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Validated Spectrophotometric Methods For The Estimation of Lurasidone Hydrochloride in Bulk And Pharmaceutical Dosage Forms

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ABSTRACT

Three new, simple and cost effective UV-Spectrophotometric methods were developed for the estimation of Lurasidone hydrochloride in bulk and pharmaceutical formulations. Lurasidone hydrochloride was estimated at 227 nm in UV-spectroscopic method (Method A), 237 nm in first order derivative spectroscopy (Method B) and scanned at 225.0 - 235.0 nm in Area under Curve method (Method C). Linearity range was found to be 5-30 g/ml (Correlation coefficient r = 0.999in method A, r = 0.999 in method B and r = 0.999 in method C) in all the three methods. These methods were tested and validated for various parameters according to ICH guidelines. The proposed Methods were successfully applied for the determination of Lurasidone hydrochloride in pharmaceutical formulation (Tablets). The results of recovery were found to be 99.44-101.28 % for method A, -100.33- -101.46% for Method B, and for Method C % Recovery was found to be 99.83-100.76% which was within limits. (98-102%). Limit of Detection and Limit of Quantification were 0.2044, 0.6196 for method A, 0.6350, 1.9245 for method B and 0.0831, 0.2521 for method C. The results demonstrated that the procedure is accurate, precise and reproducible (% relative standard deviation <2%), while being simple, cheap and less time consuming and can be suitably applied for the estimation of Lurasidone hydrochloride in tablet dosage forms.

KEYWORDS: Lurasidone hydrochloride, UV-Spectrophotometric method, first order derivative spectroscopy, Area under Curve (AUC).

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INTRODUCTION

Lurasidone [(3aR,4S,7R,7aS)-2-{(1R,2R)-2-[4-(1,2-benzisothiazol-3-yl)piperazin-1ylmethyl]cyclo hexylmethyl}hexahydro-4,7-methano- 2H-isoindole-1,3-dione hydrochloride; SM-13496] is an azapirone derivative and a novel antipsychotic candidate[1]. Lurasidone is an atypical antipsychotic developed by Dainippon Sumitomo Pharma[2]. It was approved by the U.S. Food and Drug Administration (FDA) for treatment of schizophrenia on October 28, 2010[3]. Lurasidone hydrochloride is not official in any pharmacopoeias. Lurasidone is metabolized in the liver via the enzyme CYP3A4[4]. 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.

Lurasidone acts as a D2, 5-HT2A, 5-HT7, and α2C-adrenergic receptor antagonist, and 5-HT1A receptor agonist. In animal studies, Lurasidone was found to be superior to all of the other antipsychotics examined in reversing Dizocilpine induced learning and memory impairment, including Risperidone, Olanzapine, Quetiapine, Clozapine, Aripiprazole, and Haloperidol[5,6]. As with other Atypical Neuroleptics, Lurasidone should not be used in elderly patients because it puts them at an increased risk for a stroke or transient ischemic attack[4,7]. A survey of literature revealed that only RP-HPLC[8] method for estimation of Lurasidone hydrochloride in bulk drug and formulation has been developed .The objective of the present study is to develop simple, precise, accurate and economic spectrometric methods for estimation of Lurasidone hydrochloride.

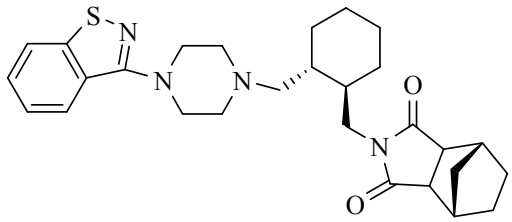


Figure 1: Structure of Lurasidone hydrochloride

MATERIALS AND METHODS

APPARATUS

Spectroscopic measurements were carried out on a computerized UV - 1800 Double beam spectrophotometer with 1 cm matched quartz cells and Shimadzu electronic balance from Uni Bloc was used for weighing the sample.

CHEMICALS

Working standard of Lurasidone hydrochloride was kindly gifted from Shodhana Laboratories Limited, Hyderabad. Tablets of Lurasidone hydrochloride (40mg) were prepared in house. Distilled water was obtained by in house distillation, AR grade Methanol was obtained from Astron Chemicals, India and AR grade Sodium Hydroxide was obtained from RFCL Ltd., India. AR grade Hydrochloric acid was obtained from Astron, Ahmedabad, India.

PROCEDURE

PREPARATION OF STANDARD STOCK SOLUTION

Standard stock solution of Lurasidone hydrochloride was prepared by dissolving 10 mg in 100 ml (1000 µg/ml) volumetric flask using methanol as solvent. Aliquots of standard stock solution were pipetted out and suitably diluted with methanol to get the final Concentration of 5, 10, 15, 20, 25, 30 g/ml of standard stock solution.

METHOD A (ZERO-ORDER DERIVATIVE SPECTROMETRY):

Series dilutions of standard solutions were prepared in 25 ml volumetric flasks with methanol to get the concentration ranging from 5-30 g/ml. The above solutions were scanned over the range of 400 nm to 200 nm against reagent blank. The λ max was found to be 230.0 nm for 30 g/ml of the drug concentration (Figure 2a). The calibration curve was constructed by plotting concentration against absorbance at 230.0 nm (Figure 3a). The optical characteristics were shown in Table 1.

METHOD B (FIRST-DERIVATIVE SPECTROMETRY):

The first order derivative spectra of 30 g/ml of the drug at n=1 showed a sharp maxima at 237.0 and minima at 227.0nm (figure 2b).The absorbance Difference at n=1 (dA/dλ) is calculated by the inbuilt software of the instrument which was directly Proportional to the concentration of the standard solution. The standard drug solution was diluted so as to get the final concentration in the range of 5-30 µg/ml and scanned in the first order derivative spectra. The calibration curve of dA/dλ against concentration of the drug showed linearity (Figure 3b). The optical characteristics were shown in Table 1.

Table 1: Optical Characteristics of Lurasidone Hydrochloride

Parameters	Method A	Method B	Method C
Beer's range (µg/ml)	5-30	5-30	5-30
Wavelength	230 nm	227nm maxima 237nm minima	230 nm (225-235 nm)
Regression Equation	Y = 0.025x - 0.101	Y = 0.002x + 0.001	Y=0.015x +0.027
Correlation coefficient	0.999	0.998	0.999
Slope	0.025	0.002	0.015
Intercept	0.101	0.001	0.027
Limit of Detection (µg/ml)	0.2044	0.6350	0.0831
Limit of Quantification (µg/ml)	0.6196	1.9245	0.2521
Intraday precision (n=3) (%RSD)	0.2116	-0.6728	0.1972
Inter day precision (n=3) (%RSD)	0.3928	-0.4073	0.4573

METHOD C (AREA UNDER CURVE):

The AUC (Area under Curve) method involves the calculation of integrated value of absorbance with respect to the wavelength between two selected wavelength 225nm and 235nm (Figure-2c). Area calculation processing item calculates the area bound by the curve and the horizontal axis. The horizontal axis is selected by entering the wavelength range over which the area has to be calculated. The wavelength range is selected on the basis of repeated observations so as to get the linearity between area under curve and concentration. Suitable dilutions of standard stock solution (30 g/ml) of the drug were prepared and scanned in the spectrum mode from the wavelength range 400-200 nm and the calibration curve was plotted(Figure-3c). The optical characteristics were shown in Table 1.

ANALYSIS OF IN-HOUSE TABLET DOSAGE FORM:

From tablets prepared by using tablet compression machine twenty tablets were weighed and powdered finely. A quantity of tablet powder equivalent to 40 mg of Lurasidone hydrochloride was accurately weighed and transferred to 10 ml volumetric flask and sonicated for 5 min with sufficient quantity in methanol and further diluted to volume. The solution was filtered through whatman filter paper. The resultant solution was diluted with methanol to get concentration 10 g/ml for all three methods. The amount of drug present in the sample solution was determined using the calibration curve of standard drug.

RESULT AND DISCUSSION

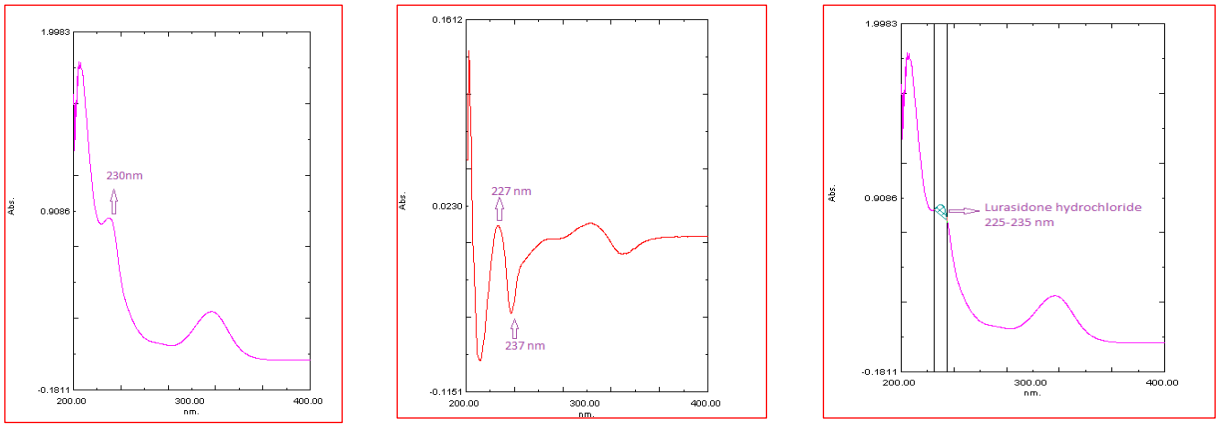
METHOD VALIDATION

LINEARITY AND RANGE

Aliquots 1.25, 2.5, 3.75, 5, 6.25and 7.5 ml of standard stock solution of Lurasidone hydrochloride was transferred to series of 25 ml volumetric flasks and made up to volume with methanol. Each solution were analysed. Linearity of the concentration was taken in range of 5-30 g/ml for tablet formulation.

PRECISION

The intraday precision was determined on three different days at three different levels 10, 15, 20 g/ml for Method-A and Method-C while 15, 20, 25 g/ml for Method-B. To record inter day variation, 3 different concentration solution within the linearity range were analyzed for 3 different days. The %RSD values were found to be less than 2% indicating that the method is more precise.



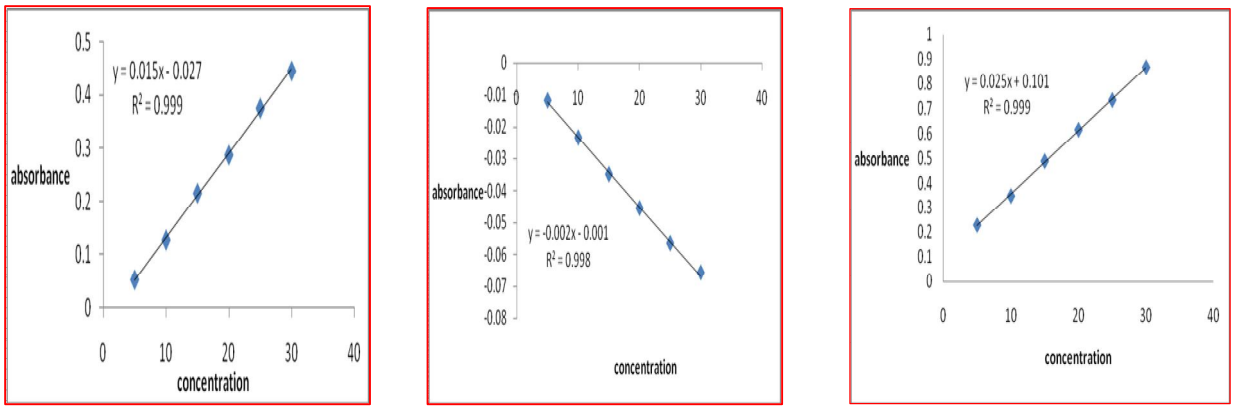
(a)Zero-derivative, (b) First order-derivative, (c) AUC

Figure 2: Absorption spectrum of Lurasidone hydrochloride in methanol (30 g/ml)

ACCURACY

Recovery studies were carried out by adding different amounts 80%, 100%, 120% of bulk sample of Lurasidone hydrochloride within the linearity range. For Method A % Recovery was found to be 99.44-101.28% and for Method B % Recovery was found to be -100.33- -101.46% for Method C % Recovery was found to be 99.83-100.76%.

The %RSD values were found to be less than 2% indicating that the method is more accurate.



(a)Zero-derivative, (b) First order-derivative, (c) AUC

Figure 3: Calibration curves of Lurasidone hydrochloride in methanol

Table 2: Recovery Study of Lurasidone Hydrochloride For Method A, B And C

Method	Level of % Recovery (n=3)	Tablet concentration (mcg/ml)	Standard concentration spiked (mcg/ml)	% Mean Recovery	% SD	% RSD
A	0	10	0	99.44	0.280	0.281
	50	10	5	100.66	0.577	0.573
	100	10	10	100.40	0.871	0.868
	150	10	15	101.28	1.027	1.028
B	0	10	0	-100.33	1.527	-1.522
	50	10	5	-100.01	1.354	-1.354
	100	10	10	-100.75	0.6614	-0.6565
	150	10	15	-101.46	0.9237	-0.9104
C	0	10	0	100.76	1.021	1.013
	50	10	5	100.06	0.2309	0.2285
	100	10	10	99.83	0.9504	0.9520
	150	10	15	100.76	0.2497	0.2479

Table 3: Analysis of Tablet Dosage Form

Method	Label amount	Amount found	% Label claim	SD	% RSD (n =3)
A	40 mg	39.75	99.39	0.1282	0.1290
B	40 mg	39.60	99.20	1.259	-1.271
C	40 mg	39.83	99.73	0.3253	0.3263

CONCLUSION

The validated three spectroscopic methods are simple, precise, accurate and can be used for determination of Lurasidone hydrochloride in bulk and tablet formulation.

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