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RESEARCH ARTICLE

Analytical Method Devlopment and Validation for Estimation of Drotaverin Hcl in Bulk and Tablet Formulation

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ABSTRACT
The present study was aimed to develop and validates for the analysis of Drotaverine HCl in bulk and tablet formulation. Drotaverine HCl in presence of acidic medium reacts with excess amount of potassium bromide bromate with crystal violet and oxidizes crystal violet. It shows the absorbance at 590nm.The Beer's law was obeyed in the concentration of 10-60mcg/ml. The method was validated for linearity, accuracy, precision and ruggedness. Proposed method was Statistically validated by recovery studies.
Keyword: Drotaverine hydrochloride, Potassium bromide bromate, Crystal violet, Beer's law.

1. INTRODUCTION:

Drotaverine Hydrochloride (1-[(3, 4-diethoxyphenyl)-methylene]-6, 7-diethoxy-1, 2, 3, 4-Tetrahydroisoquinoline[1] and molecular formula $C_{24}H_{31}NO_4$, structure is related to papaverine. It is a novel non anticholinergic smooth muscle antispasmodic which act by inhibiting phospodiesterase -4 (PDE-4) selective for smooth muscle. It is widely used to treat renal cholic and useful in helping to accelerate labor. Drotaverine may also have minor allosteric calcium channel blocking properties.

But Drotaverine is not an official drug. A number of methods like spectrophotometry[2], HPLC[3, 4], RP-HPLC [5, 6], HPTLC [7] have been reported in literature for the determination of Drotaverine. The present work is to develop, simple, precise, and accurate colorimetric method for determination of Drotaverine HCl in tablet dosage form and validated[8, 9] as per ICH[10] guidelines.

2. EXPERIMENTAL:

Instrument: The analysis was performed by Jasco V-630 series with 1cm matched glass cuvettes were used.

3. MATERIALS AND METHODS

All materials used were of AR grade and double distilled water was used throughout the work.

Drotaverine Hydrochloride was kindly provided by Indoco Remedies. Potassium bromide bromate and crystal violet were purchased from Merck Chemical, India. Doverin

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40mg tablets (Intas Laboratories Pvt Ltd) were obtained from commercial source in the local market.

3.1 Standard Stock Solution: Stock solution of 1mg/ml was prepared by dissolving 100mg of drug in 100ml of methanol. For working solution 10ml was pipette from standard stock solution into 100ml calibrated volumetric flask and made up the volume with methanol to get concentration of 100mcg/ml.

3.2 Procedure: Six different aliquots were taken from working standard stock solution diluted with methanol and 1.2ml of 330mcg/ml. Potassium bromide bromate reagent was added(kept for 15mins) to prepare series of concentration from 10-60mcg/ml. Then 0.2ml of crystal violet was added to each 10ml volumetric flask. The absorbance of the resulting solution was measured at 590nm.

3.3 Analysis of marketed formulation: 20 tablets of Doverin (marketed product) containing 40mg Drotaverine was obtained for all analytical study. Powder equivalent to 100mg Drotaverine of was weighed accurately and transferred into 100 ml volumetric flask; volume was made by methanol to give concentration of 1000mcg/ml (stock solution A). From the above Stock solution A, 1ml was pipetted out and added to a 100ml volumetric flask. (Stock solution B).From this solution 2ml was pipette out into 10ml volumetric flask to this 1.2ml of 330mcg/ml Potassium bromide bromate reagent and 0.5ml 2M HCl were added and kept aside for 15mins to allow complete reaction. After 15mins 0.2ml of 0.025% crystal violet added volume made up to 10ml with methanol. Table no.1

Formulation	Actual concentration of Drotaverine hydrochloride(µg/ml)	Amount obtained of Drotaverine hydrochloride (µg/ml)	% Drotaverine hydrochloride
tablet	15 µg/ml	14.563 µg/ml	97.07%

Table no .1. Assay Results of Marketed Formulation

4. VALIDATION

4.1 Linearity: Linearity was determined over the range of 10 to 60µg/ml. Six 10ml volumetric flasks were taken. Then 1.0, 2.0, 3.0, 4.0, 5.0, 6.0 ml working standard solution of Drotaverine Hydrochloride was added. 1.2 ml `of 330µg/ml Potassium bromide bromate reagent and 0.5ml of 2M HCL were added, kept for 15 minutes. 0.2ml of 0.025% crystal violet was added and made up the volume with methanol. Absorbance was taken at 590 nm. Table no 2. Figure no.1

Sr. no	Volume of working standard of drug (ml)	Concentration in µg/ml	Absorbance at 590nm Mean ± S.D. (n=6)
1	1.0	10	0.141±0.000980
2	2.0	20	0.2763±0.005444
3	3.0	30	0.4153±0.000696
4	4.0	40	0.5545±0.000605
5	5.0	50	0.6819±0.000705
6	6.0	60	0.8173±0.005157

Table no.2 Linearity for Drotaverine hydrochloride

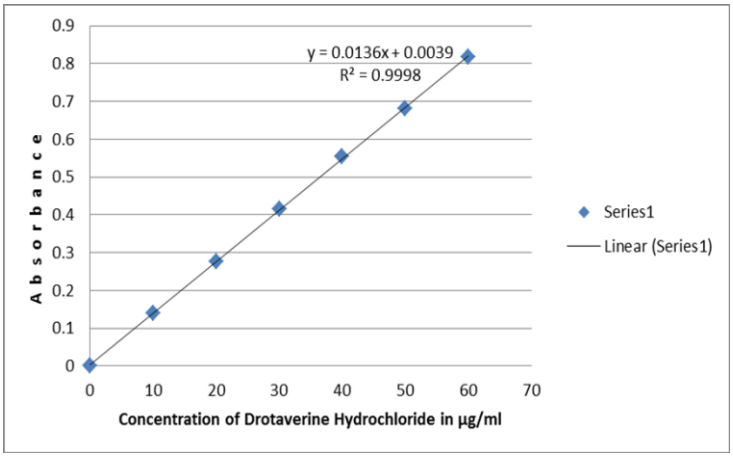

Figure no.1|Standard curve for Drotaverine Hydrochloride

4.2 Accuracy: The accuracy of the methods was determined by calculating % recovery of Drotaverine Hydrochloride by standard addition method. Known volumes of standard solutions of Drotaverine Hydrochloride were taken for recovery studies in 3 different levels 80, 100, 120% and recovery study was carried out. Table no.3

Amt. of sample Drotaverine hydrochloride µg/ml	Amt. of Pure drug Drotaverine hydrochloride %	Amt. of Pure drug Drotaverine hydrochloride µg/ml	Amt. of drug recovered Drotaverine hydrochloride µg/ml	Mean % Recovery + SD
20	80	16	15.9337	99.58±0.2577
20	100	20	19.7327	98.65±0.1305
20	120	24	23.6813	98.66±0.2478

Table.3 Accuracy data for Drotaverine hydrochloride at 590 nm

4.3 Method precision: The precision of the methods was checked by repeated measurement of the absorbance of standard solutions (n = 6) of 10 µg/ml without changing the parameters for the method. The repeatability was

expressed in terms of relative standard deviation (RSD).table no.4

Concentration	10µg/ml	20µg/ml	30µg/ml	40µg/ml	50µg/ml	60µg/ml
Absorbance	0.1413	0.2768	0.4142	0.5554	0.6814	0.8145
	0.1413	0.2794	0.4157	0.5548	0.6815	0.815
	0.1415	0.2795	0.4156	0.5537	0.682	0.8156
	0.1425	0.2789	0.4149	0.5549	0.6814	0.8163
	0.1408	0.2781	0.4153	0.5541	0.6826	0.8149
	0.1397	0.2779	0.4162	0.5545	0.6829	0.8161
Mean.	0.14102	0.27843	0.41532	0.55457	0.68197	0.8154
Std. Dev	0.00098	0.00103	0.0007	0.00061	0.00065	0.00072
RSD	0.00695	0.00369	0.00458	0.0011	0.00257	0.00088
%RSD	0.695	0.369	0.458	0.11	0.257	0.088

Table.4: Repeatability data for Drotaverine hydrochloride at 590 nm

4.4 Intermediate precision: The intraday and interday precision of the proposed methods were performed by analyzing the corresponding responses three times on the same day and on three different days over a period of one week for three different concentrations of standard solutions of Drotaverine Hydrochloride (10, 20, 30 µg/ml). The results were reported in terms of relative standard deviation (RSD). Table no.5

Serial No.	Concentration (µg/ml)	Inter-day Precision		Intra-day Precision	
		Mean ± S.D	%RSD	Mean ± S.D	%RSD
1	5	0.1282±0.00060	0.470	0.1278±0.000751	0.586
2	10	0.2378±0.0003	0.126	0.2371±0.002371	0.856
3	15	0.3245 ± 0.000945	0.291	0.3239±0.0009	0.277

Table.5: Intermediate Precision for Drotaverine hydrochloride at 605 nm

4.5 Ruggedness: To establish ruggedness of the proposed method, assays for two different concentrations of Drotaverine Hydrochloride were performed by two different analysts. The results of assays were represented as % Recovery with SD and % RSD showing the ruggedness of the proposed method. Table no.6

Serial No	Concentration (µg/ml)	Analyst I		Analyst II	
		Amount found (µg)	(%) Recovery ± SD	Amount found (µg)	(%) Recovery ± SD
1	5	4.92	98.4±0.8	4.94	98.8±0.4
2	10	9.85	98.5±0.3	9.8566	98.566±0.2081

Table 6: Ruggedness results for Drotaverine hydrochloride at 605 nm

4.6 Reproducibility: The absorbance readings of 10µg/ ml were measured at different laboratory using different Spectrophotometer by another analyst and the %RSD values obtained to verify their reproducibility. Table no.7

Concentration (µg/ml)	Instrument 1	%RSD	Instrument 1	%RSD
5	0.12806±0.000216	0.1688	0.128167±0.000175	0.1365

Table no 7: Reproducibility data for Drotaverine hydrochloride with Different Instrument at 605 nm

4.7 Limit of Detection and Limit of Quantification: The limit of detection (LOD) and limit of quantification (LOQ) of the drug were derived by calculating the signal-to-noise (i.e. 3.3 for LOD and 10 for LOQ) ratio using following

4.8 equations designated by ICH guideline:

LOD = 3.3 X σ/S and LOQ = 10 X σ/S

Where, σ = the standard deviation of the response, S = slope of the calibration curve.

4.9 Result and Discussion: For validation of analytical methods, were done as per ICH guidelines. The linearity was observed in the concentration range of 10-60mcg/ml .Marketed formulation was analyzed and amount of drug determined by proposed method ranges 98.23%.The % recovery ranges from 0.695-0.088 for Drotaverine.

Estimation of Drotaverine was based on complex with Potassium bromide bromate and the unreacted react with crystal violet, remaining molecule of crystal violet indirectly indicate the amount of drug present.

5. ACKNOWLEDGEMENT:

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Conflict of Interest: None Declared

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