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RESEARCH ARTICLE

Ultraviolet–visible Spectrophotometric and Titration Method for the Assay of Lisinopril Bulk and Pharmaceutical Dosage Form

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ABSTRACT

A simple, accurate, fast, and cheap titrimetric assay method and ultraviolet–visible (UV-Vis) spectrophotometric method have been developed for the assay of lisinopril in pharmaceutical pure and tablet dosage form. The method developed in titrimetric method is a color-based indicator method. The assay of lisinopril by UV is based on its absorbance in the UV range. Lisinopril is a long-acting angiotensin-converting enzyme inhibitor. It is used as a first-line drug to manage hypertension, congestive heart failure, and acute myocardial infarction. The titrimetric method is a type of neutralization reaction using methanol as solvent and titrating it against 0.1 N NaOH and 3–4 drops of phenolphthalein as indicator and the appearance of permanent pink color is taken as the endpoint. The average volume of 0.1 N NaOH consumed to neutralize the content in flask was noted and the percent purity of the drug in the tablet formulation was calculated. The analytical methods reported for the determination of lisinopril in tablets are generally based on spectrophotometric measurements. A UV-Vis spectroscopy is an analytical technique that measures the amount of discrete wavelengths of UV or visible light that are absorbed by or transmitted through a sample in comparison to a reference or blank sample. The assay of lisinopril was performed by ethanol and water as diluents and the absorption maxima were at 208 nm. The concentration of the sample was determined by standard calibration curve method. The titrimetric method and UV-Vis spectroscopic method developed are easy, rapid, and simple and can be used as a routine quality control test for both the pure drug and in tablet formulation.

Keywords: Ethanol, Lisinopril, NaOH, Purity, Titrimetric method, Ultraviolet–visible spectroscopy, Water

INTRODUCTION

Lisinopril chemically, (2S)-1-[(2S)-6-Amino-2-[[(1S)-1-carboxy-3 phenylpropyl]amino]hexanoyl] pyrrolidine-2-carboxylic acid;dihydrate is a lysine analog of enalaprilat [Figure 1]. Enalaprilat is the active metabolite of enalapril, which exists as a dihydrate salt.[1] Lisinopril is a long-acting angiotensin-converting enzyme (ACE) inhibitor. Lisinopril dihydrate is used as first-line drug in the management of hypertension, congestive heart failure, and acute myocardial infarction.[2,3] It is also used in preventing renal and retinal complications of diabetics. It acts by reducing peripheral vascular resistance and blood volume.

The official methods include the use of potentiometry and high-performance liquid chromatography (HPLC) for the determination of content of pure lisinopril dihydrate.[4,5] Various analytical techniques have been reported

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for the tablet dosage form; these include spectrophotometry, liquid chromatography, gas chromatography, spectrofluorimetry, capillary electrophoresis,[6-13] and fluoroimmunoassay. One of the official methods[14] is the use of titrimetric method for the determination of lisinopril. The method consisted of the titration of the aqueous solution of the tablet containing lisinopril with 0.1 M NaOH potentiometrically and requires fairly large quantities of LNP for each titration.[19]

A ultraviolet–visible (UV-Vis) spectroscopy is an analytical technique that measures the amount of discrete wavelengths of UV or visible light that are absorbed by or transmitted through a sample in comparison to a reference or blank sample.[15] Determination of the lisinopril by UV-Vis spectroscopy is a simple, easy, fast, cheap method. Lisinopril has maximum solubility in water and less solubility in alcohol. In this method of UV-Vis spectrophotometry, the solubility of lisinopril in alcohol[16,17] is increased by equal portions of water to alcohol. Lisinopril can be detected in the UV range of 200–400 nm.[18,20]

Since other methods are rather costly, time taking and require sophisticated and advanced instruments, it was required to develop a fast, effective, and economic method which can also serve as a quality control test therefore titrimetric and UV-Vis spectroscopic methods were opted.

MATERIALS AND METHODS

Reagents

Lisinopril pure drug, 0.1 N NaOH, methanol, phenolphthalein indicator, distilled water, ethanol, of AR grade were procured from SDFCL (S D Fine-Chem Limited, Mumbai, India).

Titrimetric assay

Pure lisinopril dihydrate

250 mg of pure lisinopril drug was accurately weighed and dissolved in 25 mL of methanol. It was titrated against 0.1 N NaOH. For the determination of endpoint, phenolphthalein was used as indicator. The appearance of pink color from colorless indicates the endpoint [Figure 2].

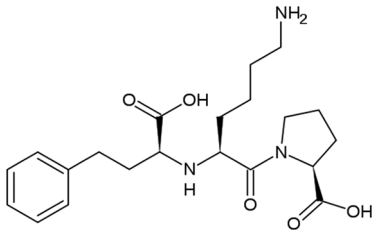

Figure 1: Structure of lisinopril

Figure 2: The appearance of pink color endpoint after titration with 0.1 N NaOH

Lisinopril tablet assay

20 tablets of lisinopril (zestril) were powdered and average weight of each tablet was calculated. The powdered tablet equivalent to 250 mg pure lisinopril was accurately weighed and then dissolved in 25 mL of methanol with shaking. 3–4 drops of phenolphthalein indicator were added. The mixture was titrated against 0.1 N NaOH till the appearance of pink color which stays even after swirling. The assay was carried out in triplicate.

UV-Vis spectroscopic method

Calibration curve method

10 mg of standard drug was taken and weighed accurately. Stock solution concentration of 1000 ppm was prepared using ethanol and water of ratio 1:1 as diluents. From stock solution, working standard solution of concentration 100 ppm was prepared using the same diluents. 10 ppm solution was prepared from the working standard solution and was scanned in UV-Vis spectrophotometer from 200 nm to 400 nm using glass cuvettes. The maximum absorbance was found to be at wavelength

208 nm. Further dilutions of concentrations 6 ppm, 9 ppm, 12 ppm, 15 ppm, 18 ppm, and 20 ppm were prepared from working standard solution using ethanol: water (1:1) as diluents. The absorbance of the prepared dilutions was measured and the calibration curve was plotted [Figure 3].

Assay

10 tablets were taken and weighed accurately. The average weight of the tablets was calculated. Tablets were then powdered using a mortar and pestle. Weight equivalent to 10 mg from the tablet label claim was weighed and taken in a volumetric flask (10 mL). The sample solution was prepared using ethanol: water (1:1) as diluents. From this solution, 10 ppm solution was prepared and the absorbance was scanned in UV-Vis spectrophotometer at 208 nm.

RESULTS AND DISCUSSION

Titrimetric method

Lisinopril, a common antihypertensive drug, is an amphoteric compound which possesses both acidic and basic properties. It has two carboxylic acids in its structure which ionizes in the basic medium. The reaction of these carboxyl groups with appropriate strength of sodium hydroxide is the basis for the proposed assay technique. The proposed titrimetric method developed was performed in triplicate and the readings [Table 1] were used to calculate the average titrant volume of 0.1 N NaOH required to neutralize the contents in the conical flask with the lisinopril tablet formulation and were found to be 11.6 mL [Table 2]. The average titrant volume was used to calculate the percentage purity of lisinopril dihydrate in the tablet sample. The assay limits in British Pharmacopoeia 2009[15] are 92.5–105.5% w/w for lisinopril. The results obtained in the proposed method were found to be within those assay limits.

Reaction involved in the titration:

$$2NaOH + C_{21}H_{31}N_3O_5 \longrightarrow C_{21}H_{29}N_3O_5 + 2H_2O$$

Each mL of 0.1 N NaOH = 0.022075 g of lisinopril

Calculations:

$$\%\ \text{Purity} = \frac{\text{Volume of NaOH consumed} \times \text{Equivalent factor} \times \text{Actual normality of NaOH}}{\text{Weight of Lisinopril} \times \text{Expected normality}} \times 100$$

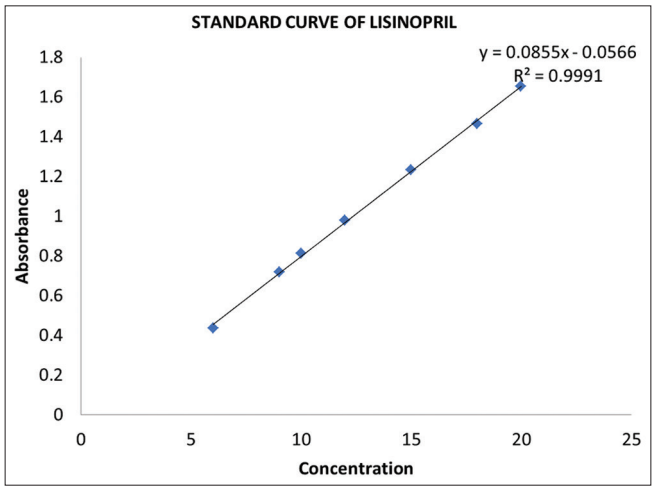

Figure 3: Standard calibration curve

Table 1: Titration data of pure lisinopril drug against 0.1N NaOH

Contents in conical flask	Burette readings		Titrant volume
	Initial	Final	
250 mg of pure lisinopril drug+25 mL of methanol+3–4 drops of phenolphthalein indicator	0	11.1	11.1
	11.1	22.4	11.3
	22.4	33.6	11.2

Table 2: Titration data of lisinopril tablet powder against 0.1 N NaOH

Contents in conical flask	Burette readings		Titrant volume
	Initial	Final	
250 mg equivalent weight of tablet powder+25 mL of methanol+3–4 drops of phenolphthalein indicator	0	11.4	11.4
	11.4	23.2	11.8
	23.2	34.8	11.6

Table 3: Absorbance of the standard and the sample

Concentration (ppm)	Absorbance
6	0.436
9	0.721
10	0.812
12	0.978
15	1.234
18	1.467
20	1.654
Unknown sample	0.953
Concentration of sample	11.80421344

% Purity of pure Lisinopril

$$\text{drug} = \frac{11.2 \times 0.022075 \times 0.1}{0.25 \times 0.1} \times 100$$

% Purity = 101.71 %

% Purity of Lisinopril tablet

$$\text{sample} = \frac{11.6 \times 0.022075 \times 0.1}{0.25 \times 0.1} \times 100$$

% purity = 102.428 %

The results obtained from this study agree with another report of titrimetric technique in the analysis of lisinopril tablets using benzene: methanol (3:1) mixture as solvent. However, the proposed method from this study with methanol as a medium has a great advantage over the earlier titrimetric report because of the issue of solvent cost and safety with regard to benzene.

UV-Vis spectroscopic method

A simple and selective spectroscopic method for the assay of lisinopril has been performed using ethanol and water of 1:1 ratio as a diluent. The maximum absorbance (λ_{max}) was found to be at 208 nm. The calibration curve was plotted and the regression coefficient was found to be 0.999. From the plotted calibration curve, the concentration of the unknown sample was determined [Table 3].

There are various methods available for the determination of lisinopril assay. The methods involved usage of sophisticated instruments as in HPLC. The other methods include fluoroimmunoassay, liquid chromatography, capillary electrophoresis, gas chromatography, and spectrofluorimetry.

CONCLUSION

All the previous methods are time taking, tedious, and meticulous. Hence, the proposed method developed using neutralization reaction titration and simple UV-Vis spectroscopic method presents an easy and effective method. This method can also be used for routine quality control test for assay of both pure drug and tablet formulation.

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