IJBPAS, October, 2025, 14(10): 5263-5270

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

ANALYTICAL METHOD DEVELOPMENT AND VALIDATION OF LUMATEPERONE TOSYLATE API BY UV SPECTROPHOTOMETRY

SALUNKHE T*, ALHAT H[1], MOHITE S[2], DHOLE S[3] AND VICHARE V[4]

1: Assistant Professor, Department of Chemistry, PES Modern College of Pharmacy (for ladies), Moshi, Pune, India

2: PES Modern College of Pharmacy (for ladies), Moshi, Pune, India

3: Principle, Department of Pharmaceutics, PES Modern College of Pharmacy (for ladies), Moshi, Pune, India

4: Head of Department, Department of Quality Assurance, PES Modern College of Pharmacy (for ladies), Moshi, Pune, India

***Corresponding Author: Dr. Tejal Ajay Salunkhe: E Mail: salunkhetejal242@gmail.com**

Received 25th July 2024; Revised 8th Sept. 2024; Accepted 1st Oct. 2024; Available online 1st Oct. 2025

https://doi.org/10.31032/IJBPAS/2025/14.10.9447

ABSTRACT

Lumateperone Tosylate is the Non-Pharmacopeial Anti-Psychotic drug which is used for the treatment of schizophrenia. A simple, precise, and cost effective UV-Spectrophotometric method was developed and validated for the estimation of Lumateperone Tosylate API. The absorbance and spectral measurements were done on a double-beam Labindia UV-Visible spectrophotometer with software UV Win. 1cm quartz cells at wavelength 250 nm and solvent system used is Methanol: Dimethyl Sulphoxide in the ratio of 70:30. The method is developed and validated for linearity, precision, robustness, LOD, LOQ. Validation was carried out as per ICH Q2(R1) guidelines.

Keywords: Lumateperone Tosylate API, Non-Pharmacopeial, Anti-Psychotic, UV, Validation, ICH Q2(R1)

INTRODUCTION

Lumateperone Tosylate is a second-generation atypical antipsychotic drug used for the treatment of schizophrenia. Schizophrenia is a debilitating psychiatric disorder characterized by positive symptoms, such as hallucinations and delusions, and negative symptoms, such as apathy, depression, and deficits in cognitive functioning **[1]**.

Lumateperone Tosylate is a Non-Pharmacopeial drug which involves mechanism of action of simultaneous modulation of dopaminergic, serotonergic, and glutamatergic neurotransmission **[2, 3]**. Lumateperone Tosylate also acts as an antagonist of serotonin 5-HT2A receptors and has a 60-fold higher affinity for 5-HT2A receptors than D2 receptors **[3, 4]**. Its dopaminergic actions involve pre-synaptic partial agonist and post-synaptic antagonist activity at dopamine D2 receptors **[5]**. This dual action at the dopamine D2 receptor is unique to Lumateperone Tosylate compared to other antipsychotics.

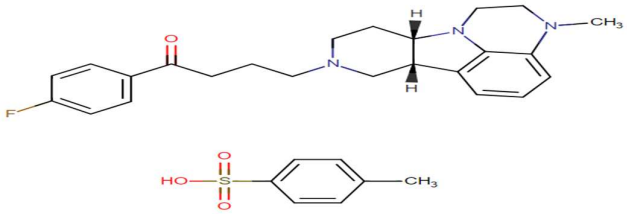

Figure 1: Structure of Lumateperone Tosylate

Lumateperone Tosylate has the structural formula as shown in **(Figure 1)**. It is chemically known as 1-(4-fluorophenyl)-4-[(10R,15S)-4-methyl-1,4,12-triazatetracyclo [7.6.1.05,16.010,15] hexadeca-5,7,9(16)-trien-12-yl] butan-1-one;4-methylbenzenesulfonic acid. It has a molecular formula of $C_{31}H_{36}FN_3O_4S$ and a molecular weight of 565.7. Lumateperone Tosylate is a White to off-white Powder which is soluble in Soluble in Organic Solvents – Ethanol, Dimethyl formamide, Dimethyl sulfoxide, Methanol.

Literature Survey revealed that the drug has been estimated by UV **[6]** and RP-HPLC **[6, 7, 8]** methods. Moreover, the reported methods for Lumateperone in bulk and pharmaceutical dosage form has been reported till now, but no UV spectrophotometric method for Lumateperone Tosylate is estimated. Therefore, method development and validation was carried out through very basic instrument (i.e. UV Spectrophotometric). Tosylate is the salt form of Lumateperone which tends to overcomes the challenges of the molecule

solubilization in particular solvent. Hence, the present work was aimed to develop and validate a simple, sensitive, precise, and specific UV Spectrophotometric method for estimation of Lumateperone Tosylate in its API.

MATERIALS AND METHODS

Instrumentation

The absorbance and spectral measurements were done on a double-beam Labindia UV-Visible spectrophotometer with software UV Win. 1cm quartz cells were used for sample handling. A digital analytical balance was used for weighing.

Materials and Reagents

Lumateperone Tosylate API was obtained from Bhisaj Pharmaceutical, Pune as a gift sample. Methanol and Dimethyl sulphoxide were procured from local market. All the chemicals and solvents used were of analytical grade.

Preparation of standard stock solution (100µg/ml)

Accurately weighed 10mg of API Lumateperone Tosylate was taken in clean, dry 100ml volumetric flask and dissolved in few ml of Methanol: Dimethyl Sulphoxide (DMSO)in the ratio of 70:30, and the volume was made up to 100ml to obtain a concentration of 100µg/ml.

Selection of Analytical wavelength

Different aliquots (12, 22, 32, 42 and 52 ml) of working standard solution were transferred to a series of 10 ml volumetric flasks and then made up to 10ml with Methanol: DMSO to obtain a concentration range of 12-52µg/ml. One of the solutions was scanned in UV range of 200-400 nm using water as a blank and the wavelength of maximum absorption was found to be 250 nm and it is selected for further analysis. The Baseline and UV spectrum of different solutions was shown in Figure 2 and 3. The UV spectrum of 32µg/ml solution was shown in **Figure 5**.

METHOD VALIDATION

The validation parameters were performed as per the ICH Q2(R1) Guideline. **[9]**

1. Linearity

Different aliquots 12, 22, 32, 42, 52 ml of working standard were transferred to a series of 10 ml volumetric flasks and then made up to 10ml with Methanol: DMSO to obtain 12, 22, 32, 42, 52µg/ml respectively. Then their absorbance was measured at 250nm. The calibration curve was plotted by taking concentration on X-axis and absorbance on Y-axis. The calibration plot was shown in **Figure 4**. And the optical characteristics and other parameters were shown in **Table 1**.

2. Precision

The precision of the method was demonstrated by intraday and inter-day studies. In the intra-day study, three different solutions of the same concentrations (32µg/ml) were prepared and analyzed thrice a day (morning, afternoon, and evening).

In the inter-day variation study, the solutions of same concentration (32µg/ml) were prepared and analyzed daily for three days, and the absorbance was recorded. The results of intra-day and inter-day study were shown in **Table 2**.

2.1 Repeatability

The method was determined by performing the six different solutions of the same concentrations (32µg/ml) were prepared and analyzed. The results of repeatability study were shown in **Table 3**.

2.2 Intermediate Precision

The method was determined by performing the same method by using different analysts at similar operational and environmental conditions. The results were reported in the table 4.

3. Robustness

Robustness is the ability of a method to remain unaffected by small deliberate variations in method parameters.

It is determined by performing the analysis at slightly different wavelengths from the selected wavelength of maximum absorption. The results were recorded in table 5.

4. Limit of Detection (LOD)

Limit of Detection (LOD) of the method was found to be 7.4254µg/ml which is calculated from the following formula,

LOD=3.3 σ/S

Where,

σ =Standard deviation of the response of the analyte,

S = Slope of the linearity plot of the analyte.

5. Limit of Quantification (LOQ)

Quantification limit is the that can be quantitated reliably with a specified level of accuracy and precision. LOQ was found to be 22.5013µg/ml and can be calculated by the following formula,

LOQ= 10 σ/S

Where,

σ = Standard deviation of the response of the analyte,

S = Slope of the linearity plot of the analyte.

6. Stability

Lumateperone Tosylate API solution was checked for stability and was found to be stable at 2-8°C for 24 hrs.

RESULTS AND DISCUSSION

Table 1: Optical Characteristics and Other Parameters

Parameters	Results
Absorption Maxima(λ max)	250 nm
Beer's-Lamber's Range(µg/ml)	12-52µg/ml
Regression Equation (y)	0.0209x+0.0695
Slope (m)	0.0209
Intercept (c)	0.0695
Correlation Co-efficient	0.9997
Limit of detection (LOD) (µg/ml)	7.4254
Limit of quantification (LOQ) (µg/ml)	22.5013

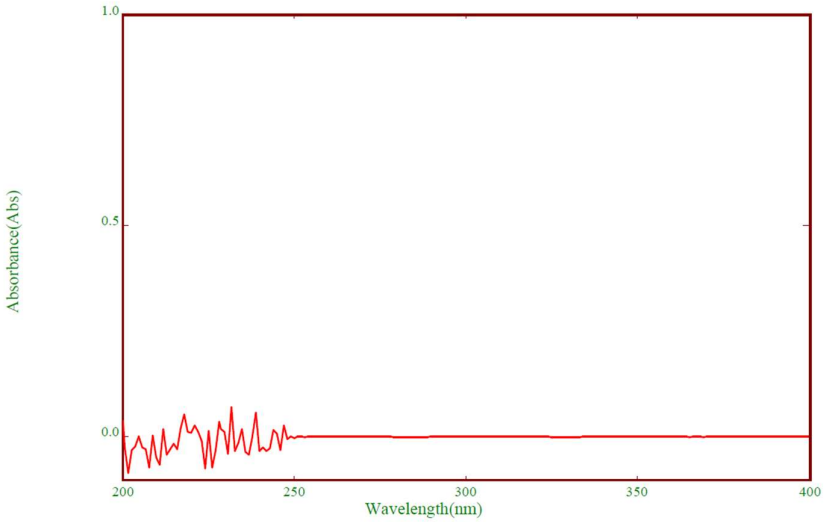

Figure 2: Baseline of Methanol: Dimethyl Sulphoxide (70:30) Solution

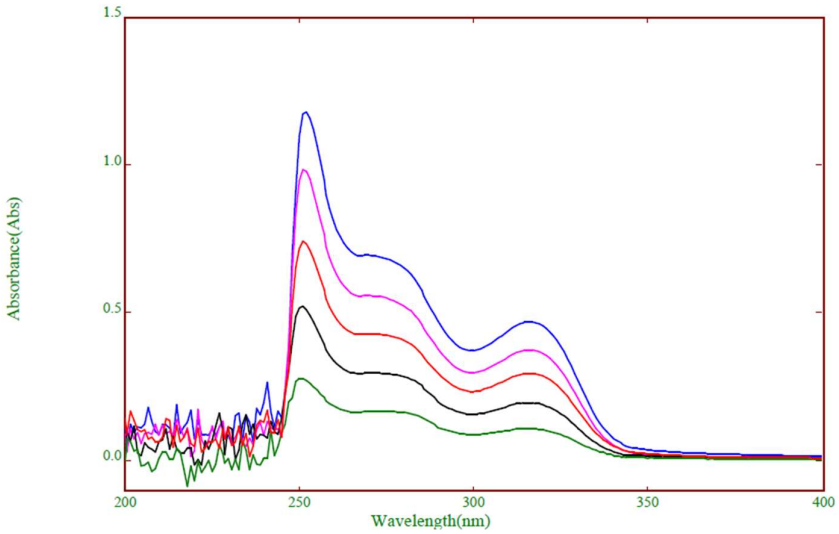

Figure 3: UV Spectrum of 12-52µg/ml Lumateperone Tosylate Solution

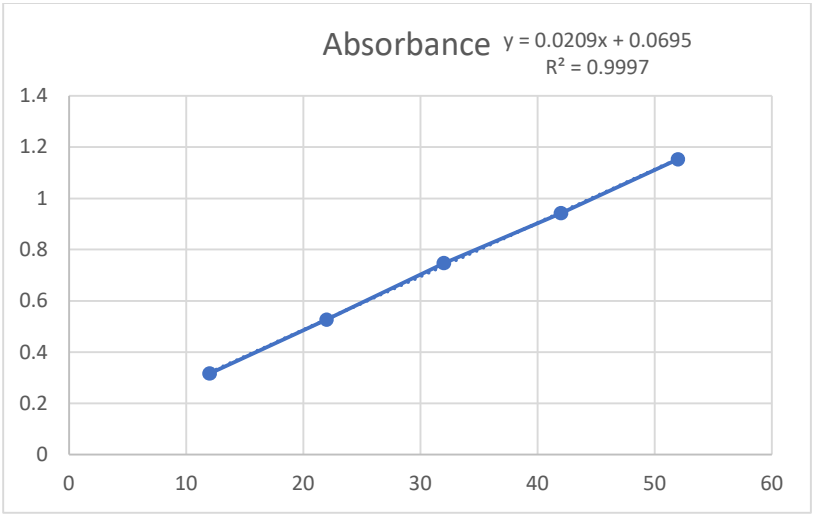

Figure 4: Calibration Curve of Lumateperone Tosylate

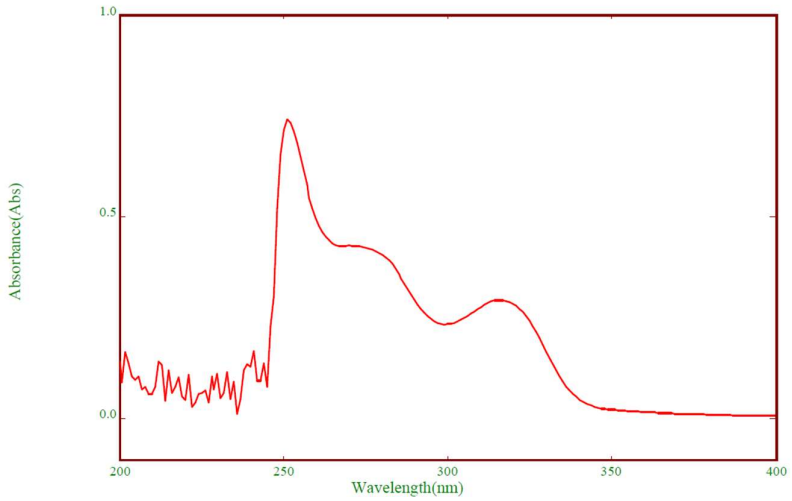

Figure 5: UV Spectrum of 32µg/ml Lumateperone Tosylate Solution

Table 2: Intra-day and Inter-day Precision Study results

Concentration (32µg/ml)	Intra-day Study			Inter-day Study		
	Morning	Afternoon	Evening	Day 1	Day 2	Day 3
Avg. Abs.	0.7322	0.7164	0.7154	0.7347	0.7219	0.7243
SD	0.0111	0.0085	0.0079	0.0118	0.0053	0.0119
%RSD	1.5159	1.1966	1.1106	1.6157	0.7461	1.6527

Table 3: Repeatability Study results

Concentration (µg/ml)	Absorbance
32	0.7111
32	0.7201
32	0.7319
32	0.7256
32	0.7318
32	0.7159
Average	0.7227
Standard Deviation	0.0085
%RSD	1.1796

Table 4: Intermediate Precision Study results

Concentration (32µg/ml)	Analyst 1	Analyst 2
Mean Abs.	0.725	0.7308
SD	0.0120	0.0052
%RSD	1.6567	0.7201

Table 5: Robustness Study results

Concentration (32µg/ml)	At 249nm	At 251nm
Mean Abs.	0.7021	0.7379
SD	0.0074	0.0053
%RSD	1.0566	0.7237

The UV spectrum of 32µg/ml Lumateperone Tosylate solution was shown in **Figure 2**. From this spectrum 250 nm was selected as the wavelength of maximum absorption (λ max).

The linearity of the method was found to be within the range of 12-52µg/ml with a correlation coefficient of 0.9997. The linearity plot was shown in **Figure 3**. Precision of the method was determined by intra-day and inter-day, repeatability, intermediate precision studies and the results were shown in **Table 2, Table 3 and Table 4**. The LOD and LOQ of the method

were calculated as 7.4254 and 22.5013µg/ml respectively. Robustness was estimated by performing analysis at slightly different wavelengths from the actual wavelength of maximum absorption and the results were reported in **Table 5**. Stability was estimated and drug was found to be stable at 2-8°C for 24 hrs.

CONCLUSION

The proposed UV- Spectrophotometric method for estimation of Lumateperone Tosylate in API and its validation was carried out as per ICH Q2(R1) guidelines. By studying various parameters and from those results we conclude that the method is simple, precise, sensitive, economic, and specific and can be applied for the determination of Lumateperone Tosylate in API. The method was found to be linear in the specified range. All the required validation parameters were estimated.

ACKNOWLEDGEMENT

The authors are thankful to the management of PES Modern college of pharmacy (for ladies), Moshi, Pune for providing necessary facilities.

REFERENCES:

[1] Maini K, Hollier JW, Gould H, Bollich V, John LaForge J, Cornett EM, Edinoff AN, Kaye AM, Kaye AD. Lumateperone tosylate, A Selective and Concurrent Modulator of Serotonin, Dopamine, and Glutamate, in the Treatment of Schizophrenia. Health Psychol Res. 2021;9(1):24932.

[2] Correll CU, Davis RE, Weingart M, Saillard J, O'Gorman C, Kane JM, Lieberman JA, Tamminga CA, Mates S, Vanover KE. Efficacy and Safety of Lumateperone for Treatment of Schizophrenia: A Randomized Clinical Trial. JAMA Psychiatry. 2020 Apr 01;77(4):349-358.

[3] Corponi F, Fabbri C, Bitter I, Montgomery S, Vieta E, Kasper S, Pallanti S, Serretti A. Novel antipsychotics specificity profile: A clinically oriented review of lurasidone, brexpiprazole, cariprazine and lumateperone. Eur Neuropsychopharmacol. 2019 Sep;29(9):971-985.

[4] Davis RE, Correll CU. ITI-007 in the treatment of schizophrenia: from novel pharmacology to clinical outcomes. *Expert Review of Neurotherapeutics*. 2016;16(6):601-614. doi:10.1080/14737175.2016.1174577

[5] Vanover KE, Davis RE, Zhou Y, Ye W, Brašić JR, Gapasin L, Saillard J, Weingart M, Litman RE, Mates S, Wong DF. Dopamine D_2 receptor occupancy of lumateperone (ITI-007): a Positron Emission Tomography Study in patients with

schizophrenia. Neuropsychopharmacology. 2019 Feb;44(3):598-605.

[6] International Journal of All Research Education and Scientific Methods (IJARESM), ISSN: 2455-6211 Volume 9, Issue 5, May -2021, Impact Factor: 7.429, Available online at: www.ijaresm.com

[7] Babu KN, Mrinalini TS. Contemporary HPLC-UV reverse phase method development and validation of anti-psychotic drug Lumateperone Tosylate, followed by forced degradation studies. Atomic Spectroscopy-Part C. 2023 Oct 21;44(3):1-1.

[8] International Journal of Novel Research and Development (IJNRD), ISSN: 2456-4184 Volume 8, Issue 7 July 2023, Available online at: www.ijnrd.org

[9] ICH, Q2 (R1) validation of analytical procedures: text and methodology, International conference on harmonization; Nov 2005.