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Validated UV spectrophotometric method for quantitative analysis of Lurasidone hydrochloride in pharmaceutical dosage form

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ABSTRACT

A simple, precise, accurate spectrophotometric method was developed and validated for the determination of Lurasidone HCl in bulk and pharmaceutical formulations. Beer's law is obeyed in the concentration range of 2-10 µg/mL with good correlation coefficient (R^2= 0.9995) and UV detection was done at 315 nm. The percentage recovery studies were performed and the percentage recovery was found to be of 98.76 -99.84 %. The method was precise and the relative standard deviation was found to be 0.98. Detection limit and Quantitation limit were found to be 0.253 µg/mL and 0.766 µg/mL respectively. The proposed method was successfully validated as per the ICH guidelines. This method can be used for the determination Lurasidone HCl in quality control laboratories without interference of excipients.

Key words: Lurasidone HCl, Spectrophotometric methods, Statistical analysis, Recovery studies.

INTRODUCTION

Lurasidone HCl is an atypical antipsychotic drug approved by the U.S. Food and Drug Administration (FDA) for treatment of Schizophrenia. Lurasidone Hydrochloride, chemically is (3aR,4S,7R,7aS)-2-[((1R,2R)-2-{[4-(1,2-benzisothiazol-3-yl)-piperazin-1–yl]methyl}cyclohexyl}hexahydro-1H-4,7-methanisoindol-1,3-dione hydrochloride. The efficacy of Lurasidone HCl in schizophrenia is mediated through a combination of central dopamine Type 2 (D2) and serotonin Type 2 (5HT2A) receptor antagonism and it gives antipsychotic activity. Lurasidone HCl is metabolized in the liver via the enzyme CYP3A44. This means that its plasma concentrations may be increased when combined with CYP3A4 inhibitors like ketoconazole or grape fruit juice, possibly leading to more side effects. As with other atypical neuroleptics, Lurasidone HCl should not be used in elderly patients because it puts them at an increased risk for a stroke or transient ischemic attack. The chemical structure of Lurasidone hydrochloride is shown in the following Figure 1.

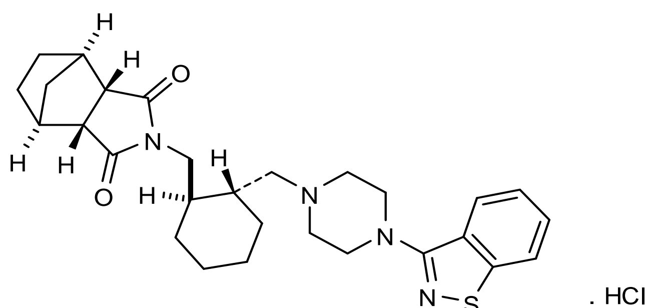

Figure 1: Chemical structure of Lurasidone HCl

A through literature survey reveals that only few spectrophotometric and chromatographic techniques have been reported recently for the determination of Lurasidone HCl in pharmaceutical dosage form. Among them, the methods for the estimation of Lurasidone HCl included UV Spectrophotometry [1-4], RP-HPLC [5-6] and LC/MS/MS [7]. However in some extent, the above stated methods are limited either low sensitivity or specificity. In fact, the specific aim of the present study is to develop and validate a simple, accurate, precise, sensitive and cost effective UV method for the estimation of Lurasidone HCl in pharmaceutical dosage form.

MATERIALS AND METHODS

Materials used

Lurasidone HCl active pharmaceutical ingredient (API) was procured from Hetero Drugs Ltd., Hyderabad, Andhra Pradesh, India. All the chemicals were analytical grade. Methanol procured from Merck specialities private Ltd., Mumbai, India and triple distilled water procured from Vignan Pharmacy College.

Instruments used

UV-Visible double beam spectrophotometer (Systronics model 2203). The UV-VIS spectrophotometer achieves a resolution of 1 nm with matched quartz cells of 1 cm path length. In addition an electronic balance (Shimadzu TX223L), digital pH- meter (Systronics model 802), a sonicator (spectra lab, model UCB 40) were used in the present study.

Preparation of solutions:

Preparation of standard stock solution

Standard stock solution was prepared by precisely 10 mg of pure drug of Lurasidone HCl was transferred into a 10 mL volumetric flask and dissolved in few mL of methanol and sonicated for 10 minutes and the volume was made to the mark with distilled water to get the stock solution of 1000 µg/mL solution. This solution was used as primary stock solution.

Preparation of working standard solution:

From the primary stock solution 1mL aliquot was pipette out in a10 mL volumetric flask and made up to the mark with methanol to obtain 100 µg/mL of working standard solution. This solution was used as working standard solution. From the working standard solution 1mL was pipette out into another 10 mL volumetric flask to obtain a solution of 10 µg/mL concentration.

Procedure for assay of tablet formulation

Twenty tablets of Latuda were weighed and powdered and average weight was determined. A quantity of tablet powder equivalent to 50 mg of Lurasidone HCl was accurately weighed and transferred into a 50 mL of methanol. The solution was sonicated for extracting the drug for about 15 minutes, filtered through a cotton wool and the filtrate was made up to volume with methanol. The volume was made up to the mark with methanol to obtain a final concentration of 1000 µg/mL. The solution was filtered through Whatmann filter paper (0.45µm) and this solution was used as Sample stock solution 'A'.

From the sample stock 'A' 1mL aliquot was pipette out and transferred to a 10 mL volumetric flask. The volume was made up to the mark with methanol to obtain a solution of concentration 100 µg/mL and this solution was used as sample stock solution 'B'. From the sample stock solution 'B' 5 mL aliquot was pipette out and transferred to a 10 mL volumetric flask. The volume was made up to the mark with methanol to obtain a solution of concentration 50 µg/mL, and analysed at the selected maximum absorption wavelength, 315 nm.

Method Development

Selection of Solvent

A number of trials were made to find out the ideal solvent system for dissolving the drug. The solvents such as water, methanol, ethyl acetoacetate and acetonitrile were tried based on the solubility of the drug. Better absorption maximum was found to be 315 nm with methanol. So methanol was selected as optimized solvent in this spectrophotometric method.

Determination of maximum absorption wave length

In order to obtained the wavelength of maximum absorption (λ_{max}) of the drug, 10µg/mL Lurasidone HCl aqueous solution was scanned using spectrophotometer within the wavelength region of 200-400 nm against methanol as blank. The resulting absorption spectra showed characteristic absorption maxima at 315 nm. This wavelength of maximum absorption (315 nm) was selected and the absorption spectrum is represented in Figure 2.

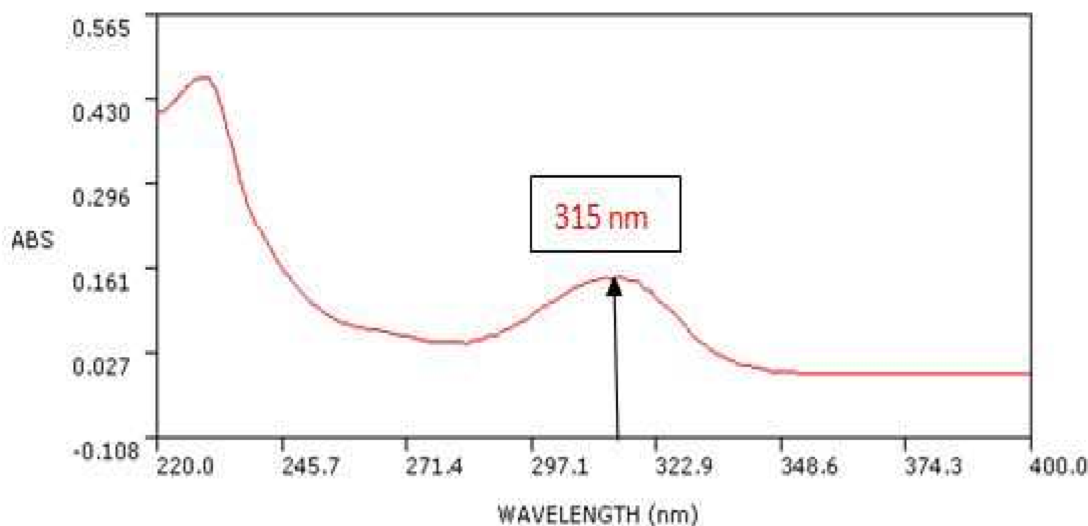

Figure 2: UV spectrum of Lurasidone HCl

Determination of Concentration Range:
A Series of dilutions were prepared by utilizing the working standard solution. From the working standard solution 0.2, 0.4, 0.6, 0.8 and 1mL were pipette out into a 10 mL volumetric flasks and diluted with methanol. The absorbances were measured and the range of 2-10 µg/mL of Lurasidone HCl was found to be linear.

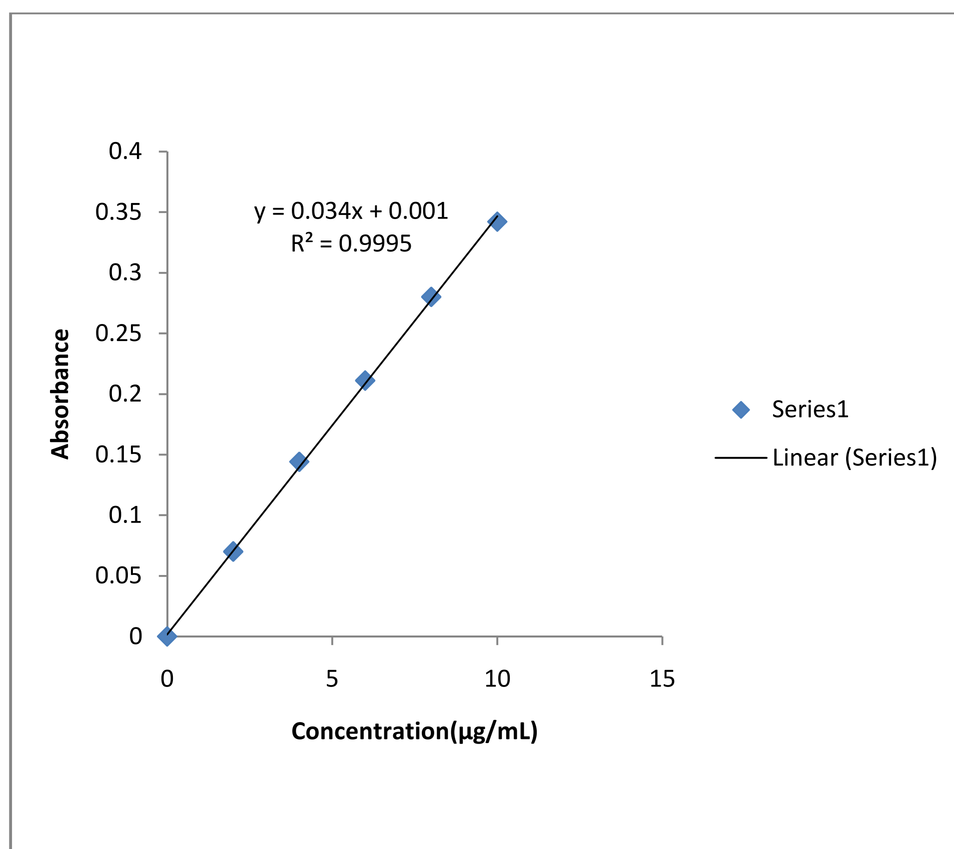

Figure 3: Calibration curve of Lurasidone HCl by UV method

METHOD VALIDATION
Linearity:
The linearity of the method was confirmed over the concentration range of 2-10 µg /mL. A Series of dilutions were prepared by using the working standard solution. From the working standard solution 0.2, 0.4, 0.6, 0.8 and 1mL were pipette out into a 10 mL volumetric flasks and diluted with methanol and finally make up to the volume with

methanol. The resulting solutions were labelled as 2, 4, 6, 8 and 10 µg /mL. The calibration curves were constructed by plotting absorbance versus concentration and the linearity was calculated by the least square regression method. The linearity data of Lurasidone HCl is presented Table 1, The linearity curve is shown in Figure 3. Optical characteristics, regression data of the proposed method is tabulated in Table 2.

Table 1: Linearity data for Lurasidone HCl

S.N0	Concentration µg/mL	Absorbance
1	2	0.07
2	4	0.144
3	6	0.211
4	8	0.280
5	10	0.342

Table 2: Optical characteristics, regression data of the proposed method

Parameter	Result
λ_{max} (nm)	315 nm
Beer's law limits (µg / mL)	2-10
Molar absorptivity (L. mole^{-1} cm^{-1})	315.66
Detection limits (µg / mL)	0.2530
Quantitation limits (µg / mL)	0.7668
Sandell's sensitivity (µg /cm^2/0.001 absorbance unit)	0.0284
Regression equation (Y = a+ bc): Slope (b)	0.0343
Standard deviation of slope (S_b)	0.00043
Intercept (a)	0.0025
Standard deviation of intercept (S_a)	0.0026
Standard error of estimation(S_e)	0.0036
Correlation coefficient (R^2)	0.9995
% Relative standard deviation*	0.2451

**Average of six determinations.*

Precision

The precision of the method was determined by repeatability (intraday) and intermediate precision (inter-day) and reported as percent RSD. For this 10 µg /mL concentration solution was prepared from the working standard solution by taking 1mL of the solution into a 10 mL volumetric flask and diluted with methanol. It was measured six times in the same day for intraday precision and on three different days for interday precision. The percent relative standard deviation (% RSD) was calculated which is within the acceptable criteria of not more than 2.0. The results for intra-day and inter-day precision are presented in Table 3 and Table 4.

Table 3: Results of Intra-day precision study

Concentration (µg/mL)	Absorbance			
	0 hour	2 hour	4 hour	6 hour
6	0.211	0.227	0.221	0.220
6	0.216	0.229	0.225	0.219
6	0.217	0.223	0.227	0.215
6	0.216	0.225	0.228	0.221
6	0.216	0.223	0.225	0.219
6	0.217	0.225	0.224	0.216
MEAN	0.2155	0.2253	0.2254	0.2183
SD	0.0022	0.0023	0.0024	0.0023
% RSD	1.04	1.03	1.08	1.07

Table 4: Results of Inter-day precision study

Concentration (µg/mL)	Absorbance		
	DAY 1	DAY 2	DAY 3
6	0.226	0.220	0.219
6	0.224	0.217	0.215
6	0.229	0.215	0.218
6	0.224	0.218	0.214
6	0.225	0.214	0.217
6	0.229	0.218	0.214
MEAN	0.2261	0.2170	0.2161
SD	0.0023	0.0021	0.0021
% RSD	1.0242	1.0096	0.9885

Accuracy (Recovery studies)
The accuracy of the method was evaluated by standard addition method. In this method the volume of the test solution was taken as constant and standard Lurasidone HCl solution was added in increasing amounts equivalent to 80%, 100% and 120% level to each test solution. Known amount of standard Lurasidone HCl of 2 µg/mL concentrations was added in pre-analyzed sample for 4, 5 and 6 µg/mL in triplicate. The percent recovery of the triplicate solutions was determined and average of the percent recovery was calculated. The results are presented in Table 5.

Procedure for the Preparation of Solution for 80% Recovery
From the working standard solution of Lurasidone HCl 0.4 mL was taken into a 10 mL volumetric flask. To this 0.2 mL of working test solution was added and mixed well. Volume was filled up to the mark with methanol.

Procedure for the Preparation of Solution for 100% Recovery
From the working standard solution of Lurasidone HCl 0.5 mL was taken into a 10 mL volumetric flask. To this 0.2 mL of working test solution was added, mixed well and volume was brought up to the mark with methanol.

Procedure for the Preparation of Solution for 120% Recovery
From the working standard solution of Lurasidone HCl 0.6 mL was taken into a 10 mL volumetric flask. To this 0.2 mL of working test solution was added, mixed well and the volume was filled up to the mark with methanol.

Table 5: Results of recovery studies

S.N0	Spiked level	Amount of drug from formulation added (µg/mL)	Amount of standard solution added (µg/mL)	Amount recovered (µg/mL)	% Recovery	% R.S.D
1	80%	2	4	12.98	99.84	0.70
				12.87	99.00	
				12.78	98.30	
2	100%	2	5	14.95	99.66	0.57
				14.89	99.26	
				14.78	98.53	
3	120%	2	6	16.97	99.82	0.53
				16.88	99.29	
				16.79	98.76	

Robustness:
The robustness of an analytical procedure is the 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. For the determination of a method's robustness, parameters such as variation in detector wavelength are varied within a realistic range and the quantitative influence of the variables is determined. If the influence of the parameter is within a previously specified tolerance, the parameter is said to be within the method's robustness range. The absorbance was measured and assay was calculated for six times. The results of robustness are presented in Table 6.

Table 6: Results for Robustness study

S.N0	λ_{max} 1	λ_{max} 2
1	0.278	0.258
2	0.274	0.256
3	0.276	0.253
Mean	0.276	0.2556
SD	0.002	0.0025
% R.S.D	0.7246	0.9843

Ruggedness:
The Ruggedness of an analytical method is degree of reproducibility of test results obtained by the analysis of the same samples under a variety of conditions, such as different analysts, instruments. 6 µg/mL standard solution was prepared as mentioned in the precision, the absorbances were measured by different analyst and different instrument. The results were noted down and tabulated. The % relative standard deviation was calculated. The Ruggedness values are presented in Table 7.

Table 7: Results for Ruggedness study

S.N0	Analyst 1	Analyst 2	Instrument 1	Instrument 2
1	0.28	0.278	0.28	0.258
2	0.279	0.274	0.279	0.256
3	0.277	0.276	0.277	0.253
4	0.28	0.275	0.28	0.254
5	0.275	0.273	0.275	0.257
6	0.277	0.271	0.277	0.258
Mean	0.278	0.274	0.278	0.256
S.D	0.002	0.0024	0.002	0.0020
% R.S.D	0.71	0.88	0.71	0.81

LOD and LOQ:
Limit of Detection is the lowest concentration in a sample that can be detected, but not necessarily quantified under the stated experimental conditions. The limit of quantitation is the lowest concentration of analyte in a sample that can be determined with acceptable precision and accuracy. Limit of detection and limit of quantitation were calculated utilizing the following formula LOD = 3.3(SD)/S and LOQ = 10 (SD)/S, where SD = standard deviation of response (absorbance) and S = slope of the calibration curve. The LOD and LOQ values are presented in Table 8.

Table 8: Results of LOD and LOQ

Parameter	Result
Limit of detection (µg/mL)	0.253
Limit of quantitation (µg/mL)	0.766

Assay of Lurasidone in tablets:
The Latuda tablets were analyzed using the developed method. Satisfactory results obtained that the mean percentage found for Lurasidone were good agreement with the label claimed. The Mean percentage found and the RSD values in Table 9 showed that the proposed method can be adopted for the determination of Lurasidone in pharmaceutical tablets.

Table 9: Assay results of Lurasidone in tablets

S.N0	Formulation	Labelled amount	Mean % ± SD	%Assay	% RSD
1.	Latuda	**40 mg**	**39.96±0.16**	**99.9**	**0.4**

RESULTS AND DISCUSSION

The proposed method was found to be linear in the range of 2-10 µg/mL with a correlation coefficient R^2 value of 0.9995 which states that the method was linear and the UV spectrum for determination of maximum absorption wavelength (315 nm) is shown in the Figure 2. Regarding precision the value of standard deviation and % R.S.D. were found to be < 2 %. The % R.S.D. for intra- day precision was found as 1.03 and for inter -day precision was 1.02 and the results are showed in the Table 3 and 4. High % recovery greater than 98 % showed that the method is free from the interference of excipients used in the formulation. The results are shown in the Table 5. The proposed method was found to be robust because with the change of solvent % R.S.D was found as 0.74 and with the change of wavelength it was found to be 0.98 and the results are shown in the Table 6. The ruggedness was performed and results are shown in the Table 7 and these robustness and ruggedness results indicate the vast applicability of the method. The percentage recovery of the drug from Tablets was found as 99.9% and results are shown in the Table 5. The limit of detection and limit of quantitation for Lurasidone was found to be 0.253 and 0.766 µg/mL respectively. High % recovery and low % RSD suggests the method can be vast applicability for the routine analysis of commercial formulations.

CONCLUSION

A validated UV spectrophotometric method has been developed for the determination of Lurasidone HCl in pharmaceutical formulations. From the above experimental data results and parameters reveals that, the developed

method has several advantages such as the time taken for preparation of standard and sample solutions is less, cheaper and robust to slight variations in experimental conditions. The developed method has acceptable accuracy and precision reproducibility and hence this method can be applicable for the analysis of Lurasidone HCl raw material and its pharmaceutical dosage form in quality control studies for routine analysis.

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REFERENCES

[1] Nirav K, Joshi, Nehal Shah, Minaxi Dumasiya and Alisha Patel, *IJPS*, **2012**, 3, 2643-2653.
[2] Muvvala S and Ratnakarm V, *RJPBS*, **2013**, 4, 609-617**.**
[3] Mali N, Patel J, Patel M, *Int J Res Pharm Sci*, **2012**, 2, 44-50.
[4] Muvvala SS and Ratnakaram VN, *Research Journal of Pharmaceutical, Biological and Chemical Sciences*, **2013**, 4, 609- 617.
[5] Joshi NK, Shah NJ, *Int J Pharm Sci*, **2012**, 3, 2886-2899.
[6] Joshi NK and Shah NJ, *Pharma Science Monitor*, **2012**, 3, 2886-2899.
[7] Ishiyama T, Tokuda K, Ishibashi T, *Eur J Pharmacol*, **2007**, 572, 160–170.
[8] International Conference on Harmonization. Validation of Analytical Procedures: Text and Methodology Q2 (R1), **2005**.