

# Spectrophotometric Method for Analysis of Valsartan

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**Abstract:** A simple, sensitive and cost effective visible spectrophotometric method has been developed for the determination of Valsartan from bulk and tablet dosage forms. The method is based on the formation of green colored coordination complex by the drug with cobalt thiocyanate which is quantitatively extractable into nitro benzene with an absorption maximum of 605nm. The Regression analysis of Beer's Law plot showed good correlation in a general concentration range of 0.5 – 3.0 ml, 400µg/ml with correlation coefficient ( $r= 0.992$ ). 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 Valsartan in tablet form without the interference of excipients.

**Keywords:** Beer's Law, Cobalt thiocyanate, Extractive Spectrophotometry, Nitrobenzene, Valsartan

## 1. Introduction

Valsartan is an Angiotensin Receptor Blocker (ARB) that shows high affinity for the angiotensin II type 1 (AT1) receptors, has a long duration of action, and has the longest half - life of any ARB. It is an angiotensin II receptor antagonist, effective in the treatment of hypertension. It is also effective when used alone or in combination with other drugs for the treatment of high blood pressure.

Diovan (Valsartan) is a nonpeptide, orally active, and specific angiotensin II receptor blocker acting on the AT1 receptor subtype. Valsartan is a white to practically white fine powder. It is soluble in ethanol and methanol and slightly soluble in water. Angiotensin II Receptor type 1 antagonists have been widely used in treatment of diseases like hypertension, heart failure, myocardial infarction and diabetic nephropathy. Their beneficial effects are related to inhibition of Angiotensin II by blockade of AT1 receptor. It was first developed by Novartis and has a wide market in the developed and the developing countries. Valsartan is an angiotensin II receptor blocker (ARB). It works by blocking a substance in the body that causes the blood vessels to tighten. Valsartan relaxes the blood vessels and lowers blood pressure. A lower blood pressure will increase the supply of blood and oxygen to the heart.

Valsartan is an ARB that selectively inhibits the binding of angiotensin II to AT1, which is found in many tissues such as vascular smooth muscle and the adrenal glands. This effectively inhibits the AT1 - mediated vasoconstrictive and aldosterone - secreting effects of angiotensin II and results in a decrease in vascular resistance and blood pressure.

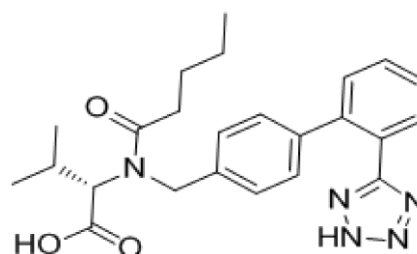


Figure 1: Showing chemical structure of VLS

## 2. Materials and Methods

### Apparatus and chemicals

A Systronics UV - Visible double beam spectrophotometer 2203 with 1 cm matched quartz cells was used for all spectral and absorbance measurements. A Systronics digital pH meter 361 was used for pH measurements. All the chemicals used were of analytical grade. Tablets were purchased from local market. CTC solution prepared by dissolving 7.25g of cobalt nitrate and 3.8gm of ammonium thiocyanate in 100ml of distilled water, nitrobenzene used as it is. Buffer P<sup>H</sup> 2.0 Solution Prepared by mixing 306 ml of trisodium citrate (0.1M) with 694 ml of HCl (0.1M) and the pH was adjusted to 2.0.

### Standard drug solution

The stock solution of drug was prepared by dissolving 100 mg in 100 ml distilled water. A portion of this stock solution was diluted stepwise with the distilled water to obtain the working standard drug solution of concentrations of 100 µg/ml. From the stock solution, a series of standards were freshly prepared during the analysis day.

### Preparation of sample solution

An accurately weighed portion of the powdered tablets equivalent to 100 mg of drug was dissolved in 20 ml of methanol (MeOH), shaken well and filtered. The filtrate was diluted to 100ml with MeOH to get 1 mg/ml solution of drug in formulations.

**Assay**

Aliquots of standard drug solution (0.5 – 3.0 ml, 400 $\mu$ g/ml) were delivered into a series of calibrated tubes. 2.0 ml of buffer (pH 2.0) and 5.0 ml of CTC solutions were added and the total volume in each tube was adjusted to 15 ml with distilled water. The solutions in the tubes were transferred to 125 ml separating funnel. To each separating funnel 10 ml of nitrobenzene was added and the contents were shaken for 2 min. The two phases were allowed to separate and the absorbance of the separated nitrobenzene layer was measured after 20 min. at  $\lambda_{\max}$  605 nm against a similar reagent blank. The amount of VLS in a sample was obtained from the Beers – Lambert's plot.

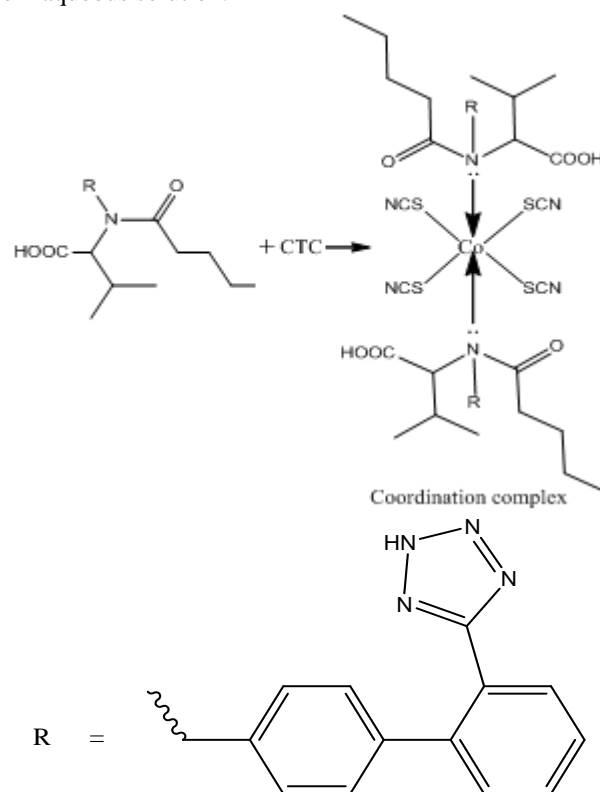
**3. Results and Discussion**

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 (CTC, Nitrobenzene) 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 3/4th of the amount of the upper Beer's law limits), Regression characteristics like standard deviation of slope ( $S_b$ ), standard deviation of intercept ( $S_a$ ), standard error of estimation ( $S_e$ ) and % range of error (0.05 and 0.01 confidence limits) were calculated and are shown in Table - 1. Commercial formulations containing FFH 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 preanalyzed 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:**

Cobalt thiocyanate (CTC) [formed from the combination of ammonium thiocyanate and cobalt nitrate] has been proved to be a valuable reagent for the determination of amino compounds. In the present investigation the colored species

formed is the co - ordination complex of tertiary amine of VLS (electron donor) and central metal of the cobalt thiocyanate (acceptor) which is extractable into nitrobenzene from aqueous solution.

**Figure 2:** Showing the Scheme**Table 1:** Optical characteristics, precision and accuracy of proposed analytical method

Parameter	Values
$\lambda_{\max}$ (nm)	605
Beer's law limits ( $\mu\text{g ml}^{-1}$ )	8 - 48
Detection limits ( $\mu\text{g ml}^{-1}$ )	3.264
Molar absorptivity ( $1 \text{ mole cm}^{-1}$ )	$1.407 \times 10^5$
Sandell's sensitivity ( $\mu\text{g cm}^{-2} / 0.001$ absorbance unit)	0.00773
Regression equation ( $Y = a + bC$ ) Slope (b)	0.013
Standard deviation of slope ( $S_b$ )	$4.54 \times 10^{-4}$
Intercept (a)	0.009
Standard deviation of intercept ( $S_a$ )	$1.414 \times 10^{-2}$
Standard error of estimation ( $S_e$ )	$1.520 \times 10^{-2}$
Correlation coefficient ( $r^2$ )	0.995
Relative standard deviation (%) *	0.6783
% Range of error (Confidence limits) *0.05 level	0.7119
0.01 level	1.1165
% Error in bulk samples **	0.386

\*: Average of six determinations considered \*\*: Average of three determinations

**Table 2:** Analysis Valsartan by proposed and reference methods

Method	Formulations	Labeled Amount (mg)	Found by Proposed Methods	t	f	Recovery by Proposed
CTC	Tablet - 1	80	79.612 $\pm$ 0.364	0.56	1.93	99.446 $\pm$ 0.263

Average  $\pm$  Standard deviation of six determinations, the t - and f - values refer to comparison of the proposed method with UV reference method. Theoretical values at 95% confidence limits t = 2.57 and f = 5.05.

**4. Conclusion**

The reagents utilized in the proposed method are cheap, readily available and the procedure does not involve any critical reaction conditions or tedious sample preparation. The proposed extractive colorimetric method is validated as

per ICH guide lines and possess reasonable precision, accuracy, simple, sensitive and can be used as alternative

method to the reported ones for the routine determination of VLS depending on the need and situation.

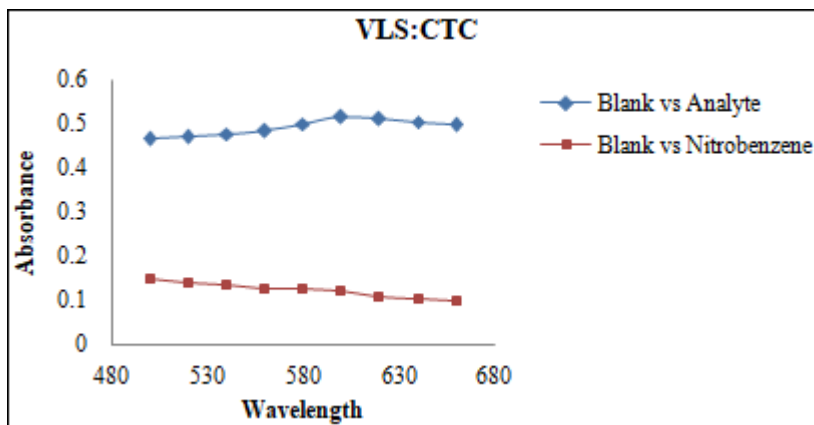


Figure 3: Absorption spectra of VLS – CTC

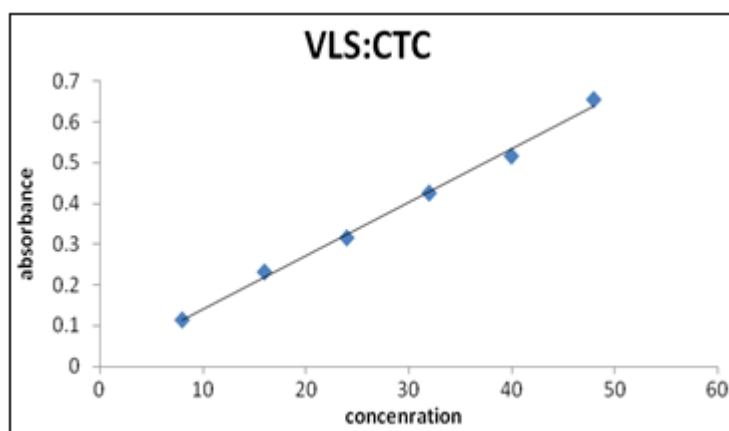


Figure 4: Beer's plot of VLS - CTC

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