Spectrophotometric Determination of Dimethindene in Pharmecutical Preparations and Water Samples

Nief Rahman Ahmed
Department of Environmental Technology / College of Environment, University of Mosul

Received 16 / 05 / 2010 **Accepted** 04 / 07 / 2010

الخلاصة

تم اختبار طريقة طيفية بسيطة وسريعة وذات حساسية ودقة عالية لتقدير الداي ميثيدين في نماذج من الماء وفي بعض مستحضراته الصيدلانية تعتمد الطريقة على أكسدة الداي ميثيدين بواسطة برمنكنات البوتاسيوم في الوسط القاعدي لتعطي ناتج ذو لون اخضر مزرق والذي له أقصى امتصاص عند 610 نانوميتر. وجد بأن قانون بير ينطبق ضمن مدى التراكيز 0.2-2.8-مايكرو غرام/ مل وبلغت قيمة الامتصاصية المولارية ٤×١٠^{٣} لتر.مول$^{-١}$.سم$^{-١}$ وتم دراسة الظروف المثلى للتفاعل وطبقت الطريقة بنجاح لتقدير الداي ميثيدين في نماذج من الماء وفي بعض مستحضراته الصيدلانية. كما وجد أن لا تأثير للمضافات الدوائية في الطريق المقترحة.

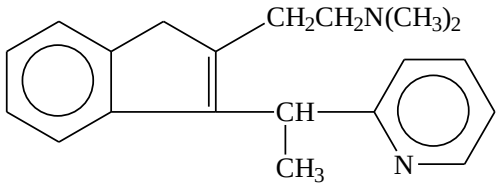
ABSTRACT

A simple, accurate, rapid and sensitive visible spectrophotometric method has been developed for the determination of dimethindene in pure and pharmaceutical preparations. The method is based on the reaction of dimethindene with potassium permanganate in alkaline solution to form a bluish green coloured chromogen with an absorption maximum at 610 nm. Beer's Law was obyed in the range of 0.2-2.8 µg/ml with molar absorbitivity of 4×10^3 L.mol.$^{-1}$.cm^{-1}. The optimum conditions for all colour development are described and the propsed method has been successfully applied for the determination of dimethindene in pharmaceutical preparations and water samples. The common excipients and additives did not interfere in the proposed method.

Key words: Dimethindene maleate, potassium permanganate, spectrophotometric

1. INTRODUCTION

Dimethindene:N,N-dimethyl-2-[3-(RS)-1-(pyridine-2-yl)ethyl]-1h-inden-2-yl]ethanamine. With a molecular formula of $C_{22}H_{24}N_2$ and molecular weight of (292.8). Its structural formula is as follows



It is antihisatamine agent and may be considered as a derivative of the unstandard propylamines [1,2], the antihistamine avtivity resides mainly in the levo-rotory isomer. It is mildly sedative and is reported to have mast-cell stabilizing properties. It is used for the symptomatic relief of allergic conditions including urticaria and angioedema and rhinitis and in pruritic skin disorders. It is also used in compound preparations for the symptomatic treatment of coughs and the common cold [3, 4]. The literature revealed that dimethindene has been determined by mean of a few analytical methods. These include HPLC [5-7], capillary electrophoresis[8]. The spectrophotometric methods using different reagents like 7,7,8,8-tetracyano-quinodimethane (TCNQ) [9], p-chloranilic acid [10], and fast green FCF[11] have also been reported for its determination. These methods suffer from some drawbacks like large number of solvent for the extraction, instability of colour, use of toxic reagents etc. in the present work, a simple sensitive spectrophotometric method for the determination of dimethindene in water samples and in pharmaceutical preparations. The method based on the oxidation of dimethindene by a potassium permanganate to form a bluish green coloured chromogen with an maximum absorption at 610nm.

2. EXPERIMENTAL

2.1 Apparatus

Optima sp-3000 plus UV-visible spectrophotometer with 1.0cm quartz cells was used for all absorption measurements.

2.2 Reagents

All chemicals used were of analytical reagent grade and all solution were prepared in distilled water. A standard solution of dimethindene (100 ppm) was prepared by dissolving 0.1g of pure drug in 1L distilled water. It was later diluted with water to get concentration of 10 ppm. Potassium permanganate 0.02M. This solution was prepared by dissolving 3.2g in 1L distilled water, Then the solution was heated to boling and then filtered

through asbestose. The filtered solution should be kept in the dark and standardized immediately before use. [12]. Sodium hydroxide (10N). This solution was prepared by dissolving 40 g of pure NaOH in 100 ml distilled water.

3. RECOMMENDED PROCEDURE

Different a liquots of standard dimethindene solution equivalent to 5-70µg were transferred into a series of 25ml volumetric flask, 7 ml of 10N NaOH and 4 ml of 0.02M $KMnO_4$ were added. The content was mixed and let stand for 5 min with occasional shaking. The volume was diluted to the mark with distilled water and mixed well. The absorbance of each solution was measured at 610nm against a reagent blank.

3.1 Procedures for pharmaceutical preparations:

3.1.1 Oral drops and syrup:

The content of 5 bottles were mixed well in 1L dried beaker. An a liquots equivalent to 10 mg of dimethindene was transferred into 1L volumetric flask and diluted with distilled water to the volume. The determination of dimethindene proceeded as desired under the recommended procedure.

3.1.2 Capsules:

The content of 10 capsules were mixed thoroughly, an accurate weight equivalent to 10mg of dimethindene was transferred in to 100 ml beaker added 50 ml of water and mixed well for 30 mint filtered, transferred quantitatively to 1L volumetric flask and completed to the volume. The determination of dimethindene proceeded as described under recommended procedure.

3.2 Procedure for water samples

Distilled and tap water samples (100ml) were fortified with 1 mg of dimethindene. the fortified water samples were analyzed as desired under recommended procedure .

4. RESULTS AND DISCUSSION

The reaction between dimethindene and $KMnO_4$ in alkaline medium yields a green colour dye due to the formation of manganate ions, which absorb at 610nm fig(1). The various experimental parameters affecting the development and stability of the reaction product was optimized by changing each variable in turn while keeping all other variables constant.

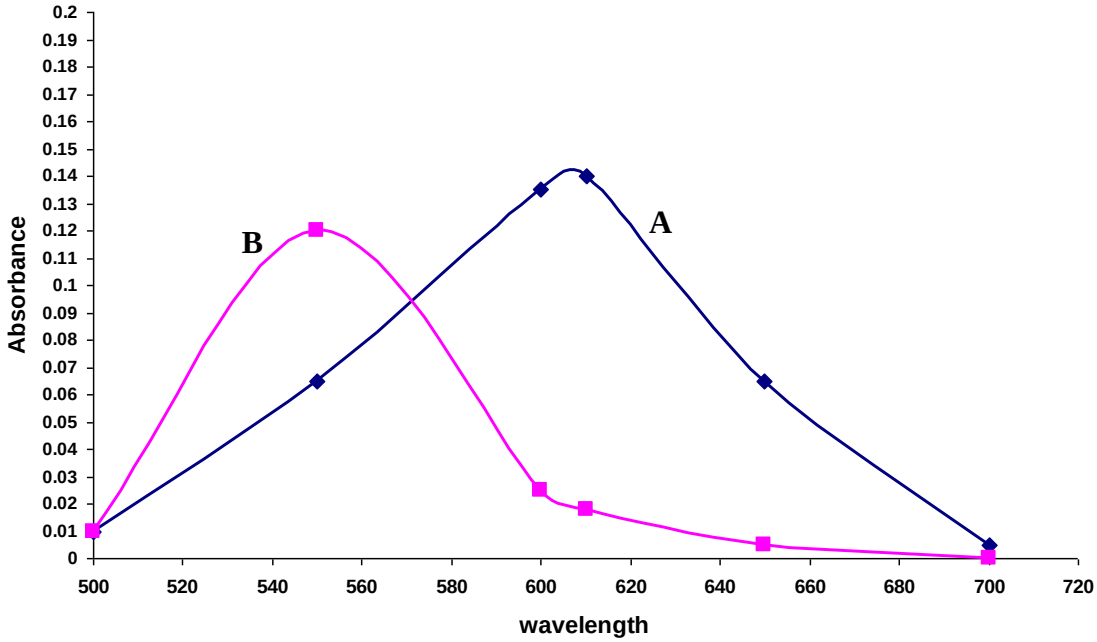


Fig. (1): Absorption Spectra of (A) 1.2 μg/ml dimethidene with $KMnO_4$ in alkaline medium against reagent blank and (B) reagent blank against distilled water

4.1 Effect of $KMnO_4$ concentration

The absorbance increase with increasing $KMnO_4$ concentration. It was found that 4 ml of 0.02M $KMnO_4$ was adequate for the maximum absorbance for the dye formed

4.2 Effect of NaOH

Trials were made to determine the drug through oxidation with $KMnO_4$ in neutral, acidic and alkaline media,but very little oxidation of dimethindene was observed in neutral and acidic solution. It was found that increasing the volume of 10M NaOH would increase absorbance of the reaction product up to 7 ml. after that NaOH has no effect on the absorbance as shown in fig (2)

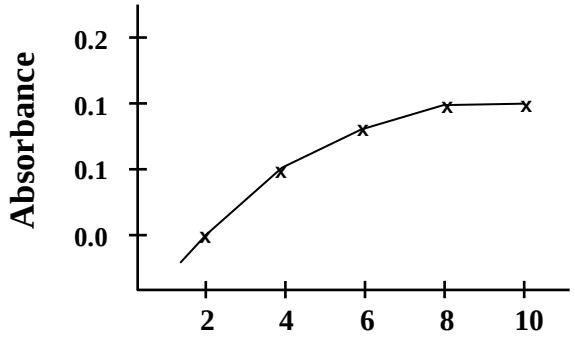


Fig (2): Effect of NaOH-dimethindene (1.2µg/ml)

4.3 Effect of temperature

The resulting product of the proposed method were studied at room temperature (25±5 C^0), Higher temperature causes turbid colour, therefore, room temperature was selected as suitable temperature.

4.4 Effect of reaction time

The colour formed immediately after addition of potassium permanganate and became stable after 5 minutes, therefor 5minutes as a development time was selected as a suitable time in the recommended procedure, the colour obtained was stable for at least 3 hours.

4.5 Effect of order of addition

To test the effect of order of the addition of the reagents on the absorbance of the product, different order were tested. The selected order was sample solution, NaOH followed by $KMnO_4$ solution which was gave high absorbance value.

4.6 Calibration graph

Employing the conditions described in the recommended procedure a linear calibration graph of dimethindene is obtained fig(3), which shows that Beer's law is obeyed over the concentration range 0.2-2.8 µg/ml with correlation coefficient of 0.9998, intercept of 0.027 and slope of 0.036 The limit of detection was evaluated as [13].

$LOD = 3.3\frac{so}{b}$ where (b) is the slope and (so) is the standard deviation of the regression line. The limit of detection was 0.016 µg/ml. The conditional molar absorptivity of the product formed was found to be 4×10^3L. $mol^{-1}.cm^{-1}$

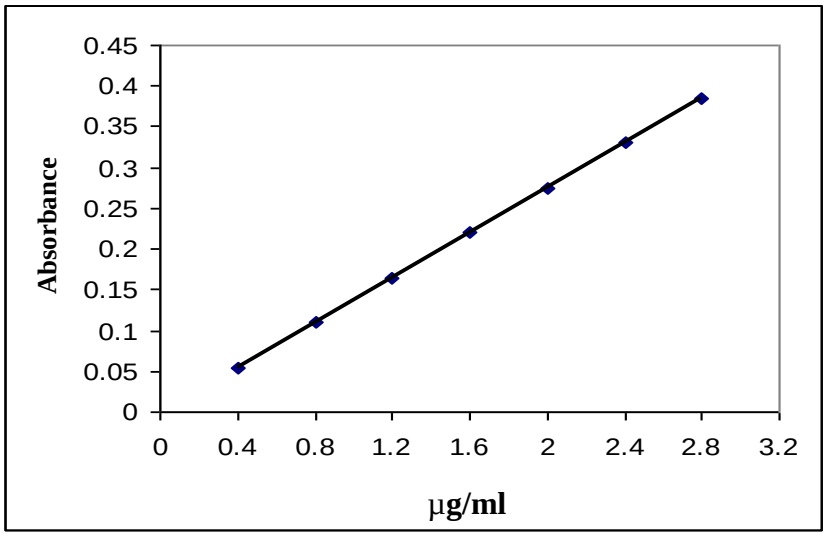


Fig. (3): Calibration graph of dimethindene

5. ACCURACY AND PRECESION OF THE PROPOSED METHOD

To evaluate the accuracy and precesion of the method, a pure drug solution was analyzed at three different concentrations, each determination being repeated six times the relative error (%) and relative standard deviation (%) values are summarized in table (1). From table (1), it is clear that the relative error of less than 1.8% and the method is found to be precise with RSD value less than 2.1%. for a better picture of reproducibility, aseries of experiments were performed in which the standard drug solution was determined at three different levels each day for six days, with all solutions being prepared a fresh each day. The day-to-day relative standard deviation values were in the range of 0.9-2.0 % and represent the best appraisal of repeatability of the proposed methods.

Table(1): Accuracy and precision of the method

Dimethindene taken µg	E_r (%)[a]	RSD %
10	1.2	1.3
20	1.3	2.0
40	1.6	1.5

a: Mean of six determinations

6. INTERFERENCE STUDIES

In order to asses the possible of the proposed method, the effect of substance that often accompany with dimethindene in various pharmaceutical products were studied by adding different amount of substances to 40µg of dimethindene. An attractive feature of the method is its relative freedom from inference by the usual diluents and expcipients in amount for in excess of their normal occurance in pharmaceutical preparations. The results are given in table (2).

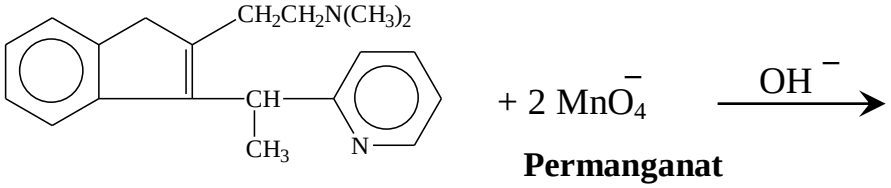
Table (2): Determination of 40µg of dimethindene in the presense of excipients and other substances.

Interfering substances	Amount added / µg	Amount of dimethindene found*	RSD %
Propylene glycol	4000	39.93	1.2
Citric acid	400	40.01	1.1
Na_2HPO_4	600	40.03	0.9
Sodium-saccharine	50	39.98	0.9
Na_2 – EDTA	60	40.05	1.5
Lactose	10000	40.02	1.3
Benzoic acid	100	39.84	1.5
Starch	10000	40.05	1.6
Sorbitol	10000	40.08	1.2
Methyl paraben	100	39.92	1.5

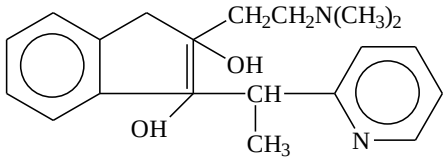
* average of six determinations

7. STOICHEIOMETRY OF THE REACTION:

The stoicheiometry of the reaction between dimethindene and $KMnO_4$ was investigated using job's and mole ratio methods, the result obtained show that 1:2 drug to $KMnO_4$ and the suggested reaction and structure of the product might be written as [14-16]



Permanganat



Manganate
Blush-green

8. ANALYTICAL APPLICATION

The proposed method was satisfactorly applied to the determination of dimethindene in its pharmaceutical formulations and water samples . the results of the assay of the pharmaceutical formulations revels that there is close agreement between the results obtained by the proposed method and the lable claim. The results were also compared statistically by student t-test and by the variance ratio F-test with those obtained by spectrophotometric literature method [17] at 95% confidence level. The calculated t- and F-values did not exceed the theoretical values indicating that there was no significant differences between the precision of the proposed and literature method as cited in table (3) , And the results of water samples table (4) show that the recovery values obtained were close to 100%.

Table(3): Determination of dimethindene in pharmaceutical formulations

Pharmaceutical formulations	Lable amount mg	Found by proposed method * mg	Literature method [17]
Oral drops	0.1%	0.098%	0.091%
Syrup	0.01%	0.01%	0.01%
capsules	4mg/cap	3.97mg/cap.	3.99mg/cap

- mean value of six determinations

Table(4): Determination of dimethindene in water samples

Water samples	Added µg/ml	Found* µg/ml	Recovery %
Tap water	0.3	0.29	96.66
	1.0	0.98	98.00
	2.5	2.47	98.88
Distilled water	0.3	0.303	101
	1.0	0.99	99
	2.5	2.5	100

* mean value of six determinations

9. CONCLUSION

The proposed method was simple, accurate, precise, sensitive and low economical cost. Furthermore, the proposed method doesn't require elaboration of procedures, which are usually associated with chromatographic methods. The proposed method could be applied successfully for determination of dimethindene in pure form as well as in different dosage forms.

REFERENCE:

1) A. F. Casy, "Chemistry of anti-HI histamine antagonists". In Rocha esilva (Edn): Hand book of experimental pharmacology, New York, Spring- Verbage, (1978)

2) Wilson and Glsvold's, "Text-book of organic Medical and pharmaceutical chemistry, 10th Edn,London. Awolter, Kluwer Company, p.670, (1998),

3) Royal pharmaceutical society, Martindal: The Extra pharmacopoeia. 34rd.Edn. London. UK:Royal Pharmaceutical society; p.431, (2005).

4) K. Schaffler, CH. Wauschkuhn & D. Rehn: Evaluation of the local anaesthetic activity of dimethindene maleate laser algesimetry in healthy volunteers, Arzneimittel Forschuny, vol. 42, 1332-1335. (1992).

5) S. Radler and G. Blachke. "Transdermal absorption of dimethindene in man", Archivder Pharmazie, 328, 127-129, (1994).

6) F. Chollet, B. Pholippe, G. Anderegg, V. Ares and R. Lanz, "Determination of dimethindene in human tears by high-performance liquid chromatography", Journal of chromatography B,707,334-337. (1998)

7) D. chollet, P. Kunstner and M. wermeille, "High-performance liquid chromatographic method for the determination of dimethindene in urine" J. Chromatagor, 15, 89-93(1993).

8) M. Heuermann and G. Blaschke, "Simultanous enantioselective determination and quantification of dimethindene and its metabolite N-demethyl-dimethindene in human urine using cyclodextrins as chiral additives in capillary electrophoresis, J. Pharm. Biomed. Anal, 12, 753-760. (1994).

9) A. Badawey, S. Abbas and H. Loutfy, "Spectrophotometric determination of some antihstaminic drugs using 7,7,8,8-tetracyano-quindimethane (TCNQ), "Journal of AOA International,89, 46-52, (2006).

10) A. El. Ragehy, M. Badawy and Z. El Khateeb, Utility of p-chloranilic acid for spectrophotometric determination of some antihistaminic drugs, Analytical letters, 28,2363-2378, (1995).

11) C. Sastry, T. Prasad and M. Suryanarayana, "Extraction-spectrophotometric determination of some antihistaminic agents with fast green FCF, "Microchimica Acta, 100, 107-112, (1990).

12) I. Kolthoff, R. Belcher, V. Stenger & G. Matsnyama, "Volumetric analysis, volume III, Interscience Publishers, New York, p.37,(1957)

13) ICH Harmonized Fripartite Guideline, ICH Topic Q_2n, validation of analytical procedures: Methodology ICH, London 1996.

14) A. Suganthi, HB. Sivakumar, SC. Vijagakumar, P. Ravimathi and TK. Ravi "Visible spectrophotometric determination of valdecoxib in tablet dosage forms", Indian Journal of pharmaceutical sciences, 168, 373-374, (2006).

15) G. C. Hiremath, R. Mulla and S. Nandibewoor, Kinetic methods of determination of atenolol in pure compound and in pharmaceutical formulations; Chem.. Anal. (warsaw), 50, 449-453, (2005).

16) K. Chitra, K. Chitra, K. Sujatha, IR. Ahmed, K. Shalini, and B. Lakshmi. Spectrophotometric estimation of tranexamic acid in bulk and pharmaceutical dosage form, Indian Journal of pharmaceutical sciences, l 66, 836-839,(2004)]

17) N. R. Ahmed, M. A. Basher and S. N. Lottfi: High performance liquid chromatographic and spectrophotometric methods for the determination of dimethindene maleate in pharmaceutical preparations:; J.Edu and Sci, 21,123-134, (2008).