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A New Extractive Spectrophotometric Method for Determination of Lansoprazole Dosage Forms Using Bromocresol Green.

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ABSTRACT

Lansoprazole is a selective inhibitor of gastric proton pump and is used for the treatment of gastrointestinal disorders. In this study, a simple, sensitive and rapid spectrophotometric method based on ion-pair complexation was used for the determination of lansoprasole. Bromocresol green was used as the complexing agent in the presence of phosphate buffer (pH 3.0) which was resulted in a 1:1 ion-pair complex. The within-day and between-day precision values were less than 2% for the calibration range of 1-20 µg/mL. The proposed spectrophotometric method was used for the determination of lansoprazole in capsule dosage forms without any interference with excipients.

Keywords: Lansoprazole, Ion-pair complexation, Bromocresol green, Spectrophotometry

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INTRODUCTION

Lansoprazole,(RS)-2-([3-methyl-4-(2,2,2-trifluoroethoxy)pyridine-2-yl]methylsulfinyl-1H-benzo[α] imidazole (figure no. 1), is a potent H^+/K^+-ATPase inhibitor. Lansoprazole selectively and irreversibly inhibits the gastric proton pump, which could reduce the gastric acid secretion. Lansoprazole is used in the treatment of gastrointestinal disorders such as ulcers and gastro esophageal reflux disease [1].

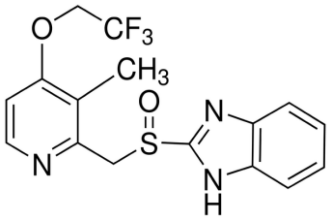

Figure 1: Chemical structure of lansoprazole and BCG.

Literature survey showed several HPLC [2-7] and LC-MS/MS [8-11] methods for the determination of lansoprazole alone, or in the presence of its metabolites or other drugs in biological fluids. Lansoprazole is official in BP and USP and HPLC methods have been described for its determination in pharmaceutical dosage forms. Other HPLC methods have also been previously reported for the determination of lansoprazole individually or in combination with other proton pump inhibitors [3, 7, 12]. Lansoprazole has also been determined using flow injection analysis spectrophotometry in pharmaceutical dosage forms [7, 13]. Few spectrophotometric methods have also been reported for the determination of lansoprazole in pharmaceutical dosage forms [14-17]. Ozaltin [14] reported zero order and derivative spectrophotometric method with a linear range of 3-25 µg/mL for determination of lansoprazole in pharmaceutical dosage forms. In the report of Moustafa [15], lansoprazole has been determined based on charge transfer complexation with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone or iodine and also ternary complex formation with eosin and copper (П) [15]. The linearity range in these methods was between 10-90, 1.5-6.7 and 3.7-16.6 µg/mL for these three reagents. Wahbi et al. [16] reported a spectrophotometric method based on chemometrics for the determination of lansoprazole with a linearity range of 0.5-3.5 µg/mL. Ceric ammonium sulphate, methyl orange and indigo carmine were also used as charge transfer complexing agent for the analysis of lansoprazole [17]. These methods were reported to be linear in the range of 0.5-7 and 0.25-3 µg/mL.

In continuation to our laboratory interest for developing simple and valid spectrophotometric methods [18-21], in this study a spectrophotometric method based on charge transfer complexation with bromocresol green (fiigure no. 2) has been developed and validated for the determination of lansoprazole in pharmaceutical dosage forms.

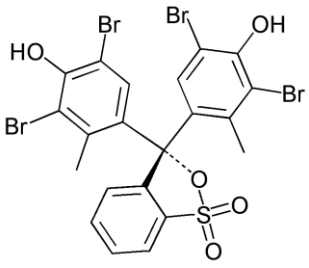

Figure 2: Chemical structure of bromocresol green

EXPERIMENTAL

Chemicals

Lansoprozole was from Sigma-Aldrich Co. and kindly provided by Food and Drug Laboratory, Ministry of Health, Tehran, Iran. Bromocresol green (BCG), chloroform and all other chemicals were of analytical grade and purchased from Merck (Darmstadt, Germany). Lansoprazole capsules containing 15 mg of lansoprazole were from Ramopharmine Pharmaceutical Company (Tehran, Iran) and purchased from a local pharmacy.

Instrumentation

Shimadzu UV-160A Spectrophotometer (Kyoto, Japan) was used for spectrophotometric measurements. Metrohm pH meter (Model 691)(Switzerland) was used for pH adjustments.

Standard Solutions

Standard solution of lansoprazole was prepared at the concentration level of 5×10^{-4} M by dissolving appropriate amount of the drug in methanol. The bromocresol green (BCG) solution was also prepared at the same concentration level (5×10^{-4} M) by dissolving 35 mg of the reagent in 100 mL water containing 0.2 mL of 0.1 M NaOH.

To prepare the phosphate buffer 0.2 M, 3.56 g of NaH_2PO_4 was dissolved in 100 mL of distilled water and the pH of the solution was adjusted to 3.0. Britton-Robinson buffers at the pH values of 2, 2.5, 3, 3.5, 4, and 5 were prepared according to the general procedure using a mixture of equal amounts of 0.1 M H_3BO_3, 0.1 M H_3PO_4 and 0.1 M CH_3COOH and adjusting the pH to the desired value.

General Procedure

Two milliliters of lansoprazole solution and one ml of phosphate buffer (pH 3.0) were pipetted into a 100 mL separating funnel. After addition of 4.5 mL of BCG reagent (5×10^{-4} M) and 2.5 mL of water, the mixture was extracted three times with 5, 3 and 2 ml of chloroform. The solution was shaken for 30 sec each time. The organic layer was passed through a layer of anhydrous sodium sulfate and transferred to a 10 mL volumetric flask. The flask was made up to volume by chloroform and the absorbance of the resulting solution was determined at 416 nm against a reagent blank solution prepared by the same procedure.

Reagent Amount

To find out the needed reagent amount for completion of the reaction, a solution of 5×10^{-4} M lansoprazole and different volumes of 5×10^{-4} M BCG reagent (0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, and 5 mL) were used.

Choice of Solvent

Different solvents including chloroform, dichloromethane, diethyl ether and ethyl acetate were used as extracting solvent using the general procedure.

Effect of pH

The absorbance of ion-pair complexes resulted from a standard solution of lansoprazole using 4.5 ml of BCG reagent in the presence of Britton-Robinson buffer at different pH values was measured and the best pH value was chosen.

Stability

The stability of the reaction product was checked over a 24 h period.

Stoichiometric Ratio of the Reaction

The stoichiometric ratio was evaluated by Jobs' method of continuous variation. A mixture of lansoprazole and BCG solutions at the same concentration level (5×10^{-4} M) was used by different molar ratios. These solutions were treated according to the general procedure. The absorbance was plotted over the molar ratio and the stoichiometric ratio evaluated.

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Linearity

Lansoprazole standard solutions at 1, 2, 4, 8, 12, 16, and 20 µg/mL were prepared and treated according to the general procedure. The calibration curve was plotted using the absorbance over the lasnsoprazole concentration. Six series of calibration solutions were determined and the statistical data for calibration curves were calculated.

Accuracy and Precision

Three sets of lansoprazole solutions at 1, 8 and 20 µg/mL were prepared and analyzed according to the general procedure and appropriate calibration curves. The within-day accuracy and precision was calculated. The same procedure was performed on three consecutive days to find out the between-day accuracy and precision of the method.

Analysis of Lansoprazole in Capsules

The content of twenty capsules of lansoprazole (15 mg) was mixed and an accurately weighed amount equal to one capsule transferred to a 100 mL volumetric flask. After addition of 70 mL of methanol and 0.1 M sodium hydroxide (40:60, v/v), the mixture was sonicated for 20 min. The volume was completed with methanol after neutralization and mixed well. After centrifugation, a portion of the solution was neutralized with hydrochloric acid and subjected to the spectrophotometric method after ten times dilution. The absorbance was compared with a standard solution of lansoprazole prepared by the same procedure. The capsules were also assayed by the official method described in the USP.

Recovery

The relative recovery of the spectrophotometric method was determined by standard addition technique. Known amount of lansoprazole standard solution was added to the capsule samples and the absorbance compared with a standard solution at the same concentration level.

RESULTS AND DISCUSSION

Absoption spectra

Lansoprazole molecule with basic nitrogen could form a colored ion-pair complex with bromocresol green in acidic medium. The formed ion-pair complex was extracted in chloroform. The ion-pair complex was formed instantly at room temperature. The absorption spectra of the resulting ion-pair complex against reagent blank showed a maximum at 416 nm which was used for spectrophotometric measurements. It was shown that this complex is stable for at least 1 h (recovery>98.5%) and did not change significantly after 8 h (recovery>96%).

Effect of pH

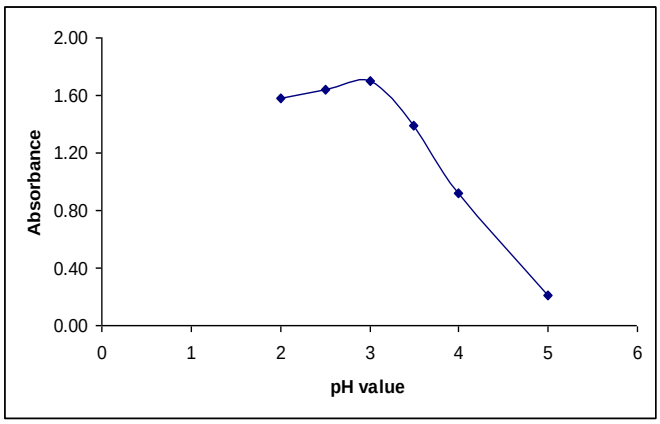

Figure 3: The effect of pH of the buffer (Britton-Rabinson) on the ion-pair complex formation.

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The ion-pair complex formation was performed in different pH values using Britton-Robinson buffer. Figure no. 3 shows that the maximum absorption occurred in the pH value of 3.0. Using different buffers at the same pH value (phosphate, phthalate, and Britton-Robinson), better results were obtained by phosphate buffer.

Effect of reagent amount

The absorbance of ion-pair complexes, prepared by using lansoprazole solutions at fixed concentration and different amounts (1-5 mL) of the reagent solution (5×10^{-4} M), were measured. Best results obtained by using 4.5 mL of the BCG reagent (5×10^{-4} M) (figure no. 4). Higher amounts did not exceed the absorbance.

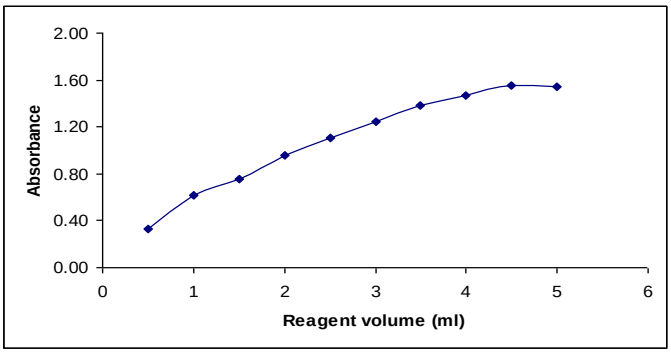

Figure 4: The effect of BCG amount on the absorbance of the ion pair complex at 416 nm.

Effect of extracting solvent

Using few organic solvents as the extracting solvent, it was shown that maximum absorbance and acceptable stability attained by chloroform. Quantitative recovery was obtained by a three step extraction procedure using 5, 3, and 2 mL of chloroform and 10 sec mixing for each step.

Stoichiometry of the reaction

The Jobs' method of continuous variation was used to study the stoichiometry of the ion-pair complexation. A 1:1 ion-pair complex was formed according to the results of this study (figure no. 5).

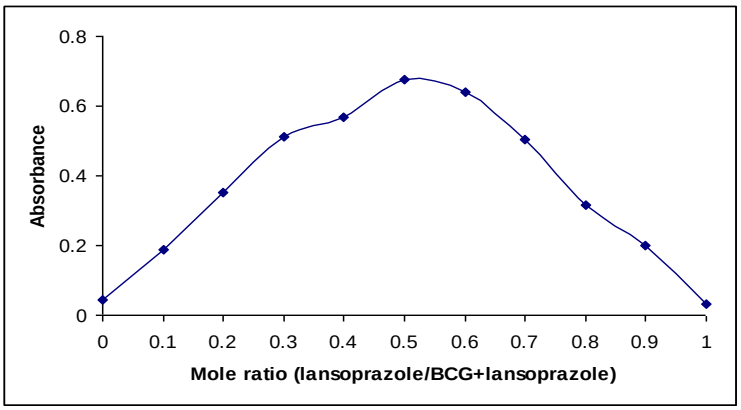

Figure 5: Stoichiometry of the ion pair complex of lansoprazole (5×10^{-4} M) and BCG (5×10^{-4} M) by Job's method of continuous variation.

Linearity

Under the specified conditions in the experimental section, six calibration curves were constructed and statistical data calculated which are shown in Table no. 1. A linear relationship was observed between the absorbance at 416 nm and lansoprazole concentration in the range of 1-20 µg/mL with a good correlation coefficient.

The quantification limit and detection limit was calculated using the following equations [22]:

$$LOQ = 10\sigma/s \quad \text{and} \quad LOD = 3.3\sigma/s$$

where σ is the standard deviation of intercept and s is the slope of the calibration graph.

Table 1: Statistical data of calibration curves of lansoprazole in standard solutions (n = 6)

Parameters	Results
Linearity range	1-20 μg/mL
Regression equation	Y=0.0092 X+ 0.0649
Standard deviation of slope	8.2×10^{-5}
Relative standard deviation of slope (%)	0.89
Standard deviation of intercept	0.0011
Correlation coefficient (r^2)	0.997
LOQ	1.19 μg/mL
LOD	0.39 μg/mL

Accuracy and precision

The within-day and between-day accuracy and precision of the spectrophotometric method performed in one day and three consecutive days, are shown in Table no. 2. The data proved the excellent accuracy and precision which is necessary for drug analysis purposes.

Table 2: Precision and accuracy of the method for determination of lansoprazole in standard solutions (n=9; 3 sets for 3 days)

Concentration added (μg/mL)	Within-day (n=3)			Between-day (n=9)		
	Found (μg/mL)	CV (%)	Error (%)	Found (μg/mL)	CV (%)	Error (%)
1.00	0.99±0.02	2.02	-1.00	1.00±0.02	2.00	0.00
8.00	8.05±0.11	1.37	-0.63	8.03±0.12	1.49	0.38
20.00	20.01±0.11	0.55	0.05	19.99±0.12	0.60	-0.05

Analysis of the Lansoprazole capsules

The amount of lansoprazole was determined using the general spectrophotometric method. The results were comparable to the HPLC method specified in the United States Pharmacopeia (Table no. 3).

Table 3: Comparison of the developed method with the reference method for the determination of Lansoprazole capsules

Compound	Label claimed(mg)	Found(mean ± sd)		Statistical Tests*
		Proposed method	HPLC method	
Lansoprazole	15.00	15.00±0.15	15.03±0.09	t = 0.758 F = 0.539

*Theoretical values of t and F at p = 0.05 are 4.303 and 19.00 respectively.

Relative recovery

By using the standard addition method, the relative recovery was found to be 98.9±0.3% with no significant interferences from the capsule excipients.

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