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Research Article

DEVELOPMENT AND VALIDATION OF UV SPECTROPHOTOMETRIC METHOD FOR THE ESTIMATION OF LOSARTAN BULK DRUG AND PHARMACEUTICAL FORMULATION

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ABSTRACT
Method validation is the process by which it is established that performance characteristics of the method meet the requirements for the intended analytical applications. Methods need to be validated or revalidated before their introduction into routine use. The current aim of the research work was to establish a simple, rapid and inexpensive method for the estimation of losartan. The parameters linearity, precision, accuracy, limit of detection and limit of quantitation were studied according to International Conference on Harmonization guidelines. UV spectroscopic determination was carried out at an absorption maximum of 237 nm using distilled water as solvent. In the UV spectroscopic method linearity over the concentration range of losartan was found to be 6-20 µg/ml with a correlation coefficient 0.990. Results of the analyses were validated statistically and by recovery studies. The proposed method is simple, rapid, precise and accurate and can be used for the reliable quantitation of Losartan in pharmaceutical formulation.
KEYWORDS: losartan, method validation, UV spectrophotometric,

INTRODUCTION

In the pharmaceutical, medical device, food, blood establishments, tissue establishments, and clinical trials industries, validation is the documented act of demonstrating that a procedure, process, and activity will consistently lead to the expected results. The validity of a specific method should be demonstrated in laboratory experiments using samples or standards that are similar to unknown samples analyzed routinely. There are many reasons for the need to validate analytical procedures. Among them are regulatory requirements, good science, and quality control requirements. The *Code of Federal Regulations* (CFR) 311.165c explicitly states that " the accuracy, sensitivity, specificity, and reproducibility of test methods employed by the firm shall be established and documented. " Of course, as scientists, we would want to apply good science to demonstrate that the analytical method used had demonstrated accuracy, sensitivity, specificity, and reproducibility. Finally management of the quality control unit would definitely want to ensure that the analytical methods that the department uses to release its products are properly validated for its intended use so the product will be safe for human use. The accuracy of an analytical procedure expresses the closeness of agreement between the value which is accepted either as a conventional true value or an accepted reference value and the value found. This is sometimes termed trueness[1-3] The precision of an analytical procedure expresses the closeness of agreement (degree of scatter) between a series of measurements obtained from multiple sampling of the same homogeneous sample under the prescribed conditions. Precision may be considered at three levels: repeatability, intermediate precision and reproducibility. Precision should be investigated using homogeneous, authentic samples. However, if it is not possible to obtain a homogeneous sample it may be investigated using artificially prepared samples or a sample solution. The precision of an analytical procedure is usually expressed as the variance, standard deviation or coefficient of variation of a series of measurements. Losartan potassium is chemically known as 2-butyl-4- chloro-1[[2 -(1H-tetrazol-5-yl)[1,1 -biphenyl]-4-yl]methyl]- 1H-imidazole-5-methanol, which belongs to the antihypertensive group of drugs known as angiotensin II receptor antagonists. It is a highly selective and orally active non-peptide antagonist used in the treatment of hypertension with heart failure or renal impairment by blocking the binding of angiotensin II to the AT1 receptor level found in vascular smooth muscles, adrenal glands, etc. It is metabolized in the body to a pharmacologically active carboxylic acid metabolite. Losartan competitively inhibits the binding of angiotensin II to AT1 in many tissues including vascular smooth muscle and the adrenal glands. Losartan is metabolized to its active metabolite, E-3174, which is 10 to 40 times more potent than losartan and acts as a non-competitive AT1 antagonist. Inhibition of angiotensin II binding to AT1 inhibits its AT1-mediated vasoconstrictive and aldosterone-secreting effects and results in decreased vascular resistance and blood pressure[3-6]

MATERIALS AND METHODS

UV double beam Spectrophotometer (UV 1700, SHIMADZU Limited, Japan) with 1 cm matched quartz cuvetes and digital balance. All reagents used were of analytical grade. Double distilled water was used throughout the work.

Methods

Standard solution of losartan

Standard losartan (100mg) was accurately weighed and transferred to 100 ml volumetric flask. It was dissolved properly and diluted up to the mark with distilled water to obtain concentration of 1 mg⁄ml. This solution was used as working standard solution. From this solution, by suitable dilution, 20 µg/ml concentration was obtained as standard solution for preparation of serial dilutions of 2 -20 µg/ml.

Measurement of absorbance and calibration curve

The absorbance of the solutions containing Losartan was determined in the uv range 100 to 400 nm using appropriate blank (distilled water) .The λmax was found to be 237nm .At

these wavelength maxima ,calibration curve was drawn by plotting graph between absorbance and concentration.

Validation of UV spectrophotometric method[5-9]

Linearity The aliquots of concentration ranging 2-20 µg/ml were prepared in triplicate, and the range of linearity was established.

Precision

It may be defined as concordance of a series of measurement of the same quality .Accuracy expresses the correctness of measurement, while precision the reproducibility of a measurement. Accuracy without precision is impossible , but precision doesn't imply accuracy. The precision of the assay was determined by repeatability (intraday) and intermediate precision (interday) and reported as % RSD. For this 4 ,6 8 µg/m lconcentration solution was measured three times a day and same was measured in next three days. The % RSD was calculated (table).

Accuracy

Accuracy is defined as the degree of agreement between a measured value and the most probable or true value. Accuracy was determined by performing recovery studies by spiking different concentrations of pure drug in the pre-analyzed powder for infusion samples within the analytical concentration range of the proposed method at three different set at level of 80%, 100% and 120%. The amount of losartan was calculated at each level and % recoveries were computed.

Limit of Detection (LOD) and Limit of Quantitation (LOQ)

The LOD and LOQ were estimated from the set of 3 calibration curves used to determine method linearity.

$$LOD = 3.3*\sigma/S \text{ and } LOQ = 10*\sigma/S$$

Where, σ = the standard deviation of y-intercepts of regression lines, S = the slope of the calibration curve.

Determination procedure for losartan potassium in commercial tablets

For sample preparation of different tablets, the mixed contents of 5.0 tablets were weighed and ground. The powder equivalent of 50 mg losartan potassium was stirred well with doubly distilled water. The solution was filtered through Whatman No. 42 filter paper (Whatman International Limited, Kent, UK) in a 100.0 mL standard volumetric flask and the residue was washed well with doubly distilled water for complete recovery of the drug. The content of each standard volumetric flask was then diluted to 100.0 mL with doubly distilled water. The recovery of the losartan potassium was calculated from the corresponding linear regression equations or calibration graphs.

RESULTS AND DISCUSSION

The two simple methods inclusive of simple UV-Spectroscopy and second derivative spectrophotometric methods were developed for the estimation of losartan potassium in pharmaceutical dosage forms. The max of losartan potassium was found to be 234nm. Linearity was found to be 6-20µg/ml. Correlation coefficient (0.990) indicate good linearity between concentration and slope area. The amplitude of the respective derivative spectrum is converted in terms of absorbance. Beer's law was obeyed by the fundamental spectrum. Both the methods were found to be simple, accurate, and economical for the routine analysis of losartan potassium and its dosage forms. Recovery studies were found to be close to 99% that indicated the accuracy and precision of the above two proposed methods. values of LOD and LOQ were found to be 0.908 and 2.75 respectively. The accuracy was calculated to be 98.2%.

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TABLE 1 calibration curve parameters

Concentration	Absorbance± SD	RSD%
2	0.120± 0.008	6.66
4	0.160± 0.004	2.50
6	0.170±0.004	2.35
8	0.230±0.004	1.73
10	0.290±0.003	1.03
12	0.350±0.003	0.85
14	0.420±0.003	0.71
16	0.470±0.005	1.06
18	0.530±0.007	1.32
20	0.620±0.004	0.64

TABLE 2 validation parameters

S.No	PARAMETER	RESULT
1	Absorption Maximum(nm)	237
2	Linearty Range(µg/ml)	2-20
3	Std.Regression Equation	Y=0.0291x +0.0182
4	Corelation Coefficient(R2)	0.9902
5	Accuracy	98.2±0.123
6	LOD(µg/ml)	0.908
7	LOQ(µg/ml)	2.75

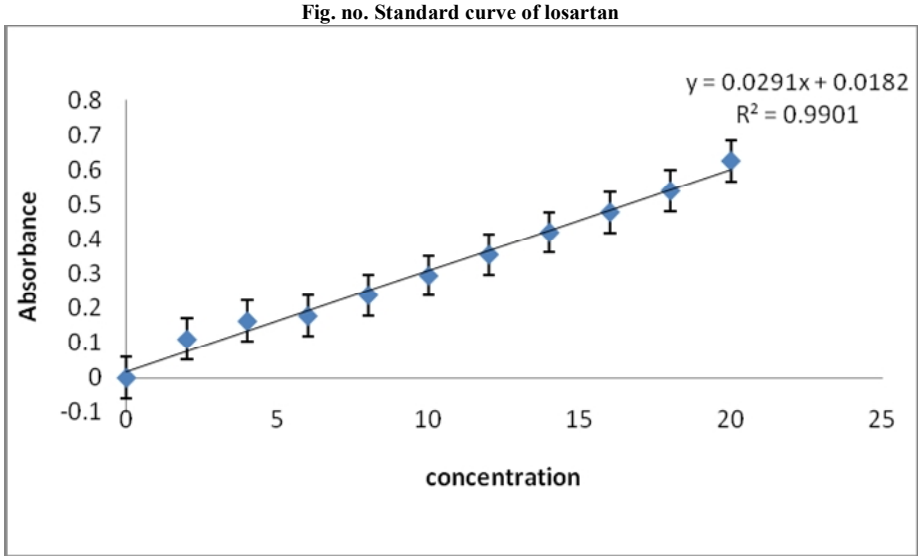
TABLE 3 INTER DAY(PRECISION)

s.no.	CONCENTRATION (µg/ml)	ABSORBANCE±SD	%RSD
1.	4	0.162±0.003	1.85
2.	6	0.177±0.003	1.69
3.	8	0.237±0.003	1.26

TABLE 4 INTRA DAY(PRECISION)

S.no.	Conc.	Absorbance ± s.d.	%RSD
1.	4	0.160±0.004	2.50
2.	6	0.170±0.004	3.35
3.	8	0.230±0.004	1.75

Fig. no. Standard curve of losartan



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