CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187

https://doi.org/10.5281/zenodo.8170995

Available online at: http://www.iajps.com *Research Article*

ANALYTICAL METHOD DEVELOPMENT AND VALIDATION FOR THE DETERMINATION OF LURASIDONE HCL IN PHARMACEUTICAL DOSAGE FORM BY RP-HPLC

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Abstract:

A simple, accurate, precise and sensitive RP-HPLC assay method have been validated for the estimation of Lurasidone HCl in bulk and marketed pharmaceutical formulation.Lurasidone HCl is separated using Symmetry C18 ODS (4.6mm×150mm) 5µm particle size column and Methanol: Phosphate Buffer (0.05M-pH-4.8) (34:66) used as a mobile phase at a flow rate of 1.0ml/ minand effluent was detected at 315 nm. Here resolution was good, theoretical plate count and symmetry was appropriate. The retention time of Lurasidone HCl was found to be 2.248 minutes.Linearity was observed over concentration range of 30-60ng ml-1. The Limit of detection and limit of quantification was found to be 1.2ng ml-1 and 3.7ngml-1 respectively. The accuracy of the proposed method was determined by recovery studies and found to be 98% to 102%. The above method was afforded excellent percentage recovery was found to be within the limits i.e. 98-102% The % RSD values were less than 2%.The validation parameters, tested in accordance with the requirements of ICH guidelines, prove the suitability of this method. The method was successfully applied for determination of drug in tablets, wherein no interference from tablet excipients was observed, indicating the specificity of the developed method.The proposed method was found to be simple, precise, accurate, rapid, economic and reproducible for the estimation of Lurasidone HCl in bulk and marketed pharmaceutical formulation.

Keywords: *Lurasidone HCl, RP-HPLC, Accuracy, Precision, ICH Guidelines.*

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Please cite this article in press Gattu Manisha et al, ***Analytical Method Development And Validation For The Determination Of Lurasidone Hcl In Pharmaceutical Dosage Form By RP-HPLC.,*** *Indo Am. J. P. Sci, 2023; 10 (06).*

INTRODUCTION:

Chromatography is a laboratory technique for the separation of a mixture. The mixture is dissolved in a fluid called the mobile phase, which carries it through a structure holding another material called the stationary phase. The various constituents of the mixture travel at different speeds, causing them to separate. The separation is based on differential partitioning between the mobile and stationary phases. Subtle differences in a compound's partition coefficient result in differential retention on the stationary phase and thus affect the separation.[1]

Chromatography may be preparative or analytical. The purpose of preparative chromatography is to separate the components of a mixture for later use, and is thus a form of purification. Analytical chromatography is done normally with smaller amounts of material and is for establishing the presence or measuring the relative proportions of analytes in a mixture. The two are not mutually exclusive.[2]

Introduction to chromatography, its types and classification Chromatography

Chromatography is a set of techniques in which separation of chemical substances takes place quantitatively as well as qualitatively.

Terminology used in Chromatography Mobile Phase:

In chromatography the substance which is introduced with or along with the sample and causes elution of the contents of the sample. It may be liquid or gas.

Stationary phase: Stationary phase of the chromatographic system refers to that part which is present before the introduction of sample or solute in the column (as in column chromatography) or on solid support (as in paper or similar chromatography). It may be liquid or solid.

Eluent: The substance which separates the components of the mixture in chromatographic technique.Eluent is that part that brings separation when the solution is passed either from the column or from thesolid support.

Eluate: The substance which is separated as a individual component of the mixture is called eluate.

Important types of Chromatographic Techniques

Following are some important types of Chromatographic separation techniques. They are defined thoroughly by explaining their general principle, application, and a brief outline of their instrumentation for a complete understanding .Following are some commonly utilized types of techniques:

i.Gas Chromatography
ii.High Pressure Liquid Chromatography
iii.Supercritical fluid Chromatography
iv. Gel Exclusion Chromatography.

High Pressure Liquid Chromatography (HPLC)

High Performance Liquid Chromatography (HPLC) is a form of column chromatography that pumps a sample mixture or analyte in a solvent (known as the mobile phase) at high pressure through a column with chromatographic packing material (stationary phase). The sample is carried by a moving carrier gas stream of helium or nitrogen. HPLC has the ability to separate, and identify compounds that are present in any sample that can be dissolved in a liquid in trace concentrations as low as parts per trillion. Because of this versatility, HPLC is used in a variety of industrial and scientific applications, such as pharmaceutical, environmental, forensics, and chemicals.

Sample retention time will vary depending on the interaction between the stationary phase, the molecules being analyzed, and the solvent, or solvents used. As the sample passes through the column it interacts between the two phases at different rate, primarily due to different polarities in the analytes. Analytes that have the least amount of interaction with the stationary phase or the most amount of interaction with the mobile phase will exit the column faster.

High-performance liquid chromatography (HPLC; formerly referred to as high-pressure liquid chromatography) is a technique in analytical chemistry used to separate, identify, and quantify each component in a mixture. It relies on pumps to pass a pressurized liquid solvent containing the sample mixture through a column filled with a solid adsorbent material. Each component in the sample interacts slightly differently with the adsorbent material, causing different flow rates for the different components and leading to the separation of the components as they flow out of the column.

HPLC has been used for manufacturing (e.g., during the production process of pharmaceutical and biological products), legal (e.g., detecting performance enhancement drugs in urine), research (e.g., separating the components of a complex biological sample, or of similar synthetic chemicals from each other), and medical (e.g., detecting vitamin D levels in blood serum) purposes.[1]

High performance liquid chromatography (HPLC) is basically a highly improved form of column liquid chromatography.

Instead of a solvent being allowed to drip through a column under gravity, it is forced through under high pressures of up to 400 atmospheres. That makes it much faster.

MATERIALS AND METHODS

Drug name- Lurasidone HCl, Formulation- Luratrend 80mg (2.5mg),Manufacturer- Sun Pharmaceuticals Ltd, Procurement-Sura labs

OPTIMIZED CHROMATOGRAPHIC CONDITIONS:

Mobile phase : Methanol: Phosphate Buffer (0.05M-pH-4.8) (34:66)
Column : Symmetry C18 ODS (4.6mm×150mm) 5µm particle size
Flow rate : 1 ml/min
Wavelength : 315 nm
Column temp : Ambient
Injection Volume : 10 µl
Run time : 6 minutes

VALIDATION

PREPARATION OF MOBILE PHASE:

Preparation of mobile phase:

Accurately measured 340 ml (34%) of HPLC Grade Methanol and 660 ml of Phosphate buffer (660%) were mixed and degassed in a digital ultra sonicater for 15 minutes and then filtered through 0.45 µ filter under vacuum filter.

Diluent Preparation:

Accurately measured 340 ml (34%) of HPLC Grade Methanol and 660 ml of Phosphate buffer (660%) were mixed and degassed in a digital ultra sonicater for 15 minutes and then filtered through 0.45 µ filter under vacuum filter.

RESULTS AND DISCUSSION:

Optimized Chromatogram (Standard)

Mobile phase : Methanol: Phosphate Buffer (0.05M-pH-4.8) (34:66)
Column : Symmetry C18 ODS (4.6mm×150mm) 5µm particle size
Flow rate : 1 ml/min
Wavelength : 315 nm
Column temp : Ambient
Injection Volume : 10 µl
Run time : 6 minutes

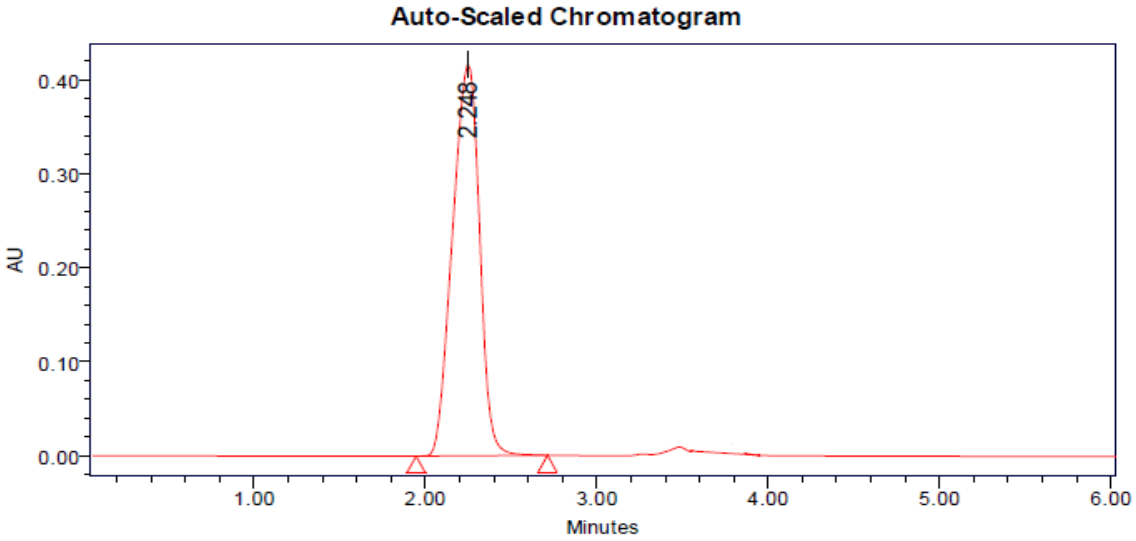

Figure1: Optimized Chromatogram (Standard)

Table 1: Results of Optimized Chromatogram (Standard)

S.No.	Name	RT	Area	Height	USP Tailing	USP Plate Count
1	Lurosidone HCl	2.248	1056524	63582	1.46	5876

Observation: In this trial it shows proper separation of peak and more plate count in the chromatogram and the tailing factor is within the limit. So it is an optimized chromatogram.

Optimized Chromatogram (Sample)

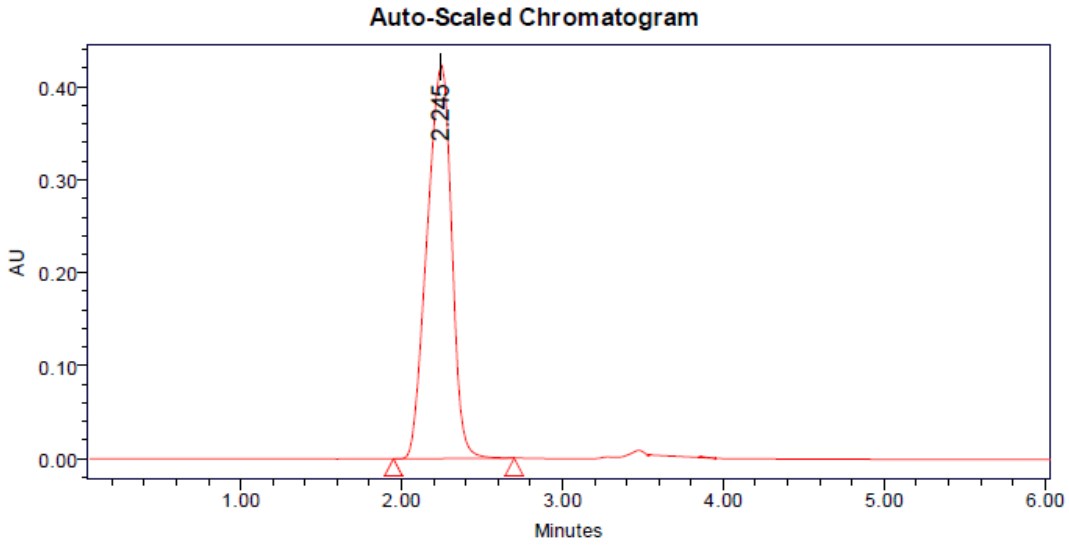

Figure2: Optimized Chromatogram (Sample)

Table2: Results of Optimized Chromatogram (Sample)

S.No.	Name	RT	Area	Height	USP Tailing	USP Plate Count
1	Lurosidone HCl	2.245	1068547	64587	1.48	5986

Acceptance criteria:

- Theoretical plates must be not less than 2000.
- Tailing factor must be not less than 2.
- It was found from above data that all the system suitability parameters for developed method were within the limit.

Assay (Standard):

Table-3: Results of system suitability for Lurosidone HCl

S.No	Name	RT	Area	Height	USP Tailing	USP Plate Count	Injection
1	Lurosidone HCl	2.241	1058745	63587	1.46	5879	1
2	Lurosidone HCl	2.246	1056854	63589	1.47	5874	2
3	Lurosidone HCl	2.245	1058462	63524	1.46	5869	3

Assay (Sample):

Table-4: Peak Results for Assay sample

S.No	Name	RT	Area	Height	USP Tailing	USP Plate Count	Injection
1	Lurosidone HCl	2.248	1065874	64874	1.47	5986	1
2	Lurosidone HCl	2.248	1066258	64258	1.48	5948	2
3	Lurosidone HCl	2.247	1069854	64587	1.48	5964	3

$$\%ASSAY = \frac{\text{Sample area}}{\text{Standard area}} \times \frac{\text{Weight of standard}}{\text{Dilution of standard}} \times \frac{\text{Dilution of sample}}{\text{Weight of sample}} \times \frac{\text{Purity}}{100} \times \frac{\text{Weight of tablet}}{\text{Label claim}} \times 100$$

The % purity of Lurosidone HCl in pharmaceutical dosage form was found to be 99.25%.

LINEARITY

CHROMATOGRAPHIC DATA FOR LINEARITY STUDY:

Table-5: Chromatographic Data for Linearity Study

Concentration µg/ml	Average Peak Area
20	548745
30	806487
40	1056528
50	1285845
60	1538542

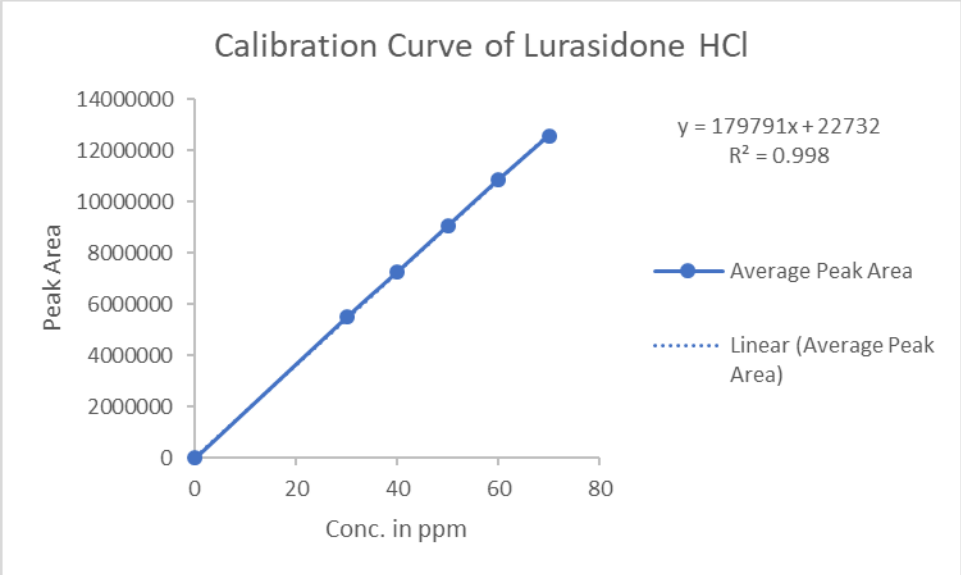

Fig 3: Calibration Curve of Lurosidone HCl

REPEATABILITY

Table6: Results of repeatability for Lurosidone HCl:

S. No.	Peak name	Retention time	Area (µV*sec)	Height (µV)	USP Plate Count	USP Tailing
1	Lurosidone HCl	2.255	1056524	63525	5869	1.46
2	Lurosidone HCl	2.258	1056485	63587	5874	1.47
3	Lurosidone HCl	2.252	1056985	63985	5896	1.47
4	Lurosidone HCl	2.253	1054874	63548	5846	1.46
5	Lurosidone HCl	2.258	1053652	63854	5863	1.46
Mean			1055704			
Std.dev			1398.475			
%RSD			0.132468			

Acceptance criteria:

- %RSD for sample should be NMT 2.
- The %RSD for the standard solution is below 1, which is within the limits hence method is precise.

Intermediate precision:

Table7: Results of Intermediate precision for Lurosidone HCl

S.No.	Peak Name	RT	Area (µV*sec)	Height (µV)	USP Plate Count	USP Tailing
1	Lurosidone HCl	2.255	1065874	65245	6154	1.48
2	Lurosidone HCl	2.262	1068547	65241	6185	1.47
3	Lurosidone HCl	2.257	1069854	65231	6158	1.48
4	Lurosidone HCl	2.260	1065341	65784	6192	1.47
5	Lurosidone HCl	2.262	1065848	65842	6154	1.48
6	Lurosidone HCl	2.263	1065232	65894	6135	1.47
Mean			1066783			
Std. Dev.			1935.366			
% RSD			0.181421			

Acceptance criteria:

- %RSD of Six different sample solutions should not more than 2.

Table 8: Results of Intermediate precision Analyst 2 for Lurosidone HCl

S.No.	Peak Name	RT	Area (µV*sec)	Height (µV)	USP Plate count	USP Tailing
1	Lurosidone HCl	2.266	1075483	65842	5986	1.47
2	Lurosidone HCl	2.275	1078564	65285	5978	1.48
3	Lurosidone HCl	2.266	1078542	65365	5982	1.48
4	Lurosidone HCl	2.267	1078547	65985	5914	1.47
5	Lurosidone HCl	2.276	1078549	65421	5974	1.48
6	Lurosidone HCl	2.270	1076545	65487	5961	1.47
Mean			1077705			
Std. Dev.			1352.23			
% RSD			0.125473			

Acceptance criteria:

- %RSD of Six different sample solutions should not more than 2.

ACCURACY:

Table 9: The accuracy results for Lurosidone HCl

%Concentration (at specification Level)	Area	Amount Added (ppm)	Amount Found (ppm)	% Recovery	Mean Recovery
50%	534704.3	20	20.078	100.390%	100.18%
100%	1043632	40	40.036	100.090%	
150%	1553443	60	60.030	100.050%	

Robustness

Table 10: Results for Robustness

Parameter used for sample analysis	Peak Area	Retention Time	Theoretical plates	Tailing factor
Actual Flow rate of 1.0 mL/min	1056524	2.248	5876	1.46
Less Flow rate of 0.9 mL/min	1098698	2.879	5986	1.42
More Flow rate of 1.1 mL/min	1021454	1.915	5784	1.45
Less organic phase	1012431	1.916	5642	1.43
More organic phase	1005874	1.950	5465	1.44

Acceptance criteria:
The tailing factor should be less than 2.0 and the number of theoretical plates (N) should be more than 2000.

CONCLUSION:

In the present investigation, a simple, sensitive, precise and accurate RP-HPLC method was developed for the quantitative estimation of Lurasidone HClin bulk drug and pharmaceutical dosage forms.

This method was simple, since diluted samples are directly used without any preliminary chemical derivatisation or purification steps.

Lurasidone HCl is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF), which should be purged with an inert gas.
Methanol: Phosphate Buffer (0.05M-pH-4.8) (34:66) was chosen as the mobile phase. The solvent system used in this method waseconomical.

The %RSD values were within 2 and the method was found to be precise.

The results expressed inTablesfor RP-HPLC method was promising. The RP-HPLC method is more sensitive, accurate and precise compared to the Spectrophotometric methods.

This method can be used for the routine determination of Lurasidone HClin bulk drug and in Pharmaceutical dosage forms.

ACKNOWLEDGEMENT

The Authors are thankful to the Management and Principal, Department of Pharmacy, Surabi dayakar rao college of pharmacy, Rimmanguda,Telangana, for extending support to carry out the research work. Finally, the authors express their gratitude to the Sura Labs, Dilsukhnagar, Hyderabad, for providing research equipment and facilities.

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