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# Spectrophotometric Determination of Drotavarine

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Three simple sensitive and reproducible visible spectrophotometric methods (**A-C**) for the determination of drotaverine in bulk samples and pharmaceutical formulations are described. Method **A** is based on the formation of coloured species with chloranil and acetaldehyde (TQ-acetaldehyde). Method **B** involves the complex formation between drotavarine and sodium nitroprusside in alkaline medium. Method **C** is based on the formation of coloured coordination complex with cobalt thiocyanate (CTC). Regression analysis of Beer's law plots showed good concentration ranges 10-50, 4-20 and 10-30 µg/mL for methods, **A**, **B** and **C**, respectively. The applicability of the methods were examined by analyzing tablets or syrup of drotaverine.

**Key Words: Spectrophotometry, Drotavarine.**

## INTRODUCTION

Drotaverine[1] is a isoquinoline antispasmodic agent for oral administration and chemically known as 1-[(3,4-diethoxyphenyl)methylene]-6,7-diethoxy-1,2,3,4-tetrahydroisoquinoline, 1-(3,4-diethoxybenzylidene)-6,7-diethoxly-1,2,3,4-tetrahydroisoquinoline. Few methods such as HPLC[2-5], spectrophotometry[6-9] TLC[10], ion exchange[11], GC[12,13] were reported for the estimation of drotaverine. Literature survey revealed few visible spectrophotometric methods are reported for its quantitative determination in bulk drug and pharmaceutical formulations. This paper describes three visible spectrophototmetric procedures by exploiting the property of secondary amine in drug [formation of vinyl amino substituted with acetaldehyde (method **A**), coloured complex formation with sodium nitroprusside-hydroxylamine (method **B**) and molecular complex formation with cobalt thiocyanate (method **C**)].

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## EXPERIMENTAL

The stock solution (mg/mL) of drotavarine as hydrochloride was prepared by dissolving 100 mg of it in 100 mL, of distilled water. A portion of this stock solution was diluted stepwise with the same solvent to obtain the working standard drotavarine solution of concentrations of 200 µg/mL.

All the chemicals and reagents were of analytical grade and the solutions were prepared in triply distilled water.

Chloranil (BDH, 0.1 %, $4.067 \times 10^{-3}$ M) was prepared by dissolving 100 mg of chloranil in 100 mL of 1,4-dioxane and acetaldehyde used as directly for method **A**. Sodium nitroprusside solution (E. Merck, 5.0 %, $1.67 \times 10^{-1}$ M) prepared by dissolving 5 g of the sodium nitroprusside in 100 mL, of water, $NH_2OH$ solution (Fluka, 5.0 %, $7.09 \times 10^{-1}$ M) prepared by dissolving 5 g of hydroxylamine monohydrochloride in 100 mL, of distilled water and $Na_2CO_3$ solution (Loba, 10 %, $9.43 \times 10^{-1}$ M) prepared by dissolving 10 g of sodium carbonate in 100 mL of distilled water for method **B**. Cobalt thiocyanate ($2.50 \times 10^{-1}$ M) solution was prepared by dissolving 7.25 g of cobalt nitrate and 3.8 g of ammonium thiocyanate in 100 mL of distilled water and trisodium citrate-HCl buffer solution of pH 2.0 were prepared in the usual way 14 for method **C**.

A Milton Roy Spectronic 1201 and Systronics 106 digital spectrophotometer with 1 cm matched quartz cells were used for the spectral and absorbance measurements. An Elico LI-120 digital pH meter was used for pH measurements.

### Recommended procedures

**Method A:** Aliquots of standard drug drotavarine solution (1.0-3.0 mL, 40 µg/mL) were taken into series of 10 mL calibrated tubes. Then 0.5 mL of acetaldehyde and 0.1 mL chloranil were added an allowed to stand for 5 min, at room temp. then solution was made upto the make with 1,4-dioxane and the absorbance were measured at 665 nm against a reagent blank prepared simultaneously. The amount was compute from the appropriate calibration curve.

**Method B:** Aliquots of standard drug solution, 200 µg/mL, ranging from 0.5-2.5 mL were transferred into a series of calibrated tubes and the volume in each tube was brought to 3.0 mL., with distilled water. 1 mL of sodium nitroprusside and 2.0 mL of hydroxylamine solutions were successively added to each tube and shaken for 2 min then 1.0 mL of sodium nitroprusside solution was added and shaken for 15-25 min. Then contents were diluted to 25 mL with distilled water and the absorbance measured after 10 min at 580 nm against the reagent blank. The amount of drug was computed from its calibration graph.

**Method C:** Aliquots of standard drotaverine solution (1.0-3.0 mL, 100 µg/mL) were delivered into a series of calibrated tubes. 2 mL of buffer of pH 2.0 and 5 mL of cobalt thiocyanate solutions were added and the total volume in each tube was adjusted 15 mL with distilled water. These solutions in the tubes were transferred to 125 mL separating funnel. To each separting funnel 10.0 mL of nitrobenzene was added and the contents were shaken for 2 min the two phases were allowed to separate and the absorbance of the separated nitrobenzene layer was measured after 20 min at 630 nm against a similar reagent blank. The amount of drug was deduced from it's calibration curve.

## RESULTS AND DISCUSSION

The optimum conditions for the colour development of methods were established by varying the parameters one at a time, keeping the others fixed and observing the effect produced on the absorbance of the coloured species.

The optical characteristics such as Beer's law limits, molar absorptivity and Sandell's sensitivity for the methods are given in Table-1. The precision of the method was found by measuring absorbance of 6 replicate samples containing known amounts of the drugs and the results obtained are incorporated in Table-1. Regression analysis using the method of least squares was made to evaluate the slope (b), intercept (a) and correlation coefficient (r) for each method and are presented in Table-1. The accuracy of the methods

TABLE-1
OPTICAL CHARACTERISTICS, PRECISION AND ACCURACY OF THE PROPOSED METHODS OF DROTAVARINE

| Parameters | Method **A** | Method **B** | Method **C** |
|---|---|---|---|
| $\lambda_{max}$ (nm) | 665 | 580 | 630 |
| Beer's Law limits (µg $mL^{-1}$) | 10-50 | 4-20 | 10-30 |
| Molar absorptivity (1 $mol^{-1}$ $cm^{-1}$) | $9.23 \times 10^3$ | $1.073 \times 10^4$ | $5.724 \times 10^3$ |
| Sandell's sensitivity (µg/$cm^2$/0.001 absorbance unit) | 0.042 | 0.0375 | 0.384 |
| Regression Equation (y = a + bc) | | | |
| Slope (b) | 0.0235 | 0.026 | 0.0141 |
| Intercept (a) | -0.0004 | 0.0006 | 0.0012 |
| Correlation coefficient (r) | 0.9999 | 0.9999 | 0.9999 |
| Relative Standard Deviation (%)* | 0.2760 | 0.5490 | 0.3630 |
| % Range error (confidence limit) | | | |
| (i) 0.05 level | 0.2310 | 0.3840 | 0.3040 |
| (ii) 0.01 level | 0.3420 | 0.5690 | 0.4510 |
| % Error in bulk sample** | 0.7910 | -0.2900 | 0.0710 |

*Average of 6 determinations considered; **Average of 3 determinations.

was ascertained by comparing the results by proposed and reference methods (UV) statistically by the t- and F-tests (Table-2). This comparison shows that there is no significant difference between the results of proposed methods and those of the reference ones. The similarity of the results is obvious evidence that during the application of these methods, the additives and excipients that are usually present in tablets do not interfere in the assay of proposed methods. As an additional check of accuracy of the proposed methods, recovery experiments were performed by adding a fixed amount of the drug to the preanalyzed formulations. The amount of drug found, the % recovery was calculated in the usual way.

TABLE-2
DETERMINATION OF DROTAVARINE IN PHARMACEUTICAL FORMULATIONS

| Formulations | Labeled amount (mg) | Amount found by proposed methods** | | | Reference Δ method | % Recovery by proposed methods*** | | |
|---|---|---|---|---|---|---|---|---|
| | | **A** | **B** | **C** | | **A** | **B** | **C** |
| Tablet I | 100 | 99.0 ± 0.91<br>F=1.76<br>T=1.9 | 99.79 ± 0.551<br>F=2.11<br>t=0.88 | 99.84 ± 0.415<br>F=2.11<br>t=0.88 | 99.1 ± 0.97 | 97.9 ± 0.54 | 99.79 ± 0.551 | 99.84 ± 0.415 |
| Tablet II | 100 | 98.1 ± 0.75<br>F=1.11<br>T=1.90 | 100.20 ± 0.551<br>F=1.12<br>t=0.84 | 99.78 ± 0.372<br>F=1.95<br>t=0.45 | 99.2 ± 0.64 | 98.7 ± 0.62 | 100.20 ± 0.551 | 99.78 ± 0.372 |
| Tablet III | 100 | 101.1 ± 1.04<br>F=2.60<br>T=1.04 | 99.91 ± 0.139<br>F=1.80<br>t=0.99 | 99.93 ± 0.107<br>F=1.06<br>t=0.99 | 99.1 ± 0.81 | 97.6 ± 0.49 | 99.91 ± 0.139 | 99.93 ± 0.107 |
| Tablet IV | 100 | 98.0 ± 0.27<br>F=1.82<br>T=0.73 | 99.95 ± 0.267<br>F=2.86<br>t=0.94 | 99.96 ± 0.230<br>F=2.10<br>t=1.12 | 100.5 ± 0.49 | 98.6 ± 0.45 | 99.95 ± 0.267 | 99.96 ± 0.230 |

*Two different batches of tablets from a pharmaceutical company.
**Average standard deviation of six determinations; the t- and F- values refer to comparison of the proposed method with the reference method. Theoretical values at 95 % confidence limit, t = 2.57, F = 5.05.
***After adding 3 different amounts of the pure labeled to the pharmaceutical formulation, each value is an average of 3 determinations.
Δ Reference method[1] (drotavarine)

## Conclusion

The proposed methods are applicable for the assay of drug drotaverine and have the advantage of wider range under Beer's law limits. The decreasing order of sensitivity and $\lambda_{max}$ among the proposed methods are B > A > C and A > C > B, respectively. The proposed methods are simple, selective and can be used in the routine determination of drotaverine in bulk samples and formulations with reasonable precision and accuracy.

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