Trade Science Inc.

June 2009 Volume 8 Issue 2

Analytical CHEMISTRY

An Indian Journal

Full Paper

ACAIJ, 8(2) 2009 [165-167]

A validated non-aqueous potentiometric titration method for the quantitative determination of rupatadine from rupatadine fumarate

R.V.Rele*, S.A.Sawant, R.N.Mali

Department of chemistry, D.G.Ruparel College, mahim , Mumbai-400016, (INDIA)

E mail : searchnil_2007@yahoo.com

Received: 28th March, 2009 ; Accepted: 2nd April, 2009

ABSTRACT

A simple precise, rapid, accurate and sensitive non-aqueous potentiometric titration method was developed for quantitative determination of rupatadine as rupatadine fumarate in pharmaceutical dosage form. The titration was carried out using standardized 0.1 N perchloric acid. The proposed method was found to be precise with % RSD <1(n = 6). The method showed strict linearity ($r^2 > 0.99$) between 20 % to 100 % of 100 mg of drug substance weight. The percentage recovery of rupatadine in the optimized method was between 98 % to 102 %. The method is also found to be rugged when checked by different analysts and using different lots of reagents and different makes of titrators.

KEYWORDS

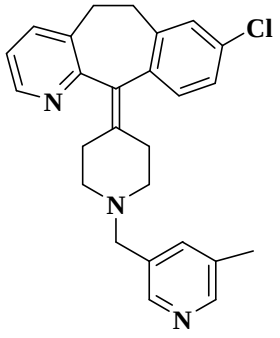
Rupatadiene;
Perchloric acid;
Potassium hydrogen phthalate;
Glacial acetic acid.

INTRODUCTION

Ruapatadine is 8 chloro 6, 11 dihydro 11-[1-(5methyl -3-pyridinyl) methyl-4-piperidinyllidene]-5 H-benzo[5,6] cyclohepta [1,2-b] pyridine. It acts as a long acting, non sedative antagonist at histaminergic H_1-receptors and also antagonizes the platelet-activating factor (PAF). Both histamine and PAF cause bronchoconstriction and lead to an increase in vascular permeability, acting as a mediator in the inflammatory process, which is responsible for the bronchial hyperactivity.

Quantitative determination of the drug is very important in pharmaceutical quality control and assurance. In the proposed method an attempt is been made to develop a suitable non-aqueous potentiometric method for quantitative determination of Rupatadine as rupatadine fumarate. The developed non-aqueous potentiometric method was subsequently validated.

Structure of rupatadine



EXPERIMENTAL

Instrumentation

A potentiometric titrator was used (VEEGO-MATIC) for assay method development and validation.

Full Paper

TABLE 1 : Method of precision

Weight of Rupatadine fumarate in g.	Weight of Rupatadine in g.	Burette reading in ml	Normality of perchloric acid	%Assay
0.1279	0.1	7.1	0.9991	98.352
0.1279	0.1	7.15	0.9991	99.045
0.1279	0.1	7.1	0.9991	98.352
0.1279	0.1	7.1	0.9991	98.335
0.1279	0.1	7.15	0.9991	99.045
0.1279	0.1	7.15	0.9991	99.045

Mean 98.695 %, Standard deviation 0.3827, % RSD 0.3877

A Sartorious analytical balance with 0.01 mg was used.

Reagents and chemical

Potassium hydrogen phthalate, perchloric acid and glacial acetic acid of A. R. grade were used.

General procedure

Standardization of 0.1 mole perchloric acid

About 0.35 mg of potassium hydrogen phthalate (previously powdered lightly, dried at 120°C for 2 hours) was weighed accurately into clean and dry titration jar. It was dissolved in 50 ml of glacial acetic acid. About 0.1 ml of crystal violet solution (0.5 % w/v in anhydrous glacial acetic acid) was added. It was titrated with 0.1 N perchloric acid until violet colour changes to emerald green. Blank determination was performed out for necessary correction.

The titration was performed in duplicate.

One ml of 0.1 N $HClO_4$ is equivalent to 0.02042 gm of potassium hydrogen phthalate ($C_8H_5KO_4$)

Normality of perchloric acid = W/ B.R. × 0.2042

Where W is weight of potassium hydrogen phthalate in g. B.R. is burette reading in ml.

Quantitative determination of rupatadine

About 0.1 g. of rupatadine test sample was weighted accurately into a clean and dried titration jar. It was dissolved in 35 ml. of anhydrous glacial acetic acid in presence of 15 ml 5% (w/v) of mercuric acetate solution.

It was titrated with 0.1 N perchloric acid potentiometrically.

Blank determination was also carried out for necessary correction.

One ml of 0.1 N perchloric acid is equivalent to 0.013865 g. of rupatadine ($C_{26}H_{26}ClN_3$) % Rupatadine on the dried basis was calculated as below :

% assay = B.R. × N × 0.013865 × 100 / 0.1 × W

Where B.R. is burette reading in ml at the potentiometric end point, N is actual normality of 0.1 N perchloric acid, W is weight of the sample taken in g.

RESULT AND DISCUSSION

Determination of rupatadine

The objective of this work was to determine accurately the content of rupatadine. The assay of rupatadine (on the dried basis) of various batches of rupatadine test sample was analyzed using the above method. It was in the range of 99.02 % to 100.41 %.

Analytical method validation

The method precision was checked after analyzing six different preparations of homogeneous test sample of Rupatadine as rupatadine fumarate. The % RSD of results obtained was found to be 0.3877.

It confirms good precision of the method. The results are presented in TABLE 1.

Linearity

For the establishment of method linearity ,five different weights of rupatadine test samples corresponding to 20 % ,40 %, 60 % , 80 % and 100 % of the about weight (0.1 g.) were taken and analyzed for % of rupatadine content. The results are in table II. The potentiometric titration was conducted once at each level. Calibration curve was drawn by plotting test sample weight in gram on x axis and titre values on y axis.

The values of correlation coefficient, slope and intercept are given in TABLE 2.

Accuracy and recovery

Accuracy was determined at five different levels i.e., 20 %, 40 %, 60 %, 80 % and 100 % of the nominal concentration. (0.1 g.) The titration was conducted in triplicate at each level and the titre value was recorded. The tire value obtained in linearity study was

TABLE 2: Linearity

Level	Weight of Rupatadinefumarate in g.	Weight of Rupatadine In g.	Burette reading ml	Normality of perchloric acid	% Assay
1	0.0255	0.020	1.45	0.09991	100.430
2	0.05115	0.040	2.9	0.09991	100.430
3	0.07674	0.060	4.3	0.09991	99.276
4	0.10232	0.080	5.7	0.09991	98.699
5	0.12790	0.100	7.15	0.09991	99.045

Mean 99.5182%, Standard deviation 0.7370, % RSD 0.7406

TABLE 3: Regression values

Correlation coefficient	0.9998
Slope (m)	0.0708
Intercept (c)	0.065
Regression equation	y = 0.0708x + 0.065

TABLE 4 : Accuracy and recovery

Level	Weight of Rupatadinefumarate added (g).	Weight of Rupatadine added (g).	Weight of Rupatadine found (g).	% Assay	Mean % assay
1	0.0255	0.020	0.01953	97.65	
	0.0255	0.020	0.02023	101.15	99.983
	0.0255	0.020	0.02023	101.15	
2	0.05115	0.040	0.04045	101.125	
	0.05115	0.040	0.04045	101.125	100.558
	0.05115	0.040	0.03977	99.425	
3	0.07674	0.060	0.05976	99.61	
	0.07674	0.060	0.06046	100.766	99.995
	0.07674	0.060	0.05976	99.61	
4	0.10232	0.080	0.08162	102.035	
	0.10232	0.080	0.08093	101.167	101.456
	0.10232	0.080	0.080934	101.167	
5	0.12785	0.100	0.100278	100.278	
	0.12785	0.100	0.09953	99.536	100.031
	0.12785	0.100	0.100278	100.278	

considered as true value during the calculation of percentage (%) recovery. The percentage recovery is calculated using following equation.

Percentage recovery = Titre value × 100/ True titre value

The percentage range recovery of rupatadine was in 99. 41 to 101.456 %. It confirms the accuracy of the proposed method. (TABLE 4).

Ruggedness

The ruggedness of the method is defined as degree of reproducibility of results obtained by analysis of rupatadine sample under variety of normal test conditions such as different laboratories, different analysts and different lots of reagents. Quantitative determination of rupatadine was conducted potentiometrically on one laboratory. It was again tested in another laboratory using different instrument by different analyst. The assays obtained in two different laboratories were well in agreement. It proved ruggedness of the proposed method.

CONCLUSION

The proposed method of non-aqueous potentiometric titration was found to be precise, accurate and rugged. The values of percentage recovery and standard deviation showed sensitivity. The method was completely validated. It showed satisfactory data for all the parameters of validation. Hence it can be applied for routine quality control application.

REFERENCES

[1] D.R.Nogueira, D'Avila Felipe, Rolim Clarice, L. Dalmora Serigo; Chromatographia, **66**, 915-919 **(2007)**.

[2] Yuan Tain, Jingjing Zhang, Hui Lin, Jiabi Lang, Zanjian Zhang, Yun Chen; J.of Pharmaceutical and Biomedical Analysis, **47**, 4-5, 899-906 **(2008)**.

[3] A.A.Shirkhendkar, R.R.Thorve, R.A.Fursule, S.J.Surana; Acta Chromatographica, **20**, 423-437 **(2008)**.

[4] D.R.Noqueira, L.M.da Silva, V.Todeschini, S.L. Dalmora; J.of separation technique, **3(16-17)**, 3098-3105 **(2008)**.