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Spectrophotometric Determination of Paracetamol in bulk and Pharmaceutical Preparations

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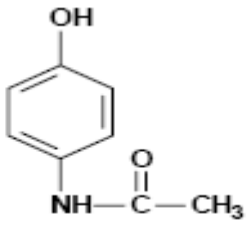
Abstract:

A simple, and rapid spectrophotometric method for the estimation of paracetamol has been developed. The methods is based on diazotisation of 2,4-dichloroaniline followed by a coupling reaction with paracetamol in sodium hydroxide medium. All variables affecting the reaction conditions were carefully studied. Beer's law is obeyed in the concentration range of 4-350 $\mu g ml^{-1}$ at 490 nm .The method is successfully employed for the determination of paracetamol in pharmaceutical preparations. No interferes observed in the proposed method. Analytical parameters such as accuracy and precision have been established for the method and evaluated statistically to assess the application of the method.

Key words: Spectrophotometric determination, Paracetamol, Diazotisation.

Introduction:

Paracetamol is 4-Acetamidophenol; with the following Structural formulae[1,2] in scheme (1)



Scheme(1):Structure of Paracetamol

Paracetamol is a common analgesic and antipyretic drug that is used for the relief of fever, headaches and other minor aches and pains [3].

It belongs to the class of drugs, known as aniline analgesics All the reported methods require expensive reagents and are time consuming.

Spectrophotometric determination is a simple, rapid and sensitive analytical method for quantitative analysis which provides practical and significant economic advantages over other methods. Therefore, they are of frequent choice for pharmaceutical analyses.

Many methods are available in literature for assay of paracetamol in different types of samples including pharmaceutical preparations, including titrimetry [4], Voltammetry[5], electrochemical [6,7], HPLC [8], and spectroscopy[9-11].

The purpose of the current study is to describe the simple Spectro-photometric analytical methods for determination of paracetamol in pharmaceutical preparations.

Materials and Methods:

Equipment:

All spectral and absorbance measurements were using a Computerize UV-Visible, shimadzu T60U Spectrophotometer, with 1cm matched quartz cell

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Chemicals and Reagents

All chemicals used were of analytical reagent grade and paracetamol standard. with (99% purity) was obtained from (BDH) it was provided from Al-Nahrain company for drug industry .

1-A stander solution of 1000 µg ml^{-1} paracetamol was freshly prepared by dissolving 0. 1gm of paracetamol with distilled water to 100 ml

2-.2,4-dichloro aniline of (98.0% purity) was obtained from (Merck) a stander solution of 1000 µg ml^{-1} was freshly prepared by dissolving 0.1gm of 2,4-dichloro aniline in 10ml absolute ethanol and then diluted with distilled water to 100 ml.

3-Sodium nitrite (99.8% purity) from (BDH) and stander solution of 1% were prepared. **4**-Sodium Hydroxide of (98% purity) from (RDL) solution of 1M was prepared by dissolving 4 gm in 100 ml distilled water **5**-1M HCl was prepared and used.

General procedure:

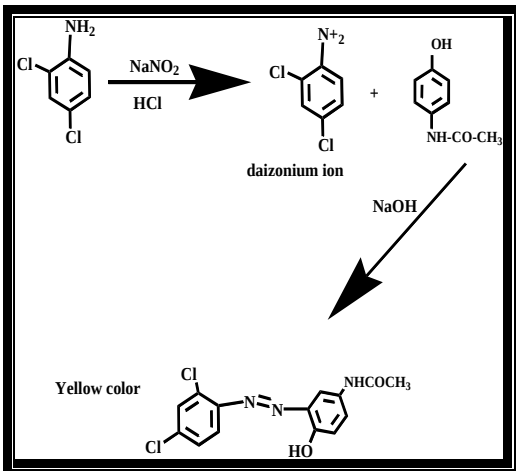
The 3.5 ml of paracetamol standard solution (1000µgml^{-1}) and 0.5 ml of 1M Sodium Hydroxide solutions were added to 1.5 ml of of 2,4-dichloroaniline and 1 ml of 1% sodium nitrite and 0.5 ml of 1M HCl were mixed and completed with distilled water to the mark in 10 ml volumetric flask and shaked for 2 minutes, with shaking and cooling in ice bath for 2 minute, after 5 minutes the yellow color is completely developed and the absorbance measurement was carried out at a wavelength at 490 nm, against a blank solution prepared in the same method but without paracetamol.

Procedure for Assay of paracetamol in Pharmaceutical Preparations

Tablets: ten tablets of paracetamol from Al-Nahrian company drug were weighed and finely powdered. A weighed amount of the powder 0.1g of paracetamol was dissolved in 10 ml ethanol and diluted up to the mark in 50 ml of volumetric flask.

The proposed mechanism

The yallow dye product obtained after coupling paracetamol with an electrophilic of 2,4-dichloroaniline diazotization ion in the presence of alkaline medium. The following mechanism has explain of the reaction as shown in scheme(2).



Scheme (2) The reaction mechanism

Results and Discussion:

The results of this investigation indicated that the reaction between paracetamol with 2,4-dichloroaniline in the presence of sodium nitrite and hydrochloric acid yield highly soluble red colored condensation products which can be utilized as a suitable assay procedure for paracetamol. The colored product has maximum absorption at 490 nm. (Figure 1,C).

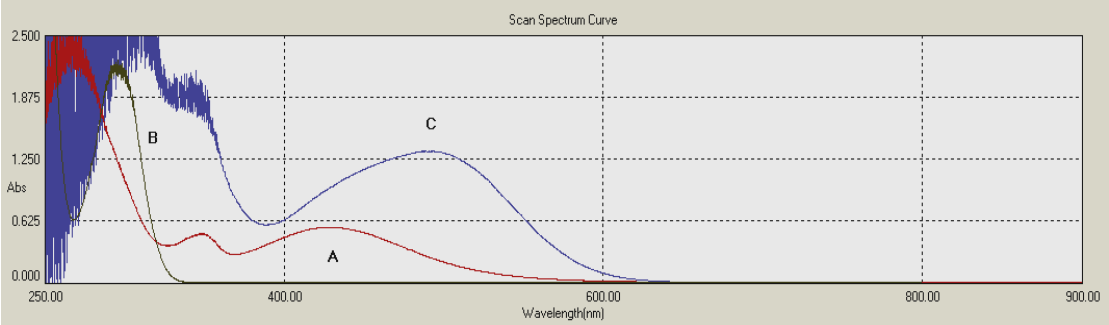


Fig. 1: A) Absorption spectrum of: 2,4-dichloroaniline. (B) Absorption spectrum of paracetamol (C) Absorption spectrum of the azo dye formed, paracetamol/ 2,4-dichloroaniline.

Development time and stability period:

The color intensity reached maximum after formation of azo dye of paracetamol. The color obtained was stable for at least 12 hours and this stability, period was sufficient to allow several measurements to be performed.

The effect of acid:

It was found experimentally that the colored product was stable by using of the amount of 0.5 ml of (1M) hydrochloric acid and then used in determination of paracetamol.

The effect of Base: It was found that the presence of a base led to increase the intensity of the colored product so; 0.5 ml of 1M of NaOH was found that the best volume to give high sensitivity which selected in subsequent experiments.

The effect of sodium nitrite

The optimum concentration of sodium nitrite solution that gave maximum absorption was found to be 1ml of 1% of sodium nitrite solution.

The effect of reagent concentration:

The effect of various concentrations of 2,4-dichloroaniline was investigated using the proposed procedure and adding 0.25-2 ml of 1000µg ml^{-1} 2,4-dichloroaniline. It was found necessary for developing the colored products 1.5 ml of 1000µg ml^{-1} of 2,4-dichloroaniline solution in final volume of 10 ml.

Calibration curve:

Employing the conditions described in the procedure, a linear calibration curve for paracetamol is obtained in Figure (2), which shows that Beer's law is obeyed over the concentration range of **4-350** µg/ml with correlation coefficient of 0.9992 and the conditional molar absorptivity of the yellow product formed was found to be **3219.69** $L.mol^{-1}.cm^{-1}$.

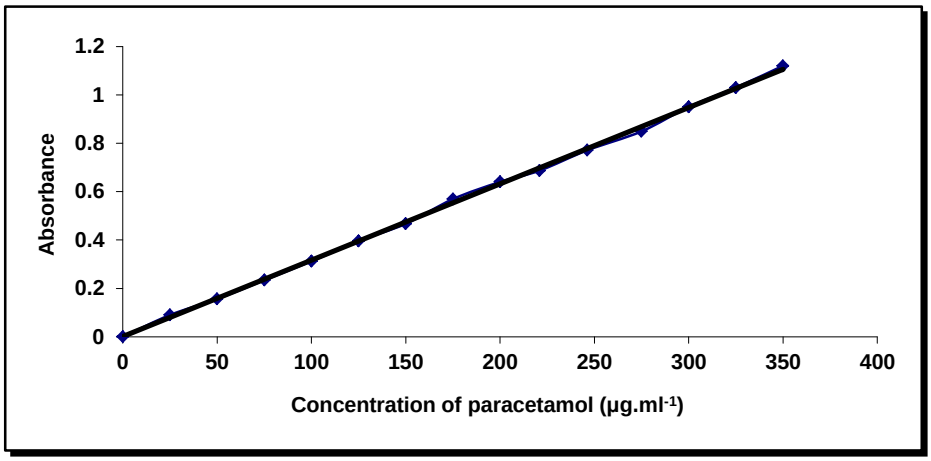


Fig.(2) The calibration curves of paracetamol.

Composition of the Formula structure:

The composition of the formula structure of azo dye was studied by the mole ratio Method [14,15]. A break of 1:1 suggested the formation of paracetamol drug with 2,4-di chloroaniline Figure(3) explain the formula of azo dye.

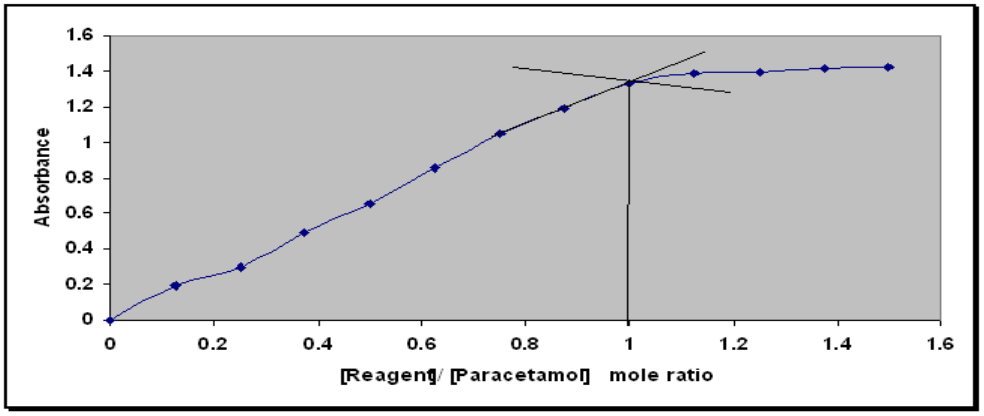


Fig. (3): Mole ratio of the azo dye of paracetamol with 2,4-di chloroaniline.

The effect of Organic solvents

The effect of organic solvents such us methanol, ethanol, ether and distill water was studied by using in the dilution and measuring the absorbances were found 1.118, 1.108, 1.046 and 1.106 respectively. We used distill water because it had best absorbance for it is abundance.

The effect of Interferences

The effete of interference by common organic compounds was determined by measuring the absorbance of a dye solution containing 2 ml of 10^{-4}M of starch, lactose and 4-chloro nitro aniline .It was found no effect of interferences

The accuracy and precision:

To determine the accuracy and high precision of the method, paracetamol is determined at three different concentrations. The results shown in Table (1) indicate that satisfactory precision and accuracy could be attained with the proposed method.

Table 1. Accuracy and precision of the proposed method.

Concentration of paracetamol µg ml^{-1} Taken	Concentration of paracetamol µg ml^{-1} Found	Recovery%	Average Rec%	%E Relative Standard error	Relative Standard Deviation* %
5	4.949	98.98	99.22	1.02	1.55
15	14.871	99.14		0.86	2.05
20	19.19	99.55		0.45	3.05

* Average of five determinations

The analytical application

The Proposed method have been used of drug containing paracetamol (tablet) and they gave good accuracy and precision as shown with table (2), the proposed method were compared with British pharmocopei as standard method, since F-test,T-test showed that there was no significant differences between the proposed method and official method[12], the results obtained were tabulated in Table (3).

Table 2: Determination of paracetamol in pharmaceutical formulations by the proposed method

Pharmaceutical Formulation	Taken µg ml^{-1}	Found µg ml^{-1}	Recovery%	AverageRec%	%E Relative Standard error	Relative Standard Deviation* %
Tablets [a] Pracetamol	10	9.945	99.45	99.415	0.55	3.5
	15	14.907	99.38		0.62	3.25

* Mean of three determinations.
a Marketed by S.D.I, Iraq.

Table 4:Comparison of %Recovery for paracetamol determination by the proposed method and standard method .

Pharmaceutical paracetamol (tablet) µg ml^{-1}	proposed method	standard method
Recovery%		
10	99.415	99.32
15		

Table4:Comparison of paracetamol determination in the proposed method and other literature methods

Reagent	$\Lambda_{max\ nm}$	ε, L mole^{-1} cm^{-1}	Linear range µg.ml^{-1}	Ref.
ammonium molybdate	670	2.6 x 10^4	up to 6	[13]
Derivative spectroscopic method	250	-	5-25	[14]
Simultaneous equation method)	256	-	5-30	[15]
1-napthol or resorcinol	505 485	1.68×10^4 2.86×10^4	Both 2-10	[16]
Simultaneous equation method)	248		3-15	[17]
3-chloro-7-hydroxy-4-methyl-2*H*-chromen-2-one	545	0.12×10^4	10-60	[18]
sodium bismuthate	550	77.27	100-300	[19]
2,4-dichloroaniline	490	3219.69	4-350	Proposed method

Conclusion:

The present study demonstrates an excellent approach for the development of spectrophotometric method for determination of paracetamol with high selectivity and excellent sensitivity than other spectroscopic methods in litretures for diazotization coupling reaction of paracetamol with 2,4-dichloroaniline. The method was applied successfully on pharmaceutical formulations as shown with table(4) .

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تقدير دواء الباراسيتمول طيفيا في المادة النقية وفي المستحضرات الصيدلانية

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جامعة بغداد / كلية العلوم للبنات / قسم الكيمياء ، بغداد ، العراق .

الخلاصة:

استخدمت طريقة طيفية بسيطة وسريعة لتعيين تركيز الباراسيتمول في المادة النقية وفي بعض المستحضرات الصيدلانية إنّ الطريقةَ تعتمد على ازدواج الباراسيتمول مع ملح الديازونيوم للكاشف 2و4- ثنائي كلورو أنيلين عند طول موجي 490 نانومتر ، قانون بير وجد مطاعاً في مدى تركيز4-350 ملغم/لتر.و درست بعناية جميع العوامل المؤثرة على التفاعل ولم يلاحظ تاثير للمتداخلات قدرت الظروف المثلى للتفاعل وكذلك الدقة والضبط ودرست احصائيا وطبقت الطريقة بنجاح لتقدير الباراسيتامول في المستحضرات الصيدلانية.

الكلمات المفتاحية: تقرير الطيفي، الباراسيتامول، Diazotisation.