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Research Article

Analytical Method Validation of Tablet Dosage Form of Lurasidone HCl

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ABSTRACT

This research is mainly focused on development of an Excellent Gradient method by reverse phase - high performance liquid chromatography (RP-HPLC) using UV Visible Detector. The main objective of method validation of Lurasidone HCl as a tablet dosage form is to validate the method as in-house method. As this tablet dosage form is not registered in any of Pharmacopeia, so the method is developed and validated for further studies. The sample is analyzed by RP-HPLC using octadecylsilane (C18) column (Inertsil LC-GC) as stationary phase with UV-Visible detector. The 'Gradient Method' is used as instrumental method. The Mobile phase (A) was prepared using potassium phosphate buffer by adjusting the pH of value 4.0 and mobile phase (B) was 100% acetonitrile; the ratio used for gradient was buffer: acetonitrile (40:60) respectively. The wavelength for λ max was selected by UV-Visible detector on spectrophotometer at wavelength 254nm. This method complies with Linearity , Accuracy , Recovery , Specificity , precision , stability , LOD , LOQ and Robustness

INTRODUCTION

A simple, rapid and sensitive analytical method was developed and validated for the analysis for Lurasidone in pharmaceutical formulations. Quality by Design approach was used for the optimization of method condition and the analysis was completed within shortest chromatographic runtime of less than 5 minutes. Statistical analysis proves that the method is suitable for the analysis of Lurasidone in pharmaceutical formulation without any interference from the excipients.

Lurasidone HCl is a potent atypical antipsychotic (Neuroleptics) drug that belongs to class of benzisothiazol **[1].** It is used in treatment of schizophrenia and also in treatment of depressive episodes that occurs in conditions of bipolar I disorder (Bipolar depression)**[2,3].** It was used firstly in when U.S Food and Administration approved Lurasidone Tablet (with Brand name

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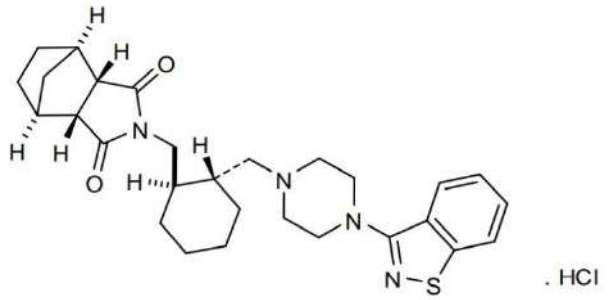


Fig. 1: Structure of Lurasidone HCl

Latuda) for treatment of adults [4-6] suffering from schizophrenia on Oct.28, 2010**[7,10].** It Usefulness comes under visuals when its tendency to treat symptoms including Hallucinations, Delusions, Disordered thinking and change in behaviour occurs **[8].** It is a white to off-white colour crystalline powder **[11].** It is slightly soluble in water, ethanol and sparingly soluble in methanol, practically insoluble in 0.1N HCl, toluene and very slightly soluble in acetone **[5].** It chemical structure is referred as [(3aR,4S,7R,7As)-2-{(1R,2R)-2-[4(1,2benzisothiazol3yl) piperazin1ylmethyl] cyclohexyl methyl} hexahydro-4-7-methano-2H-isoindole-1,3-dionehydrochloride**[9.]** It is an azapirone derivate. The chemical structure of lurasidone hydrochloride has six chiral centres. Its molecular weight is 492.67 g/l.

EXPERIMENTAL

1. Materials & Methods

1.1 Apparatus

Shimadzu Liquid chromatography (LC 2010CHT HPLC System) having UV- Visible detector Loaded with Lab Solution Software, octadecylsilane (C18) 250mm x 4.0 mm 5 µ shimpack Shimadzu stainless steel Column is used as stationary Phase, Shimadzu Analytical Balance AP Series is used for all weighing functions. Sonicator (Precioustech), Digital pH Meter (Hanna instruments), Glass wares like Pipette, Beaker, Volumetric Flask etc. manufactured and certified from Supertek. Syringes, nylon Syring filters of 0.45µ size are used, Milli Q Water System of Labjal (HPLC Grade Water System) is used.

1.2 Chemicals and Materials

Lurasidone Working reference Standard is used from Consern Pharma Pvt Ltd. Potassium di hydrogen orthophosphate of AR Grade, Acetonitrile used is of HPLC Grade, Methanol also of HPLC Grade, Milli Q Water, Orthophosphoric Acid, Lurasidone tablet 40 mg of Brand name lurasic-40(Taken from Consern Pharma Pvt Ltd)is taken for experimental purpose.

1.3 Chromatographic Conditions

For Dissolution: Medium: 0.1 M hydrochloric acid, 900 ml, R.P.M.: 100, Time: For 45 min. Paddle, Sample: 6 Tablets, C_{18} 5micron 250cmX4mm column.

Detection:- λ max: 254 nm Flow rate:- 1 ml per minute. Loop Injector:- 100 microlitre, Temperature :- Ambient

For Assay: C_{18} 5 micron 250cmX4mm column, Detection:- λ max: 254 nm, Flow rate:- 1 ml per minute, Loop injector:- 100 microlitre, Temperature:- Ambient

1.4 Preparation of Mobile Phase

Mobile Phase: Acetonitrile: Buffer: methanol (40:40:20) Respectively and adjust the final pH of the mobile phase to 4.0

Buffer preparation:- Dissolve 2.72 gm of Potassium dihydrogen orthophosphate in 400 ml of water.

1.5 Preparation of Standard solution and sample for Dissolution:

Standard solution for 40mg: - Weigh accurately about 50 mg of Lurasidone HCl WRS and transfer to a 50 ml volumetric flask. Add about 20 ml of mobile phase and shake to dissolve and make up the volume with same solvent. Dilute 1 ml to 25ml with the Medium.

Sample Solution: Transfer one tablet to each jar containing dissolution medium & operate as per described conditions & Filter the solution using

0.45µ nylon filter, discard few ml & use the solution.

Procedure: Inject the sample & standard solution & calculate the result by comparison.

1.6 Preparation of Standard solution and sample for Assay:

Standard solution: - Weigh accurately about 50 mg of Lurasidone HCl WRS and transfer to a 50 ml volumetric flask. Add about 20 ml of mobile phase and shake to dissolve and make up the volume with same solvent. Dilute 1 ml to 10 ml with the Medium

Sample Solution: Weigh accurately 20 tablets & reduce to fine powder & weigh accurately equivalent to 100 mg of Lurasidone HCl & transfer to 100 flasks, add 60ml of mobile phase & sonicate for 5 minutes & cool, dilute to the volume with same. Filter the solution using 0.45µ nylon filter, discard few ml & use the solution. Dilute 1ml of 1st dilution to 10ml volumetric flask and make the volume with mobile phase.

Procedure: Inject the sample & standard solution & calculate the result by comparison.

2.0 Analytical Method Validation of dosage form of Lurasidone 40 mg: -

So the method complies with all the parameters that are necessary for its Validation i.e Accuracy / Recovery, Specificity, Method Precision, Stability of sample and standard solution, Robustness.

RESULT & DISCUSSION:

2.1 Linearity

Linearity refers to linear results with respect to concentration used. It is found that with increase in concentration there is linear increase in Area Under Curve (AUC). Three triplicate injections of Lurasidone are injected and a linear change is observed in all at different concentration i.e 80%,90%100%,110% and 120%. The relative standard deviation that is observed is also below the limit of 2% which is good and allows to study for further Validation parameters. The R^2 Value obtained is

Concentration	1st injection area	2nd injection area	3rd injection area	Average area	Std deviation	%RSD
80ppm (80%)	631,590	632,561	629,794	631,315	1403.848639	0.222368966
90ppm(90%)	719,806	716,336	719,970	718,704	2052.386903	0.285567759
100ppm(100%)	786,700	788,611	788,464	787,925	1063.424186	0.134965154
110ppm(110%)	865,498	864,651	865,750	865,300	575.7189708	0.066534057
120ppm(120%)	945,931	944,333	946,663	945,642	1191.520597	0.12600119
						0.167087425

Table

Retention time of injections at different concentrations:

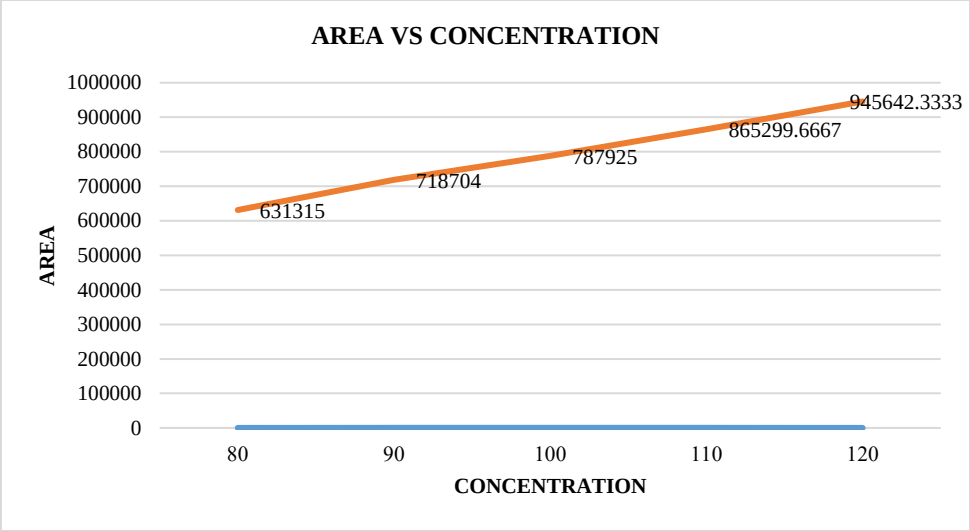
Concentration	Injections	Area	Retention Time	%RSD of Area	Avg retention time
80ppm	1st	631590	10.870	0.222	10.911
	2nd	632561	10.973		
	3rd	629794	10.890		
90ppm	1st	719806	11.398	0..286	11.054
	2nd	719336	10.840		
	3rd	719970	10.923		
100ppm	1st	786700	10.791	0.135	10.822
	2nd	788611	10.770		
	3rd	788464	10.904		

110ppm	1st	865498	10.767	0.067	10.760
	2nd	864651	10.730		
	3rd	865750	10.782		
120ppm	1st	945931	10.928	0.126	10.843
	2nd	944333	10.799		
	3rd	946663	10.803		

Table 2

Table 1 shows triplicate injection of different concentration of sample and area under curve observed of different injections. average area, standard deviation and relative standard deviation of area under curve

Table 2 shows the retention time of different peaks of sample, relative standard deviation of retention time and average retention time.



2.2 Accuracy / Recovery

Accuracy/recovery is determined by running triplicate injection of samples with concentration of 80%,90%,100%,110% and 120%. As the retention time and area observations explains the good and accurate linear change when the concentration increases by every 10%. Also the retention time remains almost similar with respect to each injection at different concentrations. So the results are mentions as per study of lurasidone tablet dosage form at different concentration are shown in Table 2.

2.3 Specificity

Specificity is defined as a specific precision for a well developed method that can be analysed again at same conditions and parameters. The other components are used to check the interference of those and the main API used. So, the placebo used in formation of tablet as per average weight of tablet is used as a reference to check whether its presence can effect the formulation or not. I it effects than one can check the area difference, amplitude of peaks obtained, might be slight change in retention time etc.

2.4 Method Precision

Six replicate injections of sample solution are injected to check whether the applied method is suitable or not. The RSD percentage should be below 2% and results obtained can be seen in Table 1 & 2. The indication of correctively of the method is precised by repeatedly applying multiple injections.

2.5 Stability of sample and standard solution

Stability of sample and standard are checked at time of analysis as firstly one analyst performs Analytical method that is developed and after that

second analysis perform the same and result obtained are .

2.6 Limit of Detection & Limit of Quantification

LOD refers to limit of detection and it's the precised limit at which a substance show its existance by absorbing radiations. LOQ is value of quantification that is calculated and found to be good.

LOD = 3.3 × σ/S , LOQ = 10 × σ/S Where, σ = the standard deviation of the response and S = slope of the calibration curve.

Value of slope in Plot 1 is 7752.5 and standard deviation is 14445.47 So , after applying values in formula , we can able to LOD and LOQ.

The LOD is found to be 13.74 µg/ml and LOQ is found to be 41.66 µg/ml.

2.6 Robustness

Robustness in an analytical method is the variational changes that are brought to check the stability of sample even after some minor changes in it. The changes or variations which are checked is change in pH by ±0.5 and cahnge in temperature by ±2.0˚C.

After checking these changes the validation has been done as the results obtained are satisfying and notable with respect to attained method.

CONCLUSION

An Excellent Gradient method is developed by RP-HPLC in which UV Visible Detector is present . The nature of method is such that it complies with Linearity , Accuracy , Recovery , Specificity , precision , stability , LOD , LOQ and Robustness. Lurasidone is detected mainly at 254 nm when 250mmx 4.0mm , 5µ C18 Column is used. Flow rate is justified at 1ml/min. with injection volume of 20µl in Assay and 100µl in Dissolution . The calibration curves shows good linearity from range 80ppm to 120ppm concentration with r^2 value of 0.9984 . Interferance of any other component is not found there in AUC of main peak of Lurasidone . Precision is attaianed by injecting multiple replicate injections and RSD obtained is below 2%. Reproducibility is good as sample tested by another analyst is found stable . Method is validated after seeing the Degradation study too as after 24 hours the same sample is injected and AUC obtained shows good responses . LOD and LOQ values is found to be 13.74957 and 41.66536 µg/ml.

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