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Degradation study of different brands of amlodipine using UV spectrophotometer

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Abstract

There are several different brands available for Amlodipine as it is the most prescribed oral antihypertensive agents that is used for primary and secondary hypertension. The objective of this study develops the degradation studies of different brands of Amlodipine besylate 5 mg. This drug was subjected to different stress conditions as per International Conference on Harmonization guidelines (ICH). An ultraviolet UV spectroscopic method was developed for analysis of the drug in the presence of the degradation products. Distilled water was used as a solvents. The amount of degraded drugs was calculated by taking the absorbance at 238 nm. According to the assay limit of USP specified that the content should not be less than 95% and not more than 105% of labelled amount. Brand 1, 2 and 5 are degraded by UV light exposure and Brand 1 and 2 degraded after the heat exposure. On basic pH brand 1, 2 ,4 and 5 showed degradation after the addition of 1N NaOH while brand 3 do not degrade as the base has no impact on Amlodipine concentration. On addition of 1N HCL brands 1, 2, 4 and 5 showed heavy degradation and brand 3 is remain nondegradable in acidic pH. The method was found to be simple and less time consuming and cost effective.

Keywords: Amlodipine besylate 5 mg, Degradation studies, Assay.

Introduction

Amlodipine besylate (AML), (4R, S)-3-ethyl-5-methyl 2-(2-amino-ethoxy-methyl)-4-(2-chlorophenyl)-1,4-dihydro-6-methyl pyridine-3,5-dicarboxylate mono benzene, sulphonate and it is a potent long-acting Ca channel blocking agent (Figure 1).[1] Amlodipine, a charged dihydropyridine-type (DHP) calcium channel blocker (CCB), has been widely used to treat angina and hypertension HT. Several meta-analyses have been evaluated the effect of CCBs on cardiovascular outcomes. Calcium channel blockers (CCB) are one of the most widely used group of anti-hypertensive drugs. Amlodipine has a long half-life (30-58 hrs) and large volume of distribution (21 L/kg). Toxicity is seen at doses up to 5-10 times the therapeutic dose and sets within 30-60 minutes following ingestion. It is more effective than β-blockers in the treatment of variant angina because it prevents and reverses the coronary spasms resulting in increased blood flow and myocardial oxygen supply. Moreover, it inhibits selectively the arterial vascular smooth muscle cell proliferation resulting in prevention of the progressive narrowing of the arteries. Amlodipine besylate is official in British Pharmacopoeia BP.[2]

Forced degradation is a process whereby the natural degradation rate of a drug product or drug substance is accelerated by an application of an additional stress.

Understanding of these products qualitatively, can assist in predicting toxicity of these degradation products and also in deciding the shelf life of the drug. The ICH guideline indicates that stress testing is designed to determine the stability of the molecule by knowing degradation pathway in order to identify the likely degradation the products. The degradation products are those formed under different conditions like effect of temperature, humidity, oxidation, photolysis and susceptibility of hydrolysis across a wide range of pH value. Even though ICH and FDA ask to include this study at phase III level. It is recommended to start this study as early as possible to provide valuable information to assess inherent stability of a drug and to improve the formulation process. Different analytical methods that have been reported for the determination of amlodipine including, HPLC, high-performance liquid chromatography,[3-8] gas chromatography coupled with mass spectrometry,[9] high-performance thin layer liquid chromatography,[10] fluorimetry,[11] capillary electrophoresis,[12] flow injection analysis,[13] differential-pulse square-wave anodic Voltammetry,[14] and enzyme immunoassay[15]. Moreover amlodipine besylate in pharmaceutical preparations was determined using the formation of Charge transfer complexes based on the reaction of ADB with an electron acceptor named DDQ.[16] Spectrophotometry because of its inherent simplicity is considered one of the most convenient alternative techniques. Our research group has done these types of degradation studies of drugs and these are very helpful for health care professionals.[17-19]

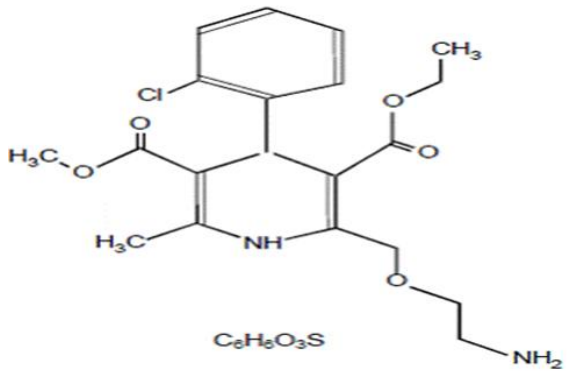

Figure 1: Structure of Amlodipine besylate

Materials and Methods

Reagents

Analytical grade reagents were used 1N sodium hydroxide, 1N hydrochloric acid and deionized water used to be double distilled, deionized and filtered.

Glasswares

Volumetric flask, funnel, beakers, Measuring cylinder, pipette, and stirrer used were of Pyrex type and were washed with chromic acid followed by thorough washing with water and finally rinsed with double distilled or de-ionized water which was freshly prepared in the laboratory.

Instruments

• Spectrophometer: PG Instrument (T80 UV/vi's spectrometer) along with a pair of 5 cm quartz

• Corvettes

• Weighing Balance: Pioneer OHAIUS (Item PA214C)

• Water Bath: DT; Digital constant temperature tank HH-4

• UV Lamp: Power: 8N, LF-204.LS ,Serial N 045571, 4W-254 nm,4W-365 nm.

UV, visible 1601 Shimadzu double beam spectrophotometer was used for measurement of spectra. The solvent, which is used for the assay was distill water.

Wavelength Selection

About 50 ppm of amlodipine besylate was accurately prepared in distill water. The wavelength maxima (λmax) was observed at 238 nm and this wavelength was adopted for absorbance measurement.

Preparation of 1N Sodium Hydroxide

Weigh 40 gm of NaOH, dissolve in small quantity of water taken in a 100ml volumetric flask and make up the volume upto mark with de ionized water

Preparation of 1N Hydrochloric Acid

Take 8.36 ml analytical grade hydrochloric acid (37%, 12N) in a volumetric flask and add de-ionized water to make up the volume.

Standard Stock Solution

The five different brands were purchased from a different Public medical store located in Karachi. All tablets of brand have the same batch number and were labeled to contain amlodipine besylate 5 mg per tablet. All the five brands have 5 year shelf life. Weigh and finally crushed tablets accurately for making primary solutions of amlodipine besylate 5 mg, Amlocard (0.2050 gm)

PharmaTech, Novasc (0.2029 gm) Pfizer, Lodopin (0.1232 gm) Merck, Zodip (0.1195 gm) Zafa pharmaceutical, Revloc (0.1493 gm) Opal laboratory, were weighed accurately and introduced in 100 ml volumetric flasks. Add distill water and shake vigorously and make up the volume upto 100 ml to make the strength of the solution 50ppm in 100 ml.

For Acid

To study the effect of acid, take 5 ml of 50 ppm solution of each brand in five separated test tubes then 5ml of 1N HCl is added in each test tube. They were then left for a period of 30 minutes. Upon completion of time period, solutions were transferred to acuvette separately and then absorbance of the solutions was recorded at the wavelength of 238 nm.

For Base

To study the effect of acid, 5 ml of 50 ppm solution of each brand in five separated test tubes then 5 ml of 1N NaOH is added in each test tube. The samples were then left for a period of 30 minutes. Upon completion of time period, solutions were transferred to a cuvette separately and then absorbance of the solutions was recorded at the wavelength of 238nm.

For UV Light

To study the effect of UV light, take 5 ml of 50 ppm solution of each brand in five separated test tubes then 5 ml water is added in each test tube and place these solutions in UV light of 365nm for 30 min and absorbance of the solutions was recorded at the wavelength of 238 nm.

For Heat

To study the effect of heat, take 5 ml of 50 ppm solution of each brand in six separated test tubes each containing 5 ml of water, than place these solutions in water bath for 30 min and absorbance of the solutions was recorded at the wavelength of 238 nm.

Result and Discussion

This research was performed with the purpose to compare the degree of degradation in five different brands of Amlodipine besylate 5 mg. Table 1 shows the variation in absorbance after the effect of different degredation parameters. The limit of assay by USP specified that the content should not be less than 95% and not more than 105% of labelled amount. Brand 1, 2, 4 and 5 are degraded in acidic and basic pH (table 2, 3) showing that pH alteration has the most degradation impact on these products. Brand 1, 2 and 5 are degraded by UV light exposure (table 4) while Brand 1 and 2 degraded after the heat exposure (table 5).

Table 1: Showing absorbance of drug in different parameters

S No.	Brand name	Absorbance of standard	Absorbance after acidic pH effect	Absorbance after basic pH effect	Absorbance after UV light effect	Absorbance after heat effect
1.	Amlocard	0.660	0.883	0.992	0.825	0.758
2.	Norvasc	0.530	0.890	0.632	0.678	0.734
3.	Lodopin	0.483	0.476	0.575	0.458	0.414
4.	Zoldip	0.611	0.673	0.687	0.694	0.573
5.	Revloc	0.668	0.825	0.74	0.717	0.695

Table 2: Showing effect of acid

S No.	Brands	% Assay
1.	Amlocard	133.7%
2.	Norvasc	167.92%
3.	Lodopin	98.55%
4.	Zoldip	110.147%
5.	Revloc	123.50%

Table 3: Showing effect of base

S No.	Brands	% Assay
1.	Amlocard	150.38%
2.	Norvasc	119.2%
3.	Lodopin	98.62%
4.	Zoldip	112.43%
5.	Revloc	110.7%

Table 4: Showing effect of UV light

S No.	Brands	% Assay
1.	Amlocard	125%
2.	Norvasc	127.92%
3.	Lodopin	94.82%
4.	Zoldip	99.56%
5.	Revloc	107.33%

Table 5: Showing effect of heat

S No.	Brands	% Assay
1.	Amlocard	114.84%
2.	Norvasc	138.49%
3.	Lodopin	85.71%
4.	Zoldip	93.78%
5.	Revloc	104.04%

Conclusion

It was used to study the stress‑degradation studies as per ICH guidelines. Amlodipine was found to be degraded in almost all types of stress conditions and was found to be less stable. The method was used is accurate and precise as well as reproducible and economical and can be successfully used degradation studies of different dosage form. It was concluded that only brand "A" showed accepted results among other brands for all the stresses applied for degradation studies.

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Conflict of Interest

There is no conflict of interest.

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