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Determination of Itopride in pharmaceutical formulations by visible spectrophotometric method

Dr.A.Venkateswara Rao,
Lecturer, Department of Chemistry, S.K.B.R.College, Amalapuram, E.G.Dt.,A.P. India

Introduction

The present study describes a simple and selective visible spectrophotometric method for the determination of the Itopride in tablet formulations. Itopride (ITP) is a prokinetic benzamide derivative unlike metoclopramide or domperidone. These drugs inhibit dopamine and have a gastrokinetic effect.[1] Itopride is indicated for the treatment of functional dyspepsia and other gastrointestinal conditions(GI).[2] It is indicated in the treatment of GI symptoms caused by reduced GI motility: dyspepsia of a non-ulcer type (gastric "fullness", discomfort, and possible pain), anorexia, heartburn, regurgitation, bloating, nausea and vomiting, other possible gastric, prolactin, or dopamine related conditions. Itropide is not official in any pharmacopoeia and a literature survey reveals a high performance liquid chromatographic method and a direct UV absorbance measurement after chloroformic clean-up for its determination in pharmaceutical tablets [2] and syrups [3], respectively. Chromatographic procedures for the determination of have been described, but these GLC [4] and HPLC [5,6,7] methods were all used for the analysis of the drug in biological fluids. No colourimetric or other spectrophotometric methods are available for the analysis of (ITP) in pharmaceutical tablets

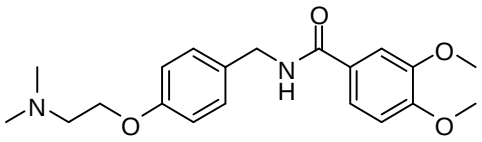

Figure 1: Chemical structure of Itopride

Materials and method

Instrumentation

Teccomp UV-2301 double beam UV-Visible spectrophotometer was used to carry out spectral analysis and the data was recorded by Hitachi software. Standard cuvettes of 10mm path length are used for analysis. Sonicator (1.5L) Ultrasonicator was used to sonicating the standard and formulation sample. Standard and sample drugs were weighed by using Denver electronic analytical balance (SI-234).

Reagents and Materials

Working standard sample Itopride was obtained from Hetero labs pvt. limited, Hyderabad, formulation sample (Gimate-50mg) was purchased from local pharmacy. Spectrophotometric coloring reagent were purchased from Merk chemicals pvt limited, Fine chemindustries, Himedia chemicals, Mumbai, India. All the chemicals used were of analytical grade. All the solutions were freshly prepared with double distilled water.

Preparation of standard stock solution (100 μg/ml)

Standard stock solution of Itopride pure drug was prepared by accurately weighing about 10mg of each drug in 10ml volumetric flask. The drug dissolved with 5ml of methanol and sonicated to dissolve it completely and made up to the mark with the same solvent, results 1000μg/ml solution was obtained. The content was mixed well and from this 1ml, 2ml, 3ml and 4ml separately in a 10ml calibrated volumetric flasks and further make up to 10ml to get a concentration of 100μg/ml. 500mg of Vanillin(VN) was weighed accurately and was dissolved in 100ml methanol.

Procedure for method :

Aliquot of the drug (0.5-4ml) was then in a series of 10ml volumetric flasks, Volume of the each test tube was make up to 3ml with methanol. Then the contents were incubated for 30min with 2ml of Vanillin. Final volume of the volumetric flask was makeup to 10ml with double distilled water. The resulting solution was scanned in UV-VIS spectrophotometer from 400-800 nm to determine the λ_{max} against the reagent blank. Then the absorbance of the formed color was measured at λ_{max} 420nm against a reagent blank. The visible spectrum was shown in Figure.2

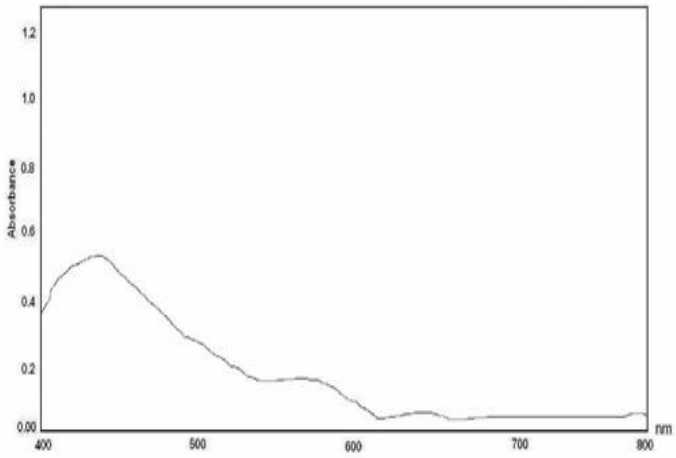

Figure 2. Absorption spectra of Itropride with Vanillin Methode

S.NO	Method	
	Con*,	Abs#
1	5	0.126
2	10	0.232
3	15	0.334
4	20	0.442
5	25	0.534
6	30	0.634
	Slope: 0.0209 Intercept:0.0151 R^2:0.9991	

Table 1. Linearity results of Itopride by the proposed method

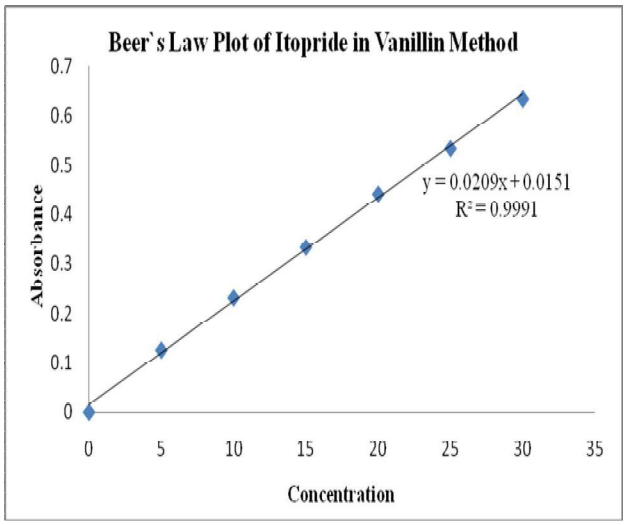

Figure 3. Linearity Graph of Itopride in Vanillin Method

Estimation of Gimate-50mg in tablet formulation

Weighed accurately about 20 tablets and triturated to fine powder. Tablet powder equivalent to 100 mg of Gimate-50mg was weighed and dissolved in 10 ml of methanol with shaking and final volume was made up to 100 ml with methanol. This was then filtered through whatmann's filter paper to get concentration of 1mg/ml solution. This was then diluted to make the working concentration of 100 µg/ml with methanol and used for method respectively. The amount of drug present in the formulation was determined from the calibration curve. The results were summarized in Table 3.

Formulation	Labelled amount	Amount found	% Recovery ± SD
Gimate-50mg	50 mg	49.86 mg	99.06 ± 0.087

Table 3: Estimation of Gimate-50mg in Pharmaceutical Formulation

Chemistry of the colored species:

Enamines are formed by a condensation reaction between a secondary amine and an aldehyde or ketone in the presence of an acid catalyst. The formation of enamine forms the basis for the spectrophotometric determination of compounds of pharmaceutical significance. Vanillin, an aromatic aldehyde, has been applied to the quantification of drugs with primary or secondary amine in acidic medium using spectrophotometry. The proposed method is based on the formation of chromogenic enamine between the secondary amino group of Itopride and aldehyde group of vanillin. The most probable condensation step for the formation of enamine between Itopride and vanillin.

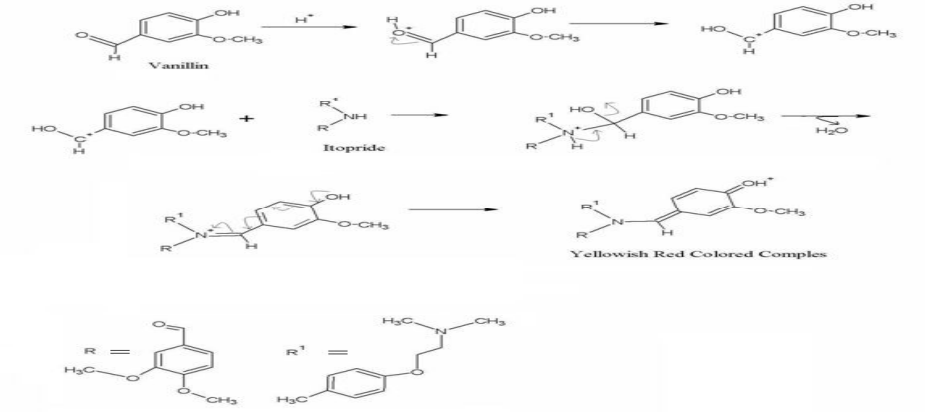

Figure 5.The proposed reaction pathway for enamine formation

Results and discussion

The optical characteristics such as Beer's law limits and molar absorptivity values, together with other analytical performance characteristics such as LOD, LOQ, regression equation parameters for method was summarized in Table.Repeatability or intra-day precision was investigated on six replicate sample solutions on the same day. Inter-day precision was assessed by analyzing newly prepared sample solutions in triplicate over three consecutive days. Both inter day and intraday precision was expressed as % RSD . The % RSD values for intraday precision for this Method 0.51. The % RSD for inter day precision 0.52. The results were summarized in Table 4. The low value of % RSD indicates the high precision of the method

S.No.	Parameter	Method
1	Regression Equation*	Y=0.0209x+0.0151
2	Slope(b)	0.0202
3	Intercept(a)	0.0151
4	Correlation Coefficient(r)	0.9991
5	%RSD**	0.35
6	Absorption Maxima(nm)	420
7	Linearity Range(µg/ml)	5-30
8	Limit of Detection (µg/ml)	0.37
9	Limit of Quantification(µg/ml)	1.25

** Y= bX+a, where X is the concentration of in Gimate-50mg in µg/ml and Y is the absorbance at respective λ_{max} ** For six replicate samples*

Table 4: Regression and optical parameters for Method

Intra-day	Inter-day			
Con. taken (µg/ml)	Con. found * (µg/ml)	%RSD	Con. found*(µg/ml)	%RSD
15	14.86	0.51	14.91	0.88

**average of six determinations*

Table 5 : Intra-day and Inter-day precision for method

The accuracy of the method was evaluated by recovery studies by adding pure Itopride to the pre-analyzed formulation. The average accuracy was found to be 99.06-99.66 % for method**.** The results are summarized in Table 6. The results implied that the method developed was accurate for the determination.

Method	Recovery	Target conc.*	Spiked conc.	Final conc.	Recovered Mean ± SD#	%RSD	%Recovery Mean ± SD	RSD of Recovery	Relative % Error
M1	50%	10	5	15	15.10±0.007	0.44	100.69±0.46	0.45	0.69
	100%	10	10	20	20.19±0.007	0.35	100.97±0.34	0.34	0.97
	150%	10	15	25	25.07±0.20	0.79	100.31±0.78	0.78	0.31

Table 6: Accuracy results for method

Commercial formulation of *Gimate-50mg* was successfully analyzed and there was no interference of additives or excipients in proposed analytical methods. The proposed methods were found to be simple, sensitive, accurate, precise and can be used for the routine quality control of this drug in bulk as well as in pharmaceutical formulation.

Conclusion

The spectrophotometric method was found to be reproducible and accurate in the analysis of Itropide in pharmaceutical tablets. Statistical analysis of the results shows that the proposed procedure has good precision and accuracy. Results of analysis of pharmaceutical formulations reveal that the proposed method suitable for their analysis with virtually no interference of the usual additives presented in pharmaceutical formulations. This method can be adopted for routine quality control of Itopride in bulk and pharmaceutical preparations

Selected readings

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