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EFFECT OF ACID AND BASE ON LOSARTAN BY UV SPECTROSCOPY

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ABSTRACT

Chemically Losartan is {2-*N*-butyl-4-chloro-5-hydroxymethyl-1-[(2′-(1*H*-tetrazol-5-yl)biphenyl-4-yl)methyl]imidazole}. it is a typical angiotensin II (Ang II) type I receptor (AT1R) blocker that has been used for regulation of blood pressure and fluid homeostasis. Forced degradation studies are used to identify reactions which may occur to degrade a processed product. Usually conducted before final formulation, forced degradation uses external stresses to rapidly screen material stabilities. The forced degradation studies on drug substance involves photo Acid/base Stress testing, photo degradation, Temperature and or with humidity, Time, pH variation (low and high).In our recent research we study degradation parameters on losartan 50mg tablets. When Losartan subjected to 0.1 N HCl and 0.1N NaOH, Losartan showed decreased availability i.e. 99.59% in the presence of acid while it showed slight changes in terms of availability i.e. 99.91% in the presence of base. it shows decreased availability i.e. 99.75% in case of UV light of 246nm.

KEYWORDS: Losartan, stress testing, U.V spectrophotometer, humidity.

INTRODUCTION

Chemically Losartan is {2-*N*-butyl-4-chloro-5-hydroxymethyl-1-[(2′-(1*H*-tetrazol-5-yl)biphenyl-4-yl)methyl]imidazole}as shown in Figure 1. it is a typical angiotensin II (AngII) type I receptor (AT1R) blocker that has been used for regulation of blood pressure and fluid homeostasis.[1] Following oral administration, this drug is almost completely absorbed and extensively metabolized mainly by the enzyme cytochrome P450 (CYP) 2C9 and 3A4 to

EXP-3174; a carboxylic acid derivative.[2] EXP-3174 is a major active metabolite in both humans and rats and it is a more potent inhibitor of angiotensin II receptor than losartan, having high-affinity receptor specificity. It has also been reported that Losartan is a substrate of P-glycoprotein (P-gp). Considering that losartan is a substrate of both P-glycoprotein and cytochrome P450 (CYP) enzymes, the modulation of P-glycoprotein and cytochrome P450 (CYP) enzymes activities may cause considerable changes in the Losatran and its active metabolite, EXP-3174 pharmacokinetic profiles.[3] Losartan and other angiotensin-receptor antagonists exhibit fetal toxicity and should be avoided during pregnancy, particularly in the second and third trimester.[4] Literature survey shows a A high-performance liquid chromatography (HPLC) method for quantification of losartan in plasma. The reported assay enables the measurement of losartan for therapeutic drug monitoring.[5]

Spectrophotometry is a simple instrument having less equipment cost and economical maintenance that is why preferred over other methods. This technique can also be use for stress degradation testing. According to International Conference of Harmonization (ICH) guideline forced degradation testing is performed on the active pharmaceutical ingredient and final products. In this technique the active pharmaceutical ingredient and final products is expressed to various conditions which are acidic, basic and light conditions.We have already performed such type of work[6] During intermediary development procedure, forced degradation activities should be performed to make sure that the method is selective to save lot of effort, time, money and to detect the responsible conditions for degradation of drug.Forced degradation is able to demonstrating that the chosen technique is stability indicating that is the technique use to identify the increase in the degradation product and the subsequent loss of active components.[7]

Parameters involve in Forced Degradation

Forced degradation studies are used to identify reactions which may occur to degrade a processed product. Usually conducted before final formulation, forced degradation uses external stresses to rapidly screen material stabilities.

Thermal and/or humidity stress testing

Thermal and/or humidity stress testing is performed by exposing the drug substance to thermal/humidity conditions in due course which causes the substance to degrade forcefully to its main components.

Degradation by UV light

UV degradation is a main problem in numerous UV-unstable products which are made up of natural and synthetic polymers as they break or disintegrate when exposed to continuous sunlight. As the attack is dependent on the degree and degree of exposure, nonstop exposure is a more serious problem than intermittent exposure.

Acid/base stress testing

Acid/base stress testing is used for the evaluation of forced degradation of a drug substance. This test involves degradation of a drug substance by exposure to basic or acidic medium over time to its primary degradation products.[7]

EXPERIMENTAL

Losartan for the purpose of degradation studies. We took active of Losartan.

Material and reagents

Pyrex glass including measuring volumetric flask, cylinder, beakers, pipette, funnel and stirrer were used. All glass wares were first washed with chromic acid then with water and finally rinsed with freshly prepared double distilled water . Reagents were of Analytical grade reagents 0.1N Sodium hydroxide, 0.1N Hydrochloric acid and de-ionized water or double distilled water.

Instruments

Ultraviolet Lamp Power of 8N, Serial NO: N 045571, LF-204.LS '4W-254 and 365 nm', Spectrophotometer with a quartz cuvette T80 UV-VI spectrometer 'PG Instrument', Weighing Balance Item PA214C: 'Pioneer OHAIUS' and Water Bath 'HH-4' having digital and constant temperature tank.

Preparation of 0.1 N Hydrochloric acid and Sodium hydroxide

Take 4 grams of sodium hydroxide and transfer it in 100ml volumetric flask and dissolve it in small quantity of water and finally make up the volume up to mark of the flask with de-ionized water. Take 8.3ml analytical grade hydrochloric acid having 37% purity and 12N normality in a volumetric flask and the make up the final volume upto the mark of flask with DI water.

Preparation of Losartan solution

Weigh the active Losartan 0.020 gm then dissolve it in small quantity of water. Transfer this solution in a 100 ml volumetric flask finally make up the volume with water. Absorbance was determined at wavelength max 246 nm.

Procedure for Degradation Studies

For Acid and Base

To determine the effect of acid and base on Losartan, 5 ml of 200 ppm solution of Losartan was transferred in to two separate test tubes then 5 ml of 0.1 N hydrochloric acid was added in one test tube and 5 ml of 0.1 N sodium hydroxide was added in another test tube respectively . Then the tubes were left for 30 minutes. the absorbance of the solution was determined using spectrophotometer at wavelength max 230nm.

For UV light and heat

To determine the effect of UV light and heat on Losartan, 5 ml of 200 ppm solution of Losartan was transferred in to two test tubes then 5 ml of de-ionized water was added in both test tubes and one test tube was left in UV light for 30 minutes and the absorbance of the solution was determined. Another test tube was kept in water bath at 50°C for 60 minutes. At different intervals of times, determine the absorbance of the solution one by one by using spectrophotometer at wavelength max 202nm.

RESULT AND DISCUSSION

We study degradation parameters on active of Losartan (Table 2 Figure 3).the absorbance for degradation parameters are given in (Table 1, figure 2). When Losartan subjected to 0.1 N HCl and 0.1N NaOH, Losartan showed decreased availability i.e. 99.59% in the presence of acid while it showed slight changes in terms of availability i.e. 99.91% in the presence of base. It shows decreased availability i.e. 99.75% in case of UV light of 246nm. (Table 2&3 figure 3&4).

From our results we can conclude that Losartan when introduced in acidic medium i.e. 0.1N HCl it degrade up to 99.59% but degrades to larger extend when subjected to basic medium i.e. 0.1N NaOH i.e. 99.91%. When Losartan exposed to U.V light (246 nm) degradation was observed i.e. 99.75%.

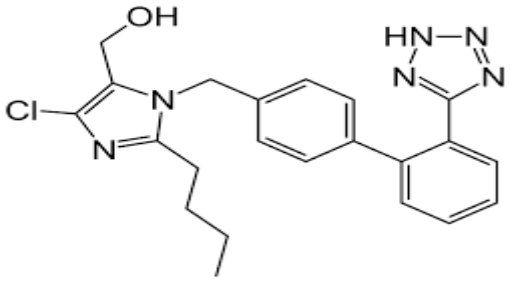

Fig-1 Structure of Losartan

Table 1: Absorbance of Losartan

Degradation Parameters	Losartan			
	1	2	3	Average
Before	2.45	2.45	2.45	2.45
After acid	2.44	2.44	2.44	2.44
After base	2.448	2.448	2.448	2.448
After U.V	2.444	2.444	2.444	2.444

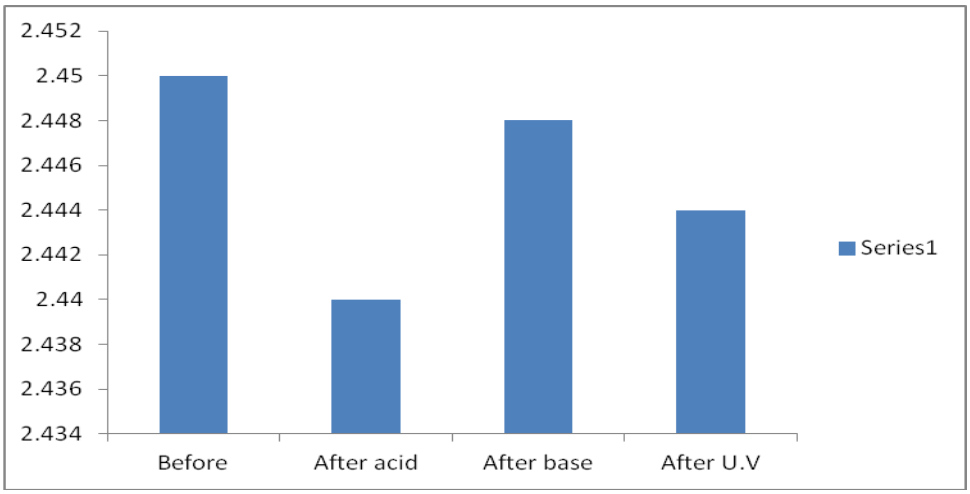

Fig 2: Absorbance of Losartan

Table 2: Degradation Pattern in Percentage of Losartan

Degradation Parameters	Losartan			
	1	2	3	Average
Before	100.00%	100.00%	100.00%	100.00%
After acid	99.59%	99.59%	99.59%	99.59%
After base	99.91%	99.91%	99.91%	99.91%
After U.V	99.75%	99.75%	99.75%	99.75%

Table 3: Effect of Heat

Effect of Heat							
Minutes	0	10	20	30	40	50	60
absorbance	2.49	2.482	2.462	2.475	2.463	2.422	2.439

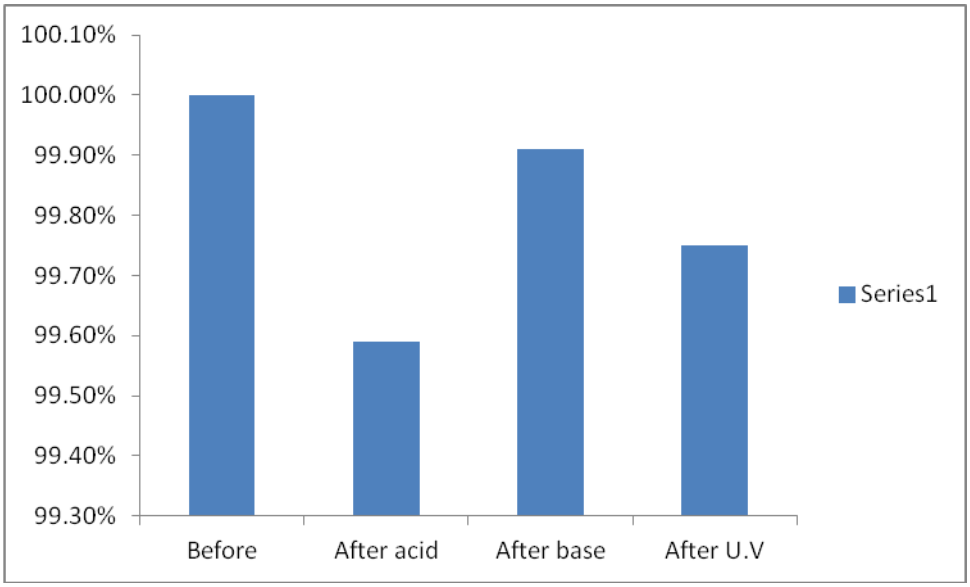

Figure 3: Degradation Pattern of Losartan

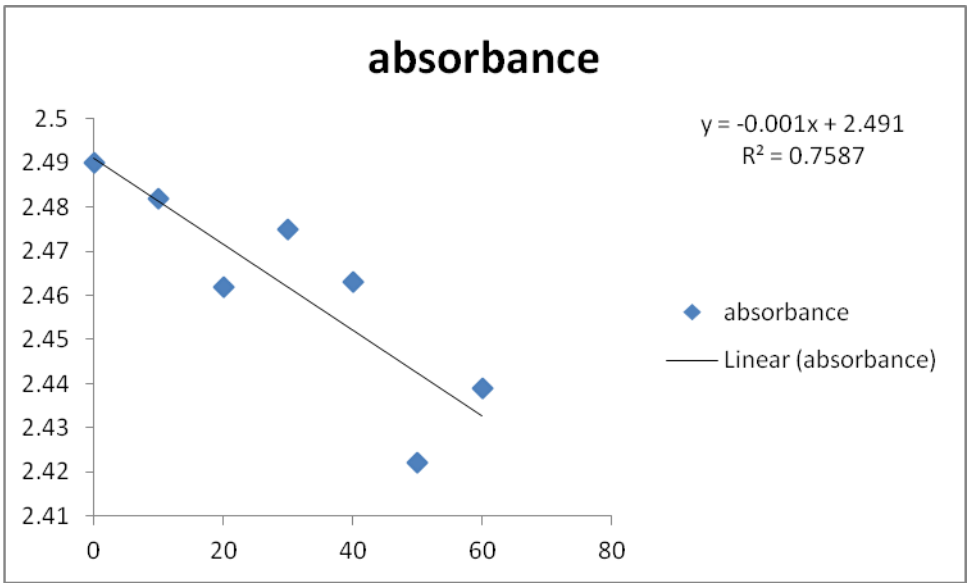

Figure 4: Effect of Heat

CONCLUSION

According to WHO monographic specification, the official assay limit of the content should not less than 95% and not more than 105% of the estimated potency. The conclusion of our result is that Losartan degrades to a very little when exposed to basic medium whereas it also degrades in the presence of acidic medium, heat and U.V light of 246nm.

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