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Short Communication

Validation of Paliperidone by Non-Aqueous Potentiometric Titration Method for Quantitative Determination from Active Pharmaceutical Ingredient and Formulation

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Abstract

A sensitive and simple potentiometric titration method by using non-aqueous solvent was described for quantification of paliperidone from active pharmaceutical ingredient and formulation. The method was carried out by using standard 0.1 N perchloric acid as titrant for quantification. A % RSD value is 0.1565 indicated precision of method. The linearity (r^2 > 0.9999) was obtained in the range 0.02 mg to 0.100 mg of paliperidone weight. The percentage recovery of paliperidone was found between 99.60% to 100.13%. The ruggedness was checked with different analysts, chemicals and different manufactures of auto-titrators.

Keywords: Paliperidone, Perchloric acid, Glacial acetic acid, acetic anhydride, Potassium hydrogen phthalate.

Introduction

Paliperidone is Chemically, (±)-3-[2-[4-(6-fluoro-1, 2 benzisoxazol-3-yl)-1-piperidinyl] ethyl]-6,7,8,9-tetrahydro-9-hydroxy-2-methyl-4*H*-pyrido [1,2- a]pyrimidin-4-one (Figure-1). It belongs to the chemical class of benzisoxazole derivatives, indicated for the treatment of schizophrenia It is a psychotropic agent. Paliperidone is the major active metabolite of risperidone. The action of mechanism of paliperidone with other drugs is not known exactly. It has been suggested that the paliperdone's therapeutic activity in schizophrenia with a combination of central dopamine Type 2 (D2) and serotonin Type 2 (5HT2A) receptor antagonism.

A literature survey reveals a spectrophotometric[1-5], HPLC[6-12], LC-MS[13,] HPTLC[14] methods. The proposed method will useful for quantitative analysis of formulation in small analytical laboratory.

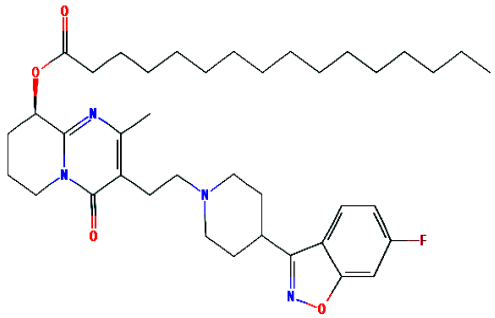

Figure-1
Structure of paliperidone

Materials and Methods

Instrumentation: An automatic titrator was used (Lab- India auto titrator) with glass electrode for proposed method. A analytical balance of Simadzu made with capacity 0.01 mg was used.

Chemicals: Paliperidone was used which was already standardized as per Pharmacopeias guidelines. Potassium hydrogen phthalate, perchloric acid acetic anhydride and glacial acetic acid of A. R. grade were used.

Determination of exact normality of 0.1 N perchloric acid: A potassium hydrogen phthalate is powdered lightly, dried at 120°C for 2 hours. It was weighed accurately about 0.350 g. into dry titration beaker. A 50 ml of glacial acetic acid was added and sonicated for 10 minutes. A titration was carried out with 0.1 N perchloric acid in automatic titrator. The replicate titrations were carried out to find out exact normality of perchloric acid. 1 ml of 0.1 N $HClO_4$ is corresponds to 0.2042 gm of potassium hydrogen phthalate.

Quantification of paliperidone: A 0.100 g. of standard paliperidone was weighted. It was transferred into a clean beaker. A 15 ml of 5% (w/v) mercuric acetate and 35 ml. of anhydrous glacial acetic acid were added.

The replicates Titration were performed with 0.1 N perchloric acid in auto titrator.

% recovery was obtained of paliperidone by using equation.

$$\% \text{ assay} = \frac{\text{Burette reading. x Normality of perchloric acid x 0.10662 x 100}}{\text{Weight of paliperidone}}$$

Results and Discussion

Quantification of paliperidone: The method was used for validation of paliperidone. It was observed in 99.60% to 100.13 %.as percentage recovery.

Method of validation: The method precision study was carried out in six replicates of test sample of paliperidone. The % RSD value was 0.1565 reports precision. The results are represented in table of study of precision (Table-1).

Table-1
Study of Precision

Sr.no	Amount of paliperidone in mg	Values in ml	perchloric acid (Normality)	Values of % assay
1	100	9.38	0.09992	99.92
2	100	9.39	0.09992	100.03
3	100	9.40	0.09992	100.13
4	100	9.37	0.09992	99.81
5	100	9.39	0.09992	100.03
6	100	9.38	0.09992	99.71
			Mean	99.93833
			Std. Deviation	0.156514
			RSD	0.1565

Study of Linearity: For linearity study, five replicate test samples corresponding to 0.02, 0.04, 0.06, 0.08 and 0.1 mg weighed and studied for linearity of paliperidone. The values are reported in Table-2.

Table-2
Linearity

Sr. No.	Paliperidone in mg.	Reading in ml	Perchloric acid(N)	% assay
1	0.020	1.86	0.09990	99.077
2	0.040	3.75	0.09990	99.876
3	0.060	5.62	0.09990	99.787
4	0.080	7.50	0.09990	100.876
5	0.100	9.38	0.09990	99.710
			Mean	99.8652
			Std. Deviation	0.64677
			RSD	0.6475

The assay was performed once different levels. Linearity curve was drawn Figure-2.

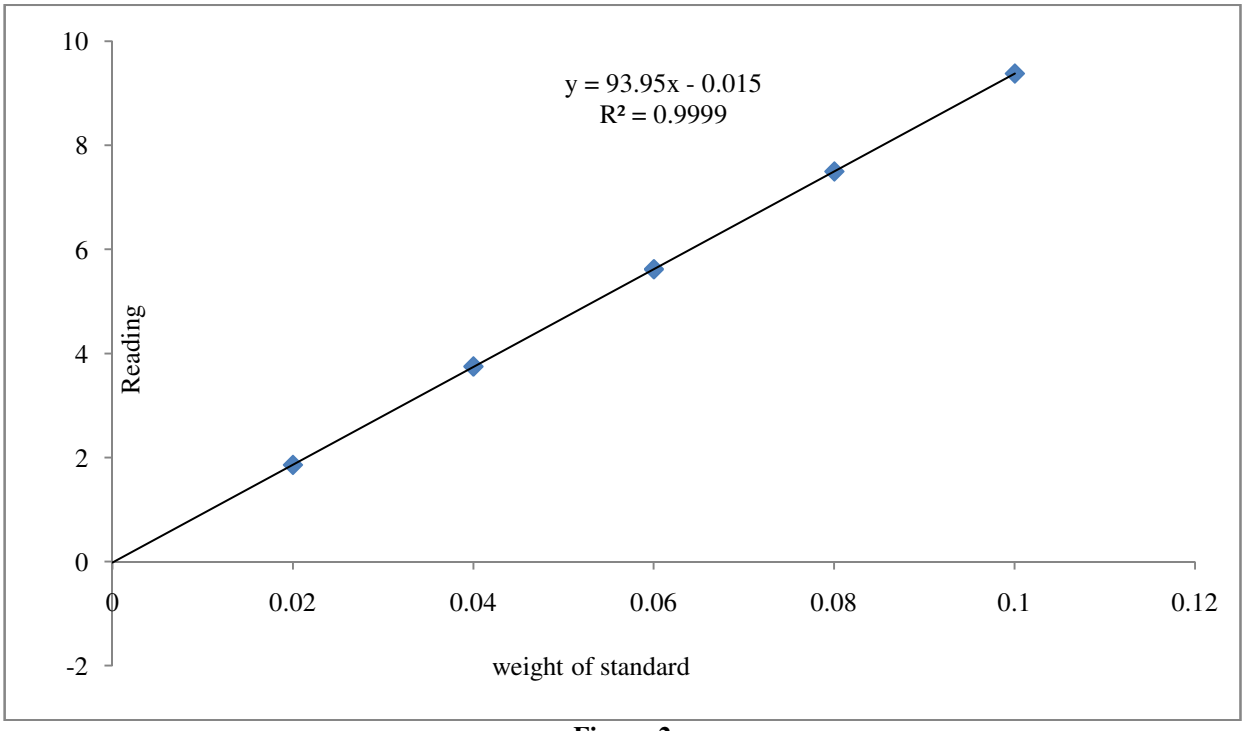

Figure-2
Linearity curve

Table-3 represents data of regression.

Table-3
Data of regression

Parameter	Values
Slope	93.95
Intercept	-0.015
Coefficient of co-relation	0.9999

Study of recovery for Accuracy: For determination of accuracy was five different amount such as 0.02, 0.04, 0.06 ,0.08 and 0.100 mg were used. The titration was performed at each level in triplicate. The burette readings values were noted. The burette reading found in linearity study were converted to true value by using blank determination. The calculation of percentage recovery following equation was used.

$$\text{Percentage recovery} = \frac{\text{Burette reading}}{\text{Titration reading} - \text{Blank reading}} \text{ x } 100$$

The recovery of paliperidone was in 99.60 to 100.18% indicates accuracy (Table-4).

Ruggedness: The degree of reproducibility of results obtained by analysis of paliperidone sample is studied for ruggedness. It is studied under variety of test conditions s as per ICH guidelines. The ruggedness results of analysis were well in agreement.

Conclusion

The precise, accurate non-aqueous titration was found to be rugged. The standard deviation and % RSD values showed sensitivity. The proposed method was validated as per ICH guidelines. Parameters of validation showed satisfactory results. Hence method is strongly recommended assay of paliperidone

Table-4
Accuracy with Precision Study

No.	Paliperidone in mg added	Paliperidone in mg found	% assay	Mean values of % assay
1	0.020	1.86	99.077	99.60867
	0.020	1.87	99.609	
	0.020	1.88	100.14	
2	0.040	3.75	99.876	100.1387
	0.040	3.76	100.14	
	0.040	3.77	100.40	
3	0.060	5.63	99.665	99.98067
	0.060	5.65	99.787	
	0.060	5.66	100.49	
4	0.080	7.51	100.01	100.1833
	0.080	7.54	100.40	
	0.080	7.52	100.14	
5	0.100	9.38	99.92	100.0267
	0.100	9.39	100.03	
	0.100	9.40	100.13	

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