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Spectrophotometric Determination of Paliperidone Palmitate in Tablets

T. Satya[1], G. K. Siva Sankara Yadav[2], S. Ramanaiah[1], I. E. Chakravarthy[1]*

[1]Department of Chemistry, Rayalaseema University, Kurnool - 518 007, Andhra Pradesh, India. [2]Department of Physics, Rayalaseema University, Kurnool - 518 007, Andhra Pradesh, India.

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ABSTRACT

The ultraviolet (UV) spectrophotometric method has been developed for the determination of paliperidone palmitate (PP) in the pharmaceutical formulation using bromocresol green (BCG) and tropeolin-oo sol (TPOO) methods. The PP chemically named as, (9RS)-3-[2-[4-(6-fluoro-1,2,benzisoxazol-3-yl)piperidin-1-yl]ethyl]-2-methyl4-oxo-6,7,8,9-tetrahydro-4H-pyridol [1,2-a] pyrimadin-9-ylhexadecanoate is an antipsychotic drug used in the treatment of schizophrenia. It works by helping to restore the balance of certain natural chemicals (neurotransmitters) in the brain. The chemical and reagents were prepared for BCG and TPOO methods. Blank solution and sample solution were prepared for the spectrophotometric metyhods. The blank and sample solutions were prepared with chloroform. PP Obey's Beer's law between the range of 0-200 mg ml^{-1}. PP solution in the BCG and TPOO shows as the wavelength of maximum absorbance at 420 nm and 410 nm, respectively. The orange color solution is obtained. The calibration graphs constructed at their wavelength of determination were found to be linear for UV spectrophotometric method.

Key words: *Spectrophotometric, Wavelength, Bromocresol green, Tropeolin-oo sol, Paliperidone palmitate.*

1. INTRODUCTION

Paliperidone palmitate (PP) is designed for treatment of schizophrenia in daily clinical practice, and it has pharmacokinetic properties [1]. Different methods have been reported for the estimation of PP. Most of the methods reported are either expensive or due not give reproducible results. This prompted the authors to propose a simple less expensive method which gives better reproducible results using a popular analytical technique namely the spectrophotometric technique [2,3]. In the present paper, the proposed method was based on the bromocresol green (BCG) and tropeolin-oo sol (TPOO) methods. Usually, the spectrophotometric technique is simple and less expensive [4-7]. The selective and sensitivity of the spectrophotometric methods depend only on the nature of chemical reactions involved in color development and not on the sophistications of the experiment. Ultraviolet (UV) and visible spectrophotometric methods are highly versatile, sensitive, and reproducible. So, we develop new spectrophotometric methods for the estimation of selected drugs having various uses in pharmaceutical preparations. In BCG initially, we prepared BCG solution and added chloroform called as a blank solution, thereafter BCG solution, chloroform added with drug solution called as a sample solution. Both blank solution and sample solution were used in a spectrophotometric method for the estimation of PP.

In TPOO, chemicals were prepared with molar ratios and solutions were used for studying of PP in the spectrophotometric method**.** The PP was clinically used in an oral formulation for daily use due to its active metabolite of risperidone. Figure 1 shows the structure of PP.

Tablets were weighed and contents well mixed, and the powder equivalent to 50 mg of PP was dissolved in chloroform, filtered, residue was washed with distilled water and the volume was adjusted to 50 ml with chloroform. This solution was further diluted as in standard solution method preparation. Thereafter, it follows BCG and TPOO methods. Further analysis was carried out as per the procedure described under calibration curve, and the amount of PP present in the sample was estimated from calibration graph. To study the accuracy and suitability of the proposed method known quantities of PP were added to the previously analyzed samples and the same mixture were reanalyzed by the proposed.

*Corresponding Author:
E-mail: iechakra@yahoo.co.in

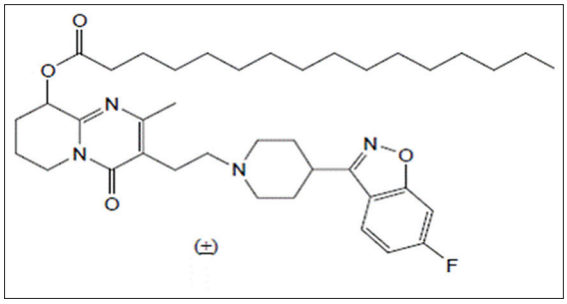

Figure 1: Schematic structure of paliperidone palmitate.

2. EXPERIMENTAL METHODS AND MATERIALS

2.1. Instrumentation

Measurements were carried out using Elico SL 164 double beam UV-visible spectrophotometer with 10 mm matched Quartz cuvettes.

Spectrophotometric analytical procedures are not generally stability indicating. However, in view of the simplicity, high sensitivity, precision accuracy, and low cost, UV-visible spectrophotometric methods are necessary for routine analysis of small scale industries and clinical laboratories.

2.2. Chemicals and Reagents

2.2.1. BCG solution

BCG solution is prepared by dissolving 500 mg of BCG in 100 ml distilled water.

2.2.2. TPOO solution

TPOO is prepared by dissolving 500 mg of TPOO (loba) in 100 ml of distilled water.

2.2.3. Buffer solution (3.5 pH)

Buffer solution is prepared 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.

2.2.4. HCl solution (0.1 M)

It is prepared by diluting 8.5 ml of concentrated HCl to 1000 ml with distilled water.

2.2.5. Standard solution

About 50 mg of pure PP was dissolved in 50 ml of chloroform (1000 mg ml^{-1}). It is further diluted to get a concentration of mg ml^{-1}.

2.3. Assay Procedure

2.3.1. BCG method

The following procedure has been adopted for obtaining the standard curve. An aliquot of 0.5, 1.0, 2.0, 2.5 ml of each flask, add 1.0 ml of 3.5 pH buffer solution, and add 1.0 ml of BCG solution were added and to this add 5 ml of chloroform uniformly. Then, the diluted water is added as 3.0, 2.5, 2.0, 1.5, and 1.0 ml to each flask. The maximum wavelength was measured at 420 nm. The calibration curve was obtained by plotting absorbance values against amount of standard drug in mg.ml. The amount of drug present in the sample was read from the calibration curve. The calibration curve was found to be linear over the concentration range of 0-200 mg ml^{-1}.

2.3.2. TPOO method

The following procedure has been adopted for obtaining the standard curve. An aliquot of 0.5, 1.0, 1.5, 2.0, and 2.5 ml of drug solution was transferred into a series of flasks. To each flask add 1.5 ml of 0.1 M HCl solution and to this add 1.0 ml of the TPOO solution to each flask. Then, the distilled water is added as 3.0, 2.5, 2.0, 1.5, and 1.0 ml to each flask and then add 5 ml of chloroform uniformly. The maximum wavelength was measured at 410 nm.

The calibration curve was obtained by plotting absorbance values against amount of standard drug in mg ml^{-1}. The amount of drug present in the sample was read from the calibration curve. The calibration curve was found to be linear over the concentration range of 0-200 mg ml^{-1}.

2.4. Pharmaceutical Formulations

Tablets were weighed accurately, and contents were well mixed, and the powder equivalent to 50 mg of PP was dissolved in chloroform, filtered, residue was washed with distilled water and the volume was adjusted to 50 ml with chloroform. This solution was further diluted as in standard solution. Thereafter, it follows BCG and TPOO methods. Furthermore, the analysis was performed as per the procedure described under calibration curve, and the amount of PP present in the sample was estimated from calibration plot. To study the accuracy and suitability of the proposed method known quantities of PP were added to the previously analyzed samples and the same mixture were reanalyzed by the proposed method.

3. RESULTS AND DISCUSSIONS

The present study was carried out to develop a simple, rapid, precise, and reproducible spectrophotometric method for the estimation of PP in pharmaceutical formulation and the results obtained by proposed method are in good agreement with the official method. Figures 2a and b shows the calibration curve of PP in both BCG and TPOO method with absorbance verses µg/ml and indicates it obeys Beer's law. Figures 3a and b indicate that colored products were quantized spectrophotometrically at 420 nm and 410 nm for BCG and TPOO method. Optimization of the different experimental conditions was conducted. Beer's law was obeyed in the concentration range 0-200 mg ml^{-1}. The calibration curve is linear over the range of 0-200 mg ml^{-1} of drug (concentration vs. absorbance).

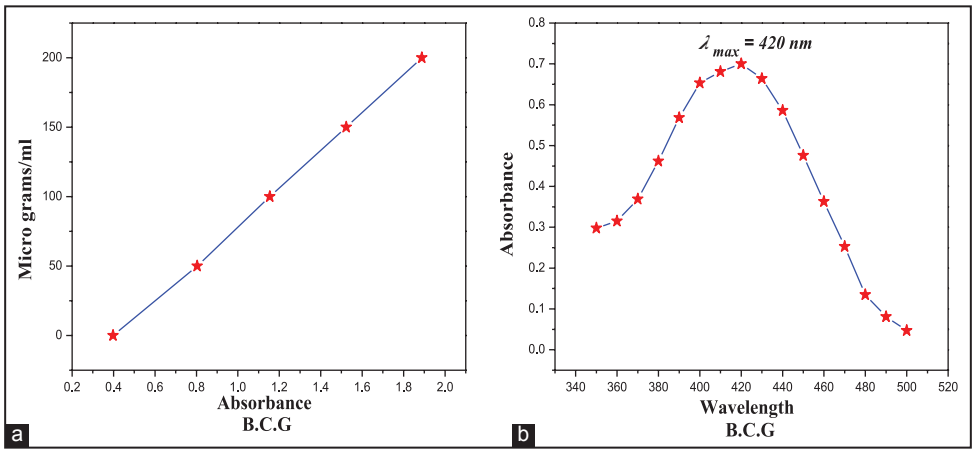

Figure 2: (a and b) Bromocresol green method.

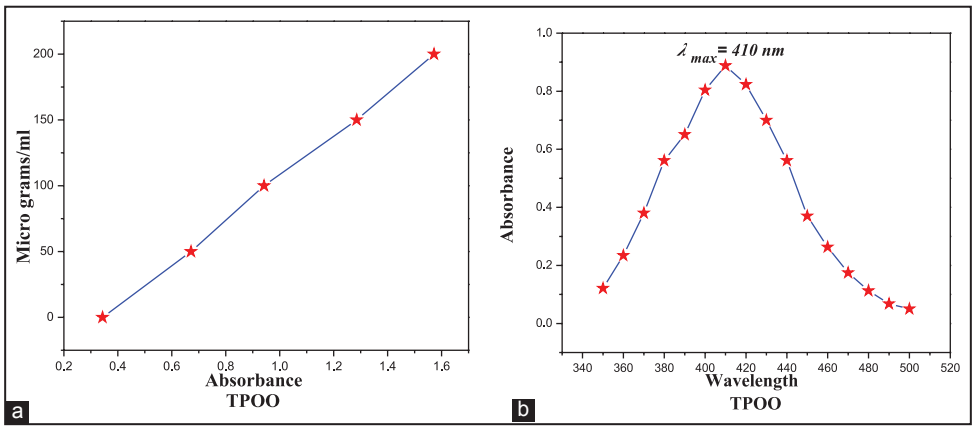

Figure 3: (a and b) Tropeolin-oo sol method.

The absorbance of the orange color solution is measured in the wavelength range of 420 nm against the reagent blank. It is clear that the drug treated with BCG solution has a maximum absorbance at 420 nm. Hence, all further studies are made at 420 nm. The amount of drug read from the calibration curve.

The recovery studies conducted by addition of different amount of pure drugs to a reanalyzed sample solution and data are tabulated in Table 1. The recovery values were ranged from 99.64 to 100.04 indicates the accuracy of the method. The additives and excipients usually present in the tables do not interface. The statistical analysis of various parameters was studied, and the results are summarized in Tables 1 and 2.

The values of standard deviation and coefficient of variation were satisfactorily low, indicates the reproducibility of the method. The data of assay values of commercial formulations in subjected to statistical evaluation of student test to study the proposed method.

An average of five determinations based on label claim. Standard deviation, coefficient of variation,

Table 1: Estimation of PP in tablets.

Sample	Labeled amount (mg)	The amount found in mg		Percentage of recovery*
		Proposed method	Official method	
Tablet 1	250	250.30	250.10	99.88
Tablet 2	250	249.80	250.00	99.64
Tablet 3	250	249.86	249.84	100.00
Tablet 4	250	248.98	248.95	100.04

*An average of five determinations based on label claim.
PP=Paliperidone palmitate

Table 2: Statistical analysis of estimation of PP.

Sample	Labeled amount (mg)	Standard deviation	Coefficient of variation	*t_{Cal}
Tablet 1	250	0.4509	0.0901	0.148
Tablet 2	250	0.3646	0.0729	1.226
Tablet 3	250	0.7124	0.1425	0.4394
Tablet 4	250	0.8955	0.0922	0.2548

PP=Paliperidone palmitate

calculated × t value by proposed method, theoretical values at 95% confidence limits, "t" 2.58. The "t" values are < "t" theoretical with 4 degress of freedom at the 5% level of significance indicates that there is no significant difference between proposed method and reference method. The proposed spectrophotometric method was found to be simple, precise, accurate, and less time consuming. Hence, the proposed method is the preferred method for routine analysis of estimation of PP in bulk drugs sample and from pharmaceutical preparations.

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