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ORIGINAL ARTICLE

A modified high-performance liquid chromatographic method for the analysis of pantoprazole sodium in pharmaceutical dosage forms using lansoprazole as internal standard

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KEYWORDS

Pantoprazole sodium;
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Abstract A Simple and rapid reversed-phase high-performance liquid chromatographic method for the direct determination of pantoprazole in pharmaceutical dosage forms was developed and validated. Lansoprazole was used as internal standard. The chromatographic separation of pantoprazole and lansoprazole was achieved on a Nucleodur C_8 column (250 × 4.6 mm i.d., 5 μm particle size) using the photodiode array detector at 280 nm. The optimized mobile phase was consisted of a mixture of 0.1 M ammonium acetate solution and methanol (42:58, v/v), pumped at a flow rate 1.0 mL min^{-1}. The retention times for pantoprazole and lansoprazole were 8.10 and 11.15 min, respectively. Linearity range was 3.06–1243.0 μg mL^{-1} with limit of detection value of 0.78 μg mL^{-1}. The precision of the method was demonstrated using intra- and inter-day assay RSD% values which were less than 2.07%, while the recovery was 99.07–103.95%. No interference from any components of pharmaceutical dosage forms or degradation products was observed. According to the validation results, the proposed method was found to be specific, accurate, precise and could be applied to the quantitative analysis of pantoprazole in tablets.

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1. Introduction

Pantoprazole, 5-difluoromethoxybenzimidazole-2-yl 3,4-dimethoxy-2-pyridylmethyl sulfoxide (CAS, 102625-70-7; MW, 383.4) is an irreversible proton pump (H^+/K^+-ATPase) inhibitor (PPI) that decreases acid secretion from gastric parietal cells (Cheer et al., 2003). It is also effective in Zollinger–Ellison syndrome and in preventing ulcer rebleeding. Thus pantoprazole is a valuable alternate to other PPIs in the treatment of acid-related disorders. The drug is officially listed in Martindale the extra pharmacopoeia (2005). A literature survey

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reveals that spectrophometric (Wahbi et al., 2002; Karljikovic-Rajic et al., 2003; Salama et al., 2003; Moustafa, 2000; Syed and Syeda, 2008), kinetic spectrophotometric (Rahman and Kashif, 2005; Rahman et al., 2006), capillary zone electrophoresis (Eberle et al., 1997; Tivesten et al., 1999) and voltammetric (Radi, 2003; Chung et al., 2003; Erk, 2003) methods for the determination of pantoprazole in drug formulations have been described. In the literature only a few high-performance liquid chromatographic methods for the determination of pantoprazole in pharmaceutical formulations have been reported (Mansour and Sorour, 2001; Tanaka et al., 1995). An increasing number of publications are appearing describing the development of methods for pantoprazole determination in biological samples (Tanaka and Yamazaki, 1996; Ramakrishna et al., 2005; Storms and Stewart, 2002; Cass et al., 2002).

The objective of this work was to develop an analytical LC procedure, which would serve as reliable and rapid method for the determination of pantoprazole in pharmaceutical preparations. This manuscript describes the development and subsequent validation of isocratic reversed-phase HPLC method using C_8 column as stationary phase for the above determination. In the proposed LC method, pantoprazole and lansoprazole (internal standard) were well separated and eluted before 12 min run time. The precision of the described method for assay of pantoprazole has been checked in terms of *F*-test using a reported method as reference.

2. Experimental

2.1. Chromatographic system

Chromatographic analysis was performed on a modular HPLC system, Hitachi (Japan) consisted of binary pump (L-2130, flow rate range of 0.000–9.999 mL min^{-1}), auto sampler (L-2200, injection volume of 0.1–100 μL), column oven (L-2350, temperature range of 1–85 °C) and ultraviolet detector (L-2455, 190–850 nm) operated at wavelength of 280 nm and a quartz flow cell (10 mm path and 17 μL volume). Separation was achieved on a reversed-phase Nucleodur C8 column (250 × 4.6 mm, 5 μm particle size, Macherey-Nagel Germany). The mobile phase was a mixture of a 0.1 M ammonium acetate and methanol (42:58, v/v) and was filtered and degassed by ultrasonic agitation before use. The mobile phase was prepared weekly and was delivered at a flow rate of 1.0 mL min^{-1}. Data were monitored and processed using automation system software. Peak areas were integrated automatically by computer using the Ezchrom Elite Hitachi software program. The injection volume was 10 μL. The system was operated at ambient temperature.

2.2. Chemicals

HPLC grade methanol and water were purchased from Merck (Darmstadt, Germany). Analytical reagent grade ammonium acetate from Merck (Darmstadt, Germany) and acetic acid glacial from SCP (England) were used to prepare the mobile phase.

2.3. Materials

Pantoprazole sodium ($C_{16}H_{35}F_2N_3NaO_4S$ = 426.52 g/mol, its purity was found to be 100.66% according to the compendial method) and the internal standard (lansoprazole USP, $C_{16}H_{14}F_3N_3O_2S$ = 369.37 g/mol, its purity was found to be 99.5%) were obtained from SL Drugs & Pharmaceuticals, India. Tablets containing pantoprazole sodium: Penta 40 mg (Alpha, Syria), Progast 40 mg (K.C. pharma, Syria) and Pantoprazol 40 mg (Amrit Medical Co., Syria).

2.4. Standard solutions

Standard solution of pantoprazole sodium (PPZ) was prepared by direct weighing of standard substance with subsequent dissolution in methanol. The concentration of the stock standard solution was 2.0 mg mL^{-1}. Stock standard solution of lansoprazole (LPZ) 1.0 mg mL^{-1} was prepared by dissolving appropriate amount of the compound in methanol. These solutions were stored in the dark at 2–8 °C and were found to be stable for one month at least. A series of working standard solutions of PPZ (3.06–1243.0 μg mL^{-1}) were prepared by diluting the stock standard solution with the methanol. In each sample 1 mL of LPZ was added. Standard solutions were found to be stable during the analysis time.

2.5. Calibration curve

To construct the calibration curve five replicates (10 μL) of each standard solution were injected immediately after preparation into the column and the peak area of the chromatograms was measured. Then, the mean peak area ratio of PPZ to that of the internal standard was plotted against the corresponding concentration of PPZ (3.06–1243.0 μg mL^{-1}) to obtain the calibration graph (Table 1).

2.6. Assay procedure for dosage forms

Twenty tablets containing PPZ were weighed and finely powdered. Five accurately weighed quantities of the powder equivalent to 50 mg of PPZ were transferred into 25 mL separated volumetric flasks. A 20 mL of methanol was then added to each flask and the mixture was sonicated for 10 min. Then, the volume of each mixture was adjusted to 25 mL with methanol. The sample solutions were filtered and a suitable concentration was prepared by diluting 0.5 mL of the filtrates with

Table 1 Calibration data for the estimation of pantoprazole by HPLC.

Parameters	Pantoprazole
Optimum concentration range (μg mL^{-1})	3.06–1243.0
Regression equation for the peak area of PPZ vs. concentration of PPZ in μg/mL, $A_{PPZ} = 0.762C_{PPZ} + 5.578$	
Correlation coefficient (r^2)	0.9999
Standard deviation of slope	0.0019
Standard deviation of intercept	0.7711
Regression equation for the ratio of peak area of PPZ to that of I.S. (LPZ) vs. concentration of PPZ in μg/mL, $R_{PPZ/LPZ} = 0.008C_{PPZ} + 0.060$	
Correlation coefficient (r^2)	0.9999
Standard deviation of slope	0.0018
Standard deviation of intercept	0.0033
Limit of quantification, LOQ (μg mL^{-1})	2.60
Limit of detection, LOD (μg mL^{-1})	0.78

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