WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 6.805
Volume 6, Issue 1, 829-834. Research Article ISSN 2277– 7105

DEVELOPMENT AND VALIDATION OF VISIBLE METHOD FOR ESTIMATION OF CILAZAPRIL IN BULK FORMULATION

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Article Received on
04 Nov. 2016,

Revised on 25 Nov. 2016,
Accepted on 16 Dec. 2016

DOI: 10.20959/wjpr20171-7595

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ABSTRACT

A simple, sensitive, accurate, precise and economical visible Spectrophotometric method was developed and validated for the estimation of Cilazapril in Bulk form. The method is based on the reaction of Cilazapril with vanillin in the presence of conc.Sulphuric acid producing orange red colour chromogen which shows maximum absorbance at 580nm against reagent blank. The Chromogen obeyed Beer's law in the concentration range of 10-50 µg/ml for Cilazapril. The results of the analysis have been validated statistically and recovery studies.

KEYWORDS: Cilazapril, vanillin (4%), conc.Sulphuric acid, Visible Spectrophotometric.

INTRODUCTION

Cilazapril is chemically (4*S*,7*S*)-7-[[(2*S*)-1-Ethoxy-1-oxo-4-phenylbutan-2-yl]amino]-6-oxo-1,2,3,4,7,8,9,10-octahydropyridazino[1,2-a]diazepine-4-carboxylic acid.[1] Cilazapril is an angiotensin-converting enzyme inhibitor (ACE inhibitor) used for the treatment of hypertension and congestive heart failure.[1] Literature survey reveals Septrophotometric[2-3] methods for estimation of Cilazapril in biological fluids and in pharmaceutical formulations. The present communication describes simple, sensitive, accurate, precise and economical visible spectrophotometric method using vanillin (4%), conc.Sulphuric acid, for the estimation of Cilazapril in bulk formulation.

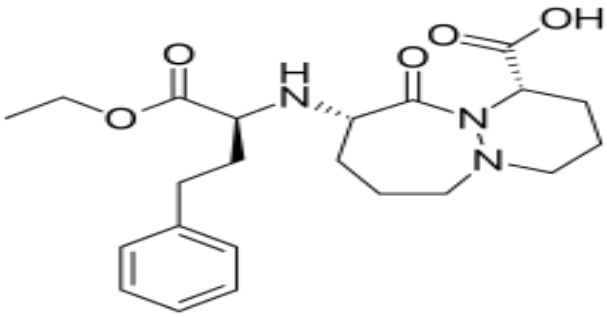

Figure 1: Cilazapril structure

Mechanism of action: Cilazapril is an angiotensin-converting enzyme inhibitor used for the treatment of hypertension and congestive heart failure. Cilazapril suppress the rennin-angiotensin-aldosterrone system and there by reduces both supine and standing systolic and diastolic blood pressure.[1]

MATERIALS AND METHODS

Apparatus: A Shimadzu model T60 double beam UV/Vis Spectrophotometer with spectral width of 2nm wave length accuracy of 0.5 nm and a pair of 10mm matched quartz cells was used to measure absorbance of the resulting solutions. Shimadzu analytical balance, an ultra sonic cleaner were used in the study.

Reagents and Materials: Cilazapril drug was procured as a gift sample from Hetero drugs Ltd. Erragudda, Hyderabad, Telangana. Vanillin and conc.Sulphuric acid [A.R.Grade, SD Fine Chemicals Ltd., Mumbai] were used in the study.

Preparation of Reagent and Working standard stock solution

4% Vanillin solution: - The solution was prepared by dissolving 4gms of vanillin in 100 ml of methanol.

Working Standard Stock Solution: Accurate weigh the 100mg of pure drug and transferred in 100 ml of volumetric flask later diluted with distilled water upto100ml gives 1000µg/ml.

Methodology: Different aliquots of working standard solution containing 10-50 µg/ml concentration of Cilizapril was transferred into series of volumetric flask. To it 1ml of 4% vanillin solution and 1ml of conc.Suphuric acid was added and volume was made up to 10 ml with distilled water. The contents of the each flask was mixed well and allowed to stand at room temperature for 10 minutes. The absorbance of coloured species was measured at 580

nm against reagent blank. The amount of drug present in the sample solution was computed from the calibration curve.[2, 3]

Reaction Mechanism: The results obtained in this method were based on the condensation of Cilizapril with vanillin in the presence conc.Sulphuric acid producing orange red coloured species which is measured at 580 nm shown in the Figure 2.

Method Validation

Linearity: Five points calibration curve were obtained in a concentration range from 10-50 µg/ml for Cilazapril. The response of the drug was found to be linear in the investigation concentration range and the linear regression equation was y = 0.009X+0.010 with correlation coefficient 0.997 results are tabulated in table No.1 & Figure 3.

Precision: Precision of the analytical method is ascertained by carrying out the analysis as per the procedure and as per normal weight taken for analysis. Repeat the analysis six times. Calculate the % assay, mean assay, % Deviation and % relative standard deviation and %RSD. The developed method was found to be precise as the %RSD values for the repeatability and intermediate precision studies were 2% and 1.095%, respectively shown results are tabulated in table No.2.

Accuracy: Accuracy of the method is ascertained by standard addition method at 3 levels. Standard quantity equivalent to 60%, 100% and 150% is to be added in sample. The result shown that best recoveries (98.5-99.12%) of the spiked drug were obtained at each added concentration, indicating that the method was accurate and results are tabulated in table No.3.

Robustness: Measure of the capacity of an analytical method to remain unaffected by small intentional variations in the operational parameters and provide an assurance of its reliability during the normal usage. It may be determined by various parameters like ph, flow rate, temperature etc. Robustness studies are performed during the method development stage. Results are tabulated in table No.4.

Sensitivity

Limit of Detection and Quantitation (LOD and LOQ):- From the linearity data calculate the limit of detection and quantitation using the following formula.

LOD = $3.3\sigma / S$

σ = Standard deviation of response.

S = Slope of the calibration curve of the analyte.

LOQ = 10σ / S

σ = Standard deviation of response.

S = Slope of the calibration curve of the analyte.

The results are tabulated in Table No.5.

RESULTS AND DISCUSSION

The analytical method was developed by studying different parameters. The method was validated for all validation parameters as per ICH guidelines. The lambda max of Cilazapril was found to be 580 nm. Linearity was found with the concentration range 10-50 µg/ml and correlation coefficients found to be 0.997 indicate good linearity between concentration and slope area. Beer's law was obeyed by the fundamental spectrum. This method was found to be simple, sensitive, accurate, precise and economical for routine analysis for the estimation of Cilazapril in Bulk form.

Recovery studies were found to be close 99% indicated the accuracy and precision of the above two proposed methods. Values of LOD and LOQ were found to be 3.66 and 11.1 respectively. The accuracy and robustness was calculated to be 99.12 and 96.2%.

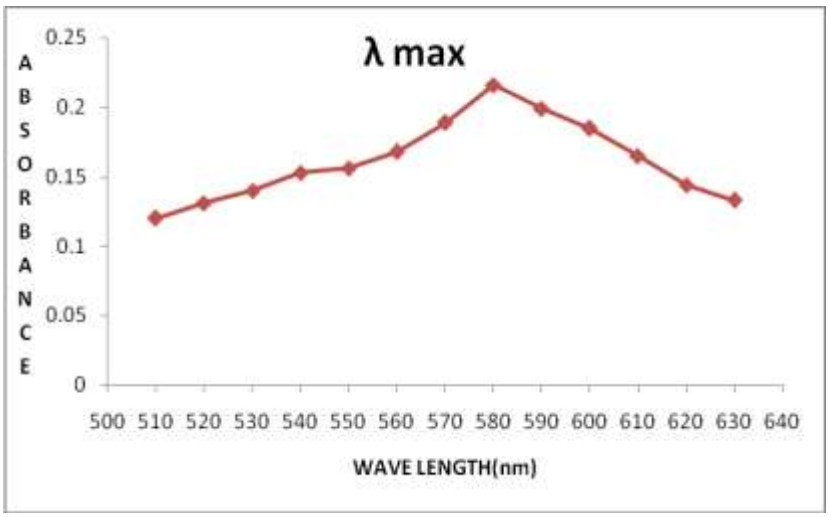

Figure 2: Reaction mechanism (λ max)

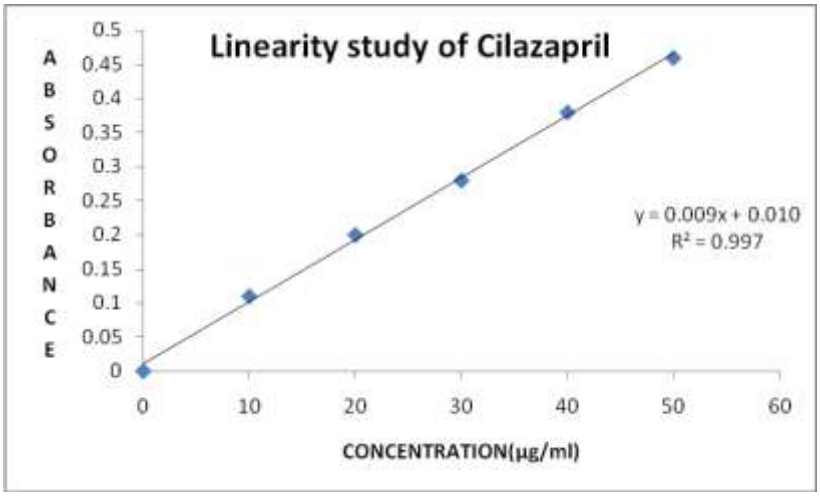

Figure 3: Linearity graph

Table No.1 – Result for Linearity

Concentration (µg/ml)	Absorbance
10	0.11
20	0.2
30	0.28
40	0.38
50	0.46
Correlation	0.997
Intercept	0.010
Slope	0.009

Table No.2 – Result for Precision

Sample No.	% Assay	
	Intra day	Inter day
10	101	100
20	105.5	102
30	100	99
40	102.7	100
50	100	99
Mean	101.8	100
SD	2.07	1.095
% RSD	2.04	1.095

Table No.3 – Result for Accuracy

% Recovery Level	% Recovery	Mean	SD	%RSD
60%	98.62	98.62	0.0081	0.0082
	98.63			
	98.61			
100%	98.56	98.55	0.0124	0.0126
	98.57			
	98.54			

150%	99.13	99.12	0.0081	0.0082
	99.11			
	99.12			

Table No.4 – Result for Robustness

Parameter	Amount of Cilazapril (µg/ml)		%Recovery	SD	%RSD
	Taken	Found			
2 ml of 4% vanillin and 2 ml of conc.Sulphuric acid	30	28.8	96.2	0.92	0.97
	40	37.7	94.4		

Table No.5 Result for Lod and Loq

LOD ((µg/ml)	3.66
LOQ ((µg/ml)	11.1

CONCLUSION

The proposed visible spectrophotometric method was found to be simple, sensitive, accurate, precise and economic for determination of Cilazapril in bulk formulation. Hence it can be conveniently adopted for routine quality analysis of drug in pharmaceutical dosage form.

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