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Visible Spectrophotometri determination of Valsartan in Pharmaceutical Formulations

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Abstract:

A simple, rapid, sensitive, and accurate extractive spectrophotometric method has been developed for the determination of Valsartan in pure forms as well as their pharmaceutical dosage forms. The method depends on the formation of an intensely colored ion-pair complex between the acidic drug and methylene blue in alkaline medium The complex is stable and extractable into methylene chloride. All parameters were optimized. Beer-Lambert's law was obeyed in concentrations ranging from 0.5.-3.0 ml, 200 µg/ml. Statistical analysis of the calibration data was carried out, and correlation coefficients were in the range from 0.9996 to 0.9998. The developed method was fully validated according to International Conference on Harmonization guidelines, and complied with U.S. Pharmacopeia guidelines. The proposed method was applied to the analysis of the investigated drugs in their pharmaceutical formulations, and good recoveries were obtained. The results obtained were compared with those of reported and official methods, and no significant differences were found with *t*- and *F*-tests. The method is applied successfully for the estimation Valsartan in tablet form without the interference of excipients.

Key words: Spectrophotometry, Valsartan, ion-pair complex, Beer-Lambert's law,methylene blue, U.S. Pharmacopeia guidelines.

Introdution

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.

Very limited referencespublished 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. 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.

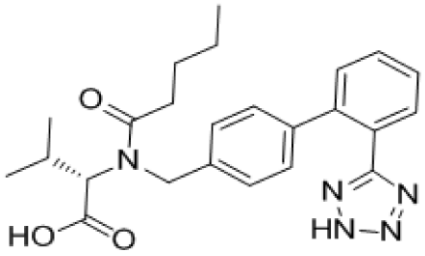


Figure1 chemical structure of Valsartan

EXPERIMENTAL

Instrument used

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.

Preparation of standard drug solutions:

The stock solution (1mg/ml) of VLS was prepared by dissolving 100mg of it in 100ml of methanol. A portion of this stock solution was diluted stepwise with the methanol to obtain the working standard VLS solution of concentrations 200 µg/ml .

Sample drug 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.Two ml of this solution was further diluted to 50 ml to get 40 µg/ml solution.

Preparation of reagents:

All the chemicals and reagents were of analytical grade and all solutions were freshly prepared in Millipore distilled water.

MB Solution (0.01%) : Prepared by dissolving 10 mg of methylene blue in 100ml of distilled water and subsequently washed with chloroform to remove chloroform soluble impurities

Buffer(pH =9.8) : Prepared by mixing 7 g of ammonium chloride with 6.8 ml of liquor ammonia solution and diluted with 100 ml distilled water and pH adjusted to 9.8 solution

Chloroform: AR grade chloroform was used as it is.

Recommended Procedures

Into a series of 125 ml separating funnels containing aliquots of standard VLS solution (0.5.-3.0 ml, 200 µg/ml); 1 ml of buffer (pH = 9.8) and 5 ml of MB (Methylene blue) were added and the volume was made up to 15 ml with distilled water and 10 ml of chloroform was added. . The contents were shaken for 2minutes. The two phases were allowed to separate and the absorbances of the separated organic layers were measured at λ_{max}666nm

against a similar reagent blank. The colored species was stable for 1 hour. The amount of VLS in sample solution was calculatedfrom the Beer-Lambert's plot Fig 2.

RESULTS AND DISCUSSION

Spectral characteristics

In order to ascertain the optimum wavelength of maximum absorption (λ_{max}) of the colored species formed in each of the above methods, specified amounts of VLS in final dilution 200 µg/ml were taken and the colors were developed (or diminished) separately following the above mentioned procedures. The absorption spectra were scanned in the wavelength region of 360 - 850 nm against a corresponding reagent blank. The reagent blank absorption spectrum of each method was also recorded against distilled water. The absorption curves of colored species formed in each method shows characteristic absorption maximum whereas the blank in each method has low or no absorption in this region.

In developing these methods, a systematic study of the effects of various relevant parameters in the methods concerned were undertaken by varying one parameter at a time and controlling all other parameters to get maximum color development, minimum blank color, reproducibility and the reasonable period of stability of final colored species formed. The following studies were conducted for this purpose.

The optimum conditions in the method was fixed basing on the study of the effects of various parameters such as type of acid or buffer, concentration of the acid, concentration of dye MB choice of organic solvent, ratio of organic phase to aqueous phase, shaking time and step, intensity and stability of the colored species in organic phase by measuring the absorbance at appropriate λ_m666nm. The optimum conditions developed and the actual conditions chosen for the procedure were recorded in Table1.

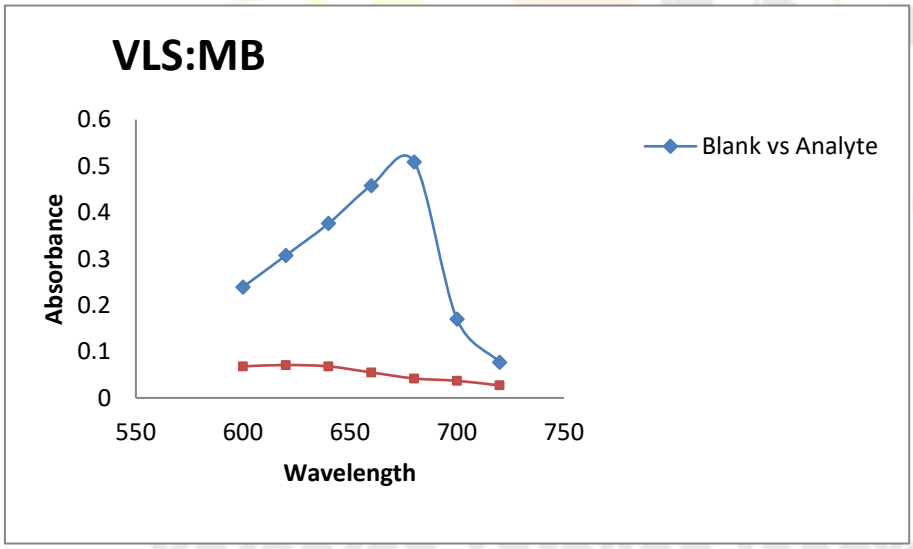


Fig.2: Absorption spectra of VLS: MB

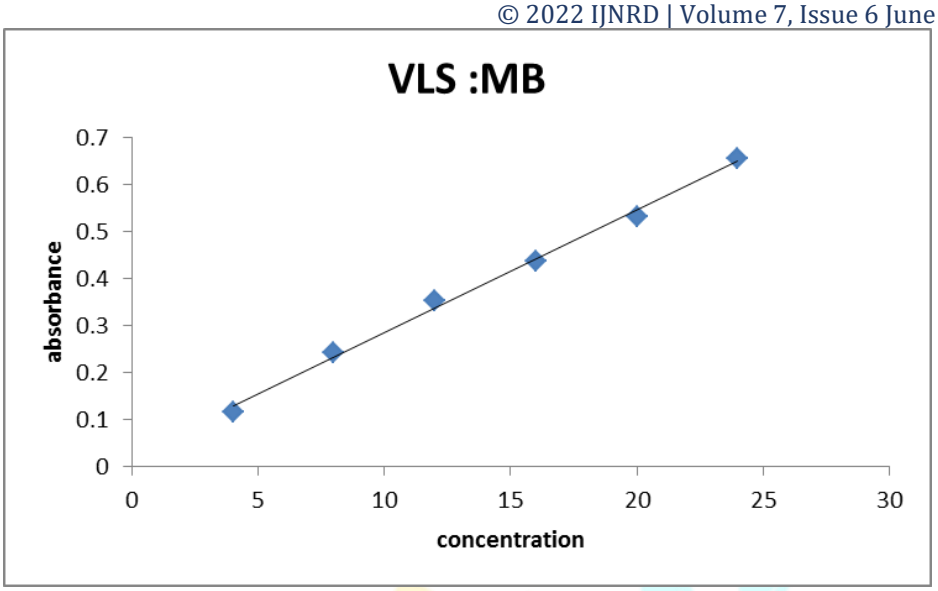


Fig 3: Beer's law plot of VLS: MB

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

Parameter	Results
λ_{max} (nm)	666
Beer's law limits (µg ml^{-1})	4-24
Detection limits (µg ml^{-1})	1.44
Molar absorptivity (1 mole cm^{-1})	$2.8962x10^{5}$
Sandell's sensitivity (µg cm^{-2} / 0.001 absorbance unit)	0.00751
Regressionequation (Y = a + bC) Slope (b)	0.026
Standard deviation of slope (S_b)	$8.043x10^{-4}$
Intercept (a)	0.023
Standard deviation of intercept (S_a)	$1.253x10^{-2}$
Standard error of estimation (S_e)	$1.34x10^{-2}$
Correlation coefficient (r^2)	0.996
Relative standard deviation (%)*	0.599

% Range of error (Confidence limits)*0.05 level	0.629
0.01 level	0.986
Error in bulk samples **	0.375

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

Table 2: ASSAY OF VLS IN PHARMACEUTICAL FORMULATIONS

samle	Amount taken(mg)	Amount found by proposed methods*	Reference methods $	Percentage recovery by proposed methods**
Tablet I	80	79.446± 0.342 F=1.70 t =0.82	79.552± 0.262	99.443± 0.119

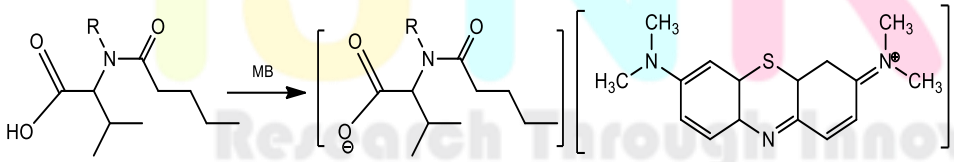
*: Average ± standard deviation of six determinations; the t- and F- values refer to comparison of the proposed method with the reference method. Theoretical values at 95% confidence limit t=2.57, F=5.05.

**: After adding 2 different amounts of the pure labeled to the pharmaceutical formulations, each value is an average of 3 determinations

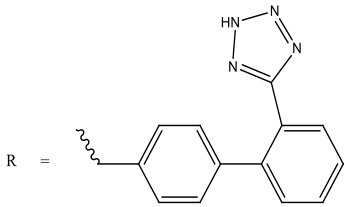
$: UVreference method

Chemistry of the colored species:

As VLS contains carboxylic acid group, it forms an ion association complex with a basic dye (MB) which is extractable into chloroform from aqueous phase. The cationic form of the dye (MB, M_4) involves in the formation of neutral colored ion- association complex by positive charge of the dye with negative charge due to acid group of the drug which is extractable into chloroform. It behaves as a single unit being held together by electrostatic attraction. It is supported by slope ratio method which was obtained as 1: 1.



Ion pair complex formed between OLS and MB



Conclusion:

The proposed method is simple, precise, accurate and economic with good precision and accuracy. With this method one can do analysis simply with cheap chemicals without losing accuracy. This method provides sensitivity comparable to that achieved by sophisticated and expensive techniques like HPLC. Hence this method can be employed as alternative for routine analysis of bulk sample and tablets.

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