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LACOSAMIDE ESTIMATION IN BULK AND PHARMACEUTICAL DOSAGE FORM: A REVIEW

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ABSTRACT

Epilepsy is a central nervous system (neurological) disorder in which brain activity becomes abnormal, causing seizures or periods of surprising behaviour, sensations, and usually loss of awareness. Lacosamide (LCM) is a drug approved for the treatment of partial onset seizures. Lacosamide is used alone and in combination with other medication to control certain types of seizures. There are several analytical strategies including UV spectroscopy, HPLC and HPTLC reported for determination of lacosamide in bulk and its pharmaceutical dosage forms. The review focuses on validated UV and HPLC methods for lacosamide estimation.

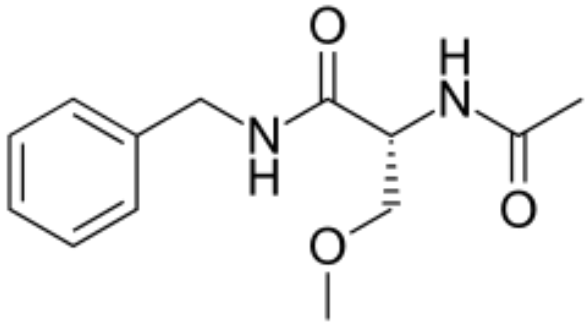
INTRODUCTION

The word “epilepsy” is a Greek word means seized or attacked. Epilepsy is a brain disorder during in which a person has repeated seizures over time. Seizures are episodes of uncontrolled and abnormal firing of brain cells that cause changes in movement, behaviour and sensation. Brain disorder could develop once specific identifiable three event (e.g. head injury, meningitis, asphyxia) epilepsy are divided into three groups such as idiopathic epilepsies, symptomatic epilepsies and cryptogenic epilepsies. Lacosamide provide new mechanisms of action and favourable pharmacokinetic and safety profiles.[1] Lacosamide is approved for connected use in partial onset seizures in patients of seventeen years of age and older four. It is completely different from all other approved AEDs (Anti-epileptic drugs) in that it has novel mechanisms of action and favourable pharmacokinetic and safety profiles. The potential for drug interactions with other AEDs and presently prescribed medications is

very low. Overall there is a minimal dosing and clinical observation demand with Lacosamide.[2]

Chemistry of lacosamide[3,4]

Lacosamide is a functionalized amino acid compound specifically synthesized as an anticonvulsive drug. The chemical name of lacosamide is (R)-2-acetamido- N -benzyl-3-methoxypropionamide. Lacosamide is a powder, white to light yellow crystalline compound. Molecular mass of lacosamide is 250.294 g/mol. Its melting point is 140-146˚C.



Chemical structure of lacosamide

Solubility of lacosamide

Lacosamideis has high solubility in water and DMSO, with a solubility of 20.1 mg/mL in phosphate-buffered saline (PBS, pH 7.5 at 25 °C). It is equally soluble in organic solvent like ethyl alcohol, acetonitrile, dimethyl formamide.[5,6]

Mechanism of action

It is assumed that lacosamide's inhibition of Na (sodium) channels is responsible for physiological action of Lacosamide. It could also be selective for inhibiting depolarized neurons instead of neurons with traditional resting potentials. It would be targeting pain and nociceptor hyper excitability area unit related to neural membrane depolarization. Lacosamide binds to collapsin response between protein-2 (CRMP-2), a protein that's expressed primarily inside the nervous system and is involved in neuronal differentiation and management of nerve fibre outgrowth.[7,8]

Pharmacokinetics[9]

1. Absorption

Lacosamide shows a negligible 1st pass effect with bioavailability of about 100%. The maximum Lacosamide plasma concentrations reaches in 1 to 4 hours after oral administration

and the pharmacokinetics of Lacosamide are dose proportional. Food doesn't have an effect on its absorption.

2. Distribution

Volume of distribution is more or less 0.6 L /kg.

3. Metabolism

Lacosamideis a CYP2C19 substrate. The relative contribution of variousCYP isoforms or non-CYP enzymes among the metabolism of lacosamide is not identified. Primary compounds excreted were unchanged lacosamide (approximately 40% of the dose), its O-dimethylsubstance (approximately 30%), and a structurally unknown polar fraction (~20%).

4. Elimination

Lacosamide is eliminated primarily from the circulation by biotransformation and renal (kidney) excretion.

Contraindication

Contraindicated in patients with severe liver drawback and hypersensitivity.

Drug interaction[10]

Drug Interaction using lacosamide with ethanol might increase side effects like dizziness, drowsiness, confusion, and difficulty concentrating.

No food–drug or drug–drug interactions with different marketed agents (i.e., digoxin, metformin, omeprazole, and oral contraceptives containing ethinyl estradiol and levonorgestrel) that could be affected by the CYP2C19 pathway or protein binding at therapeutic levels are known

Side effects[11]

- Dizziness
- Loss of balance management
- Mood or mental changes
- Blurred vision
- Nausea Vomiting
- Diarrhea
- Heartburn trouble with sleeping

Analytical method development

Various analytical methods and validation plays important role in the discovery development and manufacture of pharmaceuticals. Analytical methods used to ensure the identity, purity, potency, and performance of drug products.[12]

Ultraviolet spectroscopy

- Lacosamide has been analysed by UVspectroscopy using water as solvent at 257nm Beer's law was found to be obeyed in the concentration range of 300-900µg/mL.[13]
- A simple method using acetonitrile and water as solvent has been performed at a wavelength 230 nm and this method was found to be linear at concentration ranging from 12-40µg/ml.[13]
- Another simple method using sodium dihydrogen phosphate monohydrate buffer (pH adjusted to 3.0 with diluted orthophosphoric acid) and Acetonitrile as a solvent has been performed at a wavelength 210nm and this method was found to be linear at concentration ranging from 3.99-47.95µg/ml.[14]

HPLC using UV detector

- This method is performed using Develosil ODS HG-5 ((Make: Nomura chemicals (Japan); 150 mmx4.6 mm I.D; particle size 5 µm)) Column and Sodium di-hydrogen phosphate monohydrate buffer (pH adjusted to 3.0 with diluted orthophosphoric acid): Acetonitrile (700:300) v/v as eluent at flow rate 1.0 mL/min and the Column temperature was 40°C. UV detection was performed at 210nm and sample temperature was maintained at 5°C. the retention time of drug was 3.09min.The method is simple, rapid, and selective. The described method of Lacosamide is linear over a range of 3.996 µg/ml to 47.952 µg/ml. The method precision for the determination of assay was below 2.0% RSD. The percentage recoveries of active pharmaceutical ingredient (API) from dosage forms ranged from 100.0 to 101.3%.[14]

- This method has been developed for estimation of Lacosamide in its bulk and tablet dosage form. Chromatography was applied on a Symmetry C18 (4.6 x150mm, 5 µm) column employing a mixture of Methanol and phosphate buffer (65:35 v/v) as the mobile phase at a rate of flow 0.7 mL/min, the detection was carried out at 215nm. The Retention time of drug was 2.56±0.02 min. The method creates linear responses within the

concentration range of 10-60 µg/ml of Lacosamide. The strategy precision for the determination of assay was below 2.0%RSD.[15]

- Another isocratic reverse phase liquid chromatography technique has been developed for the determination of Lacosamide in Bulk and its pharmaceutical formulation. Separation was achieved using Xterra RP-8 column (make: water corporation; 150 mm×4.6 mm I.D; particle size 5µm) and sodium di-hydrogen phosphate monohydrate buffer (PH adjusted to 3.0 with diluted orthophosphoric acid) : Acetonitrile (800:200) v/vas a mobile phase at a flow rate of 1.0ml/min. Ultraviolet detection was performed at 230nm.the retention time of drug was 4.0min. The described technique of lacosamide is linear over a range of 12.0µg/ml to 37.85µg/ml. the strategy precision for the determination of assay was below 1.0%RSD.[16]

Stability indicating HPLC Method

- A novel stability-indicating reverse phase high pressure liquid chromatographic assay method was developed and validated for the determination of Lacosamide (LCM). This method was developed based on forced degradation data obtained by HPLC analysis. Lacosamide was subjected to stress under the conditions of hydrolysis (acidic, basicand neutral), oxidation, thermal and photolysis the separation of degradation products from Lacosamide was accomplished on Hypersil BDS C18 Column using (250 x 4.6mm, 5µm) 0.01 M mono basic potassium phosphates for adjusting the pH to 4.0 with orthophosphoric acid: acetonitrile (30:70,v/v) as mobile phase. The flow rate was1.0 mL/min and the detection were carried out at 215 nm.[16]
- An isocratic stability indicating reversed phase liquid chromatographic determination was developed for the quantitative determination of Lacosamide in the pharmaceutical dosage form. A Hypersil C-18, 4.5 µm column with mobile phase containing acetonitrile-water (20:80,v/v) was used in this method. The flow rate was 1.0 mL min-1 and effluents were monitored at 258nm. time of Lacosamide The retention was 8.9 min. The method was found to be linear in the concentration range of 5-100µg/ml and the recovery was found to be in the range of 99.15- –100.09%. The limit of detection and limit of quantification were found to be 2 and 5 µg/ml, respectively. Lacosamide stock solutions were subjected to acid and alkali hydrolysis, chemical oxidation and dry heat degradation. The drug was found to be stable to the dry heat and acidic condition attempted.[17]

CONCLUSION

Lacosamide is a water soluble drug so polar solvent system can be used to develop simple rapid and accurate method for estimation of Lacosamide in bulk and its pharmaceutical dosage form. The drug was found to be stable to the dry heat and acidic condition. Lacosamide is estimated in bulk and pharmaceutical dosage form with accuracy and precision using UV spectrophotometry and HPLC.

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