International Journal of Recent Research and Review, Vol. XI, Issue 2, June 2018

ISSN 2277 – 8322

Using of 2,5-Dihydroxy Benzyldehyde in Spectrophotometric Assay of Paracetamol in Pharmaceutical Preparations

Mohammed. S. Younis, Nabeel .S.Othman

Department of Chemistry, College of Science, University of Mosul, Iraq

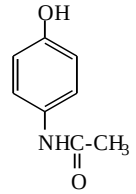
Email : nsn20002004@yahoo.com

***Abstract*- A simple, accurate and sensitive indirect spectrophotometric method for the determination of paracetamol (PAR) in aqueous solution, the method was based on the oxidative coupling reaction of p-amino phenol (PAP) which resulted from acid hydrolysis of PAR with 2,5-di-hydroxy benzaldehyde (2,5-DHB) in presence of potassium periodate as oxidizing agent to produce colored compound, water-soluble and stable product, which exhibit maximum absorption at 534 nm. Beer's law was obeyed over the range 0.25-3.0 μg.ml^{-1} of PAR in final volume of 10 ml, with a molar absorptivity of 0.347×10^{4} l.mol^{-1}.cm^{-1} and Sandell's sensitivity index of 0.04348 μg.cm^{-2}, limit of detection (LOD) 0.0479 μg.ml^{-1} ,limit of quantitation (LOQ) 0.159μg.ml^{-1} , a relative error of 1.33 to 2.14 and relative standard deviation not more than 2.52 % depending on the concentration level. The method has been successfully applied to the determination of PAR in pharmaceutical preparations.**

***Keywords*- spectrophotometric, paracetamol, 2,5-dihydroxy benzaldehyde, oxidative coupling.**

I INTRODUCTION

Paracetamol [acetaminophen, N-acetyl-p-aminophenol, 4-acetamidophenol] ,it has analgesic and antipyretic properties with week anti-inflammatory activity, it is used in the symptomatic management of moderate pain and fever [1]. PAR has the following chemical structure [2].



Paracetamol,N-(4-Hydroxyphenyl) acetamide

The assay of PAR is still the object of investigation, a survey of the literature showed that various methods have been used for quantitative determination of PAR ,these methods included: HPLC [3-6], voltametric [7-10] and electrochemical [11]. Spectrophotometry is considered as the most convenient analytical technique in pharmaceutical analysis because of its intrinsic, simplicity and availability in most quality control laboratories [12-19]. The objective of the investigated reported in this paper is to evaluated simple and accurate spectrophotometric method for the determination of PAR. The method is based on oxidative coupling of PAP with 2,5-DHB reagent in presence of KIO4 as an oxidizing agent to produced an a soluble and stable colored product.

II. EXPIMENTAL SETUP

All spectrophotometric measurements were performed on Jasco V-630(Japan) spectrophotometer using 1 cm glass and quartz cells, pH meter type HANNA PH 211 was used for pH reading.

Reagents -

All chemicals used in this investigation are of analytical – reagent grade, and paracetamol standard material was

provided from General Establishment for Medical Appliance and Drugs / SDI – Samaraa / Iraq.

Solutions -

2,5- DHB , 0.1 % - This solution was prepared daily by dissolving 0.1 g of 2,5-DHB(Fluka) in 100 ml distilled water.

KIO4 0.01 M –

This solution was prepared by dissolving 0.1 g of KIO4 (Fluka) in 100 ml distilled water.

Standard solution of paracetamol, 1000 $\mu g.ml^{-1}$ –

This solution was prepared by dissolving 0.25g of paracetamol in 10 ml ethanol, then the solution was completed to 250 ml in a volumetric flask with distilled water .

Solution of hydrolyzed- PAR,100 $\mu g.ml^{-1}$ *(HPAR,PAP)*-

This solution was prepared by transferring 150 ml of 1000 $\mu g.ml^{-1}$ PAR into 250 ml round-bottomed flask provided with condenser, 25 ml of hydrochloric acid(11.8N) was added then refluxed for 1 hour, after that the cold solution was neutralized with 20% of sodium carbonate solution and diluted to 250 ml with distilled water in a volumetric flask. To prepare a solution equivalent to 25 $\mu g.ml^{-1}$ PAR, 4.15 ml of the above solution was diluted to 100 ml in a volumetric flask using distilled water [20].

Standard drugs solutions -

The various dosage forms used in this investigation where tablets, injections, and syrup.

Tablets, 100 $\mu g.ml^{-1}$ -

A 10 tablets where powdered and the powder equivalent to 250 mg of PAR was weighed and dissolved in 10 ml ethanol,then100-150 ml distilled water was added, shaking to increase the solubility, filtered into 250 ml calibrated flask, then the solution was completed to the mark with a distilled water, and proceed as mentioned above in preparation of HPAR solution [20].

Syrup solution, solution, 100 $\mu g.ml^{-1}$ –

A 10.41 ml of antipyrol syrup(each 5ml contain 120 mg PAR) was diluted to 250 ml with distilled water in a volumetric flask, then 150 ml was taken and proceed as mentioned above in preparation of HPAR solution.

Injection solution, 100 $\mu g.ml^{-1}$ –

250 mg equivalent of injection was transferred to a 250 ml volumetric flask and diluted to the mark with distilled water, then 150 ml was taken and proceed as mentioned above in preparation of HPAR solution.

Procedure and calibration graph-

To a series of 10 ml calibrated flasks, transfer 0.1 – 1.2 ml (25 $\mu g.ml^{-1}$) of hydrolysed paracetamol solution , after that a 1 ml of $1.25x10^{-3}$ M of 2,5- DHB solution and 1 ml of KIO4 (0.015M) were added . The volumes were completed to the mark with distilled water and the absorbance was read at 534 nm against the reagent blank. A linear calibration graph was obtained over the concentration range of 0.25 – 3 μg PAR ml^{-1} (Fig. I).

III .RESULTS AND DISCUSSION

During the investigation, HPAR solution equivalent to 25 μg ml^{-1} PAR, was taken and the final volumes were brought to 10 ml with distilled water.

Study of the optimum reaction conditions-

The various parameters affecting and related to the color intensity of the dye have been studied and optimum conditions are selected.

Choice the oxidizing agent-

Several oxidizing agents have been tested ((KIO4 ,K2Cr2O7 , NaIO4,N-Chlorosuccinimide KIO4 give the most sensitive reaction with high color contrast.(Table I).

Effect of pH value-

The effect of pH value on the absorbance of the product has been investigated. The results in Table II indicated that the reaction needs neutral to week alkaline

medium(pH= 7.54), This pH value can be obtained by adding the reaction components without the addition of acid or base and therefore, it has been fixed for the subsequent experiments.

Effect of 2,5- DHB amount-

The effect of the amount of 2,5- DHB on the intensity of the colored product has been studied, the results showed that 1ml of 2,5-DHB solution gives high intensity and it selected for the subsequent experiment. (TableIII).

Effect of potassium periodate amount-

The effect of potassium periodate amount on the absorbance has been investigated , The suggested procedure has been carried out with different amount of KIO4 , the high intensity of the colored product achieved by using 0.5 ml of 0.005 M KIO4 , therefore it has been selected for the subsequent experiment.(TableIV).

Effect of time on oxidation-

The effect of the time needed to give complete has been tested, 20 minute was enough to complete oxidation (TableV).

Effect of temperature-

Some of the oxidative-coupling reactions depend heavily on the degree of temperature, so the reaction was conducted at different temperatures and the results showed that the reaction was not adopted on the temperature significantly, so investigation continued at room temperature (TableVI).

Final absorption spectra –

Under the above optimized conditions absorption spectra of the colored product formed from the reaction of HPAR with 2,5-DHB in presence of potassium periodate against its corresponding reagent blank showed a maximum absorption at 534 nm. , and this wavelength was selected on the subsequent experiments (Fig.II).

Analytical application-

The proposed method was applied to determine PAR in different pharmaceutical preparations. On applying proposed procedure, good recovery was obtained as shown in (TableVII).

IV.CONCLUSION

The suggested procedure for PAR determination was sensitive, accurate and can be used in determination different types of formulations without extraction or separation.

V. REFERENCES

[1] S.C.Sweetman.Martindale:The Complete Drug Reference 36th Edn.,The Pharmaceutical Press, London, p2.

[2] "British Pharmacopeia on CD-ROM", 3rd Edn., System Simulation Ltd, the stationary office, London, (2000).

[3] M. Topkafa , H.F. Ayyildiz , H.F Memon and H. Kara, J.of Separation Science, (2016), 39(13),2451.

[4] A.M. Khosroshahi, F. Aflaki, N. Saemiyan,A. Abdollahpour, R.Asgharin,J.Pharmaceutical and Health Science,(2016), 4(1):61.

[5] E.A.Abdelaleem, I.A.Naguib, S.E.Hassan and N.W.Ali, J.Pharmaceutical and Biomedical Analysis, (114),22.

[6] P.Scaria ,A.Poomali,Indian Journal of Pharmacy and Pharmacology, (2016), 3(4),16.

[7] P.K.Kalambate, B.J.Sanghavi, S.P.Karna and A.K.Srivastava,J. Sensors and Actuators B: Chemical,(2015),(213),285.

[8] A.Yigit, Y.Yardim , Z.Senturk, IEEE Sensors Journal, (2016), (16),1674.

[9] S.Chitravathi , N.Munichandraia J.Electroanalytical Chemistry, (2016), (764),93.

[10] A.B.Lima , M.F.C.Livia , C.Guimaraes, W.Dos santos, J. Braz. Chem. Soc. (2014),25,3

[11] H.Wang ,S.Zhang ,S.Li, Talanta,(2018),177,188-194

[12] K. Delvadia, R.Kimbahune,P.Kabra ,K.Sunil and P.Patel Int.J. of Pharm.and Pharm.Scien.,(2011),3.3

[13] S.Behera, S.Ghanty and S. Banerjee J.Anal Bioanal Techniques, (2012),3,6

[14] V.Vichare ,P.Mujgond, V.Tambe and S.N.Dhole Inter.J of Pharm. Tech. Research,(2010), 2,4

[15] O.A.Lawrence, A.G.Olufemi ,O.D. Alex and .T.Kayode, J. Research in Envir. Sci. and Toxicology,(2012), 1,10 ,251.
[16] A. M.Saeed .Int. J Pharm.Sci.Rev.(2017),42,2
[17] B.R.Shrestha and R.R.Pradhananga J.Nepal Chem.Soc.,(2009),24
[18] E.A.M.Alshwaiyat Jordan J. of Chem.,(2013),8,2,79.
[19] R.K.Ahmed , S.S.Muhammad and E.A.Khodaer Baghdad Science Journal,(2015),12,2.
[20] N. S. Othman ,S. A.Zakaria. J.Edu.Sci.(2007),19 (3),21

Table I

Oxidizing agent*, 0.015M	Absorbance	$\Delta\lambda^{**}_{max}$, nm
KIO_4	0.59	170
$K_2Cr_2O_7$	0.01	25
N-Chlorosuccinimide.	0.08	71
$NaIO_4$	0.40	78

* 1 ml of oxidizing agent solution used.

** $\Delta\lambda = \lambda_{maxS} - \lambda_{max}$ B when S=The colored product B= The blank.

Table II
Effect of the medium of reaction on absorbance

Medium	Volume	A	λ_{max}, nm	pH
Without	----------	0.58	534	7.54
Acidic (1M HCl)	0.3	0.52	536	3.15
	0.5	0.53	527	3.03
	1.0	0.46	535	2.90
Alkaline (1M NaOH)	0.3	0.11	642	12.21
	0.5	0.08	654	12.40
	1.0	0.06	654	12.50

Table III

Effect of 2,5-DHB amount on absorbance

2,5- DHB. (ml of 5×10^{-3}M)	Absorbance/μg paracetamol in 10 ml						R^2
	2.5	5	7.5	10	12.5	25	
0.5	0.11	0.138	0.177	0.197	0.22	0.25	0.9134
1.0	0.23	0.26	0.30	0.36	0.41	0.60	0.9971
1.5	0.11	0.16	0.31	0.43	0.54	0.55	0.8415

Table IV

Effect of KIO_4 amount on absorbance

Potassium periodate (ml of 0.005M)	Absorbance/μg paracetamol in 10ml					R^2
	2.5	5	10	12.5	25	
0.4	0.07	0.13	0.27	0.32	0.56	0.9955
0.5	0.09	0.16	0.31	0.34	0.62	0.9963
1.0	0.08	0.15	0.20	0.32	0.57	0.9911

Table V

Effect of time on oxidation

Time, minutes	5	10	15	20	25	30	35	40
Absorbance	0.58	0.58	0.59	0.59	0.56	0.57	0.56	0.53

Table VI

Effect of temperature

Temperature °C	20	30	40	50	60
Absorbance	0.60	0.59	0.55	0.54	0.52

Table VII

Results of application part

Pharmaceutical preparation	µg paracetamol present/10ml	µg paracetamol measured/10ml	Recovery*%	RSD*%
Paracetamol injection *500 mg / 5 ml* *India*	12.5	12.2	97.6	1.7
	25	25.4	101.6	2.1
Dala cold .500 mg/Tablet *India*	12.5	12.7	101.6	2.2
	25	25.2	100.8	2.9
Antipyrol-syrap 120 mg *SDI/Iraq*	12.5	12.9	103.2	1.3
	25	25.6	97.6	2.4

*Average of five determinations.

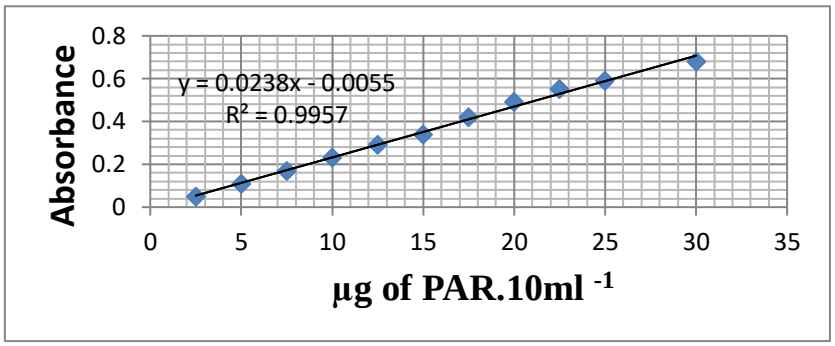


Fig.1. Calibration graph of PAR determination

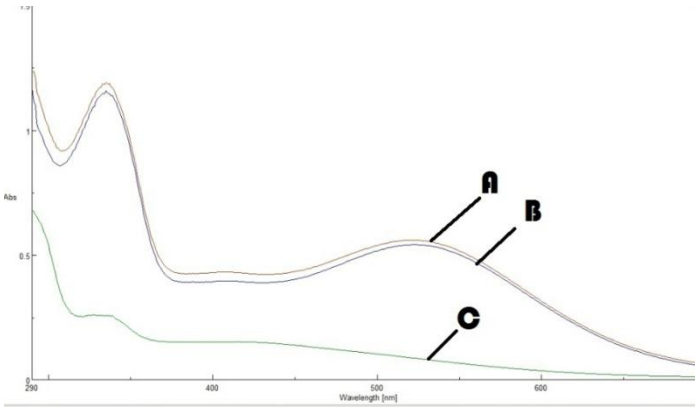


Fig. 2

Absorption spectra of 25µg PAR / 10ml treated according to the recommended procedure and measured against (A) reagent blank, (B) distilled water and (C) reagent blank measured against distilled water