

Original Research Article

SIMULTANEOUS ESTIMATION OF PANTOPRAZOLE AND ITOPRIDE IN BULK AND PHARMACEUTICAL DOSAGE FORMS BY RPHPLC METHOD

ABSTRACT:

Objectives: The objective of the present work is to develop and validate a HPLC method with PDA detector to determine Pantoprazole and Itopride in bulk and tablet formulation.

Method: This Chromatographic method uses Phenomenex Luna C18 (4.6mm×250mm) having particle size(5µm) column and mobile phase selected after optimization is Methanol: Phosphate Buffer (pH-4.2) (37:63% v/v) with flow rate of 1.0ml/min and detection was carried out at 260 nm.

Results: The retention time of the Pantoprazole and Itopride was found to be 2.133, 3.692±0.02 min respectively. The maximum wavelength (λ_{max}) was found to be 290nm for Pantaprazole and 301nm for Itopride. Linearity is seen in concentration range of 20-60mg/ml for Pantoprazole and 10-30mg/ml for Itopride. Validation was performed as per ICH guidelines for linearity , accuracy , precision , LOD and LOQ. The calculated limit of detection (LOD) values were 1.04 and 3.12 µg/mL and limit of quantitation (LOQ) values were 2.1 and 6.3 µg/mL. The inter-day and intra-day precisions were found to be within limits. The method precision for the determination of Pantaprazole and Itopride was below 2.0%RSD.

Conclusion: The present method under study is simple yet sensitive, precise, accurate and useful for routine analysis of Pantoprazole and Itopride formulation. This method is simple as diluted samples can be directly used without any preliminary chemical derivatisation or purification steps.

Keywords: Pantoprazole and Itopride, RP-HPLC, Validation, Accuracy, Precision.

INTRODUCTION:

“Pantoprazole is chemically expressed as (RS)-6-(Difluoro methoxy)-2-[(3,4-dimethoxy pyridin-2-yl) methyl sulfinyl]-1H-benzo[d]imidazole”.⁽¹⁾ “It works as proton pump inhibitor and treats heart burn also acid reflux and short-term treatment for patients having gastroesophageal reflux disease (GERD) with a history of erosive esophagitis. Pantaprazole also binds covalently to the

existing sulfhydryl groups of cysteines and it is also found on the (H⁺,K⁺)-ATPase enzyme”^(2,3).

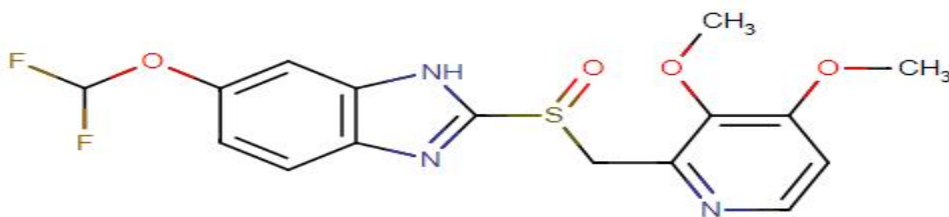


Image 1: Pantoprazole

“**Itopride** is known as N-{{4-[2-(dimethyl amino) ethoxy] phenyl} methyl}-3,4-dimethoxy benzamide. It is the gastroprokinetic agent indicated for the treatment of disorders associated with reduced gastrointestinal motility”^(4,5).

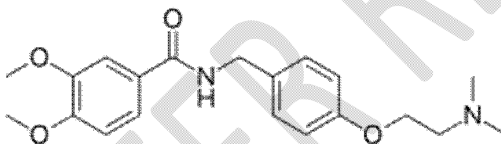


Image 2: Itopride

UV Spectrophotometric method, HPLC, HPTLC and LC-MS methods^(6,7,8) for the estimation of Pantoprazole and Itopride are already existing but in almost all existing methods either acetonitrile or combination with buffers are used. In this method Methanol was used. As it is polar protic solvent it participates in hydrogen bonding which is a powerful intermolecular force. They have high dielectric constant and high dipole moment. As most of the pharmaceutical products are polar, separation of components are favoured if we select a polar protic solvent like methanol. Hence this method stands unique, simple and specific. Validation of the proposed method was carried out according to ICH guidelines.^(9,10)

MATERIALS AND METHODS:

CHROMATOGRAPHIC CONDITIONS

This Chromatographic method uses Phenomenex Luna C18 (4.6mm×250mm) having particle size(5µm) column and mobile phase after optimization is Methanol: Phosphate Buffer (pH-4.2) (37:63% v/v) with flow rate of 1.0ml/min.

COMMERCIAL FORMULATION

“Pantoprazole and Itopride Tablets used for the present study was PANTOCID-IT of label claim Pantoprazole (40mg) Itopride hydrochloride (150mg). The samples were thoroughly checked for their manufacturing date, license number, batch numbers, production and expiry dates”.^(11,12)

PREPARATION OF STANDARD SOLUTION

150mg Itopride and 40mg Pantoprazole was dissolved in 100 ml of methanol and was further diluted to get stock solution of Itopride and Pantoprazole . Solution containing mixture of Itopride and pantoprazole with concentrations 50%,75%, 100% 125%, and 150% were prepared in the same way.

PREPARATION OF SAMPLE SOLUTION

Twenty tablets were taken and crushed in a mortar by using pestle and weight 10 mg equivalent weight of Pantoprazole and Itopride sample and make volume up to the mark with the same solvent. Filter the sample solution by using injection filter which contains 0.45 μ pore size. Further pipette out 0.4ml of Pantoprazole and 0.2ml of Itopride from the above stock solutions into a 10ml volumetric flask and dilute up to the mark with Diluent.

VALIDATION OF HPLC METHOD

“The experiment was carried out according to the official specifications of USP-30, ICH- 1996 and Global Quality Guidelines-2002. The method was validated for the parameters like system suitability , selectivity, linearity, accuracy, precision ,LOD, LOQ, and robustness”.¹³

SYSTEM SUITABILITY

“System suitability study of the method was carried out by six replicate of solution containing 100% target concentration of Pantoprazole and Itopride . Various chromatographic parameters such as retention time, peak area tailing factor, theoretical plates (Tangent) of the column and resolution between the peaks were determined and the method was evaluated by analyzing these parameters”.¹⁴

LINEARITY

Linearity of the method was determined by constructing calibration curves. Standard solutions of Pantoprazole and Itopride of different concentrations level (50%, 75%, 100%,125%, and 150%) were used for this purpose. Each measurement was carried out in six replicates and the peak areas of the chromatograms were plotted against the concentrations to obtain the calibration curves and correlation coefficients.

ACCURACY (RECOVERY STUDIES)

To check the degree of accuracy of the method, recovery studies were performed in triplicate by standard addition method at 50%, 100% and 150%. Known amounts of standard Pantoprazole and Itopride were added to pre-analyzed samples and were subjected to the proposed HPLC method.

PRECISION

Precision was evaluated by carrying out six independent sample preparation of a single lot of formulation. Percentage relative standard deviation (%RSD) was found to be less than 2% for within a day and day to day variations, which proves that method is precise.

RESULTS AND DISCUSSIONS

Table 1: Chromatogram for Standard solution

S.No.	Name	RT	Area	Height	USP Tailing	USP Plate Count	Resolution
1	Pantoprazole	2.133	526389	86756	1.56	5679	
2	Itopride	3.692	1687285	367532	1.79	8685	9.8

Fig 1: Standard chromatogram peak

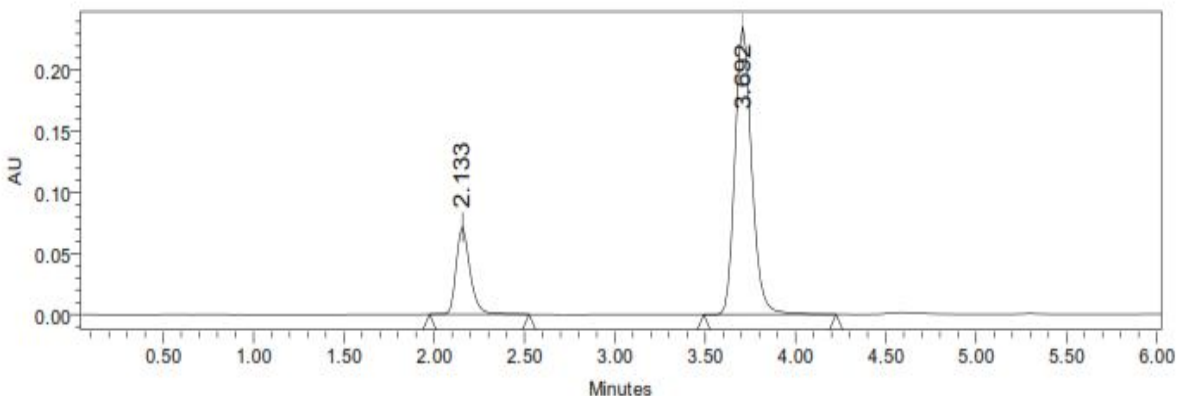


Table 2: Chromatogram for Sample solution

S.No.	Name	Rt	Area	Height	USP Tailing	USP Plate Count	Resolution
1	Pantoprazole	2.166	536587	77464	1.57	5789	
2	Itopride	3.629	1695846	378564	1.80	8795	10.01

Fig 2: Sample chromatogram peak

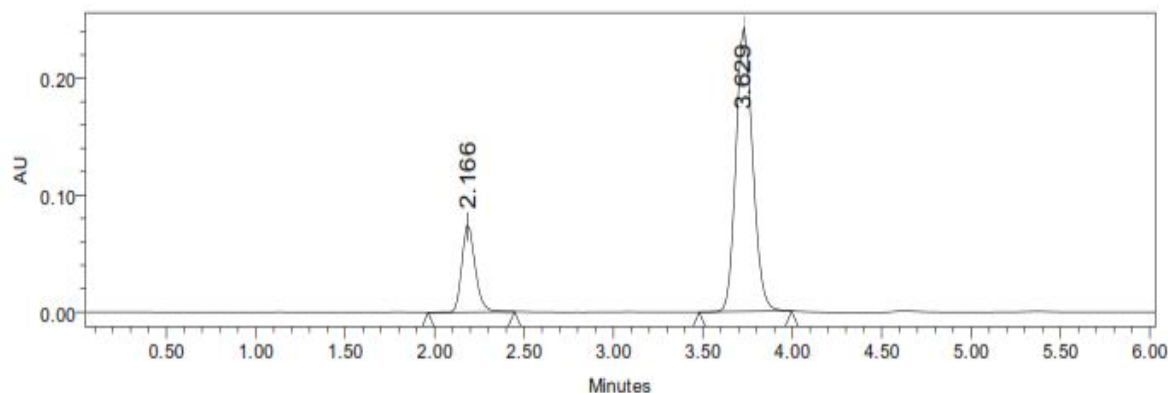


Table 3: Peak results for Assay sample of Pantoprazole

S.No	Name	RT	Area	Height	USP Tailing	USP Plate Count	Injectio
1	Pantoprazole	2.152	536859	87584	1.58	5789	1
2	Pantoprazole	2.150	532654	87965	1.59	5784	2
3	Pantoprazole	2.187	532685	87465	1.58	5769	3

Table 4: Peak results for Assay sample of Itopride

S.No	Name	RT	Area	Height	USP Tailing	USP Plate Count	Injectio
1	Itopride	3.646	1698568	378562	1.81	8759	1
2	Itopride	3.651	1698574	375847	1.80	8795	2
3	Itopride	3.601	1698547	376584	1.81	8745	3

The % purity of Pantoprazole and Itopride in pharmaceutical dosage form was found to be 99.89%. By altering the chromatographic conditions, the standard and samples of Pantoprazole and Itopride were injected. There was no discernible change in parameters such as resolution, tailing factor, or plate count. **DISCUSSION**

To quantify Pantoprazole and Itopride few methods were reported in literature and there are UV spectroscopy, TLC and HPLC with acetonitrile. These methods were tedious. The present method is simple very economical and solvents used were also easily available in market. Methanol: Phosphate Buffer (pH-4.2) (37:63 v/v) was chosen

as the mobile phase. Comparing the RP-HPLC method to Spectrophotometric approaches, the RP-HPLC method is more sensitive, accurate, and precise. This technique can be used to regularly determine the presence of Pantoprazole and Itopride in pharmaceutical dosage forms and bulk drugs. **CONCLUSION**

Estimation of Pantoprazole and Itopride in bulk drug and pharmaceutical dosage forms was done by different combinations of mobile phase, flow rate and modifying chromatographic conditions. The %RSD values were within 2 and the method was found to be precise.

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