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SPECTROPHOTOMETRIC DETERMINATION OF METHYLPHENIDATE IN A PHARMACEUTICAL PREPARATION BY POTASSIUM PERMANGANATE AND SULPHANILIC ACID

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ABSTRACT

Two simple and sensitive Spectrophotometric methods are developed for detection of Methylphenidate Hydrochloride. The first method A is based on oxidation of the drug with alkaline potassium permanganate at room temperature (25±°c). The decrease in absorbance of colored Manganate ions was measured at 610 nm. The second Method B is based on the formation of orange color as a result of reaction between drug and diazotised Sulfanilic acid. The absorbance was measured at 510 nm. All parameters affecting the development of the color were investigated and the conditions were optimized. Under the optimum condition, Beer's law was obeyed in the concentration range 2-18 µg/ml and 6-18 µg/ml for method A and B respectively. Molar absorptivity was found to be 7.014×10^3 L $mol^{-1}cm^{-1}$ and 5.395×10^3 L mol^{-1} cm^{-1} respectively. The proposed methods are well suited for determination of Methylphenidate in pharmaceutical formulations.

KEYWORDS: Methylphenidate Hydrochloride, Spectrophotometry, Potassium Permanganate, Daizotised Sulphanilic Acid, Oxidation.

INTRODUCTION

Methylphenidate [methyl α-phenyl-α (2-piperidyl acetate, (Ritalin) has pharmacological properties similar to those of Dextroamphetamine)[1] and has been used to treat children with Hyperkinesis[2] as well as patients with depression. According to recent estimates from the United States, 1-2 % of the children labeled as hyperactive are currently receiving this medication.[3] Its name is often shorten to MPH. MPH stimulates the central nervous system. It does these by increasing dopamine transmission in the brain.[4] The drug is commonly used to treat attention deflect hyperactivity disorders and narcolepsy. Sometimes this drug is used

together with other drug to treat depression. Various methods for analysis such as IR[5], LC-MS[6],HPLC[7,8],MS[9], LC-UV[10],GC[11] have been reported for assaying MPH in pharmaceuticals and in blood serum.

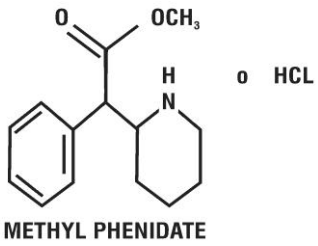

Fig-1:- Structure of Methylphenidate Hydrochloride.

The present investigation describe two visible Spectrophotometric methods using $KMnO_4$ as an oxidizing agent and Sulphanilic Acid as a coloring reagent respectively. Simplicity, sensitivity, wide linear ranges, mild experimental conditions and above all cost effectiveness characterize the proposed methods. Further the methods were found to possess adequate accuracy and precision.

The aim of the present work is to develop simple method for the determination of Methylphenidate in different dosage form. The proposed methods are comparable with reported method with respect to sensitivity moreover the methods neither require extraction nor prior separation of the drug.

MATERIALS AND METHODS

a) Apparatus

A model specord 600 spectrophotometer with 1 cm matched quartz cell was used for all absorbance measurements.

b) Reagents and Materials

All chemicals used were of analytical grade reagent and double distilled water was used to prepare all solutions. Potassium Permanganate (5×10^{-3}) mol/lit was prepared by dissolving about 0.079 gm of chemical (Merck, Mumbai, India) in water and diluting to 100 ml, and standardized.[12] using H.A Brights Procedure (A.I. Vogel, 3rd edition, 1961, pg.no280). Sodium Hydroxide solution (0.5 mol/lit) was prepared by dissolving the chemical (Merck, Mumbai, India) in water. Pharmaceutical grade Methylphenidate certified to be 99.90% pure

was kindly provided by Sandoz Pvt. Limited, Mumbai as a gift and a solution of 100 µg/ml and 40 µg/ml was prepared from it. Sulfanilic Acid: Into a 100 ml volumetric flask, 200 mg of sodium nitrite was taken and dissolved in 60 ml of distilled water. One ml of hydrochloride acid was added and allowed to stand for one hr. Sulfanilic acid, 500 mg, was then added and the final volume was made up to the mark with purified water. This reagent was used after 30 minutes of preparation. This reagent should be freshly prepared for analytical work.

Methods

Method A: Different aliquots of standard solution (O.5 to 4.5 ml, 100 µg/ml) of pure MPH were transferred into a series of 25 ml calibrated flask by means of micro burette. A volume of 1 ml of (0.5 mol/lit NaOH was added to each flask accurately. To each flask was added 2 ml of (5×10^{-3}) mol /lit $KMnO_4$.The final volume made to 25 ml with D/W. The flasks were kept aside for 10 minutes with occasional shaking. The absorbance was recorded at 610 nm against the reagent blank.[13]

Method B: Into a series of 20 ml calibrated flasks (3 to 9 ml, 40µg/ml) of pure MPH were buretted and 10 ml of coloring reagent was added. The final volume was made to 20 ml with NaOH (1M). The absorbance was measured at 510 nm after 5.0 minutes after dilution.[14]

Assay Procedure for Tablet

Ten tablets were accurately weighed and powdered. A Portion of tablet powder equivalent to 40mg of MPH was accurately weighed into a 250 ml calibrated flask.40 ml of D/W was added and shaken for 20 minutes. Then the volume was make to 250 ml with D/W. Mixed well and filtered using Whatman filter paper no-42 and a convenient aliquot of filtrate (2 to 3 ml) was subjected to analysis by the procedure described under method A. Another portion of tablet containing 40 mg MPH was accurately weighed and dissolved in 1M Sodium Hydroxide and diluted to 250 ml with 1M NaOH. Then it was filtered through Whatman Filter paper no 42 and a suitable aliquot (2 to 3 ml) was subjected to analysis by the procedure described under method- B. The assay was completed as described in procedure for calibration curve.

THE RESULT AND DISCUSSIONS

The method A is based on the oxidation of Methylphenidate by $KMnO_4$ in a alkaline medium followed by measurement of the residual Paramagnate at 610 nm in method A (Fig-

2) and in method B coloring reagent was prepared by diazotization reaction with Sulphanilic Acid. In second method reaction proceeds with increasing absorbance (Fig-4) This reagent react with Methylphenidate to form Orange colored complex The stability of complex was estimated with respect to time and is evident from figs the complex is stable between 10 to 30 minutes for Method – A and 5 to 10 minutes for Method B Fig-3,5.

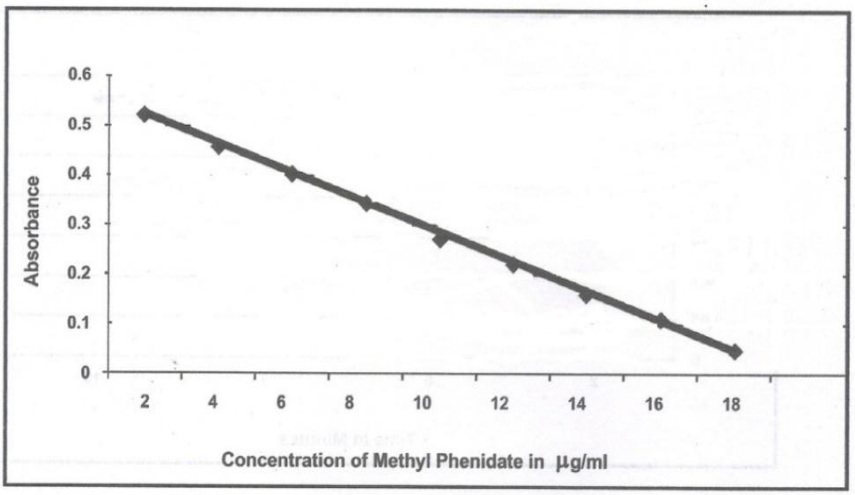

Fig-2:- Calibration Curve for Method A

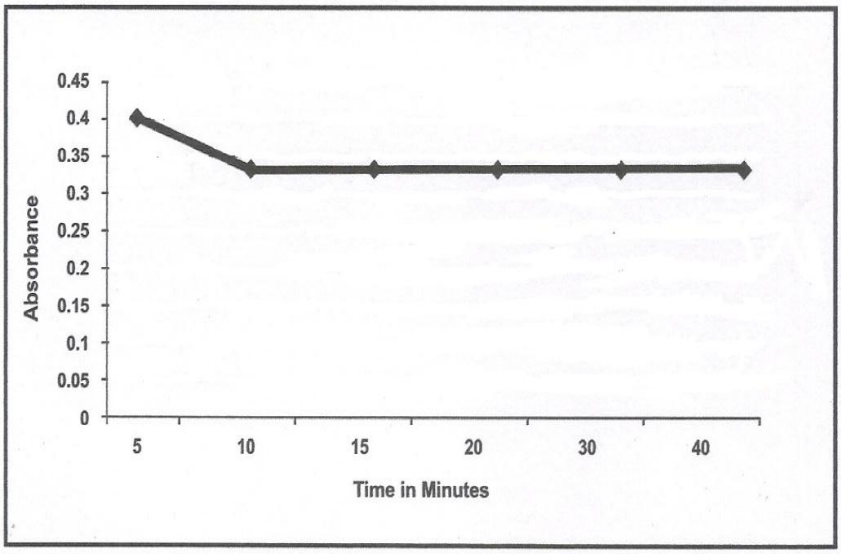

Fig-3:- Stability of Complex in Method A

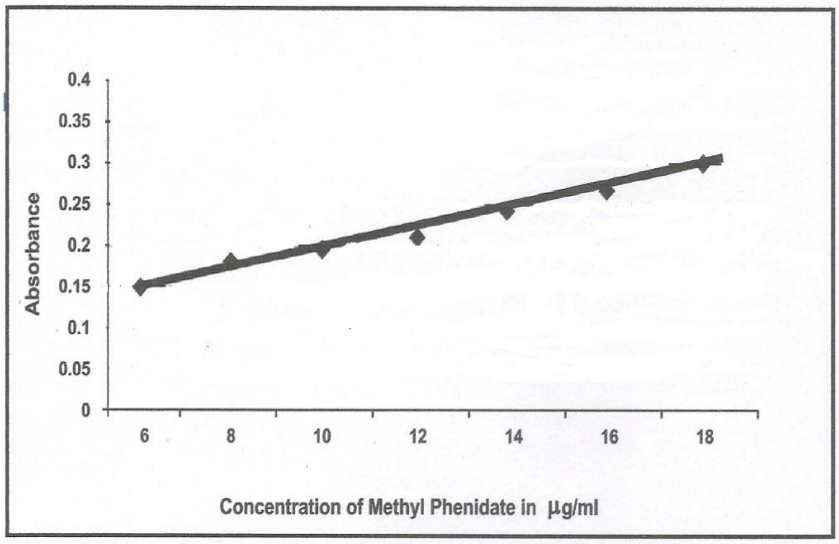

Fig-4:- Calibration Curve for Method B

Optimisation of Parameters

In Method A, when a fix concentration of Permanganate was reacted with increasing concentration of MPH in basic medium there occurred a concomitant fall in the concentration of Permanganate as revealed by decreasing absorbance at 610 nm.

The reaction between MPH and $KMnO_4$ in basic medium was complete in 10 minutes and the absorbance of the magnate ions at 610 nm was found to be stable up to 30 minutes thereafter (Fig -3)

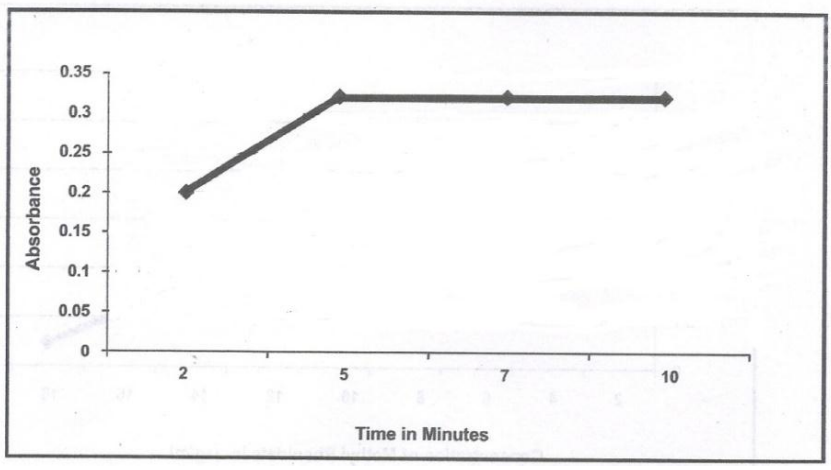

Fig-5:- Stability of Complex For Method – B (Effect of time on the stability of color product in method B)

All the optimization parameters are estimated at room temp, in method A. The investigations were carried out to establish the most favorable conditions for the formation of colored

product. The influence of the concentration as well as the volume of the reagent on the reaction has been studied. Different concentration and different volume were tried for all the reagents by varying one parameter at a time.

1) The influence of $KMnO_4$

The reaction rate and absorbance increases with increasing $KMnO_4$ concentration. The absorbance was studied in the range 1×10^{-4} to 1×10^{-3} mol/L keeping all other parameters constant. It was found that 7.5×10^{-4} mol/L $KMnO_4$ is the optimum concentration for the absorbance of Methylphenidate as shown in (Fig-6) .The effect of the color development was investigated by adding different volume (0.1- 2.0 ml) of 7.5 $\times10^{-4}$ mol/L. potassium permanganate to a drug. The maximum absorbance of the green color was attained with 1.6 ml of the coloring reagent, and remained constant even when higher volumes were added (Fig-7). Therefore, 2 ml of the reagent was used for the experimental investigations.

Two ml of $KMnO_4$ must be accurately added in all the reaction flask since $KMnO_4$ absorbs maximally at the analytical wave length, and small changes in the volume of $KMnO_4$ have a critical effect on the absorbance reading.

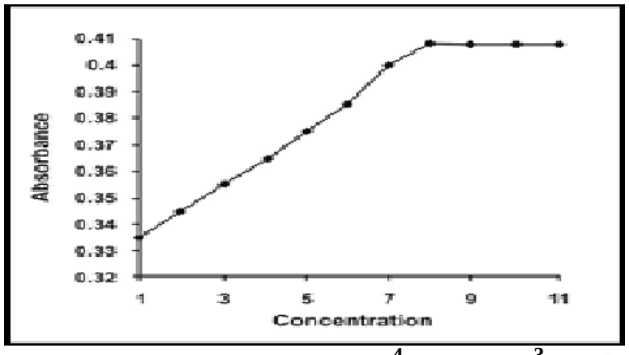

Fig-6: Effect of the concentration ranges 1×10^{-4} to 1×10^{-3} mol/L of $KMnO_4$ on the intensity of the color produced during the reaction (MPH 25 µg/ ml ; 1ml of 0.5 mol/L NaOH)

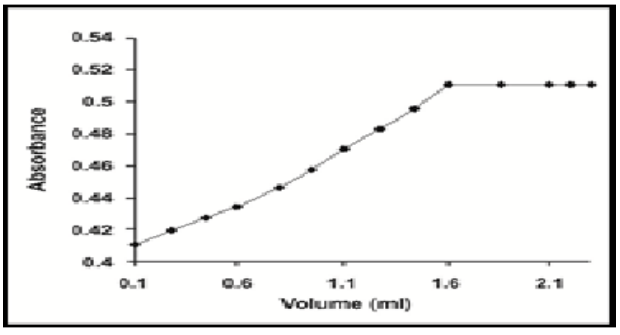

Fig-7: Effect of the volume of 2 mol/L $KMnO_4$ on the intensity of the color produced during the reaction (MPH 25 µg/ml; 1ml of 0.5 mol/l NaOH)

Influence of the NaOH

The reaction rate and absorbance increases with increasing $KMnO_4$ concentration on the formation of MnO_4^{-2} was also examined at constant concentration of drug, Permanganate ion and varying volume (0.2-2.0 ml) of O.5 Mol/L NaOH at 25°C.The optimum absorbance was obtain with 0.9 ml of of 0.5 mol/l NaOH after which increase in volume of NaOH caused no changed in absorbance. Hence 1 ml of 0.5 mol/L NaOH was used throughout the experimental investigation (Fig-8)

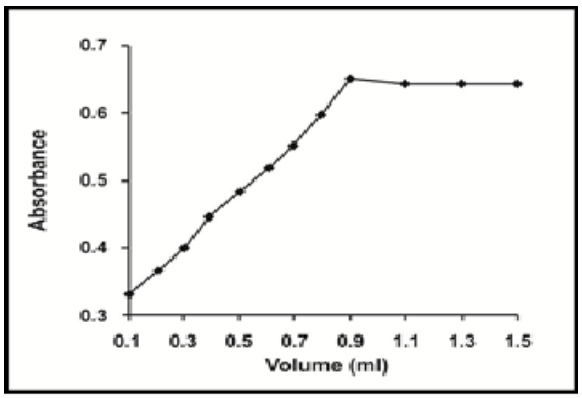

Fig-8:- Effect of the volume of 0.5 mol/L NaOH On the intensity of the color produced during the reaction (MPH 25 µg/ml: 2 ml 5×10^{-3} mol/L $KMnO_4$)

For Method A

The optimum concentration of $KMNO_4$ was 5×10^{-3} M, and optimum volume is 2 ml. The absorbance was measured 10 minutes after the final dilution. The resulted product is stable for 30 minutes thereafter. Alkalinity is maintained with 1ml of 0.5 mol/L of NaOH.

For Method B

The optimum concentration of Sulphanilic acid was 500 mg and of Sodium Nitrite was 200 mg, optimum volume of coloring reagent was 10 ml. The absorbance was measured between first 10 minutes.

Method Validation

The developed method were validated for it's accuracy, precision, reproducibility and selectivity. Also the experiment was repeated three times in a day to determine intra-day precision and on three different days to determine inter-day precision. The percent relative standard deviation was calculated at each concentration level and the results are tabulated. The Reproducibility was confirmed by repeating the three different analyst and the % RSD was calculated

Table 1: Evaluation of Precision of the proposed spectrophotometric methods for MPH

METHOD A		
Amount taken (µg/ml)	**Amount found (µg/ml)**	**% Recovery**
1) 10	10.06±.12	100.02
2) 20	19.94±.18	99.95
METHOD-B		
1) 10	9.72±.18	99.86
2) 20	19.76±.24	99.70

1) Accuracy and Precision of the proposed methods

Accuracy and precision was checked according to USP validation guidelines (TUSP, 2002) at three concentration levels within the specified range, six replicates measurements were recorded at concentration levels. The results are summarized in (table-1) below.

Table 2: Analytical parameters for spectrophotometric determination of MPH in the tablet form by applying methods A and B.

Parameters Optical characteristic.	**Method A**	**Method B**
Maximum wavelength (nm), λmax	610	510
Linearity Range (µg/ml)	2-18	6-18
Intercept (a)	0.575	.14
Std deviation on intercept (Sa)	0.006	.026
Slope (b)	0.03	.06
Std deviation on slope (Sb)	.028	.055
Correlation Coefficient (r)	-0.9987	0.9975
LOD (µg/ml)	0.66	1.43
LOQ (µg/ml)	2.0	4.33
Molar absorptivity L/mol.Cm	5.395×10^{3}	7.014×10^{3}

2) Limit of detection (LOD)

LOD was calculated based on standard deviation of response and the slope of calibration curve. The limit of detection was expressed as.

$$LOD= 3.3\times \sigma/S$$

Where σ is the standard deviation of intercept, S is the standard deviation of slope of calibration curve. The results were summarized in table above indicating good sensitivity of proposed method. According to USP validation guidelines (TUSP, 2002).

3) Limit of Quantitation (LOQ)

LOQ was calculated based on standard deviation of intercept and slope of calibration curve. In this method the limit of quantitation is expressed as.

$$LOQ = 10 \times \sigma/s$$

The result was summarized in table indicating good sensitivity of the proposed method according to USP validation guidelines (TUSP, 2002).

TABLE 3

Tablet of the MPH analyzed by the proposed method as per the procedure described earlier. The result obtained are comparable with standard method

Sample	**MPH FOUND**		
Addwize Tablets.	**Method-A**	**Method-B**	**Standard method[15]**
10.0 mg	10.06mg	9.67mg	10.02mg

CONCLUSION

Two simple, rapid, fairly accurate precise and sensitive Spectrophotometric methods were developed for the determination of MPH in bulk drug and in tablets. The methods are free, rigid over experimental conditions and are characterized by wide linear dynamic ranges and has high sensitivity and employ inexpensive and easily available chemicals. The low detection and quantification limits, simplicity and selectivity make the method suitable for quality control in pharmaceutical industry for routine analysis.

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