طريقة مباشرة وطريقة غير مباشرة لتعيين البراسيتامول في مستحضرات صيدلانية بالازدواج التأكسدي مع بارا-امينو-2-هيدروكسي بنزوات الصوديوم

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الخلاصة

طورت طريقتان طيفيتان سهلتان وحساستان لتقدير الباراسيتامول في الوسط المائي. تعتمد الطريقة على اقترانه مع كاشف بارا-امينو-2-هيدروكسي بنزوات الصوديوم (AHB) بوجود العامل المؤكسد بيريودات الصوديوم في الوسط الحامضي لتكوين مركب ذي لون بني برتقالي ذائب في الماء التي يقاس امتصاصها عند الطول الموجي λ_{max}= 470 نانوميتر. وقد بلغت قيمة معامل الامتصاص المولاري 3371 لتر.مول$^{-1}$.سم$^{-1}$ ، ودلالة ساندل تساوي 0.0449 مكغم .سم$^{-2}$ واتبعت الطريقة قانون بير في مدى من التراكيز يتراوح بين 12.5 – 500.0 مكغم من الباراسيتامول في حجم محلول نهائي 25 مل اي 0.5 – 20.0 مكغم.مل$^{-1}$ وتراوح الانحراف القياسي النسبي للطريقة بين0.26 –4.70% ، بينما بلغت دقتها المعبر عنها بنسبة الاسترجاع المئوية بين 95 – 106 %ولخمسة مستويات من تراكيز الباراسيتامول

أما الطريقة الثانية فتعتمد على تقديرالباراسيتامول بصورة غير مباشرة من خلال إجراء تحلل مائي حامضي للباراسيتامول ثم مفاعلة ناتج التحلل (البارا -امينوفينول) مع كاشف بارا-امينو-2-هيدركسي بنزوات الصوديوم (AHB) بوجود بيريودات الصوديوم في الوسط القاعدي، إذ يتكون مركب نو لون بنفسجي مزرق ذائب في الماء يقاس أقصى امتصاص لها عند طول موجي λ_{max}=580 نانوميتر وبامتصاصية مولارية مقدارها 11884 لتر.مول$^{-1}$.سم$^{-1}$ ودلالة ساندل 0.0127 مكغم .سم$^{-2}$. وكانت حدود تطبيق قانون بير بين 12.5–500.0 مكغم من الباراسيتامول في حجم نهائي 25 مل أي 0.5– 20.0 مكغم.مل$^{-1}$ وبمعدل نسبة استرجاع مئوية تراوح بين 94.28–101.60 % وانحراف قياسي نسبي 0.6 –1.1%. طبقت الطريقتان بنجاح على بعض المستحضرات الصيدلانية الحاوية على الباراسيتامول وبالطريقين المباشرة والإضافة القياسية ولثلاثة مستويات من التراكيز.

Direct and Indirect Spectrophotometric Determination of Paracetamol in Pharmaceutical Preparations By Oxidative Coupling With p-Amino-2-hydroxy Sodium Benzoate

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Abstract

New simple and sensitive spectrophotometric methods for the determination of paracetamol in aqueous medium were developed. The first method is based on coupling of paracetamol with p-amino-2-hydroxy sodium benzoate (AHB) in the presence of sodium periodate, as oxidizing agent, to form a brownish-orange compound which shows a λ_{max} at 470 nm. The molar absorptivity (ε_{max}) of the colored product was found to be (3371) $l.mole^{-1}.cm^{-1}$ and Sandel's index 0.0449 $\mu g.cm^{-2}$. The method follows Beer's law in the concentration range of 12.5-500.0 µg of paracetamol in a final volume of 25 ml (0.5-20.0) $\mu g.ml^{-1}$ with relative standard deviation percent (R.S.D%) ranged between 0.26-4.71% and accuracy, expressed by recovery percent, 95-106% for five levels of parcetamol concentration.

The second method is based on indirect spectrophotometric procedure for the determination of paracetamol, after its hydrolysis in acidic medium and the reaction of hydrolyzed product (p-aminophenol) with p-amino-2-hydroxy sodium benzoate in the presence of sodium periodate in alkaline medium. A bluish-violet water soluble compound is formed with λ_{max} =580nm and ε_{max} =11884 $l.mole^{-1}.cm^{-1}$ and Sandel's index 0.0127 $\mu g.cm^{-2}$. Beer's law is applicable for concentration range of paracetamol 12.5-500.0 µg per 25 ml volume of solution (0.5-20.0) $\mu g.ml^{-1}$ with (R.S.D %) ranged between 0.60-1.10 % and recovery percent 94.28-101.6% for three levels of parcetamol concentration. The proposed methods were successfully applied for the determination of paracetamol in pharmaceutical preparations by both direct and standard addition method and for three levels of concentration.

Introduction

Paracetamole chemically known as N-(4-hydroxyphenyl)acetamide is used therapeutically as an analgesic-antipyretic agent alone or associated with other drugs[1], it is effective in

treating mild to moderate pain such as headache, neuralgia, and pain of musculo-skeletal orgin[2].

Several analytical methods have been reported for the analysis of paracetamol in pharmaceutical or biological fluids, include titrimetric [3-6], fluoremetric[7-11], chromatographic[12-14], spectophotometric[15-19] and other procedures[20-23]. Some of these procedures are not simple for routine analysis and require expensive or sophisticated instruments.

Oxidative coupling reactions, which rely on the coupling of two organic compounds in the presence of oxidizing agent under suitable conditions, could be considered as a type among the most important organic reactions which have wide applications in analytical chemistry[24,25].

The present work describes a spectrophotometric procedures for the assay of paracetamol. The first one is based on coupling with p-amino-2-hydroxysodium benzoate in the presence of sodium perchlorate, while the second depends on the oxidative coupling of the acid hydrolyzed product of paracetamol with p-amino-2-hydroxysodium benzoate in alkaline medium.

Experimental

Apparatus

All absorbance measurements were performed by using a Spectronic 21D Uv-visible spectrophotometer, while the spectral measurements were carried out with Centra-5 double-beam spectrophotometer using 1-cm silica match cells. The pH measurements were taken with Jenway pH-meter3310.

Reagents

All reagents were of analytical grade.

1. Paracetamol stock solution (1000 $\mu g.mL^{-1}$) was prepared by dissolving) 0.1gm of pure paracetamol powder (obtained from the state company for drug industries and medical appliance (S.D.I.), Samara-Iraq)in 10 mL of ethanol and diluted to 100 mL with distilled water. Working solutions were freshly prepared by subsequent dilutions.

2. P-amino-2-hydroxy sodium benzoate (AHB) solution (1.0×10^{-2} M) was prepared by dissolving 0.2111gm of the reagent in distilled water and diluted to 100 mL in a volumetric flask.

3. Sodium periodate solution (1.0×10^{-1}M) was prepared by dissolving 2.1389 gm of the salt in 100 mL of distilled water.

4. Acetate buffer solution (pH = 4) was prepared by dissolving 13.7 gm of sodium acetate in 6 mL of glacial acetic acid and making the volume to 100 mL in a calibrated flask. The pH of the resulted buffer mixture was adjusted to pH = 4 ± 0.2 via the addition of glacial acetic acid using a pH-meter.

5. Solutions of pharmaceutical preparations containing paracetamol:
Different pharmaceutical preparations from different sources containing paracetamol were obtained from local market (Table (1)).

a. Solution for tablet analysis: 10 tablets were weighted out , grinded and mixed well. A portion of the resulted powder (containing 0.1 gm of paracetamol) was used for the

preparation of the solution as described before. The resulted solution was filtered off and subsequently diluted to obtain working solutions.

b. Solution for suppositories analysis: The containing of five suppositories was mixed well and a weight from the resulted mixture containing 0.1 gm of paracetamol was dissolved in 10 mL of ethanol and a little amount of hot distilled water. The solution was then diluted to 100 mL with hot distilled water and the volume was checked after the solution been cooled. Working solutions were prepared after filtration of the prepared stock solution.

c. Hydrolyzed paracetamol solution: 25 mL of concentrated hydrochloric solution was added to 150 mL of 1000 $\mu g.mL^{-1}$ of stock paracetamol solution in a round bottom flask. The mixture was refluxed for 1hr and after cooling the volume was diluted to 250 mL with distilled water. A 600 $\mu g.mL^{-1}$ of the hydrolyzed paracetamol (as p-aminophenol) stock solution was obtained and working solution were freshly prepared after neutralizing (pH = 7) the required aliquots of stock solution with 20% sodium carbonate solution before dilution with distilled water.

d. Solutions of drugs for analysis by direct and standard addition methods: To 60 mL of 1000 $\mu g.mL^{-1}$ solution of drug (tablet or suppositories), which is prepared as described before, 10 mL of concentrated HCl solution (11.8 M) was added and the mixture was refluxed for 1 hr. After cooling the mixture was diluted with distilled water in a 100 mL volumetric flask. Working solutions were freshly prepared for each drug (100 $\mu g.mL^{-1}$) after adjusting the pH to 7 with 20% sodium carbonate solution.

Recommended Procedures

1.Direct Determination of Paracetamol :

a.Calibration curve procedure: To a series of 25-mL volumetric flasks, different volumes (0.25 – 10 mL) of standard 50 $\mu g.mL^{-1}$ of paracetamol solution were added followed by the addition of 1.6 mL of 0.1 M of $NaIO_4$ solution, 0.6 mL of AHB reagent solution (1×10^{-2} M) and 2.0 mL of acetate buffer solution. The volume in each flask was diluted with distilled water and the absorbance of the formed colored compound was measured at 470 nm against reagent blank solution after 30 minutes. Figure (3) shows that linear calibration graph was obtained in the range of paractamol solution of (0.5 – 20.0 $\mu g.mL^{-1}$) while higher concentrations show negative deviations from Beer's law.

b. Standard addition procedure: Standard addition procedure was used for the assay of paracetamol contained in pharmaceutical preparations at three concentration levels (viz. 1, 5 and 10 $\mu g.mL^{-1}$) as follows; to a series of five 25-mL calibrated flasks, aliquots of the sought drug solution containing (25 or 125 or 250 µg) of paracetamol were transferred followed by the addition of (0, 0.5, 1.0, 1.5 and 2.0 mL) of standard paracetamol solution (100 $\mu g.mL^{-1}$) respectively. The resulted mixtures were then treated as described in the calibration curve procedure and the absorbances were measured at 470 nm after standing for 30 minutes.

2.Indirect Determination of Paracetamol :

a.Calibration curve procedure: To a series of 25 mL calibrated flasks, different volumes (0.25 – 10 mL) of 50 $\mu g.mL^{-1}$ of the hydrolyzed paracetamol solution were added followed by the

addition of of 0.2 mL of $NaIO_4$ solution (0.1 M), 3 mL of AHB solution (1.0×10^{-2} M) and 2 mL of NaOH solution (1.0 M). Dilution was made with distilled water and the absorbance was measured after 20 minutes at λ_{max} = 580 nm against reagent blank. Figure (6) shows the calibration curve which is linear in the concentration range of (0.5 – 20 $\mu g.mL^{-1}$) of paracetamol.

b. Standard addition procedure: The method was applied to cover three concentration levels of paracetamol (hydrolyzed as described before) in the studied druges (viz. 2.0, 4.0 and 10.0 $\mu g.mL^{-1}$) applying the following procedure; to a series of five 25 mL calibrated flasks aliquots of the studied drug solution (hydrolyzed as described before) containing (50 or 100 or 250 µg) of paracetamol were transferred, followed by the addition of (0, 1, 2, 3 and 4 mL) of standard hydrolyzed paracetamol solution (50 $\mu g.mL^{-1}$) resepectively. The resulted mixtures were treated as described in calibration curve procedure and the absorbances were measured at 580nm after standing for 20 minutes.

Results and Discussion

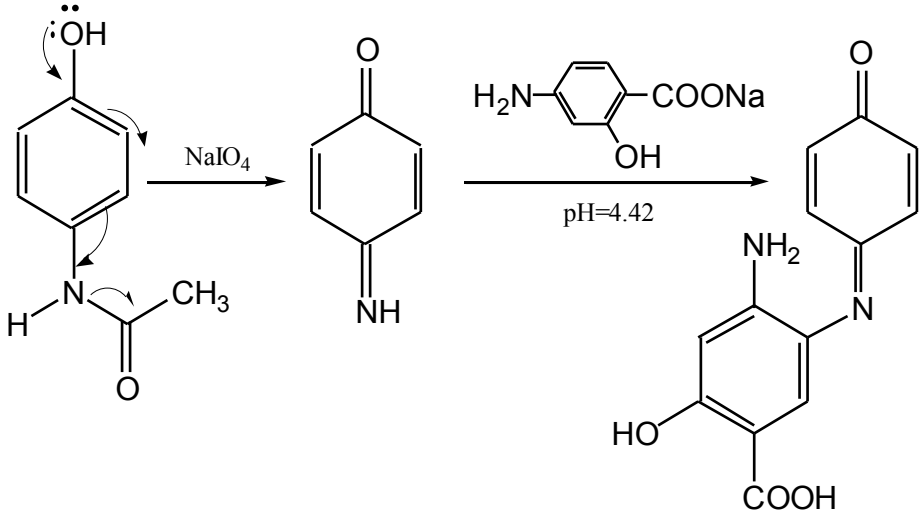
1.Direct Determination of Paracetamol

The present work depends on quantitative oxidative-coupling of paracetamol via reaction with 4-amino-2-hydroxy sodium benzoate followed by spectrophotometric determination of the resulted colored compound. Preliminary investigations showed that a brownish-orange product resulted upon treating paracetamol solution with AHB and $NaIO_4$ in acidic medium. The absorbance of the colored product was measured at 470 nm against reagent blank solution and its absorbance was found to be stable after 30 minutes of mixing(Fig. 1 a).

A univariate study of the variables affecting the color development of reaction product, namely the amount of reagent for the range of (0.2 – 1.2 mL) of 0.1 M, the amount of oxidizing agent for the range (0.2 – 2.0 mL) of 0.1 M, the pH of the oxidation medium by using different volumes (0.2 – 6.0 mL) of acetate buffer (pH = 4.47), the order of mixing of analyte and reagent solutions and the of reaction temperature (17.5 ºC, 20 ºC, 25 ºC, 30 ºC, 40 ºC), was performed on a 20 $\mu g.mL^{-1}$ of the analyte solution.

One milliliter of AHB reagent solution was selected as an optimum amount (Fig.1b), and was used subsequently. Among different types and amounts of oxidizing agents which were investigated, 1.6 mL of 0.1 M solution of $NaIO_4$ was found to be the optimum (Fig.1c). Different types of buffer solutions (acidic and basic) were tested to control the pH of reaction medium. The study showed that using 2 mL of acetate buffer (pH = 4.42) gave the best result (Fig.1d). Table (2) illustrates the results obtained when different orders of mixing of analyte and reagents solutions were followed. The optimum order which gave the highest absorbance was: paracetamol solution(S) + $NaIO_4$ solution (O) + AHB reagent solution (R) + acetate buffer solution (B).

A suggested mechanism for the reaction is proposed in which paracetamol oxidized in the presence of $NaIO_4$ to form a benzoquinon immine which in turn couples with AHB through ortho-position to $-NH_2$ group in acidic medium as shown in the following scheme.



Final Absorption Spectrum

Absorption spectrum of the colored product formed under optimum reaction conditions shows a maximnm absorption at 470 nm in contrast to reagent blank Fig (2).

Calibration Graph

Applying the conditions described in the recommended procedure, a linear calibration plot for paracetamol concentration in the range of (0.5 – 20 $\mu g.mL^{-1}$) against the measured absorbance is obtained (Fig.(3)) with correlation coefficient of 0.9995. The conditional molar absorptivity was found to be 3.371×10^3 liter. $mole^{-1}$. cm^{-1} and Sandle's index 0.0449 $\mu g.cm^{-2}$.

Interferences

To assess the possibility of the analytical application of the proposed method, the effect of the presence of some foreign substances (viz. talk, glucose, lactose, starch) was studied by adding different amounts of the mentioned compounds to 15 $\mu g.mL^{-1}$ of paracetamol solution and applying the recommended procedure for color development. Each of the studied compounds was considered not to interfere if its addition causes a relative error less than 5%. It was found the presence of 200 $\mu g.mL^{-1}$ of each of the compounds is tolerated in the determination of paracetamol.

Precision and Accuracy

To check the precision and accuracy of the proposed method, three replicate of paracetamol solution were determined under the established conditions at five concentration levels. The results are listed in Table 3.

Analytical Applications

Five types of commercially available paracetamol containing pharmaceutical preparations were analyzed. On applying the recommended procedure, good recoveries were obtained (Table 4).

Comparison with Other Methods

To assess the validity of the proposed method which was checked by comparing the results with those obtained by standard methods (Table 5). Moreover, F-test and t-test show that there were no significant difference between the proposed and standard methods.

2.Indirect Determination of Paracetamol

In this procedure, the acid hydrolysis product of paracetamol (i.e. p-aminophenol) is oxidized by sodium periodate and coupled with AHB in sodium hydroxide medium to yield a brownish-violetwater soluble dye which absorbs at 580 nm.

The experimental conditions for the color producing reaction were optimized by following the same steps mentioned in the direct method starting with arbitrary conditions (i.e. mixing 1.0 mL of 0.1 M of $NaIO_4$ solution, 1.0 mL of 1 x 10^{-2}M of AHB solution and 1.0 mL of NaOH solution in a volumetric flask containing 300 µg of the analyte) and measuring the absorbance of the colored product after 20 minutes at 580 nm against reagent blank solution(Fig. 4 a).

The effect of using different volumes of coupling reagent solution(1.0 x 10^{-2} M) was investigated, and the results show that 3.0 mL gave the highest absorbance (Fig.4 b) which was used as a subsequent work.

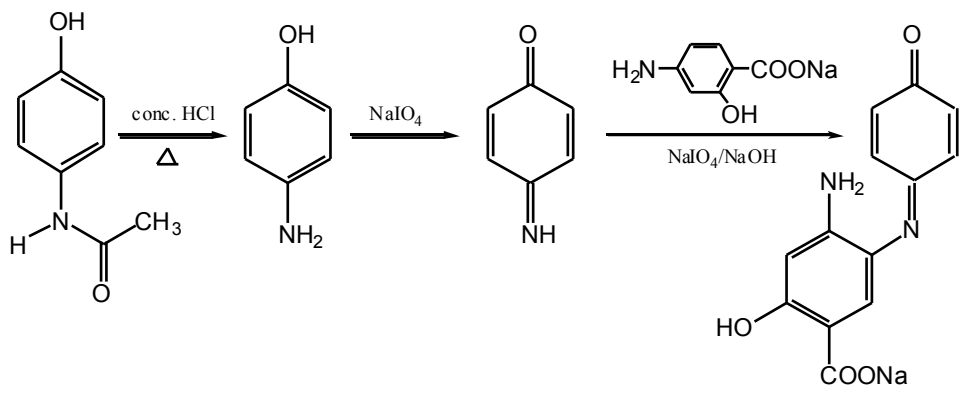
The results obtained from using various volumes (0.1 – 2.0 mL) of 0.1M of $NaIO_4$ (Fig.4 c), indicate that 0.2 mL of the oxidizing reagent was the optimum.

The study shows that a stable color product could only be obtained in alkaline medium, therefore, the reaction was carried out in the presence of ammonium buffer (pH range 9 – 12) and in the presence of NaOH. Figure (4 d) shows that using 2.0 mL of 1.0 M NaOH solution resulted in obtaining the best results.

The order of addition of the reacting solutions shows that the following order : (S) + (O) + (R) + (B) must be followed to obtain the highest absorbanc (Table 6).

Finally, the effect of temperature on the color reaction was investigated in at the given values (20 ºC, 25 ºC, 30 ºC, 40 ºC and 50 ºC). The investigation shows that the colored product is not stable at elevated temperatures, therefor, the reaction was carried out at room temperature (i.e. 20 ºC).

A mechanism was suggested for the oxidation of the hydrolysis product of paracetamol via $NaIO_4$ and coupling with AHB to form the coloed product in alkaline medium as follows:



Final Absorption Spectrum

The absorption spectrum of the colored product was recorded, for the range (400 – 700 nm), under established optimum conditions against reagent blank solution. Figure (5) shows a spectrum with wavelength of maximum absorption(λ_{max}) at 580.

Calibration Graph

Employing the recommended procedure, Beer's law is obyed over the range of (12.5 – 500 $\mu g.mL^{-1}$) of paracetamol per 25 mL of solution with correlation coefficient of 0.9956 (Fig. 6). The conditional molar absorptivity for the colored product was found to be 11884 liter. $mole^{-1}.cm^{-1}$ and Sandl's index was 0.0127 $\mu g.cm^{-2}$.

Interferences

The presence of 250 $\mu g.mL^{-1}$ of foreign substances (talk, lactose and starch) can be tolerated in the analysis of 12 $\mu g.mL^{-1}$ of paracetamol solution since it would cause relative error percent less than 5%.

Precision and accuracy

The precision of the proposed method was calculated in term of R.S.D.% and its accuracy in term of relative error percent for three replicates of solution at three concentration levels (2, 10 and 20 $\mu g.mL^{-1}$). Satisfactory results were obtained under optimum conditions (Table 7).

Analytical application

Table (8) shows the results obtained upon application of the proposed method in the determination of five drugs containing paracetamol.

Comparison with other methods

Table (9) shows the results obtained by the proposed and other standared methods. Both F-test and t-test were applied and showed that there were no significant differences between the results obtained in comparison with standard methods.

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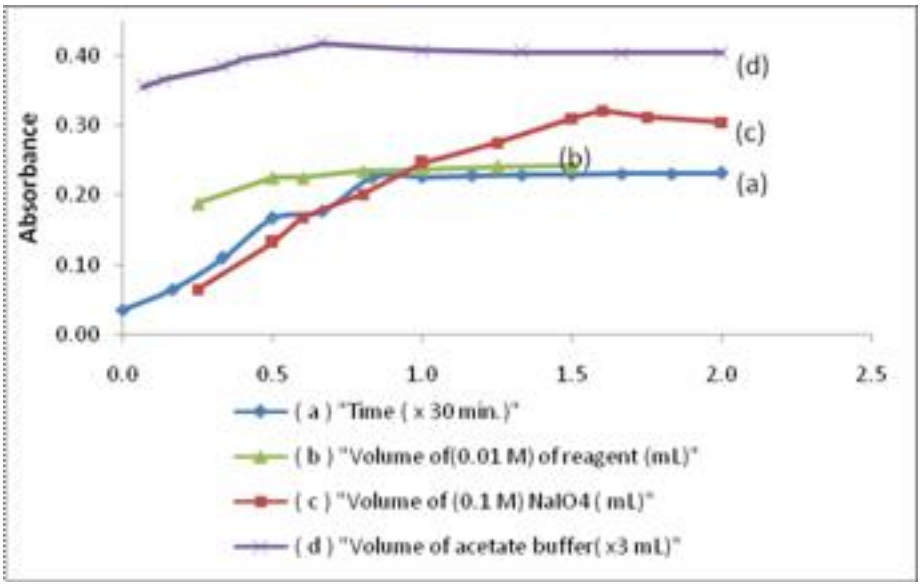

Fig. (1): Optimization of experimental conditions.

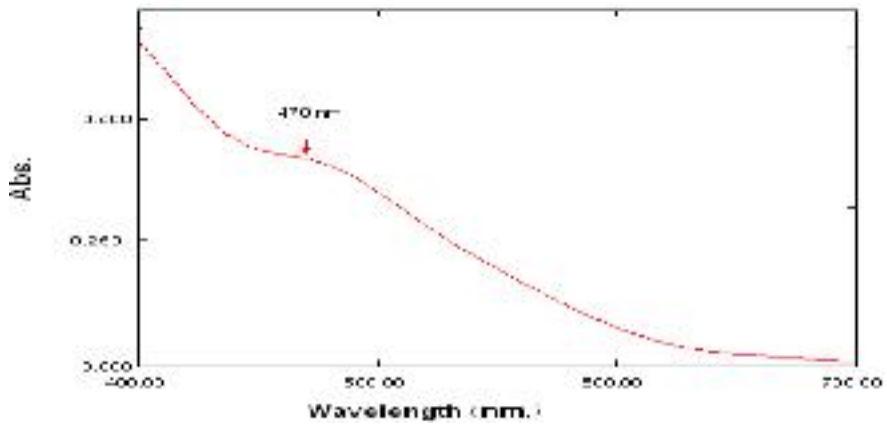

Fig. (2): Final absorption spectrum.

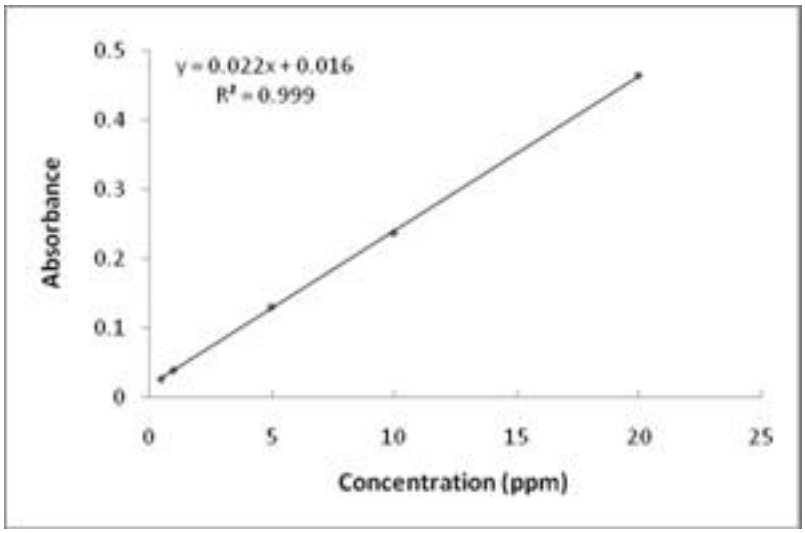

Fig. (3): Calibration graph of paracetamol

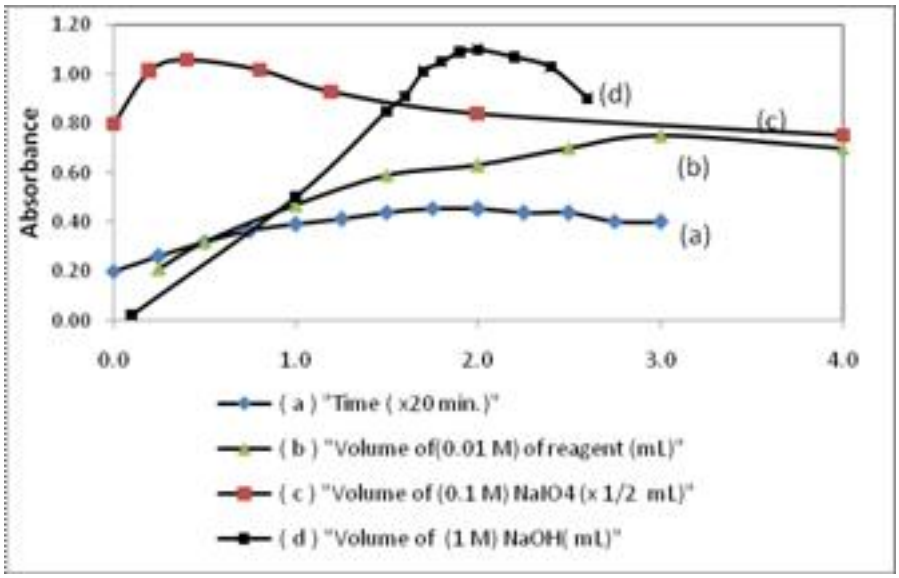

Fig. (4): Optimization of experimental conditions.

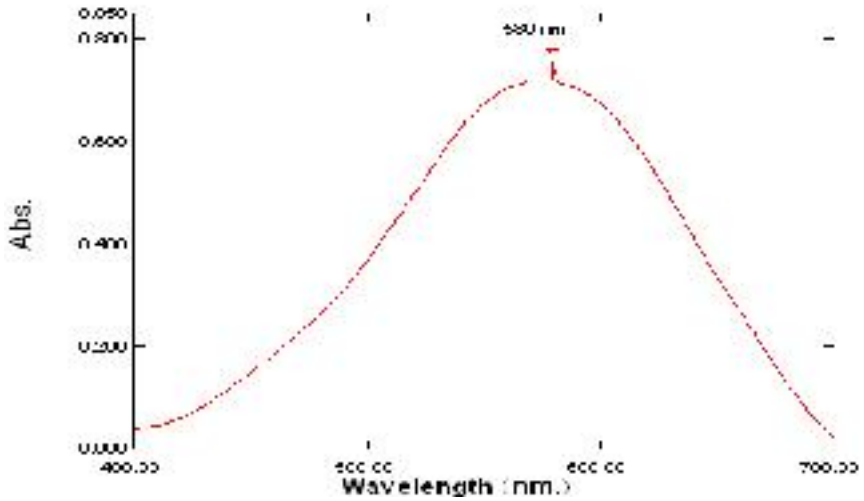

Fig.(5): Final absorption spectrum.

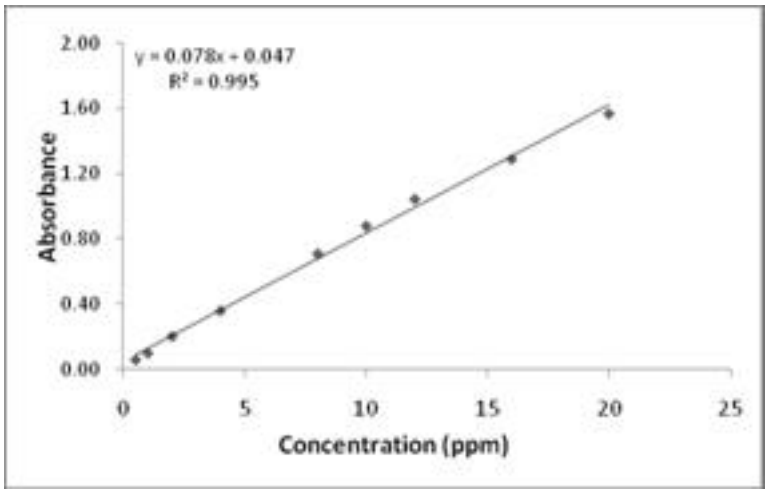

Fig. (6): Calibration graph of paracetamol.

Order of addition	Absorbance
S+O+R+B	0.466
O+S+R+B	0.465
R+S+O+B	0.459
B+S+O+R	0.389
O+R+B+S	0.431
R+O+S+B	0.445

Table (1): Pharmaceutical preparations used

Pharmaceutical preparation	Contains	Company
Paracetamol tablets	500 mg paracetamol	S.D.I -Iraq
Algesic tablets	350 mg paracetamol 50 mg caffeine 10 mg codeine phosphate	S.D.I -Iraq
Paramol tablets	500 mg paracetamol	U.K- London
Kanagesic tablets	450 mg paracetamol 35 mg orphenadrine citrate	M.P.K- Syria
Panatol delta Suppositories	250mg paracetamol	S.A.R

Table (2): Effect of order of mixing

Table(3): Precision and accuracy of the method

Taken Conc. (ppm)	Found Conc. (ppm)			Average	Recovery (%)	Error (%)	R.S.D (%)
0.5	0.4909	0.4507	0.4839	0.4751	95.0202	-4.9798	4.5156
1	1.1261	1.0334	1.0456	1.0684	106.8377	+6.8377	4.7155
5	5.0876	5.1125	5.0904	5.0968	101.9363	+1.9363	0.2681
10	9.6469	9.8640	9.8092	9.7734	97.7341	-2.2659	1.1549
20	20.1984	20.0394	20.7091	20.0863	100.4315	+0.4315	0.2796

Table (4): Analytical application of the direct and standard addition methods.

Pharmaceutical preparation	Procedure	Amount			Recovery (%)	
		Certified value (mg)	Conc. Of Paracetamol (µg/ml)	Found Value(mg)	Each assay	Average
Paracetamol tablets S.D.I –Iraq	Calibration curve	500	10	522.8460	104.5690	101.2435
			5	509.0640	101.8120	
			1	486.7421	97.3484	
	Standard addition		10	507.591	101.5182	99.3506
			5	490.675	98.1350	
			1	492.00	98.4000	
Algesic tablets S.D.I –Iraq	Calibration curve	350	10	365.5990	104.456	102.0797
			5	364.2092	104.059	
			1	342.0296	97.7226	
	Standard addition		10	351.583	100.4523	100.2193
			5	351.344	100.3840	
			1	349.376	99.82172	
Paramol tablets U.K- London	Calibration curve	500	10	485.3933	97.0787	98.7492
			5	501.5730	100.314	
			1	494.2322	98.8464	
	Standard addition		10	502.4390	100.4878	100.5014
			5	502.7851	100.5570	
			1	502.2971	100.4594	

Kanagesic tablets M.P.K- Syria	Calibration curve	450	10	453.7079	100.823	100.3779
			5	458.1573	101.812	
			1	443.1236	98.4969	
	Standard Addition		10	452.1344	100.4743	100.5266
			5	453.4599	100.7688	
			1	451.5152	100.3367	
Panatol delta S.A.R	Calibration curve	250	10	261.4232	104.569	104.3645
			5	260.1498	104.059	
			1	261.1610	104.464	
	Standard addition		10	249.2453	99.69812	100.3144
			5	250.9978	100.3991	
			1	252.1151	100.8460	

Table (5): Comparison with other methods

Drug samples	Recovery %	
	The proposed method	Standard method
Pure Paracetamol	100.394	101.000*
Paracetamol tablets S.D.I –Iraq	101.243	99.000*
Algesic tablts S.D.I –Iraq	102.079	97.970**
Paramol tablts U.K- London	98.749	100.501***
kanagesic tablts M.P.K- Syria	100.377	100.526***
Panatol delta S.A.R	104.364	100.314***

* British Pharmacopoeia B.P, ** S.D.I standard methods ,

*** Oxidative coupling versus standard addition value.

Table (6): Effect of order of mixing

Order of Addition	Absorbance
S + O + R + B	1.062
S + R + O + B	1.026
S + B + O + R	0.872
R + O + S + B	0.950
R + S + B + O	0.954
B + S + O + R	0.898
O + S + R + B	1.020
O + R + B + S	0.794

Table (7): Precision and accuracy of the method.

Taken Conc. (ppm)	Found Conc. ($\mu g.ml^{-1}$)			Average	Recovery (%)	Error(%)	R.S.D(%)
2	1.8651	1.8899	1.9022	1.8857	94.2863	-5.7137	1.0025
10	10.0582	10.1448	10.2809	10.1613	101.6130	+ 1.6130	1.1052
20	19.9839	19.8601	20.1077	19.9839	99.9196	-0.0804	0.6193

Table (8): Analytical application of the direct and standard addition methods.

Pharmaceutical preparation	Procedure	Amount			Recovery (%)	
		Certified value (mg)	Conc. of Paracetamol (µg/ml)	Found Value(mg)	Each assay	Average
Paracetamol tablets S.D.I –Iraq	Calibration curve	500	10	506.8948	101.3789	99.7617
			4	493.2985	98.6597	
			2	496.2322	99.2464	
	Standard addition		10	504.8823	100.9764	100.9449
			4	504.9708	100.9941	
			2	504.3217	100.8643	
Algesic tablets S.D.I –Iraq	Calibration curve	350	10	336.4066	96.1161	99.2741
			4	348.4753	99.5643	
			2	357.4970	102.1421	
	Standard addition		10	356.9930	101.9980	101.5203
			4	354.3256	101.2359	
			2	354.6450	101.3271	
Paramol tablets U.K- London	Calibration curve	500	10	486.9397	97.3879	99.3166
			4	491.4631	98.2926	
			2	511.3459	102.2692	
	Standard addition		10	505.4348	101.1087	101.0055
			4	502.8191	100.5638	

			2	506.7203	101.3440	
Kanagesic tablets M.P.K- Syria	Calibration curve	450	10	458.2759	101.8391	100.8003
			4	448.0397	99.5644	
			2	454.4884	100.9474	
	Standard Addition		10	453.9413	100.8758	99.6598
			4	450.9009	100.2002	
			2	440.4731	97.8829	
Panatol delta S.A.R	Calibration curve	250	10	257.7771	103.1108	103.6618
			4	264.0131	105.6052	
			2	255.6730	102.2692	
	Standard addition		10	246.2356	98.4942	100.3073
			4	252.5189	101.0076	
			2	253.5550	101.4220	

Table(9): Comparison with other methods.

Drug samples	Recovery %	
	The proposed method	Standard method
Pure Paracetamol	99.7617	101.0000*
Paracetamol tablets S.D.I –Iraq	98.6000	99.0000*
Algesic tablts S.D.I –Iraq	99.2741	97.9700**
Paramol tablts U.K- London	99.3165	100.5014**
kanagesic tablts M.P.K- Syria	100.8002	100.5260***
Panatol delta S.A.R	103.6617	100.3140***

* British Pharmacopoeia B.P, ** S.D.I standard methods ,

*** Oxidative coupling versus standard addition value.