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DEVELOPMENT AND VALIDATION OF ANALYTICAL TECHNIQUE FOR ANTI HYPERTENSIVES BY HIGH PERFORMANCE LIQUID CHROMATOGRAPHY (HPLC)

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ABSTRACT

Drug analysis plays an important role in the development of drugs, their manufacture and therapeutic use. Pharmaceutical industries rely upon quantitative chemical analysis to ensure that the raw material used and final products obtained meet the required specifications. The number of drugs and drug formulations introduced into the market has been increasing at an alarming rate. These drugs or formulations may be either new entities or partial structural modifications of the existing ones or novel dosage forms (controlled/ sustained release formulations) or multi component dosage forms. Very often, there is a time lag from the date of introduction of a drug into the market to the date of its inclusion in pharmacopoeias. This happens because of the possible uncertainties in the continuous and wider usage of these drugs, reports of new toxicities (resulting in their withdrawal from the market), development of patient resistance and introduction of better drugs by competitors. Under these conditions, standards and analytical procedures for these drugs may not available in pharmacopoeias. It becomes necessary, therefore, to develop newer analytical methods for such drugs. Considering all these views some drug formulations from Anti hypertensives were selected for the present study. An extensive literature survey was carried out and it is evident that methods like High Performance Liquid Chromatography (HPLC) have been reported for the estimation of these drugs in their biological fluids[15-17]. There are however, no reports for their estimation by HPLC in their formulations. It becomes essential, therefore, to develop newer rapid analytical methods by HPLC[1-14].

KEYWORDS: *Anti hypertensive drugs, analytical technique, development, validation, HPLC*

INTRODUCTION

DRUG PROFILE

TELMISARTAN

It is 4'- [(1,4'-Dimethyl 2'-propyl [2,6'-bi-1H-benzimidazol]-1'-yl) methyl] [1,1'-biphenyl]-2-carboxylic acid; 4'-[[4-metyl-6-(1-methyl-2-benzimi-dazolyl)-2-propyl-1 benzimidazolyl]methyl]-2-biphenylcarboxylic acid;

It is obtained as a white crystalline powder with m.p. **221-223°C**.

Telmisartan is a new angiotensin II receptor antagonist (like candesartan, irbesartan, losartan and valsartan) licensed for the treatment of essential hypertension only. Telmisartan lowers systolic/diastolic blood pressure in patients with hypertension by up to 12/9mm Hg at 40mg once daily, and up to 13/10mm Hg at 80mg once daily. It is at least as effective as enalapril, lisinopril, amlodipine, and losartan in the treatment of mild to moderate hypertension. Telmisartan gave better 24-hour control of blood pressure than amlodipine and losartan, particularly for the 18 to 24 hour period after dosing when serum levels are lowest and the risk of cardiovascular events is likely to be greatest.

Clinical trials show that the drug is well tolerated and has a lower incidence of cough than ACE inhibitors, although further evidence is required before the complete adverse drug reaction profile is known.

Telmisartan costs less than other angiotensin II receptor antagonists. Low dose thiazide diuretics or beta-blockers are preferred as first line therapy for the majority of hypertensive patients. ACE inhibitors are particularly appropriate for use in patients with heart failure, left ventricular dysfunction and type 1 diabetic nephropathy. Angiotensin II receptor antagonists are recommended for hypertension when patients cannot tolerate ACE inhibitors.Telmisartan

warrants consideration for these patients if current evidence is confirmed in further trials.

MATERIALS AND METHOD (EXPERIMENTAL)

ESTIMATION OF TELMISARTAN BY REVERSE PHASE HPLC METHOD

Instrument: HPLC (Waters)

Chemicals & Reagents:

Standard Telmisartan drug was procured from Glenmark pharma ltd. (Nasik).and formulations were obtained from drug stores in market. Acetonitrile HPLC grade and methanol HPLC grade from Merck were used.

Mobile phase

700.0 ml of Acetonitrile of HPLC grade and 300.0ml of Methanol of HPLC grade were taken and both were mixed and sonicated for 15 minutes and they are filtered through 4.5micron filter paper and further sonicated for 5 minutes.

Standard preparation

10mg of standard drug was taken in 10ml standard volumetric flask and dissolved in the mobile phase using sonicator. And the stock solution was further diluted to micro gram level concentration with the mobile phase.

Linearity of detector response

Linearity study was carried out at five different concentrations and it was found to be linear in range of 4 to 12 micro gram concentration (4mcg/ml, 6mcg/ml, 8mcg/ml, 10mcg/ml, 12mcg/ml) were prepared for Telmisartan and the **peak areas** Vs **concentrations** are plotted in the **Figure 1**.

Chromatography

The flow rate was maintained at 1ml/min. Temperature of the column (Thermo hypurity C18, 50*4.6mm, 5µ) was ambient, the average pressure was 1225 psi and the effluents were monitored at 245nm. The mobile phase used was Acetonitrile and methanol (70:30).

Calibration curve was constructed for Telmisartan by plotting the peak area of drug i.e. (y axis) against the concentration of drug µg/ml (x axis), **Figure 1.**

Experiment

Assay of twenty tablets of different manufacturer`s were procured from market, weighed and triturated finely, the powder equivalent to 40mg of the pure drug (347.8mg) was dissolved in mobile phase to get 10mcg/ml concentrations.

Twenty microlitres of sample preparation was injected into injector of liquid chromatography. From the peak response of Telmisartan the amount of drug in sample was computed.

Formula:

$$\%\text{Of Sample} = \frac{\text{Mean Area of Sample}}{\text{Mean Area of Standard}} \times \frac{\text{Weight of Standard}}{\text{Dilution Factor}} \times \frac{\text{Dilution Factor of Sample}}{\text{Weight of Sample}} \times \text{Label Claimed}$$

Recovery experiment

To study the accuracy, reproducibility and the precision of the proposed method recovery experiments were carried out. A fixed amount of pre analyzed sample was taken and standard drug was added at three different concentrations and each level repeated for 4 times.

RESULTS AND DISCUSSION

The present method is a high performance liquid chromatography method to determine Telmisartan from its formulations, various experiments were carried out to separate them and mobile phase Acetonitrile and Methanol in proportion of (70:30), is found to be ideal for the separation and elution of Telmisartan at (RT/1.52). The mean recovery of Telmisartan was 100.05% and 100.13%. The values of percent recovery and standard deviation shown that the proposed method is accurate, reproducible and precise. The summary of final results was given in **Table no.1, 2&3.**

Figure 1. Linearity Response of Detector for Telmisartan

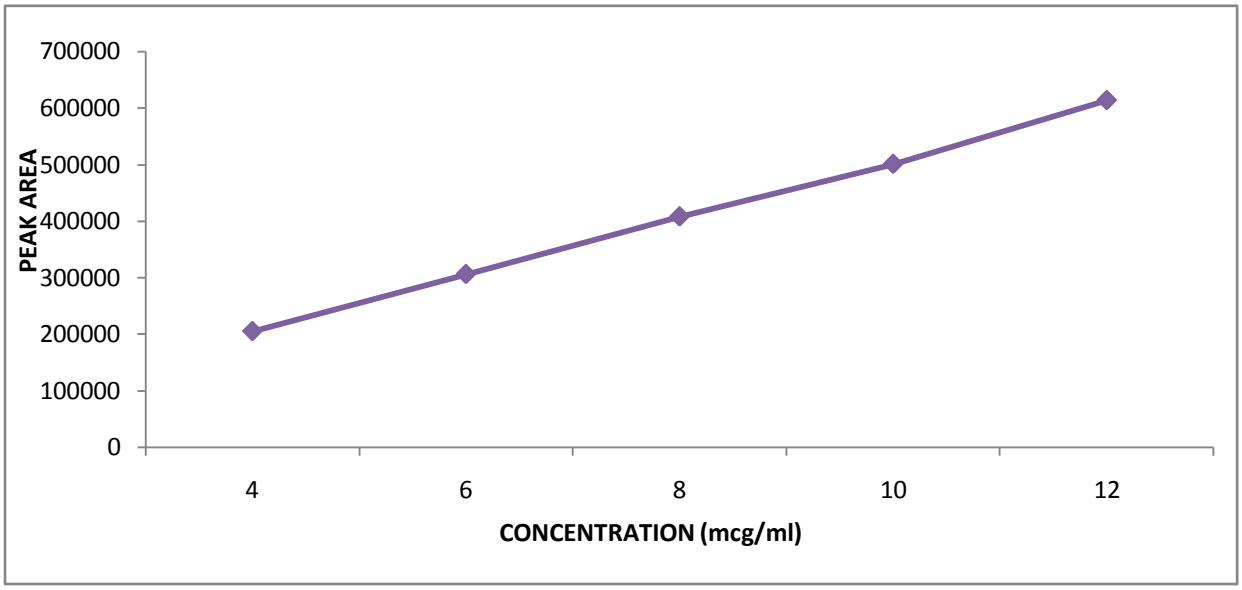

Table 1. Reproducibility experiment for Telmisartan

Sl. No	Name of company	Amount found Mg/ tablet + SD	%RSD	Percentage of Assay
1	TEL 1	40.089+0.293	0.22	100.22
2	TEL 2	40.178+0.422	0.44	100.44

Table 2. Recovery experiment for Telmisartan (TEL1)

Label claim amount of std added in mg	Amount of standard drug added in mg	Amount recovered in mg	% of recovery
40	0.0	39.99	99.97
40	5	44.98	99.95
40	10	50.06	100.12
40	15	55.09	100.16

Table: 3. Recovery experiment TEL 2

Label claim amount of std added in mg	Amount of standard drug added in mg	Amount recovered in mg	% of recovery
40	0.0	40.06	100.15
40	5	45.16	100.35
40	10	49.99	99.98
40	15	55.03	100.05

CONCLUSIONS

The accuracy of the method was noted and it was felt that method can be suitably adapted for other drugs and combinations in further studies.

HPLC method has been accurate and it gives details with regards best separation and calculation of concentration simultaneously.

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