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DEVELOPMENT AND VALIDATION OF DERIVATIVE UV-SPECTROPHOTOMETRIC METHODS FOR QUANTITATIVE ESTIMATION OF ILOPERIDONE IN BULK AND PHARMACEUTICAL DOSAGE FORM

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ABSTRACT

First and second order derivative UV-Spectrophotometric methods have been developed and validated for the estimation of Iloperidone in bulk and its tablet formulations. The solutions of standard and sample were prepared in methanol. The Iloperidone solution was showed the maximum absorbance at 262nm and 248nm for the first and second order UV-Spectrophotometric methods respectively. Beer's law was obeyed in the concentration range of 4- 12 µg / ml with r^2 value 0.999 for both the methods. These methods were tested and validated for various parameters according to ICH guidelines. The precision expressed as relative standard deviation and was found within the range of 0.13 % to 1.7 % for the both methods. Limit of detection was 0.0133 µg/ml (first order), 0.0216 µg/ml (second order) and limit of quantification was found to be 0.0403 µg/ml (first order), 0.0657 µg/ml (second order). Recovery of Iloperidone was found to be within the range of 99.51 – 100.16 % for the two methods. The proposed methods were successfully applied for the determination of Iloperidone in tablet formulations. In addition, the proposed methods are simple, easy to apply, low cost, and requires relatively inexpensive instruments.

Keywords: Iloperidone, Method Validation, Derivative UV-Spectrophotometric methods.

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INTRODUCTION

Iloperidone[1, 2] is chemically, 1-[4-[3-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl] propoxy]-3-methoxyphenyl]ethanone. It is an atypical antipsychotic drug that is chemically belongs to the class of piperidinyl-benzisoxazole derivative and it is used in the treatment of schizophrenia. The structure of Iloperidone is shown in Figure 1.

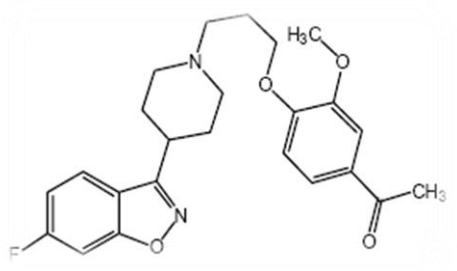

Figure 1: Chemical Structure of Iloperidone

It has potent selective antagonist activity for the noradrenaline (α_{2C}), dopamine (D_{2A} and D_3) and serotonin (5-HT_{1A} and 5-HT_6) receptors. From the literature survey, it was found that Iloperidone was estimated by reversed-phase high-performance liquid chromatographic (RP-HPLC) method[3] and liquid chromatographic-mass spectrometric (LC-MS) method [4]. Apart from this, no other methods were reported for the estimation of Iloperidone. In view of the above fact, we have developed a UV spectrophotometric method which is simple, precise, specific, accurate, and reproducible. For the estimation of Iloperidone in pharmaceutical formulations.

MATERIAL AND METHODS

Instrument and reagents

Spectral scan were made on a Shimadzu UV spectrophotometer, model 1800 (Schimadzu, Japan) with spectral bandwidth of 0.5 nm, wavelength accuracy of $\pm$ 0.3 nm with automatic wavelength corrections using a pair of 10 mm quartz cells. All Spectral measurements were done using UV-Probe 2.33 software. An analytically pure sample of Iloperidone was procured from Ranbaxy pharma, Ahmadabad. Methanol (AR) was used as a solvent for dilution.

Preparation of standard drug solution

100 mg standard Iloperidone was weighed accurately and transferred to a 100 ml volumetric flask and dissolved in methanol. The flask was shaken and volume was made up to the mark with methanol to give a solution of 1000 µg/ml. From this solution, 10 ml of solution was pipetted out and placed into 100 ml volumetric flask. The volume was made up to mark with methanol to give a solution containing 100 µg/ml. Further dilutions with methanol were made from this stock solution to get required concentration.

Preparation of sample solution

To determine the content of Iloperidone in conventional tablet (Brand name: Fanapt®; Label claim: 12 mg), twenty tablets were weighed, their mean weight was determined and finely powdered.. Tablet powder equivalent to 100 mg of Iloperidone was weighed and transfer into 100 ml volumetric flask then dissolved with methanol and further diluted upto the mark. It was kept for ultra-sonication for 30 min; this was filtered through Whatman filter paper No. 41 and then the final dilution was made with methanol to get the final stock solution of 1000 µg/ml. From this stock solution, various dilutions of the sample solution were prepared and analyzed.

First order and second order derivative Spectrophotometry

The various concentrations of Iloperidone solution was prepared by appropriate dilution of standard stock solution and scanned in the spectrum mode from 400 nm to 200 nm. First order and second order derivative spectra showed the absorption maxima [λmax] at 262 nm and 248 nm which are illustrated in **Figure2** & **Figure 4**, respectively.

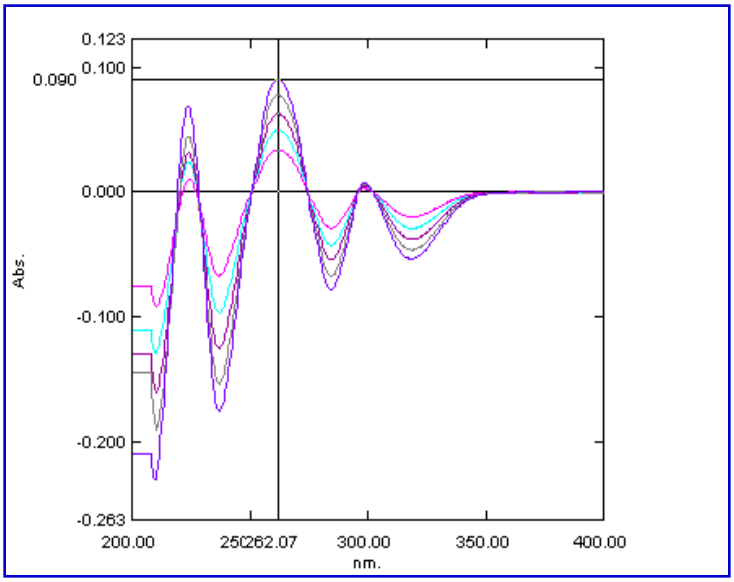

Figure 2: Overlay first order derivative spectra of Iloperidone showing absorbance at 262nm

Calibration curve was obtained by plotting absorbance at 262nm (for first order) and 248 nm (for second order) against the various concentrations of Iloperidone**,** which are shown in **Figure 3** & **Figure 5**, respectively. Beer's- Lamberts law was obeyed in the concentration range of 4-12 µg/ml for both the methods. The regression equation and correlation coefficient were determined from the calibration. The concentration of the sample solution was determined using the regression equation.

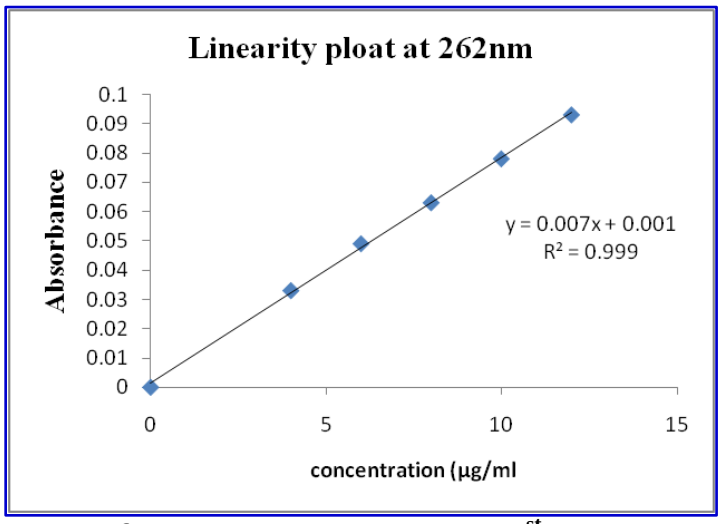

Figure 3. Calibration curve for Iloperidone at 262nm by 1st order derivative spectroscopy

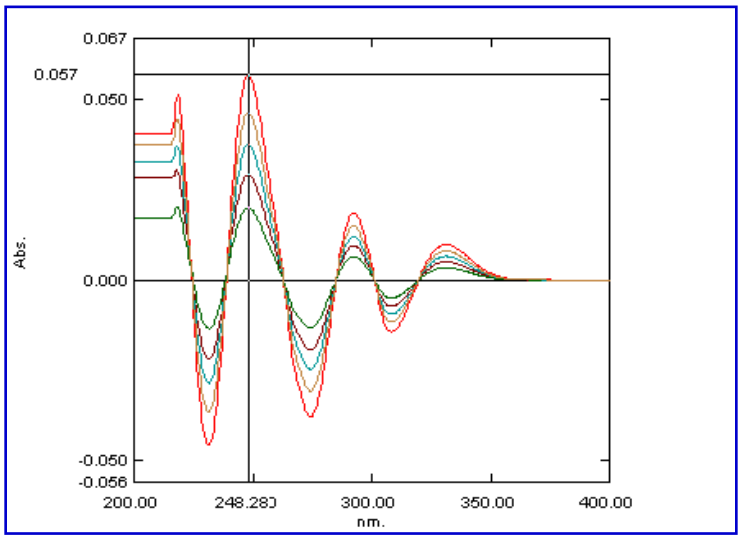

Figure 4: Overlay Second order derivative spectra of Iloperidone showing absorbance at 248 nm

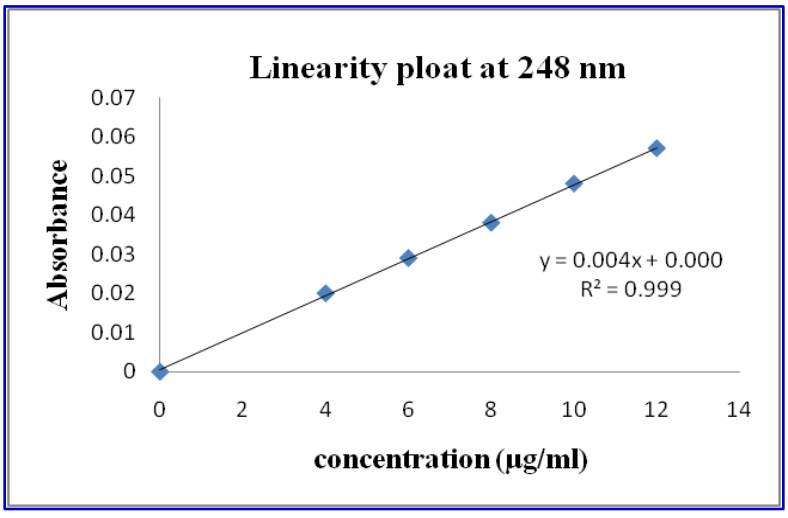

Figure 5. Calibration curve for Iloperidone at 248nm by Second order derivative spectroscopy

VALIDATION

Method validation was done in accordance with ICH guidelines.[5, 6, 7]. Linearity (correlation coefficient) was tested in the range of 4-12 µg/ml for each method. Intraday (repeatability) and Interday precisions were obtained as % relative standard deviation (% RSD) using six replicates. We have established accuracy (% recovery and SD) by spiked placebo recovery method. Limits of detection (LOD) and quantification (LOQ) were calculated for Iloperidone by using standard deviation of intercept. To establish ruggedness of the proposed methods, the estimation was done by two different analyst on two different days.

RESULTS AND DISCUSSION:

The proposed methods were found to be simple, accurate and reproducible. Results obtained from the validation parameters are given in **Table-1**. The accuracy of the methods was assessed by recovery studies at three different levels i.e. 50%, 100%, 150%. The values of standard deviation were satisfactory and the recovery studies were close to 100%. The % RSD values obtained for all the methods are less than 1.1, which indicate good precision of the methods. Results found for the LOD and LOQ shows good sensitivity of the methods. First and second order derivate methods were successfully applied for the estimation of Iloperidone tablets (Fanapt®) and the results obtained are shown in **Table-2**.

Table-1: Validation Parameters.

Validation Parameters		First order derivative method	Second order derivative method
Detection Wavelength (nm)		262	248
Linearity	Range (µg/ml)	4-12	4-12
	Slope	0.00770	0.00473
	Intercept	0.00128	0.00042
	Correlation coefficient	0.999	0.999
Limit of Detection (µg/ml)		0.01333	0.02169
Limit of Quantification (µg/ml)		0.04039	0.06573
% RSD of Intraday Precision	4 µg/ml	0.22	0.37
	8 µg/ml	0.67	0.19
	12 µg/ml	1.06	0.13
% RSD of Interday Precision	4 µg/ml	0.33	0.517
	8 µg/ml	0.86	0.23
	12 µg/ml	1.04	1.70
Accuracy* (% Recovery ± SD)	4 µg/ml (50%)	99.90±0.23	100.48±0.35
	8 µg/ml (100%)	100.09±0.29	99.51±0.35
	12 µg/ml (150%)	99.96±0.09	100.16±0.11

* Mean ±SD are obtained from 6 determinations.

Table: 2. Analysis of tablet formulation

Method	Label claimed(mg)	Amount found (mg)	%Recovery ± SD**
First order derivative method	12	11.99	99.96 ± 0.09
Second order derivative method	12	12.07	100.16 ± 0.11

**Average of six determinations

CONCLUSION

The most striking features of two methods are its simplicity and rapidity, not requiring tedious sample preparations such as extraction of solvents, heating, degassing which are needed for HPLC procedure. It can be concluded that the proposed methods are fully validated and found to be simple, sensitive, accurate, precise, reproducible, rugged and robust and relatively inexpensive. So, the developed methods can be easily applied for the routine quality control analysis of Iloperidone in pharmaceutical formulations

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