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SPECTROPHOTOMETRIC DETERMINATION OF PROCHLORPERAZINE MALEATE USING CRYSTAL VIOLET DYE IN THE PURE FORM AND IN PHARMACEUTICAL PREPARATIONS

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Abstract. In this study, a simple and sensitive A new spectroscopic method has been developed for the determination of prochlorperazine (PCZM) in aqueous solutions. The method is based on the oxidation of the drug using a potassium bromate/potassium bromide ($KBrO_3$/KBr) mixture in an acidic medium, followed by a reaction with crystal violet to form a stable, water-soluble blue product. Spectral analysis of the coloured product showed that the maximum absorption was observed at a wavelength of 590 nanometres. The results showed that the relationship between absorbance and drug concentration was linear within the range 3–105 µg/ml, in accordance with Beer–Lambert's law. The molar absorptivity was 10,148.44 $L \cdot mol^{-1} \cdot cm^{-1}$, whilst the Sandel sensitivity was 0.059 $\mu g \cdot cm^{-2}$. The limit of detection (LOD) and limit of quantification (LOQ) were 0.089 and 0.29 micrograms/ml, respectively. Application of the method to tablets containing prochlorperazine maleate demonstrated its effectiveness in providing accurate and reliable results. This highlights the method's effectiveness in determining the content of prochlorperazine in pharmaceutical preparations.

Keywords: Prochlorperazine Maleate, Crystal Violet, Spectrophotometric

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Introduction

Phenothiazine compounds are an important class of drugs that are widely used in the treatment of psychiatric disorders, and they represent one of the prominent chemical groups in pharmacological literature. Their widespread use has led researchers to develop various analytical methods for their characterisation and quantification in pharmaceutical preparations and biological samples. These methods include: electroanalytical techniques [1], [2], spectrophotometry [3], [4], [5], chemiluminescence [6], and high-performance liquid chromatography (HPLC) [7]. Prochlorperazine maleate is defined as the maleate salt of the compound prochlorperazine; it is characterised by its efficacy as an antipsychotic and antiemetic, in addition to its sedative effect [8], [9]. Some studies suggest that long-term use of this drug may affect bone metabolism and mineralisation in psychiatric patients [10]. Treatment with this drug may also be associated with a number of undesirable effects, such as drowsiness and dizziness, menstrual disorders, skin reactions, hypotension, neuromuscular disorders, akathisia, contact dermatitis, and, in some cases, cholestatic jaundice [11]. Figure (1) shows the chemical formula of prochlorperazine maleate:

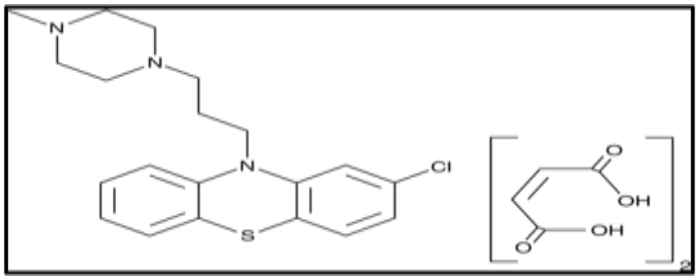

Figure 1. Chemical structure of Prochlorperazine Maleate

The molecular formula is C28H32ClN3O8S and molar mass 606.1 g.mol-1 and melting point of around 187 to 190 °C [12], Prochlorperazine has attracted considerable attention in the field of analytical chemistry, leading to the development of numerous analytical methods for its determination in raw materials, pharmaceutical preparations and biological samples. These methods have varied to include volumetric titrations [13], [14], [15], spectroscopic measurements [16], [17], [18], [19], [20], kinetic methods [21], fluorometric measurements [22], [23], [24], [25], [26] and electrochemical techniques [27], [28], as well as the use of liquid chromatography coupled with various extraction methods, such as liquid–liquid extraction and solid-phase extraction, utilising a variety of reagents and detectors to achieve greater accuracy and sensitivity [29], [30].

In this study the Crystal Violet dye was used in spectrophotometric determination of Prochlorperazine Maleate, the goal of this research was to develop a swift, sensitive, simple and efficient process for quantitative estimation of Prochlorperazine Maleate in its pure and pharmaceutical formulations.

Methods

All spectral measurements were carried out using a T90 UV–Vis spectrophotometer manufactured by PG Instruments Ltd. (United Kingdom), utilising quartz cells with a light path length of 10 mm. Weighing was carried out using a Sartorius 210S electronic balance (Kern), whilst a water bath was used to maintain reaction conditions where necessary during the experiments.

All reagents and chemicals were of analytical grade, supplied by Aldrich and Fluka, and were used directly without undergoing any further purification. A standard solution of prochlorperazine malate was prepared at a concentration of (1000 micrograms/ml) by dissolving (0.1000 g) of the substance in an appropriate volume of distilled water; The solution was then transferred to a 100 ml volumetric flask and made up to the mark with distilled water.The required working solutions were prepared by appropriate dilution of this solution.A

violet crystal solution with a concentration of (1×10^{-6} molar) was prepared by dissolving (0.00004 g) of the dye in a 100 ml volumetric flask, then making up the volume with distilled water to the mark., then making up the volume to 100 ml in a volumetric flask. As for the bromide–bromate solution, it was prepared by dissolving 1.0 g of potassium bromide and Dissolve (0.1 g) of potassium bromate in a suitable volume of distilled water in a 100 ml volumetric flask, then make up to the mark with distilled water. Thereafter, 3 ml of this solution was transferred to a 100 ml volumetric flask and diluted with distilled water to the mark to obtain the working solution.To prepare a solution of prochlorperazine maleate at a concentration of 300 micrograms/ml, the standard solution was suitably diluted with distilled water in a 100-ml volumetric flask. Furthermore, 0.1 molar solutions of nitric acid, hydrochloric acid and acetic acid were prepared in accordance with standard procedures.

To prepare samples of the pharmaceutical preparation, ten tablets of Nautisol were selected, each containing 5 mg of prochlorperazine maleate, with a total weight of 6.30 g. The tablets were ground to a uniform powder; 3.784 g of this powder was then weighed and transferred to a volumetric flask, and an appropriate amount of distilled water was added to dissolve it. The solution was then filtered to remove undissolved material, The final volume of the solution was adjusted to 100 ml using distilled water, resulting in a solution with a concentration of 300 micrograms per millilitre. The concentrations required for subsequent experiments were prepared by serially diluting this solution with distilled water.

Results and Discussion

Upon adding (1 ml) of a (KBr : KBrO3) solution to (1.5 ml) of a Prochlorperazine Maleate solution (300 µg/mL) in the presence of (0.5 ml) of (0.1 M) sulfuric acid, and subsequently adding (1 ml) of the Crystal Violet dye solution (10^{-6} M), a blue-colored product is formed. Measuring the absorption spectrum of the colored product after diluting it with distilled water to the mark in a (10 ml) volumetric flask and allowing it to stand for (15 minutes) revealed maximum absorbance at a wavelength of (590 nm) .The study involved examining the experimental factors influencing the reaction in order to select the conditions that yield the best analytical performance.

The effect of the volume of the oxidising agent (KBr:$KBrO_3$) was evaluated within the range (0.1–3 ml) to investigate its role in the formation of the coloured product. The results showed that the use of 1.5 mL of the oxidising agent yielded the highest absorbance value at a wavelength of 590 nm; therefore, this volume was adopted as the optimum volume in all subsequent experiments, as shown in Figure 2.

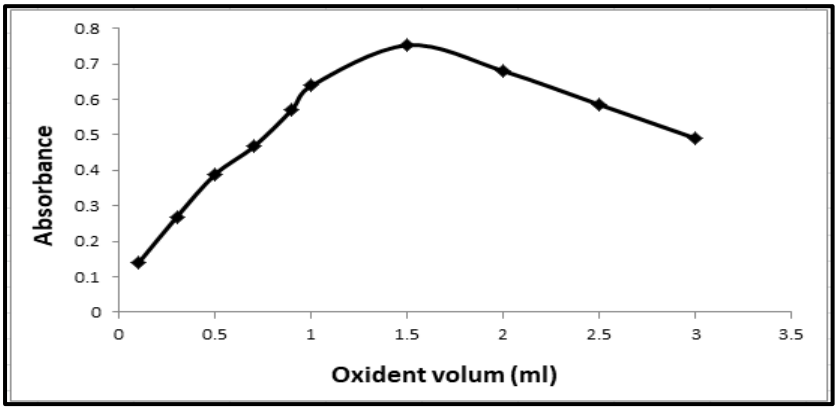

Figure 2. The effect of Oxidizing agent on absorbance

An assessment was carried out of the effect of acid type on the oxidation process was investigated by using four types of acids each at a concentration of (0.1 M) and reacting them with the drug, oxidizing agent and the dye. Absorbance measurements were taken ; as shown in Table (1) Sulfuric acid was the most effective acid, yielding the highest absorbance value.

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Table 1. The effect of acid

Type of acid	Absorbance	Λmax
H_2SO_4	0.752	590
HNO_3	0.692	590
HCl	0.681	590
CH_3COOH	0.526	590

The effect of acid volume was investigated by using varying volumes of sulfuric acid, ranging from (0.1 - 3 ml) . The absorbance values of the prepared solutions were recorded at a wavelength of 590 nm. The data shown in Figure 3 indicated that the use of 1.0 ml of acid yielded the highest spectral response; therefore, this volume was adopted for all subsequent experiments.

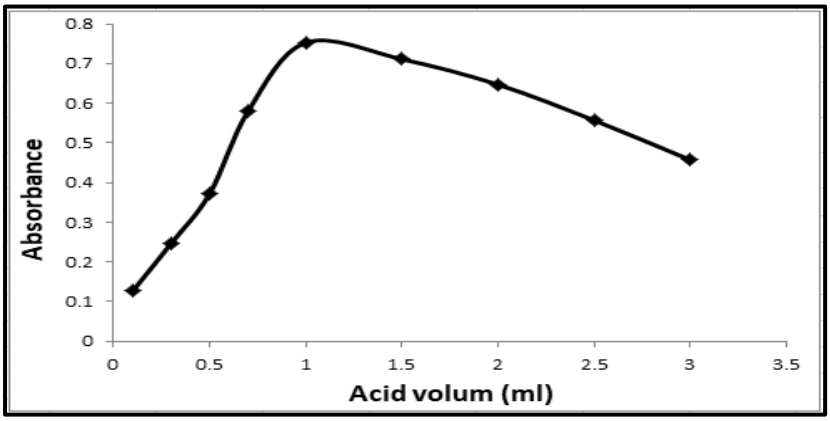

Figure 3. The effect of acid volume

The effect of the amount of Crystal Violet dye was investigated by using varying volumes of the dye solution ranging from (0.5 - 4 ml) at a concentration of (10^{-6} M) in combination with the Prochlorperazine Maleate drug solution, the oxidizing agent (KBr : $KBrO_3$), and Sulfuric acid. Figure (4) demonstrates that a dye volume of (2 ml) yields the optimal absorbance value.

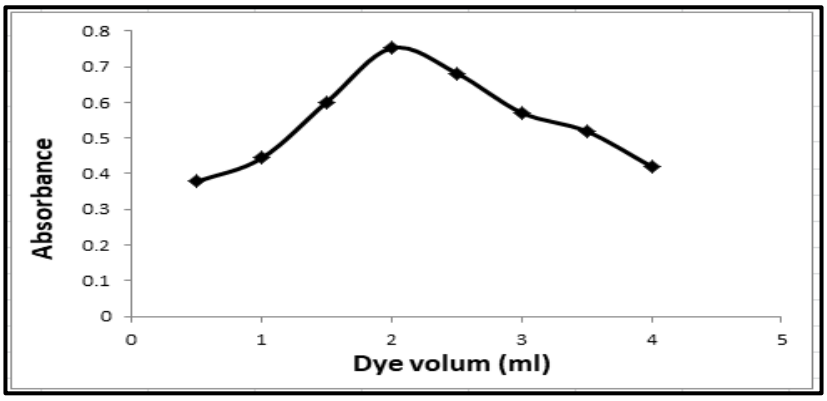

Figure 4. The effect of Crystal Violet dye volume

The response of the coloured product was evaluated at different temperatures to investigate the effect of temperature on its spectral properties. and the results are shown in Figure (5).; therefore, the use of room temperature (25°C) is recommended for subsequent experiments.

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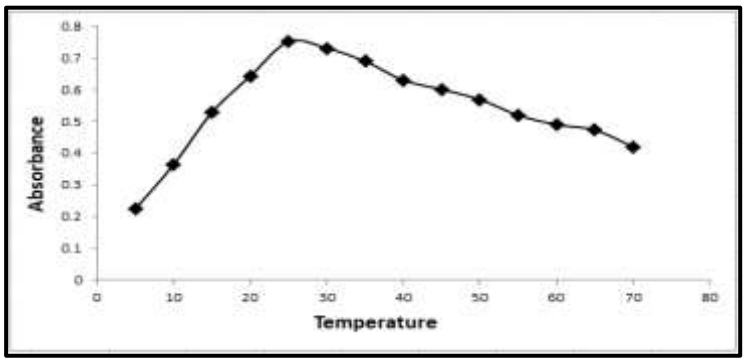

Figure 5. The effect of Temperature

The Stability of the resulting product was investigated over various time intervals. Specifically, Prochlorperazine Maleate (1.5 ml) of oxidizing agent (KBr : $KBrO_3$),Preparation of the mixture began by adding (1.0 ml) of sulphuric acid and (2.0 ml) of crystal violet solution to a (10 ml) volumetric flask, then making up the volume with distilled water to the mark, as shown in Table 2. The product was found to remain stable for approximately 60 minutes (one hour), a duration considered sufficient for performing the necessary calculations.

Table 2. The effect of Stability.

Time	Direct	5	10	15	20	25	30	35	40	45	50	60
Abs	0.740	0.746	0.750	0.752	0.752	0.753	0.753	0.751	0.751	0.750	0.750	0.750

The order of reagent addition was evaluated by testing a number of different sequences, with the aim of determining their effect on the spectral response of the product. The results indicated that sequence (3) was superior in terms of absorbance value, which led to its adoption for the remainder of the experiments, as shown in Table (3).

Table 3. The effect of Order of addition.

No.	Order of addition	Absorbance
1	K + P + C + S	0.651
2	C + P + S + K	0.587
3	P + K + S + C	0.752
4	S + C + K + P	0.683
5	P + S + C + K	0.698

(P) Prochlorperazine Maleate, (K) (KBr : $KBrO_3$), (S) Sulfuric acid (C) Crystal Violet

To construct a calibration curve, a series of volumetric flasks with concentrations of (3-105 µg/ml) of Prochlorperazine Maleate were prepared, and (1.5ml) of the oxidizing agent (KBr : $KBrO_3$), (1ml) of Sulfuric acid and (2ml) of Crystal Violet dye were added to each flask. The solutions were left for (15 minutes) before completing the volume with distilled water and measuring the absorbance at (590 nm) The calibration curve was based on the average absorbance values of the coloured product and showed an excellent linear relationship with a correlation coefficient of (0.9991). The molar absorbance was 10,148.44 $L \cdot mol^{-1} \cdot cm^{-1}$, whilst the Sandel sensitivity was recorded as 0.0597 $\mu g \cdot cm^{-2}$. Figure 6 shows the resulting calibration curve.

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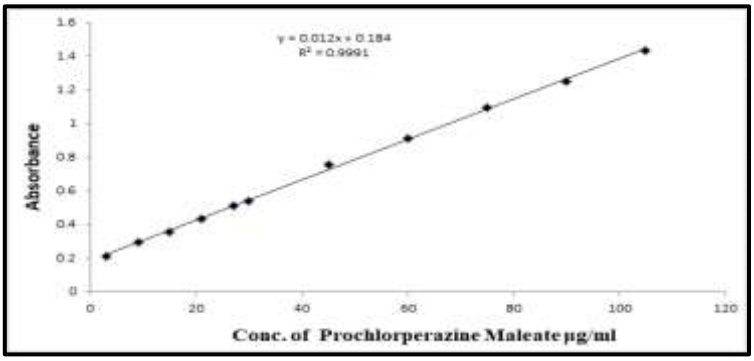

Figure 6. Calibration curve for determination Prochlorperazine Maleate

The figure 7 shows the absorption spectrum recorded for the product formed by the reaction of malate with prochlorperazine once all optimal reaction conditions had been met.

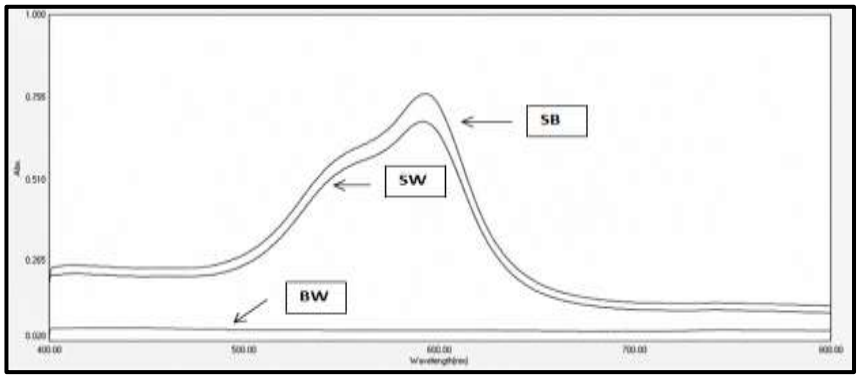

Figure 7. Absorption spectrum of the coloured product formed by the reaction of prochlorperazine malate under optimal experimental conditions.

SB: Absorbance of the coloured product relative to the blank solution.
SW: Absorbance of the coloured product relative to distilled water.
BW: Absorbance of the blank solution relative to distilled water.

The accuracy and precision of a method for measuring the absorption of a drug were studied by taking Six absorption measurements at (590 nm) For three different concentrations of prochlorperazine within the linear range, in accordance with the Beer–Lambert law.. The average recovery was found to be (99.21%), indicating high accuracy and precision. Tables (4) and (5) show the results of the analytical performance evaluation of the method; Table (4) specifically presents data on accuracy and precision. including the observed and expected concentrations of Prochlorperazine Maleate, as well as the recovery and Er% values. Table 5 shows the results of the detection limits, including the LOQ, LOD, and concentration values.

Table 4. Results of accuracy and precision

Conc. of Prochlorperazine Maleate µg /ml	Conc. Prochlorperazine Maleate Observed*	Recovery*%	Er%
9	8.83	98.11	-1.88
60	60.4	100.66	0.666
105	103.8	98.88	-1.11

*n=6

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Table 5. Results of Detection limits

Concentration µg /ml	LOD µg/ml	LOQ µg/ml
3	0.0874	0.2914

To determine the Equivalence of the colored product formed and the binding ratio between the drug Prochlorperazine Maleate and the Crystal Violet dye, The stoichiometric ratio of the product was determined using both the continuous changes (Joubert) method and the molar ratio method, with solutions of prochlorperazine and crystal violet prepared at a standard concentration of (1×10^{-5} M) for both methods. To determine the stoichiometric ratio using the Jopp method, a series of solutions was prepared such that the volume of the prochlorperazine malate solution varied gradually from (0.5–4.5 ml), whilst the volume of the crystal violet solution was adjusted accordingly within the same range, keeping the total volume constant. Thereafter, 1.5 ml of a KBr/$KBrO_3$ mixture and 1 ml of sulphuric acid solution were added to each flask, and the volume was made up to 10 ml with distilled water. Absorbance values were recorded at λmax = 590 nm, and the results shown in Figure (8) indicate that the reaction proceeds in a 1:1 molar ratio.

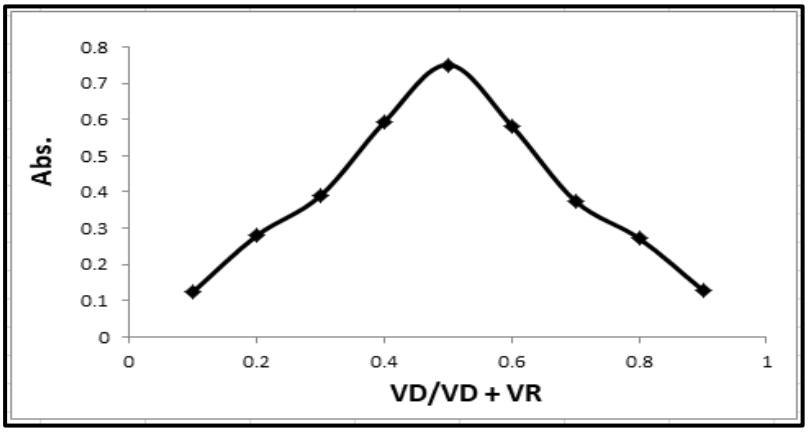

Figure 8. Continuous variations in output method (Job's method)

The mole-ratio method involved adding a fixed volume (1.5 ml) of the drug (at a concentration of (1×10^{-5} M) to increasing volumes (ranging from 0.5 to 4.5 ml) of the Crystal Violet dye (also at 1×10^{-5} M). Subsequently, (1.5ml) of the oxidizing agent (KBr : $KBrO_3$). To each 10 ml volumetric flask, 1 ml of sulphuric acid was added, and the volume was then made up to the mark with distilled water. After preparing all the solutions, spectrophotometric measurements were carried out at a wavelength of 590 nm, using the corresponding blank solution for each sample as a reference. The results obtained via the mole-ratio method were consistent with those from the continuous variations method, confirming a (1:1) binding ratio, as illustrated in Figure (9).

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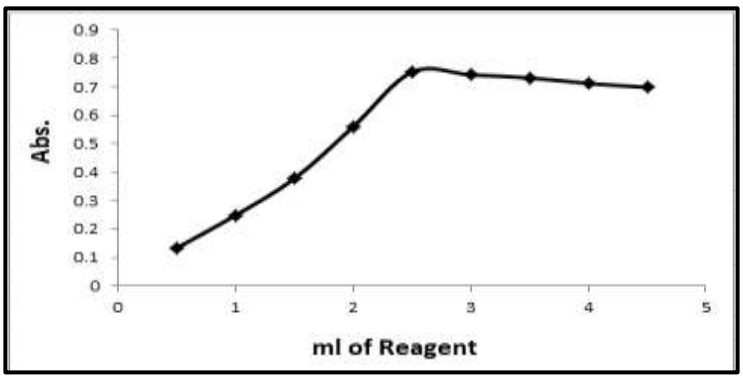

Figure 9. Molar ratio method for the product

Both methods confirmed a 1:1 binding ratio between the drug and the dye, and the proposed reaction can be represented by the following equation Figure (10):

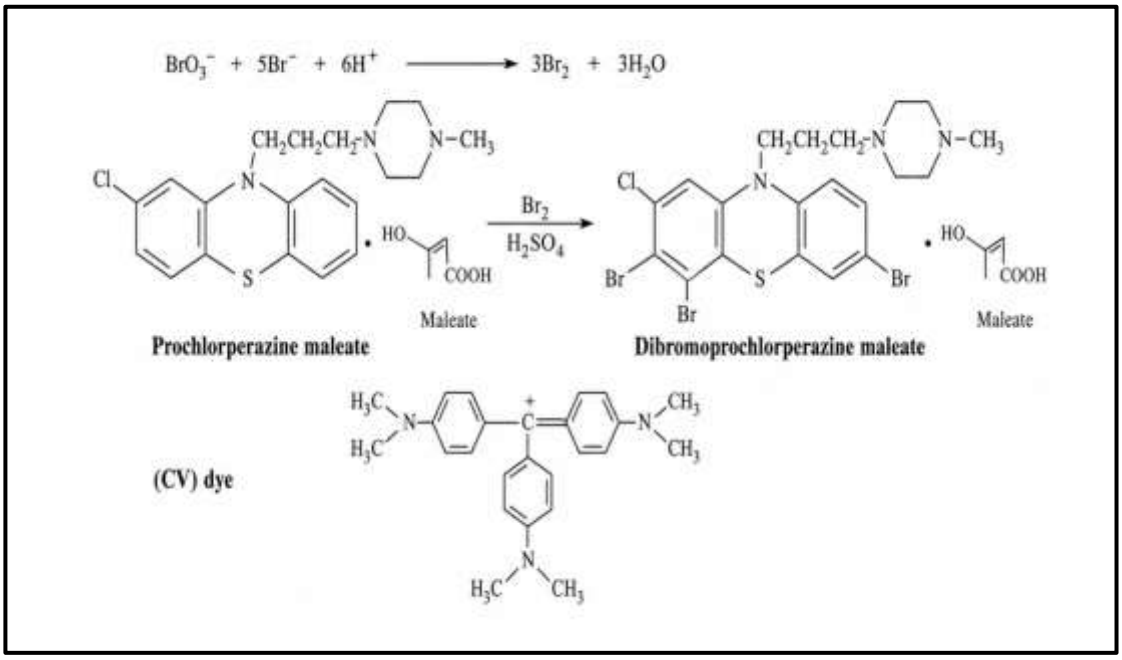

Figure 10. Final reaction equation

The method was applied to determine Prochlorperazine Maleate in the pharmaceutical preparation in tablet form. Ten tablets weighing (6.3068 g) were ground into a fine powder. A (3.7841 g) sample was dissolved in distilled water, filtered, and the volume was completed to (100 ml) to obtain a (300 µg /ml) solution. The solution was filtered, and three concentrations of the filtrate were used to determine with regard to the determination of the prochlorperazine content in the pharmaceutical preparation, the results are set out in Table 6.

Table 6. Determination of Prochlorperazine Maleate in pharmaceutical

Conc. of Prochlorperazine Maleate µg/mL	Conc. of Prochlorperazine Maleate Observed µg/mL*	Er%
15	14.33	- 4.66
30	30.5	1.66
90	89.8	- 0.22

* n=3

The results in Table (6) indicate that the developed method is successful in determining the content of prochlorperazine in the pharmaceutical preparation, whilst achieving satisfactory analytical performance.

Conclusion

A simple, sensitive, accurate, and economical spectrophotometric method was successfully developed for the determination of prochlorperazine maleate in its pure form and pharmaceutical preparations. The method is based on the oxidation of prochlorperazine maleate using a potassium bromide–potassium bromate mixture in an acidic medium, followed by its reaction with crystal violet to produce a stable blue-coloured product with maximum absorbance at 590 nm. Under the optimum experimental conditions, the method obeyed Beer–Lambert's law over the concentration range of 3–105 µg/mL, with a correlation coefficient of 0.9991, a molar absorptivity of 10,148.44 $L \cdot mol^{-1} \cdot cm^{-1}$, and a Sandell sensitivity of 0.0597 $\mu g \cdot cm^{-2}$. The limits of detection and quantification were 0.0874 and 0.2914 µg/mL, respectively, while the average recovery was 99.21%, confirming the satisfactory accuracy and precision of the proposed procedure. Job's continuous variation and mole-ratio methods demonstrated that the reaction product was formed at a 1:1 molar ratio between prochlorperazine maleate and crystal violet and remained stable for approximately 60 minutes. The successful application of the method to commercial tablet formulations demonstrated that it is suitable for routine quality-control analysis because it requires readily available reagents, simple instrumentation, and no complicated extraction or separation procedures.

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