INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACY AND CHEMISTRY

Available online at www.ijrpc.com

Research Article

DOI: https://dx.doi.org/10.33289/IJRPC.12.2.2022.12(31)

A NEW CHROMATOGRAPHY SEPERATION TECHNIQUE FOR ESTIMATION OF VALSARTAN IN ITS BULK AND DOSAGE FORM

Sireesha Gangi*, Tulasi Ruttala, Baby Jahnavi Sabbi,

Sravani Sappa, Satyasuma Sunkara and Veera Satyakala Surisetti

Department of Pharmaceutical Analysis, VJ'S college of Pharmacy, Diwancheruvu, Rajahmundry, Andhra Pradesh, India.

ABSTRACT

A simple, Accurate, precise method was developed for the simultaneous estimation of the Valsartan in Tablet dosage form. Chromatogram was run through Symmetry (4.6 x 150mm, 5µm). Mobile phase containing Buffer Acetonitrile and 0.1% TEA in the ratio of 30:70 was pumped through column at a flow rate of 1.0 ml/min. Temperature was maintained at 30°C. Optimized wavelength for Valsartan was 250nm. Retention time of Valsartan were found to be 4.269 min. %RSD of the Valsartan were found to be 0.5. %Recover was Obtained as 99.67% for Valsartan. Retention times are decreased and that run time was decreased so the method developed was simple and economical that can be adopted in regular Quality control test in Industries.

Keywords: Valsartan, RP-HPLC, Chromatography and retention time.

INTRODUCTION

'Health is wealth'. It is vital fact that a healthy body is desire of every human being. Good health is first condition to enjoy the life and all other things which mankind is having. Nowadays peoples are more concentrating towards health. Even governmental bodies of different countries and World health organization (WHO) are also focusing for health of human being.

HPLC was commonly used for the separation of chemical compounds. New techniques improved separation, identification, purification and quantification far above the previous techniques. Computers and automation added to the convenience of HPLC. Improvements in type of columns and thus reproducibility were made as such terms as micro-column, affinity columns, and Fast HPLC began to immerge.

Today's HPLC requires very special apparatus which includes the following.

1. Extremely precise gradient mixers.
2. HPLC high pressure pumps with very constant flow.
3. Unique high accuracy, low dispersion, HPLC sample valves.
4. Very high efficiency HPLC columns with inert packing materials.
5. High sensitivity low dispersion HPLC detectors.
6. High speed data acquisition systems.
7. Low dispersion connecting tubes for valve to column and column to detector.

HPLC Gradient mixtures

HPLC gradient mixers must provide a very precise control of solvent composition to maintain a reproducible gradient profile. This can be complicated in HPLC by the small elution volumes required by many systems. It is much more difficult to produce a constant gradient when mixing small volumes then when mixing large volumes. For low pressure systems this requires great precision in the operation of the miniature mixing General Introduction valves used and low dispersion flows throughout the mixer. For multi-pump

high pressure systems it requires a very precise control of the flow rate while making very small changes of the flow rate.

HPLC Sample Valves

Since sample valves come between the pump and the column it follows that HPLC sample valves must also tolerate pressures upto 10,000psi. For analytical HPLC, the sample volume should be selectable from sub micro liter to a few micro liters, whereas in preparative HPLC the sample volume may be even greater than 10 ml. To maintain system efficiency the sample valve must be designed to have very low dispersion characteristics, this is true not only for flow dispersion but also for the less obvious problems of dispersion caused by sample adsorption/ desorption on valve surfaces and diffusion of sample into and out of the mating surfaces between valve moving parts. It goes without saying that the valves must deliver a very constant sample size but this is usually attatched.

HPLC Columns

HPLC columns are packed with very fine particles (usually a few microns in diameter). The very fine particles are required to attain the low dispersion that give the high plate counts expected of modern HPLC. Plate counts in excess of 25,000 plates per column are possible with modern columns, however, these very high efficiencies are very rarely found with real samples because of the dispersion associated with injection valves, detectors, data acquisition systems and the dispersion due to the higher molecular weight of real samples as opposed to the common test samples. Packing these small particles into the column is a difficult technical problem but even with good packing a great amount of care must be given to the column end fittings. The main consideration with HPLCS is the much wider variety of solvents and packing materials that can be utilized because of the much lower quantities of both which are required. In particular very expensive optically pure compounds can be used to make Chiral HPLC stationary phases and may even be used as (disposable) HPLC solvents.

Table 1: Instruments used

SL.No	Instruments	Model
1	HPLC	WATERS, sciftware: Empower, 2695
2	IJV/VIS spectrophotometer	L Il4DLAIJ SOOO
3	pH meter	Adwa—AD1020
4	Weighing machine	AfiosotER-2OOA
5	Pipettes and Burette s	
6	Beakers	

Table 2: Chemicals used

SL. No	Chemical	Company Name
1	Valsartan	PHA ATRAIN
2	Water for HPLC	FINER chemical LTD
3	Methanol for HPLC	LICHROSOLV (MERCK)
4	Acetonitrile for HPLC	MOLYCHEM
5	TEA	MERCK
6	NaOH	FINER chemical LTD

Parameters for Method Validation

The parameters for method validation have

been defined in different working groups of national and internationalcommitteesandaredescribedintheliterature.Anattemptatharmonizationwasmadefor pharmaceutical applications through the ICH. The defined validation parameters by the ICH and other regulatorybodiesaresummarizedasunder:a)Specificitystudyb)Linearityandrangestudyc)Limitof detection and Limit of quantitation study d) Precision study e) Accuracy study f) Robustness study g) Solution stability study h) System suitability

Mechanism of action of valsartan

Valsartan selectively acts on AT1, the subtype receptor that mediates the cardiovascular actions of angiotensin II, the main vasoactive hormone of the renin-angiotensin-system. The AT2 receptor subtype, which can be found in tissues such as the brain, endometrium, myometrium, and fetal kidney and adrenals, plays no known role in cardiovascular homeostasis at this time. Angiotensin II contributes to vasoconstrictor activity and sodium/water retention, which contribute to hypertension. Through the inhibition of response to angiotensin II by actions on the AT1 receptor, valsartan is able to decrease blood pressure. The cardioprotective effects of valsartan are thought to occur through inverse agonist activity of valsartan on the AT1receptor, which plays an important role in cardiac remodeling (causing ventricular hypertrophy). Inverse agonists such as valsartan inactivate this receptor, preventing cardio vascular remodeling.

Preparation of Buffer and Mobile Phase

Preparation of 0.1% TEA buffer

Take 1mL of TEA in 1000ml of HPLC water, pH was adjusted with NaOH up to 3.5. Final solution was filtered through 0.45 membrane filter and sonicate it for 10mins.

Preparation of mobile phase

Accurately measured 300 mL of Acetonitrile (30%) and 700 mL of above buffer (70%) were mixed and degassed in an ultrasonic water bath for 10minutes and then filtered through 0.45µ filter under vacuum filtration.

Diluent Preparation

The Mobile phase was used as the diluent.

Standard Solution Preparation

Accurately weigh and transfer 80 mg of Valsartan working standard into a 50 ml clean dry volumetric flask add about 25 ml of diluent and sonicate to dissolve it completely and make volume up to the mark with the same solvent. (Stock solution) Further pipette 2.5 ml of the above stock solutions into a 25 ml volumetric flask and dilute up to the mark with diluent. Further pipette 3 ml of the above stock solutions into a 10 ml volumetric flask and dilute up to the mark with diluent. (48 ppm Valsartan)

Sample Solution Preparation

Accurately weigh 10 tablets crush in motor and pestle and transfer equivalent to 80 mg (200 mg of tablet power) of Valsartan sample into a 50 ml clean dry volumetric flask add about 25 ml of diluent and sonicate it up to 30 mins to dissolve it completely and make volume up to the mark with the same solvent. Then it is filtered through 0.45 micron injection filter. (Stock solution)

Further pipette 2.5 ml of the above stock solutions into a 25 ml volumetric flask and dilute upto the mark with diluent. Further pipette 3ml of the above stock solutions into a10 ml volumetric flask and dilute up to the mark with diluent. (48 ppm Valsartan).

VALIDATION PARAMETERS

LINEARITY

Preparation of stock solution

Accurately weigh and transfer 80mg of Valsartan working standard into a 50 mL clean dry volumetric flask add about 25 ml of diluent and sonicate to dissolve it completely and make volume up to the mark with the same solvent. (Stock solution) Further pipette 2.5 ml of the above stock solutions into a 25 ml volumetric flask and dilute up to the mark with diluent.

Preparation of Level – I (16 ppm of Valsartan)

1 mL of above stock solutions has taken in 10 ml of volumetric flask, dilute up to the mark with diluent.

Preparation of Level – II (32 ppm of Valsartan)

2 mL of above stock solutions has taken in 10 ml of volumetric flask, dilute up to the mark with diluent.

Preparation of Level – III (48 ppm of Valsartan)

3 mL of above stock solutions has taken in 10 ml of volumetric flask, dilute up to the mark withdiluent.

Preparation of Level – IV (64 ppm of Valsartan)

4 mL of above stock solutions has taken in 10 ml of volumetric flask, dilute up to the mark withdiluent.

Preparation of Level – V (80 ppm of Valsartan)

5 mL of above stock solutions has taken in 10 ml of volumetric flask, dilute up to the mark withdiluent.

Procedure

Inject each level into the chromatographic system and measure the peak area. Plot a graph of peak area versus concentration (on X-axis concentration and on Y-axis Peak area) and calculate the correlation coefficient. Acceptance Criteria: Correlation coefficient should be not less than 0.99.

PRECISION

Preparation of stock solution

Accurately weigh and transfer 80 mg of Valsartan working standard into a 50 ml clean dry volumetric flask add about 25 mL of diluent and sonicate to dissolve it completely and make volume upto the mark with the same solvent. (Stock solution).

Further pipette 2.5 ml of the above stock solutions into a 25 ml volumetric flask and dilute up to the mark with diluent. Further pipette 3 ml of the above stock solutions into a 10 ml volumetric flask and dilute up to the mark with diluent. (48 ppm Valsartan)

Procedure

The standard solution was injected for six times and measured the area for all six. Injections in HPLC. The %RSD for the area of six replicate injections was found to be within the specified limits. Acceptance Criteria: The % RSD for the area of six standard injections results should not be more than 2%.

INTERMEDIATE PRECISION/RUGGEDNESS

To evaluate the intermediate precision (also known as Ruggedness) of the method, Precision was performed on different day.

Preparation of stock solution

Accurately weigh and transfer 80 mg of Valsartan working standard into a 50 mL clean dry volumetric flask add about 25 mL of diluent and sonicate to dissolve it completely and make volume up to the mark with the same solvent. (Stock solution)

Further pipette 2.5 mL of the above stock solutions into a 25 mL volumetric flask and dilute up to the mark with diluent. Further pipette 3 mL of the above stock solutions into a10 mL volumetric flask and dilute up to the mark with diluent. (48 ppm Valsartan).

Procedure

The standard solutions prepared in the precision was injected on the other day, for six times and measured the area for all six injections in HPLC. The %RSD for the area of six replicate injections was found to be within the specified limits.

RESULTS AND DISCUSSION

SYSTEM SUITABILITY

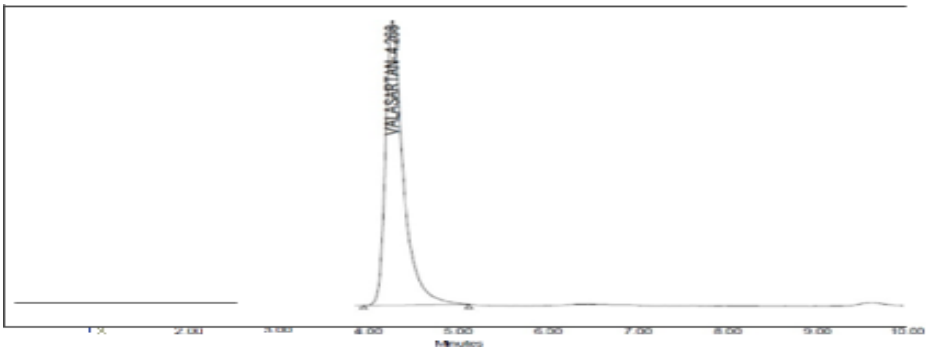

Fig. 1: Chromatogram for system suitability

Table 3: Result of system suitability

S. No.	Name	RT(min)	Area (µV sec)	Height (µV)	USP tailing	USP plate count
1	Valsartan	4.269	468236	23851	1.06	5429.17

Acceptance criteria:

- Theoretical plates must be not less than 2000.
- Tailing factor must be not more than 2.
- It was found from above data that all the system suitability parameters for developed method were within the limit.

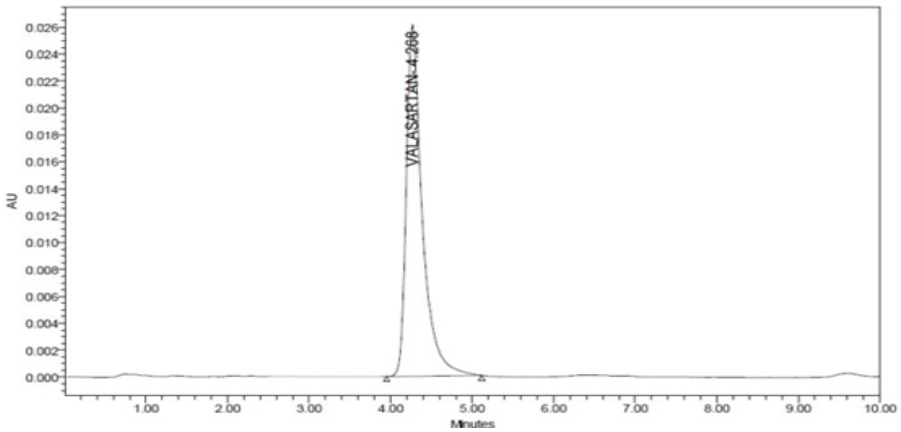

Fig. 2: Chromatogram of standard

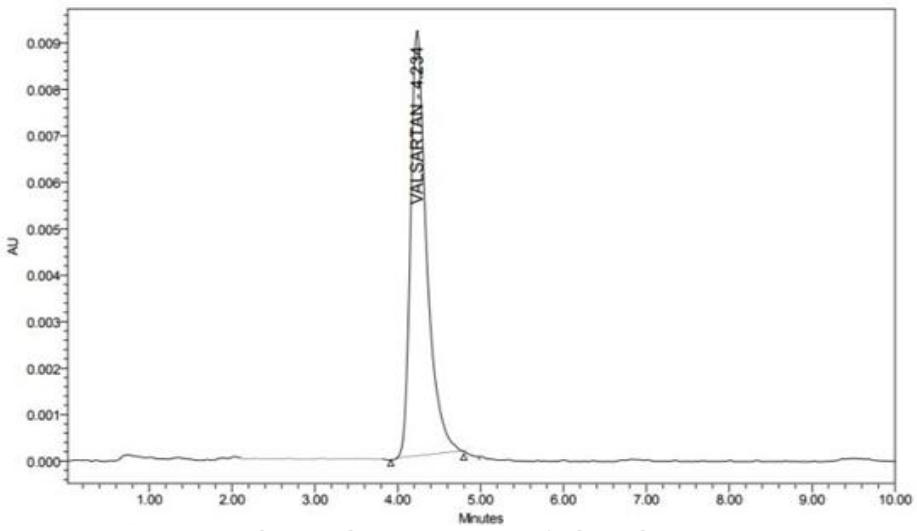

Fig. 3: Chromatogram of Linearity -1

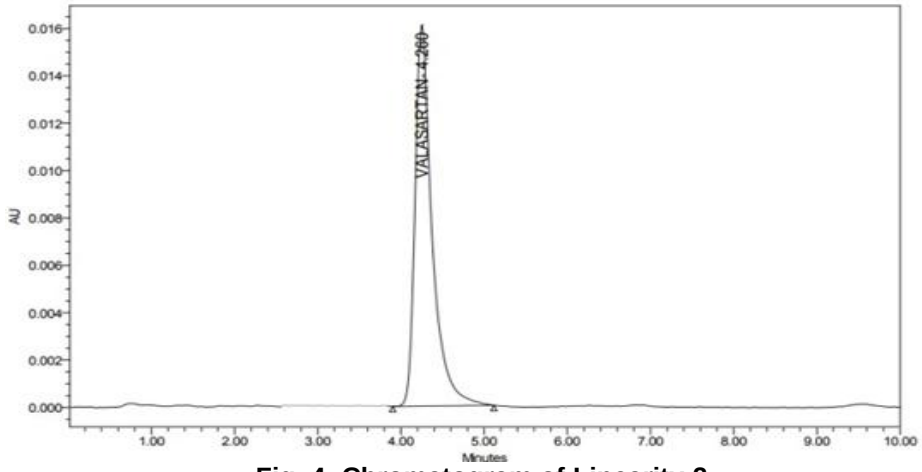

Fig. 4: Chromatogram of Linearity-2

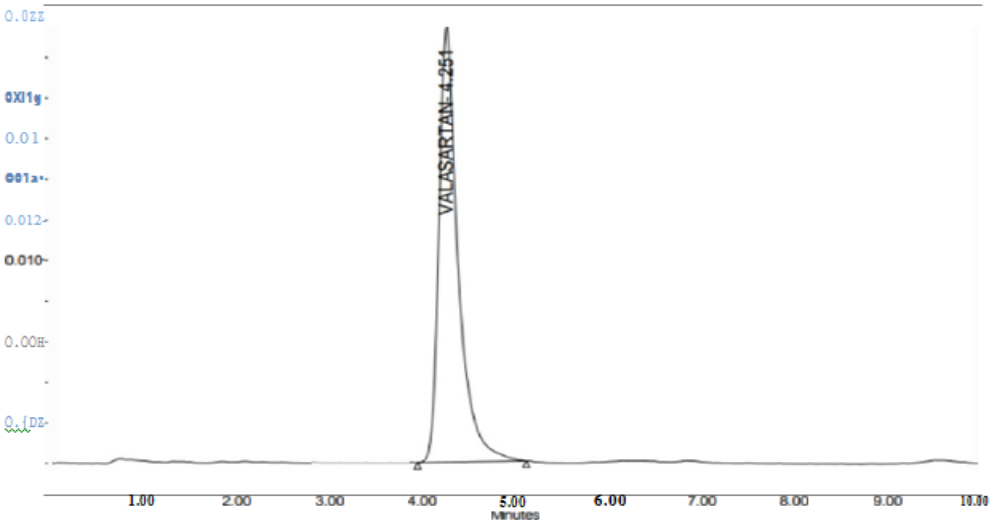

Fig. 5: Chromatogram of Linearity-3

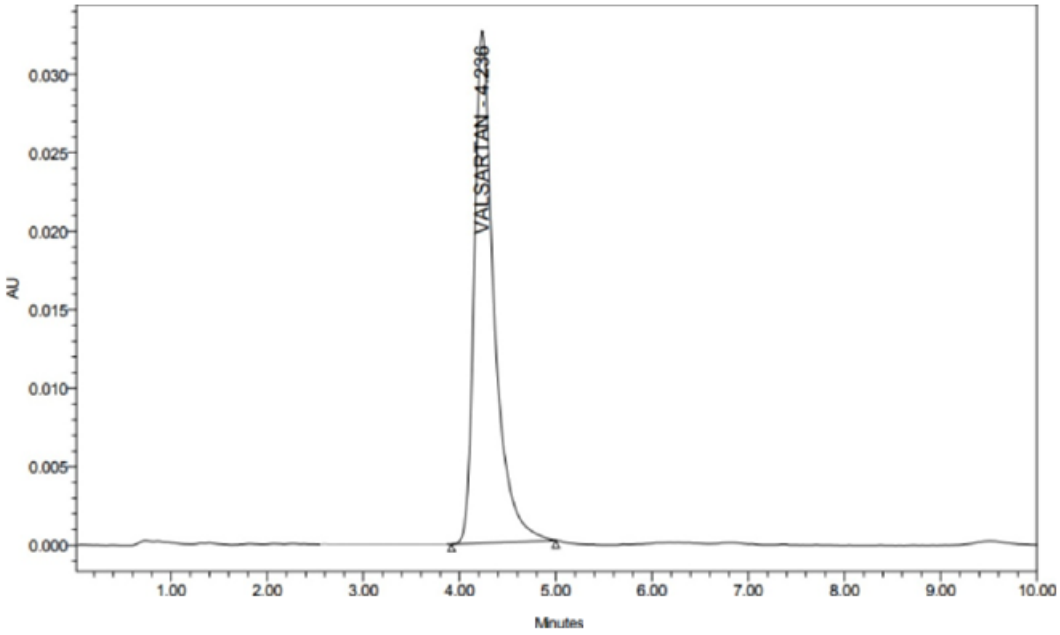

Fig. 6: Chromatogram of Linearity-4

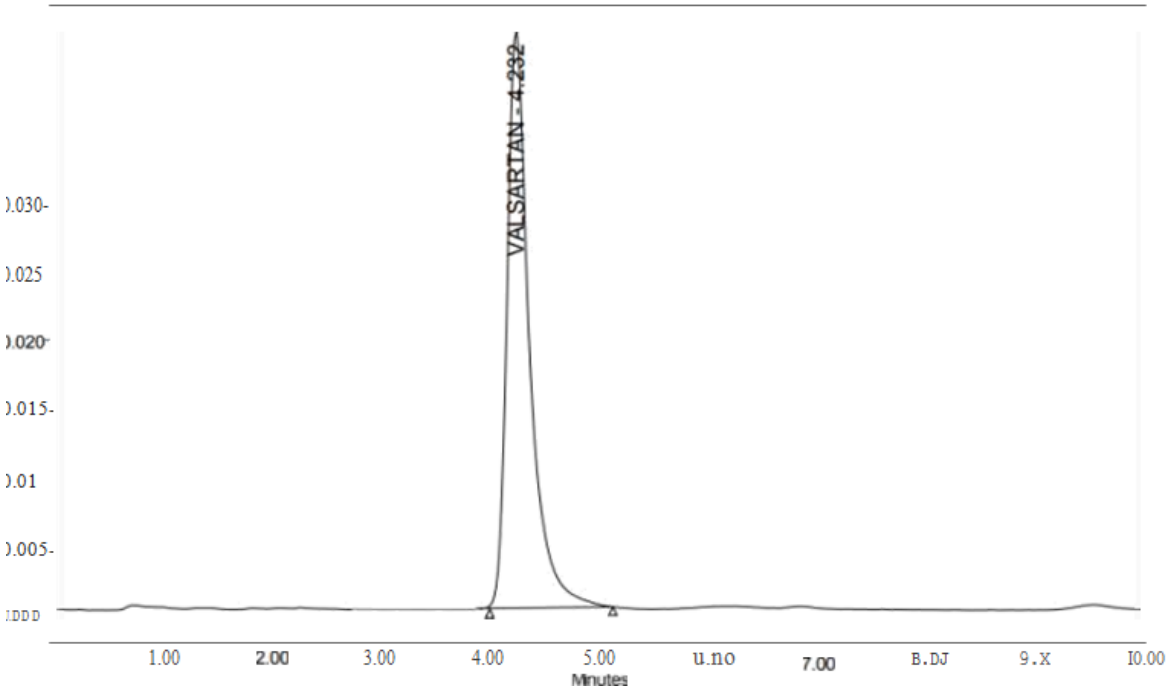

Fig. 7: Chromatogram of Linearity-5

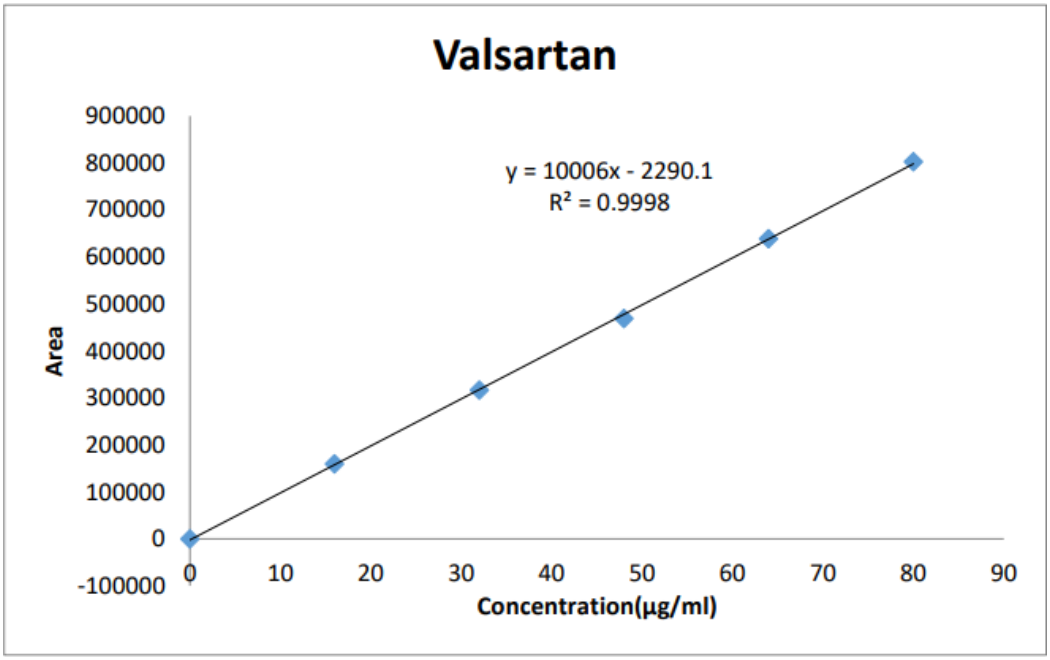

Fig. 8: Calibration Graph for Valsartan

Table 4: Area of different concentrations of Valsaratan

S. No	Valsartan	
	Concentration (µg/ml)	Area
1	0	0
2	16	159692
3	32	316982
4	48	469362
5	64	638978
6	80	802571

Parameters	Valsartan
Slope (m)	10006
Intercept (c)	2290.1
Correlation coefficient (R^2)	0.999

Acceptance criteria:

Correlation coefficient (R^2) should not be less than 0.999

- The correlation coefficient obtained was 0.999 which is in the acceptance limit.

CONCLUSION

The estimation of Valsartan was done by RP-HPLC. The assay of Valsartan was performed with tablets and the %assay was found to be 99.67 which show that the method is useful for routine analysis. The linearity of Valsartan was found to be linear with a correlation coefficient of 0.999, which shows that the method is capable of producing good sensitivity. The acceptance criteria of precision is RSD should be not more than 2.0% and the method show precision 0.5 for Valsartan which shows that the method is precise. The acceptance criteria of intermediate precision is RSD should be not more than 2.0% and the method show precision 0.4 for Valsartan which shows that the method is repeatable when performed in different days also. The accuracy limit is the percentage recovery should be in the range of 98.0% - 102.0%. The total recovery was found to be 100.34% for Valsartan. The validation of developed method shows that the accuracy is well within the limit, which shows that the method is capable of showing good accuracy and reproducibility. The robustness limit for mobile phase variation and flow rate variation are well within the limit, which shows that the method is having good system suitability and precision under given set of conditions.

REFERENCES

1. Brahmankar M and Sunil.
2. Jaiswal B. Biopharmaceutics Pharmacokinetics, A Treatise, 1st ed, Vallabh Prakasan, Delhi, 2005;27:5-6.
3. James Swarbrick and James C Boylan. Encyclopedia of Pharmaceutical Technology, 2nd edition. 1:8.
4. Christian Leuner and Jennifer Dressmann. Improving drug solubility for oral delivery using solid dispersions. European Journal of Pharmaceutics and Biopharmaceutics. 2000;50:47-48.
5. Leon Shargel and Andrew BC. Applied Biopharmaceutics and Pharmacokinetics, Appleton Century-Crofts, 4th Ed. 1985;134.
6. Gare Kani HA, Sadeghi F, Badiee A, Mostafa SA and Rajabisiahboomi AR. Crystal habit modifications of Ibuprofen and their Physicochemical Characteristics. Drug Development and Industrial Pharmacy. 2001;27(8):803-809.
7. Leon Shargel and Andrew BC. Applied Biopharmaceutics and Pharmacokinetics. Appleton Century-Crofts, 4th Ed. 1985;135.
8. Brahmankar DM and Sunil B Jaiswal. Biopharmaceutics and Pharmakokinetics. A Treatise, 1st ed, Vallabh Prakasan, Delhi. 2005;27:29-30.
9. Nandita G Das and Sudip K Das. Formulation of Poorly Soluble Drugs. Drug Delivery Report Spring/Summer. 2006;52-55.
10. Chiou WL and Riegelman SJ. J Pharm Sci. 1971;60:1283-1297.