Journal of Pharmaceutical Analysis 2011;1(4):275–283

Contents lists available at ScienceDirect

Journal of Pharmaceutical Analysis

www.elsevier.com/locate/jpa
www.sciencedirect.com

ORIGINAL ARTICLE

# Stability indicating high performance thin-layer chromatographic method for simultaneous estimation of pantoprazole sodium and itopride hydrochloride in combined dosage form

**Deepak Bageshwar, Vineeta Khanvilkar*, Vilasrao Kadam**

*Bharati Vidyapeeth's College of Pharmacy, Sector-8, CBD Belapur, Navi Mumbai 400614, India*

Received 11 July 2011; accepted 16 September 2011
Available online 6 November 2011

**KEYWORDS**

Gastroesophageal reflux disease (GERD);
Itopride hydrochloride;
Pantoprazole sodium;
High performance thin layer chromatography (HPTLC);
Stability indicating;
Forced degradation

**Abstract** A specific, precise and stability indicating high-performance thin-layer chromatographic method for simultaneous estimation of pantoprazole sodium and itopride hydrochloride in pharmaceutical formulations was developed and validated. The method employed TLC aluminium plates precoated with silica gel $60F_{254}$ as the stationary phase. The solvent system consisted of methanol:water:ammonium acetate; 4.0:1.0:0.5 (v/v/v). This system was found to give compact and dense spots for both itopride hydrochloride ($R_f$ value of $0.55\pm0.02$) and pantoprazole sodium ($R_f$ value of $0.85\pm0.04$). Densitometric analysis of both drugs was carried out in the reflectance–absorbance mode at 289 nm. The linear regression analysis data for the calibration plots showed a good linear relationship with $R^2=0.9988\pm0.0012$ in the concentration range of 100–400 ng for pantoprazole sodium. Also, the linear regression analysis data for the calibration plots showed a good linear relationship with $R^2=0.9990\pm0.0008$ in the concentration range of 200–1200 ng for itopride hydrochloride. The method was validated for specificity, precision, robustness and recovery. Statistical analysis proves that the method is repeatable and selective for the estimation of both the said drugs. As the method could effectively separate the drug from its degradation products, it can be employed as a stability indicating method.



*Corresponding author.
E-mail address: vineetakhanvilkar@gmail.com (V. Khanvilkar).



Peer review under responsibility of Xi'an Jiaotong University.
doi:10.1016/j.jpha.2011.09.012

Production and hosting by Elsevier

## 1. Introduction

Reflux of gastric contents into the oesophagus is a normal phenomenon in most individuals, but it becomes pathological when it causes troublesome symptoms or complications. Since the introduction of proton pump inhibitors (PPIs), the treatment of patients with gastroesophageal reflux disease (GERD) has dramatically improved [1]. GERD is very common and advances in drug development over recent years have markedly improved

GERD management. A wide range of medications are currently used in GERD treatment, including antacids, Gaviscon, sucralfate, histamine-2 receptor antagonists and prokinetics. However, proton pump inhibitors (PPIs) remain the mainstay of treatment for GERD owing to their profound and consistent inhibitory effect on acid secretion. Despite the presence of a wide armamentarium of therapeutic modalities for GERD, many areas of unmet needs remain. Drug development has focused primarily on improving PPI efficacy, reducing the transient lower oesophageal sphincter relaxation rate, attenuating oesophageal sensitivity and developing oesophageal mucosal protectants [2].

Thus, many formulations are available for treatment of GERD. Combination of pantoprazole sodium and itopride hydrochloride is also available for treatment of GERD [2,3]. So, it is necessary to have an analytical method so as to estimate both drugs simultaneously from its combined dosage form.

Literature survey reveals that spectrophotometric [4,5], HPLC [6–9] and high performance thin layer chromatography (HPTLC) [10,11] methods for the estimation of itopride hydrochloride from bulk drugs and pharmaceutical formulation have been developed whereas spectrophotometric [12], HPLC [13,14], RP-HPLC [15], HPTLC [16] methods for the estimation of pantoprazole alone or in combination with other drugs from pharmaceutical formulation have been developed. However, no stability indicating method has been reported so far for simultaneous estimation of both drugs in combined pharmaceutical dosage form by HPTLC. This work presents a stability indicating HPTLC method for the simultaneous estimation of both drugs in their combined pharmaceutical dosage form, which can be used for its routine analysis in laboratory.

The advantage of HPTLC is that large number of samples can be simultaneously analysed in a shorter time period. Unlike HPLC, this method utilises less quantities of solvents, thus lowering the cost of analysis [17].

An ideal stability indicating chromatographic method should estimate the drug and also be able to resolve the drug from its degradation products. Hence an attempt has been made to develop an accurate, rapid and reproducible method for the determination of itopride hydrochloride and pantoprazole sodium in presence of their degradation products for their content analysis in pharmaceutical dosage forms containing this combination as per ICH [18] guidelines.

## 2. Materials and methods

### 2.1. Chemicals and reagents

Itopride hydrochloride and pantoprazole sodium were procured as a gift sample. All other solvents and reagents were purchased from S.D. Fine chemicals, Mumbai, India and were of analytical grade.

### 2.2. Instrumentation

Spotting was done using Camag Linomat 5 sample applicator (CAMAG, Switzerland) and Camag Hamilton Bonaduz microlitre syringe (100 µl) on HPTLC aluminium plates precoated with silica gel $60F_{254}$ (20 cm × 10 cm with 250 µm thickness; Merck, Germany). The plates were prewashed with methanol for 30 min in a Camag twin trough glass chamber closed with lid. The plates were activated at 110 °C for 30 min. The samples were spotted in the form of narrow bands having length of 6 mm. The application position *X* and *Y* were kept at 10 mm and 12 mm, respectively, to avoid edge effect. The distance between the two bands was 10 mm. Spots were applied at a constant rate of 15 nL/s using a nitrogen aspirator. Linear ascending development of chromatogram was carried out in a Camag twin trough glass chamber saturated with the mobile phase for 15 min and chromatogram run was kept up to 90 mm. Spectrodensitometric analysis of the separated components was carried out using Camag TLC Scanner 3 in the reflectance–absorbance mode at 289 nm using a $D_2$ lamp. The slit dimension used was 6.0 mm × 0.3 mm and sensitivity was kept at auto mode. Scanning speed was 100 nm/s. Integration of the chromatogram was carried out using Planar chromatography manager-winCATS (CAMAG).

### 2.3. Calibration plots

#### 2.3.1. Calibration plot of pantoprazole sodium in methanol

A total of 10 mg of pantoprazole sodium was dissolved in 100 mL of methanol to obtain stock solution of 100 µg/mL. Appropriate quantities of this stock solution were spotted to obtain the concentration in the range of 100–400 ng.

#### 2.3.2. Calibration plot of itopride hydrochloride in methanol

A total of 10 mg of itopride hydrochloride was dissolved in 100 mL of methanol to obtain stock solution of 100 µg/mL. Appropriate quantities of this stock solution were spotted to obtain the concentration in the range of 200–1200 ng.

### 2.4. Analysis of marketed formulation

To determine the content of itopride hydrochloride and pantoprazole sodium in marketed capsules (label claim: pantoprazole sodium 40 mg/capsule and itopride hydrochloride 150 mg/capsule), the contents of 20 capsules were weighed and their average weight was determined. The content of capsules containing sustained released pellets was finely powdered.

Solution A: an amount equivalent to average weight of capsule contents was transferred into a 100 mL volumetric flask containing 50 mL methanol. It was sonicated for 10 min and contents were diluted to 100 mL with methanol. The resulting solution was centrifuged at 3000 rpm for 5 min and supernatant was collected.

Solution B: 1 mL of solution A was diluted to 10 mL of methanol in a 10 mL volumetric flask. 5 µL of solution B (200 ng of pantoprazole sodium and 750 ng of itopride hydrochloride) was applied on the TLC plate followed by development and scanning. The analysis was repeated for six times.

## 3. Method validation

### 3.1. Specificity

The specificity of the HPTLC method was ascertained by analysing standard drug and sample solutions (marketed formulation). The retention factor of pantoprazole sodium