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Research Article

ESTIMATION OF TRIMEBUTINE MALEATE IN TABLET DOSAGE FORM BY RP-HPLC

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ABSTRACT
A simple, precise, rapid and accurate reverse phase HPLC method was developed for the estimation of Trimebutine Maleate in tablet dosage form. An XTerra(R) C18 analytical column (250 x 4.6 mm, 5 µm partical size) with mobile phase consisting of mixture of buffer 0.02M Ammonium Acetate in water and acetonitrile in the gradient program was used. The flow rate was 1.0 mL/min and the effluents were monitored at 275 nm. The retention time was 17.0 minutes. The detector response was linear in the concentration of 20-300 mcg/mL. The respective linear regression equation being y = 1914.1 x -1911. The limit of detection and limit of quantification was 0.5 mcg/mL and 1.5 mcg/mL respectively. The percentage assay of Trimebutine Maleate was 99.8 %. The method was validated by determining its accuracy, precision and system suitability. The results of the study showed that the proposed RP-HPLC method is simple, rapid, precise and accurate, which is useful for the routine determination of Trimebutine Maleate in bulk drug and in its pharmaceutical dosage form.
Keywords: Trimebutine Maleate, RP-HPLC and Tablets.

INTRODUCTION

Trimebutine Maleate, the active pharmaceutical ingredient in Gast-reg® (Trimebutine Maleate 100 mg tablets) Tablets, Trimebutine is a drug with antimuscarinic and weak mu opioid agonist effects[1,2]. The maleic acid salt of trimebutine is marketed under the trademark of Debridat, Recutin, Polybutin, or Modulon for treatment of irritable bowel syndrome and other gastrointestinal disorders. The major product from drug metabolism of trimebutine in human beings is nor-trimebutine, which comes from removal of one of the methyl groups attached to nitrogen. Both Trimebutine and its metabolite are commercially available. Trimebutine Maleate is off-white to light yellow crystals or crystalline powder. The chemical name of Trimebutine Maleate is 2-(Dimethylamino)-2-phenylbutyl 3,4,5-trimethoxybenzoate (Figure 1) and the molecular formula[2] is $C_{22}H_{29}NO_5$ with a molecular weight of 387.47. Literature survey[3-7] reveals no chromatographic methods for the estimation of Trimebutine Maleate from pharmaceutical tablet dosage forms. The availability of an HPLC method with high sensitivity and selectivity will be very useful for the determination of Trimebutine Maleate in tablet dosage form. The aim of the study was to develop a simple, precise and accurate reversed-phase HPLC method for the estimation of Trimebutine Maleate in bulk drug samples and in pharmaceutical tablet dosage form.

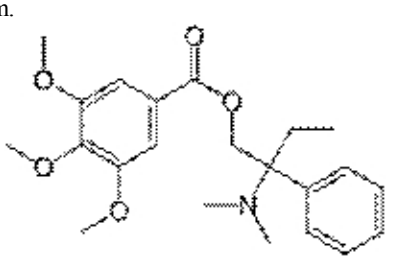

Figure 1: Structure of Trimebutine

MATERIALS AND METHODS

Trimebutine Maleate was obtained as a gift sample from M/s. Vishnu Chemicals Ltd, Hyderabad, India. Acetonitrile, Ammonium acetate and water used were of HPLC grade (Qualigens). Commercially available Trimebutine Maleate tablets (Gast-reg® Trimebutine Maleate 100 mg tablets) were procured from local market.

Instrument

Quantitative HPLC was performed on liquid Chromatograph, Shimadzu LC 2010 dual λ detector equipped with automatic injector with injection volume 20 µL. The HPLC system was equipped with LC solution Software.

HPLC Conditions

The contents of the mobile phase were mixture of buffer 0.02 M Ammonium acetate in water and acetonitrile in the gradient program (shown in Table 4). They were filtered before use through a 0.45 µm membrane filter, and pumped from the respective solvent reservoirs to the column at a flow rate of 1.0 mL/min. The run time was set at 30.0 minutes and the column temperature was ambient. Prior to the injection of the drug solution, the column was equilibrated for at least 30 minutes with the mobile phase flowing through the system. The eluents were monitored at 275 nm.

Preparation of Standard Stock solution

A standard stock solution of the drug was prepared by dissolving 10 mg of Trimebutine Maleate in 10 mL volumetric flask and dissolved in diluent (Acetonitrile and Water:50:50), sonicated for about 15 minutes and then made up to 10 mL with diluent get 1000 mcg/mL standard stock solution.

Working Standard solution

2 mL of the above stock solution was taken in 10 mL volumetric flask and thereafter made up to 10 mL with

diluent (Acetonitrile and Water: 50:50) to get a concentration of 200 mcg/mL.

Preparation of Sample solution

Twenty tablets (Gast-reg® Trimebutine Maleate 100 mg tablets) were weighed, and then powdered. A sample of the powdered tablets, equivalent to 50 mg of the active ingredient, was mixed with 30 mL of diluent in 50 mL volumetric flask. The mixture was allowed to stand for 15 minutes with intermittent sonication to ensure complete solubility of the drug, and then filtered through a 0.45 µm membrane filter, followed by adding diluent up 50 mL to obtain a stock solution of 1000 mcg/mL. 10 mL of the above solution was taken and further diluted with diluent up to 50 mL to get working sample solution of 200 mcg/mL.

Linearity

Aliquots of standard Trimebutine Maleate stock solution were taken in different 10 mL volumetric flasks and diluted up to the mark with the mobile phase such that the final concentrations of Trimebutine Maleate are in the range of 20-300 mcg/mL. Each of these drug solutions (20 µL) was injected three times into the column, and the peak areas and retention times were recorded. Evaluation was performed with PDA detector at 275 nm and a Calibration graph was obtained by plotting peak area versus concentration of Trimebutine Maleate (Figure 3). The plot of peak area of each sample against respective concentration of Trimebutine Maleate was found to be linear in the range of 20–3000 mcg/mL with correlation coefficient of 0.9999. Linear regression least square fit data obtained from the measurements are given in Table 1. The respective linear regression equation being y = 1914.1 x -1911. The regression characteristics, such as slope, intercept, and % RSD were calculated for this method and given in Table 1.

Assay

20 µL of sample solution was injected into the injector of liquid chromatograph. The retention time was found to be 17.0 minutes. The amount of drug present per tablet was calculated by comparing the peak area of the sample solution with that of the standard solution. The data are presented in Table 2.

Recovery Studies

Accuracy was determined by recovery studies of Trimebutine Maleate, known amount of standard was added to the pre analyzed sample and subjected to the proposed HPLC analysis. Results of recovery study are shown in Table 2. The study was done at three different concentration levels.

Table 1: Linear Regression Data for Calibration curves

Drug	Trimebutine Maleate
Concentration range (mcg/mL)	20-300
Slope (m)	1914.1
Intercept (b)	-1911
Correlation coefficient	0.9999
% RSD	0.83

Table 2: Results of HPLC Assay and Recovery studies

Sample	Amount claim (mg/tablet)	% found by the proposed method	% Recovery*
1.	100	99.85	99.12
2.	100	99.92	98.96
3.	100	99.63	99.22

*Average of three different concentration levels

Table 3: Validation Summary

Validation Parameter	Results
System Suitability	
Theoretical Plates (N)	8688
Tailing factor	1.20
Retention time in minutes	17.0
% Area	99.96
LOD (mcg/mL)	0.5
LOQ (mcg/mL)	1.5

Table 4: Gradient Program in HPLC method

Time in minutes	Buffer	Acetonotrile
0	80	20
5	80	20
12	30	70
20	30	70
25	80	20
30	80	20

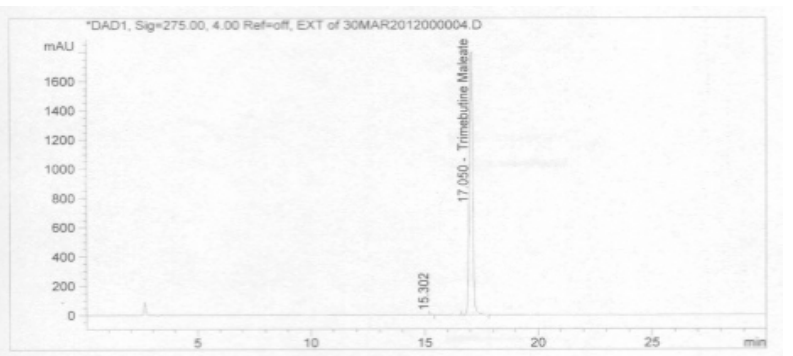

Figure 2: Typical Chromatogram of Trimebutine Maleate by HPLC

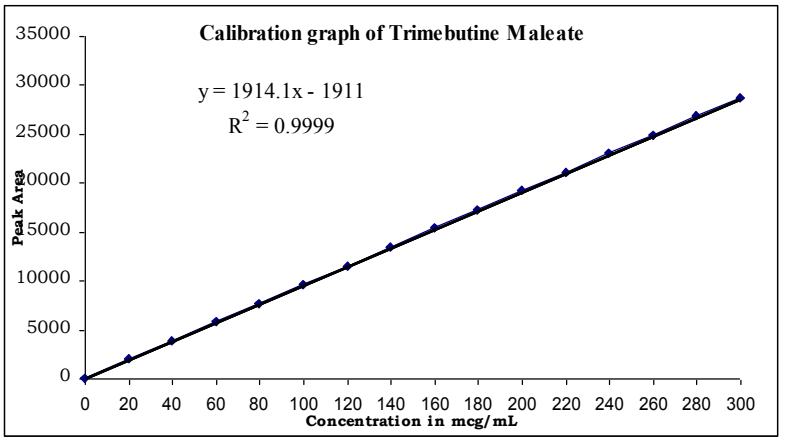

Figure 3: Calibration curve of the Trimebutine Maleate by RP-HPLC

RESULTS AND DISCUSSION

The system suitability tests were carried out on freshly prepared standard stock solution of Trimebutine Maleate. Parameters that were studied to evaluate the suitability of the system are given in Table 3.

Limit of Detection (LOD) and Limit of Quantification (LOQ)

The limit of detection (LOD) and limit of quantification (LOQ) for Trimebutine Maleate were found to be 0.5 mcg/mL and 1.5 mcg/mL respectively. The signal to noise ratio is 3 for LOD and 10 for LOQ. From the typical chromatogram of Trimebutine Maleate as shown in Figure 2, it was found that the retention time was 17.0 minutes. A mixture of buffer 0.02 M Ammonium acetate in water and acetonitrile in the gradient program (shown in Table 4) was found to be most suitable to obtain a peak well defined and free from tailing. In the present developed HPLC method, the standard and sample preparation required less time and no tedious extractions were involved. A good linear relationship (r^2 = 0.9999) was observed between the concentration range of 20-300 mcg/mL. Low values of standard deviation are indicative of the high precision of the method. The assay of Trimebutine Maleate tablets was found to be 99.8 %. From the recovery studies it was found that about 99.1 % of Trimebutine Maleate was recovered which indicates high accuracy of the method. The absence of additional peaks in the chromatogram indicates non-interference of the common excipients used in the tablets. This demonstrates that the developed HPLC method is simple, linear, accurate, sensitive and reproducible. Thus, the developed method can be easily used for the routine quality control of bulk and tablet dosage forms of Trimebutine Maleate within a short analysis time.

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REFERENCES

1. Roman FJ, Lanet S, Hamon J *et al*. Pharmacological properties of trimebutine and N-monodesmethyltrimebutine. J Pharmacol Exp Ther 1999; 289: 1391-7.
2. Delvaux M, Wingate D. Trimebutine: mechanism of ac- tion, effects on gastrointestinal function and clinical results. JInt Med Res 1997; 25: 225-46.
3. Jhee OH, Lee YS, Shaw LM, Jeon YC, Lee MH, Lee SH, Kang JS. Pharmacokinetic and bio equivalence evaluation of two formulations of 100 mg trimebutine maleate (Recutin and Polybutin) in healthy male volunteers using the LC-MS/MS method. Clin Chim Acta 2007; 375(1-2): 69-75. http://dx.doi.org/10.1016/j.cca.2006.06.006
4. Eun Hee J, Woo Ik C, Injoon O, Sang Chul S, Han Kwang N, Yong Bok L. High-performance liquid chromatographic determination of trimebutine and its major metabolite, N-monodesmethyl trimebutine, in rat and human plasma. J. Chromatogr. B 1999; 723: 239-46.
5. Wang H, Zhou H, Horimoto S, Jiang J, Mayumi T, Hu P. Quantitative determination of rimebutine maleate and its three metabolites in human plasma by liquid chromatography-tandem mass spectrometry. J. Chromatogr. B 2002; 779: 173-87. http://dx.doi.org/10.1016/S1570-0232(02)00369-0
6. Astier A, Deutsch AM. Quantitative high- performance liquid chromatographic determination of antispasmodic trimebutine in human plasma: pharmacokinetic studies after intravenous administration in humans. J Chromatogr 1981; 224: 149-55. http://dx.doi.org/10.1016/S0378-4347(00)80150-4
7. Jiang H, Ding L, Yang J, Huang X, Liu GY, Zhang ZX. Pharmacokinetic and bio equivalence of trimebutine dispersive tablet in healthy subjects. Yao Xue Xue Bao 2004; 39: 208-11.

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