ANALYTICAL METHOD DEVELOPMENT AND VALIDATION OF LOSARTAN POTASSIUM TABLET BY RP-HPLC

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ABSTRACT

Analytical methods development of validation plays important roles in the discovery, development and manufacture of Pharmaceutical. The official test methods that result from those processes are used by quality control laboratories to ensure the identify, purity, potency performance of drug product. Method validation is defined as the process of method proving through scientific studies that an analytical methods is acceptable for it intended in recent years, a great deal of efforts has been devoted to the homonization of Pharmaceutical use. The objective of this validation of an analytical procedure is to demonstrate that the drug Losartan Potassium is suitable for its intended purpose. The analytical method development recommends the quality, purity and specificity of the drug Losartan Potassium tablet form during the manufacturing process and hence the standard of the drug may not vary, which produce the desirable therapeutic effect.

Keywords: *Losartan Potassium, Glacial Acetic acid, Acetonitrile, Phosphoric Acid*

INTRODUCTION

Validation is a concept that has been evolving continuously since in first formal appearance in the United States in 1978. Validation is a rapidly growing and evolving subject. Validation in a requirement that has always made sense from both a regulatory and quality perspective.[1,7] It extended to those process steps determined to be critical to the quality purity of the final products. Analytical methods rely on scrupulous attention to cleanliness, sample preparation accuracy and precision. A standard method for analysis of concentration involves the creation of calibration curve. In the concentration of elements of compound in a sample is too high for the detection range of a technique, it can simply be diluted in a pure solvent. If the amount in sample is below an instruments range of measurement, the method of addition can be used. In this method a known quantity of the elements or compound under study is added, and the concentration observed in the amount actually in the sample. Analytical chemistry research is largely driven by performance of sensitivity, selectivity, robustness, linear range, accuracy, precision, speed, cost of purchase, operation, training, time and space. Validation is founded on but not specifically prescribed by regulatory requirements and is best viewed as an important and integral part of cGMP. Validation is therefore one element of quality assurance programmed associated with particular process. As the process differs so widely there is no universal approach to validation regulatory bodies such as FDA and EC for medicinal products have developed general non-mandatory guidelines.[2,8] The most compelling reason for validation should is to guarantee as for as possible that all processes and machinery in the Pharmaceutical manufacturing process are being used in a way which will ensure safety, integrity, quality and strength of the product for use by the general public.[3,9]

EXPERIMENTAL

The analytical method development and the validation procedure for the drug Losartan potassium tablet dosage form-Reverse Phase HPLC. Method development trials were given in the Table-1.

Table – 1: Method Development Trials

Trial No.	Buffer	pH	Mobile phase / solvent	Column used	flow rate	R_t
1.	Ammonium Acetate	4.9	Glacial Acetic acid and Acetonitrile (50:50)	C_{18}	1.0 ml / min	Not found
2.	Ammonium Acetate	4.9	Glacial Acetic acid and Acetonitrile (50:50)	C_{18}	2.0 ml / min	Not found
3.	Ammonium Dihydrogen phosphate	3.0	Phosphoric Acid, and Acetonitrile (80 : 20)	C_{18}	1.0 ml/ min	Not found
4.	Ammonium Dihydrogen phosphate	3.0	Phosphoric Acid, and Acetonitrile (75 :25)	C_{18}	1.0 ml/ min	Not found
5.	Ammonium Dihydrogen phosphate	3.0	Phosphoric Acid, and Acetonitrile (70:30)	C_{18}	1.0 ml/ min	52 min with peak split
6.	Ammonium Dihydrogen phosphate	3.0	Phosphoric Acid, and Acetonitrile (70:30)	C_{18}	1.5 ml/ min	32 min
7.	Ammonium Dihydrogen phosphate	3.0	Phosphoric Acid, and Acetonitrile (65 : 35)	C_{18}	1.5 ml/ min	7.5 min

Peak of Losartan potassium was well resolved with solvent system of buffer and acetonitrile (65 : 35)

Chromatographic parameters:

Instrument	:	Water alliance 2695 separation module
Column	:	Spherisorh C_{18}, 250 X 4.6 mm, 5μ
Flow rate	:	1.5 ml/m
Wavelength	:	254 nm
Injection volume	:	20 μ L.
Column temperature	:	Ambient
Run time	:	20 mints.

Analytical method validation of Losartan Potassium

Preparation of mobile phase

a. Preparation of ammonium dihydrogen phosphate buffer pH 3.0

Weigh about 8.62 g ammonium dihydrogen phosphate to a 1000 ml volumetric flask, dissolve and dilute to volume with water and mix. Adjust to pH 3.0 ± 0.1 with phosphoric acid.

b. Preparation of mobile phase

Prepare a mixture of buffer and acetonitrile (65:35). Filter through 0.45 μ membrane filter and degas.

Determination of retention time

a. Preparation of standard solution

Weight accurately about 50 mg of Losartan Potassium WS in 50 ml volumetric flask. Add about 40 ml mobile phase, sonicate to dissolve and dilute to volume with mobile phase and mix. Further dilute 10.0 ml of this solution to 50 ml with mobile phase and mix.

b. Preparation of test solution

Weight accurately about 306.4 mg Losartan Potassium and transfer it in to a 100 ml volumetric flask. Add about 80 ml water, sonicate to dissolve and dilute to volume with water and mix. Filter through Whatman filter paper no. 1. Discard first few ml of the filtrate. Further dilute 10.0 ml of the filtrate to 50 ml with Mobile phase and mix.

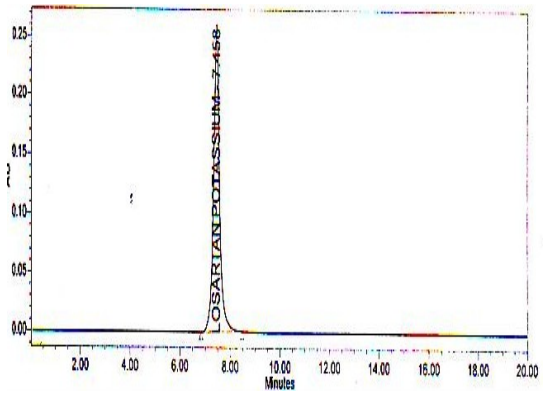
RESULTS AND DISCUSSION

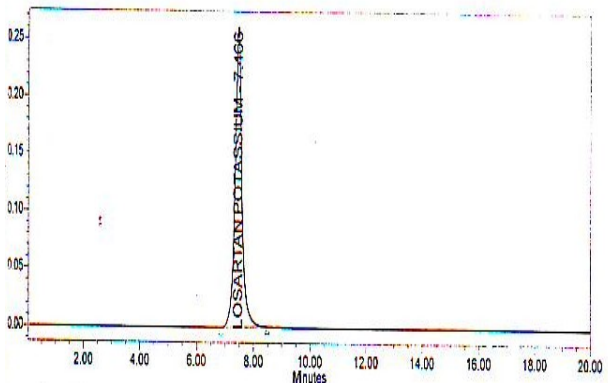
The analytical method development and validation for the drug Losartan Potassium was done, which shows the best elution of the peak. The specificity test studies shows that the analyte chromatographic peak is not attributable to more than one components. The linearity calibration curve shows linear response over the range of concentration used. The precision data shows that the reproducibility of the assay procedure was satisfactory. The accuracy of the method was determined by recovery studies. The recovery studies were carried out of the percentage recovery was calculated. The Robustness studies show that there were no marked changes in the chromatogram. The Ruggedness of the method was determined for the same sample under different laboratory, different analysis and using operational and environmental conditions, the degree of reproducibility will shows results within their limits. Further there was no interference due to excipients. The system suitability studies were also carried out to determine column efficiency resolution and peak asymmetry.

Table – 2:Summary of Results

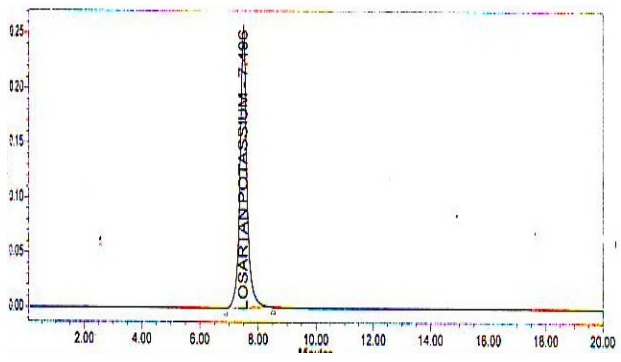
Parameters	Acceptance criteria	% RSD	Results
Accuracy	% recovery should be between 98.0 to 102.0	-	% recovery should be between 99.0 to 100.0
Precision	RSD should not be more than 2%	0.4	The result are found to be will within the acceptance limit.
Linearity	Correlation co-efficient should be not less than 0.99	-	Correlation co-efficient is found to be 0.999975.
	% curve fitting should not less than 99.99		% curve fitting is found to be 99.99
Specificity	The number of theoretical plates determined for Losartan Potassium is atleast 5500.	0.2	The number of theoretical plates determined for Losartan Potassium is 5845
	The tailing factor for Losartan Potassium should be less than 2.0	-	The tailing factor for Losartan Potassium is found to be 1 %

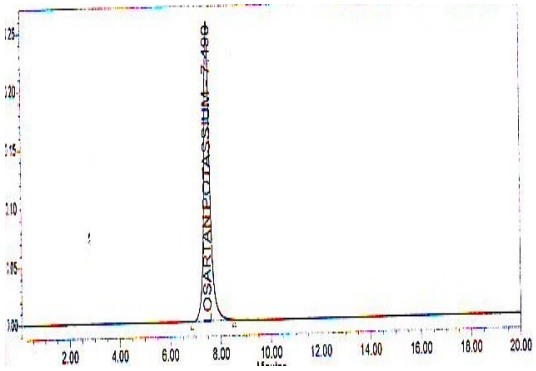
	The R_t determined for Losartan Potassium is atleast 7.0	-	The R_t determined for Losartan Potassium is 7.496
Ruggedness	% RSD of assay result obtained should be NMT 2.0	-	The result are found to be will within the acceptance limit.
Robustness	The number of theoretical plates determined for Losartan Potassium should be between 5500 to 6500.	-	The number of theoretical plates determined for Losartan Potassium should be between 5580 to 5760.
	The tailing factor for Losartan Potassium should be less than 2.0	-	The tailing factor for Losartan Potassium is 1.0.





The peaks of Losartan Potassium are found well separated at 7.493 respectively. In analytical method development and validation of Losartan Potassium by reverse phase HPLC proposed method is found to be satisfactory and could be used for the routine pharmaceutical analysis of Losartan Potassium tablet.





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The failure to read good books both enfeebles the vision and strengthens our most fatal tendency - the belief that the here and now is all there is.
-Allan Bloom