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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 color complex is measured at the wavelength of maximum absorbance of the complex against the reagent blank treated similarly. These methods have different linearity ranges observed in the concentration ranges of 8 – 28 and 4 – 14 µg/mL with correlation coefficients 0.9995 and 0.9998 respectively. Statistical analysis proves that the proposed methods are reproducible and selective for the estimation of Paliperidone in bulk drug and in its tablet dosage form.

Introduction

Paliperidone is a tricyclic dopamine antagonist of the atypical antipsychotic class of medications[1-3] and is also known as 9-hydroxy risperidone and its structure is given in Fig.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. People react differently and adverse effects vary between individual users. 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.

Molecular formula of Paliperidone is $C_{23}H_{27}FN_4O_3$

Molecular weight is 426.484 g/mol

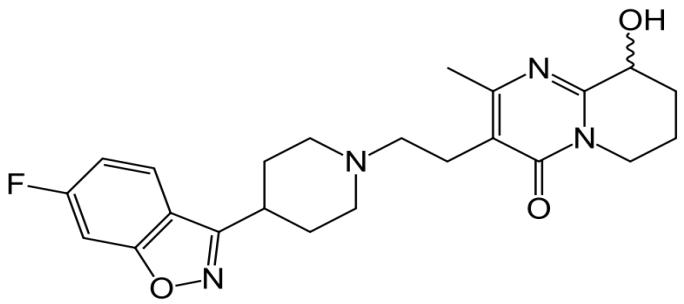

Fig.1 Structure of Paliperidone

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:

BTB Method:

Preparation of Standard drug solution:

10mg of the drug was taken in 10mL of methanol. 2ml of it was made to 10mL to get a concentration of 200µg/mL and is used as a stock solution.

Preparation of reagents:

Bromo thymol blue reagent : 0.1mL of Aliquots of Bromo thymol blue solution was dissolved in 10mL of alcohol and made to 100mL with distilled water.

Procedure:

Standard solution was transferred into a series of 125mL separating funnels, to each flask 1mL of the brorno thymol blue dyer and 2mL of ortho phosphoric acid buffer (1M) were added and diluted to 15mL with distilled water. The formed coloured chromogen was extracted into 10mL of dichloro methane solvent and the absorbance was measured at 415nm, against the reagent blank prepared simultaneously omitting the drug solution.

Tropaeolin-ooo Method:

Preparation of Standard drug solution:

10mg of the drug was taken in 10mL of double distilled water. From this 1mL was makeup to 10mL to get a concentration of 100µg/mL. this solution is used as a stock solution.

Preparation of reagents:

Tropaeolin-ooo solution: 200 mg of Tropaeolin-ooo (Tpooo) was weighed and dissolved in 100mL of distilled water.

HCl Solution: 8.6 mL of concentrated hydrochloric acid was dissolved in 1000 mL of distill water.

Procedure:

A series of 125 mL separating funnels containing aliquots of standard drug solution was taken. To this 6mLof HCl solution and 2mL of Tpooo solutions were added successively. The total volume of the aqueous phase in each separating funnel was adjusted to 15mL with distill water. To each separating funnel

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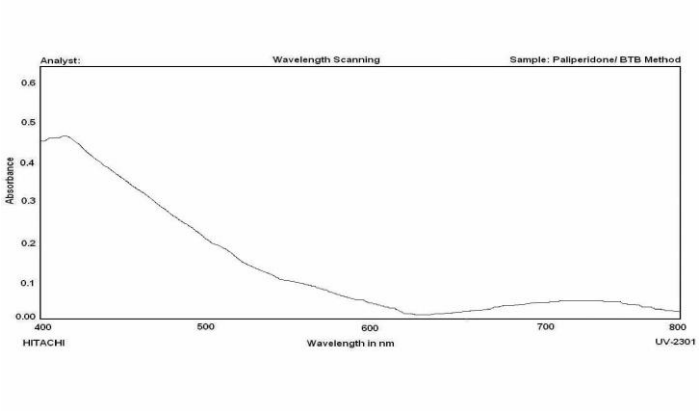
10mL of chloroform was added and the contents were shaken for 2 min. the two phases were allowed to separate and the absorbance of the separated chloroform layer was measured at 495nm against a similar reagent blank.

Results & Discussion:

Method Validation:

Selection of analytical concentration ranges: (linearity test)

Linearity test was evaluated 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 color formation, absorbance of each concentration was measured at wavelength found for the proposed method. Results were shown in Table 1 and Table 2 for BTB and Tpooo methods respectively and Standard graphs of linearity for proposed methods were shown below.



Wavelength Scan [BTB Method]

Table.1 Linearity

S.NO	Concentration in µg/mL	Absorbance
1	8	0.231
2	12	0.345
3	16	0.482
4	20	0.584
5	24	0.704
6	28	0.803
	Slope: 0.029 Intercept:0.002 Correlation Coefficient:0.9995	

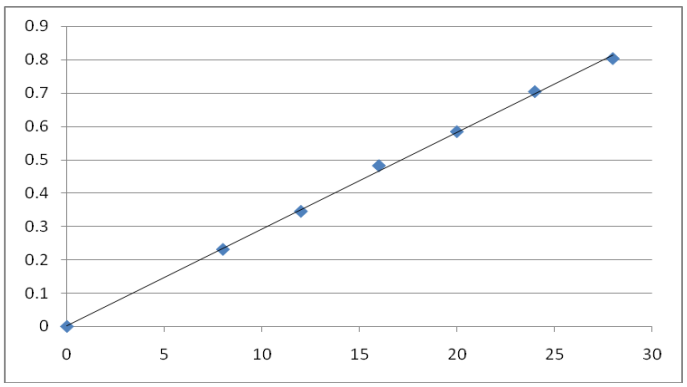
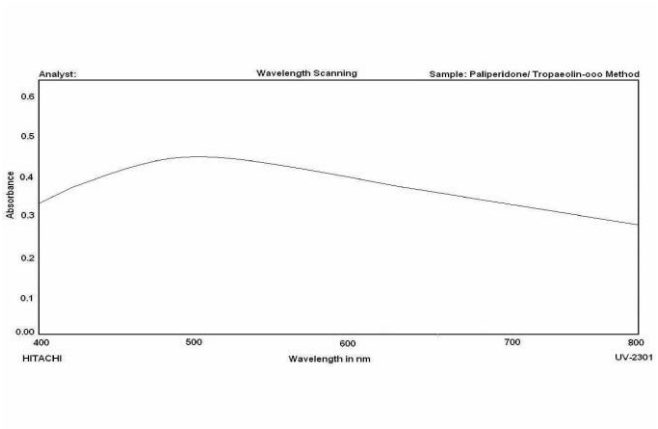


Figure 2: Calibration curves for the proposed methods.



Wavelength scan [Tpooo Method]

Table.2 Linearity

S.NO	Concentration in µg/ml	Absorbance
1	4	0.231
2	6	0.335
3	8	0.442
4	10	0.549
5	12	0.668
6	14	0.779
	Slope: 0.055 Intercept:0.002 Correlation Coefficient:0.9998	

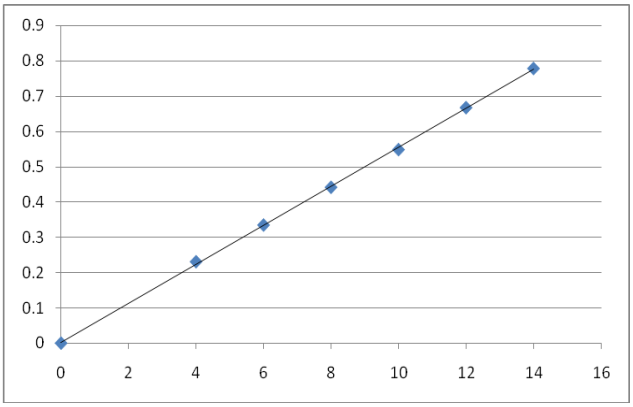


Figure 3: Calibration curves for the proposed methods

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 [BTB Method]

S.NO	Concentration in µg/mL	ABSORBANCE	
		Intraday Precision	Interday precision
1	16	0.492	0.478
2	16	0.495	0.475
3	16	0.496	0.474
4	16	0.494	0.476
5	16	0.493	0.473
6	16	0.489	0.477
	S.D: **Mean:** **RSD:**	**0.002** **0.49** **0.50**	**0.0018** **0.47** **0.39**

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.4 Precision study [TPooo Method]

S.NO	Concentration in µg/mL	Intraday Precision (Absorbance)	Interday precision (Absorbance)
1	8	0.449	0.512
2	8	0.446	0.514
3	8	0.447	0.509
4	8	0.448	0.507
5	8	0.444	0.508
6	8	0.445	0.51
	S.D: **Mean:** **RSD:**	**0.0018** **0.44** **0.41**	**0.0026** **0.51** **0.51**

Table 5: Recovery results of the BTB method

% of Recovery	Target Conc., (µg/mL)	Spiked conc., (µg/mL)	Final Conc., (µg/mL)	Conc., Obtained	% Recovery
50%	8	4	12	12.13	101.15
	8	4	12	12.03	100.28
	8	4	12	12.06	100.57
100%	8	8	16	16.13	100.82
	8	8	16	16.19	101.24
	8	8	16	16.16	101.03
150%	8	12	20	20.17	100.85
	8	12	20	20.23	101.19
	8	12	20	20.102	100.51

Table 6: Recovery results of the proposed TPooo method

% of Recovery	Target Conc., (µg/mL)	Spiked conc., (µg/mL)	Final Conc., (µg/mL)	Conc., Obtained	% Recovery
50%	4	2	6	6.071	101.19
	4	2	6	6.10	101.79
	4	2	6	6.03	100.59
100%	4	4	8	8.10	101.35
	4	4	8	8.14	101.81
	4	4	8	8.07	100.90
150%	4	6	10	10.054	100.54
	4	6	10	10.01	100.18
	4	6	10	10.036	100.36

Stability studies

The stability of the formed colour for the proposed methods was also studied and found to be 90 Min for the BTB Method [98.13% Assay] and for TPooo method it is found to be 45 min [99.32 % Assay] and the details of the study given in Table 7 & 8 respectively.

Table 7 Stability Study [BTB Method]

S.NO	Time	Absorbance found	% Assay
1	0	0.482	100
2	10	0.491	101.86
3	20	0.486	100.82
4	30	0.487	101.03
5	40	0.485	100.62
6	50	0.481	99.79
7	60	0.49	101.6
8	70	0.488	101.24
9	80	0.489	101.45
10	90	0.473	98.13
11	100	0.471	97.71

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 8 Stability Study [Tpooo Method]

S.NO	Time	Absorbance found	% Assay
1	0	0.442	100
2	5	0.448	101.35
3	10	0.449	101.58
4	15	0.446	100.90
5	20	0.45	101.8
6	25	0.447	101.13
7	30	0.445	100.67
8	35	0.443	100.22
9	40	0.444	100.45
10	45	0.439	99.32
11	50	0.432	97.73

Table.9: LOD & LOQ

	BTB Method	TPooo Method
LOD	0.6µg/mL	0.3µg/mL
LOQ	2µg/mL	1µg/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 close agreement between the results obtained by the proposed methods and the label claim. The 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	Concen tration	Amount found	% Assay
1	BTB	INVEGA	Tablet	9.0mg	16µg/ml	15.87	99.1
2.	Tpooo	INVEGA	Tablet	9.0mg	8µg/ml	7.94	99.25

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