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Development and Validation of new analytical methods for the estimation of Lacosamide by UV Spectroscopy

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A B S T R A C T

A rapid and sensitive UV-Visible spectroscopic method was developed for the estimation of Lacosamide in bulk and its pharmaceutical formulation. The method was validated as per International Conference on Harmonization [ICH] guidelines. The Lacosamide was monitored at 230 nm with UV detection and there is no interference of diluent at 230 nm for lacosamide. The method was linear (r^2=0.999) at concentration ranging from 12 to 40µg/mL, precise (intra and inter-day RSD values < 1.0%), accurate (mean recovery = 99.9%), specific and robust. The results showed that the proposed method is suitable for the precise, accurate and rapid determination of lacosamide in bulk and tablet dosage forms.

Keywords: Lacosamide, UV-Visible spectroscopy, Validation, Dosage form

A R T I C L E I N F O

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C o n t e n t s

1. Introduction:

Lacosamide is a new antiepileptic drug (AED) for use as adjunctive therapy in the treatment of partial onset seizures with or without secondary generalization in patients with epilepsy aged 16 years or older [1-3]. Like many other new AEDs lacosamide has not been compared to any currently used antiepileptic. Clinicians who manage epileptic patients suggest that lacosamide should be used when all other AEDs have failed. Adverse effects are dose related, classed as mild to moderate and affect the central nervous system (dizziness, headache, fatigue, ataxia, vertigo) or gastrointestinal adverse system (nausea, vomiting). Lacosamide can cause a small dose related increase in mean PR interval. When choosing an AED, the seizure type, concomitant medication, age and sex should be taken into account. Carbamazepine, lamotrigine, oxcarbazepine, sodium valproate and topiramate are the drugs of choice for partial seizures. The chemical name of lacosamide is (R)-2-acetamido-N- benzyl-3methoxypropionamide (Fig.1) and its molecular weight is 250.30. Lacosamide is a white to light yellow powder. It is sparingly soluble in water and slightly soluble in acetonitrile and ethanol. It is not official in any pharmacopoeia, few liquid chromatography procedures have been reported for the determination of lacosamide [4,5]. Literature survey also reveals the saliva and serum concentration of lacosamide in patient with epilepsy [6].

The objective of this study is to develop a new, simple and rapid UV-Visible spectroscopy method to quantify lacosamide in bulk and capsule dosage forms. The developed method has been validated as per ICH guidelines.

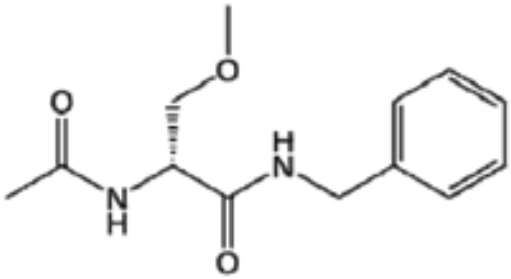

Fig.1 Chemical structure of Lacosamide

2. Methodology

Drug Samples (Raw material)

Lacosamide was obtained as a gift sample from Alkem Pharma, Mumbai.

Formulation used

LACOSAM tablets (Torrent pharmaceuticals, Mumbai) containing Lacosamide 100 mg was procured from OM pharmacy, Chennai.

Chemicals and solvents used

Distilled water, Potassium dihydrogen orthophosphate (AR Grade), Methanol (HPLC grade), Water (HPLC grade), Acetonitrile (HPLC grade), were purchased from Qualigens India Pvt. Limited & Loba Chemie India Limited, Mumbai.

Instruments used

Different instruments used to carry out the present work such as: Shimadzu AUX- 220 Digital balance, Shimadzu - 1700 Double Beam UV - Visible spectrophotometer with pair of10 mm matched quartz cells, ELICO SL-210 Double Beam UV-Visible spectrophotometer with pair of10 mm matched quartz cells, ELICO pH meter (ModelLI-120), SOLTECH–Sonica ultrasonic cleaner –Model 2200 MH, REMI–Centrifuge apparatus, CYBERLAB– Micropipette.

Methods

In the present work an attempt was made to develop and validate simple, precise and accurate methods for the estimation of Lacosamide in pure form and in tablet dosage form by First Order Derivative Spectrophotometric Method.

3. Results and Discussion

Table :1 Optical characteristics of lacosamide by first order derivative spectrophotometric method

S.no	Parameters	Derivatives
1	max(nm)	216.5 nm
2	Beer's law limit(µg/mL)	10-50
3	Correlation coefficient(r)	0.999878769
4	Regression equation (y=mx+c)	Y=0.003420429 x-0.000875397
5	Slope (m)	0.003461429
6	Intercept(c)	0.000875397
7	LOD(µg/mL)	0.32951216.53
8	LOQ(µg/mL)	0.998522132
9	Sandell sensitivity(µg/cm^{2}0.001A.U)	0.292400562
10	Standard error of mean	0.000183206

Table:2 Quantification of formulation (lacosam) by first order derivative spectrophotometric method

S. No	Labeled Amount	Amount Found	% Obtained	Average % Found	S.D	% R.S.D	S.E
1	100 mg	97.97 mg	97.97	99.55	1.1795	1.1848	0.0327
2	100 mg	100.7 mg	100.7				
3	100 mg	100.7 mg	100.7				
4	100 mg	98.27 mg	98.27				
5	100 mg	99.93 mg	99.93				
6	100 mg	99.73 mg	99.73				

Table:3 Intraday precision analysis of formulation (lacosam) by first order derivative spectrophotometric method

Drug	S. No	Labeled amount (mg/tab)	Amount found (mg/tab)	Percentage obtained	Average percentage	S.D	% R.S.D	S.E
Lacosamide	1	100	101.4	101.40	100.93	0.4163	0.4124	0.0462
	2	100	100.8	100.80				
	3	100	100.6	100.60				

*mean of three observation

Table:4 Interday precision analysis of formulation method

Drug	S. No	Labeled amount (mg/tab)	Amount found (mg/tab)	Percentage obtained	Avg %	S.D	% R.S.D	S.E

Lacosamide	1	100	100.9	100.90	100.7	0.2	0.1986	0.0222
	2	100	100.7	100.70				
	3	100	100.5	100.50				

*mean of three observation

Table:5 Ruggedness analysis of formulation (lacosam 100mg) by first order derivative spectrophotometric method

Drug	Condition	Sample No	Labelled Amount (Mg/Tab)	Amount Found (Mg/Tab)	Avg(%) Obtained	S.D	% R.S.D	S.E
Lacosamide	ANALYST 1	1	100	100.70	100.56	0.1250	0.1243	0.0034
		2	100	100.60				
		3	100	100.43				
		4	100	100.50				
		5	100	100.70				
		6	100	100.43				
	ANALYST 2	1	100	100.43	100.36	0.0816	0.0813	0.0022
		2	100	100.33				
		3	100	100.43				
		4	100	100.33				
		5	100	100.23				
		6	100	100.43				

*Mean of six observation

Table:6 Ruggedness analysis of formulation (lacosam 100mg) by first order derivative spectrophotometric method

Drug	Condition	Sample No	Labelled Amount (Mg/Tab)	Amount Found (Mg/Tab)	Avg(%) Obtained	S.D	% R.S.D	S.E
Lacosamide	Instrument 1	1	100	100.60	100.51	0.1124	0.1118	0.0031
		2	100	100.43				
		3	100	100.60				
		4	100	100.50				
		5	100	100.33				
		6	100	100.60				
	Instrument 2	1	100	100.43	100.46	0.0909	0.0905	0.0025
		2	100	100.50				
		3	100	100.33				
		4	100	100.60				
		5	100	100.43				
		6	100	100.50				

Drug	%	Amt present (µg/mL)	Amt added (µg/mL)	Amt estimated	Amt recovery	% recovery	Avg % recovery	S.D	% R.S.D	S.E
Lacosamide	80	14.92	24	38.80	23.88	99.50	99.81	0.2936	0.2941	0.032
		14.92	24	38.89	23.97	99.87				
		14.92	24	38.94	24.02	100.08				
	100	14.92	30	44.56	29.64	98.80	99.18	1.0356	1.0441	0.115
		14.92	30	44.44	29.52	98.40				
		14.92	30	45.03	30.11	100.36				
	120	14.92	36	50.87	35.95	99.80	99.89	0.1824	0.1826	0.020
		14.92	36	50.96	36.04	100.1				
		14.92	36	50.84	35.92	99.77				

*mean of three observation

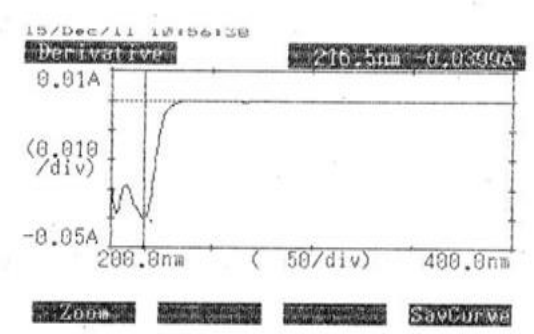

Fig:1 First order derivative spectrum of lacosamide in distilled water

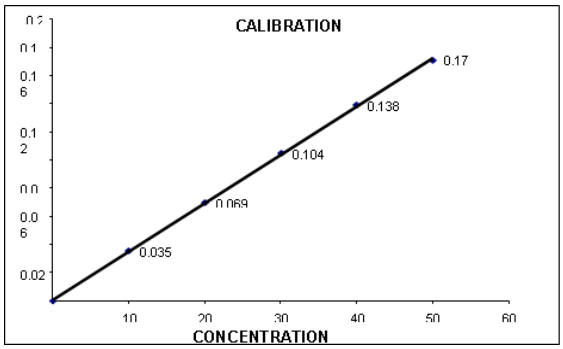

Fig:2 Calibration curve of lacosamide by first order derivative spectrophotometric method using distilled water

Discussion:

The zero-order spectra were converted into first-order derivative spectra for Lacosamide analysis. The first-order derivative spectrum showed maximum absorbance at 216.5 nm (Figure 1). Calibration curves were constructed using concentrations ranging from 10 to 50µg/mL, with measurements taken at 216.5nm. The correlation coefficient exceeded 0.9998, indicating compliance with Beer's law within the chosen concentration range (Table 1). Quantification was performed at 30 µg/mL, yielding a tablet purity of 99.55% ± 1.1795 with a % RSD of 1.1848 (Table 2). Intraday and interday analyses demonstrated % RSD values of 0.4124 and 0.1986, respectively, confirming method precision (Tables 3 and 4). Ruggedness was validated by different analysts and instruments, with % RSD values ranging from 0.0813 to 0.1243 (Table 5 & 6). Recovery studies revealed percentage recovery within 99.18% to 99.89%, with an average % RSD of 0.5069, indicating high accuracy. Intermediate precision was confirmed by % RSD values of 0.3502 for intraday and 1.4218 for interday analysis of Lacosamide formulations.

4. Conclusion

A UV-Visible spectroscopic method was developed to estimate Lacosamide in both its bulk pure form and tablet dosage form. The method employed for the analysis of Lacosamide was the first-order derivative spectrophotometric method. Based on the solubility profile, distilled water was selected as the solvent for Lacosamide estimation. A sample solution containing 10µg/mL of Lacosamide in distilled water was prepared and scanned in the UV region, ranging from 200 to 400 nm, with methanol used as the blank. Analysis revealed Lacosamide's maximum absorbance at 216.5 nm. The percentage of label claim present in the capsule formulation was determined to be 99.55% ± 1.1795%. Recovery studies indicated a percentage recovery within the range of 99.18% to 99.89%.

A sensitive & selective RP-HPLC method has been developed & validated for the analysis of Mobocertinib API. Further the proposed RP-HPLC method has excellent sensitivity, precision and reproducibility. The result shows the developed method is yet another suitable method for assay, purity which can help in the analysis of Mobocertinib in different formulations.

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