Original Research Article

A SIMPLE AND VALIDATED RP-HPLC METHOD FOR THE SIMULTANEOUS ESTIMATION OF PANTOPRAZOLE AND ITOPRIDE IN BULK AND PHARMACEUTICAL DOSAGE FORMS

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: Chromatography was carried out on a Phenomenex Luna C18 (4.6mm×250mm) 5µm particle size column using a mixture of Methanol: Phosphate Buffer (pH-4.2) (37:63% v/v) as the mobile phase at a flow rate of 1.0ml/min, the 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 method produce linear responses in the concentration range of 20-60mg/ml of Pantoprazole and 10-30mg/ml of Itopride .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 proposed method was simple, sensitive, precise, accurate, quick and useful for routine analysis of Pantoprazole and Itopride in bulk and tablet dosage forms. This method was simple, since diluted samples are 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, acid reflux and short-term treatment (7-10 days) of patients having gastroesophageal reflux disease (GERD) with a history of erosive esophagitis. Pantaprazole also binds covalently to sulfhydryl groups of cysteines and it is found on the [H+,K+]-ATPase enzyme.[2,3]

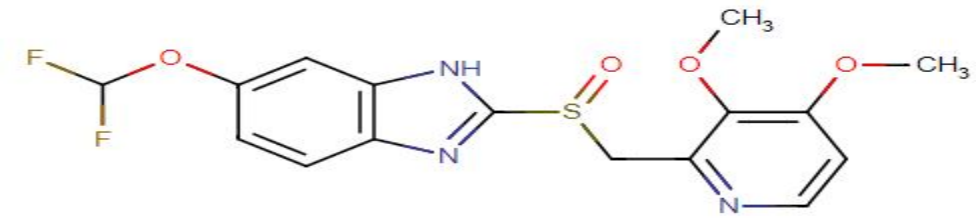

Image 1: Pantoprazole

Itopride is chemically 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]

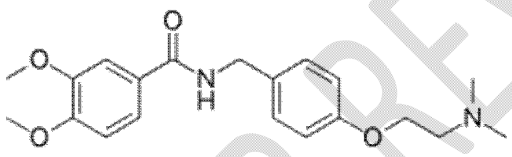

Image 2: Itopride

To quantify Pantoprazole and itopride separately and in combination with other drugs several methods have been proposed . A few of them are UV spectroscopy, TLC and HPLC with acetonitrile has been reported so far.[6,7,8]

To our knowledge direct, precise and economical analytical method for simultaneous estimation of Pantoprazole and Itopride has not been reported so far. So attempt were made to develop and validate an economic, rapid RP-HPLC method. The method was validated and found to be accurate, precise and reproducible.

MATERIALS AND METHODS:

CHROMATOGRAPHIC CONDITIONS

The mobile phase was optimized to Methanol: Phosphate Buffer (pH-4.2) (37:63 v/v) in proportion 37:63 v/v respectively. The method was performed with Phenomenex Luna C18 (4.6mm×250mm) 5µm particle size. It gives good peak shape and resolution at 1ml/min flow.

COMMERCIAL FORMULATION

Pantoprazole and Itopride Tablets used for the present study was PANTOCID-IT of label claim Pantoprazole (40mg) Itopride hydrocholride (150mg). The samples were properly checked for their manufacturing license numbers, batch numbers, production, expiry dates and stored properly.

PREPARATION OF STANDARD SOLUTION

150mg Itopride and 40mg Pantoprazole was dissolved in 100 ml of Diluent (methanol) and was further diluted to get stock solution of Itopride and Pantoprazole (300 µg/ml and 250 µg/ml respectively). This is taken as a 100% concentration. Solution containing mixture of Itopride and pantoprazole of different concentrations (50%,75%, 100% 125%, and 150% of target concentration) 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 into a 10ml clean dry volumetric flask and add about 7mL of Diluent and sonicate to dissolve it completely and make volume up to the mark with the same solvent. Filter the sample solution by using injection filter which contains 0.45µ 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.

DEVELOPMENT AND VALIDATION OF HPLC METHOD

Present study was conducted to obtain a new, affordable, cost-effective and convenient method for HPLC determination of Pantoprazole and Itopride in tablet dosage form. 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.

RESULTS

Table 1: Optimized Chromatogram (Standard)

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

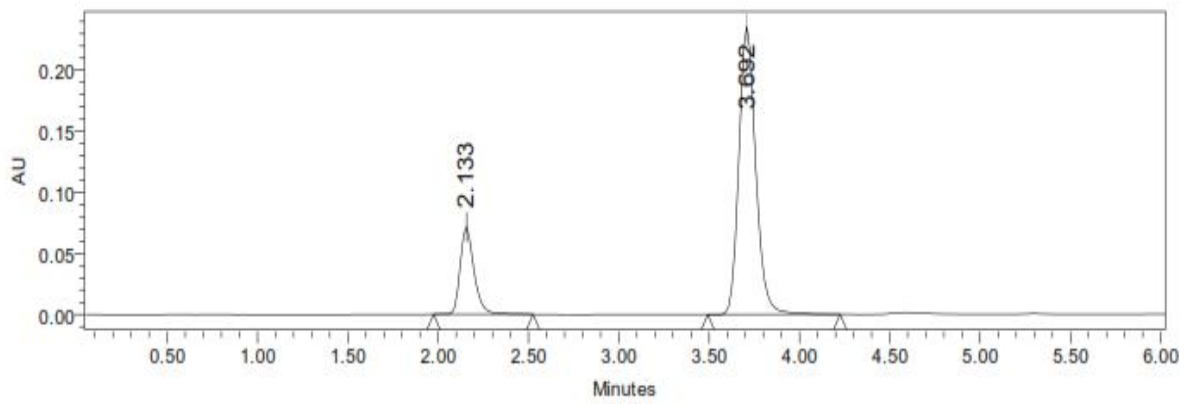

Table 2: Optimized Chromatogram (Sample)

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

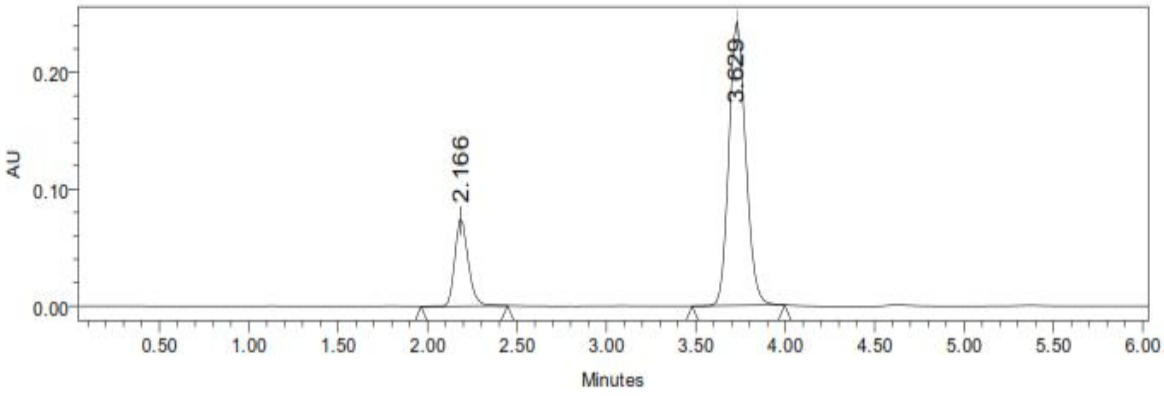

Table 3: Peak results for Assay sample of Pantoprazole

S.No	Name	RT	Area	Height	USP Tailing	USP Plate Count	Injection
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	Injection
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%. The standard and samples of Pantoprazole and Itopride were injected by changing the conditions of chromatography. There was no significant change in the parameters like resolution, tailing factor and plate count.

Table 5: Summary of Validation data for Pantoprazole:

S.No.	Parameter	Observation	Acceptance Criteria
1	**System suitability** Theoretical plates Tailing %RSD	 5679 1.56 0.14	 Not less than 2000 Not more than 2 Not more than 2.0%
2	**Specificity** %Assay	 99.89%	 98-102%
3	**Method Precision** (%RSD)	0.29	Not more than 2.0%
4	**Linearity** Slope Correlation coefficient(r^2)	20-60 µg/ml 12802 0.999	 ≤0.99
5	**Accuracy** Mean % recovery	 100.28%	 98 - 102%
6	**Robustness** a) Flow rate variation b) Organic phase variation	All the system suitability parameters are within the limits.	

Table 6: Summary of validation data for Itopride:

S.No	Parameter	Observation	Acceptance criteria
1	**System suitability** Theoretical plates Tailing %RSD	 8685 1.79 0.11	 Not less than 2000 Not more than 2 Not more than 2.0%
2	**Specificity** %Assay	 99.89%	 98-102%
3	**Method Precision** (%RSD)	0.044	Not more than 2.0%
4	**Linearity** Slope Correlation coefficient(r^2)	10-30 µg/ml 93626 0.999	 ≤0.99
5	**Accuracy** Mean % recovery	 100.48%	 98 - 102%
6	**Robustness** a) Flow rate variation b) Organic phase variation	All the system suitability parameters are within the limits.	

DISCUSSION

To quantify Pantaprazole 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. The RP-HPLC method is more sensitive, accurate and precise compared to the Spectrophotometric methods. This method can be used for the routine determination of Pantoprazole and Itopride in bulk drug and in Pharmaceutical dosage forms.

CONCLUSION

In the present investigation, a simple, sensitive, precise and accurate RP-HPLC method was developed for the quantitative estimation of Pantoprazole and Itopride in bulk drug and pharmaceutical dosage forms. The %RSD values were within 2 and the method was found to be precise.

BIBLIOGRAPHY

1. Snyder LR, Kirkland JJ, Glach JL. Practical HPLC Method Development, John Wiley and Sons, New York, 1997; 158-192.
2. McpolinOona.an Introduction to HPLC for Pharmaceutical Analysis. Mourne Training Service. 11-12.
3. Charde MS, Welankiwar AS and Kumar J. Method development by liquid chromatography with validation. International Journal of Pharmaceutical Chemistry.2014; 4(2):57-61.
4. Sánchez MLF. Chromatographic techniques, European RTN Project, GLADNET, retrieved on 05-09-2013.
5. Snyder LR, Kirkland JJ, Dolan JW. Introduction to modern liquid chromatography. John Wiley & Sons. New York. 2011.
6. Weston A, Brown PR. HPLC and CE Principles and Practice. Academic press California; 1997.
7. Shah RS, Pawar RB, Gayakar PP. An analytical method development of HPLC. International Journal of Institutional Pharmacy and Life Sciences. 2015; 5(5): 506-513.
8. ICH Q2A. Text on Validation of Analytical Procedures, International Conference on Harmonization. Geneva; 1994.