
Extractive Spectrophotometric Determination of Pentazocine, Orphenadrine and Doxepin Hydrochloride

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A new spectrophotometric method is proposed for the determination of pentazocine, orphenadrine and doxepin hydrochlorides based on the formation of stable ion-pair complexes between the drugs and cobalt-thiocyanate in 2N-hydrochloric acid medium. Statistical comparison of the results of the assay of the drugs in pure and dosage forms with those of an official method shows an excellent agreement and indicates no significant difference in precision.

PENTAZOCINE hydrochloride (PZH) is an analgesic and has narcotic antagonist action. It is used as a pre and post-operative anaesthetic. Orphenadrine hydrochloride (ORPH) is used in the symptomatic management of Parkinson's disease. It reduces sialorrhoea, diaphoresis, voluntary muscle spasm, spasticity and blepharospasm. Doxepin hydrochloride (DOX) is an antidepressive agent. Pentazocine has been analysed by various methods in biological fluids and pharmaceutical preparations.¹ The official compendia^{2,3} describe spectrophotometric assay method. A few more procedure have also been reported for PZH⁴⁻⁷, ORPH⁸ and DOX⁹. Sethi et al¹⁰ have recommended the spectrophotometric determination of PZH in pharmaceutical formulations through copper(II) and cobalt(II) chelation. More recently titrimetric¹¹ and HPLC¹² methods have also been reported in literature. In the present communication a new extractive spectrophotometric method based on the formation of a stable blue coloured ion-pair complex with cobalt-thiocyanate in 2N-hydrochloric acid medium, is described.

EXPERIMENTAL

Apparatus JASCO model UVIDEK-610 and ELICO model CL-27 digital spectrophotometers were used for absorbance measurements.

Standard solutions Stock solutions of PZH, ORPH (M/s Biddle-Sawyer Ltd., Bombay) and DOX (Intas Laboratories Pvt. Ltd., Ahmedabad) were prepared by dissolving requisite amount of the sample in doubly distilled water.

Cobalt thiocyanate Pure solid cobalt thiocyanate was prepared as described earlier.¹³

Standard curve Suitable volumes of standard drug solution containing 25 to 250 μg of PZH/ORPH or 15 to 250 μg of DOX were transferred into a series of 100ml separatory funnels. A 10 ml volumes of 10% cobalt thiocyanate and 1 ml of 2N-hydrochloric acid were added to it and mixed well. The contents were extracted with three 3ml portions of 1,2-dichloroethane. The organic layer was separated and dried with anhydrous sodium sulphate and transferred into a 10 ml flask, diluted to the mark with 1,2-dichloroethane and mixed well. The absorbance of the organic layer was measured at 625 nm against reagent blank. The standard curve was drawn by plotting concentration vs absorbance.

Procedure for Drug in Formulations:

The sample (pure drug, tablet powder and capsules) equivalent to about 50 mg of active ingredient

Table 1- Optical characteristics and precision data

	PZH	ORPH	DOX
Beer's law limits ($\mu\text{g/ml}$)	2-25	2.5-25	0.5-30
Molar absorptivity ($\times 10^3 \text{ l/mol/cm}$)	3.54	5.28	2.65
Sandell's sensitivity ($\mu\text{g/cm}^2/0.001 \text{ abs.unit}$)	0.09	0.057	0.121
Pure drug:			
Taken ($\mu\text{g/ml}$)	20.0	20.0	25.0
Found ($\mu\text{g/ml}$)	19.8	19.9	25.1
Standard deviation	± 0.3184	± 0.617	± 0.75
Error	0.99	0.70	0.62
Coefficient of variation	1.6	3.1	3.0
Regression equation(Y^*)			
Slope (b)	0.00897	0.0135	0.010138
Intercept (a)	0.004	0.01212	-0.01965
Correlation coefficient (r)	0.99	0.989	0.99

$Y^* = a+bx$, where x is the concentration in $\mu\text{g/ml}$

Table 2-Recovery studies of drugs in pharmaceutical preparations.

Drug present in Tablets/Caps	Label claim (mg)	Found (mg)	Recovery(%)	
			B.P.	Proposed*
PZH	25	25.10	98.8	100.4
ORPH	50	49.80	99.0	99.6
DOX	75	74.85	99.5	99.8
	25	25.10	—	100.4

* Average of five determinations

PZH, ORPH and DOX was dissolved in distilled water and filtered using a G-4 sintered glass filter. The combined filtrate and washings were diluted to 100ml

with distilled water. The drug content was determined from this solution as described under the standard curve and the results are presented in Table 2.

RESULTS AND DISCUSSION

Cobalt thiocyanate reacts with PZH, ORPH and DOX in acid medium to yield a stable blue coloured ion-pair complex which when extracted into organic layer exhibits maximum absorption at 625 nm. 1,2-dichloro ethane was found to be an effective solvent for the extraction. The colour of the compound in the organic layer remains constant over a period of 6,2 h and 45 min in the temperature range 5-40° for PZH, ORPH and DOX, respectively. Beer's law ranges, the molar absorptivities, slope, intercept and correlation coefficients obtained by a linear least-squares treatment of the results are presented in **Table 1**.

The effect of common excipients in the assay was investigated and the results indicate that the excipients like talc, starch, dextrose, stearic acid, sodium alginate, gum acacia and gelatin did not interfere.

The proposed procedure has been employed for the determination of pure drugs and their dosage forms and the results are presented in **Table 2**. It can be seen that the values obtained compare favourably with those obtained by official methods.^{2,3} The precision data also indicates no significant differences.

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