

A Review on Analytical methods: Levetiracetam

Malla Krishna Prasad* and Mukthinuthalapati Mathrusri Annapurna

Department of Pharmaceutical Analysis and Quality Assurance, GITAM Institute of Pharmacy, GITAM (Deemed to be University), Visakhapatnam, Andhra Pradesh, India

*Corresponding Author: Malla Krishna Prasad, Department of Pharmaceutical Analysis and Quality Assurance, GITAM Institute of Pharmacy, GITAM (Deemed to be University), Visakhapatnam, Andhra Pradesh, India.

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Abstract

Levetiracetam is a second-generation anti-epileptic drug which belongs to pyrrolidone family with wide spectrum of action. In 1999 Levetiracetam was approved by US Food and Drug Administration as a broad spectrum antiepileptic drug. Levetiracetam is different from other older antiepileptic drugs in its structure with hydrophilic groups. The present review summarizes the analytical techniques used for the analysis of Levetiracetam.

Keywords: Levetiracetam; Antiepileptic Drug; Spectrophotometry; HPLC; LC-MS

Introduction

Levetiracetam is an anti-epileptic agent [1] and chemically known as (S)-2-(2-oxopyrrolidin-1-yl) butanamide (Figure 1) and it has a molecular formula ($C_8H_{14}N_2O_2$). Levetiracetam is very soluble in water and freely soluble in methanol and chloroform. In n-hexane Levetiracetam is insoluble practically. Levetiracetam acts by modulating the synaptic neurotransmitter release and by binding itself to synaptic vesicle protein SV2A in the brain. Levetiracetam was approved by the US FDA. Levetiracetam is absorbed completely after the oral administration and about 100% bio-availability was reported. Levetiracetam undergoes metabolism through enzymatic hydrolysis of acetamide group. Levetiracetam maintains a large margin of safety and no interactions were reported with other anticonvulsants [2] and due to this Levetiracetam is used as an adjunctive therapy for the treatment of epileptic seizures.

The authors have summarised the analytical methods developed for the quantification of Levetiracetam in the present review article. These analytical methods include spectrophotometry [3-6], HPLC [7-12], UPLC [13], UHPLC [14], HPTLC [15], LC-MS/MS

[16,17] and UPLC-MS/MS [18] for the estimation of Levetiracetam in pharmaceutical formulations and biological fluids such as human plasma and human serum (Table 1).

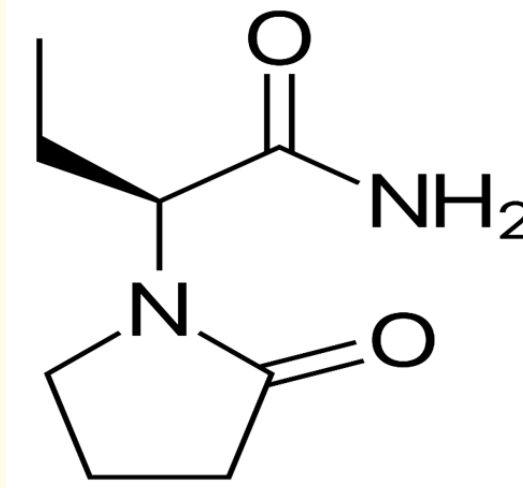


Figure 1: Structure of Levetiracetam.

| Reagent/Mobile phase (v/v) | λ (nm) | Linearity ($\mu\text{g/ml}$) | Remarks | Ref |
|---|----------------|--------------------------------|-----------------------------|-----|
| Spectrophotometric methods | | | | |
| Water | 209 | 2-10 | | 3 |
| 2-Chloro phenyl hydrazine and 2 ml (0.25 %) Anthranilic acid | 560 485 | - | | 4 |
| 2,4- Dinitrophenylhydrazine | 455 | 30-130 | | 5 |
| Glacial acetic acid | 221 | 30-90 | | 6 |
| Liquid chromatographic methods | | | | |
| Potassium dihydrogen phosphate and sodium 1-heptane sulphonate buffer (pH adjusted to 2.8 with ortho phosphoric acid): Acetonitrile (90:10) | 215 | 45-270 | HPLC | 7 |
| Acetonitrile: water (Gradient mode) Internal standard | 205 | 2.5-29.7 | HPLC and GLC Human serum | 8 |
| Acetonitrile: 0.03 M potassium dihydrogen phosphate (pH adjusted to 3.0 with ortho phosphoric acid) (15: 85) | 210 | 20-240 | HPLC | 9 |
| 0.05M KH_2PO_4 buffer (pH adjusted to 3.0 with ortho phosphoric acid): Methanol (70:30) | 210 | 20-120 | HPLC | 10 |
| Water: acetonitrile (90:10) | 200 | 0.8-8.0 | HPLC | 11 |
| Methanol: Ammonium acetate buffer (pH 4.0) (80:20) Ritonavir (Internal standard) | 240 | 5-350 | HPLC | 12 |
| Buffer (KH_2PO_4 + Heptan sulphonic acid salt) (pH 2.4): Acetonitrile (90: 10) | 200 | 45-135 | UPLC | 13 |
| Acetonitrile: water (80: 20) Lamivudine (Internal standard) | 205 | 0.05-1 | UHPLC Human serum | 14 |
| Toluene: Ethyl acetate: Methanol (2:1:1) | 204 | 0.1-1.0 | HPTLC | 15 |
| Liquid chromatography-Mass spectrometric methods | | | | |
| 5 mM Ammonium acetate (adjusted to pH 3.2 with Glacial acetic acid): Acetonitrile (20: 80) Clonazepam (Internal standard) | - | 0.5-50 | LC-MS/MS Human plasma | 16 |
| 0.1% Formic acid in Ammonium acetate: Methanol (10: 90) Lamivudine (Internal standard) | - | 0.50-80.0 | LC-MS/MS Human plasma | 17 |
| [0.1%formic acid -10 mM Ammonium formate (pH 3.5)]: [0.1%formic acid in methanol] (Gradient mode) | - | 0.5-150 | UPLC-MS/MS Human plasma | 18 |

Table 1: Review of analytical methods for the determination of Levetiracetam.

Conclusion

Different analytical methods such as UV, HPLC, HPTLC, UPLC, UHPLC and hyphenated techniques such as GC-MS, LC-MS methods

were reported for the estimation of Levetiracetam in bulk, pharmaceutical formulations and biological samples. This review article is very much useful for the readers for understanding the analytical techniques so far reported for the quantification of Levetiracetam.

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