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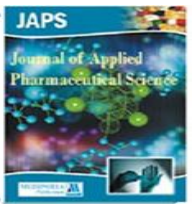

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Quantitative determination of lamotrigi1ne in bulk and dosage form by UV Spectrophotometry

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ABSTRACT

A new simple, rapid and precise spectroscopic method in UV region was developed for the quantitative determination of lamotrigine in bulk and in dosage form. In 0.1 M NaOH, Lamotrigine shows maximum absorbance at 307 nm. In proposed method Lamotrigine follows linearity in the concentration range 5-50 mcg/ml.The correlation coefficient for lamotrigine was found to be 0.99. The method was validated for Linearity, Precision and Accuracy.

Key words: Lamotrigine, UV, Spectroscopic Method.

INTRODUCTION

Lamotrigine is chemically, (6-(2, 3-dichlorophenyl)-1, 2, 4-triazine-3,5-diamine) which has chemical formula $C_9H_7C_{l2}N_5$, mol. wt. 256.09 is an anticonvulsant drug used in the treatment of epilepsy and bipolar disorder(IP, 2007; USP, 2000; Sweetman et al., 2005). It is used to treat partial seizures, primary and secondary tonic-clonic seizures and seizures associated with Lennox-Gastaut syndrome. Lamotrigine also acts as a mood stabilizer. It is the first medicament since lithium approved by food and drug administration (FDA) for the maintenance treatment of bipolar type I disorder. Chemically unrelated to other anticonvulsants, lamotrigine has relatively few side-effects and does not require blood monitoring (Ramse et al., 1991; Morris et al., 1998). A very few methods in literature were reported for the determination of lamotrigine and its metabolites in human plasma. Literature reported methods on HPLC (Puvvada et.al, 2010; Sallustio et al., 1997; Magda et al., 2010; Kumar et al., 2010; Beck et al., 2006; Stoforidis et al., 1999; Manuela et al., 2005; Emami et al., 2006; Hart et al., 1997), LC-MS (Jimenez et al., 2009; Olof et al., 2006; Murali et al., 2008), HPTLC (Patil et al., 2004) and Spectrophotometry (Alizadeh et al., 2008; Talekar et al., 2000; Rajput et al., 2004) for the determination of lamotrigine individually and in combination with other drugs and related substances in dosage forms and biological fluids. The objective of the present work is to develop simple, rapid and precise UV spectroscopic method for the determination of lamotrigine in bulk and in dosage forms.

MATERIALS

Lamotrigine as the reference standard was provided by Torrent Pharma as a gift sample. The chemicals of analytical reagent grade purchased from various sources. Doubly distilled water was used to prepare all solutions. Freshly prepared solutions were employed. The Lamotrigine tablets were purchased from local Pharmacies. UV Spectrophotometer (Shimadzu, model1800) was employed for spectra measurements.

METHODS

Lamotrigine Stock Solution

50 mg of Lamotrigine was weighed and dissolved in 20 ml of 0.1 M NaOH, sonicated for 20 min. Then final volume to100 ml was made up with 0.1 M NaOH to get concentration of 500 µg/ml. 2ml of this solution was further diluted with 0.1 M NaOH to make the volume 100ml to get the standard stock solution of concentration 100 µg/ml.

Method Development

Aliquots of stock solution were further diluted with 0.1 M NaOH to get working solution of 5, 10, 20, 30, 40 and 50 µg/ml and the working standards were scanned between 275 - 350 nm which shows the maximum absorbance at 307 nm. (Figure 1)

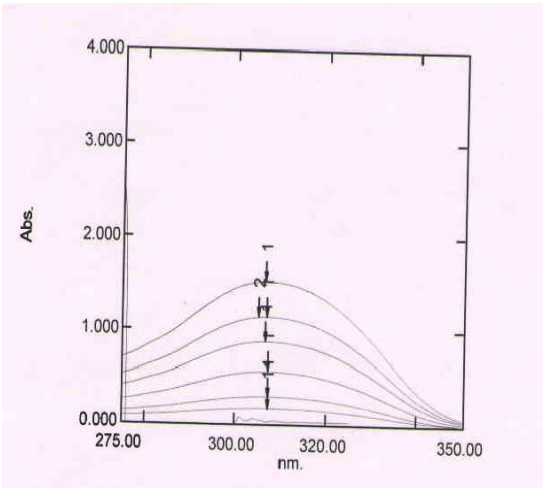

Fig 1. UV spectrum of Lamotrigine

Procedure for Calibration Curve

Aliquots of stock solution were further diluted with 0.1 M NaOH to get working solution of 5, 10, 20, 30, 40 and 50 µg/ml. Subsequently, the prepared standards were measured after standing for 5 min at λ max as recorded in (Table 1) in each case against a solvent blank similarly prepared. A calibration curve of the absorbance against the concentration of the drug was plotted. This was shown in Figure 2.

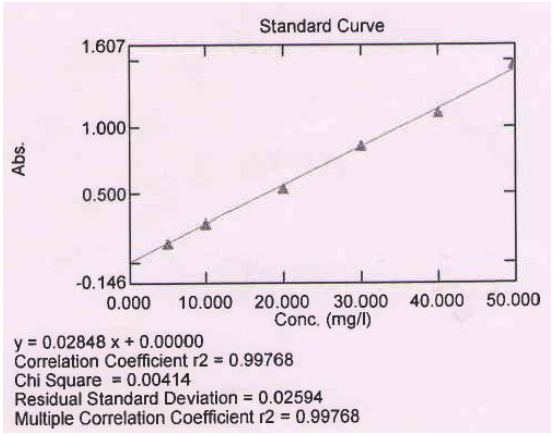

Fig 2. Calibration Curve of Lamotrigine

Table 1. Optical characteristics of method

Parameter	Value
λ max, nm	307
Beer's Law limit, µg/ml	5-50
Molar absorptivity, $Lmol^{-1}cm^{-1}$	2848
Regression equation, slope(b)	0.02848
Intercept(a)	0.0000
Correlation coefficient (r)	0.99768

Procedure for Pharmaceutical Preparations

For analysis of dosage form; twenty tablets were taken and powdered. The powder equivalent to 50 mg of Lamotrigine was accurately weighed or measured and transferred to 100 ml volumetric flask and dissolved in 20 ml 0.1 M NaOH . Then the solution was sonicated for 20 min. The resulting solution was further diluted to 100 ml with0.1 M NaOH and filtered through Whatman filter paper no. 41. 2 ml of the above solution was pipetted out into 100 ml volumetric flask and made up to the mark with 0.1 M NaOH. 5 ml of the above solution was pipetted out into 50 ml volumetric flask and made up to the mark with 0.1 M NaOH. The absorbance was measured at 307 nm against the blank. The amount of the drug in a sample was calculated from the calibration curve. The results are reported in Table 2.

Validation Method

The precision of the method for the drug was found by measuring the absorbance of 6 separate samples containing known amount of drug. The method was validated by studying the following parameters as ICH guidelines (ICH guidelines., 1995) for method validation. The slope, intercept, correlation coefficient and optical characteristic are summarized in Table 1.

Table 2. Results of assay of Lamotrigine Tablet Dosage Form

Brand	Forms	Label Claim (mg)	*Found(mg) ±S.D	% Label Claim	%RSD
Lamitor OD100	Tablet	100	99.55 ±0.132	99.55%	0.130

*mean±SD of three observations

Precision

Inter-day precision: This was done by analyzing formulation for six days subsequently. The %RSD values are shown in Table 3.

Table 3. Intraday and Interday Precision of Method

*Amount Found (mg)		% RSD	
Intraday	Interday	Intraday	Interday
98.701± 0.618	98.558±0.699	0.626	0.709

**mean±SD of Six observations*

Intra-day Precision: This was done by analyzing formulation in same day for six times. The %RSD and data are shown in Table 3. Recovery studies were carried out by adding 8 mg, 10mg and 12 mg of pure drug to different samples of tablet powder containing equivalent to10 mg of drug. From the amount of drug found, percentage recovery was calculated. The % recovery and the % RSD values are shown in Table 4.

Table 4. Results of Recovery Studies

Formulation Amount Present (µg/ml)	Amount of Standard drug Added (µg/ml)	% Recovery	SD	%RSD
10	8	98.39	0.4874	0.3950
10	10	99.40	0.4497	0.4523
10	12	98.51	0.2478	0.2515

mean±SD of three observations

RESULT AND DISCUSSION

It can be seen from Figure 1 that the spectrum of lamotrigine has a maximum absorbance at 307 nm in 0.1 M NaOH. The method obeys Beer - Lambert law within the range of 5 - 50 µg/ml and the calibration curve showed linearity as shown in Figure 2. It can be observed from Table 1 that the slope and intercept of the equation of the regression line are 0.02848 and 0.000 respectively. Correlation coefficient was found to be 0.99768.

The relative standard deviation 0.626 was observed for analysis of 6 replicate samples. The results of recovery studies were expressed as percent recoveries and the means were 98.39, 99.40 and 98.51%. These values showed the good accuracy of the UV proposed method.

CONCLUSION

The developed method is found to be simple, sensitive, accurate, precise and reproducible and being most economical due to use of solvent 0.1 M NaOH and less time consuming, can be used for routine determination of lamotrigine in bulk and dosage form.

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