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Extractive Spectrophotometric Determination of Itopride Hydrochloride

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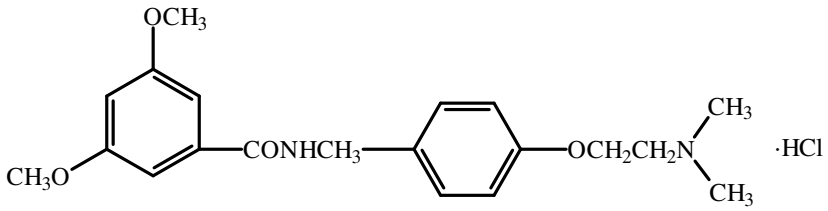
A simple and sensitive extractive spectrophotometric method has been developed for the quantitative determination of itopride hydrochloride in bulk drug and pharmaceutical formulations. The developed method involves formation of coloured chloroform extractable complex of drug with bromocresol green in acidic medium. The complex in chloroform has showed absorption maximum at 419.8 nm. Beer's law is obeyed in the concentration range of 2-10 μg/mL. The results of analysis of the above method have been validated statistically and by recovery studies.

Key Words: Spectrophotometric determination, Itopride hydrochloride.

INTRODUCTION

Itopride hydrochloride[1] is a novel prokinetic drug indicated in the treatment of gastrointestinal symptoms caused by reduced gastrointestinal motility like feeling gastric fullness, upper abdominal pain, anorexia, nausea and vomiting in non-ulcer dyspepsia[2-7]. It is chemically, N-{P-[2-(dimethyl amino)ethoxy]benzyl}veratramide hydrochloride with a molecular formula, $C_{20}H_{26}N_2O_4$. HCl, molecular weight, 394.9 and molecular structure as follows:



Literature survey revealed that visible spectrophotometric methods have not been reported for its quantitative determination in bulk drug and pharmaceutical formulations. In the present investigation, a simple and sensitive extractive spectrophotometric method has been dveloped for the

quantitative determination of itopride hydrochloride in bulk drug and pharmaceutical formulations. The developed method involves formation of coloured chloroform extractable complex of drug with bromocresol green in acidic medium. The complex in chloroform has showed absorption maximum at 419.8 nm. Beer's law is obeyed in the concentration range of 2-10 µg/mL. The results of analysis for the method have been validated statistically and by recovery studies.

EXPERIMENTAL

All spectral measurements were done on Shimadzu UV/Vis spectrophotometer model No. 1700.

Preparation of reagents

Buffer solution: pH 2.8 buffer solution was prepared as per I.P. mixing appropriate quantities of 0.2 M potassium hydrogen phthalate and 0.2 M sodium hydroxide; **Bromocresol green solution:** 0.1 % solution was prepared by dissolving 100 mg of bromocresol green in a mixture of 0.72 mL of 0.1 M NaOH and 20 mL of alcohol (95 %) and made up to 100 mL with water; Chloroform; Double distilled water; Authentic sample of itopride hydrochloride (Unichem, Mumbai, India).

Standard and sample solution: About 100 mg of itopride hydrochloride (pure or equivalent tablet powder) was weighed accurately and dissolved in 20 mL of distilled water and made up to 100 mL with distilled water. Further dilutions were made with distilled water to get working standard solution of 100 µg/mL. In case of sample, 20 tablets each containing 50 mg of drug were taken and average weight was calculated. The tablets were powdered in a glass mortar. The tablet powder equivalent to 100 mg was taken.

Assay: From standard solution (100 mcg/mL) 0.5, 1.0, 1.5, 2.0, 2.5 mL were pipetted separately into 5 seperating funnels. The volume was adjusted to 5 mL with distilled water to each separating funnel. 1 mL of buffer (pH 2.8) and 4 mL of (0.1 %) dye solution were added. 10 mL of chloroform was added and funnel was shaken for 2 min. The contents were allowed to separate. The lower chloroform layer was collected in a separate 25 mL volumetric flask. The aqueous layer was extracted again with 10 mL of chloroform. The chloroform layers were combined and the volume was made up to 25 mL with chloroform. So, the concentration of the drug would be 2, 4, 6, 8, 10 mcg/mL. Absorbance was measured at 419.8 nm against reagent blank solution obtained in the same way omitting the drug. The amount of itopride hydrochloride present in the sample was computed from the calibrtion curve. Results are reported in Tables 1 and 2.

RESULTS AND DISCUSSION

The optical characteristics such as absorption maxima, Beer's law limits, molar absorptivity and Sandell's sensitivity are presented in Table-1. the regression analysis using the method of least squares was made for the slope (b), intercept (a) and correlation (r) obtained from different concentration and the results are summarized in Table-1. The per cent relative standard deviation and per cent range of error (0.05 and 0.01 level of confidence limits), calculated from the eight measurements.

TABLE-1
OPTICAL CHARACTERISTICS AND PRECISION

Parameters		
λ_{max} (nm)		419.8
Beer's law limit (μg/mL)		2-10
Molar absorptivity (L mol^{-1} cm^{-1})		1.6887×10^4
Sandell's sensitivity (μg/cm^2 0.001 absorption units)		0.086×10^3
Regression equation (y*)	Slope (b)	0.0483
	Intercept (a)	0.0176
	Correlation coefficient (r)	0.9935
RSD (%)		8.297
Range of errors**	Confidence limit with 0.05 level	± 0.015
	Confidence limit with 0.01 level	± 0.015

*y = bc + a where c is the concentration of itopride hydrochloride in μg/mL and y is the absorbance at the respective λ_{max}; **for 8 measurements.

The values obtained for the determination of itopride hydrochloride in pharmaceutical formulations (tablets) by the proposed and UV methods are compared in Table-2. To evaluate the validity and reproducibility of the methods, known amounts of pure drug were added to the previously analyzed pharmaceutical formulations and the mixtures were analyzed by the proposed methods and the recoveries (average of 8 determinations) are given in Table-2. Interference studies reveal that the common excipients and the additives usually present in the dosage forms did not interfere in the proposed methods.

The coloured complexes, which are being extracted in chloroform layer are due to the formation of drug: dye complexes between the acidic dye and basic drug itopride hydrochloride.

The results indicate that the proposed method is a simple, sensitive, reproducible and accurate and can be used for the routine determination of itopride hydrochloride in bulk drug and dosage forms.

TABLE-2
EVALUATION OF ITOPRIDE HYDROCHLORIDE IN PHARMACEUTICAL PREPARATIONS

Sample*	Labelled amount (mg)	Amount obtained (mg)		Recovery** (%)
		UV method#	Proposed method	
T_1	50.00	49.66	49.41	99.46 ± 0.02
T_2	50.00	50.67	49.82	99.31 ± 0.01
T_3	50.00	50.16	49.37	99.42 ± 0.02
T_4	50.00	49.32	49.90	99.61 ± 0.03
T_5	50.00	49.37	49.58	99.52 ± 0.04

*Tablets from different manufacturers; **Average ± SD of 8 determinations; **50 mg of pure drug was added and recovered; #As the drug is not official in any pharmacopoeia, official method is not available for comparison. Hence, UV method developed in our laboratory was selected.

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