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DEVELOPMENT AND VALIDATION OF UV/VISIBLE SPECTROPHOTOMETRIC METHOD FOR THE ESTIMATION OF LAMOTRIGINE IN BULK AND PHARMACEUTICAL FORMULATIONS

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ABSTRACT

A simple, sensitive, accurate and reproducible UV/ visible Spectrophotometric method was developed for the determination of Lamotrigine in bulk and pharmaceutical dosage forms. The solvent used was acetonitrile and wavelength corresponding to maximum absorbance for the drug was found at 422nm. Drug obeyed beers law in the concentration range of 2-10µg/ml. with a correlation coefficient of 1. The linear regression equation obtained was y= 0.017x, where y is the absorbance and x is the concentration of the pure drug solution. The method was validated for several parameters such as linearity, accuracy, precision and robustness as per the ICH guidelines. The % recovery value which is close to 100% indicates reproducibility of the method and absence of interference of the excipients present in the formulation. The authors conclude that the proposed spectrophotometric method for the estimation of Lamotrigine can be used for routine analysis of Lamotrigine in bulk as well in tablet dosage form.

KEYWORDS: Lamotrigine, spectroscope, absorbance, wavelength and ICH guidelines.

1. INTRODUCTION

The chemical formula for lamotrigine is 6-(2,3-chlorophenyl)-1,2,4-triazine-3,5-diamine and it is shown in fig.1.[1] An anticonvulsant medication called Lamotrigine is used to treat bipolar disorder and epilepsy.[2] It is used to treat partial seizures, lennox-gastaut syndrome-related seizures, and primary and secondary tonic-clonic seizures in people with epilepsy.[3] Different chemically from other anticonvulsants (since lamotrigine is a phenyl triazine). When used as a monotherapy, Lamotrigine has comparatively little side effects and doesn't require blood monitoring. Moreover, Lamotrigine stabilizes mood.[4] For epilepsy, a starting dose of less than 1 mg is advised. For epilepsy, the usual therapeutic range is 300–500 mg per day.[5] The usual practice is to raise and decrease Lamotrigine dosages gradually.[6] As with most other psychiatric drugs, extremely modest variations in dosage frequently have dramatically different effects; as little as 10% more or less may make a visible difference. A therapeutic response may need weeks or months of consecutive dose escalations. The UV approach provided by the previously published Spectrophotometric method, as seen in the literature review, uses acetonitrile as a solvent, which may not be appropriate for an oral dose form. Because of this, the current interaction which uses distilled water as a solvent—is more practical, precise, and repeatable.

Fig. 1: Lamotrigine structural formula.

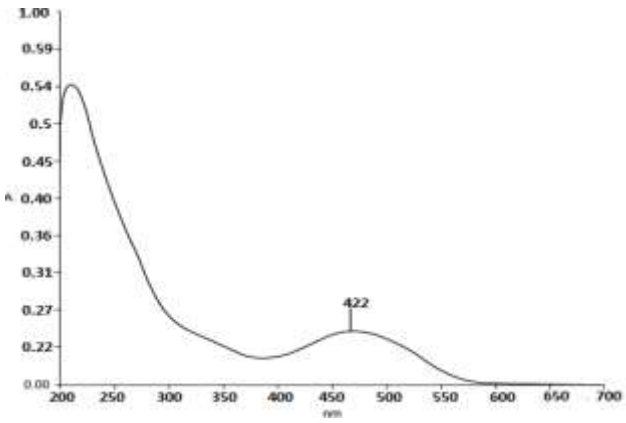

Fig. 2: Lamotrigine showed maximum absorbance at 422nm.

2. MATERIALS AND METHODS

2.1. Instrumentation

A visible double beam spectrophotometer with a matched pair of 1cm quartz cell was employed for measuring the absorbance of all the solutions.

2.1.1. Chemicals and Reagents

Lamotrigine was obtained as a gift sample from Vaagdevi Pharmacy College Bollikunta (Telangana) and analytical reagent grade, Acetonitrile.

2.1.2. Preparation of Standard Stock Solution

Standard stock solution was prepared by dissolving 10mg of Lamotrigine in 10ml of AR grade acetonitrile. The final concentration of this stock solution being 100µg/ml.

2.1.3. Determination of Wavelength of Lamotrigine

By appropriate dilution of standard stock solutions of lamotrigine in acetonitrile containing 10g/ml of lamotrigine, dilutions were made and scanned on chromo a visible double beam spectrophotometer in the range of 200-800nm against acetonitrile as blank. Wavelength of maximum absorption was determined for drug. Lamotrigine showed maximum absorbance at 422nm and it was depicted in fig.2.

2.1.4. Preparation of Standard Solution

Stock solution samples were diluted with acetonitrile to prepare a series of concentration of 2-10 g/ml. The solutions were scanned and their absorbencies were measured at 422nm using acetonitrile as a blank. All estimations were done in triplicate and the average values were reported.

3. Method Validation

The method was validated for several parameters like linearity, accuracy, precision, robustness according to ICH guidelines.

4. RESULT AND DISCUSSION

4.1. Linearity

The linearity of the analytical method was its ability to elicit test results which are directly proportional to analyte concentration in samples within a given range. To establish the linearity of the proposed method, various aliquots of the standard solution of the drug were prepared from stock solution and analyzed.

The calibration graphs were obtained by plotting the absorbance versus the concentration data and were treated by linear regression analysis. The drug showed linearity in the range of 2-10µg/ml with a correlation coefficient of 0.017. The slope, correlation-coefficient and optical characteristics are summarized in table 1 and 2 and figure 1.

Table 1: Concentrion and absorbance obtained for standard lot of lamotrigine in acetonitrile.

S.No	Concentration in ml	Absorbance
1	2	0.035
2	4	0.07
3	6	0.105
4	8	0.14
5	10	0.175

Table 2: Optimum conditions, optical characteristics and statistical data of the regression equation for Lamotrigine.

SNo	Parameters	Value
1	Absorption maximum(nm)	422
2	Beer ‘s law limit(mcg/ml)	2-8
3	Correlation co-efficient	1
4	Regression equation	y=Ax-b
5	Slope(A)	0.017

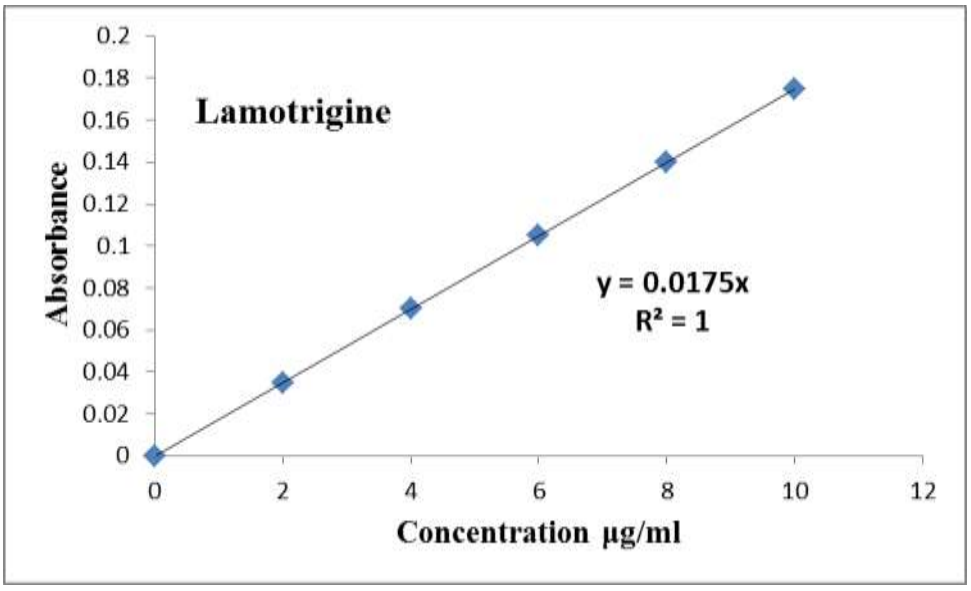

Fig. 1: Linearity of Lamotrigine.

4.1.1. Accuracy

Accuracy of the proposed method was determined using recovery studies. Accuracy was determined by known amounts of the analyte into the formulation (F1,F2 and F3) across the

specified range of the analytical procedure to obtain 4,5 and 6g/ml(4,5 and 6). At each level, solutions were prepared in triplicate and the accuracy was evaluated in terms of percent recovery (table 3). Percent recovery was calculated using the formula, [%recovery= 100 x mean experimental concentration theoretical concentration]

Table 3: Percentage recovery for Lamotrigine according to the proposed method.

S.NO	Initial amount (mg/ml)	Add of known qty of pure drug (to 100ml of formulation)	Total theoretical drug concentration in µg/ml	Mean experimental drug concentration found in µg/ml	%Recovery
1	0mg	4mg	4	4.12	102
2	0mg	5mg	5	4.11	98
3	0mg	6mg	6	6.17	102

4.1.2. Precision

Precision studies were carried out to ascertain the reproducibility of the proposed method. The precision of the assay method was determined by repeatability (intra-day) and intermediate precision was evaluated by analyzing six samples of 5µg/ml of the test concentration (n=6) at an interval of half an hour each.

Similarly inter day precision was evaluated on two consecutive days (n=12). Inter day precision was evaluated by 3 samples at an interval at an interval of 1 hour on day 2. The concentration of the drug was determined and the value of relative standard deviation (%R.S.D) of the assay method was calculated. The precision result showed a good repeatability with percent relative standard deviation less than 2. (table 4 and 5).

Table 4: Intraday Precision for Lamotrigine.

Time in mins	Absorbance (n=3)	Total theoretical drug concentration in µg/ml	Total experimental drug concentration found in µg/ml
30	0.083	5	4.88
90	0.081	5	4.7
150	0.082	5	4.8

Table 5: Inter-day precision for Lamotrigine.

Time in mins	Absorbance (n=3)	Total theoretical drug concentration in µg/ml	Total experimental drug concentration found in µg/ml
30	0.083	5	4.88
90	0.081	5	4.7
150	0.082	5	4.8

4.1.3. Robustness

Robustness was determined by carrying out analysis by two different analyst and also by carrying out the analysis on two different instruments and the respective absorbance was noted and the results was indicated as SD. Four sample solutions each containing 5g/ml were prepared and analyzed in two different UV/ visible spectrophotometers immediately after preparation. (Table 6)

Table 6: Robustness data for Lamotrigine.

S.NO	Spectrophotometer 1		Spectrophotometer 2	
	Abs	conc	Abs	conc
1	0.081	4.7	0.083	4.88
2	0.082	4.8	0.082	4.8

5. SUMMARY

6. CONCLUSION

The linear calibration curve was obtained at concentration range 2-10g/ml with a coefficient (1) and slope (0.017 xs). The proposed method was reproducible because results obtained with in inter-day and intra-day were in acceptable limit. The results of assay and % recovery were found to be satisfactory, indicating that the proposed method is precise and accurate and hence can be used for the routine analysis of Lamotrigine in bulk and pharmaceutical formulation.

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