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## A Novel Method for Estimation of Valsartan in Bulk and Pharmaceutical Preparations by Visible Spectrophotometry



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### ABSTRACT

A simple and sensitive visible spectrophotometric method is described for the determination of Valsartan in bulk and pharmaceutical preparations based on the formation of dark green colored molecular complex with sodium nitroprusside in presence of hydroxylamine under alkaline conditions and exhibiting  $\lambda$  max at 720nm. The Regression analysis of Beer's Law plot showed good correlation in a general concentration range of 8-24 $\mu$ g/ml with correlation coefficient ( $r=0.999$ ). The proposed method is validated with respect to accuracy, precision, linearity and limit of detection. The suggested procedure is successfully applied to the determination of the drug in pharmaceutical preparation, with high percentage of recovery, good accuracy and precision. The results of analysis have been validated statistically by repeatability and recovery studies. The results are found satisfactory and reproducible. The method is applied successfully for the estimation of Valsartan in tablet form without the interference of excipients.

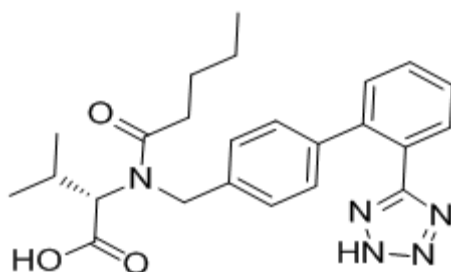


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## INTRODUCTION

Valsartan is a non-peptide, orally active and specific angiotensin II receptor blocker acting on the AT1 receptor subtype. Valsartan chemically described as N-(1-oxopentyl)-N-[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]4-yl methyl]L-valine. Valsartan is used for the treatment of hypertension, can be used alone or in combination with other antihypertensive drugs. Only LC-MS in human plasma<sup>2</sup>, Colorimetric estimation<sup>3</sup>, RP-HPLC<sup>4</sup> and degradation studies by isocratic HPLC<sup>5</sup> has been reported so far. The aim of this work is to develop simple, accurate, precise spectrophotometric methods for the routine determination of valsartan in bulk and tablet dosage form.



**Fig. 1: Structure of valsartan**

The proposed method is based on the formation of molecular complex of drug with sodium nitroprusside in presence of hydroxylamine hydrochloride under alkaline conditions. The method can be extended for the routine assay of VLS formulations.

## MATERIALS AND METHODS

A Systronics UV/Visible spectrophotometer model -2203 with 10mm matched quartz cells were used for all spectral measurements. All the chemicals used were of analytical grade. SNP (Sd Fine, 0.4%,  $1.34 \times 10^{-2}$  M, solution prepared by dissolving 400mg of SNP in 100ml distilled water), Hydroxylamine hydrochloride (Loba, 0.4%,  $5.75 \times 10^{-2}$  M solution prepared by dissolving 400mg of hydroxylamine hydrochloride in 100ml of distilled water), sodium carbonate (Loba, 10%,  $9.43 \times 10^{-1}$  M solution prepared by dissolving 10g of sodium carbonate in 100ml of distilled water) were prepared.

**Standard drug solution:** Standard drug solution of VLS was prepared by dissolving 20mg in 4ml of 0.1M NaOH, followed by dilution to 100ml with distilled water to obtain 200 $\mu$ g/ml solution.

### **Sample solution**

In order to determine the contents of VLS in commercial dosage forms (label claim: 40 and 80mg tablet), the contents of ten tablets were weighed accurately and ground into a fine powder. An amount of powder equivalent to 10mg of VLS was accurately weighed and transferred into two separate 100mL calibrated flasks and 30mL of methanol was added. The content was shaken for about 30min; the volume was diluted to the mark with methanol and mixed well and filtered using a Whatman no.41 filter paper. The filtrate containing VLS at a concentration of 100 $\mu$ g/mL.

**Assay:** Aliquots of standard VLS solution (1.0ml-3.0ml, 200 $\mu$ g/ml) were transferred into a series of 25ml calibrated tubes and the volume in each tube was brought to 5.0ml with distilled water. One ml each of (1.324 $\times 10^{-2}$ M) SNP and (5.75 $\times 10^{-2}$ M) hydroxylamine hydrochloride Solutions were successively added to each test tube and shaken for 2 minutes.

Then 1.0ml of (9.43  $\times 10^{-1}$  M) Na<sub>2</sub>CO<sub>3</sub> solution was added and further shaken for 15 minutes. The contents were diluted to the mark with distilled water and the absorbances were measured at 720nm against a reagent blank within the stability period (immediate-120 min). (Fig-2 showing absorption spectra). The amount of VAL in the sample solution was computed from its calibration graph (Fig.3 showing Beer's Law plot).

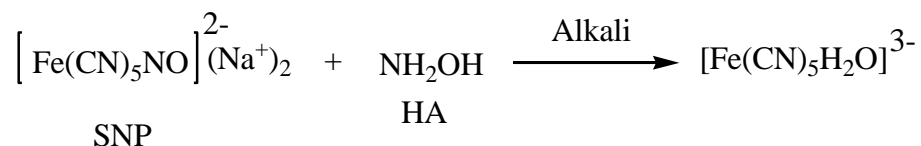
### **RESULTS AND DISCUSSION**

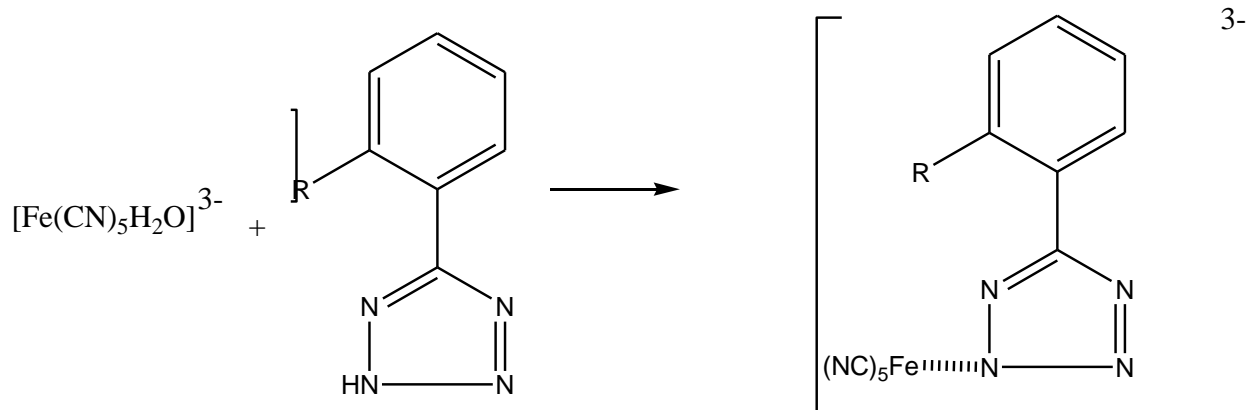
In developing this method, a systematic study of the effects of various parameters were undertaken by varying one parameter at a time and controlling all others fixed. The effect of various parameters such as time, temperature, volume and strength of SNP, NH<sub>2</sub>OH, Na<sub>2</sub>CO<sub>3</sub> reagents, order of addition of reagents on color development and solvent for final dilution of the colored species were studied and the optimum conditions were established. Other water miscible solvents like methanol, ethanol, propan-2-ol and acetonitrile were found to provide no additional advantage. The optical characteristics such as Beer's law limit, Sandell's sensitivity, molar absorptivity, percent relative standard deviation (calculated from the six measurements

containing 3/4<sup>th</sup> of the amount of the upper Beer's law limits), Regression characteristics like standard deviation of slope (Sb), standard deviation of intercept (Sa), standard error of estimation (Se) and % range of error (0.05 and 0.01 confidence limits) were calculated and are shown in Table-1. Commercial formulations containing VAL were successfully analyzed by the proposed method. The values obtained by the proposed and reference method (reported UV method in methanol,  $\lambda_{max}$  289nm) for formulations were compared statistically by the t-and f-test and found not to differ significantly. As an additional demonstration of accuracy, recovery experiments were performed by adding a fixed amount of the drug to the pre-analyzed formulations at three different concentration levels. These results are summarized in Table-2. The ingredients usually present in formulations of VLS did not interfere with the proposed analytical method.

### Chemistry of colored species

In the present investigation, VLS functions as a donor due to the presence of cyclic tertiary nitrogen in piperidine portion. Sodium nitroprusside in the presence of hydroxylamine and alkali exists as aquoferrocyanide  $[\text{Fe}(\text{CN})_5\text{H}_2\text{O}]^{3-}$ . In a general way, it may be expected that the electron transfer depends upon the extent of delocalization of the donor and acceptor metal orbitals of the intervening ligands. From this standpoint, ligands such as water and ammonia, which contain single bonds, are expected to be much less effective in conducting electrons between metal ions than unsaturated ligands such as  $\text{CN}^-$  whose complexes are characterized by high degree of covalency and electron delocalization. Based on the analogy, the probable sequence of reactions is presented in scheme (Fig-4).





**Table 1:** Analytical and regression parameters of the proposed methods

**Parameter Values**

$\lambda$ max (nm)	720nm
Beer's law limit ( $\mu\text{g/ml}$ )	8-24
Sandell's sensitivity ( $\mu\text{g/cm}^2/0.001$ abs. unit)	0.046404
Molar absorptivity (Litre/mole/cm)	10991.58
Regression equation (Y)*	
Intercept (a)	0.107
Slope (b)	0.027
Correlation Coefficient ( $R^2$ )	0.999
% RSD	0.8648
% Range of errors (95% Confidence limits)	
0.05 significance level	0.9077
0.01 significance level	1.4235

**CONCLUSION**

The reagents utilized in the proposed method are cheap and readily available and the procedure does not involve any critical reaction conditions or tedious sample preparation. The proposed analytical method is validated as per ICH guidelines and possesses reasonable precision, accuracy, simple, sensitive and can be used as an alternative method to the reported ones for the routine determination of VLS depending on the need and situation.

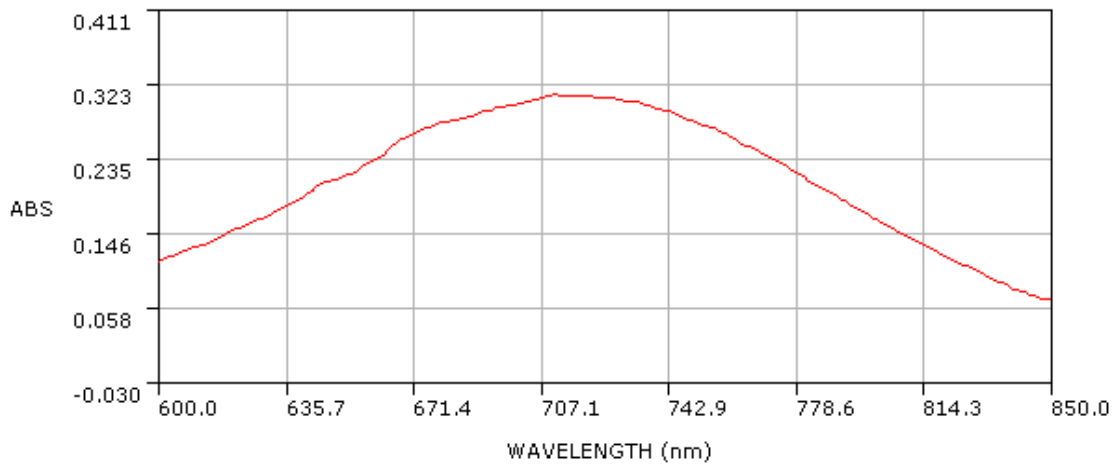


Fig. 2. Showing Absorption Spectra of VLS-SNP-NH<sub>2</sub>OH

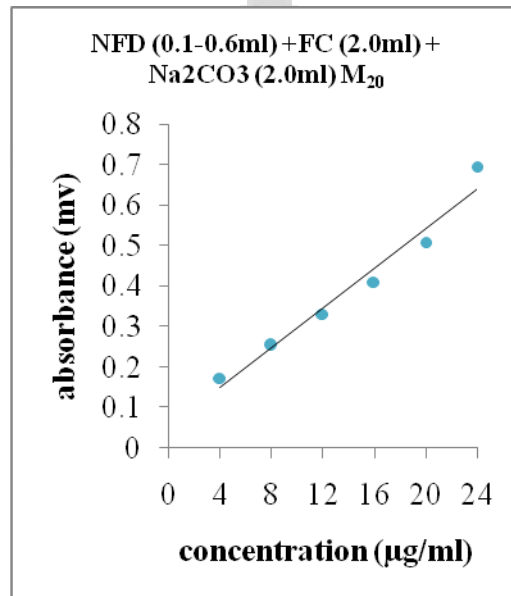


Fig. 3. Showing Beer's Law Plot

Table 2: Results of determination of VLS in tablets and statistical comparison with the reference method

Tablet brand Name	Nominal amount mg per tablet	Reference method	Proposed method
VALZAAR	40	100.88±0.48	99.62±0.704 t = 1.68, F = 2.15

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