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# Development of a novel UV spectrophotometric method for the estimation of lacosamide in both bulk and solid dosage forms

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## ABSTRACT

The present study aims to develop a simple, precise and accurate UV spectrophotometric method for the estimation of Lacosamide in both bulk and in pharmaceutical dosage form. From the solubility profile, phosphate buffer with pH 3 was chosen as a solvent for the estimation of Lacosamide by ultraviolet spectroscopy. From the spectra, Lacosamide showed maximum absorbance at 210 nm.The proposed method was validated in accordance with the ICH guidelines and successfully applied for the tablet formulation. The percentage label claim present in tablet formulation was found to be 99.08 ± 0.6568%. The percentage recovery was found to be in the range of 99.06 ± 0.5386 %. From the high recovery values (> 98%) it can be inferred that the method is free from the interference of excipients used in the formulation. Based on the results obtained, the proposed method can be regarded as simple, accurate, precise, reliable and cost effective which can be employed for routine quality control of Lacosamide in tablet dosage forms.

**Keywords:** UV method development, Lacosamide, phosphate buffer, ICH guidelines

## INTRODUCTION

The quality of pharmaceuticals has been a concern of the World Health Organization (WHO) since its inception. The setting of global standards is requested in the WHO Constitution, which cites as one of the organization's function that it should "develop, establish and promote international standards with respect to food, biological, pharmaceutical and similar products". In the drug industry at large, quality management is usually defined as the aspect of management function that determines and implements the "quality policy", i.e. the overall intention and direction of an organization regarding quality, as formally expressed and authorized by top management. Analytical method development being a vital part of preformulation-formulation research and development obviates the need to development reliable, effective, ecofriendly and cost effective methodologies for routine analysis of active pharmaceutical ingredients for both small and large scale pharmaceutical industries world wide. [1-15] Sophisticated chromatographic methods with HPLC, HPTLC which are being employed for analysis are relatively expensive; many methods necessitate analyte extraction from respective sample matrices thus necessitating complicated sample preparation steps, use of internal standards for analysis increases the time required and error in recovery . UV-vis spectrophotometric method is one of the earliest, yet easy, sensitive, relatively cost effective method applied for drug estimations in both small and large scale pharmaceutical R&Ds.Lacosamide[18], is an antiepileptic drug approved in the USA, European several other countries as adjunctive therapy for partial-onset seizures.Lacosamidechemically (2R)-N-benzyl-2-acetamido-3-methoxy propenamide (Fig.1), with molecular weight of about 250.29 g/mole and chemical formula $C_{13}H_{18}N_2O_3$. Lacosamide is a functionalized amino acid molecule that has high solubility Ω in water and DMSO, with a solubility of 20.1mg/ml in phosphate buffer saline (PBS,$p^H$-7.5, 25$^O$C). Its mechanism of action is by inhibition of $Na^+$ channels responisible for analgesia. Lacosamide may be selective for inhibiting the depolarized neurons rather than neurons with normal resting potentials. Pain and nociceptor hyper excitability are

assiocated with neural membrane deploarisation. It binds to collapsing response mediator protein-2 (CRMP-2), a phosphoprotein which is expressed primarily in the nervous system and is involved in neuronal differentiation and control of axonal outgrowth. The maximum lacosamide plasma concentration occur about 1-4 hours after oral administration, and the pharmacokinetics of lacosamide are dose proportional food does not affect absorption. Literature[19-23] reports various HPLC and UV methods for the estimation of Lacosamide, but the present study aims at developing a simpl, reliable and cost effective method.

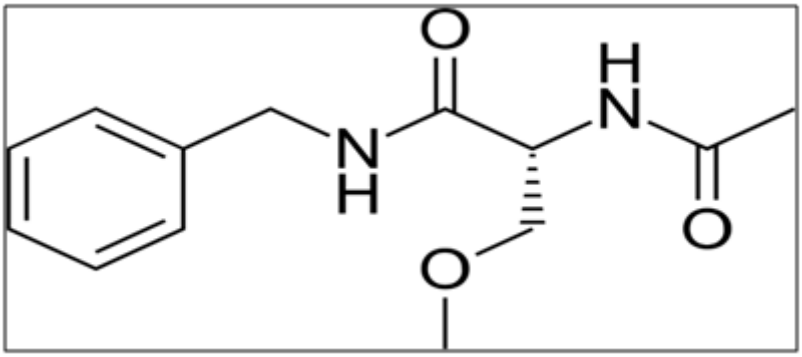


**Fig : 1 – Structure of Lacosamide**

## MATERIALS AND METHODS

### Instruments used

Electronic digital balance (ESSAE,AJ220E), U.V double beam spectrophotometer (SYSTRONICS 2003), Digital $p^H$ meter (ELICO, L1120), plus); Ultrasonic bath sonicator (Biotechnics) were used in the study.

### Reagent and chemicals

Analytical pure drug of Lacosamide were obtained as kind gift samples from Hetero drugs , Hyderabad, India. The tablet formulation called Lacosam, with a labeled claim of 100 mg, were obtained from local drug store. Reagents of analytical grade were purchased from Merck, Mumbai.

### Selection of solvent

The solubility of Lacosamide was determined in a variety of solvents as per Indian Pharmacopeia standards. Solubility was carried out in polar and non polar solvents. From the solubility data, phosphate buffer $p^H$-3 was selected as the best solvent for the analysis of Lacosamide, as the analytical properties of Lacosamide were reflected well in it.

### Preparation of phosphate buffer

An accurately weighed amount of 7.8g of sodium dihydrogen phosphate was taken in a 1000ml volumetric flask. A few ml of distilled water was added to dissolve and made upto 900ml.The pH was adjusted to 3.0 by using orthophosphoric acid and the volume of the solution was made upto the mark with distilled water.

### Preparation of standard stock solution

50 mg of Lacosamide was weighed accurately and transferred in to 100 ml volumetric flask and dissolved in phosphate buffer $p^H$-3 and made up to the volume with phosphate buffer. This solution contains 500 µg / ml concentration of Lacosamide.

### Selection of wavelength for estimation

The standard stock solution was further diluted with phosphate buffer to get the concentration of 10µg /ml and the solution was scanned between 200 and 400 nm phosphate buffer $p^H$-3 as blank. From the spectra obtained, 210 nm was selected as an analytical wavelength, as the drug showed maximum absorbance at this wavelength.

### Preparation of calibration graph

From the standard stock solution of Lacosamide (500µg / ml), 0.1, 0.2, 0.3, 0.4 and 0.5ml was transferred into series of 10 ml volumetric flasks and made up to the volume with phosphate buffer $p^H$-3 and it gave 5,10, 15, 20 and 25µg /ml solutions respectively. The absorbances of these solutions were measured at 210 nm. The calibration curve was constructed by plotting concentration Vs absorbance.

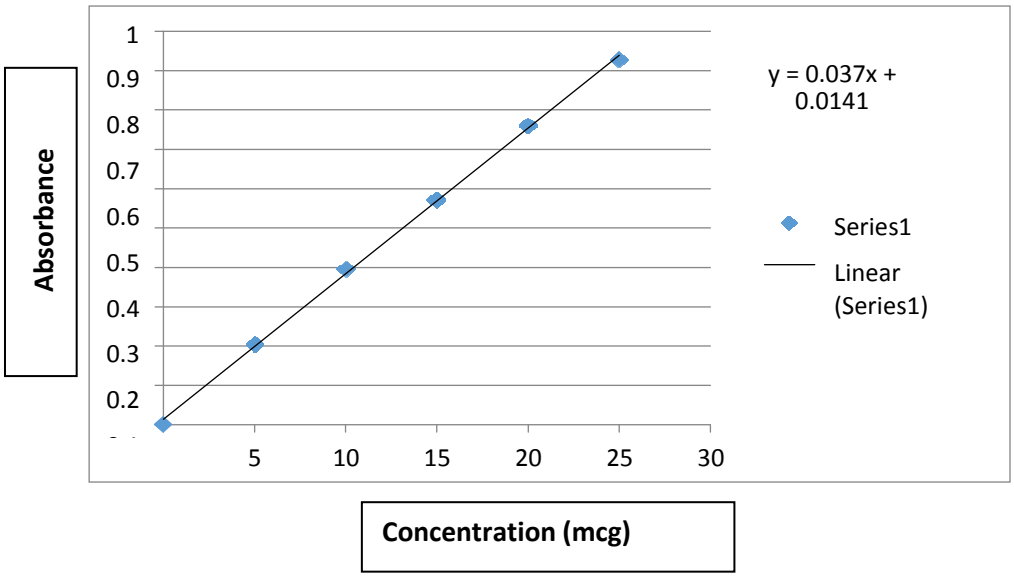


**Fig: 2 Standard Calibration curve for Lacosamide**

## Preparation of sample solutions

Twenty tablets (LACOSAM) were weighed accurately and the average weight was found. The tablets were then powdered well in a motor and pestle. The tablet powder weight equivalent to 50 mg of Lacosamide was weighed and transferred into 100 ml volumetric flask. A minimum quantity of phosphate buffer was added to the powder to dissolve it and the solution was further sonicated for 15 minutes, to ensure the solubility of the drug. The solution was then made up to the mark with the solvent. The solution was filtered through Whatman filter paper No: 41. From the clear solution, further dilutions were made by diluting 0.2 mL into 10 mL with phosphate buffer pH – 3 to obtain 10 µg/ mL solution theFrom the clear solution, further dilutions were made by diluting 0.2 mL into 10 mL with phosphate buffer pH – 3 to obtain 10 µg/ mL solution theoretically. The absorbances of three replicates were measured and the amount was calculated.

## Method validation

The proposed method was validated as per ICH guidelines in terms of linearity, precision, accuracy [30]

## Linearity

A series of solutions were prepared in the concentration range of 5- 25µg/ml and the respective absorbances were plotted against concentration, to ensure the linearity of the result obtained. Lacosamide was linear in the concentration range of 5- 25µg/ml

## Accuracy

Accuracy of the method was confirmed by recovery studies. To the preanalyzed formulation, a known quantity of working standard of Lacosamide was added and the procedure was followed as per the analysis of formulation. From the sample solution containing 500µg/ml of Lacosamide, a volume of 0.2ml was transferred to three 10ml volumetric flasks containing 0.1, 0.2, 0.3, ml of Lacosamide standard solution. The amount of each drug recovered was calculated. This procedure was repeated for three times for each concentration. The % RSD was calculated.

## Precision

Precision of the developed method was established through intra and inter day studies. A 10µg/ml solution of Lacosamide working standard was prepared in six replicates and were analysed on the same day and for three consecutive days. The percentage RSD for the results obtained was calculated.

## LOD and LOQ

The linearity study was carried out for six times. The LOD and LOQ were calculated based upon the calibration curve method. The LOD and LOQ were calculated by using the average of slope and standard deviation of intercept.

Ruggedness

Ruggedness of the method was confirmed by the analysis of formulation by using different analysts. The amount and % RSD were calculated.

## Robustness

The robustness of an analytical procedure is a measure of its capacity to remain unaffected by small, but deliberate variations in method parameters and provides an indication of its reliability during normal usage

# RESULTS

The Standard Calibration curve and linearity ranges for Lacosamide are represented in Table – 1 and Fig - 2 . In method validation, the results of accuracy of Lacosamide are depicted in Table – 2 and precision of inter and intraday variations in Table – 3. The Assay results of Lacosamide are in Table – 4. The remaining validation parameters LOD, LOQ, RUGGEDNESS, ROBUSTNESS) of Lacosamide are presented in Table – 5.

# DISCUSSION

The current research article aims to develop a UV

method for estimation of Lacosamide in commercially available tablets dosage form. From the solubility profile of Lacosamide, phosphate buffer pH 3 was selected as a solvent. From the spectra, 210nm was selected as sample wavelength for Lacosamide. The simplicity and reliability of method requires knowledge very accurate.

From the assay result, the amount of Lacosamide in tablet dosage form was found to be 99.009mg.

The method was validated as per ICH guidelines. Linearity was obtained at concentration range of 5-25µg/ml for Lacosamide, shown in Table – 1. The %RSD for intra and interday variations for Lacosamide was found to be 1.302 and 1.66, 1.242 respectively. It indicates that the developed UV method has good precision. While validating the accuracy of method (table – 3), it was found that the mean % recovery for Lacosamide were found to be 99%. Based on the results obtained the proposed method can be regarded as simple, accurate, precise, and reliable which can be employed for routine quality control of Lacosamide in bulk and combined formulation.

**Table 1 : Table for Calibration curve of Lacosamide**

| S.No | Concentration(mcg) | Absorbance |
|---|---|---|
| 1. | 5 | 0.205 |
| 2. | 10 | 0.396 |
| 3. | 15 | 0.572 |
| 4. | 20 | 0.760 |
| 5. | 25 | 0.927 |

**Table 2 : Table for precision data of Lacosamide**

| Precision studies | Concentration (µg/ml) | Absorbance | %RSD |
|---|---|---|---|
| Intraday studies | 10 | 0.420 | 1.302147 |
| | 10 | 0.407 | |
| | 10 | 0.415 | |
| | 10 | 0.414 | |
| | 10 | 0.419 | |
| | 10 | 0.422 | |
| Interday studies | 10 | 0.416 | 1.6671 |
| | 10 | 0.412 | |
| | 10 | 0.414 | |
| | 10 | 0.422 | |
| | 10 | 0.401 | |
| | 10 | 0.412 | |
| | 10 | 0.401 | 1.242785 |
| | 10 | 0.412 | |
| | 10 | 0.411 | |
| | 10 | 0.416 | |
| | 10 | 0.407 | |
| | 10 | 0.41 | |

**Table 3 : Table for Accuracy of Lacosamide:**

| S.No | % spiked | Amount added (µg/ml) | Amount recovered (µg/ml) | % mean recovery | Statistical analysis |
|---|---|---|---|---|---|
| 1 | 50 | 5 | 4.95122 | 99.02439 | MEAN: 98.86% |
| 2 | 50 | 5 | 5.04878 | 100.9756 | SD: 1.290 |
| 3 | 50 | 5 | 4.829268 | 96.58537 | %RSD: 1.296 |
| 4 | 100 | 10 | 10.05051 | 100.5050505 | MEAN: 98.65 |
| 5 | 100 | 10 | 9.79798 | 97.97979798 | SD:1.62 |
| 6 | 100 | 10 | 9.747475 | 97.47474747 | %RSD:1.65 |
| 7 | 150 | 15 | 15.26224 | 101.7482517 | MEAN: 99.76 |
| 8 | 150 | 15 | 14.73776 | 98.25174825 | SD: 1.794 |
| 9 | 150 | 15 | 14.8951 | 99.3006993 | %RSD: 1.798 |

**Table 4 : Table for Assay of Lacosamide**

| Concentration (µg/ml) | Amount Found (mg) | Label Claim(mg) | % purity | % RSD |
|---|---|---|---|---|
| 10 | 96.46465 | 100 | 96.46465 | |
| 10 | 99.24242 | 100 | 99.24242 | 1.434991 |
| 10 | 98.23232 | 100 | 98.23232 | |

**Table 5: Table for LOD and LOQ**

| S.No | Parameters | Results |
|---|---|---|
| 1. | LOD | 1.467111 |
| 2. | LOQ | 4.44579 |

**Table 6 : Table for Ruggedness**

| Analyst | Samples | Absorbance | Parameters | Results |
|---|---|---|---|---|
| I. | 10 | 0.392 | MEAN | 0.386 |
| II. | 10 | 0.388 | SD | 0.005 |
| III. | 10 | 0.381 | RSD | 1.438 |

**Table 7 : Table for Robustness**

| S.no | Wavelength (nm) | Concentration (mcg) | Absorbance | Parameters | Results |
|---|---|---|---|---|---|
| 1. | 208 | 20 | 0.722 | MEAN | 0.731 |
| 2. | 210 | 20 | 0.74 | SD | 0.009 |
| 3. | 212 | 20 | 0.732 | RSD | 1.233 |

## CONCLUSION

Properly validated simple, cost effective, time saving UV method developments are of immense benefit for the pharmaceutical R & Ds for routine drug estimation and in various phases of preformulation and formulation studies. The current properly validated UV methodology for the estimation of Lacosamide in the marketed formulations is beneficial for its routine estimation.

## REFERENCES


1. World Health Organization, Quality assurance of pharmaceuticals, A compendium of guidelines and related materials. 2nd edition, volume 2 Good manufacturing practices and inspection. p. 1, 15-16.
2. 2. MD. Shahidullah, quality control and quality assurance [internet]. 2011. Available from: http://www.scribd.com/doc/72928556/QC-and-QA.2011. [cited 10 Augest 2012].
3. Satinder Ahuja, Stephen Scypinski. Hand book of modern pharmaceutical analysis. volume 3. London: Academic Press. Page num:1-2.
4. Dr. G. Devala Rao. A Text book of Advanced Pharmaceutical analysis. Birla publications, page num:1-3.
5. A. A Napoleon, Pharmaceutical Titrimetric analysis theory and practical, Klaimani publishers and Distributers. Page num: 3.5 – 3.7.
6. Kamboj, P. C. Pharmaceutical Analysis. 2nd edition, Volume I, Vallabh Publication, New Delhi, 2003, page num:1 - 3.
7. Beckett A. H. and Stenlake J.B. Practical Pharmaceutical Chemistry. 4th edition, volume 2, CBS Publishers and Distributors, New Delhi, 2007, page num: 85, 255 - 272, 277 -307.
8. Sharma B. K. Spectroscopy. Goel Publishing House, A Unit of Krishna Prakashan Media (P) Ltd., Meerut, 2007, S-71.
9. Y.R Sharma Elementary organic spectroscopy principles and chemical application, Revised edition, S. Chand publications.
10. Gurdeep R. Chatwal, and Sham K. Anand. Instrumental Methods of Chemical Analysis. 5th revised edition, Himalaya Publishing House, Mumbai, 2000, 2.107 – 2.120, 2.149 – 2.170, 2.566 – 2.568.
11. JagMohan. Organic Spectroscopy. 2nd edition, Narosa Publishing House Pvt.Ltd.,22 Daryagani, Delhi Medical Association Road, New Delhi, 2005,page num: 131-132.
12. Mendham, J., Denney, R. C., Barnes, J. D. and Thomas, M. J. K. Vogel□s Text Book of Quantitative Chemical Analysis. 6th edition, Pearson education, New Delhi, 2002, page num: 133 – 140, 269 – 275, 653.
13. Hobert H. Willard, Lynne L. Meritt, Jr., Jorn A. Dean, Frank A. Settle, Jr. Instrumental Methods of Analysis. 7th edition, CBS Publisers and Distributors, New Delhi, 1986,page num: 3 and 5.
14. Ashutoshkar. Pharmaceutical Drug Analysis, 2nd edition, New Age International (P) Limited, New Delhi, 2005,page num: 293-311.
15. Douglas A. Skoog, Donald M. West, James Holler F. and Stanley R. Crouch. Fundamentals of Analytical Chemistry. 8th

edition,. Thomson Asia Pvt. Ltd. 2005, page num: 975-979
16. Code Q2A, Text on Validation of Analytical Procedures. ICH Harmonized Tripartite Guidelines, Geneva, Switzerland, 1994, page num: 1 - 5.
17. Code Q2B, Validation of Analytical Procedures; Methodology. ICH Harmonized Tripartite Guidelines, Geneva, Switzerland, 1996,page num: 1 - 8.
18. (The Merck index,2006, http://toxwiki.wikispace/lacosamide.com, www.drugs.com /ppa/lacosamide.html).
19. Bala NN Rao Attili, G. Rohini Reddy, S.K Chaitanya, M.D. Abdul Shoeb UVVisible spectrophotometric method for the determination of lacosamide in its pure and tablet dosage form. January 2012, 4(6):1737-1741.
20. R. Valarmathi, S. Faraisha Banu, Rathinam Senthamarai, C.S Dhivya Dhharshini, Simple UV spectrophotometric method development and validation for determination of lacosamide in bulk and its tablet dosage form. International Journal of drug development and research march 2013. 5(1):373-376 ·
21. Kestelyn C1, Lastelle M, Higuet N, Dell'Aiera S, Staelens L, Boulanger P, Boekens H, Smith S, A Simple UV HPLC method for estimation of Lacosamide.PUB MED November 2011. 3(22):2515-22.
22. V. Kalyan Chakravarthy* and D. Gowri Shankar, HPLC method for determination of lacosamide s(-)enantiomer in bulk and pharmaceutical formulation. Rasayan jouranal.com Vol.4, No.4 (2011), 744-752.
23. Ravishankar P, Gowthami S and Devala Rao G: A review on analytical method development. Indian Journal of Research in Pharmacy and Biotechnology 2014; 2: 1183- 1195.