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A COMPARATIVE STUDY ON THE QUALITY OF DIFFERENT VALSARTAN TABLETS AVAILABLE IN THE SHIVAMOGGA DISTRICT

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Abstract:

Objective: Valsartan (VAL) is a potent, orally active nonpeptide tetrazole derivative and selectively inhibits angiotensin II receptor type 1 which causes reduction in blood pressure and is used in treatment of hypertension. This study aims to determine the purity of valsartan in ethical and generic formulation by UV spectrophotometric methods.

Methods: Three UV spectrophotometric methods have been performed such as zero order, second order and AUC and apply the same for their determination in generic and ethical pharmaceutical formulations.

Results: All the methods showed nearly 100 % purity for VALZAAR - 40 mg (ethical formulation) and near 98.57 % purity for Valsartan Tablets IP 40 mg (generic formulation).

Conclusion: All tablets complied with the pharmacopoeia standards. This study demonstrated that price variations do not always correlate with differences in quality.

Index Terms – Valsartan, zero order derivative, second order derivative, AUC method.

I. INTRODUTION:

Hypertension is considered as a '**silent killer'**. Hypertension, also known as high or raised blood pressure, is a condition in which the blood vessels have persistently raised pressure. Blood is carried from the heart to all parts of the body through blood vessels. Each time the heart beats, it pumps the blood into blood vessels. Blood pressure is created by the force of blood pushing against the walls of blood vessels (arteries) as it is pumped by the heart. Higher the pressure, harder the heart has to pump the blood. There is an abnormal increase in systolic and/or diastolic pressure i.e., systolic blood pressure ≥140 mmHg, diastolic blood pressure

≥90 mmHg. The number of adults aged 30–79 years with hypertension has increased from 650 million to 1.28 billion in the last thirty years. It is a major cause of premature death worldwide, with upwards of 1 in 4 men and 1 in 5 women – over a billion people – having the condition.

Valsartan is chemically (2S)-3-methyl-2-[pentanoyl-[[4-[2-(2H-tetrazol-5-yl)phenyl] phenyl] methyl] amino]butanoic acid. It is white or almost white, hygroscopic powder which is practically insoluble in water, sparingly soluble in methylene chloride and freely soluble in ethanol and methanol belongs to the category angiotensin II receptor blocker (ARB).

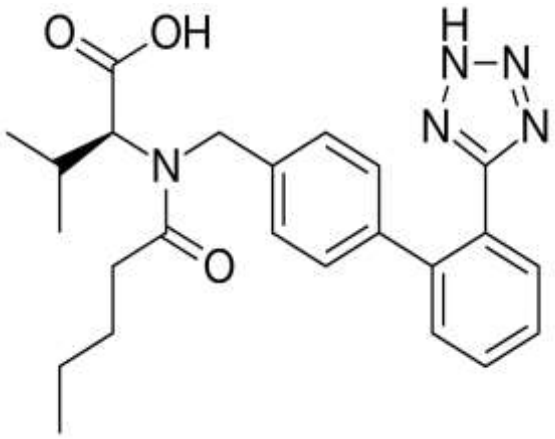

Fig 01: CHEMICAL STRUCTURE OF VALSARTAN

II. EXPERIMENTAL

2.1 Reagents and Chemicals:

Valsartan pure sample was obtained as a gift sample from Chempure Pharmaceuticals Ltd., Mumbai, India. The marketed formulation VALZAAR - 40 mg (ethical formulation) film coated tablets contains Valsartan 40 mg manufactured by Torrent Pharma Ltd and Valsartan Tablets IP 40 mg (generic formulation) each film coated Tablet contains 40 mg of valsartan manufactured by Ausmed Life Sciences, Bharatiya Janaushadi Kendra, Shivamogga were used. Both of these tablets are procured from the local market. Ethanol was procured from SD fine chemicals, Mumbai, India. All chemicals and reagents used were of analytical grade.

2.2 Instrumentation:

The developed method was performed on a Shimadzu model 1800 double-beam UV-visible spectrophotometer having a pair of quartz cuvettes with a 1 cm path length.

III. MATERIALS AND METHODS

3.1 Preparation of standard stock solution VAL:

100 mg of VAL was weighed and transferred into 100 ml volumetric flask. The drug was dissolved in 60 ml of ethanol by sonication and then volume was made upto the mark with ethanol to obtain a concentration of 1000 mcg/ml of VAL (Std Stock A solution). From the above stock 'A' solution 10 ml of aliquot was pipetted out into a 100 mL volumetric flask and the volume was made upto the mark with ethanol to obtain a concentration of 100 mcg/ml of VAL (Std Stock B solution).

3.2 Preparation of sample stock solutions using formulation:

Twenty tablets of VAL were weighed and average weight was determined. The tablets were crushed to fine powder and tablet powder equivalent to 50 mg of VAL was weighed and transferred to 50 ml volumetric flask, dissolved in 30 ml of ethanol and the content was kept in sonicator for 15 min. The solution was filtered

through Whatmann filter paper NO.41. Finally, the volume was made upto the mark with ethanol to get a concentration of 1000 µg/ml of VAL (sample stock solution A). From the above sample stock 'A' solution, 5 ml of the aliquot was pipetted out and transferred to a 50 ml volumetric flask. The volume was made upto 50 ml with ethanol to obtain a concentration of 100 µg/ml of VAL (sample stock solution B).

3.3 Selection of analytical concentration range.

Appropriate aliquot was pipetted out from the standard stock 'B' solution into a series of 10 ml volumetric flasks. The volume was made upto the mark with ethanol to get a set of solutions having a concentrations range of 2-10 µg/ml of VAL. Absorbance of above solutions was measured at 254.0 nm and a calibration curve of absorbance against concentration was plotted. The drug VAL obeyed the beer's law in the concentration range of 2 to 10 µg/ml. For method development a concentration of 2,4,6,8 and 10 µg/ml was selected as working concentrations for VAL.

3.4 Analysis of tablet formulation.

Appropriate aliquots were prepared from the sample stock 'B' solution to get a concentration of 6 µg/ml of VAL for zero order, second order derivative method and 8 µg/ml for AUC method. Above preparations were analysed at the selected analytical wavelength of 254.0 nm for zero order, second order derivative method and 249 to 259 nm for AUC method respectively.

IV. VALIDATION PARAMETERS

The developed approach was validated for the following parameters in compliance with ICH recommendations.

4.1 Linearity:

The linearity of an analytical procedure is its ability to obtain test results that are directly proportional to the concentration of analyte in the sample. Five different concentrations were used to evaluate the method's linearity; the linearity ranges for VAL were found to be 2-10 µg/ml for all the three methods. The overlain spectrum and calibration curves for VAL along with UV spectrum of generic and ethical formulations are displayed in Fig. 2-13. The result of the Statistical data of Valsartan at 254 nm is shown in Table no. 1 and Table no. 2 for zero order derivative method and Second order derivative method respectively. The statistical data of valsartan at 249 to 259 nm is shown in table no. 03 for AUC method.

4.2 Limit of Detection and Limit of Quantification:

LOD stands for the amount of the analyte that can be detected. LOQ is the least amount of the analyte that can be quantified. The drug's limit of detection and quantification was determined using the formula below;

LOD = 3.3* SD /Slope
LOQ = 10* SD /Slope
SD = Standard deviation

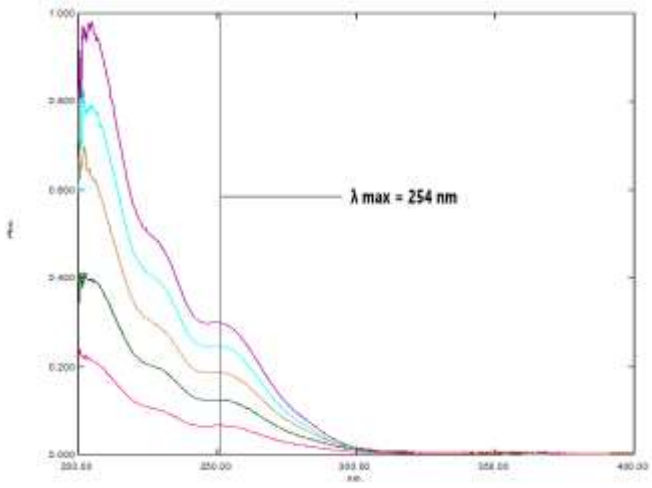

Fig. 02: Overlay spectrum of Valsartan at 254 nm by Zero order derivative method.

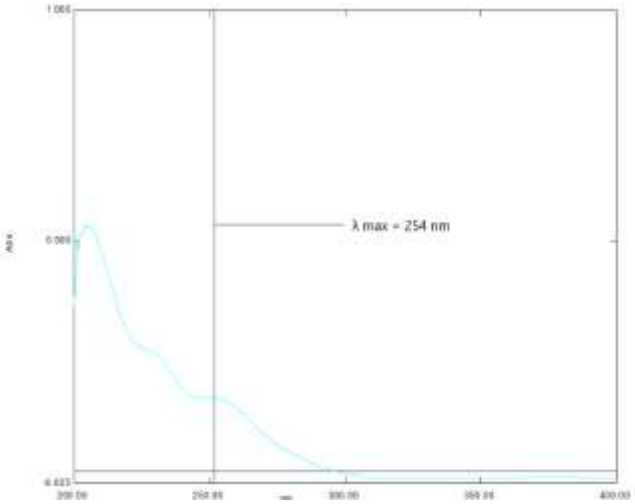

Fig. 03: UV spectrum of Valsartan (6 mcg) in generic formulation at 254 nm by Zero order derivative method.

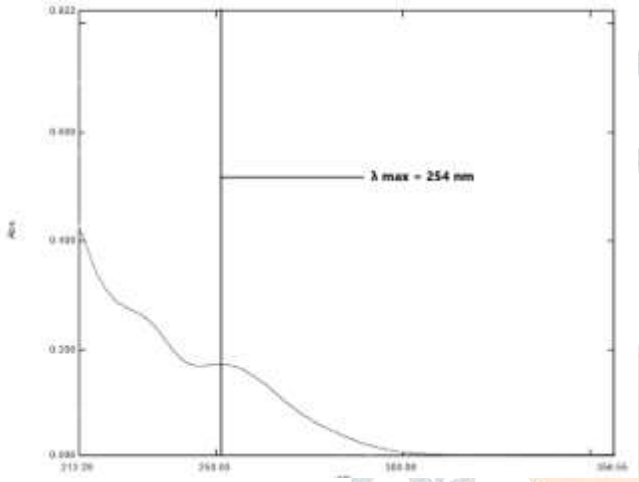

Fig. 04: UV spectrum of Valsartan (6 mcg) in Ethical formulation at 254 nm byZero order derivative method.

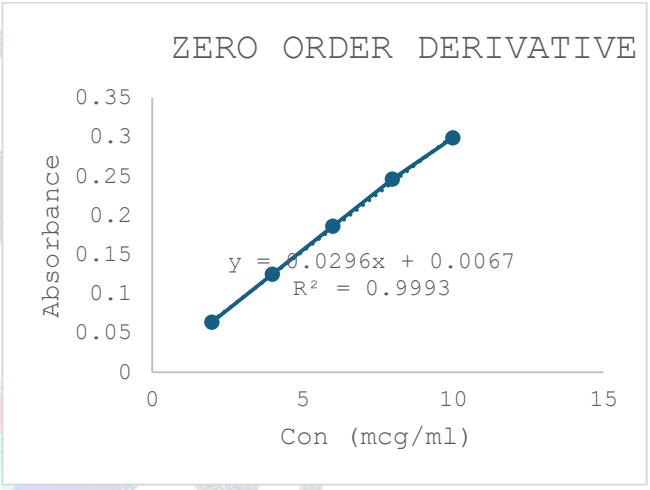

Fig. 05: Calibration curve of Valsartan at 254 nm by Zero order derivativemethod.

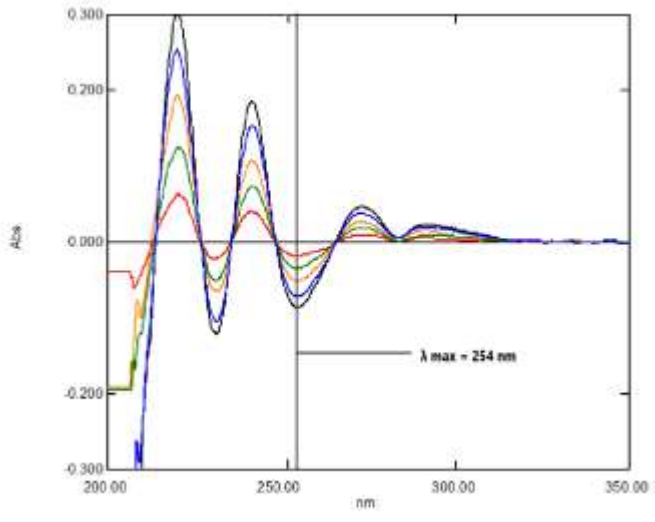

Fig. 06: Overlay spectrum of Valsartan at 254 nm by Second order derivative method.

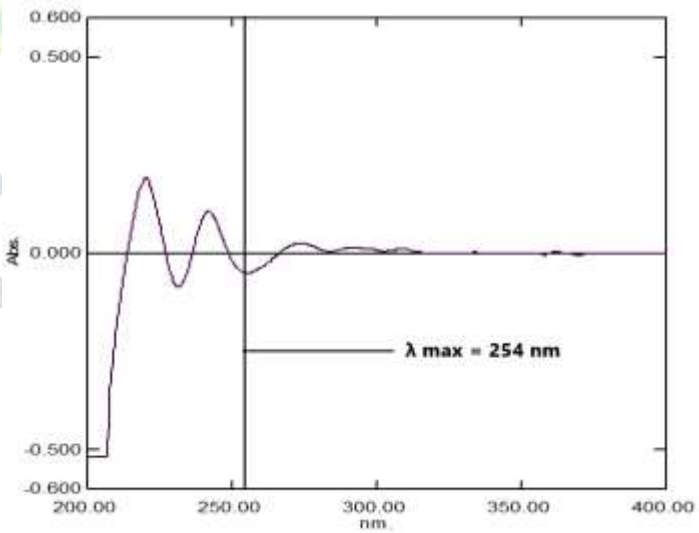

Fig. 07: UV spectrum of Valsartan in Generic formulation at 254 nm by Second order derivative method.

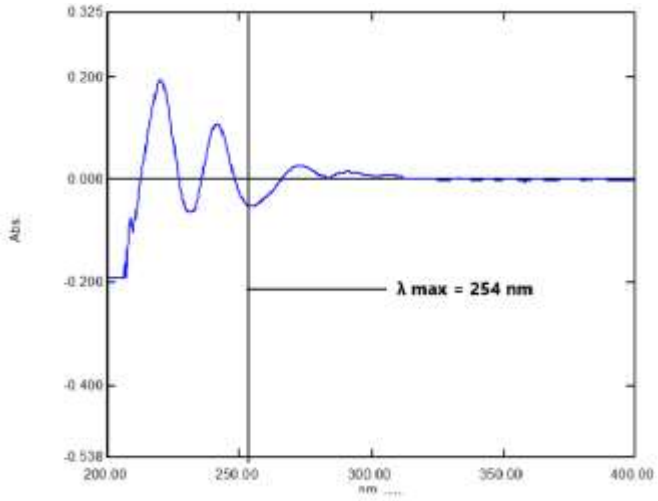

Fig. 08: UV spectrum of Valsartan in Ethical formulation at 254 nm by Second order derivative method.

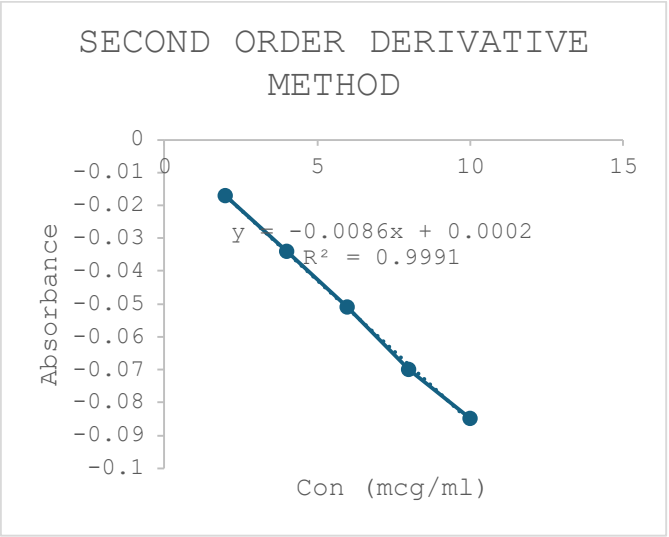

Fig. 09: Calibration curve of Valsartan at 254 nm by Second order derivativemethod.

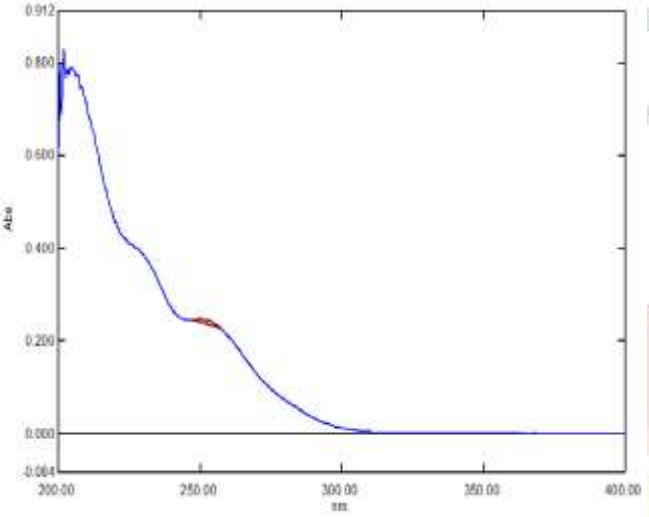

Fig. 10: Area of Valsartan (8 mcg/ ml) Pure drug in the wavelength range of 249-259 nm.

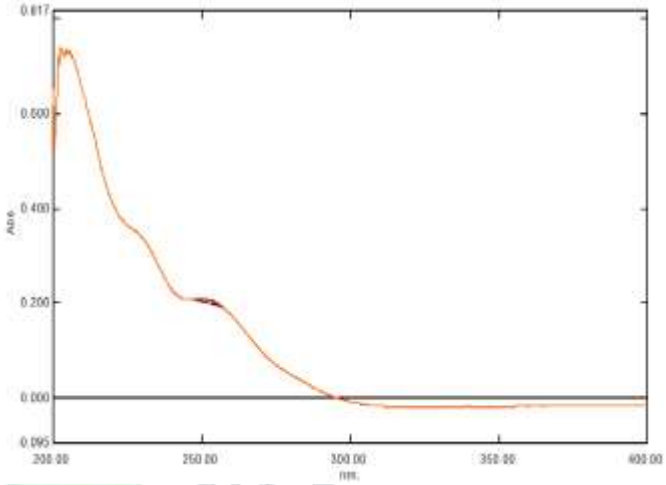

Fig. 11: Area of Valsartan (8 mcg/ ml) in Generic formulation in the wave length rang of 249-259 nm.

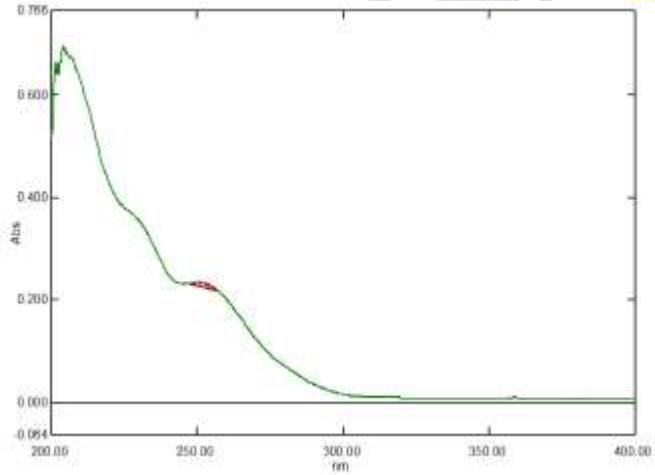

Fig. 12: Area of Valsartan (8 mcg/ ml) in Ethical formulation in the wavelengthrange of 249-259 nm.

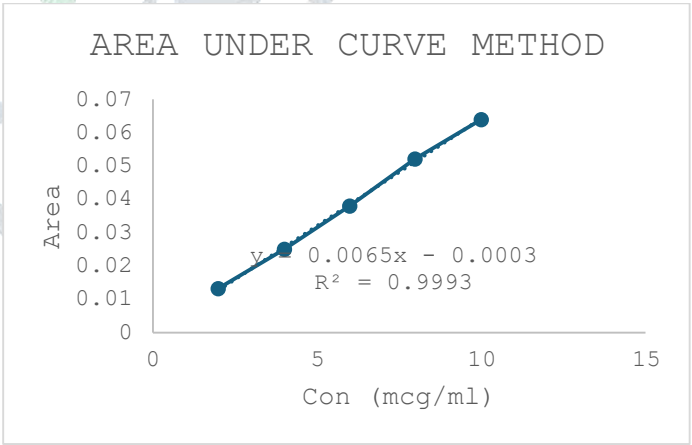

Fig. 13: Calibration curve of Valsartan at 249-259 nm by Area Under Curve method.

Table no. 01: Statistical data of Valsartan at 254 nm by Zero order derivativemethod.

Parameter	Valsartan at 254 nm
Linear range (µg/ml)	2.0-10.0
Slope	0.0296
Intercept	0.0067
Limit of detection (µg/ml)	0.33454
Limit of quantification(µg/ml)	1.0131
% Purity (Pure VAL drug)	100.2
% Purity (Generic formulation)	98.34
% Purity (Ethical formulation)	100.34

Table no. 02: Statistical data of Valsartan at 254 nm by Second order derivative method.

Parameter	Valsartan at 254 nm
Linear range(µg/ml)	2.0-10.0
Slope	-0.0086
Intercept	0.0002
Limit of detection(µg/ml)	0.370
Limit of quantification(µg/ml)	1.123
% Purity (Pure VAL drug)	99.71
% Purity (Generic formulation)	98.34
% Purity (Ethical formulation)	100.32

Table no. 03: Statistical data of Valsartan at 249-259nm by AUC method.

Parameter	VAL at 249-259 nm
Linear range(µg/ml)	2-10 µg/mL
Slope	0.0065
Intercept	0.0003
Limit of detection (µg/ml)	0.3074
Limit of quantification (µg/ml)	0.9315
% Purity (Pure VAL drug)	100.07
% Purity (Generic formulation)	99.1
% Purity (Ethical formulation)	100.04

V. RESULTS & DISCUSSION

It was discovered that the suggested procedure was simple, reliable and reproducible. The method was validated for linearity, % purity, LOD and LOQ according to ICH guidelines. The linearity was discovered in the concentration range between 2 to 10 µg/ml. The regression equation of the calibration curve for VAL was y = 0.0296x + 0.0067 for zero order derivative method, y = -0.0086x + 0.0002 for second order derivative method and y = 0.0065x – 0.0003 for AUC method. The regression coefficient values of the calibration curve for VAL were found to be 0.9993, 0.9991 and 0.9993 for the zero-order, second order and AUC method respectively. The standard deviation numbers were acceptable, and the recovery studies were close to 100%. The accuracy of the procedure was confirmed by the percentage recoveries for VAL which were found to be 100.2 % purity for pure valsartan drug, 98.34 % purity for valsartan Tablets IP 40 mg (generic formulation) and 100.34 % purity for VALZAAR - 40 mg (ethical formulation). LOD & LOQ was found to be 0.3345 mcg/ml & 1.013 mcg/ml for Valsartan for zero order derivative method. For Second order derivative method

standard valsartan showed 99.71 % purity, valsartan tablets IP 40 mg (generic formulation) showed 98.34 % purity and VALZAAR - 40 mg (ethical formulation) showed 100.32 % purity. LOD & LOQ was found to be 0.37 mcg/ml & 1.123 mcg/ml. For AUC method standard valsartan showed 100.07 % purity, valsartan tablets IP 40 mg (generic formulation) showed 99.1 % purity and VALZAAR - 40 mg (ethical formulation) showed 100.04 % purity. LOD & LOQ was found to be 0.307 mcg/ml & 0.931 mcg/ml.

VI. CONCLUSION

All the methods showed near 100 % purity for VALZAAR - 40 mg (ethical formulation) and near 98.57 % purity for Valsartan Tablets IP 40 mg (generic formulation).

VII. ACKNOWLEDGEMENT

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