



## SPECTROPHOTOMETRIC DETERMINATION OF LISINOPRIL DOSAGE FORM BY CONDENSATION REACTION

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### ABSTRACT

A precise, accurate, simple spectrophotometric method is developed for determination of Lisinopril in dosage form. This is based upon the formation of coupled product with *o*-phenylenediamine and diketone piperazine a degraded product of Lisinopril which absorbs at 399.5 nm. Linearity was observed in the range of 2 µg to 30 µg, with regression coefficient of 0.9998, RSD 0.81710084. The effect of temperature, concentration of coupling agent and the time of reaction completion were studied. Tablet dosage form was estimated, and percentage recovery was 97-100%. The method was validated for linearity, precision, accuracy, specificity and recovery studies limit.

**Keywords:** Lisinopril, Degradation, *O*-Phenylenediamine, Spectrophotometry

### INTRODUCTION

Lisinopril is an angiotensin converting enzyme inhibitor which is popular antihypertensive agent<sup>1-4</sup>.

The analytical methods described in the official books for the determination of Lisinopril are potentiometric titration and HPLC with mobile phase, mixture of buffer pH 5 and acetonitrile (96:4) and Dimethyloctylsilane column at UV range of 210 nm. Various spectrophotometric methods based on reaction between Lisinopril and different reagents including ninhydrin, chloranil, dichlone and acetylacetone with formaldehyde, phenylhydrazine have been described and comparative study of these methods revealed by Basavaiah K and coworkers were remarked<sup>5-17</sup>.

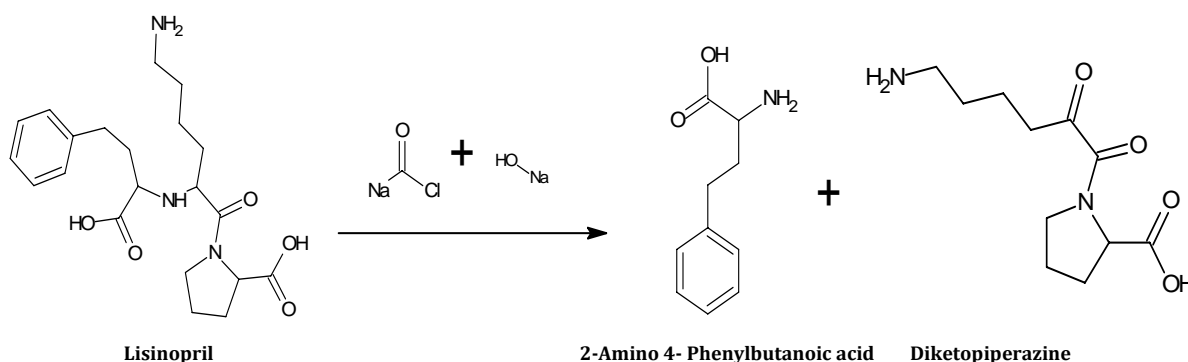
The first, second derivative spectrophotometric and spectrofluorometric methods were reported for the single or multicomponent dosage forms or for the pure drug have been developed. The chromatographic methods of analysis such as micellar electrokinetic chromatography and gas liquid chromatography have been described. The other methods such as Capillary electrophoresis, fluoroimmunoassay and fluoroenzymatic assay have also been reported<sup>18-29</sup>.

The HPLC methods are complicated, associated with low reliability due to isomerisation of Lisinopril, these are often non affordable and require expertise to perform. Lisinopril shows very low absorption in the UV region ( $\lambda_{max}$  193 nm) as result the conventional UV method cannot be used. The spectrophotometric methods developed so far

require non aqueous solvents, pH dependent, less sensitive and measurement at lower wavelength. The estimation with ninhydrin in sodium hydroxide and sodium carbonate associated with interference of concentrated blank solution in absorption and is time consuming. The spectrophotometric method developed by Alaa El Gindy and coworkers is involves estimation of Lisinopril by the condensation with Phenyhydrazine makes the measurement in the range of UV region.

The objective of present study is to develop simple, accurate, precise, specific methods. Spectrophotometric method developed under present study to determine the Lisinopril in pure form or in formulation by coupling with *o*-phenylenediamine to convert the Lisinopril to a more sensitive form which can be measured in Visible region its by using aqueous solvents.

The spectrophotometric method developed involves the degradation of Lisinopril to produce diketopiperazine, by the sodium hypochlorite solution in the alkaline media<sup>7</sup>. Then it was subjected to condensation with *o*-Phenylenediamine to form complex that showed reddish-yellow color (Figure 1). The diketone-*o*-phenylenediamine complex thus formed was soluble in acidic and basic solvents. It was determined by spectrophotometrically at  $\lambda_{max}$  399.5 nm in alkaline media and displays linearity with Beer's range of 2 µg to 30 µg, the factors like temperature, reaction duration, pH of solvent are optimized(Figure 2). The stability of reaction mixture was determined. The developed method was validated as per the ICH guidelines.



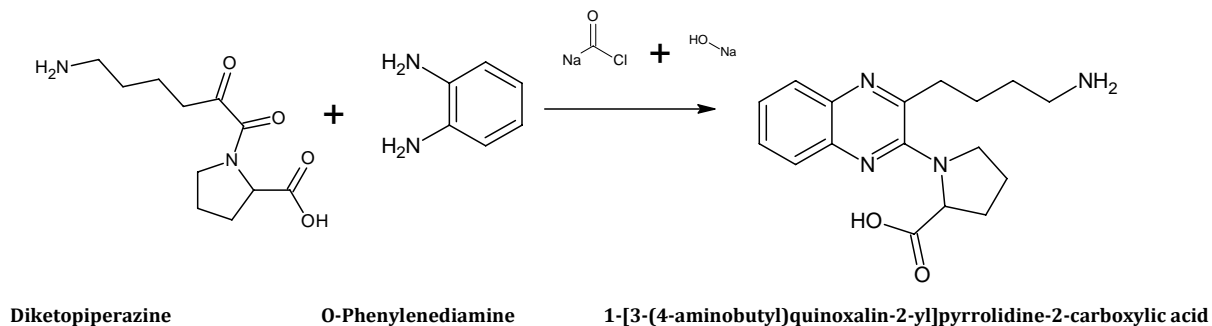


Fig. 1: Proposed reaction pathway for the spectrophotometric complex formation of Lisinopril

## MATERIALS AND METHODS

### Instrumentation

A double beam Elico SL 159 UV-visible spectrophotometer with recording software Spectral treats SL 159 was used. The wavelength range used for scanning was 190 nm to 800 nm. The absorption of test and reference solutions was recorded in 1-cm borosilicate cells.

### Materials and reagents

Lisinopril dihydrate standard drug was procured from the Unimark Pharmaceuticals Ltd, Vapi, Gujarat, India, and certified to contain 99.3%. All the chemicals, solvents and reagents used in the study were of analytical grade. 0.2 N sodium hypochlorite solution was prepared by diluting 4% solution of sodium hypochlorite, 2% w/v solution of sodium sulphite, 0.5% w/v of sodium hydroxide solutions were prepared. The solution of coupling agent *o*-phenylenediamine (1mg/ml) was prepared in 1N H<sub>2</sub>SO<sub>4</sub>. The three different marketed formulations of brand names Lislril 5mg, Lipril 10 mg and Lisiril 5mg were used for sample estimation.

### Preparation of the degradation solution

The working primary standard (1 mg/ml) was prepared by dissolving 50 mg of Lisinopril in 10 ml of 0.1N Sodium hydroxide and 8 ml of sodium hypochlorite was added, stirred and then the mixture was heated at 85° C to allow the reaction to complete for 5 minutes. The mixture was cooled and excess sodium hypochlorite was naturalized with sodium sulphite solution. The final volume was made with sodium sulphite to 50 ml mark.

### Standard solutions and calibration graphs

The various dilutions in the range of 2µg - 30 µg were prepared in 50 ml volumetric flask. The 4 ml of *o*-phenylenediamine solution was added. The mixture was heated at 80°C for 25 minutes. All the flasks were cooled to room temperature and final volume was made to the mark with 0.5 N sodium hydroxide solutions. The absorption of each dilution was recorded at 399.5 nm. The absorption maximum of coupling agent was found to be 233 nm.

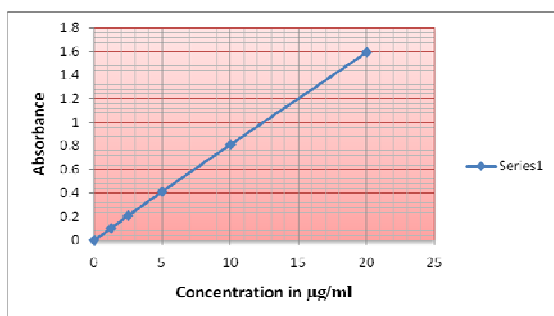


Fig. 2: Linearity curve of Spectrophotometric determination.

Table 1: Statistical observations of developed methods

Parameter	Observation
Linearity range, µg/ml	2µg - 30 µg
Relative Standard Deviation	0.81710084
Slope (b)	0.07921
Intercept (a)	0.010125
Correlation co-efficient	0.9998
Percentage of recovery	97-100
Sandell sensitivity	0.001369 µg/cm <sup>2</sup>

Equation of linearity for % Relative Intensity = Slope x Concentration + Intercept.

The method was compared with standard method and statistically expressed.

T-test value is 0.285431 (table value at 0.05, d<sub>r</sub> 12 is 2.18)

### Procedure for estimation in commercial tablets

Weigh accurately 20 tablets of Lisinopril and ground to fine powder. The tablet powder equivalent to 50 mg was weighed and 10 ml of 0.1 N NaOH solution added, shaken and filtered with Whatman filter paper No.42 into 50 ml volumetric flask. Add 8 ml of sodium hypochlorite, stirred well and heated the mixture for 5 min at 85°C. The final volume was made with sodium sulphite solution. This solution was used as sample stock solution to prepare different unknown concentrations in 50 ml volumetric flasks and to each unknown concentration 4 ml of *o*-phenylenediamine was added. The mixture was heated at 80°C for 20 minutes to complete the reaction. The final volume was made with 0.5N NaOH.

## RESULTS AND DISCUSSION

The developed spectroscopic method was validated as per ICH guidelines for the parameters such as precision, accuracy, specificity and ruggedness. The analytical data on statistical calculation shows the relative standard deviation 0.817, correlation coefficient was 0.999, the percentage recovery was 97-100 and method was compared with standard method the data found to be within specified limit (Table 1). Thus the developed method can be applied for routine analysis of Lisinopril and formulations.

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