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A Non-Aqueous Potentiometric Titration Method for Validation of Drotaverine Hydrochloride from Pharmaceutical Dosages

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Abstract : A simple precise, rapid accurate and sensitive non-aqueous potentiometric titration method was developed for quantitative determination of Drotaverine hydrochloride from pharmaceutical dosage form. The titration was carried out using standardized0.1 N perchloric acid. The proposed method was found to be precise with % RSD <1 (n = 6). The method showed strict linearity (r^2> 0.999) between 20 % to 100 % of 500 mg of drug substance weight. The percentage recovery of Drotaverine hydrochloride in the optimized method was between 99.747 to 100.325%. The method is also found to be rugged when checked by different analysts and using different lots of reagents and different makes of titrators.
Key-Words : Drotaverine hydrochloride, Perchloric acid, Potassium hydrogen phthalate, Glacial acetic acid.

Introduction

Drotaverine hydrochloride is[(1 - (3, 4 – diethoxybenzylidene) - 6, 7 – diethoxy - 1, 2, 3, 4 tetrahydro isoquinoline) hydrochloride], a benzylisoquinoline derivative. It is a highly potent spasmolytic drug. It shows excellent properties of smooth muscle relaxant. Its antispasmodic activity is due to inhibition of phosphodiesterase enzyme IV. It causes smoothmuscle relaxation by increasing intracellular levels of cyclic adenosine mono-phosphate (cAMP) secondary to inhibition of phosphodiesterase.

According to the literature review several methods has been developed for drug, like spectroscopy methods[1-8].HPLC[9-12] and miscellaneous[13-18]. A simple precise, rapid accurate and sensitive non-aqueous potentiometric titration method was developed for quantitative determination of drotaverine hydrochloride from bulk drug and pharmaceutical formulation. The developed method will useful for pharmaceutical industries and research organizations.

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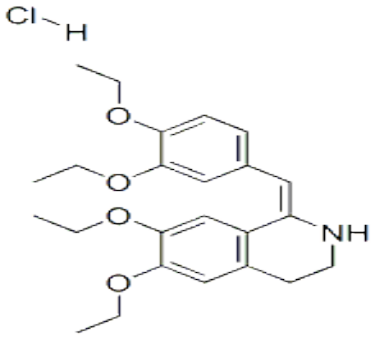
Structure of drotaverine



Experimental

Instrumentation

An potentiometric titrator was used used (Lab- India auto titrator)for assay method development and validation.

A Simadzu analytical balance with 0.01 mg was used.

Reagents and chemical

Reference standard of drotaverine hydrochloride was obtained from reputed firm with certificate of analysis.

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

General procedure

Standardization of 0.1 N perchloric acid

About 0.350 mg of potassium hydrogen phthalate (previously powdered lightly, dried at 120^{o}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 0.2042 gm of potassium hydrogen phthalate ($C_8H_5KO_4$)

$$\text{Normality of perchloric acid} = \frac{W}{\text{B.R.} \times 0.2042}$$

Where W is weight of potassium hydrogen phthalate in g.

B.R. is burette reading in ml.

Quantitative determination of drotaverine hydrochloride

About 0.500 g. of drotaverine hydrochloride test sample was weighted accurately into a clean and dried titration jar. It was dissolved in 35 ml. of anhydrous glacial acetic acid and 15 ml of 5% (w/v) mercuric acetate.

It was titrated with 0.1 N perchloric acid potentiometrically.

Blank determination was also carried out for necessary correction.

One ml of 1 N perchloric acid is equivalent to 0.501656 g. of drotaverine hydrochloride

% (Percentage) Drotaverine hydrochloride on the dried basis was calculated as below

$$\% \text{ assay} = \frac{\text{B.R.} \times N \times 0.4339 \times 100}{W}$$

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 drotaverine hydrochloride

The objective of this work was to determine accurately the content of drotaverine hydrochloride. The assay of drotaverine hydrochloride (on the dried basis) of various batches of drotaverine hydrochloride test sample was analyzed using the above method. It was in the range of 99.739 % to 101.724 %.

Analytical method validation

The method precision was checked after analyzing six different preparations of homogeneous test sample of drotaverine hydrochloride. The % RSD of results obtained was found to be 0.6743.It confirms good precision of the method. The results are presented in table 1.

Table No. 1: Method of Precision

Weight of drotaverine hydrochloride in g.	**Burette Reading in ml.**	**Normality of per chloric acid**	**% Assay**
0.100	2.30	0.09995	99.74
0.100	2.31	0.09995	100.18
0.100	2.30	0.09995	99.74
0.100	2.29	0.09995	99.31
0.100	2.30	0.09995	99.74
0.100	2.31	0.09995	10.81
		Mean	99.92
		Standard deviation	0.5155
		% RSD	0.5159

Linearity

For the establishment of method linearity ,five different weights of drotaverine hydrochloride test samples corresponding to 20 % ,40 %, 60 % , 80 % and 100 % of the about weight (0.500 g.) were taken and analyzed for % (percentage) of drotaverine hydrochloride content. The results are in table 2.

Table No.2: Linearity

Level	**Weight of drotaverine hydrochloride in mg.**	**Burrete reading in ml.**	**Normality of perchloric acid**	**% Assay**
1	50	1.15	0.09995	100.240
2	100	2.3	0.09995	98.987
3	150	3.45	0.09995	101.076
4	200	4.6	0.09995	100.240
5	250	5.75	0.09995	100.240
			Mean	100.116
			Standard deviation	0.8267
			% RSD	0.8257

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 3. And graph is given in fig no. 1

Table No. 3 : Regression values

Correlation Coefficient	0.9999
Slope (m)	0.023
Intercept (c)	0.003
Regression equation	y = 0.023x + 0.003

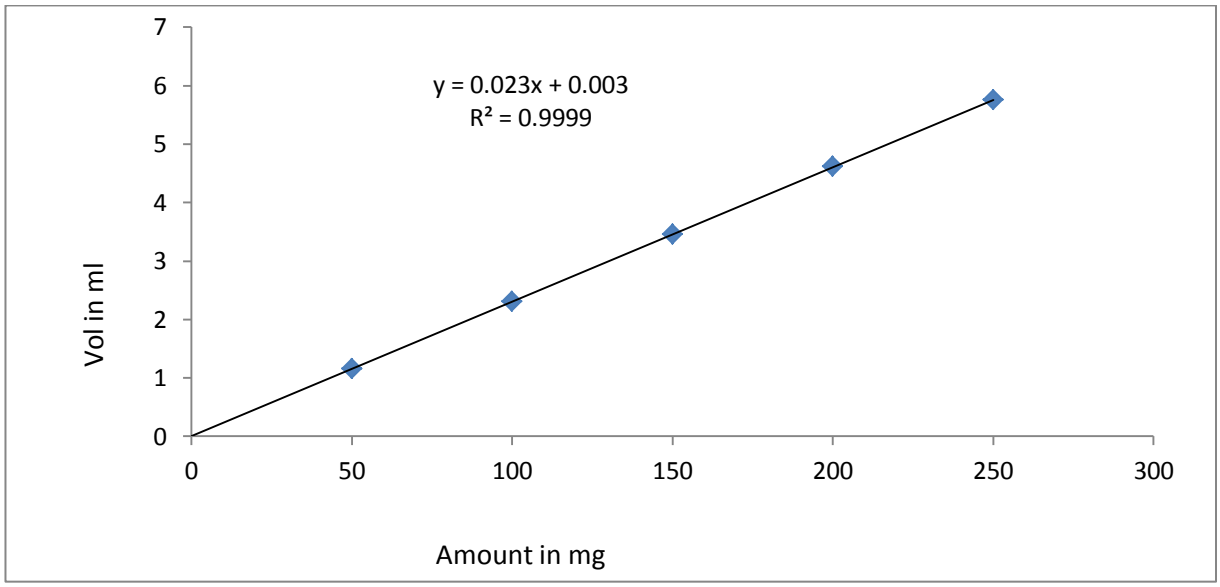


Fig no. 1: Linearity graph

Accuracy and recovery

Accuracy was determined at five different levels i.e., 20 %, 40%, 60%, 80 % and 100 % of the nominal concentration. (0.250 g.) The titration was conducted in triplicate at each level and the titre value was recorded. The tire value obtained in linearity study was considered as true value during the calculation of percentage (%) recovery. The percentage recovery is calculated using following equation.

$$\text{Percentage recovery} = \frac{\text{Titre value} \times 100}{\text{True titre value}}$$

The percentage range recovery of drotaverine hydrochloride was in 99.747 to 100.325 %. It confirms the accuracy of the proposed method. (Table 4).

Table No 4 Accuracy and Recovery

Level	Volume in ml	Weight of drotaverine hydrochloride added in g.	Weight of Drotaverine hydrochloride found in g.	% Assay	Mean % assay
1	1.15	0.05	0.0501	99.7471	
	1.16	0.05	0.05012	100.614	99.7471
	1.14	0.05	0.05008	98.8797	
2	2.3	0.1	0.10012	99.7471	
	2.31	0.1	0.10008	100.181	99.8917
	2.3	0.1	0.1004	99.7471	
3	3.45	0.15	0.1501	99.7471	
	3.46	0.15	0.15011	100.036	99.7471
	3.44	0.15	0.15007	99.458	
4	4.62	0.2	0.2009	100.181	
	4.63	0.2	0.20005	100.398	100.325
	4.63	0.2	0.20006	100.398	
5	5.75	0.25	0.2502	99.7471	
	5.74	0.25	0.25004	99.5736	99.6893
	5.75	0.25	0.25005	99.7471	

Ruggedness

The ruggedness of the method is defined as degree of reproducibility of results obtained by analysis of drotaverine hydrochloride sample under variety of normal test conditions such as different laboratories, different analysts and different lots of reagents. Quantitative determination of drotaverine hydrochloride 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.

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