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RESEARCH ARTICLE

Spectrophotometric Methods for the Quantitative Estimation of Paliperidone in Formulations

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Abstract: Two simple, sensitive and economical spectrophotometric methods have been developed and validated for the determination of paliperidone in pharmaceutical dosage forms. The methods were based on the formation of colored complex of Paliperidone with different reagents. The absorbance of the formed colored complex is measured at the wavelength of maximum absorbance of the complex 665 nm and 555 nm respectively against the reagent blank treated similarly. These methods have different linearity ranges observed in the concentration ranges of 1-6 and 10-60 µg/mL with correlation coefficient of 0.998 for both the methods. Statistical analysis indicates that the proposed methods are reproducible and selective for the estimation of Paliperidone in bulk drug and in its tablet dosage form.

Keywords: Paliperidone, Spectrophotometric Methods, Isatin, Chloranilic acid

Introduction

Paliperidone is a tricyclic dopamine antagonist of the atypical antipsychotic class of medications[1-3] and is also known as 9-hydroxy risperidone (Figure 1). Paliperidone is used to treat mania and at lower doses as maintenance for bipolar disorder. It is also used for schizophrenia and schizoaffective disorder. Paliperidone (9-OH-risperidone) is a receptor monoaminergic antagonist that exhibits the characteristic dopamine type 2 (D2) and serotonin (5-hydroxytryptamine 5-HT) type 2A (5-HT2A) antagonism of antipsychotic drugs[4,5]. An extensive literature survey is carried out and very few spectrophotometric[6] methods were found so far. Some LC–MS/MS methods[7,8], HPTLC methods[9,10], HPLC method[11,12] and a UPLC method[13] for the determination of risperidone and the enantiomers of 9-hydroxyrisperidone in plasma, urine and pharmaceutical formulations respectively are available. We report two spectrophotometric methods for the determination of the drug. Molecular formula of paliperidone is $C_{23}H_{27}FN_4O_3$, Molecular weight is 426.484 g/mol.

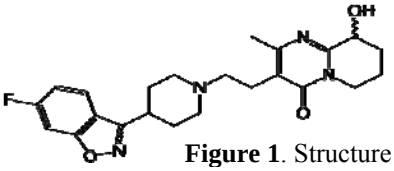

Figure 1. Structure of paliperidone

Experimental

All chemicals used were of analytical reagent grade and double distilled water was used to prepare all solutions. Double beam UV-Visible spectrophotometer is used for measuring the absorbance of the color formed during the analysis.

Preparation of reagents

Isatin Method

Preparation of standard drug solution

10 mg of the drug was taken in 10 mL of methanol. From this 1 mL was made up to 20 mL to get a concentration of 50 µg/mL and is used as a stock solution.

Isatin solution

40 mg of Isatin was dissolved in 100 mL of acetic acid.

Procedure

Aliquot of the drug solution was taken in a series of 10 mL volumetric flasks and to this 1 mL of Isatin was added and shaken well for 10 min. To this, 1 mL of H_2SO_4 was added and shaken well for 5 min. Final volume of the volumetric flask was made up to 10 mL with double distilled water. Then the absorbance of the colored solution was measured at 665 nm against a reagent blank.

Chloranilic acid method

Preparation of standard drug solution

10 mg of the drug was taken in 10 mL of methanol. From this, 2 mL was made up to 10 mL to get a concentration of 200 µg/mL. This solution is used as a stock solution. Chloranilic acid solution (CA): Prepared by dissolving 100 mg of chloranilic acid in 20 mL isopropanol initially followed by dilution with methanol to 100 mL.

Procedure

Aliquots of standard drug solution were delivered into 10 mL graduated tubes. 2.0 mL of CA in methanol was added and kept aside for 5 minutes. Then the volumes of the contents were made up to the mark with methanol. The absorbance was measured against a reagent blank at 555 nm.

Results and Discussion

Method validation

Selection of analytical concentration ranges: (Linearity test)

Linearity test was carried out by measuring the absorbance values of standard solutions. From the standard stock solution of paliperidone, appropriate aliquots were pipetted out in to a series of volumetric flasks and added the required solutions in the prescribed amounts for each individual method. After the color formation, absorbance of each concentration was measured at their corresponding wavelengths of maximum absorbance found (Figure 2 and 4) for the proposed methods. Results were shown in Table 1 and Table 2 for Isatin and chloralinic acid methods respectively and standard graphs of linearity for proposed methods were given in Figure 3 and 5 respectively.

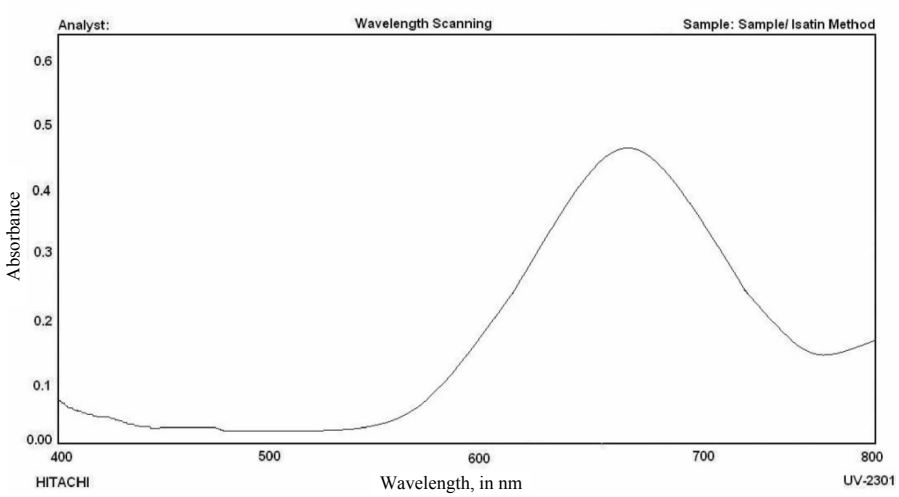

Figure 2. Wavelength Scan (Isatin Method)

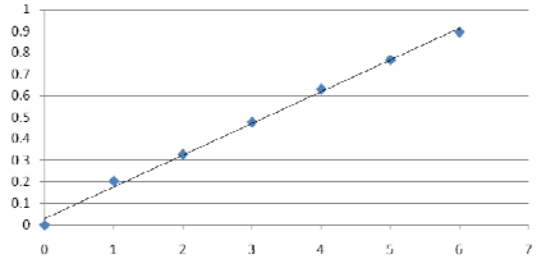

Figure 3. Calibration curves for the proposed methods

Table 1. Linearity - Isatin method

S. No	Concentration in µg/mL	Absorbance
1	1	0.204
2	2	0.328
3	3	0.478
4	4	0.632
5	5	0.767
6	6	0.897
Slope: 0.147 Intercept:0.03 Correlation Coefficient:0.998		

Table 2. Linearity - CA method

S. No	Concentration in µg/mL	Absorbance
1	10	0.156
2	20	0.301
3	30	0.426
4	40	0.556
5	50	0.684
6	60	0.824
Slope: 0.013, Intercept:0.015, Correlation, Coefficient:0.998		

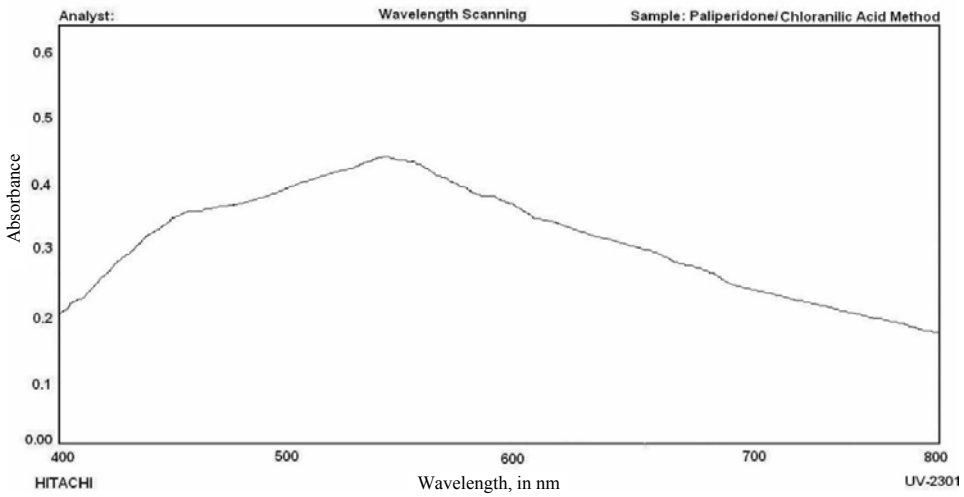

Figure 4. Wavelength scan (Chloranilic acid method)

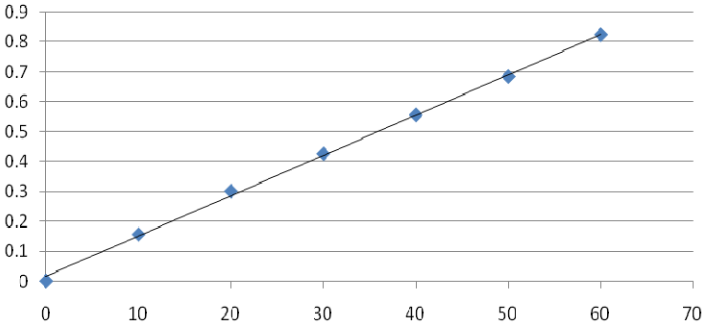

Figure 5. Calibration curves for the proposed methods

Precision

To evaluate the accuracy and precision of the methods, pure drug solution (Within the working limits) was analyzed and being repeated six times. The relative error (%) and relative standard deviation (%) were less than 2.0 and indicate the high accuracy and precision for the proposed methods (Table 3 and Table 4).

Table 3. Precision study (Isatin method)

S.No	Concentration in µg/mL	Absorbance	
		Intraday Precision	Interday precision
1	3	0.472	0.468
2	3	0.475	0.465
3	3	0.476	0.466
4	3	0.477	0.467
5	3	0.474	0.464
6	3	0.473	0.461
	SD:	0.001	0.002
	Mean:	0.47	0.46
	RSD:	0.35	0.48

Table 4. Precision study (Chloranilic acid method)

S. No	Concentration in µg/mL	Absorbance	
		Intraday Precision	Interday precision
1	30	0.428	0.416
2	30	0.425	0.413
3	30	0.427	0.415
4	30	0.424	0.414
5	30	0.423	0.412
6	30	0.426	0.411
	S.D	0.001	0.0017
	Mean:	0.425	0.41
	RSD:	0.40	0.41

Recovery studies

To ensure the accuracy and reproducibility of the results obtained, known amounts of pure drug was added to the previously analyzed formulation samples and these samples were reanalyzed by the proposed methods and also performed recovery experiments. The Percentage recoveries thus obtained were given in Table 5 and Table 6.

Table 5. Recovery results of the Isatin method

% of Recovery	Target Conc., µg/mL	Spiked conc., µg/mL	Final Conc., µg/mL	Conc., Obtained	% Recovery
	2	1	3	3.03	101.04
50%	2	1	3	3.01	100.62
	2	1	3	3.006	100.20
	2	2	4	4.04	101.10
100%	2	2	4	4.03	100.79
	2	2	4	4.01	100.31
	2	3	5	4.98	99.73
150%	2	3	5	5.02	100.52
	2	3	5	5.05	101.17

Table 6. Recovery results of the proposed Chloranilic acid method

% of Recovery	Target Conc., µg/mL	Spiked Conc., µg/mL	Final Conc., µg/mL	Conc., Obtained	% Recovery
	20	10	30	30.35	101.17
50%	20	10	30	30.14	100.46
	20	10	30	29.92	99.76
	20	20	40	40.35	100.8
100%	20	20	40	40.57	101.43
	20	20	40	40.50	101.2
	20	30	50	50.51	101.02
150%	20	30	50	50.29	100.58
	20	30	50	50.58	101.16

Stability studies

The stability of the formed colour for the proposed methods was also studied and found to be 35 min for the Isatin method (99.16% Assay) and for chloranilic acid method it is found to be 45 min (98.35% Assay) and the details of the study were given in Table 7 & 8 respectively.

Table 7. Stability Study (Isatin method)

S.No	Time, min	Absorbance found	% Assay
1	0	0.478	100
2	5	0.483	101.04
3	10	0.481	100.62
4	15	0.479	100.20
5	20	0.484	101.25
6	25	0.476	99.58
7	30	0.475	99.37
8	35	0.474	99.16
9	40	0.468	97.90

Table 8. Stability study

S.No	Time, min	Absorbance found	% Assay
1	0	0.426	100
2	5	0.429	100.70
3	10	0.428	100.46
4	15	0.425	99.76
5	20	0.427	100.23
6	25	0.423	99.29
7	30	0.421	98.82
8	35	0.424	99.53
9	40	0.42	98.59
10	45	0.419	98.35
11	50	0.416	97.65

L.O.Q and L.O.D

The limits of detection and quantification of the two proposed methods were also analysed and reported in Table 9.

Table 9. LOD & LOQ

	Isatin method	Chloranilic acid method
LOD	0.075 µg/mL	0.75 µg/mL
LOQ	0.25 µg/mL	2.5 µg/mL

Application to analysis of commercial sample

In order to check the validity of the proposed methods, paliperidone was determined in commercial formulation. From the results of the determination, it is clear that there is a close agreement between the results obtained by the proposed methods and the labelled claim. These results given in Table 10 indicate that there was no significant difference between the proposed methods and the reference methods in respect to accuracy and precision.

Table 10. % Assay

S.No	Method	Brand name	Available form	Label claim	Concentration	Amount found, µg/mL	% Assay
1.	Isatin	INVEGA	Tablet	9.0 mg	3 µg/ml	2.96	98.6
2.	Chloranilic Acid	INVEGA	Tablet	9.0 mg	30 µg/ml	29.87	99.5

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