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Original Article

USE OF ION ASSOCIATION COMPLEX FORMATION FOR THE SPECTROPHOTOMETRIC DETERMINATION OF ITOPRIDE HCL IN BULK AND ITS PHARMACEUTICAL PREPARATIONS

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ABSTRACT

Objective: The authors report two simple, accurate and economic spectrophotometric methods A and B for the determination of Itopride hydrochloride in bulk and dosage forms.

Methods: The proposed methods are based on the formation of chloroform soluble ion-associates in the presence of acidic dyes namely BPB (Method A) and BCP (Method B) exhibiting λ_{max} at 418 and 418 nm respectively.

Results: Beer's law is found to be obeyed in the concentration range of 2.0-10.0 µg/ml and 2.0-10.0 µg/ml. The molar absorptivities are found to be $1.42x10^4$ and $9.61x10^3$L/mol. cm for methods A and B. These methods are successfully applied for the assay of Itopride hydrochloride in pharmaceutical formulations.

Keywords: Itopride hydrochloride, BPB, BCP, Spectrophotometry

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INTRODUCTION

Itopride hydrochloride (*N*-[4-[2-(dimethylamino)-ethoxy] benzyl]-3, 4-dimethoxybenzamide hydrochloride) [1-3] is a prokinetic benzamide derivative, unlike metoclopramide or domperidone. These drugs inhibit dopamine and have gastrokinetic effect[4]. Itopride HCl is prescribed for non-ulcer dyspepsia, chronic indigestion and gastro-esophageal reflux disease. Itopride is effective in reducing bloating, abdominal pain and burning sensation and other gastrointestinal disorders[5]. Itopride increases acetylcholine concentration by inhibiting dopamine D_2-receptors and acetylcholinesterase. Higher acetylcholine increases gastrointestinal peristalsis, increase the lower esophageal sphincter pressure, increases gastric emptying, stimulates gastric motility and improves gastroduodenal co-ordination. Literature survey reveals that for the determination of itopride HCl and its related substances in biological fluids like plasma, blood, urine and pharmaceutical dosage forms by spectrophotometry [6-8], High Performance Liquid Chromatography (RP-HPLC) with UV detection[9], chemiluminescence detection [10], fluorimetric detection [11-13], Photo Diode Array detection [14] and Liquid Chromatography-Mass Spectrometry [15], HPTLC [16-18].

However, very few analytical methods were reported in the literature for the determination of itopride HCl in bulk and pharmaceutical dosage forms. The present manuscript describes two simple, sensitive, accurate and rapid for the determination of ITP.

MATERIALS AND METHODS

Instruments

Spectral measurements were performed on Elico SL-159 model, 2 nm high resolution, double beam, 1 cm length quartz coated optics; Wavelength range190-800 nm.

High stability, linearity, the precision instrument was used for all the spectral measurements. All the chemicals and reagents used for the studies were of analytical grade and the freshly prepared solutions were always employed in the investigations.

Chemicals and reagents

Aqueous solutions of (0.2%, $3.203x10^{-3}$M) Bromo Phenol Blue (BPB), (0.2%, $7.16x10^{-4}$M) Bromo Cresol Purple (BCP) and 0.1M HCl were prepared by dissolving 8.6 ml of Conc. HCl to 1 litre. Chloroform was used in both methods A and B.

Preparation of standard drug solution

A stock solution of 1% drug solution was freshly prepared by transferring accurately weighing 100 mg of Itopride hydrochloride into 100 ml volumetric flask and dissolved in double distilled water, and then made up to the mark. Then working standard solutions 100µg. ml^{-1} are prepared by transferring 10.0 ml of the stock solutions into two 100 ml standard flasks respectively and made up to the mark.

Table 1: Optical and regression characteristics of the proposed methods for Itopride hydrochloride

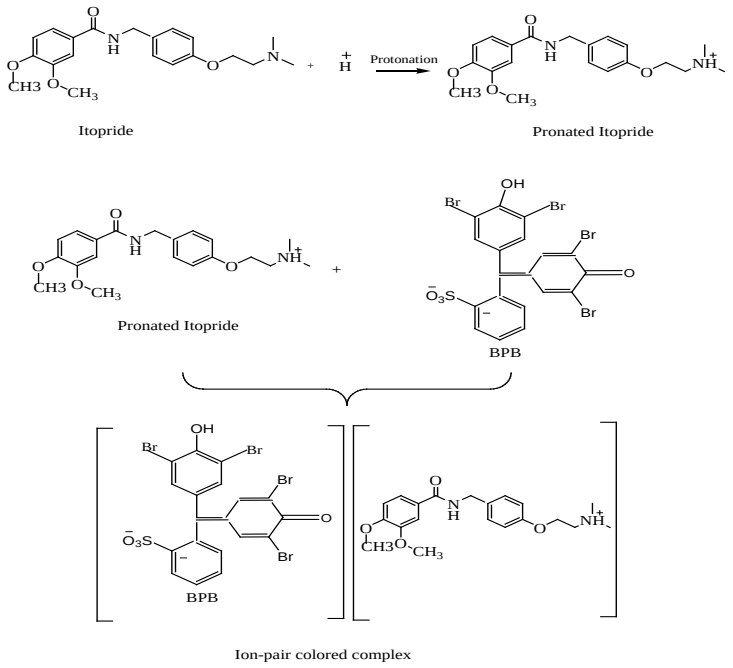
Name of the parameter	Method M_{1a}	Method M_{1b}
Maximum wavelength (λ_{max}) nm	418	418
Beer's law limits µg. ml^{-1}	2.0-10.0	2.0-10.0
Sandell's sensitivity(µg/cm^2/0.001 Absorbance)	2.38E-02	1.34E-02
Molar absorptivity (lit/mole/cm)	1.66E+04	2.61E+04
Slope (b)	4.13E-02	7.32E-02
Intercept(a)	3.00E-04	3.10E-03
Standard deviation on slope(S_b)	1.89E-04	3.50E-04
Standard deviation on intercept(S_a)	1.26E-03	2.32E-03
Standard error on estimation(S_e)	2.21E-02	2.19E-02
Correlation coefficient (r)	0.9999	0.9999
Limit of detection (LOD) µg. ml^{-1}	0.0911	0.0951
Limit of quantification (LOQ) µg. ml^{-1}	0.3038	0.3169

Recommended procedures for the Methods A and B

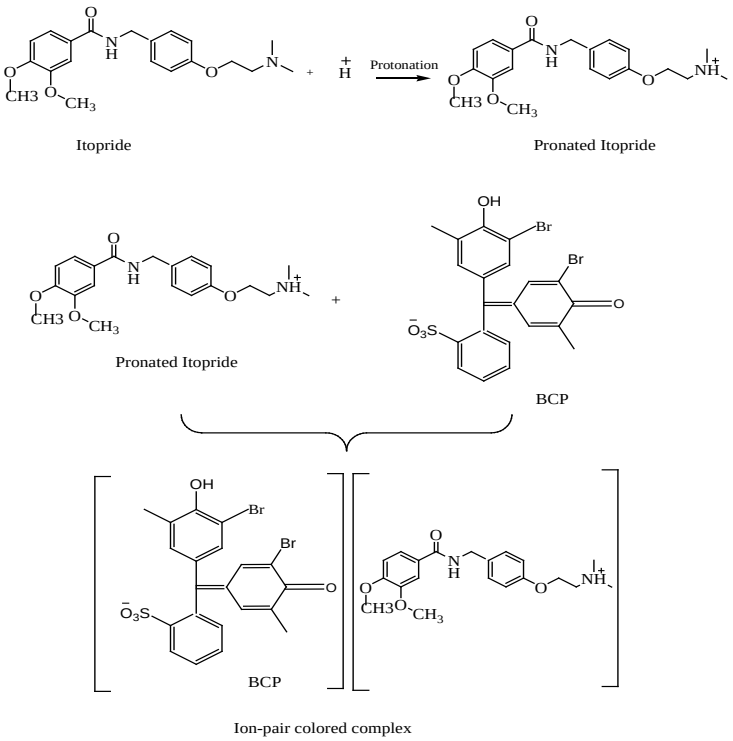
Different aliquots (0.5-2.5 ml) of standard drug solution were transferred into a series of 125 ml separating flask. To this, 6.0 ml of 0.1 M HCl solution and 5.0 ml of 0.2% dye solution were added successively. The total volume of the aqueous phase in each separating funnel was adjusted to 15 ml with distilled water and an organic layer to 10 ml with $CHCl_3$. The contents were shaken for 2 min. The two phases were allowed to separate, and the absorbance of the separated chloroform layer was measured at λ_{max} 418 nm (Method A) and 418 nm (Method B) against a similar reagent blank. The amount of ITP present was deduced from the appropriate calibration curve (fig. 1 and 2).

Reaction mechanism methods: A and B

Method-A: BPB



Method-B: BCP



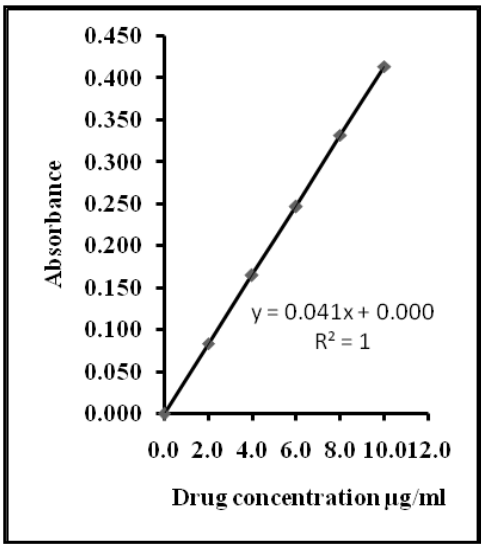


Fig. 1: Beer's Law plot of ITP with BPB (Method-A)

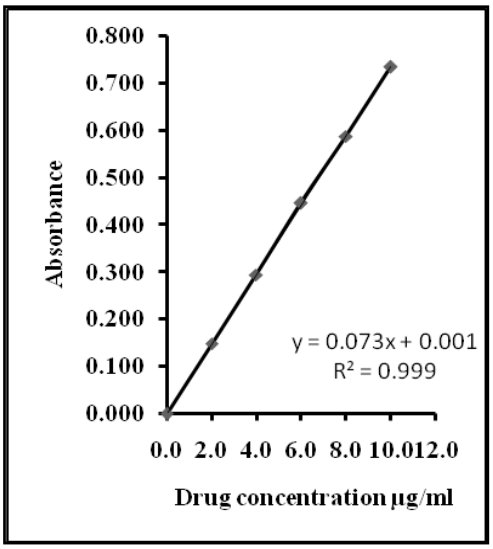


Fig. 2: Beer's Law plot of ITP with BCP (Method-B)

Table 2: Assay of Itopride hydrochloride in pharmaceutical formulations

Formulations*	Amount taken (mg)	Amount found by proposed methods**		Reference method	Percentage recovery by proposed methods***	
		M_{1a}	M_{1b}		M_{1a}	M_{1b}
Tablet	50	49.74+0.65 F=1.96 t=1.53	49.75+0.47 F=3.75 t=1.45	49.81+0.91	99.86+0.57	99.88+0.26

* * Average of six determinations considered

RESULTS AND DISCUSSION

An ion association complex is a form of the molecular complex resulting from two components extractable into organic solvents from aqueous phase at a suitable pH. In present methods A and B, the two dyes (BPB) and (BCP) produce the stable anionic component in an aqueous medium, which interact with the protonated nitrogen of the drug in acidic medium forming more stable complex due to electrostatic interactions. Ion-pair extractive spectrophotometry has attracted considerable attention for quantitative analysis of many pharmaceutically active compounds. Optimisations of the spectrophotometric conditions were intended to take into account the various goals of method development and to weigh each goal accurately. The optical characteristics such as Beer's law limits, Sandell's sensitivity, molar absorptivity, % relative standard deviation and regression characteristics like standard deviation of slope (Sb), standard deviation of intercept (Sa), standard error of estimation (S), and detection limit were calculated for the formulation ITP of was successfully analyzed by the proposed methods. The values obtained by the proposed methods are presented in table 1. The Beer's law was obeyed in the concentration ranges. The values obtained for the determination of Itopride hydrochloride in tablet sample 1 by the proposed and U. V methods are compared in table 2**.** To evaluate the validity and reproducibility of the methods, known amounts of the pure drug were added to the previously analysed pharmaceutical preparation and the mixtures were analysed by the proposed methods. The statistical analysis in terms of t-test and F-test indicates that the reported methods are not significantly different from that of literature method in terms of accuracy and precision table 2**.**

CONCLUSION

The reported methods are found to be simple, sensitive, accurate and precise. The present methods involve the formation of highly stable colored species which makes it easier for the determination of ITP from pharmaceutical dosage forms in a routine manner. Further, statistical parameters and the recovery study data clearly indicate the reproducibility and accuracy of the methods.

CONFLICT OF INTERESTS

Declared none

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