



A SIMPLE SPECTROPHOTOMETRIC METHOD FOR THE ASSAY OF RAMIPRIL IN PHARMACEUTICAL FORMULATIONS

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ABSTRACT

A simple and sensitive spectrophotometric method for the estimation of ramipril is developed by the formation of ion pair complexes with bromocresol green. The ion pair complex is formed by the interaction of drug with bromocresol green. Bromocresol green is insoluble in water and soluble in chloroform. The organic layer is extracted from chloroform and the absorbance of organic layer is measured at 420 nm against chloroform blank.

Key words: Spectrophotometry, Bromocresol green, Ramipril, Pharmaceutical dosage form.

INTRODUCTION

Ramipril, 2-[N-[(S)-1-(ethoxycarbonyl)-3-phenylpropyl] - L-alanyl]-(1S, 3S, 5S)-2-azabicyclo [3-3-0] octane carboxylic acid, is used in the treatment of hypertensive patients. The methods used for determination of ramipril include Spectrophotometric method¹⁻⁹, Spectrophotometric and spectrofluorimetric method¹⁰, Spectrophotometric and atomic absorption spectrometric determination¹¹, RP-HPLC method¹²⁻¹³, Liquid chromatography mass spectrometry method¹⁴, Radio immunoassay¹⁵ potentiometry^{16,17}, Gas Chromatography^{18,19}, HPLC method²⁰⁻²⁵, HPTLC Method²⁶.

In the present work, the ion pair complex is formed by the interaction of drug with bromocresol green. Bromocresol green is insoluble in water and soluble in chloroform. The organic layer is extracted from chloroform and the absorbance of organic layer is measured at 420 nm against chloroform blank.

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In developing the proposed methods a systematic study of the effects of various relevant parameters in the methods concerned, concentration of reagents, order of addition, time and temperature required for reaction, pH of buffer, nature of solvents for final dilution, stability of reagents of the coloured species are undertaken by varying one parameter at a time and controlling all other parameters to get a maximum colours development and minimum black colours, reproducibility and the reasonable period of stability of final coloured species formed.

After systematic and detailed study of the various parameters mentioned above, the following procedures are recommended for the determination of ramipril in bulk samples and pharmaceutical formulations.

EXPERIMENTAL

Instrument

A Milton Roy 1001 plus spectrophotometer with 1 cm quartz cells was used for all measurements. An Eutech pH meter model : cyber scan ECPH 1000 is used for pH measurements.

Chemicals and reagents

All the chemicals and reagents used were of AR grade. Double distilled water was used throughout the investigation. AR grade chloroform is used throughout the investigation. Buffer solution (pH 3.5) was obtained by diluting a mixture of 50 mL of 0.2 M potassium acid phthalate and 8.4 mL of 0.2 M HCl to 200 mL with distilled water and the pH is adjusted to 3.5. Bromocresol green (0.5% w/v) solution was prepared by dissolving 500 mg of bromocresol green (Loba) in 100 mL of distilled water.

Calibration curve procedure

Pure ramipril (50 mg) was dissolving in 50 mL methanol. This stock solution was further diluted with methanol to get desired concentration. Into a series of 10 mL volumetric flasks, aliquot samples of ramipril ranging from 0.5 to 2.0 mL (1 mL containing 100 mg) were transferred. To each flask, 2 mL buffer solution and 2 mL bromocresol green solution were added. The final volume was brought to 10 mL with distilled water. The solution in each flask is shaken well with 5 mL chloroform and allowed to separate two layers. The absorbance of the organic layer was measured at 420 nm against chloroform bulk. The amount of ramipril present in the sample was read from calibration curve.

Pharmaceutical formulations

Twenty tablets of ramipril were weighed and powdered. The powdered equivalent to 50 mg of ramipril was transferred into 50 mL volumetric flask, shaken thoroughly with 30 mL methanol and filtered. The filtrate was diluted to 50 mL with methanol. This stock solution is further diluted to obtain the working concentration of 100 $\mu\text{g/mL}$. Different aliquots of solutions were taken and analyzed by using the procedure described earlier and the amount of ramipril present in sample was read from calibration graph. The results are tabulated in Table 1.

Table 1: Assay of ramipril in Tablets

Sample (mg)	*Amount found (mg)	Percentage of label claim	S.D*	* t_{cal}
10	10.02	100.2	0.1524	0.2936
10	9.96	99.6	0.2408	0.3717
10	10.01	100.1	0.2301	0.0971
10	9.98	99.8	0.2167	0.2063

*Average of five determinations based on the label claim

RESULTS AND DISCUSSION

In the proposed method ramipril and bromocresol was treated with chloroform at pH 3.5 to form ion pair complex. The ion pair complex is soluble in chloroform and the complex is extracted from the chloroform layer. The absorbance of blue chloroform layer was measured at 420 nm against reagent blank. Beer's law is obeyed in the concentration range of 50-200 $\mu\text{g/mL}$ of ramipril. The results shown in Table 1 are in good agreement with those obtained with the earlier reported methods. The optimum conditions were established by varying one parameter and keeping others fixed and observing the effect of produced on the absorbance of the solution. The effect of buffer solution concentration and reagent concentration were studied through controlled experiments and optimum conditions were incorporated in the procedure. The common excipients employed do not interfere in the estimation of ramipril. The statistical analysis was studied by proposed method.

The developed visible spectrophotometric methods were simple, sensitive, accurate, precise and reproducible and can be successfully applied for the routine estimation of ramipril in bulk and pharmaceutical dosage forms.

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