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STABILITY INDICATING ASSAY METHOD DEVELOPMENT AND VALIDATION OF FIRST ORDER DERIVATIVE SPECTROPHOTOMETRIC METHOD FOR ESTIMATION OF LACOSAMIDE IN BULK AND TABLET DOSAGE FORM

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ABSTRACT

To develop a simple, precise, accurate, less time consuming & economical first order derivative spectroscopic method. Development of SIAM using developed first order derivative method. Distilled water was selected as a solvent for estimation of Lacosamide with the absorption at 250 nm. The linearity was established over the concentration range of 5-25 µg/ml. The correlation coefficient (r^2) for Lacosamide was found to be 1. The mean % recovery was found to be 100% for Lacosamide. The results of analysis have been validated statistically and recovery studies confirmed the accuracy of the proposed method. The method was validated as per the International Conference on Harmonization (ICH) guidelines. The proposed method is recommended for routine analysis since it is rapid, simple, accurate, sensitive and specific.

KEYWORDS: Lacosamide, Spectrophotometry, First order derivative, Validation.

INTRODUCTION

Lacosamide is chemically (2R)-N-benzyl-2-acetamido-3-methoxypropanamide (Figure 1), a functionalized amino acid that has activity in the maximal electroshock seizure test (MES). Indicated for the adjunctive treatment of partial-onset seizures and diabetic neuropathic pain.

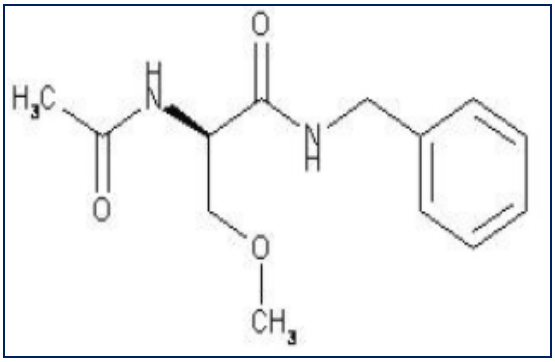

Fig 1: Chemical Structure of Lacosamide

Lacosamide only affects those neurons which are depolarized or active for long periods of time, typical of neurons at the focus of an epileptic seizure, as opposed to other antiepileptic drugs such as carbamazepine or lamotrigine which slow the recovery from inactivation and reduce the ability of neurons to fire action potentials.[1]

Literature review suggested several HPLC-UV, stability indicating HPLC, HPTLC, RP-UPLC, bioanalytical methods that have been reported for the estimation of Lacosamide.[2, 3, 4, 5, 6] Literature review also suggested that there is no Stability indicating assay method is not reported with the help of UV Derivative spectrophotometry. The objective of the work was to develop simple, accurate, precise and economic Stability indicating assay method is not reported with the help of UV Derivative spectrophotometry to estimate the Lacosamide in bulk. The method should be simple, accurate, precise, reproducible and statistically valid.

Distilled water was used as a solvent, thus making method very cost effective. The literature review prompted to develop an accurate, precise and simple method for the estimation of Lacosamide in bulk form. The work was extending to tablet formulation.

Thus, the objectives of project:

I. To develop a simple, precise, accurate method, less time consuming & economical derivative spectroscopic method.
II. Under derivative spectroscopy, the development of First order analytical derivative Method.
III. Development of SIAM using developed first order derivative method.
IV. Validation of developed method using common parameters:

a. Linearity
b. Precision
c. Accuracy

d. Sensitivity
e. Limit of Detection (LOD)
f. Limit of Quantification (LOQ)

MATERIALS AND METHODS

DRUG

The standard sample of Lacosamide was obtained as gift sample.

INSTRUMENT SPECIFICATIONS

UV Spectrophotometer, Shimadzu, Model 1800. A shimadzu UV/Vis 1800 double beam spectrophotometer is used with wavelength accuracy (± 0.3 nm), 1 cm matched quartz cells and UV probe 2.34 software was used for all the spectral measurements. Calibrated analytical Balance Denver SI234, Germany, was used for weighing purpose.

CHEMICALS AND REAGENTS USED

Distilled water.

FOR FIRST ORDER DERIVATIVE SPECTROSCOPY; PREPARATION OF STOCK SOLUTION

The stock solution of lacosamide is prepared by dissolving 100 mg of drug in 100 ml distilled water in volumetric flask with continuous shaking.

WAVELENGTH SCANNING AND DETERMINATION OF ABSORPTION MAXIMUM

- With the stock solution of Lacosamide, known concentration of 10µg/ml plasma standard is prepared by suitable dilution with distilled water.
- Wavelength scanned for the maximum absorption of drug solution using UV-Visible spectrophotometer within the wavelength region of 200–400 nm against blank.
- Convert the normal mode obtained spectra to first order derivative. The wavelength that shows the peak with a highest absorbance is considered as absorbance maximum of the drug.

METHOD VALIDATION

The validation of method was carried out by establishing linearity, limit of detection (LOD) and limit of quantification (LOQ) and within- and between- day precision and accuracy.

LINEARITY STUDIES FOR ANALYTICAL METHOD

- Standard solutions were prepared of concentrations 5µg/ml, 10µg/ml, 15µg/ml, 20µg/ml, 25µg/ml, 30µg/ml 35µg/ml, 40µg/ml, 45µg/ml 50µg/ml. Convert the normal mode obtained spectra to first order derivative.
- The results are tabulated and the linearity curve was constructed by plotting concentration vs. D^1 value. The result is presented in table 1 and fig. 2.
- Figure 4 presents the linearity obtained from the derivative spectra.

Table 1: Linearity of Lacosamide

S.NO.	Concentration (µg/ml)	D^1 value at detection wavelength (250 nm)
1	5	0.003
2	10	0.005
3	15	0.007
4	20	0.009
5	25	0.011

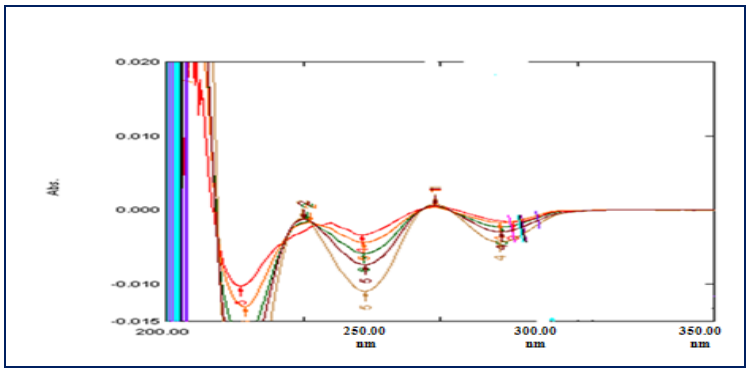

Fig 2: Depicting the linearity for the concentration range (5 – 25 µg/ml)

PRECISION

The precision of method was ascertained; the percent relative standard deviation were calculated and presented.

INTER DAY AND INTRADAY STUDIES FOR ANALYTICAL METHOD

The prepared stock solution was subsequently diluted to get 5µg/ml, 10µg/ml, 15µg/ml, 20µg/ml, 25µg/ml. The resulting solutions absorbance was measured at detection wavelength of 250 nm using double beam UV spectrophotometer against blank. The findings was made at different time intervals in a day times in a day and performed continuously for six days. Convert the normal mode obtained spectra to first order derivative. The results obtained were tabulated and studied for inter day and intraday variation. The results are presented in table 2 (a) and 2 (b).

Table 2 (a): Intraday precision for first order

S. No.	Concentration (µg/ml)	Time	D^1 value at 250 nm			
			I	II	III	Mean
1	20	1:30 PM	0.009	0.009	0.009	0.009
2	20	1:45 PM	0.009	0.008	0.009	0.00866
3	20	2:00 PM	0.008	0.009	0.009	0.00866
4	20	2:30 PM	0.009	0.009	0.008	0.00866
5	20	3:30 PM	0.009	0.009	0.008	0.00866
6	20	4:30 PM	0.009	0.009	0.009	0.009
Mean =						**0.009**
SD =						**0.000175**
% RSD =						**1.94**

Table 2 (b): Inter day precision for first order

S.NO	Concentration (µg/ml)	Days & Date	D^1 value at 250 nm			
			I	II	III	Mean
1	20	2.04.2012	0.008	0.008	0.008	0.008
2	20	3.04.2012	0.008	0.008	0.008	0.008
3	20	4.04.2012	0.009	0.009	0.009	0.009
4	20	5.04.2012	0.009	0.009	0.009	0.009
5	20	6.04.2012	0.009	0.009	0.009	0.009
6	20	7.04.2012	0.009	0.009	0.009	0.009
Mean =						**0.009**
SD =						**0.000140**
% RSD =						**1.55**

ACCURACY STUDIES

The accuracy/recovery studies were carried out with the commercial preparation and percentage recoveries was calculated. Convert the normal mode obtained spectra to first order derivative. The reproducibility of estimation was determined by performing the drug content of different samples. The results of accuracy studies were expressed in %. The result is presented in table 3.

Table 3: Depicting the accuracy studies for first order

S.NO.	Test (µg/ml)	Standard (µg/ml)	D^1 value at 250 nm	Conc. (µg/ml)	Amount of test recovered (µg/ml)	% Recovery
1	5	15	0.007	20	5	100
2	10	20	0.009	30	10	100
3	15	25	0.011	40	15	100

ASSAY STUDIES

The assay studies were carried out with the help of commercial preparation The percentage purity was calculated. Convert the normal mode obtained spectra to first order derivative. The reproducibility of estimation was determined by performing the drug content of different samples. The results of assay studies were expressed in %. The result is presented in table 4.

Table 4: Depicting the assay study

S.NO.	Conc. (µg/ml)	D^1 value at 250 nm	Conc. of drug in test solution (µg/ml)	% Purity (w/w)
1	10	0.005	10	100
2	10	0.005	10	100
3	10	0.005	10	100

PREPARATION OF DEGRADATION SAMPLES

- **For Acid Degradation**

  Lacosamide sample was refluxed with 1N HCl at 60°C for 1hour and then neutralized with 1N NaOH. The Sample was prepared as per sample preparation. The Solution was further diluted to required concentration with diluent.

- **For Base Degradation**

  Lacosamide sample was refluxed with 0.1N NaOH at 60°C for 1hour and then neutralized with 0.1N HCl. The Sample was prepared as per sample preparation. The Solution was further diluted to required concentration with diluent.

- **For Oxidative Degradation**

  Lacosamide sample was refluxed with 6% H_2O_2 by heating on water bath at 60°C for 1hour. The Sample was prepared as per sample preparation. The Solution was further diluted to required concentration with diluent.

- **For Photolytic Degradation**

  Lacosamide sample was exposed to UV (200watt- hr/m^2) and Visible (1.2 million Lux hours) as per ICH Guidelines. The Sample was prepared as per sample preparation.

- **For Thermal Degradation**

  Lacosamide sample was exposed to Temperatures at 105°C for 3days. The Sample was prepared as per sample preparation.

- **For Water Degradation**

  Lacosamide sample was refluxed with water by heating on water bath at 60°C for 1hour. The Sample was prepared as per sample preparation.

❖ **For Humidity Degradation**

Lacosamide sample was exposed to 85% Humidity (Prepared potassium nitrate saturated solution) at 3days. The Sample was prepared as per sample preparation.

The results are presented as follows.

Table 5: Depicting the Stability studies

S. No.	Parameters	Obtained Results (Degradation)	Acceptance of results
1	Acidic stress (1 N HCl)	5 % degradation	✓
2	Basic stress (0.1 N NaOH)	16 % degradation	✓
3	Oxidative stress (6% H_2O_2)	1 % degradation	✓
4	Thermal stress (Hot air oven; 105 ^oC)	No degradation	✓
5	Aqueous hydrolysis (distilled water)	No degradation	✓
6	Photolytic stress (UV and Visible)	No degradation	✓
7	Humdity degradation (85% saturated KNO_3)	5% degradation	✓

CONCLUSION

In the present study a simple, accurate, precise and economic first order analytical derivative spectroscopic method was developed to estimate the Lacosamide in bulk and pharmaceutical dosage forms. The developed analytical method by using first order derivative spectroscopy is found to simple, rapid and selective and the amount of drug recovered were same as the label claim and precise. It can be conveniently employed for the routine analysis and quantification. A validated SIAM was also developed as per ICH guidelines.

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