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Polarographic Determination of Paracetamol by Calibration Method using Hydrocloric Acid and Different Maxima Suppressors

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Abstract

Paracetamol is a common analgesic and antipyretic drug their determination in pharmaceuticals is of paramount importance, since an overdose of paracetamol can cause toxic effects. The aim of the present study is to do polarographic determination of paracetamol by calibration method using hydrocloric acid and different maxima suppressors such as fuchsion, methyl red, thymol blue and bromocresol green. 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. Calibration method has been developed and applied for the determination of paracetamol present in some synthetic as well as medicinal samples using selected maxima suppressor-supporting electrolyte system. Polarograms of all system were recorded on D.C. Recording Polarograph using Omniscribe recorder between 200 to 1300 mV using Rotating Platinum micro Electrode as anode and Saturated Calomel Electrode as cathode. 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 as indicated by low values of standard deviations. It is possible to carry out a polarographic analysis even in the presence of colouring matters and comparable amounts of other ingredients.*

Keywords: Paracetamol, Hydrocloric acid, Fuchsion, Methyl red, Thymol blue, Bromocresol green.

Introduction

A flow injection-spectrophotometric determination of paracetamol, the determination of paracetamol in pharmaceutical formulations and the influence of foreign species were reported by Calatayud et al[1]. A rapid, simple and accurate method for the simultaneous determination of paracetamol, caffeine and ascorbic acid in drug formulations has been developed[2]. The determination of paracetamol in several pharmaceutical formulations are also reported[3]. A sensitive and simple, micro-assay for paracetamol in plasma and blood is described and the method was applied to a study of gastric emptying in patients before and after cardiac surgery[4]. A polarographic procedure was described for the determination of salicylamide and paracetamol 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[5].

A simple and fast analytical procedure was proposed for the simultaneous determination of acetylsalicylic acid, caffeine and paracetamol, in pharmaceuticals[6]. 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[7]. A voltammetric method, aided by chemometrics, was developed for the simultaneous determination of phenobarbital and paracetamol in pharmaceuticals and the proposed method was verified by an established HPLC method, and its practical application was demonstrated with the determination of Phenobarbital and paracetamol in several commercial tablets with satisfactory results[8]. The utility of different techniques for quantification of paracetamol content in pharmaceutical formulations and biological samples wer evaluated by Bosch et al[9].

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 have been applied to the determination of paracetamol in effervescent dosage samples[10]. Effect of supporting electrolytes and maxima suppressors on polarographic anodic waves of paracetamol was done[11,12] 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[13].

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 do polarographic determination of paracetamol by calibration method using hydrocloric acid and different maxima suppressors such as fuchsion, methyl red, thymol blue and bromocresol green.

Methodology

Under different experimental conditions of maxima suppressor-supporting electrolyte combination as given in Table-1 standard solutions of different concentrations of the paracetamol were prepared. 50 ml total volume was maintained for each measurement. Similar solutions were prepared for medicinal samples. 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
1.5 x 10^{-3} % Fuchsin	0.1 M HCI
2.5 x 10^{-4} % Methyl red	0.01 M HCI
1.25 x 10^{-3} % Thymol blue	1.0 M HCl
3.78 x 10^{-3} % Bromocresol green	1.0 M HCl

Observation: 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 hydrocloric acid and different maxima suppressors such as fuchsion, methyl red, thymol blue and bromocresol green are shown in Figure- 1 to 4.

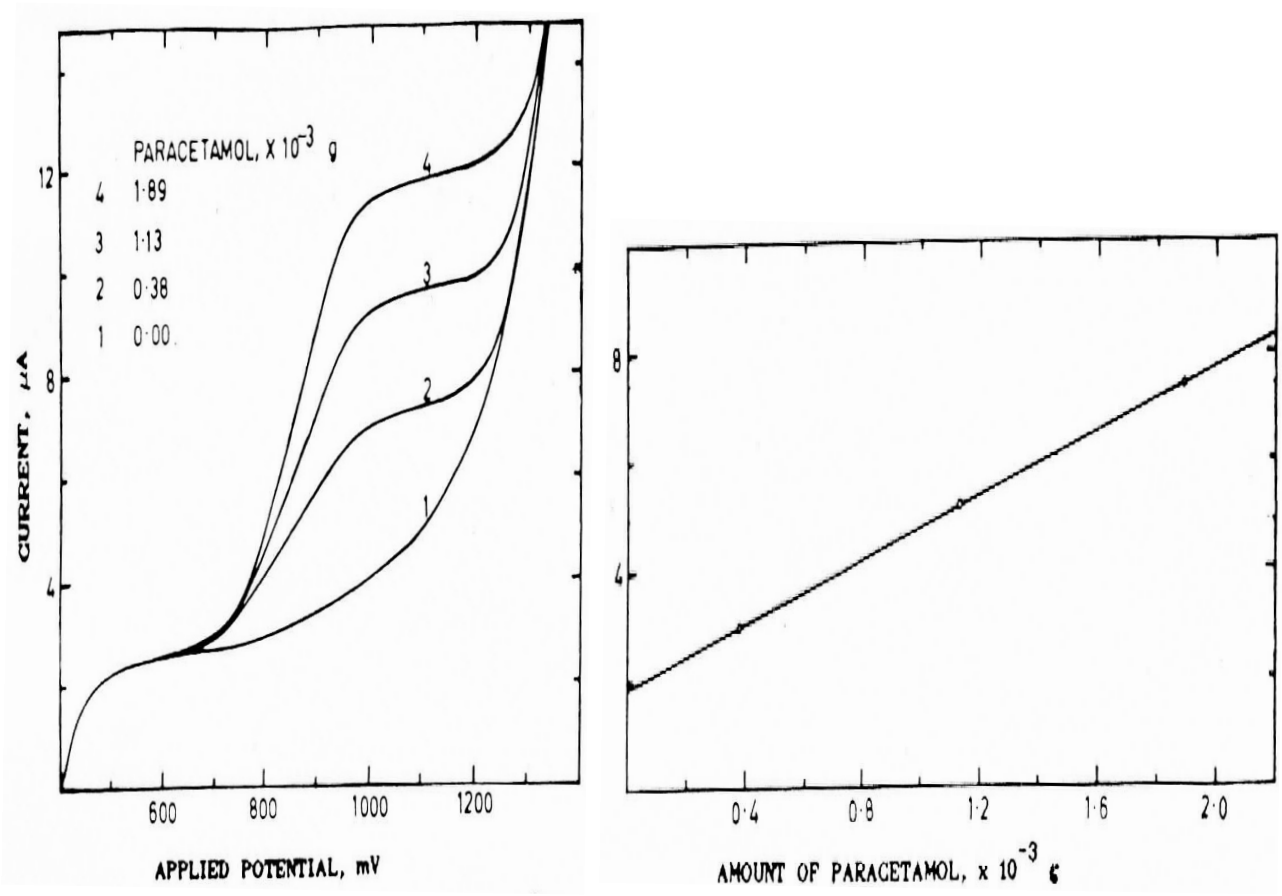

Figure-1
(a) Calibration polarogram for Paracetamol determination in 0.1 M HCl with 1.5 x 10^{-3} % Fuchsin;
(b) Calibration curve for Paracetamol

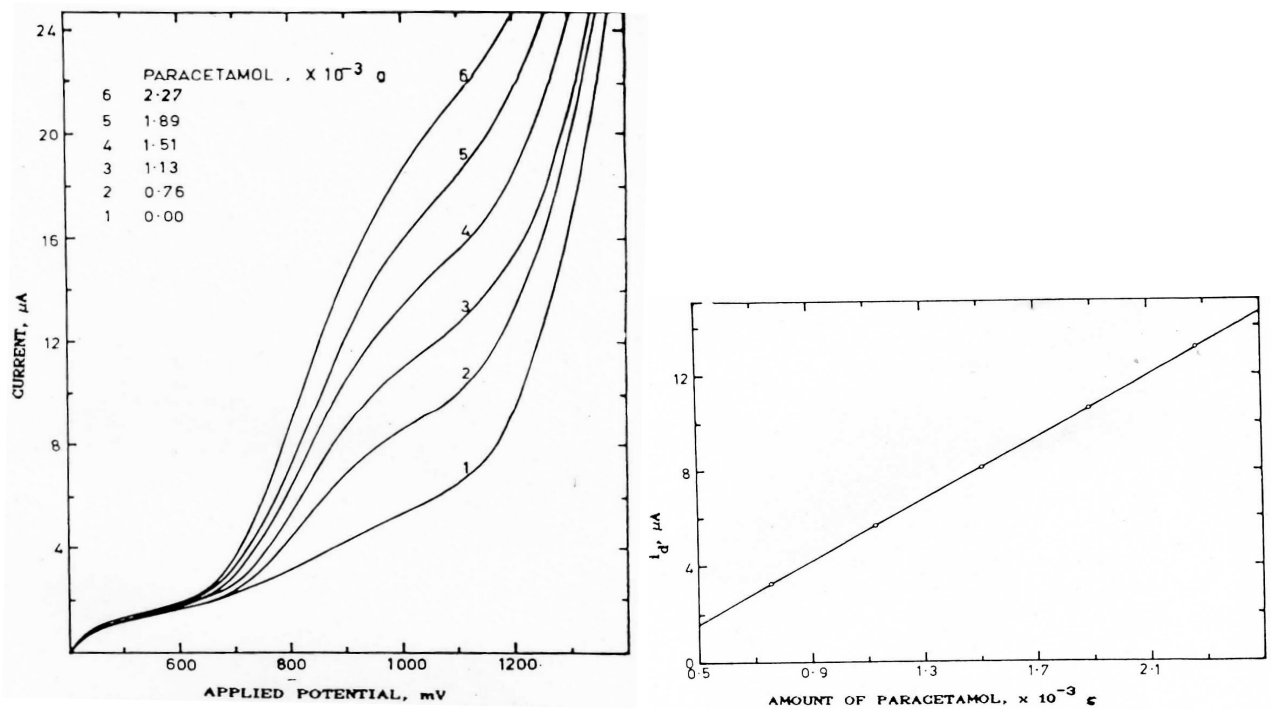

Figure-2
(a) Calibration polarogram for Paracetamol determination in 0.01 M HCl with 2.5 x 10^{-4} % methyl red;
(b) Calibration curve for Paracetamol

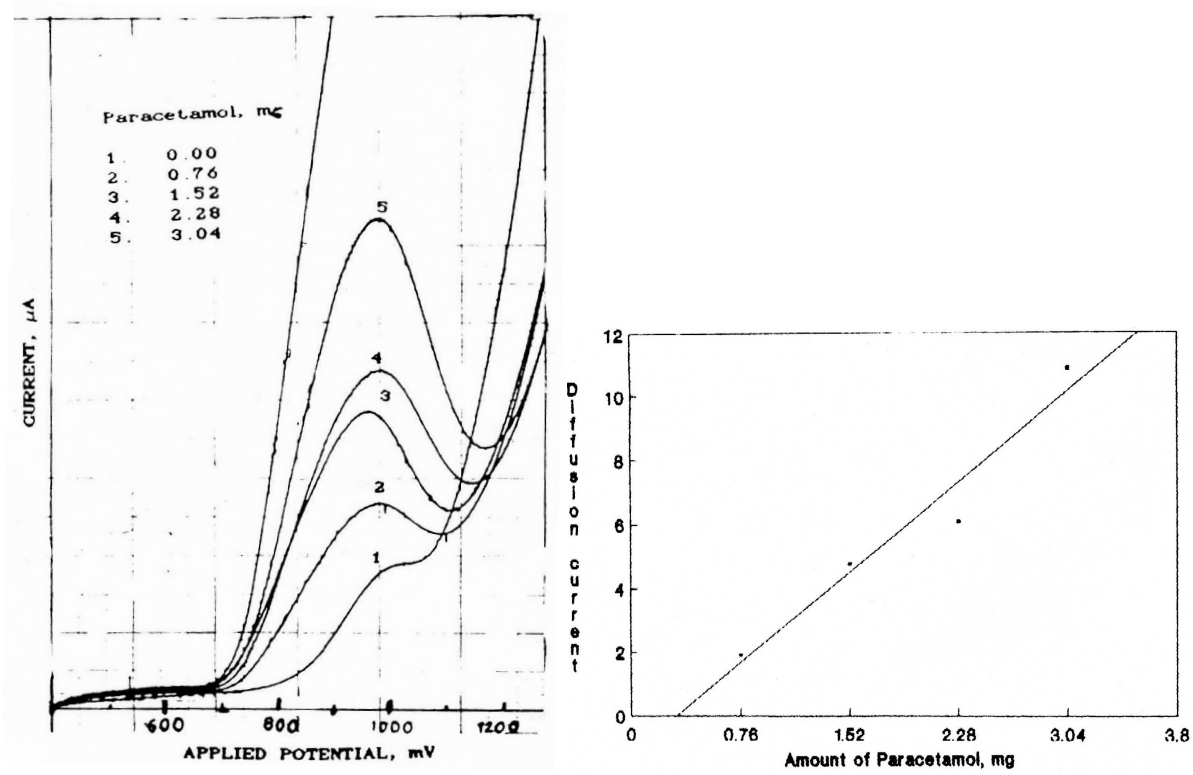

Figure-3
(a) Calibration polarogram for Paracetamol determination in 1 M HCl with 1.25 x 10^{-3} % Thymol blue;
(b) Calibration curve for Paracetamol

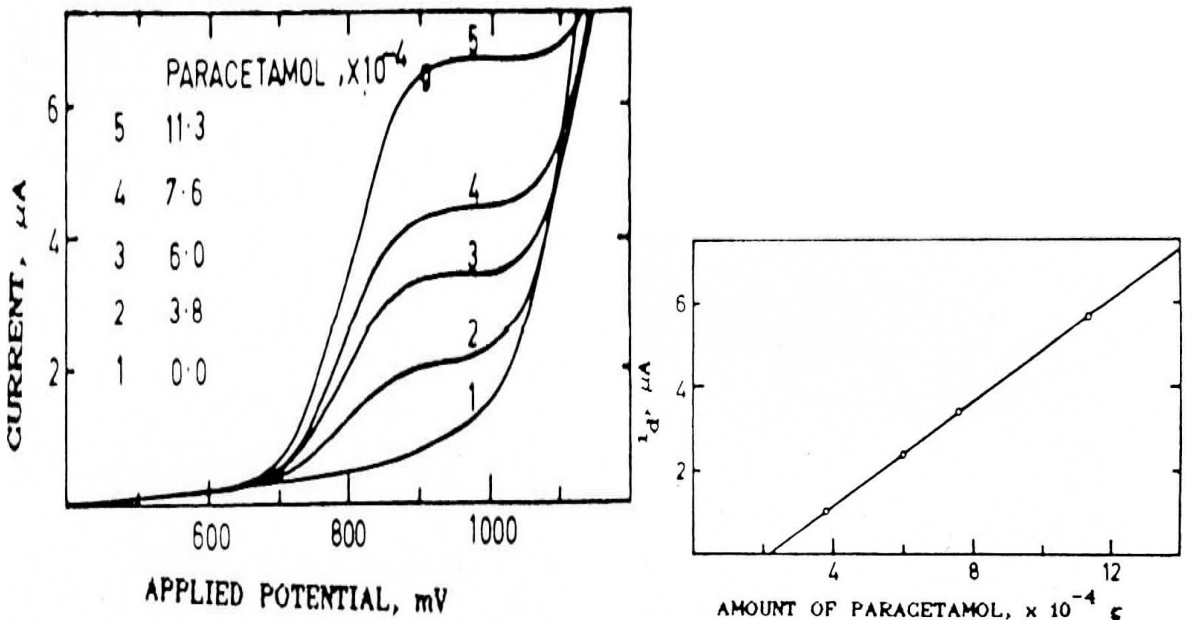

Figure-4
(a) Calibration polarogram for Paracetamol determination in 1 M HCl with 3.78 x 10^{-3} % bromocresol green;
(b) Calibration curve for Paracetamol

Results and Discussion

Calibration method has been developed and applied for the determination of paracetamol present in some synthetic as well as medicinal samples using selected maxima suppressor-supporting electrolyte system. 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.

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 Parvon-Spas, Pyrigesic, Ultragin and Veganin. Ergotamine; in case of Vasograin. Oxyphenbutazone, phenylbutazone and Ibuprofen; in case of Xeroflam. Chlorpheniramine and Phenylephrine; in case of Seumol-Plus 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.

Calibration method in Hydrochloric acid medium Method can be applied effectively to paracetamol determination in medicinal samples using 0.1 M HCI as supporting electrolyte and 1.5 x 10^{-3}% fuchsin as maxima suppressor (Figure-1 a and b). As an example Seumol plus and Ultragin show 80% recovery with a standard deviation of ± 0.1 to 0.2 (Table-3). The determination of paracetamol is best carried out in 0.012 M HCI and 2.5 x 10^{-4} % methyl red (Figure- 2 a and b). Interferences in the determination of paracetamol in some of the medicinal samples may be caused by other ingradients such as Analgin (present in Ultragin) and Ibuprofen (present in Xeroflam) which also give anodic waves under these conditions (Table-4). Hence excess recovery due to increased diffusion current than normal are obtained. In solutions of 1 M HCI and 1.25 x 10^{-3} % Thymol blue the presence of paracetamol results in a round maximum may be of catalytic origin.

Table-2
Palarographic determination of Paracetamol by Calibation method in Hydrocloric acid and different 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 HCl and 1.5 x 10-3 % Fuchsin				
Seumol-Plus (Blue Shield) Tablet	0.6634	–	0.5	0.4 ± 0.2
Ultragin (Manners) Tablet	0.6327	–	0.25	0.2 ± 0.1
In 0.01 M HCl and 2.5 x 10-4 % Methyl red				
Parvon-Spas (Jagson Pal) Capsule	0.5412	0.0903	0.4	0.46 ± 0.08
Pyrigesic (East India) Tablet	0.6224	–	0.5	0.554 ± 0.003
Ultragin (Manners) Tablet	0.6327	–	0.25	0.38 ± 0.05
Xeroflam (Helios) Tablet	1.1024	–	0.5	1.1 ± 0.1
In 1 M HCl and 1.25 x 10-3 % Thymol blue				
Parvon-Spas (Jagson Pal) Capsule	0.5412	0.0903	0.4	0.51 ± 0.08
In 1 M HCl and 3.78 x 10-3 % Bromocresol green				
Vasograin (Cadila) Tablet	0.5094	–	0.25	0.23 ± 0.01
Veganin (Warner) Tablet	0.7654	–	0.25	0.22 ± 0.01

Table-3
Calibration data for Paracetamol in 0.1 M HCl - 1.5 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
0.38	–	2.95	8	–	–
1.13	–	5.15	5	–	–
1.89	–	7.35	4	–	–
			5 ± 2		
1.508 mg Seumol - Plus (Blue Shield) Tablet					
1.136	0.6	3.6	3	0.5	0.3
1.136	0.725	3.95	3	0.5	0.3
1.136	1	4.75	4	0.5	0.4
1.136	1.46	6.1	5	0.5	0.6
			4 ± 1		0.4 ± 0.2
2.871 mg Ultragin (Manners) Tablet					
1.134	0.54	3.4	3	0.25	0.1
1.134	0.78	4.1	4	0.25	0.2
1.134	1.31	5.65	5	0.25	0.3
1.134	1.65	6.65	6	0.25	0.4
			4 ± 1		0.2 ± 0.1

Table-4
Calibration data for Paracetamol in 0.01 M HCl - 2.5 x 10-4 % Methyl red 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
0.76	–	3.225	4.2	–	–
1.13	–	5.6	5	–	–
1.51	–	8.05	5.3	–	–
1.89	–	10.5	5.6	–	–
2.27	–	13	5.7	–	–
			5.2 ± 0.6		
1.545 mg parvon - spas (Jagson Pal) Capsule					
1.142	1.015	4.85	4	0.4	0.36
1.142	1.295	6.65	6	0.4	0.45
1.142	1.395	7.3	6	0.4	0.49
1.142	1.525	8.15	7	0.4	0.53
			6 ± 1		0.46 ± 0.08
1.88 mg Pyrigesic (East India) Tablet					
1.51	1.665	9.05	5.99	0.5	0.551
1.51	1.665	9.05	5.99	0.5	0.551
1.51	1.68	9.15	6.06	0.5	0.556
1.51	1.68	9.15	6.06	0.5	0.556
			6.03 ± 0.04		0.554 ± 0.003
4.798 mg Ultragin (Manners) Tablet					
1.896	2.4	–	–	0.25	0.32
1.896	2.71	–	–	0.25	0.36
1.896	3	–	–	0.25	0.4
1.896	3.33	–	–	0.25	0.44
					0.38 ± 0.05
3.845 mg Xeroflam (Helios) Tablet					
1.899	3.63	–	–	0.5	1
1.899	3.895	–	–	0.5	1
1.899	4.29	–	–	0.5	1.1
1.899	4.66	–	–	0.5	1.2
					1.1 ± 0.1

The increase in paracetamol concentration results in the increase of the rounded maximum at about 958.33 mV (Figure- 3 a). From the height of the maximum it is possible to construct a calibration curve, which is linear, and to determine the paracetamol concentration. The calibration graph (Figure- 3 b) is used for determining paracetamol in medicinal samples with a standard deviation of ± 0.09 (Table-5). In 1 M HCI – 3.78 x 10^{-3} % Bromocresol green solution (Figure-4 a and b) results found are in good agreement with the quoted values. The method is precise as indicated by low values of standard deviations (Table-6).

Table-5
Calibration data for Paracetamol in 1 M HCl - 1.25 x 10-3 % Thymol blue and its application to Medicinal Samples

Paracetamol, mg		id at maximum height		id/C	Amount of Paracetamol per Tablet / Capsule, g	
Taken	Found	Observed	Corrected		Quoted	Found
0		4.675	–	–	–	–
0.76	–	6.55	1.875	2.4671	–	–
1.51	–	9.45	4.775	3.1623	–	–
2.27	–	10.775	6.1	2.6872	–	–
3.02	–	15.55	10.875	3.601	–	–
				3.0 ± 0.5		
2.058 mg parvon spas (jagson Pal) Capsule						
1.521	1.015	7.55	2.875	1.9	0.4	0.27
1.521	1.375	8.95	4.275	2.8	0.4	0.36
1.521	1.56	9.65	4.975	3.3	0.4	0.41
1.521	1.875	10.85	6.175	2.7	0.4	0.49
				2.7 ± 0.6		0.38 ± 0.09
1.904 mg Pyrigesic (East India) Tablet						
1.53	1.76	10.4	5.725	3.7	0.5	0.58
1.53	2.225	12.2	7.525	4.9	0.5	0.73
1.53	2.32	12.55	7.875	5.1	0.5	0.76
1.53	2.38	12.8	8.125	5.3	0.5	0.78
				4.8 ± 0.7		0.71 ± 0.09

Table-6
Calibration data for Paracetamol in 1 M HCl - 3.78 x 10-3 % Bromocresol green 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
0.38	–	1	3	–	–
0.6	–	2.35	4	–	–
0.76	–	3.35	4	–	–
1.13	–	5.6	5	–	–
			4 ± 1		
0.769 mg Vasograin (Cadila) Tablet					
0.377	0.33	0.7	1.9	0.25	0.22
0.377	0.36	0.85	2.3	0.25	0.24
			2.1 ± 0.3		0.23 ± 0.01
1.158 mg Veganin (Warner) Tablet					
0.378	0.325	0.65	1.7	0.25	0.21
0.378	0.325	0.8	2.1	0.25	0.23
			1.9 ± 0.3		0.22 ± 0.01

Conclusion

Calibration method has been developed and applied for the determination of paracetamol present in some synthetic as well as medicinal samples using selected maxima suppressor-supporting electrolyte system. 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.

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