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# ROLE OF ALKALOIDAL PRECIPITANTS FOR THE ASSAY OF QUINAPRIL HYDROCHLORIDE IN BULK AND PHARMACEUTICAL FORMULATIONS BY SPECTPOSCOPY

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## ABSTRACT

Simple spectrophotometric methods (A-C) for the assay of Quinapril (QUI) based on the formation of its complexes with alkaloidal precipitants are described. QUI under go quantitative precipitation in the form of molecular complexes with iodine ($I_2$, method A), ammonium molybdate (AM, method B) or phosphomolybdic acid (PMA, method C) when used in excess. In addition to precipitation reactions, color reactions have also been combined to estimate QUI. They are based on the color formation with either unreacted precipitant of the filtrate ($I_2$) or released precipitant from the molecular complex (AM or PMA) with chromogenic reagent such as P-N-methyl amino phenol sulphate (PMAP)-sulphanilic acid (SAc) (for $I_2$), potassium thiocyanate (for AM), cobalt nitrate (Co(II))-disodium salt of ethylene diamine tetra acetic acid (EDTA) complex (for PMA).

**KEYWORDS:** Alkaloidal, Molybdate, Phosphomolybdic, Sulphate, Thiocyanate.

## INTRODUCTION

Alkaloids are detected with the aid of group of reactions due to their chemical properties, structure and presence of functional groups. These reactions are based on the ability of the alkaloid to yield insoluble complexes mainly with AM, $I_2$ and PMA and hence these reagents are named as alkaloidal precipitants.[1] The precipitate is ascribed due to the formation of a molecular complex resulting from the interaction of the unshared electron on nitrogen in

amine with an unoccupied molecular orbital of the alkaloidal precipitant molecule. Quinapril (QUI) is a which is an angiotensin-converting enzyme (ACE) inhibitor and chemically it is [3S-[2[R*(R*)],3R*]]-2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-,2,3,4-tetrahydro-3-isoquinoline carboxylic acid. literature survey reveals that HPLC[1,13], UPLC[14], LC-MS[15,19], GC-MS[20-22], derivative spectrophotometry[23,24], Capillary Electrophoresis[25], Voltametry[26] methods were reported for the determination of QUI in its formulation and in biological fluids. The aim of the present work is to provide simple and sensitive visible spectrophotometric method, for the estimation of QUI in bulk form and formulations. The effects in this accord resulted to develop the present methods. QUI furnish precipitates with alkaloidal precipitants given above, since it contains the nitrogen containing groups (tertiary amino groups). In addition to precipitation reactions color reactions have also been combined to estimate QUI. They are based on the chemical reaction with either released alkaloidal precipitant from the precipitated with acetone (AM) or un reacted precipitant in the filtrate ($I_2$ or SA) with chromogenic reagents such as potassium thiocyanate[8] (for AM) PMAP-SA[9] (for $I_2$) or PMA-Co-II-EDTA[10]. The results are statistically validated.

## EXPERIMENTAL

### INSTRUMENTS

Spectral and absorbance measurements were made on Systronics UV- Visible Spectrophotometer 117 with 10mm matched quartz cells.

### REAGENTS

All the chemicals and reagents used analytical grade and the solutions were freshly prepared. Aqueous solution of $I_2$ (0.089%) in 0.83% of potassium iodide (KI), PMAP (2%), SAc (0.4%), hydrochloric acid (HCl) (1M) for method A; AM (2%), PTC (10%), conc.HCl (used as it is) for method B; PMA (4%) Co(II) (3%),EDTA (4%) for method C, 0.01 M HCl for methods B and C were prepared in triple distilled water. A one mg/ml solution was prepared by dissolving 100 mg of pure QUI in 100 ml of distilled water and this stock solution was diluted stepwise with distilled water to obtain the working standard solution of concentrations 50 μg/ml for method A, 400 μg/ml for method B and C respectively.

## RECOMMENDED PROCEDURES

### Method A

Aliquots of working standard solution (1.0-3.0 ml, 200 µg/ml) were delivered into a series of centrifuge tubes and the volume in each tube was adjusted to 3.0 ml with distilled water. Then 2.0 ml each of 1M HCl and $I_2$ were added successively and centrifuged for 5 min. The precipitate was collected by filtration and subsequently washed with 2 ml distilled water. The filtrate and washings were collected in 25 ml graduated test tubes. Then 3.0 ml of PMAP solution and 2.0 ml SAc solution were added successively and the volume was made up to the mark with distilled water. The absorbance was measured during next 30 min. at 520 nm against distilled water. A blank experiment was also carried out omitting the drug. The decrease in absorbance and inturn drug concentration was obtained by subtracting the absorbance of the test solution from blank. The amount of drug was calculated from calibration graph.

### Method B

Aliquots of working standard solution (1.0-3.0 ml, 200µg/ml) were delivered into a series of centrifuge tubes and the volume in each tube was adjusted to 3.0 ml with 0.01 m HCl. Then 1.0 ml of AM was added and centrifuged for 5 min. The precipitate was collected by filtration followed by washing with 50% alcohol until it is free from the reagent. The precipitate in each tube was dissolved in 5.0 ml of acetone and transferred into 25.0 ml graduated tube. The 5 ml of conc. HCl and 3 ml PTC solution were successively added and kept aside for 30 min and then volume in each tube was made up to the mark with distilled water. The absorbance was measured at 480 nm against a similar reagent blank. The amount of drug QUI was calculated form the calibration graph.

### Method C

Aliquots of working standard solution (0.5-2.5 ml, 200µg/ml) were delivered into a series of centrifuge tubes and volume in each tube was adjusted to 3.0 ml with 0.01m HCl. The 2.0 ml PMA was added and centrifuged for5 min. the precipitate was collected by filtration followed by washing with distilled water until it is free from the reagent. The precipitate in each tube was dissolved in 5 ml of acetone and transferred into 25 ml graduated tubes. One ml each of Co (II) and EDTA solutions were successively added and the tubes were heated for 15 min. at 60$^{o}$C in water bath. The tubes were cooled and the solution each tube was made upto the

mark with distilled water. The absorbance was measured at 840 nm against a similar reagent blank. The amount of drug was calculated from its calibration graph.

## RESUTLS AND DISCUSSION

The optimum conditions for the color development of methods (A, B and C) were established by varying the parameters one at a time keeping the others fixed and observing the effect produced on the absorbance of the colored species.

The optical characteristics such as Beer's law limits; molar absorptivity and Sandell's sensitivity for each method (A-C) are given in table1. The precision of each method to the drug was found by measuring the absorbance of six separate samples containing known amounts of drug and the results obtained are incorporated in table1. Regression analysis using the method of least squares was made to evaluate the slope (b), intercept (a), correlation coefficient (r) and standard error of estimation ($S_{e)}$ for each system and is presented in table1. The accuracy of the methods was ascertained by comparing the results by proposed and reference methods (UV) statistically by t- and F-tests (Table 2). The comparison shows that there is no significant difference between the results of studied methods and those of reference ones. The similarity of the results is obvious evidence that during the application of these methods, the excipients that are usually present in pharmaceutical formulations do not interfere in the assay of proposed methods. As an additional check of accuracy of the proposed methods recovery experiments were carried out. The recoveries of the added amounts of standard drug were studied at 3 different levels. Each level was repeated for 6 times. From the amount of drug found, the % recovery was calculated in the usual way.

The higher $\lambda_{max}$ values of all the proposed methods have a decessive advantage since the interference from the associated ingredients should be generally less at higher wavelengths than at lower wavelengths. Thus the proposed visible spectrophotometric methods are simple and sensitive with reasonable precision, accuracy and constitute better alternatives to the existing ones to the routine determination of QUI in bulk forms and pharmaceutical formulations.

**Table 1: Optical Characteristics, Precision and Accuracy of the Proposed Methods for QUI**

| Parameters | Method A | Method B | Method C |
|---|---|---|---|
| $\lambda_{max}$ (nm) | 520 | 480 | 840 |
| Beer's Law limits (µg/ml) | 4-24 | 20-80 | 4-24 |
| Molar absorptivity (l mole$^{-1}$cm$^{-1}$) | 1.359x10$^4$ | 90191x10$^3$ | 1.097x10$^4$ |
| Sandell's sensitivity (µg/cm$^2$/0.001 absorbance unit) | 0.035 | 0.052 | 0.043 |
| Regression Equation y = a + bc*<br>Slope (b)<br>Intercept (a) | <br>0.0286<br>-0.0011 | <br>0.0192<br>0.0018 | <br>0.0231<br>0.0006 |
| Correlation coefficient (r) | 0.9999 | 0.9998 | 0.9998 |
| Relative Standard Deviation (%)** | 0.2024 | 0.3084 | 0.2779 |
| % Range of error **<br>(0.05 level confidence limit) | <br>0.169 | <br>0.258 | <br>0.232 |

*Y = a+bc, where c is the concentration in µg/ml.

**From six determinations.

**TABLE 2: Determination Of *Qui* In Pharmaceutical Formulations.**

| Sample$^{\Delta}$ (Tablets) | Labeled method (mg) | UV* Method | Amount obtained (mg) | | | Recovery (%) | | |
|---|---|---|---|---|---|---|---|---|
| | | | Proposed method | | | | | |
| | | | A | B | C | A | B | C |
| $T_1$ | 5 | 4.98±0.022 | 4.99±0.010<br>F=2.57<br>t=0.22 | 5.01±0.026<br>F=1.43<br>t=0.87 | 4.99± 0.010<br>F=2.67<br>t=0.22 | 99.97 | 100.22 | 99.97 |
| $T_2$ | 5 | 4.99±0.006 | 5.01±0.020<br>F=1.36<br>t=0.78 | 4.99±0.024<br>F=1.25<br>t=1.08 | 5.00±0.031<br>F=2.06<br>t=1.16 | 100.1 | 99.97 | 100.13 |
| $T_3$ | 5 | 4.99±0.009 | 4.98±0.027<br>F=1.54<br>t=0.46 | 5.00±0.032<br>F=2.07<br>t=1.15 | 4.98±0.033<br>F=2.09<br>t=1.14 | 99.88 | 99.87 | 100.13 |
| $T_4$ | 5 | 4.98±0.034 | 5.00±0.006<br>F=1.18<br>t=0.99 | 4.99±0.027<br>F=1.46<br>t=0.38 | 5.01±0.025<br>F=1.42<br>t=0.88 | 99.99 | 99.89 | 100.22 |

$^{\Delta}$Four different batches of tablets from a pharmaceutical company.

## CONCLUSION

Even though there are very few methods for the determination of QNP, there were no reports utilising spectrophotometric technique. Hence then proposed methods are valuable. They were developed based on the characteristic properties of different functional groups present in QNP. Each method uses a specific reagent and the $\lambda_{max}$ and $\varepsilon_{max}$ values of each

method are different. Statistical analysis of the results show that the proposed procedures are in good precision and accuracy. Results of the analysis of pharmaceutical formulation revealed that the proposed methods are suitable for their analysis with virtually no interference of the usual additives.

All the proposed methods are simple, sensitive, and reliable and can be used for the routine determination of QNP in bulk samples and pharmaceutical formulations depending upon the needs of the specific situation.

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