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Novel spectrophotometric method for the assay of Pitavastatin calcium in pharmaceutical formulations

B. S. Virupaxappa[1]*, K. H. Shivaprasad[1], M. S. Latha[2]

[1]*Department of Chemistry PG Centre, Bellary, Gulbarga University, Gulbarga, Karnataka, (INDIA)*
[2]*Department of Chemistry G M Institute of Technology, Davangere, Karnataka, (INDIA)*

ABSTRACT

A simple, sensitive and rapid spectrophotometric method for the determination of pitavastatin calcium by using Acidic potassium permanganate is described. The method is based on the reduction of permanganate by pitavastatin in acidic medium, and the unreacted oxidant was measured at 550 nm. The Beer's law is obeyed in the range of 8.0 – 18.0 µg/ml for PTV using acidic potassium permanganate reagent. In this method, the amount of permanganate reacted corresponds to the PTV content and the absorbance was found to decrease linearly with the Concentration. The sandells sensitivity, detection limit and quantization limit were also calculated. The optimum reaction conditions and other analytical parameters were evaluated.

Keywords: Spectophotometry, Pitavastatin, Toluidine Blue.

INTRODUCTION

Pitavastatin calcium [1] (PTV), mono calciumbis {(3R, 5S, 6E)-7-[2-cyclopropyl-4-(4-flurophenyl)-3-quinolyl]-3-5-dihydroxy-6-heptenoate}, is a lipid-lowering agent [2], used in hyperlipidemia. The analytical methods reported in literature includes HPLC [3] and polarographic methods [4] for CPH and LC/MS method [5] for PTC, however, no spectrophotometric method has so far been reported for these drugs. Hence, it was thought worthwhile to develop advanced spectrophotometric method for the same. This paper describes difference spectrophotometric methods for the estimation of CPH and PTC separately in bulk and their tablet formulations. All the chemicals were of analytical reagent grade and solutions were prepared with purified water of IP [6] grade. The solutions of 0.1N HCl and 0.1N NaOH were prepared in water as per IP [7].

Several analytical techniques have been used for the determination of Pitavastatin, which rely upon sophisticated and expensive instrumentation. The low cost and the case of operation make the spectrophotometric techniques highly desirable for the determination of Pitavastatin in

pharmaceuticals. Simple and facile method for the determination of Pitavastatin in pharmaceuticals has been developed. The proposed methods are simple, accurate and easy to apply to routine used.

MATERIALS AND METHODS

APPARATUS

A Peltier Accessory (Temperature controlled) Varian Cary 50 model UV-Vis spectrophotometer equipped with 1 cm quartz cell was used for all spectral measurements. Systronics pH meter were used for the accurate pH determinations.

REAGENTS

All solutions were prepared with doubly distilled water. Chemicals used were of analytical reagent grade. Potassium permanganate (1X 10^{-2} M) was prepared

By dissolving 0.395g of the chemical (Merck, Mumbai, India) in water, the solution was boiled for 10 min to remove any residual manganese (IV) ions, cooled, filtered and diluted to 250 ml and standardized using oxalic acid titrimetrically. It was diluted to get 500 µg ml^{-1}. 10 %Acetic acid was prepared by diluting 10 ml glacial Acetic acid in 100ml distilled water.

Pitavastatin: A 1000 µg ml^{-1} standard Pitavastatin drug (Fig 1) solution was first prepared by dissolving 0.1 g in methanol and diluting to the mark in 100 ml calibrated flask. The stock solution was diluted approximately to get the working concentration.

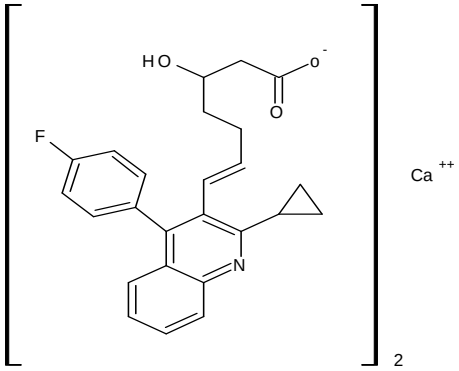

Figure1. Structure of studied Pitavastatin calcium.

Recommended Procedure

Determination of Pitavastatin using potassium permanganate as reagent: Different aliquots (8.0 – 18.0 µg ml^{-1}) of Pitavastatin prepared in acetic acid were transferred into a series of 10 ml calibrated flasks by means of micro burette and the total volume was adjusted to 4.0 ml with 10 % Acetic acid. To each flask, 1ml of % 5M H_2SO_4 was added followed by 1 ml of 500 µg ml^{-1} $KMnO_4$, the latter being measured accurately. The flasks were kept aside for 10 min with occasional shaking before diluting to the mark with water. The absorbance was recorded at 550 nm against water blank.

Analysis of formulations

The calibration graph was used for the determination of drugs in pharmaceutical formulations. An accurately weighed amount equivalent to each 100 mg of drug from composite of 05 powdered tablets was transferred into a 100 ml volumetric flask. Dissolved in about 30 ml of

acetone was added and the mixture was shaken for 5 min. The mixture was filtered using Whatman No. 42 filter paper and the filtrate was evaporated to dryness on a water bath. The residue was washed thoroughly several times with water before dissolving it in 10% Acetic acid. The solution was then transferred into a 50 ml volumetric flask, made up to the mark with 10% Acetic acid and suitable aliquot was then subjected to analysis using the procedure described as above.

RESULTS AND DISCUSSION

Potassium permanganate is a strong oxidizing agent that can react with several organic substances, the tablet excipients in the analyzed samples did not interfere in this method. Recently, permanganate was studied to determine pharmaceutical active compounds in formulations both in acidic medium [8, 9] and as well as in alkaline medium [10-13].

Optimization of Experimental conditions

In this method a fixed concentration of permanganate was reacted with increasing concentration of PTV in H_2SO_4 medium, a simultaneous decrease in the concentration of permanganate occurred as revealed by the decreasing absorbance at 550 nm (Fig 2 & 3), which served as the basis for quantification. Blank was prepared by taking 4.0 ml of 10% acetic acid, 1 ml of H_2SO_4 and 1 ml of 500 µg ml^{-1} $KMnO_4$ in a total volume of 10 ml (adjusted by water). This shows maximum absorbance reading at 550 nm against water.

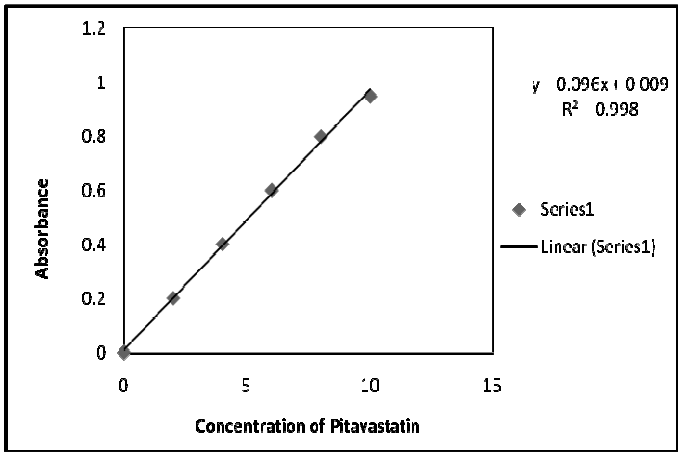

Figure 2. Calibration graph of Pitavastatin

Table1. Analytical parameters

Parameters	Pitavastatin
λ max (nm)	550
The Beer's law limits (µg/ml)	8.0-18.0
The Sandell sensitivity (µg/ml)	0.000056
Limits of detection (µg/ml)	0.5222
Limits of quantification (µg/ml)	1.9531
Regression Equation	y = a + bx
Slope(b)	0.0096
Intercept(a)	0.009
Correlation coefficient (R)	0.998

Analytical data

A linear relation was found between absorbance at λ_{max} and concentration ranges given in (Table 1). Regression analysis of the Beer's law data using the method of least squares was made to evaluate the slope (b), intercept (a) and correlation coefficients (R), for each system of pitavastatin, which are also presented in Table 1. Sensitivity parameters such a molar absorptivity, the Sandell sensitivity, detection and quantification were calculated according to ICH guidelines. The accuracy of the method was established by analyzing the pure drug at the three levels (within working limits) and the precision was ascertained by calculating the relative standard deviation of five replicate determinations on the same solution containing the drug at three levels (Table. 2)

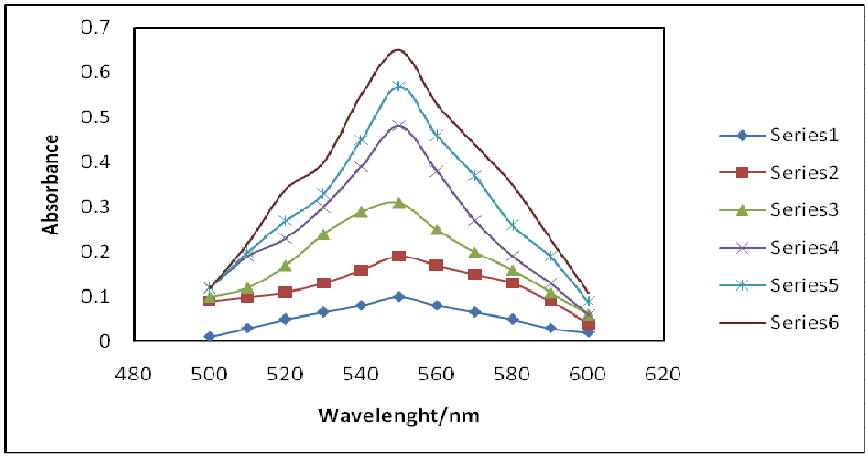

Figure 3. Absorption spectrum of Potassium permanganate Solution

Interference study: In the pharmaceutical analysis, it is important to test the selectivity towards the recipients and fillers added to the pharmaceutical preparations. Several species which can occur in the real samples together with drug were investigated. The level of interference was considered acceptable. Commonly encountered excipients such as starch, glucose, lactose did not interfere in the determination.

Table 2 .Analysis of Artenimol in pharmaceutical formulations
(Found values[a] ± SD% and comparison with the official method).

Drug	Labelled	Found (X ± SD) Proposed method
Pituva (Zydus candilla)	**2 mg/Tab**	**1.9 ± 0.85 t = 1.13, F = 1.09**

Applications

The proposed method can be used for the determination of Pitavastatin in bulk and pharmaceuticals.

CONCLUSION

Simple and rapid methods for the determination of Pitavastatin using Potassium permanganate reagent have been developed. The method is simple and easy to perform compared too many other method and do not entail any stringent experimental variables which affect the reliability of results. The methods can thus be used for the dete4rmnation of Atorvastatin in pure and dosage forms.

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