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Research Article

Second Order Derivative Spectrophotometric Method for Estimation of Lurasidone in Bulk and Pharmaceutical Formulation

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Abstract

Simple, precise, rapid and novel spectrophotometric second order derivative method using AUC technique has been developed for the determination of Lurasidone in bulk and pharmaceutical formulation. No single UV spectrophotometric second order derivative method using AUC is reported for estimation of lurasidone. Present study focused on the development of Simple spectrophotometric method using area under curve (AUC) in between 303 - 333 nm. The drug follows Beer- Lambert's law in concentration range of 10 to 60 μg/mL in solvent methanol ($r^2 = 0.9988$). The method was validated according to ICH guidelines for accuracy, precision, sensitivity and ruggedness. There was no significant difference between performance of the proposed methods regarding mean values and standard deviation. The percent relative standard deviation was not more than 2%. The proposed method is simple, easy to apply, low cost and require relatively inexpensive instruments. The method is suitable for routine quality control.

Keywords: Lurasidone, second order UV spectroscopic method, area under curve (AUC), method validation, second order derivative method

Introduction

Lurasidone[(3aR,4S,7R,7aS)-2-{(1R,2R)-2-[4-(1,2-benzisothiazol-3-yl)piperazin-1-ylmethyl] cyclohexylmethyl}hexahydro-4,7-methano-2H-isoindole-1,3-dione hydrochloride (Figure 1) is an azapirone derivative and a novel antipsychotic candidate.

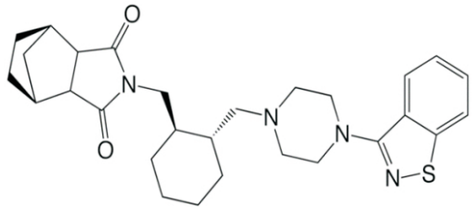

Figure1: Chemical Structure of Lurasidone

The objective of the current studies was to investigate the in vitro and in vivo pharmacological properties of Lurasidone. Receptor binding affinities of Lurasidone and several antipsychotic drugs were tested under comparable assay conditions using cloned human receptors or membrane fractions prepared from animal tissue. Lurasidone was found to have potent binding affinity for dopamine D2, 5-hydroxytryptamine 2A (5-HT2A), 5-HT7, 5-HT1A, and nor adrenaline 2C receptors. Affinity for noradrenaline 1, 2A, and 5-HT2C receptors was weak, whereas affinity for histamine H1 and muscarinic acetylcholine receptors was negligible. In vitro functional assays demonstrated that Lurasidone acts as an antagonist at D2 and 5-HT7 receptors and as a partial agonist at the 5-HT1A receptor subtype. Lurasidone showed potent effects predictive of antipsychotic activity, such as inhibition of methamphetamine induced hyperactivity and apomorphine induced stereo typed behaviour in rats, similar to other antipsychotics. Furthermore, Lurasidone had only weak extra pyramidal effects in rodent models. In animal models of anxiety disorders and depression, treatment with Lurasidone was associated with significant improvement. Lurasidone showed a preferential effect on the frontal cortex (versus striatum) in increasing dopamine turnover. Antiadrenergic, anticholinergic and central nervous system depressant actions of Lurasidone were also very weak. These results demonstrate that Lurasidone possesses antipsychotic activity and antidepressant or anxiolytic like effects with potentially reduced liability for extra pyramidal and CNS depressant side effects [1].

Lurasidone is practically insoluble in water, has poor bioavailability and slow onset of action and as a result could not be given in emergency clinical situations like schizophrenia. Bioavailability of poorly water soluble drug can be enhanced through different techniques similar to solid dispersion and mixed hydrotrophy. These techniques are useful in improving bioavailability as a result of increasing solubility. Solid dispersion is defined as dispersion of drug in a matrix of hydrophilic carrier. The solid dispersion technique is essentially used for BCS class II drugs. Drugs which come under BCS class II have low water solubility and high permeability and these drugs have solubility as the rate limiting step. So, if we promote solubility of the drug subsequently bioavailability of drug will also increase. Hence there is need to enhance the solubility of Lurasidone [2].

There are several research work has been published so far as per our knowledge [3]. Techniques like UV-Visible Spectrophotometry [4-6], high performance liquid chromatography (HPLC) [7-10], high performance thin layer chromatography (HPTLC) [11] and Liquid chromatography – mass spectroscopy (LC-MS) [12] with ESI have been used for analysis, from which it can be witnessed that high performance liquid chromatography methods have been applied most expansively. The proposed method was validated as per International Council for Harmonisation (ICH) guidelines [13].

Material and Methods

Chemicals and reagents

A gift sample of Lurasidone was obtained from Glen Mark Pvt. Ltd., Mumbai, India.

Pharmaceutical formulation of Lurasidone (20 mg) tablet was formulated by in house preparation. Methanol (HPLC grade) was purchased from Merck (India) Ltd. Mumbai, India.

Instrumentation

UV – visible spectrophotometer

Double beam UV Spectrophotometer (Shimadzu – 1700) with 10 mm match quartz cell and UV probe 2.21software.

Weighing balance: Shimadzu Aux 220

Radwag LC/GC analytical balance and ultra sonic cleaner (Equitron) were used during the study.

Selection of solvent

Methanol was selected as solvent on the basis of solubility, stability and cost.

UV Spectrophotometric Second Order Derivative (AUC) Method

Accurately weighed portion of Lurasidone (10 mg) was transferred to a separate 10 mL volumetric flask, dissolved, sonicated for three minutes and diluted to the mark with methanol to obtain standard solution having concentrations of Lurasidone (1000 µg/mL). From this stock solution 1 mL of volume was withdraw and added to 10 mL volumetric flask and methanol is added up to mark to make 100 µg/mL. Now from this stock solution volume of mL withdraw as1, 2, 3, 4, 5 and 6 mL and added to 10 mL volumetric flask respectively to obtain concentration in the range 10, 20, 30, 40, 50, and 60 µg/mL respectively. According to the certain parameters, Lurasidone solution was scanned in UV region i.e. 200 to 400 nm. After performing zero order derivatives, the curve was derivatized to second order with scaling factor 5 in UV Spectrophotometer. Two wavelengths 303 to 333 nm were selected for determination of AUC of Lurasidone (Figure 2).

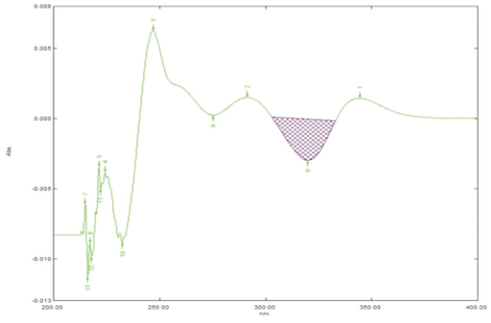

Figure 2 : Wavelength range selected for 30 μg/mL Lurasidone at 303 nm - 333 nm as AUC method

Linearity

The working standard solution of 10μg/mL was scanned in the UV range 200 to 400 nm. For the determination of linearity concentrations in the range 10-60 μg/mL were prepared and AUC were determined by analyzing all concentrations in between 303 to 333 nm. The calibration curve was plotted using concentration against AUC (Figure 3) and results of linearity study are mentioned in Table 1.

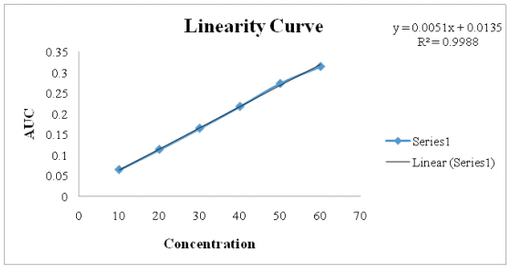

Figure 3 : Calibration curve of Lurasidone at 303 nm - 333 nm for area under curve method

Table 1: Results of linearity study

Parameters	Area Under Curve
Wavelength Range(nm)	303-333
Concentration range (µg/mL)	10-60
Linearity equation	y = 0.0051x – 0.0135
Slope (m)	0.0051
Intercept ©	0.0135
Correlation coefficient (r2)	

Table 2: Results of analysis of bulk drug and pharmaceutical formulation

Second order derivative (AUC)	z	%RSD (n=6)
Bulk	100.71	0.65
Formulation	98.56	0.69

* *n*: number of estimations

$y = mx + c$ ..... (1)

Where, y is absorbance or AUC of standard solution, x is found concentration in 10 μg/mL solution, m and c are slope and intercept of line respectively.

The percent drug content was determined by using equation,

% drug content = [found conc. (μg/mL) / actual conc. (μg/mL)] $\times$ 100 ..... (2)

Accuracy

Accuracy of the proposed method was carried as on the basis of recovery studies. It is performed by the standard addition method. Recovery studies were performed by adding standard drug at three different levels i.e. 80, 100 and 120 % to the pre analyzed tablets powder solution and the proposed method was followed. From the amount of the drug estimated, the percentage recovery was calculated (Table 3).

Table 3: Accuracy studies

Drug	Initial Amount	Amount Added	Amount Recovered	% Amount Recovered	% RSD (n=6)
Lurasidone	20	16	35.98	99.94	0.23
	20	20	39.54	98.85	0.56
	20	24	44.05	100.11	0.24

* *n*: number of estimations

Precision

Precision of the method was studied as repeatability, intraday and interday precision.

Lurasidone solutions at a concentration 20, 30 and 40 µg/mL were analyzed in group of three in morning, afternoon and evening for area under the curve spectrophotometric method. Solutions for the standard curves were prepared fresh every day (Table 4 & 5).

Table 4: Results of repeatability

Drug	Amount Taken [µg/mL]	Amount Found [µg/mL]	%Amount Found [µg/mL]	% RSD (n=6)
Lurasidone	40	39.77	99.425	0.68

* *n*: number of estimations

Table 5: Precision studies (intra day and inter day)

Drug	Concentration [µg/mL]	Intra day		Intra day	
		% Amount Found [µg/mL]	% RSD (n=6)	% Amount Found [µg/mL]	% RSD (n=6)
Lurasidone	20	20.21	0.26	19.96	0.54
	30	30.45	0.54	29.86	0.85
	40	40.25	0.58	39.58	0.95

* *n*: number of estimations

Repeatability

Repeatability was determined by analysing 40 µg/mL concentration of standard Lurasidone solution for six times. Results are shown in Table 4.

Sensitivity

Sensitivity of the proposed method was estimated in terms of LOD (Limit of detection) which is the lowest amount of analyte to be detected and LOQ (Limit of quantification) which is the lowest amount of analyte which can be measured. The sensitivity of measurement of lurasidone by the use of proposed method was estimated in terms of (LOD) and (LOQ) which were calculated using formulae "LOQ = 10 × N/ B" and "LOD = 3.3 × N/ B" where "N" is standard deviation of AUC of lurasidone (n=3) taken as a measure of noise, and "B" is the slope of the corresponding calibration curve (Table 6).

Table 6: Sensitivity

Parameter	Second order derivative AUC Method (n=6)
LOD	1.36 µg/mL
LOQ	4.45 µg/mL

* *n*: number of estimations

Ruggedness

Ruggedness of the developed method was determined by two different analysts (variables) keeping same operational and environmental conditions. It was being analysed using 40 µg/mL concentration of standard lurasidone (Table 7).

Table 7: Ruggedness

Lurasidone	Analyst	Second order derivative	AUC Method (n=6)
% RSD	I	0.33	0.08
	II	0.29	0.15

* *n*: number of estimations

Results and Discussion

In the experimental studies, UV spectrophotometric second order derivative spectra were recorded in between 303-333 nm (Figure 2). The drug follows linear relationship in 10 - 60 μg/mL showing regression equations of calibration curves, $y = 0.0051x - 0.0135$ ($R^2 = 0.9988$) (Figure 3). Both pure drug and pharmaceutical formulation analyzed and percentage of drug content were found as 100.71% in bulk and 98.56% in formulation (Table 2).The method has been validated according to ICH guidelines and results were compared statistically. Accuracy was carried out by addition of standard drug solution at three different levels of sample solution and percentage of recovery was calculated and it ranges from 98.85-100.11% (Table 3). Precision was determined in terms of repeatability, intraday and inter day analysis shows variation not more than 2 % RSD (Percent relative standard deviation) (Table 4-5). The sensitivity shows minimum amount to be measured and detected that was LOD and LOQ 1.36 and 4.45 (Table 6). Proposed method was unaffected due to change in operator and results were interpreted by calculating the % RSD value and found to be within range (Table 7).

Conclusion

No any UV spectrophotometric AUC method has been described for the determination of Lurasidone .This method was developed for determination of Lurasidone based on analytical technique, UV Spectrophotometric derivative and AUC method. The method was validated and found to be simple, sensitive, accurate, and precise. Therefore simple, fast and reliable Area under Curve spectrophotometric method was developed for the routine determination of Lurasidone. The developed method can be concluded as simple, accurate, sensitive and precise and can be easily applied to the pharmaceutical formulation.

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Conflicts of interest

The authors declare that there is no competing interest regarding publication of this paper.

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