Academic Sciences International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 3, Issue 4, 2011

Research Article

DEVELOPMENT AND VALIDATION OF RP-HPLC METHOD FOR SIMULTANEOUS ESTIMATION OF TELMISARTAN AND HYDROCHLOROTHIAZIDE IN TABLETS: IT'S APPLICATION TO ROUTINE QUALITY CONTROL ANALYSIS

J. KAVITHA[1]*, J.S.K. NAGARAJAN[2], S. MURALIDHARAN[3] AND B. SURESH[4]

***[1]SRM College of Pharmacy, Kattankulathur, Kanchipuram Dist, Tamilnadu, India, [2,3 & 4]J.S.S.College of Pharmacy, Rocklands, Ootacamund, Tamilnadu, India. *Email: kavitha0208@yahoo.com**

Received: 6 June 2011, Revised and Accepted: 5 July 2011

ABSTRACT

A very simple, rapid and sensitive RP-HPLC method has been developed and validated for the analysis of Telmisartan and Hydrochlorothiazide in tablet formulation. Best chromatographic resolution was achieved on a reverse-phase Princeton SPHER C_{18} column using acetonitrile: 50mM potassium dihydrogen ortho phosphate (pH 3.5) ratio 50:50 as mobile phase with a flow rate of 1mL/min and isocratic elution with a total run time of 10 minutes. Sulphadoxine was selected as internal standard. The retention time of Telmisartan, Hydrochlorothiazide and Internal Standard was found to be 4.71, 7.06 and 9.56 respectively. Detection of the multicompounds was carried out at 270nm. The present newly developed method was found to be accurate, precise and can be useful for routine Quality control analysis.

Keywords: Telmisartan, Hydrochlorothiazide, Sulphadoxine, RP-HPLC.

INTRODUCTION

Telmisartan is chemically[1] 2-(4-{[4-methyl-6-(1-methyl-1*H*-1,3-benzodiazol-2-yl)-2-propyl-1*H*-1,3-benzodiazol-1-yl]methyl}phenyl)benzoic acid. Telmisartan is an angiotensin II receptor antagonist (ARB) used in the management of hypertension. Hydrochlorothiazide (HCT) is chemically[1] 6-chloro-1,1-dioxo-3,4-dihydro-2H-1,2,4-benzothiadiazine-7-sulfonamide. HCT is a popular diuretic drug of the thiazide class. It is often used in the treatment of hypertension, congestive heart failure, symptomatic edema and in the prevention of kidney stones. Many methods[2-12] have been reported on individual as well as simultaneous estimation on these drugs. The present method is relatively very simple, rapid and highly sensitive for the analysis of Telmisartan and Hydrochlorothiazide in bulk or in any other formulations. The present method developed is also validated as per ICH guidelines in the analysis of the multicomponents of interest and it can be used for routine Quality control analysis in laboratories.

MATERIALS AND METHODS

Telmisartan (purity: 98.91%), Hydrochlorothiazide (purity: 99.97%) and Sulphadoxine (purity: 99.81%) were obtained from Micro labs (Bangalore, India), Saimira (Chennai, India) and Micro labs (Bangalore, India) respectively. Acetonitrile was of HPLC grade and obtained from E.merck (Mumbai, India) and all other chemicals used were of analytical grade. Purified water from Milli-Q-system (Millipore, Bangalore, India) was used throughout the analysis.

Instrumentation and Analytical Conditions

HPLC Chromatographic separation was performed on a Shimadzu® liquid chromatographic system equipped with a LC-10AT-vp solvent delivery system (pump), SPD M-10AVP photo diode array detector, Rheodyne 7725i injector with 50 µl loop volume. Class-VP 6.01 data station was applied for data collecting and processing (Shimadzu, Japan). Best HPLC separation was carried out using reverse phase C_{18} Princeton SPHER (250 × 4.6 mm) column of 5µ, using acetonitrile : 50 mM Potassium dihydrogen orthophosphate (pH 3.5) in the ratio (50 : 50) as mobile phase at a flow rate of 1.0 ml/min and detection and detection carried out at 270 nm. The mobile phase was filtered through a 0.45 µm membrane filter (Millipore®).

Preparation of standard solutions

Standard solutions were prepared (each) by accurately weighing 100.00 mg of each of the reference drug and transferred to 100.00 ml volumetric flask and dissolved in a mixture of acetonitrile : water (1:1v/v) to give a final concentration of 1 mg/mL, stored at 4°C and can be suitably diluted used for further analysis.

Preparation of Sample Solution

Twenty tablets, (Brand name: Arbitel-H) each containing 40 mg Telmisartan and 12.5 mg Hydrochlorothiazide were weighed and average weight was calculated. One fourth of the average weight was accurately weighed and transferred to 100.00 ml volumetric flask and dissolved by sonication in a mixture of acetonitrile : water (1:1v/v) to give a final concentration of 1 mg/mL. The solution was stored at 4°C and suitably diluted for further analysis.

Method validation

The objective of method validation is to demonstrate that the method is suitable for its intended purpose as it is stated in ICH guidelines. The method was validated for linearity, precision (repeatability and intermediate precision), accuracy specificity, short-term stability and system suitability. Telmisartan standard plots were constructed with six concentrations in the range of 10–60 µg/mL prepared in triplicates to test linearity. Hydrochlorothiazide standard plots were constructed with six concentrations in the rangµe of 2.5–15 µg/mL prepared in triplicates to test linearity. The ratio of peak area signal of each drug to that of IS was plotted against the corresponding concentration to obtain the calibration graph. The linearity was evaluated by linear regression analysis that was calculated by the least square regression method. The precision of the assay was studied with respect to both repeatability and intermediate precision. Repeatability was calculated from six replicate injections of each freshly prepared standard solution in the same equipment at a concentration 50 µg/mL of the intended test concentration value on the same day. The experiment was repeated by assaying freshly prepared solution at the same concentration additionally on two consecutive days to determine intermediate precision. Peak area ratios of each standard to that of IS were determined and precision was reported as % R.S.D. Method accuracy was tested (% recovery and % R.S.D. of individual measurements) by analyzing samples of each drug at three different levels in pure solutions using three preparations for each level. The results were expressed as the percentage of each drug recovered in the samples. Specificity was assessed by comparing the chromatograms obtained from sample of pharmaceutical preparation and standard solution with those obtained from excipients which take part in the commercial tablets and verifying the absence of interferences. Sample solution short-term stability was tested at ambient temperature (20±1°C) for three days. In order to confirm the stability of both standard solutions at 100% level and tablets sample solutions, both solutions protected from light were re-injected after 24 and 48 h at ambient temperature and compared with freshly prepared solutions. System suitability test was performed by six replicate injections of the standard solution at a concentration of 50 µg/mL

verifying IS/DI resolution >2; %R.S.D. of peak area ratios of each standard to that of IS ±2%; %R.S.D. of each peak retention time ±2%.

RESULTS AND DISCUSSION

Validation of methods

Linearity

Six point's calibration graphs were constructed covering a concentration range 10–60 and 2.5-15 µg/mL of Telmisartan and Hydrochlorothiazide respectively. Three independent determinations were performed at each concentration. Linear relationships between the ratio of the peak area signal of each Standard to that of IS versus the corresponding drug concentration were observed. The standard deviations of the slope and intercept were low. The determination coefficient (r^2) exceeded 0.99 (Fig. 1).

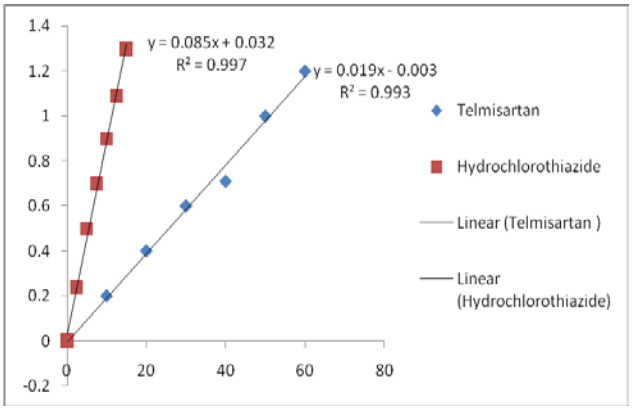

Fig. 1: Calibration Curve

(Concentration Vs Response factor)

Precision

The repeatability study (n = 6) carried out showed a %RSD of 0.858% for the peak area ratios of each standard to that of IS obtained, thus showing that the equipment used for the study worked correctly for the developed analytical method and being highly repetitive. For the intermediate precision, a study carried out by the same analyst working on two consecutive days (n = 3) indicated a %RSD of 0.744%. Both values were far below 5%, the limit percentage set for the precision and indicated a good method precision.

Stability

The stability of Telmisartan and Hydrochlorothiazide in standard and sample solutions containing IS was determined by storing the solutions at ambient temperature (20±1°C) protected from light. The solutions were checked in triplicate after three successive days of storage and the data were compared with freshly prepared samples. In each case, it could be noticed that solutions were stable for 72 h, as during this time the results did not decrease below 97%. This denotes that the drugs are stable in both standard and sample solutions for at least 3 days at ambient temperature, protected from light and is compatible with IS.

Accuracy

The data for accuracy were expressed in terms of percentage recoveries of Telmisartan and Hydrochlorothiazide in the real samples. These results are summarized in Table 1.

Table 1: Accuracy study for Arbitel-H (n=5)

Nominal Concentration (µg/mL)	Observed Concentration (µg/mL)	% Purity
Telmisartan		
10	9.9083±0.18	99.1
30	29.4405±0.68	98.1
60	59.3188±1.44	98.9
Hydrochlorothiazide		
2.5	2.499±0.10	100.0
7.5	7.4513±0.14	99.4
15	14.9017±0.41	99.3

Specificity

The HPLC chromatogram recorded for the mixture of the drug excipients revealed no peak within a retention time range of 15 min. The results showed that the developed method was specific as none of the excipients interfered with the analytes of interest.

System suitability

The resolution factor between IS and each Drug, in the developed method, was above 2. The % RSD of peak area ratios of each drug to that of IS and retention times for both drug and IS were within 2% indicating the suitability of the system (Table 2). These results indicate the applicability of this method to routine with no problems, its suitability being proved. The statistical evaluation of the proposed method revealed its good linearity, reproducibility and its validation for different parameters and led us to the conclusion that it could be used for the rapid and reliable determination of Telmisartan and Hydrochlorothiazide in pharmaceutical forms.

Table 2: System Suitability

Parameters	Telmisartan	Hydrochlorothiazide
Theoretical plate/meter	6525	5249
Asymmetric factor	0.92	1.04
LOD (µg/mL)	0.98	0.05
LOQ (µg/mL)	2.98	0.17

Assay of tablets

The validated method was applied for the assay of commercial tablets containing 40 mg of Telmisartan and 12.5 mg of Hydrochlorothiazide (Arbitel-H) each sample was analyzed in triplicate after extracting the drug as mentioned in assay sample preparation of the experimental section and injections were carried out in triplicate. Chromatogram of the sample solution was given in Fig. 2; it also showed that none of the tablet ingredients interfered with the analyte peak.

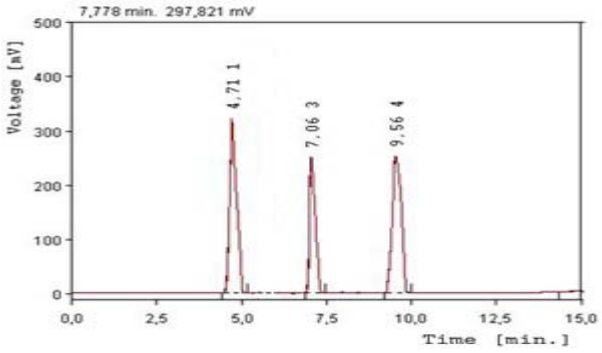

Fig. 2: Sample Chromatogram

CONCLUSION

A validated isocratic RP-HPLC method has been developed for the determination of Telmisartan and Hydrochlorothiazide in dosage forms. The proposed method is very simple, rapid, accurate, precise and specific. Its chromatographic run time of 10 mins allows the analysis of a large number of samples in a short period of time. Therefore, it is suitable for the routine analysis of pharmaceutical dosage forms. The simplicity of the method allows for application in laboratories that lack sophisticated analytical instruments such as LC–MS/MS or GC–MS/MS that are complicated, costly and time consuming rather than a simple HPLC–UV method. Considering the possible worldwide development of counterfeit Arbitel-H, the proposed method could be useful for the national quality control laboratories in developing countries.

ACKNOWLEDGEMENT

The Authors are grateful to Dr.B.Suresh, Vice-chancellor, JSS University and Dr.K.Elango, Principal, JSS College of Pharmacy, JSS University, Ootacamund, Tamil Nadu, for providing necessary facilities to carry out this work.

REFERENCE

1. Indian Pharmacopoeia; 1996. p. 371-372.
2. Indian Pharmacopoeia; 2010. p. 2187-2188.
3. http://en.wikipedia.org.
4. Sujana K, Gowri Sankar D, Bala Souri O, Swathi Rani G. Stability indicating RP-HPLC method for the determination of Telmisartan in pure and pharmaceutical formulation. International Journal of Pharmacy and Pharmaceutical Sciences 2011; 3 Suppl 2: 164-167.
5. Gangola R, Singh N, Gaurav A, Maithani M, Singh R. Spectrophotometric simultaneous determination of hydrochlorothiazide and telmisartan in combined dosage form by dual wavelength method. International journal of comprehensive pharmacy 2011. 2 Suppl 2: 1-3.
6. Sunil J, Jeyalakshmi K, Krishnamurthy T, Kumar Y. Development and Validation of Simultaneous HPLC method for Estimation of Telmisartan and Ramipril in Pharmaceutical Formulations. International Journal of PharmTech Research 2010; 2 Suppl 2: 1625-1633.
7. Phani Kishore Ch, Bhanuprakash Reddy V, Dhanashri M Kale. Development and validation of stability indicating HPLC method for the estimation of Telmisartan related substances in tablets formulation. International Journal of Research and Pharmaceutical Sciences 2010; 1 Suppl 4: 493-501.
8. Patel G, Patel S, Prajapiti D, Rajendra Mehta *S.* RP-HPLC Method for Simultaneous Estimation of Amlodipine Besylate and Hydrochlorothiazide in Combined Dosage Forms. Journal of Pharmaceutical Sciences 2010; 3 Suppl 1: 49-53.
9. Bhatia NM, Shinde HV, Bhatia MS, Choudhari PB, Ingale KB. Development and validation of spectrophotometric and ion pair chromatographic techniques for estimation of telmisartan and hydrochlorothiazide. Ars Pharmaceutica 2010; 51 Suppl 3: 145-154.
10. Bankey S, Tapadiya GG, Saboo SS, Bindaiya S, Deepti jain, Khadbadi SS. Simultaneous determination of ramipril, hydrochlorothizide and telmisartan by Spectrophotometry. International Journal of ChemTech Research 2009; 1 Suppl 2: 183-188.
11. Kurade VP, Pai MG, Gude R. RP-HPLC estimation of ramipril and telmisartan in tablets. Indian Journal of Pharmaceutical Sciences 2009; 71 Suppl 2: 148.
12. Gupta Y, Shrivastava A. Isocratic RP-HPLC-UV method development and validation for the simultaneous estimation ramipril and telmisartan in tablet dosage form. Asian Journal of Pharmaceutical and Clinical Research 2009; 2 Suppl 4: 104-111.
13. Patil UP, Gandhi SV, Sengar MR, Rajmane VS. Simultaneous determination of atorvastatin calcium and telmisartan in tablet dosage form by spectrophotometry. International Journal of ChemTech Research 2009; 1 Suppl 4: 970-973.
14. Suresh B, Meyyanathan SN, Rajan S, Muralidharan S, Arunadevi S birajdar. A validated RP-HPLC method for simultaneous estimation of nebivolol and hydrochlorothiazide in tablets. Indian Journal of Pharmaceutical Sciences 2008; 70 Suppl 5: 687-689.
15. Wankhede SB, Tajne MR, Gupta KR, Wadodkar SG. RP-HPLC method for simultaneous estimation of telmisartan and hydrochlorothiazide in tablet dosage form. Indian Journal of Pharmaceutical Sciences 2007; 69 Suppl 2: 298-300.
16. Idress F. Al-moman. Determination of Hydrochlorothiazide and Enalapril Maleate in Tablet Formulations by Reversed-Phase HPLC. Turkey Journal of Chemistry 2001; 25: 49- 54.