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New Spectrophotometric Determination of Lamotrigine in Bulk and Pharmaceutical Dosage Form

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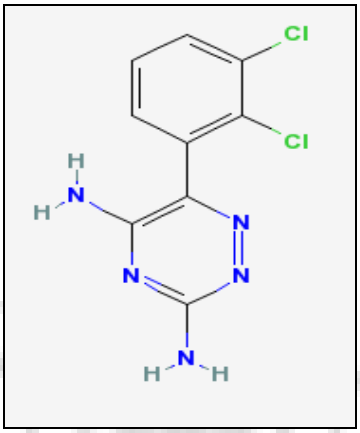
ABSTRACT

The new, selective and sensitive visible spectrophotometric method has been developed for the estimation of Lamotrigine in bulk and pharmaceutical preparations. The amino group in Lamotrigine is diazotized with sodium nitrite and hydrochloric acid at 0^0C temperature. After diazotisation, the diazonium salt is coupled with resorcinol. The orange coloured chromogen formed in the method is stable for more than 24 hours. The orange coloured chromogen is used to determine the Lamotrigine spectrophotometrically.

INTRODUCTION

Lamotrigine chemically, 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine. It is a novel anticonvulsant drug. Molecular formula of lamotrigine is $C_9H_7Cl_2N_5$. It is freely soluble in water and in methanol, sparingly soluble in ethanol. Lamotrigine is used in the treatment of depression and bipolar disorder. Lamotrigine tablets of 25mg, 100mg, 150mg and 200mg are available in different trade names. Permanent staining of teeth, nausea, rash, dysphagia, photosensitivity, hypersensitivity, haemolytic anaemia, raised blood urea, liver enzymes and bilirubin are the adverse effects. The structure of lamotrigine is as follows.



Structure of Lamotrigine

Various spectrophotometric methods are available in the literature for estimation of drugs by diazotisation and coupling reaction. The reagents such as acetylacetone[4], benzoyl acetone[5] dibenzyl methane[7], 1-naphthyl ethylene diamine[14] 1:1 ammonia: water solution[11], 2-napthol[40], 3-amino phenol[47] etc., are used for the estimation of drugs by diazotisation method. But all have certain limitations. In these methods more steps are involved, heating is necessary; the colour development is not instant and not reproducible values. The recently proposed method using 1:1 ammonia: water solution is less sensitive, time consuming and involves several steps.

No method is reported in the literature for estimation of the selected drugs by using resorcinol as the coupling reagent. Hence, it is proposed to use resorcinol as coupling reagent for the estimation of the selected drugs by spectrophotometry. The method is simple, rapid, reproducible, precise, and needs no extraction or heating, colour development is instantaneous, and the colour is stable for more than 24 hours. Further, the controlling of experimental conditions is minimum.

MATERIALS AND METHODS

The proposed method's general procedure: The drug containing amino group is treated with cold solution of sodium nitrite in acidic medium at 0-5^{o}C temperature. The resultant solution is allowed to stand for five minutes for the diazotisation to complete. Then the drug is treated with resorcinol to produce coloured species. The absorbance of the coloured species is measured at the wavelength of maximum absorbance for each drug against the reagent blank (prepared in a similar manner devoid of drug solution) and the amount of drug is determined from the calibration curve made between the absorbance and the amount of drug.

EXPERIMENT

Spectrum of diazotised lamotrigine treated with resorcinol

The wavelength of maximum absorbance of the diazotised drug treated with resorcinol solution is ascertained by the following procedure.

1 ml of lamotrigine solution (200 µg/ml) is transferred into a 10 ml volumetric flask. To this, 2.0 ml of 0.1N hydrochloric acid and 1.0 ml of cold 0.1N sodium nitrite solution are added. The resultant solution is well mixed, and then allowed to stand for five minutes at 0-5^{o}C temperature for diazotisation. To this solution 1.0 ml of 1% urea solution is added and shaken frequently for nitrogen gas to escape. Then 1.0 ml of 0.5N sodium carbonate and 1.0 ml of 1% resorcinol solution are added and the volume is made to 10 ml with methanol. The absorbance of the orange colour formed is measured in the wavelength range of 380 to 590 nm, against the reagent blank. The spectrum is given in Fig. 1.

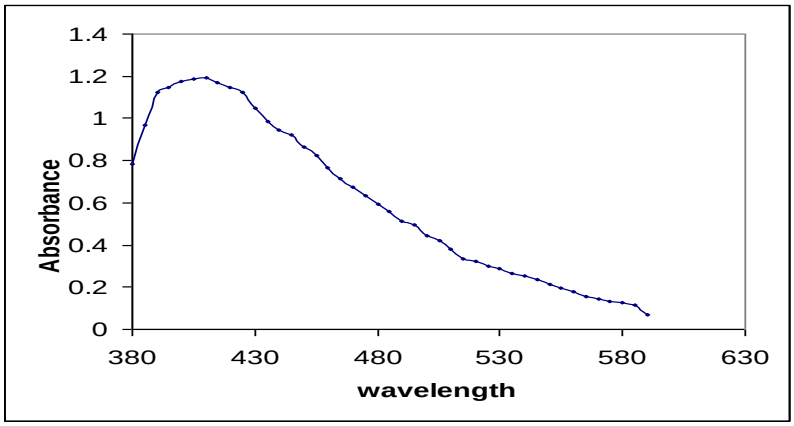


Figure 1. Spectrum of Diazotised Lamotrigine Treated with Resorcinol

From the above spectrum, it is clear that the diazotised drug treated with resorcinol solution has maximum absorbance at 410 nm. Hence, all further studies are made at 410 nm.

The optimal conditions for the determination of lamotrigine are arrived at by the following steps.

Various aliquots of the standard lamotrigine solution ranging from 0.2-1.0 ml are transferred into a series of 10 ml volumetric flasks. To each flask, 2.0 ml of 0.1N hydrochloric acid solution and 1.0 ml of cold 0.1N sodium nitrite solution are added. The resultant solution in each flask is well shaken and allowed to stand for five minutes at 0-5^{0}C temperature for diazotisation to complete. 1.0 ml of 1% urea solution is added to each flask and the solution is shaken frequently to allow nitrogen gas to escape. Then 1.0 ml of 0.5N sodium carbonate solution and 1.0 ml of 1% resorcinol solution are added and the volume in each flask is made upto 10 ml with methanol. An orange colour is formed. The maximum absorbance of the orange colour solution is measured at 410 nm against the reagent blank. Calibration graph is obtained by plotting absorbance values against the concentration of lamotrigine solution. The calibration curve is found to be linear over a concentration range of 40 to 200 μg/ml of lamotrigine. The amount of lamotrigine present in the sample is estimated from the calibration graph. The results are presented in the following Fig. 2.

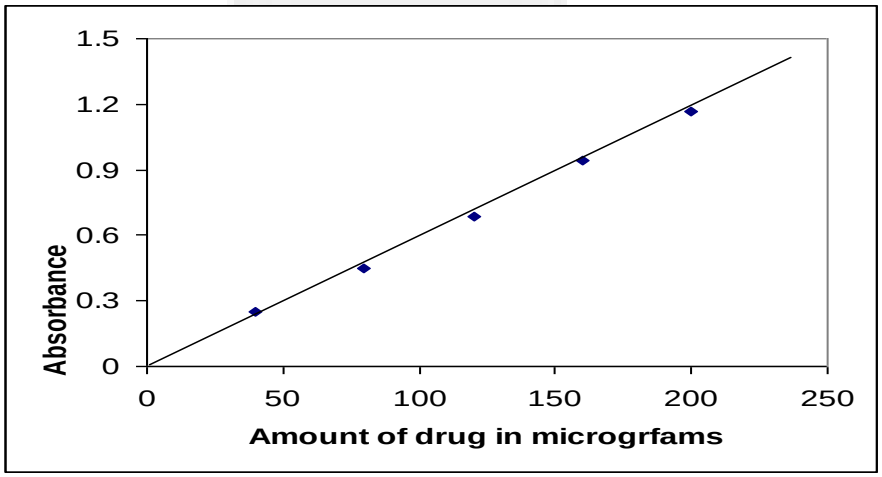


Figure 2. Calibration Curve of Lamotrigine

Assay of Lamotrigine in Pharmaceutical Formulations

The proposed procedure for the assay of lamotrigine is applied for its determination in commercial tablets.

Preparation of the Sample Solution

Powdered tablet equivalent to 50 mg of the drug is weighed accurately and transferred into a 50 ml beaker and mixed well with 30 ml of methanol. The solution is filtered and transferred into a 50 ml volumetric flask and the volume is made up to 50 ml with methanol. The concentration of the drug solutions is now 1 mg/ml. This stock solution is further diluted to obtain the working concentration of 200 μg/ml.

The pharmaceutical preparation as prepared above is analysed by the following procedure.

Assay Procedure: Known volumes of the drug formulation prepared as above are transferred into a series of 10 ml volumetric flasks and 2 ml of 0.1N hydrochloric acid solution, 1.0 ml of 0.1N sodium nitrite solution are added. The resultant solution in each flask is shaken well and allowed to stand for five minutes at 0-5^{0}C temperature for diazotisation. Then 1.0 ml of 1% urea solution, 1 ml of 0.5N sodium carbonate and 1.0 ml of 1% resorcinol solution is added. The absorbance of the resultant solution is measured at 410 nm. The amount of lamotrigine in the pharmaceutical formulation is evaluated from the predetermined calibration plot. The results are presented in the following table.

Assay of Lamotrigine in Tablets

S.No	Sample (mg)	*Amount Found(mg) ±S.D*	Percentage of Label claim	C.V*	*t_{cal}
1	200	200.02±0.40	100.01	0.1980	0.1186
2	220	200.04±0.51	100.02	0.2509	0.1778
3	100	99.96±0.36	99.9	0.3647	0.2453
4	100	99.94±0.39	99.94	0.3913	0.3430

***Average of five determination based on the label claim**

RESULTS AND DISCUSSION

Lamotrigine undergoes diazotisation when treated with sodium nitrite and hydrochloric acid. The excess nitrous acid during the diazotisation is removed by the addition of urea solution. The

solution was shaken frequently to allow the nitrogen gas to escape. The diazonium cation reacts with the coupling reagent, resorcinol by electrophilic substitution at the o-position of the coupling agent to produce an orange azo product. This orange colour product shows maximum absorbance at 410 nm. The colour of the product is stable for more than 24 hours. The calibration curve (concentration v/s absorbance) is linear over the range of 40-200 µg/ml of lamotrigine. The values of standard deviation, coefficient of variation values are low, indicates high accuracy and reproducibility of the method. The 't' calculated values are compares well with the theoretical value of 2.78 there by indicating that the precision of the method is good. There is no effect of additives and excipients such starch, calcium lactose and glucose in the concentrations those present in general pharmaceutical preparations.

CONCLUSION

The proposed method is found to be simple, precise, accurate and time saving, reproducible and can be conveniently adopted for routine analysis of estimation of lamotrigine in bulk drug samples and pharmaceutical formulations.

ACKNOLEDGEMENTS

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