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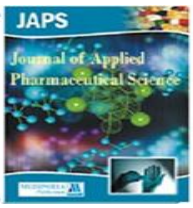

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A validated stability indicating HPLC method for the determination of Valsartan in tablet dosage forms.

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ABSTRACT

A simple, specific, rapid, precise and robust HPLC method has been developed for the quantitation of valsartan in tablet dosage form on a C_{18} column (250 x 4.6 mm) using a mobile phase consisting of ammonium dihydrogen phosphate buffer : methanol (33.5:66.5) adjusted to pH 3 with formic acid at a flow rate of 1.0 ml/min and detection at 265 nm. The retention time of valsartan was found to be at 11.9 min. The validation of above method was also done. Percentage label claim of the tablet formulations were found to be 100.8%. So the proposed method provides a faster and cost effective quality control tool for routine analysis of valsartan from formulations.

Key words: Valsartan, HPLC, ammonium dihydrogen phosphate buffer, methanol, validation.

INTRODUCTION

Valsartan is the second class of drug known as angiotensin receptor blockers (ARBs) which is 3-methyl-2-[pentanoyl-[[4-[2-(2H-tetrazol-5-yl)phenyl]phenyl] methyl]amino]butanoic acid and is used for treating high blood pressure. It acts by blocking the vasoconstrictor and aldosterone secreting effects of angiotensin II by selectively blocking the binding of angiotensin II to the ATI receptor in many tissues, such as vascular smooth muscle and adrenal gland. Literature survey revealed a number of estimation procedures of various combination of valsartan by both spectroscopy (Nevin., 2002) and chromatography (Flesch et al., 1997; Macek et al., 2006; Gonzalez et al., 2002). Derivative spectroscopic determinations include simultaneous estimations of valsartan(Tatar et al., 2002) with hydrochlorothiazide. A stripping voltammetric determination of valsartan using a hanging mercury drop electrode Habib et al., 2008)and Chromatographic determinations of valsartan combinations include ketoprofen, pantoprazole by HPLC (Kocyigit et al., 2006)was also described.Present work describes a validated stability indicating indicating method for valsartan from formulations.

MATERIALS AND METHODS

Present study was an attempt to develop a sensitive, rapid, less expensive and an accurate HPLC method for estimation of valsartan from dosage forms. Development of a validated HPLC method for valsartan in dosage forms was carried out using optimized chromatographic conditions. All solvents were of HPLC grade filtered through 0.45 µ membrane filter. Recovery studies gave results between 99 to 100%. Valsartan in pure

form was obtained as a gift sample from Torrent pharmaceuticals, Ahmedabad. Analysis was performed on a SHIMADZU model LC-2010HT with a PDA detector and C_{18} column of 250 x 4.6 mm and 5 µm dimensions and detection was carried at 265 nm. Valsartan 40 mg and 80 mg tablets manufactured and marketed by Torrent Pharmaceuticals were estimated.

Buffer solutions of mobile phase were prepared by taking 0.1M Ammonium dihydrogen phosphate and adjust to 3.0 with formic acid. Mobile phase was prepared by transferring 335ml of buffer solution into 665ml of methanol. Filtered and degassed the mixture.

Preparation of Standard and Sample solution

The standard solutions were prepared by taking accurately weighed 10 mg of valsartan standard into a 10 ml of volumetric flask. Dissolved and made up the volume with methanol and took 1 ml of the above solution and made up to 10 ml with mobile phase. The column was equilibrated for 30 min with mobile phase at a flow rate of 1.0 ml/min and kept the data processor in an area normalisation mode. 20 µl of methanol as a blank was injected in to the system and recorded the chromatogram to run time of 25 min and the data processor were programmed to inhibit the integration peaks due to blank and 20 µl of standard preparation is injected into the system and recorded the chromatogram to run time of 25 min. Retention time of valsartan is noted at 11.09 min and peak shapes were good. (fig1).

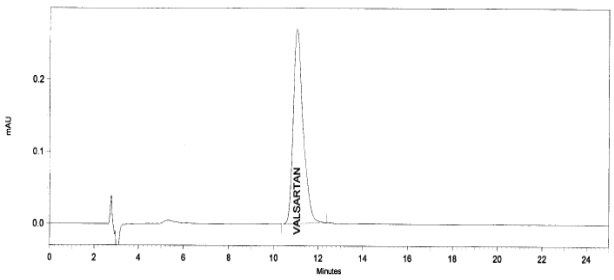

Fig.1: Chromatogram of valsartan ina conc. of 0.1 µg/ml

Different concentrations of standard solutions were made with mobile phase. These standard solutions were injected and peak areas were measured. The calibration curve was prepared by plotting concentration of valsartan versus peak area of the standard solution. Linearity graph was plotted and correlation coefficient was found as 0.999 and System suitability was performed by analysing six replicate injections of valsartan working standard solution. Relative standard deviations for six peak area was found to be 0.05.

20 tablets of Valsartan 40 mg and 80 mg were accurately weighed and average weights of the tablets were calculated. Weight of the powder equivalent to 10 mg was accurately weighed out and transferred to a volumetric flask and dissolved in 10 ml methanol HPLC grade and kept in an ultrasonic bath for a period of 20 min. Further dilutions were done with mobile phase. Finally 20 µl of assay preparation was injected in the system and recorded the area count for valsartan peak. The amount of valsartan present per tablet and percentage label claim was calculated (Table. 1).

Validation of the method

The method was validated as per specificity, linearity, precision, accuracy and system suitability parameters(Huber 1998). For specificity, placebo solutions and sample solutions were analysed and no peak was observed at the retention time of valsartan in the placebo chromatogram. Peak purity data indicated that the peak is homogeneous and there is no co-eluting peak. Stability of the solution is tested by storing valsartan working standard solution at room temperature for 12 h and analysing the sample on HPLC every 2 h for that period of storage.

The stability analysis proves that solution was stable for at least 12 h. Hence an extended period of analysis due to unavoidable circumstances would not interfere with the results of assay. Stability studies of valsartan were carried out under acidic (0.1 N HCL 40^0 C) basic (0.1 N NaOH 40^0 C), and oxidizing conditions (3% V/V H_2O_2, 40^0 C) it showed good stability in basic condition. Accuracy of the method was studied by recovery studies at 3 different levels mainly 50, 100 and 150%. Percentage recovery was calculated (Table.1). Precision study was performed by analysing six different samples of valsartan tablets on HPLC and relative standard deviation was calculated as 0.04. The LOD and LOQ of the drug valsartan were found to be 6 ng/ml and 18 ng/ml respectively.

TABLE 1: ANALYSIS OF FORMULATIONS AND RECOVERY STUDIES

Brand name (manufacturer)	Label claim (mg/tablet)	Estimated*		Relative Standard Deviation	%Recovery**
		mg/ tablet	%label claim		
Valzaar	80	80.65	100.81	0.04	99.4
Valzaar	40	40.35	100.88	0.05	100.6

*Mean (%RSD) of six observations, **Mean (%RSD) of three observations

RESULTS AND DISCUSSION

The results of analysis were treated statistically as per ICH guidelines for validation of analytical procedures. The results were found to be accurate and free from interference of tablet excipients. The high percentage recovery and low percentage deviation shows the accuracy, reliability and suitability of the method. Hence this will serve as a rapid, convenient and reliable method which can be applicable for routine analysis of valsartan in pharmaceutical dosage forms and may be extended to determine the concentration of valsartan in body fluids also.

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