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A SENSITIVE ANALYTICAL METHOD AND VALIDATION OF VALSARTAN BY UV SPECTROSCOPY IN SOLID DOSAGE FORMS

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ABSTRACT

Simple precise accurate UV Spectroscopic method has been developed and validated for estimation of valsartan in bulk and tablet dosage form. UV Spectroscopic method which is based on measurement of absorption of UV light, the spectra of valsartan in methanol and water (1:1) showed maximum wave length at 250nm and calibration graphs were plotted over the concentrations ranging from 2-10µg/ml of valsartan with correlation coefficient 0.9999 validation was performed as per ICH guidelines for linearity, accuracy, precision and percentage recovery. The limit of detection (LOD) and limit of quantification (LOQ) were found to be 1.95 and 5.91 respectively by simple UV Spectroscopy .The proposed method was validated.

Key Words:- valsartan, methanol, distilled water, UV spectroscopic method, validation.

INTRODUCTION

Valsartan is an angiotensin II receptor antagonist with particularly high affinity for the type I (AT_1) angiotensin receptor. By blocking the action of angiotensin, valsartan dilates blood vessels and reduces blood pressure (Anonymous 1). Valsartan is chemically(*S*)-3-methyl-2-(*N*-{[2'-(2*H*-1,2,3,4-tetrazol-5-yl) biphenyl-4-yl] methyl}pentan amido) butanoic acid. It is a white crystalline powder with formula $C_{24}H_{29}N_5O_3$ and molecular mass 435.52g/mol (Anonymous 1). Bioavailability was found to be 25%, up to 95% it binds to the protein molecule, it shelf life is about 6hrs. It is used as a potent angiotensin receptor blocker used as an antihypertensive i.e., used at high BP Conditions and also can be used in treatment of congestive heart failure Post myocardial infarction (Anonymous 2). High performance liquid chromatographic (HPLC) determination of valsartan in biological fluids was studied (Gonzales *et al*., 2000) and also a chiral HPLC method was developed (Francotte *et al*., 1996). Valsartan and hydrochlorothiazide were determined in tablets simultaneously by HPLC (Carlucci G *et al*., 2000; Sibel A *et al*., 2001), Capillary Electrophoresis and a very few Spectrofluorimetric method was developed for determination of valsartan in human urine (Gagigal *et al*., 2001).Valsartan is used to control high blood pressure, treats congestive heart failure, and improve survival rates for people who have had a heart attack. Also, by lowering blood pressure, valsartan can lower the risks that accompany long-term high blood pressure (Anonymous 3).

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MATERIALS AND METHODS

The spectrophotometric measurements were carried out using a UV 3000+ UV/VIS Spectrophotometer (LABINDIA, Mumbai, India) with 1 cm matched quartz cell.

Reagents

Reference sample of Valsartan was obtained as gift sample from Alembic pharmaceuticals, ltd Vadodara. Methanol AR grade and distilled water was used as

solvent throughout the experimentation. Satrval 80mg was purchased from local pharmacy (Nataraj *et al*., 2005).

Selection of media

Main criteria for selection of media solubility and stability i.e., drug should be soluble as well as stable for sufficient time in selected media. Valsartan was freely soluble in distilled water and was soluble in dichloromethane, chloroform, and ethanol-water mixture. It was slightly soluble in methanol, methanol-water and was considerably stable (Gupta *et al*., 2010).

Preparation and determination of Standard solutions

Standard solutions of valsartan are prepared accurately by dissolving 100mg of drug in 100 ml of solvent. Solvent is prepared by using Methanol and distilled water in (1:1) ratio. The standard solution of valsartan having concentration of 10µg/ml was scanned in the UV range (400-200 nm) in 1.0 cm cell against solvent blank and spectra's were recorded, and the dilutions were prepared in the concentration range of 2-10µg/ml from the standard stock solution prepared, using solvent (1:1 ratio Methanol and Distilled water). The absorbance was measured at 250nm against blank. Calibration graph was constructed by plotting absorbance against concentration of valsartan.

Preparation and determination of sample solution

Valsartan tablets were weighed accurately and finely powdered. The quantity equivalent to 100mg was taken and extracted by shaking with Methanol and Distilled water (1:1 ratio) followed by another two extractions each with 10ml of solvent. The extracted solution was filtered using 0.45µm pore filter and the solution was diluted with distilled water to obtain concentration of 100µg/ml, and The dilutions were prepared in the concentration range of 2-10µg/ml from the standard stock solution prepared, using solvent (1:1 ratio Methanol and Distilled water). The absorbance was measured at 250nm against blank. Calibration graph was constructed by plotting absorbance against concentration of valsartan.

Method of Validation

Linearity

Linearity was obtained between2-10µg/ml concentration. Graph was plotted for concentration and absorbance. The equation of calibration curve obtained was Y=0.0238x+0.0074. The correlation coefficient (R^2) was 0.9999 shown in fig.2

Accuracy

The accuracy of the proposed method was established by performing intraday method by determining the content of valsartan in bulk and pharmaceutical formulation. The samples of three different concentrations were taken and absorbance was measured at three different were calculated.

Precision

Precision was calculated for intraday and inter-day of pure drug, the data shows that the method is sufficiently precise shown in table 4 .

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

The LOD and LOQ of valsartan were determined by using standard deviation of response and slope approach as defined by ICH guidelines. The LOD and LOQ were found to be 1.95 and 5.91 respectively shown in table 5.

Stability

The standard stock solution of Valsartan 10 µg/ml in Methanol: Water (1:1) was subjected to heat at 40^0C, 50^0C for 10 minutes then diluted up to the mark and absorbance was measured. The absorbance of initial and after heating is obtained the same. Hence concluded the drug is stable in Methanol and water.

Fig 1. Structure of Valsartan

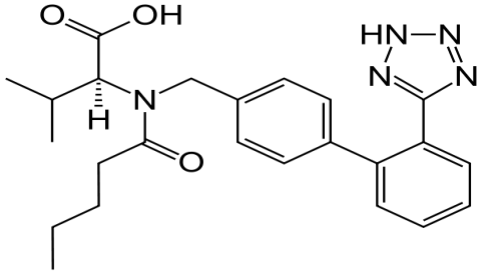

Fig 2. Scanned Spectrum Curve of Valsartan

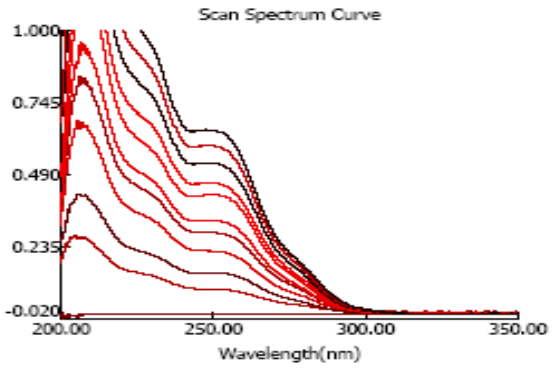

Fig 3. Calibration Curve of Valsartan

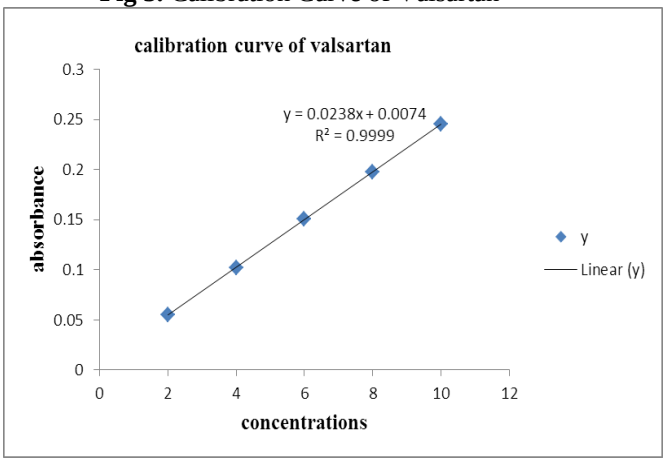

Table 1. Calibration data for Analysis of Valsartan in Methanol and Water at λ250

S.No	Concentration (µg/ml)	Absorbance
1	2µg/ml	0.05
2	4µg/ml	0.102
3	6µg/ml	0.151
4	8µg/ml	0.198
5	10µg/ml	0.245

Method Validation

Table 2. Validation parameters

S.No	Parameters	Result
1	Absorption maxima λmax(nm)	250nm
2	Linearity range(µg/ml)	2-10(µg/ml)
3	Standard regression equation	Y=0.0238x+0.0074
4	Correlation coefficient(r^2)	0.9999

Table 3. Determination of Accuracy by percentage recovery method

Drug	Tablet amount (µg/ml)	Level of addition(%)	Amount added(mg)	Drug found(µg/ml)	% recovery
Valsartan	10	10	100%	20.24 µg	101.1%
	10	15	150%	24.66 µg	99.02%

Table 4. Results of Intraday and Interday precision of Valsartan (in Methanol and Water)

S.No	Concentration (µg/ml)	% RSD		%Amount Recovered	
		Intraday*	Interday*	Intraday	Interday
1	6	1.3	1.2	100	103.2
2	8	1.0	1.0	100	100
3	10	0.8	0.7	99.8	100.4

***Each value is mean of three observations

Table 5. Lowest Limit of detection and lowest limit of quantification

LOD (µg/ml)	LOQ (µg/ml)
1.95	5.91

RESULTS AND DISCUSSION

Attempt has been made to develop rapid sensitive, economic, precise and accurate analytical method for valsartan in pure and pharmaceutical dosage form. The UV spectrum of standard solutions of valsartan was studied in methanol and water. Maximum absorbance was found to be at 250nm. LOD and LOQ were found to be 1.95 and 5.91 respectively. Beer's law was obeyed in concentrations ranging from 2-10µg/ml. The correlation co-efficient values were above 0.9999 which shows that absorbance was linear with concentration. The optical characteristics such as Beer's law limits correlation co-efficient, slope, intercept and molar absorptivity were calculated and validated. To study interference of various excipients recovery was done for formulation. It showed that there is no interference of excipients on the pure drug. The percentage label claim present in tablet formulation was confirmed by repeated analysis of formulation. % RSD values were found to be less than 2. From all the validation parameters, the developed method was found to be simple, economical, precise and accurate. Hence proposed method could be effectively applied for analysis of valsartan in bulk and formulated tablet dosage form.

CONCLUSION

A spectrophotometric method for quantifying Valsartan in pure and tablet has been developed and validated .The method is selective, precise, accurate and linear over the concentration range studied. The method is simple and suitable for the determination of Valsartan in formulation, without interference from excipients or from common degradation products, suggesting its application in IPQC and pharmacokinetic studies.

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