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Development and Validation of RP-HPLC Method for Estimation of Zolmitriptan in Tablet Dosage Forms

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A rapid, simple and precise reversed phase high performance liquid chromatography (RP-HPLC) method was developed for the estimation of zolmitriptan in tablets. The quantification was carried out using a X-Terra RP C-18 column (150 mm × 4.6 mm i.d., 5 µm particle size) in isocratic mode with mobile phase comprising of phosphate buffer, acetonitrile and methanol in the ratio of 65:15:20 (v/v) at a flow rate of 1 mL/min. The eluent was monitored at 225 nm. The retention time of the drug was 4.278 min. The calibration curve was linear in the concentration range of 5-70 µg/mL and per cent recovery ranged from 99.8-100.08.

Key Words: Zolmitriptan, RP-HPLC, Tablets.

INTRODUCTION

Zolmitriptan[1] is chemically (S)-4-[[3-[2-(dimethylamino)ethyl]-1*H*-indol-5-yl]-methyl]-2-oxazolidinone. It binds with high affinity to 5-HT_{1D} and 5-HT_{1B} receptors and is used for acute treatment of migraine attacks. Literature survey reveals that few HPLC[2-4] and CE[5,6] methods have been reported for estimation of zolmitriptan in pharmaceutical formulations and biological fluids. The proposed method is simple, rapid, highly accurate and precise for estimation of zolmitriptan in tablets.

EXPERIMENTAL

An isocratic high performance liquid chromatograph (Waters Alliance 2695 separations module) equipped with 600e controller pump, 776 autosampler, 2487 dual λ absorbance detector was used. The chromatographic column used was 150 mm × 4.6 mm i.d., X-Terra RP C-18 column with 5 µm particles. The system was equipped with Empower software on Pentium computer.

HPLC grade acetonitrile, methanol, sodium dihydrogen phosphate from E. Merck (India) Ltd., Mumbai, potassium dihydrogen ortho phosphate of AR grade (rankem Ltd.) and milli-Q water were used for preparing the mobile phase.

pH 9.85 buffer preparation: 0.3g of potassium di-hydrogen phosphate and 0.5 g of sodium dihydrogen phosphate was diluted to 1000 mL with milli-Q water and adjusted to pH 9.85 with 10 % sodium hydroxide solution.

Chromatographic conditions: The mobile phase consists of phosphate buffer, acetonitrile and methanol in the ratio of 65:15:20 (v/v). The mobile phases was mixed thoroughly and filtered through 0.45 µ membrane filter and sonicated before use. The flow rate of mobile phase was maintained at 1 mL/min and run time was set at 8 min. The column was maintained at 25 ± 2 °C and the volume of each injection was 10 µL. Prior to injecting solutions, the column was equilibrated for at least 0.5 h with mobile phase flow through the system. The eluent was monitored at 225 nm.

Procedure: About 25 mg of pure sample of zolmitriptan was weighed accurately and transferred to 250 mL volumetric flask and dissolved in 100 mL of mobile phase. The solution was sonicated for 5 min and then the volume made up with further quantity of mobile phase to get 100 µg/mL solution. Subsequent dilutions of this solution ranging from 5-70 µg/mL were made in 10 mL volumetric flasks. The solutions were filtered through 0.45 µm membrane filter and then 10 µL of filtrate was injected each time into the column at flow rate of 1 mL/min. Evaluation of the drug was performed at 225 nm. Peak area was recorded for all peaks. A plot of peak area *versus* the respective concentration gives the calibration curve. The regression of drug concentration over the peak area was computed. The regression equation was used to estimate the amount of zolmitriptan in tablets.

Estimation of zolmitriptan in tablet dosage forms: Tablet powder equivalent to 25 mg was taken in 250 mL volumetric flask and 100 mL of mobile phase was added. The solution was sonicated for complete solubility of the drug, made up to the mark with the mobile phase and filtered through a 0.45 µm membrane filter. From the filtrate, different aliquots were taken in separate 10 mL volumetric flasks. The contents of the flask were made up to volume with mobile phase and mixed well. Each of the solutions (10 µL) was then injected five times into the column. From the peak areas, the drug content in tablets was quantified using the regression equation obtained from pure sample.

RESULTS AND DISCUSSION

The present study was carried out to develop a simple, rapid, accurate and precise HPLC method for the analysis of zolmitriptan in tablet dosage forms. The run time of the method was set at 8 min and the retention time for zolmitriptan was 4.278 min. This indicates that the present HPLC method is rapid, which in turn shows that the method consumes less volume of HPLC solvents. When same drug solution was injected 6 times, the retention time of the drug was same.

The peak areas from such different concentrations set up above were calculated and are shown in Table-1. A good linear relationship (r = 0.9999) was observed between the concentration of zolmitriptan and the respective peak area. The regression curve was constructed by linear regression fitting and its mathematical expression was y = 136368x - 732.38 (where y is peak area and x is the concentration of zolmitriptan).The intra-day and inter-day variations of the method were determined

TABLE-1
CALIBRATION OF THE PROPOSED METHOD

Drug concentration (µg/mL)	Peak area	Drug concentration (µg/mL)	Peak area
5	680257	40	5448481
10	1360216	50	6870552
20	2720524	60	8182506
30	4080936	70	9516407

Regression Equation from 5-70 µg/mL; Y = 136368X – 732.38 (r = 0.9999).

using three replicate injections of four different concentrations, which were prepared and analyzed on the same day and three different days over a period of two weeks, a low coefficient of variation was observed (Table-2). This shows that the present HPLC method is highly precise.

TABLE-2
PRECISION OF THE PROPOSED METHOD

Concentration of zolmitriptan (µg/mL)	Observed concentration of zolmitriptan (µg/mL)			
	Intra-day		Inter-day	
	Mean (n = 3)	CV (%)	Mean (n = 3)	CV (%)
10	9.95	0.402	9.89	0.267
20	19.97	0.321	19.88	0.126
30	30.01	0.216	29.87	0.153
40	39.71	0.737	39.81	0.566

To ensure reliability and accuracy of the method, recovery studies were carried out mixing a known quantity of drug with preanalyzed sample and the contents were reanalyzed by the proposed method. The values are shown in Table-3. About 99.8 % of zolmitriptan could be recovered from the preanalyzed samples indicating the high accuracy of the proposed HPLC method.

TABLE-3
RESULTS OF THE RECOVERY STUDY

Amount of drug added (µg)	Recovery from drug solution		Recovery from tablet formulation	
	Mean amount found (n = 3)	Mean % recovery	Mean amount found (n = 3)	Mean % recovery
10	9.986	99.86	9.96	99.66
20	19.950	99.78	19.97	99.88
30	30.020	100.07	30.01	100.04

The drug content in tablets was quantified using the proposed analytical method and the results are shown in Table-4. No interfering peaks were found in the chromatogram indicating that the tablet excipients did not interfere with the estimation of the drug by proposed method (Fig. 1). The tablets were found to contain 99.6-100.08 % of the drug. It can be concluded that the proposed HPLC method is sufficiently sensitive and reproducible for the analysis of zolmitriptan in tablet dosage forms with a short analysis time.

TABLE-4
ASSAY OF ZOLMITRIPTAN IN TABLET DOSAGE FORMS

S. No.	Labeled amount of drug (mg)	Mean (± SD) amount (mg) by the proposed method (n = 5)	Mean (± SD) % labeled amount (n = 5)
Tablet-1	5.0	4.98 ± 0.049	99.6 ± 0.88
Tablet-2	5.0	4.99 ± 0.050	99.84 ± 0.95
Tablet-3	2.5	2.502 ± 0.080	100.08 ± 0.33
Tablet-4	2.5	2.49 ± 0.011	99.76 ± 0.45

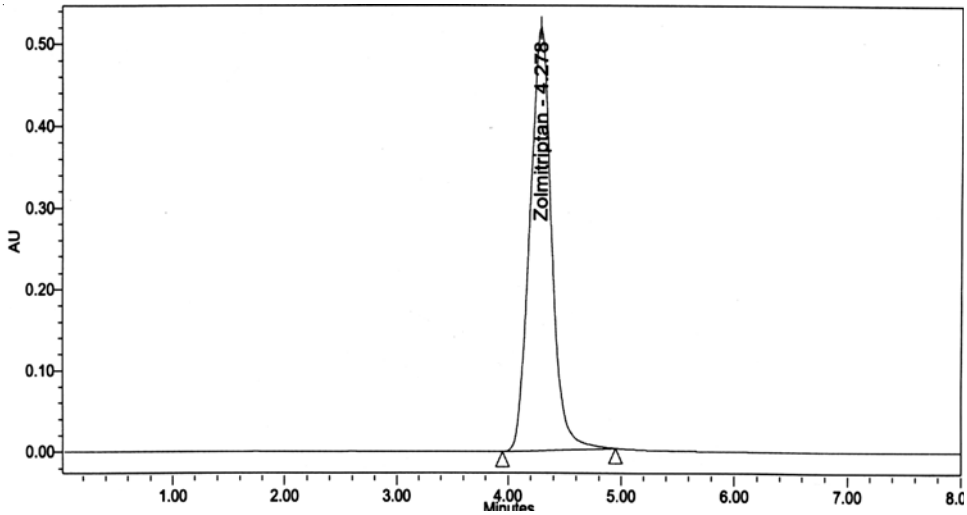

Fig. 1. Representative chromatogram of zolmitriptan

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