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RESEARCH ARTICLE

Polarographic determination of Paracetamol by Calibration method using Fuchsin and different supporting electrolytes

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ABSTRACT

In, medicinal field paracetamol can be used in so many varieties of drugs which can be effective to various body system such as Central nervous system, Cardiovascular system, Musculo-skeletal system and Respiratory system. Polarographic Calibration method has been developed and applied for the determination of paracetamol present in some synthetic as well as medicinal samples using optimum concentration of fuchsin as maxima suppressor and different supporting electrolytes such as perchloric acid, Borate buffer, Sulphuric acid and Nitric acid.

The method is strictly empirical, and no assumptions, except correspondence with the conditions of the calibration are made. The oxidation of paracetamol at rotating platinum electrode is irreversible. Results obtained with synthetic as well as medicinal samples are in good agreement with the quoted values. In borate buffered solutions of paracetamol, catalytic waves are obtained. In order to get most pronounced effect, direct comparison method is found to be suitable for determination of paracetamol. Best calibration polrograms are obtained using 0.99 M H_2SO_4 as a supporting electrolyte and 0.0125% fuchsin as maxima suppressor. Fairly accurate results with low values of standard deviations are obtained.

Keywords: Paracetamol, Fuchsin, Perchloric acid, Borate buffer, Sulphuric acid, Nitric acid.

INTRODUCTION

A flow injection-spectrophotometric determination of paracetamol, the influence of foreign species and the determination of paracetamol in several pharmaceutical formulations were reported by Calatayud et al. (1986). A simple, rapid and accurate method for the simultaneous determination of ascorbic acid, caffeine and paracetamol in drug formulations has been developed and results are reported for several commercially available drugs (Lau et al. 1989). A flow-injection spectrofluorimetric determination of paracetamol, the influence of foreign species and the determination of paracetamol in several pharm-

-aceutical formulations are also reported (Calatayud and Benito, 1990). A simple, but sensitive, micro-assay for paracetamol in blood and plasma is described and the method was applied to a study of gastric emptying in patients before and after cardiac surgery (Whelpton et al. 1993). A polarographic procedure was described for the determination of paracetamol and salicylamide after treatment with nitrous acid and different experimental parameters affecting the derivatization process and the polarographic analysis were studied and the procedure was applied to the analysis of some pharmaceutical dosage forms (Walash et al., 1994). A simple and fast analytical procedure was proposed for the simultaneous determination of paracetamol, acetylsalicylic acid and caffeine in pharmaceuticals by means the partial least square treatment of the spectrophotometric absorbance data between 216 and 300 nm, taken at 5 nm intervals (Bouhsain et al., 1997). After a large drug scanning, the system Luminol–H_2O_2–$Fe(CN)_6^{3-}$ was proposed for first time for the indirect determination of paracetamol and the influence of foreign compounds was studied and, the method was applied to determination of the drug in three different pharmaceutical formulations (Alapont et al. 1999). A voltammetric method, aided by chemometrics, was developed for the simultaneous determination of paracetamol and phenobarbital in pharmaceuticals and the proposed method was verified by an established HPLC method, and its practical application was demonstrated with the determination of paracetamol and phenobarbital in several commercial tablets with satisfactory results (Ni et al. 2004). Bosch et al evaluated the utility of different techniques for quantification of paracetamol content in pharmaceutical formulations and biological samples (Bosch et al. 2006). A novel type of carbon-coated nickel magnetic nanoparticles modified glass carbon electrodes (C–Ni/GCE) was fabricated and the electrochemical properties of paracetamol were studied on the C–Ni/GCE and has been applied to the determination of paracetamol in effervescent dosage samples (Wang et al., 2007). Effect of supporting electrolytes and maxima suppressors on polarographic anodic waves of paracetamol was done (Gupta, 2014a; 2014b; 2015) so that these data can be utilized for development of procedures for their quantitative estimations and applications to various pharmaceutical preparations. Polarographic determination of paracetamol in pharmaceutical preparations using 0.008% gelatin as maxima suppressor and 0.1 M $HClO_4$as supporting electrolyte by calibration as well as internal standard addition method was done (Gupta, 2014c).

Paracetamol is a common analgesic and antipyretic drug that is used for the relief of fever, headaches and other minor aches and pains. Their determination in pharmaceuticals is of paramount importance, since an overdose of paracetamol can cause fulminating hepatic necrosis and other toxic effects. The aim of the present study is to determine polarographically paracetamol in pharmaceutical preparations by calibration method using optimum concentration of fuchsin as maxima suppressor and different supporting electrolytes.such as perchloric acid, borate buffer, sulphuric acid and nitric acid.

MATERIALS AND METHODS

Standard solutions of different concentrations of the paracetamol were prepared, under different experimental conditions of maxima suppressor-supporting electrolyte combination as given in Table 1. Similar solutions were prepared for medicinal samples. 50 ml total volume was maintained for each measurement. Polarograms of all system were recorded on D.C. Recording Polarograph using Omniscribe recorder between 200 to 1300 mV using Rotating Platinum micro Electrode (RPE) as anode and Saturated Calomel Electrode (S.C.E.) as cathode. The heights of the waves obtained were measured and plotted as a function of the concentration.

Table 1 Optimum concentration of Maxima Suppressor-Supporting Electrolyte for Paracetamol determination.

Maxima Suppressor	Supporting electrolyte
3.75 x 10^{-4} % Fuchsin	0.1 M $HClO_4$
2.5 x 10^{-5} % Fuchsin	Borate Buffer of pH 10
1.25 x 10^{-2} % Fuchsin	0.99 M H2SO4
1 x 10^{-3} % Fuchsin	0.1 M HNO3

RESULTS AND DISCUSSION

Paracetamol from six categories of drugs are analyzed by this method and they are Analgesics and antipyretics, Sedatives and tranquillisers, Vasoconstrictors and migraine treatments, Non-steroid anti-inflammatory drugs, Muscle relaxants, Expectorants, cough-suppressants, mucolytics and decongestants. Current vs applied potential graph of different amount of paracetamol using optimum

concentration of fuchsin as maxima suppressor and different supporting electrolytes.such as perchloric acid, borate buffer, sulphuric acid and nitric acid are shown in Fig. 1 to 4.

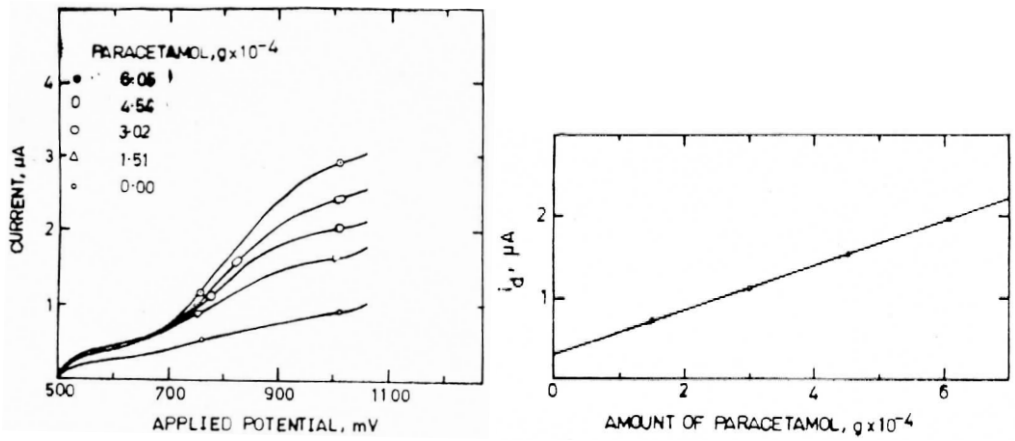

Fig. 1. (a) Calibration polarogram for Paracetamol determination in 0.1 M $HClO_4$ with 3.75 x 10^{-4} % Fuchsin; (b) Calibration curve for Paracetamol

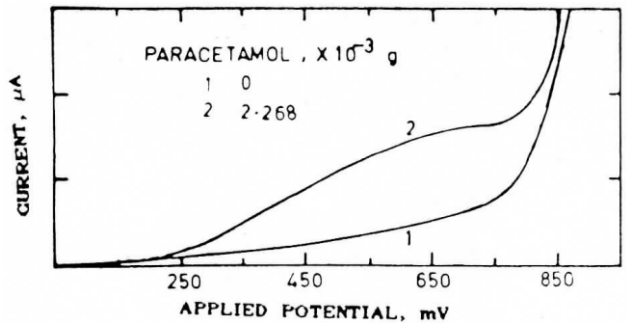

Fig. 2. Polarographic determination of Paracetamol in Borate buffer of pH 10 with 2.5 x 10^{-5} % Fuchsin by Direct comparison method

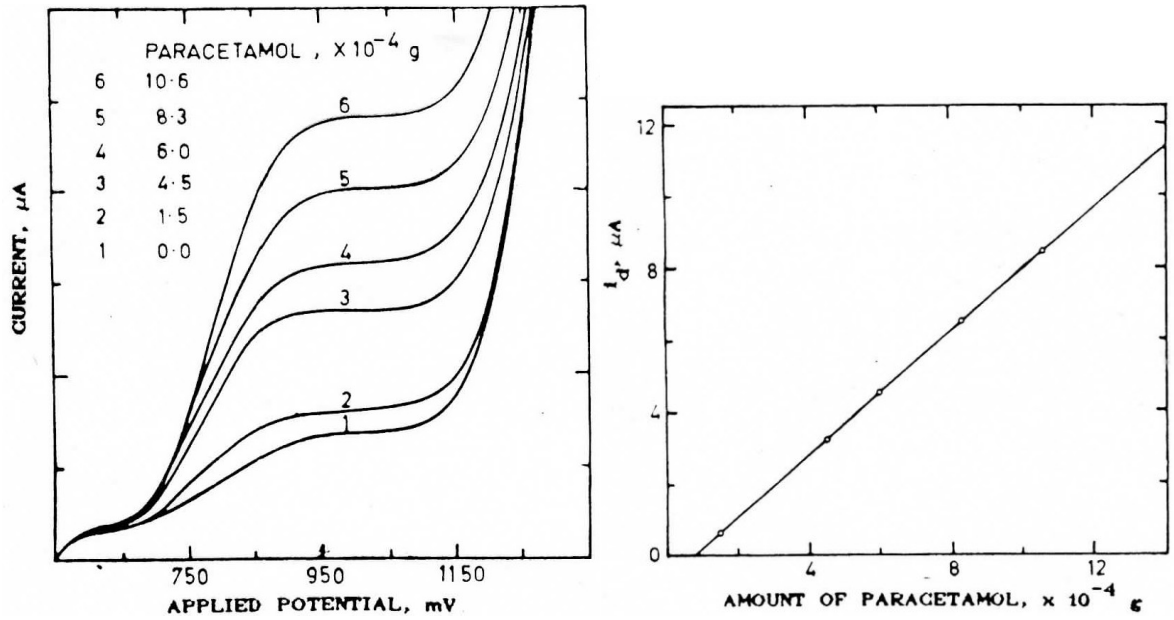

Fig. 3. (a) Calibration polarogram for Paracetamol determination in 0.99 M H_2SO_4 with 1.25 x 10^{-2} % Fuchsin; (b) Calibration curve for Paracetamol

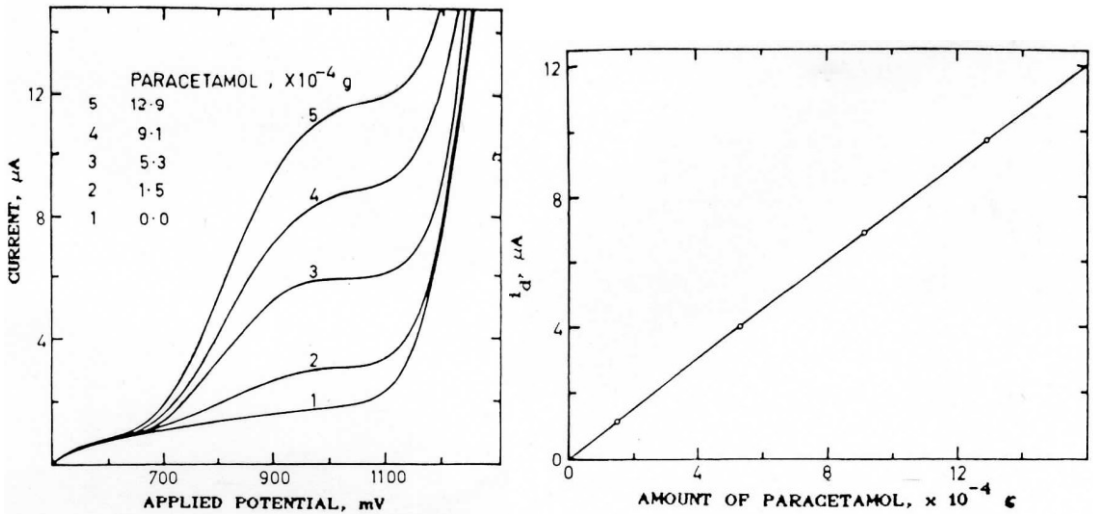

Fig. 4. (a) Calibration polarogram for Paracetamol determination in 0.1 M HNO_3 with 1 x 10^{-3} % Fuchsin; (b) Calibration curve for Paracetamol

Paracetamol the name approved by the British Pharmacopoeia Commission (para-acetylaminophenol; N-acetyl-para-aminophenol (APAP); acetaminophen, para-acetamidophenol; para-hydroxyacetanilide), is the most extensively used analgesic and antipyretic drug. It exerts analgesic and antipyretic activity, however it do not exert significant anti-inflammatory activity. It is used for relief of mild pain and antipyresis. In, medicinal field paracetamol can be used in so many varieties of drugs which can be effective to various body system such as Central nervous system, Cardiovascular system, Musculo-skeletal system and Respiratory system. For example paracetamol present in analgesics, antipyretics, sedatives and tranqullisers act through central nervous system; Vasoconstrictors and drugs used for migraine treatments act through Cardiovascular system; non-steroid anti-inflammatory drugs and muscle relaxants are usually meant for musculo-skeletal disorders; while expectorants, cough-suppressants, mucolytics and decongestants act through respiratory system.

Polarographic calibration method has been developed and applied for the determination of paracetamol present in some synthetic as well as medicinal samples using optimum concentration of fuchsin as maxima suppressor and different supporting electrolytes such as perchloric acid, borate buffer, sulphuric acid and nitric acid. The method is strictly empirical, and no assumptions, except correspondence with the conditions of the calibration are made. According to the Ilkovic equation, with all other factors constant.

$$i_d = kC$$

Where k is a constant defined by Ilkovic equation. This relation is the foundation of quantitative polarographic analysis and its general validity is well established. The results of polarographic determination of paracetamol from synthetic and medicinal samples by calibration method are in good agreement with the quoted values. A summary of the results of calibration method is given in Table 2. The method is precise as indicated by low values of standard deviations.

The advantages of the application of polarography in the analysis of medicine (paracetamol) are speed, sensitivity, which enables trace analysis to be carried out, and to follow changes in the composition of the preparation, the small sample requirements and selectivity. It is possible to carry out a polarographic analysis even in the presence of colouring matters and comparable amounts of other ingredients such as - Salicyaltes (aspirin), pentazocine; dextropropoxyphene, codeine and dicyclomie hydrochloride; as in case of Veganin. Ergotamine; in case of Vasograin. Chlorpheniramine and Phenylephrine; in case of Paracodrate, Ralcidin etc.

p-hydroxyacetanilide i.e. paracetamol produces anodic waves at the rotating platinum electrode. The oxidation yields the N-acetyl-p-benzoquinoneimine and represents a irreversible reaction. Polarographically a value of 600-700 mv is found for decomposition potential of paracetamol, whereas potentiometrically a value of 429 mV is calculated for the same. The presence of oxygen does not affect the wave. The apparent diffusion currents of paracetamol often increase markedly with increasing applied e.m.f. . This is due to the increase of the residual current with increasing applied e.m.f. and when the proper

correction is applied for the residual current the corrected diffusion current is found to be practically constant. There are instances, however, in which this correction does not produce a constant limiting current, indicating that the limiting current is not entirely diffusion controlled. Even in such cases, it is found that the limiting current is strictly proportional to concentration when care is taken to measure the current at exactly the same potential with the different concentrations.

Table 2. Palarographic determination of Paracetamol by Calibation method in different Supporting Electrolyte-Maxima suppressor system

Medicinal Sample	Weight of Tablet / Capsule material, gm	Weight of Empty Capsule, gm	Amount of Parcetamol per Tablet / Capsule, gm	
			Quoted	Found
In 0.1 M HClO4 & 3.75 x 10-4 % Fuchsin				
Paracodrate (H.Jules) Tablet	0.6047	–	0.325	0.15 ± 0.03
Ralcidin (Rallis) Tablet	0.4218	–	0.3	0.14 ± 0.03
In Borate buffer of pH 10 & 2.5 x 10-5 % Fuchsin				
Vasograin (Cadila) Tablet	0.5094	–	0.25	0.26 ± 0.02
Veganin (Warner) Tablet	0.7654	–	0.25	0.26 ± 0.02
In 0.99 M H2SO4 & 1.25 x 10-2 % Fuchsin				
Paracodrate (H.Jules) Tablet	0.6047	–	0.325	0.35 ± 0.05
Veganin (Warner) Tablet	0.7654	–	0.25	0.27 ± 0.03
In 0.1 M HNO3 & 1 x 10-3 % Fuchsin				
Paracodrate (H.Jules) Tablet	0.6047	–	0.325	0.30 ± 0.02
Vasograin (Cadila) Tablet	0.5094	–	0.25	0.32 ± 0.03

Table 3. Calibration data for Paracetamol in 0.1 M HClO4 - 3.75 x 10-4 % Fuchsin and its application to Medicinal Samples.

Paracetamol, mg		id	id/C	E1/2, mg	Slope of E Vs log (id-i) / i plots, V		Value of n		Paracetamol per tablet, g	
Taken	Found				Theoretical	Experimental	Theoretical	Experimental	Quoted	Found
0	–	–	–	–	–	–	–	–	–	–
0.151	–	0.7	4.6	760	0.03	0.15	2	0.394	–	–
0.302	–	1.125	3.7	785	0.03	0.147	2	0.402	–	–
0.605	–	2	3.3	815	0.03	0.134	2	0.441	–	–
			3.9 ± 0.7							
0.702 mg Paracodrate (H.Jules) Tablet										
0.377	0.133	0.65	1.7	–	–	–	–	–	0.325	0.18
0.377	0.185	0.8	2	–	–	–	–	–	0.325	0.16
0.377	0.21	0.875	2.4	–	–	–	–	–	0.325	0.11
			2 ± 0.3							0.15 ± 0.03
0.534 mg Ralcidin (Rallis) Tablet										
0.379	0.143	0.675	1.8	–	–	–	–	–	0.3	0.11
0.379	0.168	0.75	2	–	–	–	–	–	0.3	0.13
0.379	0.22	0.9	2.4	–	–	–	–	–	0.3	0.17
			2 ± 0.3							0.14 ± 0.03

Calibration method in Perchloric acid medium In 0.1 M $HClO_4$ - 3.75 x 10^{-4} % Fuchsin system, diffusion currents were measured at 1025 mV vs S.C.E. and the values listed in Table 3 have been corrected for the residual current of the blank. In this case i_d/C is constant to ± 17.9 % over a 4-fold range of paracetamol concentration. The plot of E against log i_d-i/i yields a straight line (Fig. 5). A slight shift of the half-wave potential to more positive values with increasing paracetamol concentrations was found, which was in agreement with the shift calculated from the following equation –

$$E = E^0 + 0.030 \log i_d - i / i \quad (25^0C)$$

With increasing paracetamol concentrations the slope became closer to the theoretical value but did not become equal to it. From the above it is evident that the oxidation of paracetamol at the R.P.E. is irreversible. Medicinal samples analyzed in this medium are Paracodrate and Ralicidin, both of which

contain Tatrazine as colouring matter which has suppressing capacity for paracetamol wave in 0.1 $HClO_4$ – 3.75 x 10^{-4} % Fuchsin media, therefore lower values of diffusion currents, are obtained. Hence observed weight of paracetamol per tablet found are quite low. 53 % less recovery is observed in both cases.

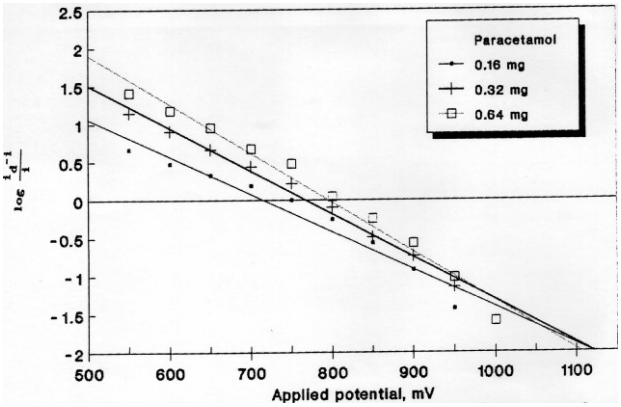

Fig. 5. Test of equation of the wave of Paracetamol in 0.1 M $HClO_4$ with 3.75 x 10-4 % Fuchsin; Experimental points from Fig. 1 a.

Direct comparison method in Borate buffer medium In buffered solutions of paracetamol, catalytic waves are obtained. Because the catalytic effects are not a specific property of a catalyst and because the height of a catalytic wave can depend on the type and concentration of other substances present in the solution, the application of catalytic waves for practical analyses is restricted. There is no strict proportionality between the catalytic current and the concentration of paracetamol. In order to get the most pronounced effect, direct comparison method is found to be suitable for determination of paracetamol. Polarograms are made of 3 x 10^{-4} M paracetamol in a borate buffer of pH 10 in the presence of 2.5 x 10^{-5} % fuchsin (Fig. 2). At higher concentrations of paracetamol (>3 x 10^{-4} M) a decrease in diffusion current with increasing positive potential is observed (due to which quantitative measurement becomes complicated), but the catalytic wave appears before the flat minimum is attained. The minimum observed at pH 10 is seem to be related to the electrolyte content of the solution. The current-voltage curves of a standard solution of the paracetamol under the same conditions as the unknown (medicinal sample) are recorded. Then, using the Ilkovic equation in the simplest form, the diffusion current quotient, i_d/C, can be computed. When divided into the height of the unknown wave, it yields the concentration of paracetamol in the unknown. The unknown is most accurately determined when the concentration of the comparison standard is about the same as that of the unknown as may be seen from Table 4. The diffusion current decreases with time since the red form of fuchsin is changed into the colourless carbinol form hence polarograms are recorded immediately after preparation of each system. In polarograms of system containing 0, 1.512 and 3.024, mg of paracetamol recorded after 2 hour of its preparation diffusion current decreases so much that only the catalytic wave is observed.

Calibration method in Sulphuric acid medium Paracetamol present in different medicinal smaples, viz., Paracodrate and Veganin can be estimated effectively using 0.99 M H_2SO_4 as supporting electrolyte and 0.0125% fuchsin as maxima suppressor. Best calibration polarograms are obtained in these instances (Fig. 3 a). Fairly accurate results with low values of standard deviations are obtained (Table 5).

Calibration method in Nitric acid medium
Well defined calibration polarograms of various concentrations of paracetamol in 0.1 M nitric acid with 1 x 10^{-3}% fuchsin are obtained as may be seen from Fig. 4 a. In this case i_d/C is constant to $\pm$ 0.8 % over a 8.6-fold range of paracetamol concentration. Excess recovery obtained in case of Vasograin (Cadila) Tablet may be attributed to the presence of comparable amount of Caffeine which show a wave on the polarographic curves at the same potential as may be oxidized and causing the excess recovery (Table 6).

Table 4. Calibration data for Paracetamol by direct Comparison Method in Borate buffer of pH 10 with 2.5 x 10-5 % Fuchsin and its application to Medicinal Samples.

Paracetamol, mg		id at 700 mV	id/C	Amount of Paracetamol per Tablet / Capsule, g	
Taken	Found			Quoted	Found
2.268	–	2.4	1.0582	–	–
4.653 mg Vasograin (Cadila) Tablet					
2.284	2.268	2.4	1.05	0.25	0.248
2.284	2.363	2.5	1.09	0.25	0.259
			1.07 ± 0.03		0.253 ± 0.007
6.978 mg Veganin (Warner) Tablet					
2.279	2.079	2.2	0.97	0.25	0.23
2.279	2.363	2.5	1.1	0.25	0.26
			1.03 ± 0.09		0.24 ± 0.02

Table 5. Calibration data for Paracetamol in 0.99 M H2SO4 - 0.0125 % Fuchsin and its application to Medicinal Samples.

Paracetamol, mg		id at 1100 mV	id/C	Amount of Paraceetamol per Tablet / Capsule, g	
Taken	Found			Quoted	Found
0.15	–	0.625	4	–	–
0.45	–	3.2	7	–	–
0.6	–	4.5	8	–	–
0.83	–	6.5	8	–	–
1.06	–	8.45	8	–	–
			7 ± 2		
0.985 mg Paracodrate (H. Jules) Tablet					
0.529	0.495	3.6	7	0.325	0.3
0.529	0.535	3.95	7	0.325	0.33
0.529	0.61	4.6	9	0.325	0.37
0.529	0.665	5.05	10	0.325	0.41
			8 ± 1		0.35 ± 0.05
1.621. mg Veganin (Warner) Tablet					
0.529	0.513	3.75	7.1	0.25	0.24
0.529	0.6	4.5	8.5	0.25	0.28
0.529	0.618	4.65	8.8	0.25	0.29
			8.1 ± 0.9		0.27 ± 0.03

Table 6. Calibration data for Paracetamol in 0.1 M HNO3 - 1 x 10-3 % Fuchsin and its application to Medicinal Samples.

Paracetamol, mg		id at 1100 mV	id/C	Amount of Paraceetamol per Tablet / Capsule, g	
Taken	Found			Quoted	Found
0.15	–	1.15	7.67	–	–
0.53	–	4	7.55	–	–
0.91	–	6.9	7.58	–	–
1.29	–	9.725	7.54	–	–
			7.58 ± 0.06		
0.988 mg Paracodrate (H. Jules) Tablet					
0.531	0.455	3.45	6.5	0.325	0.28
0.531	0.493	3.725	7	0.325	0.3
0.531	0.495	3.75	7.1	0.325	0.3
0.531	0.54	4.1	7.7	0.325	0.33
			7.1 ± 0.5		0.3 ± 0.02
1.082 mg Vasograin (Cadila) Tablet					
0.531	0.613	4.625	8.7	0.25	0.29
0.531	0.653	4.925	9.3	0.25	0.31
0.531	0.725	5.5	10.4	0.25	0.34
0.531	0.738	5.575	10.5	0.25	0.35
			9.7 ± 0.9		0.32 ± 0.03

CONCLUSIONS

Polarographic calibration method has been developed and applied for the determination of paracetamol present in some synthetic as well as medicinal samples using optimum concentration of fuchsin as maxima suppressor and different supporting electrolytes such as perchloric acid, borate buffer, sulphuric acid and nitric acid. The method is strictly empirical, and no assumptions, except correspondence with the conditions of the calibration are made. The oxidation of paracetamol at rotating platinum electrode is irreversible. Results obtained with synthetic as well as medicinal samples are in good agreement with the quoted values. The method is precise.

Calibration method in Perchloric acid medium In 0.1 M $HClO_4$ - 3.75 x 10^{-4} % Fuchsin system i_d/C is constant to ± 17.9 % over a 4-fold range of paracetamol concentration. Medicinal samples analyzed in this medium are Paracodrate and Ralicidin, both of which contain Tatrazine as colouring matter which has suppressing capacity for paracetamol wave in 0.1 $HClO_4$ – 3.75 x 10^{-4} % Fuchsin media, therefore lower values of diffusion currents, are obtained. Hence observed weight of paracetamol per tablet found are quite low. 53 % less recovery is observed in both cases.

Direct comparison method in Borate buffer medium In buffered solutions of paracetamol, catalytic waves are obtained. There is no strict proportionality

between the catalytic current and the concentration of paracetamol. In order to get the most pronounced effect, direct comparison method is found to be suitable for determination of paracetamol. Polarograms are made of 3 x 10^{-4} M paracetamol in a borate buffer of pH 10 in the presence of 2.5 x 10^{-5} % fuchsin. The diffusion current decreases with time since the red form of fuchsin is changed into the colourless carbinol form hence polarograms are recorded immediately after preparation of each system.

Calibration method in Sulphuric acid medium Paracetamol present in different medicinal smaples, viz., Paracodrate and Veganin can be estimated effectively using 0.99 M H_2SO_4 as supporting electrolyte and 0.0125% fuchsin as maxima suppressor. Best calibration polarograms are obtained in these instances. Fairly accurate results with low values of standard deviations are obtained.

Calibration method in Nitric acid medium Well defined calibration polarograms of various concentrations of paracetamol in 0.1 M nitric acid with 1 x 10^{-3}% fuchsin are obtained. In this case i_d/C is constant to $\pm$ 0.8 % over a 8.6-fold range of paracetamol concentration. Excess recovery obtained in case of Vasograin (Cadila) Tablet may be attributed to the presence of comparable amount of Caffeine which show a wave on the polarographic curves at the same potential as may be oxidized and causing the excess recovery.

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