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Estimation of drotaverine in bulk and pharmaceutical formulations by precipitation reagents

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ABSTRACT - Three simple accurate visible sepectrophotometric methods (A.B and C) have been developed for the estimation of Drotaverine (DRT) in bulk and pharmaceutical formulations. The estimation was done based on its complex formation with alkaloids using spectrophotometric methods. Drotaverine forms a molecular complex with SNP (Sodium Nitro Prusside) in method-A, CTC (Cobalt thiocyanate) in method B and DDQ (2,3-dichloro-dicyano-1,4-benzoquinone) in method C during its quantitative precipitation. The absorbance of nitrobenzene layer was measured at the respective wavelength of maximum absorbance against the reagent blank. To determine Drotaverine colour reaction was used in addition to precipitation reaction. They are based on the colour formation with either unreacted precipitant of the filtrate or released precipitant from the molecular complex. All the variables have been optimized. The proposed methods are validated statistically. Recovery studies were carried out by standard addition method.

Key words - Drotaverine, SNP, CTC, DDQ and Spectrophotometer

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Drotaverine is an antiparnodic drug an analog of papaverine with smooth muscle relaxit properties. It is a selective inhibitor of phosphodiesterase 4 and has no anticholinergic effects. Chemically, Drotaverine is (1-(3,4-diethoxybenzylidene)-6,7-diethoxy-1,2,3,4-tetrahydroisoquinolene) an isoquinolene derivative. It is considered as a highly potent spasmolytic agent[1].

It is accompanied by a mild calcium channel blocking effect. The mild impact of Drotaverine is hypotension vertigo, nausea and palpitation. Some studies stated that drotaverine was effective nearly 80,s in treating renal colic[2]. According to the literature survey it is revealed that few methods such as HPLC[3-6], Spectrophotometry[7-9], TLC[10], ion exchange[11], GC[12-13] were used for the estimation of drotarverine.

Since there is no much literature reported for the estimation of drotaverine by visible spectrophotometric methods. In the present work successful attempt was made to assess quantitatively bulk drug and pharmaceutical formulations by precipitation reagents.

EXPERIMENTAL METHODOLOGY

In the present work systronics UV-Visible spectrophotometric instrument of model number 117 was used with a pair of 10mm matched quartz cells. For pH measurements an Elico LI.120 digital pH meter was used.

Preparation of stock solution:

All the chemicals used were analytical grade and the solutions were prepared with distill water.

Method A:

SNP (Sodium Nitro Prusside) solution was prepared by dissolving 5g in 100ml of water. 5 per cent ($1.67x10^{-1}$M), 5g of hydroxylamine monohydrochloride was dissolved in 100ml of

distill water ($7.09x10^{-1}$M). 10g of sodium carbonate is dissolved in 100ml of distill water ($9.43x10^{-1}$M).

Method B:

CTC (Cobalt thiocyanate) solution was prepared by dissolving 7.25g of cobalt nitrate and 3.8g of ammonium in 100ml of distill water ($2.5x10^{-1}$M). pH 2.0 solution was prepared by taking 306 ml of trisodium citrate. 0.1M dissolved in 694ml of HCl. Nitrobenzene was prepared by using AR grade nitrobenzene.

Method C:

DDQ solution was prepared by dissolving 100mg of DDQ in 10ml of DMP followed by dilution to 100ml with dioxane.

Recommended procedure:

Method-A

Aliquot of standard drug solution 200µg/ml ranging from 0.5 to 2.5 ml were pipetted out into a series of calibrated tubes in the volume in the each tube was adjusted to 3ml with distill water. 1ml of sodium nitropruside solution and 2ml of hydroxylamine solutions were successively added to each tube and shaken for 2 minutes then 1ml of sodium carbonate solution was added and mixed thoroughly for 15-20 minutes. Then the contents were diluted with 25ml of distill water. The absorbance was measured within one hour of complex extraction. At 580nm against the reagent blank prepared in a similar manner. The amount of drug was computed from the calibration graph.

Method-B:

Aliquot of drotaverine solution (1.0, 2.0, 3.0, 100 µg/ml were delivered into a series of calibrated tubes. 2ml of pH 2 solution and 5ml of cobalt thiosulphate solution was added and the total volume in each tube was adjusted to 15ml of distill water and these solutions were transferred to separating funnels. To each separating funnel 10ml of nitrobenzene was added and thoroughly mixed for 2 minutes. The two phases were allowed to separate and the absorbance of separated nitrobenzene layer was measured at 630nm against a similar reagent blank after 20 minutes.

Method-C:

In a series of 10ml calibrated tubes aliquots of drug solution of 0.5-2.5ml, 200µg/ml was prepared by using DMP-dioxane (1:9) were transferred and the volume in each tube was adjusted to 3.0 ml with dioxane. Then 1.0 ml of DDQ solution was added and the total volume in each tube was adjusted with dioxane. The absorbance of the coloured species was measured at 460 nm against a reagent blank during the stability period (immediate to 40 min.). The amount of the drug was calculated from Bees-Lambert's plot.

EXPERIMENTAL FINDINGS AND ANALYSIS

The optimum conditions for the colour development of methods (A, B and C) 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 (A-C) are given in Table 1. The precision of the each method to the drug was found by measuring the absorbance of 6 separate samples containing known amounts of drug 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 ® and standard error of estimation (Se) for each system and is presented in Table 1.

The accuracy of the methods was ascertained by comparing the results by proposed and reference methods (UV) statistically by the T- and F-tests (Table 2). The comparison shows that there is no significant difference between the results of studied methods and those of the reference once. The similarity of the results is an obvious

Table 1 : Optical characteristics, precision and accuracy of the proposed methods for drotaverine

Sr. No.	Optical characteristics	Method A	Method B	Method C
1.	λ max (nm)	580	630	460
2.	Beer's Law	4-20	10-30	10-15
3.	Molar absorptivity (1 mol^{-1} cm^{-1})	$1.073x10^4$	$5.724x10^3$	$4.214x10^3$
4.	Correlation co-efficient ®	0.9999	0.9999	0.9999
5.	Sandell's sensitivity (/absorbance unity)	0.03756	0.04125	0.01044
6.	Regression equation (Y=a+bc)	0.02655	0.04125	0.096
7.	Optimum photometric range (µg/ml)	6-18	14-26	15-45
8.	Relative standard deviation*	0.4598	0.3634	0.314
9.	% of range error (confidence limit (i) 0.05 level (ii) 0.01 level	0.384	0.304	0.263
10.	% error in bulk sample**	-0.029	0.071	0

*Y=a+bc, where c is the concentration in µg/ml. ** From six determinations.

Table 2 : Determination of DRT in pharmaceutical formulations

Sample	Amount taken (mg)	Amount found by proposed Methods			Ref. method	% Recovery by Proposed methods		
		Method A	Method B	Method C		Method A	Method B	Method C
Tab I	100	99.77±0.551	99.84±0.415	99.2±1.34	99.74±0.604	99.79. ±0.551	99.84±0.415	99.1±0.31
		F=1.20 T=0.89	F=2.11 T=0.88	F=1.84 F=1.30				
Tab II	100	100.20±0.551	99.78±0.372	98.5±1.0	99.69±0.520	100.20±0.551	99.78±0.372	98.9±0.25
		F=1.12 T=0.84	F=1.95 T=0.45	F=2.10 T=1.3				
Tab III	100	99.9±0.139	99.93±0.107	98.4±1.56	99.91±0.103	99.91±0.139	99.93±0.107	98.8±0.39
		F=1.80 T=.99	F=1.06 T=0.99	F=2.30 T=0.54				
Tab IV	100	99.95±0.267	99.96±0.230	98.1±0.76	100.5±0.49	99.95±0.26	99.96±0.23	99.2±0.28
		F=2.86 T=0.94	F=2.10 T=1.12	F=2.44 T=1.22				

*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.

evidence that during the application of these methods, the excipients are usually present methods. As an additional check of accuracy of the proposed methods, recovery experiments were carried out. The recovery of the added amounts of standard drug was studied at 3 different levels. Each level was repeated for 6 times. From the amount of drug found, the per cent recovery was calculated in the usual way.

The higher λ max values of all the proposed methods have a decisive advantage since the interference from the associated ingredients should be generally less at higher wavelengths than at lower wavelengths. Thus the proposed visible spectrophotometric methods are simple and sensitive with reasonable precision, accuracy and constitute better alternatives to the existing ones to the routine determination of Drotaverine in bulk forms and pharmaceutical formulations.

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