuretics being on the top but Amlodipine, an antihypertension drug of calcium channel blocker has been among the first choice of drug in the treatment of hypertension in most of the cases with least side effects be it even pregnant or lactating mothers. Amlodipine has been found to be most effective in controlling symptoms like anginal pain, hypertension as compared to other calcium channel blockers.

The total market share of amlodipine has been remarkable with the global Amlodipine Market value in the year 2019 was evaluated as US$ 1049.6 Mn which increased to US$ 1,083 million in the year 2020.

Also, where covid pandemic has not left any industry untouched still amlodipine share is increasing and as per the expert's prediction, Amlodipine market value should grow at the significant CAGR of 3.4% during the forecast period 2021 to 2027 and estimated to reach over US$ 1300 million by the end of 2027 giving the great scope of profit in this sector with the lucrative area of growth being North America and India. There is a lot a positive scope in this market in yielding good profit to pharmaceutical companies in the future ahead.

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