Spectrophotometric method for estimation of Valsartan in bulk and tablet dosage form

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Abstract **- Simple, accurate, rapid and sensitive method has been developed for the estimation of Valsartan in bulk and pharmaceutical formulations. The method is based on the formation of ion association complex of the drug with eriochrome black-T in acidic buffer of pH 3.5 followed by extraction into chloroform. The linearity range of Valsartan with eriochrome black-T was found to be 50 – 250 µg/mL. The developed method was found to be precise and accurate from the statistical validation of the analytical data. The proposed method has been successfully applied for analysis of dosage formulations.**

Index Terms **- Valsartan, Eriochrome black-T and Spectrophotometric method.**

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.

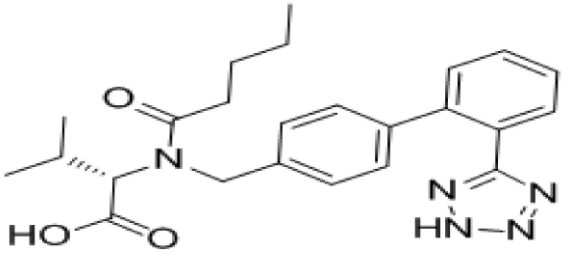


Fig 1 Valsartan

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.

Very limited references published on physico-chemical methods in the literature for the assay of VLS in biological fluids and pharmaceutical formulations. Most of them are based on HPLC, IC, CE, and UV-spectrophotometric methods. The analytically useful functional groups in VLS have not been fully exploited for designing suitable visible spectrophotometric methods and so still offer a scope to develop more visible spectrophotometric methods with better sensitivity, precision and accuracy. The author has made some attempts in this direction and succeeded in developing nine methods. All these methods have extended pharmaceutical formulations as well.

UV spectrophotometric method in methanol has been adopted for the determination of VLS in pharmaceutical formulations (Tablet), which has been made use of as a reference method to compare the results obtained by the proposed visible spectrophotometric methods.

EXPERIMENTAL MATERIALS AND METHODS

Instrument

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 and the solutions were freshly prepared with double distilled water.

Preparation of reagents:

Preparation of standard solution (1mg/mL): 100 mg of each drug was accurately weighed and transferred to separate 100 mL volumetric flasks. To dissolve the drug 5 mL of methanol was added to each flask and the volume was made up to the mark with distilled water.

Eriochrome black-T solution (0. 1%): 100 mg of eriochrome black-T was dissolved in 100 mL of distilled water and washed with chloroform to remove chloroform soluble impurities.

Acetate buffer (pH 3.5): 0.4 gm of anhydrous sodium acetate in 84 mL of distilled water and sufficient amount of glacial acetic acid to adjust pH to 3.5 (about 15 mL) and the volume was made up to 100 mL with distilled water.

Chloroform AR grade chloroform was used as it is

Selection of wavelength

In order to select the wavelength of maximum absorbance, Valsartan solutions were scanned in the range from 450-750 nm against the respective reagent blank to record the absorption spectra. The resulting spectra were shown in Fig 2 and the absorption curve showed characteristic absorption maxima at 660 nm for the drug.

Method :

Into a series of 125 ml separating funnels containing aliquots of standard VLS solution (0.5 – 3.0 ml; 200 µg/ml),. To each funnel 2.0 ml of buffer (pH = 3.5) and 2.0 ml of 0.1% w/v Eriochrome black-T were added. 10 ml of chloroform was added to each funnel. The solutions were shaken for 2 minutes thorough mixing of the two phases and were allowed to stand for clear separation of the layers The absorbance values of the chloroform layers were measured against their respective reagent blank at the wavelength of the maximum absorbance at λmax 660nm The colored species was stabled. The amount of VLS in sample solution was calculated by using Beers-Lambert's plot Fig 3.

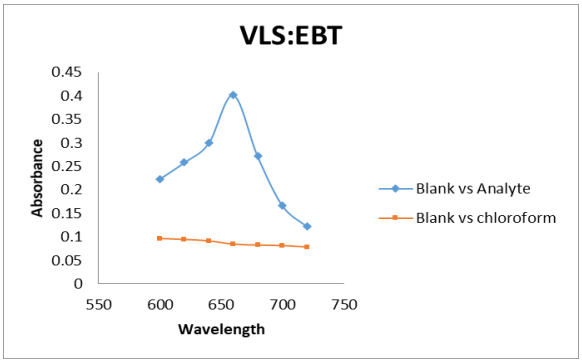


Fig.2. Absorption spectra of VLS: EBT

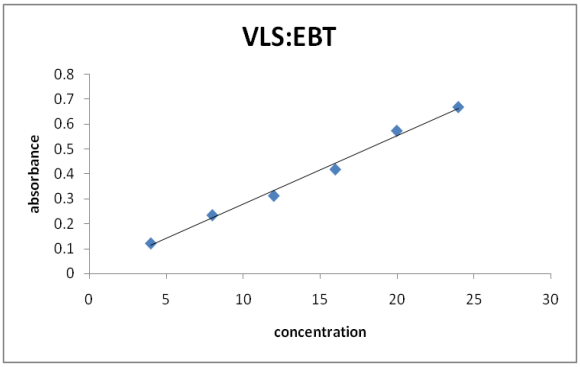


Fig 3. Beer's plot of VLS: EBT

Table 1: Optical and Regression characteristics, precision and accuracy of the proposed method for VLS

Parameter	Values
λ_{max} (nm)	660
Beer's law limits (µg ml^{-1})	4-24
Detection limits (µg ml^{-1})	2.637
Molar absorptivity (1 mole cm^{-1})	$2.844x10^5$
Sandell's sensitivity (µg cm^{-2} / 0.001 absorbance unit)	0.00956
Regression equation (Y = a + bC) Slope (b)	0.027
Standard deviation of slope (S_b)	$1.524x10^{-2}$
Intercept (a)	0.001
Standard deviation of intercept (S_a)	$2.374x10^{-2}$
Standard error of estimation (S_e)	$2.55x10^{-2}$
Correlation coefficient (r^2)	0.992
Relative standard deviation (%)*	1.0109
% Range of error (Confidence limits)*0.05 level	1.0611
0.01 level	1.6640
Error in bulk samples **	0.478

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

Table 2: ASSAY OF VLS IN PHARMACEUTICAL FORMULATIONS

Sample	Amount taken (mg)	Amount found by proposed method*	Reference method$	Percentage recovery by proposed method**
Tablet I	80	79.246± 0.386 F=2.17 t =1.12	79.552± 0.262	99.567± 0.167
Tablet II	80	79.748± 0.092 F=2.51 t =1.52	79.682± 0.146	99.208± 0.153

*: Average ± standard deviation of six determinations; the t- and F- values refer to comparison of the proposed method with the reference method. Theoretical values at 95% confidence limit t=2.57, F=5.05.

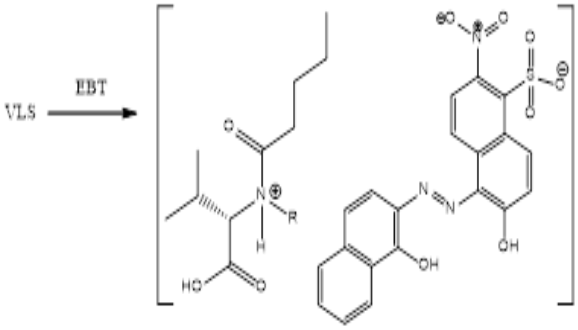
**: After adding2different amounts of the pure labeled to the pharmaceutical formulations, each value is an average of 3 determinations.

$: UV reference method

Chemistry of the colored species:

Valsartan possesses different functional moieties such as tertiary amino group and tetrazole group The proposed method is based on the reactivity of either tertiary amine (ion association complex formation with acid dye EBT)

Valsartan under slightly acidic conditions forms ion-association complex with acid dyes which is extractable into chloroform from aqueous phase. The protonated nitrogen (positive charge) of Valsartan is expected to attract the oppositely charged part of the dye and behave as a single unit being held together by electrostatic attraction as represented in the scheme.



Purple colored ion-pair complex

RESULTS AND DISCUSSION

The optimum conditions in the method is fixed basing on the study of the effects of various parameters such as type of acid or buffer, concentrations of acid, concentration of dye [EBT] choice of organic solvent, ratio of organic phase to aqueous phase, shaking time, temperature, intensity and stability of the colored species in organic phase. The author performed control experiments by measuring the absorbance's at appropriate λ_{max}660nmof a series of solutions varying one and fixing the other parameters and the results are presented in Table 1.

CONCLUSION

The proposed method is simple, rapid, sensitive and can be successfully applied for estimation of these drugs in pharmaceutical dosage form. The proposed reagent is cheaper and easily available and the method does not need any heating for color development.

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