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Polarographic Determination of Paracetamol in Pharmaceutical Preparations Using 0.008% Gelatin and 0.1 M $HClO_4$

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Abstract. Paracetamol is the most extensively used 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 determine polarographicallyparacetamol 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. The results are in good agreement with the quoted values. The method is precise as indicated by low values of standard deviations.The oxidation of paracetamol at rotating platinum electrode is irreversible.

Keywords: paracetamol, gelatin, HClO4, calibration method, internal standard addition method.

1. Introduction

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 [1].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 [2].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 [3]. Bosch et al. evaluated the utility of different techniques for quantification of paracetamol content in pharmaceutical formulations and biological samples [4]. A novel type of carbon-coated nickel magnetic nanoparticles modified glass carbon electrodes (C–Ni/GCE) was fabricated and the electrochemical properties of paracetamolwere studied on the C–Ni/GCE and has been applied to the determination of paracetamol in effervescent dosage samples [5].

Paracetamol is the most extensively used analgesic and antipyretic drug. 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. 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 determine

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polarographicallyparacetamol 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.

2. Methodology

Paracetamol from six different categories Analgesics and antipyretics, Sedatives and tranquillisers, Vasoconstrictors and migraine treatments, Non-steroid anti-inflammatory drugs, Muscle relaxants, Expectorants, cough-suppressants, mucolytics and decongestants of drugs were analyzed. 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. Standard solutions of different concentrations of the paracetamol were prepared, by taking 0.008% gelatin as maxima suppressor and 0.1 M $HClO_4$ as supporting electrolyte. 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 Omniscriberecorder 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. Similar procedure was followed for polarographic determination of paracetamol in synthetic samples by internal standard addition method in 0.1 M $HClO_4$ and 0.008 % Gelatin.

3. Results and Discussion

3.1. Calibration method in Perchloric acid medium

A typical set of data illustrating the calibration method in 0.14 M $HClO_4$ with 0.008 % Gelatin is shown in Fig. 1. (a). It is found that the values of diffusion current increase with increase in concentration of paracetmol. The plot of Applied potential (E) against log $(i_d-i)/i$yields straight lines (Fig. 2), which however, did not have the theoretical slope. For example in the analysis of the wave in 0.14 M $HClO_4$ - 0.008 % Gelatin system which contains 0.076 mg paracetamol the slope was found to be 0.180 instead of 0.030 (Table 1). With increasing paracetamol concentrations the deviation from the theoretical value became greater. A slight shift of the half-wave potential to more positive values with increasing paracetamol concentrations confirmed that the oxidation of paracetamol at rotating platinum electrode is irreversible.

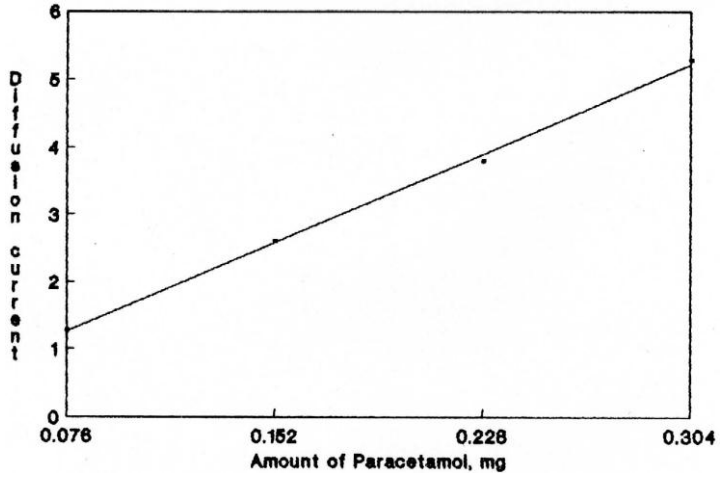

Fig. 1: (a) Calibration polarogram for Paracetamol; (b) Calibration curve for Paracetamol

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. The results of calibration method is given in Table 2. The method is precise as indicated by low values of standard deviations.

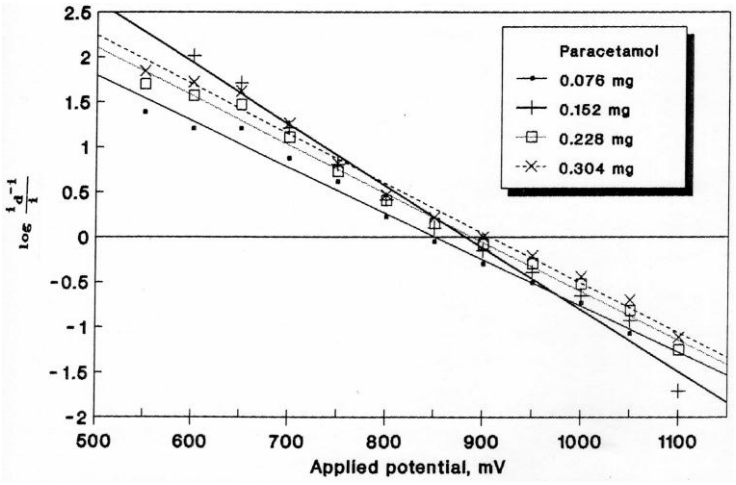

Fig. 2: Test of equation of the wave of Paracetamol in 0.14 M $HClO_4$ with 0.008 % Gelatin; Experimental points from Fig. 1. (a).

Table 1: Calibration Data for Paracetamol; Experimental points from Fig. 1. (a).

Paracetamol, mg	id	id/C	E1/2, mV	Slope of E Vs log(id-i)/i plots, V		Value of n	
				Theoretical	Experimental	Theoretical	Experimental
0.076	1.275	16.9	857.5	0.03	0.18	2	0.328
0.152	2.6	17.2	877.5	0.03	0.187	2	0.317
0.228	3.8	16.8	882.5	0.03	0.204	2	0.289
0.304	5.275	17.4	900	0.03	0.229	2	0.258
Average …….id/C = 17.1 ± 0.3							

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 Beserol, Calpol, Carbutyl, Crocin, Cyclopam, Foracet, Fortagesic, Malidens, Metacin, Norgesic, Paramet, Parvon, Parvon-Spas, Proxyvon, Pyrigesic, Pyrispam, Spasmo-Proxyvon, Sudhinol, Ultragin, Veganin and Walagesic.
- Dichloralphenazone; in case of Sedokid.
- Ergotamine; in case of Migranil and Vasograin.
- Oxyphenbutazone, phenylbutazone and Ibuprofen; in case of Actimol, Anaflam, Bestophen, Brupal 300, Bufex plus, Combiflam, Diclogesic, Duoflam, Parazolandin, Parvon Forte, Rumatin and Xeroflam.
- Chlorzoxazone; in case of Doudil and Parafon.
- Chlorpheniramine and Phenylephrine; in case of Cinaryl, Contac-CC, Paracodrate, Ralcidin, Seumol-Plus, Sinarest, Vicks Action 500, Vikoryl 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 emf. 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: Polarographicdetermmination of Paracetmol by Calibration method in 0.14 M HClO4 with 0.008 % Gelatin

Medicinal Sample	Weight of Tablet / Capsule material, gm	Weight of Empty Capsule, gm	Amount of Parcetamol per Tablet / Capsule, gm	
			Quoted	Found
Analgesics and Antipyretics				
Beserol (Win-Medicare) Tablet	0.61	–	0.45	0.42 ± 0.01
Calpol (Wellcome) Tablet	0.6687	–	0.5	0.48 ± 0.01
Corbutyl (Roussel) Tablet	1.0646	–	0.65	0.60 ± 0.03
Crocin (Duphar) Tablet	0.6243	–	0.5	0.53 ± 0.01
Cyclopam (Indoco) Tablet	0.6257	–	0.5	0.43 ± 0.03
Foracet (Ranbaxy) Tablet	0.6652	–	0.5	0.503 ± 0.008
Fortagesic (Win-Medicare) Tablet	0.6464	–	0.5	0.472 ± 0.003
Malidens (Nicholas) Tablet	0.7082	–	0.5	0.52 ± 0.01
Metacin (Themis) Tablet	0.585	–	0.5	0.47 ± 0.02
Norgesic (Cipla) Tablet	0.4258	–	0.325	0.31 ± 0.01
Paramet (Wallace) Tablet	0.64	–	0.5	0.46 ± 0.05
Parvon (Jagson Pal) Capsule	0.5765	0.095	0.4	0.46 ± 0.02
Parvon-Spas (Jagson Pal) Capsule	0.5258	0.101	0.4	0.388 ± 0.009
Proxyvon (Wockhardt) Capsule	0.526	0.0996	0.4	0.389 ± 0.004
Pyrigesic (East India) Tablet	0.608	–	0.5	0.466 ± 0.007
Pyrispam (Biddle Sawyer) Capsule	0.5353	0.0996	0.5	0.51 ± 0.01
Sapasmo-Proxyvon (Wockhardt) Capsule	0.5326	0.0964	0.4	0.329 ± 0.006
Sudhinol (Ranbaxy) Tablet	0.5555	–	0.325	0.269 ± 0.004
Ultragin (Manners) Tablet	0.6554	–	0.25	0.24 ± 0.01
Veganin (Warner) Tablet	0.7769	–	0.25	0.22 ± 0.01
Walagesic (Wallace) Capsule	0.4877	0.0968	0.4	0.36 ± 0.01
Sedatives and Tranquillisers				
Sedokid (IPCA) Syrup	–	–	0.1 / 5 ml	0.10 ± 0.01
Vasoconstrictors and Migraine treatments				
Migranil (INGA) Tablet	0.609	–	0.25	0.24 ± 0.01
Vasograin (Cadila) Tablet	0.5079	–	0.25	0.212 ± 0.005
Non-steroid anti-inflammatory drugs				
Actimol (Pharmed) Tablet	0.6646	–	0.5	0.5 ± 0.01
Anaflam (Albert David) Tablet	0.9084	–	0.325	0.29 ± 0.02
Bestophen (Biological E) Tablet	0.8856	–	0.325	0.41 ± 0.04
Brupal 300 (Geno) Tablet	0.8424	–	0.325	0.33 ± 0.04
Bufer plus (CFL) Tablet	0.9829	–	0.5	0.43 ± 0.02
Combiflam (Roussel) Tablet	0.9341	–	0.325	0.30 ± 0.02
Diclogesic (Torrent) Tablet	0.614	–	0.5	0.58 ± 0.04
Duoflam (Sigma) Tablet	1.0338	–	0.5	0.53 ± 0.05
Parazolandin (SG) Tablet	0.7271	–	0.5	0.47 ± 0.03
Parvon Forte (Jagson Pal) Capsule	0.439	0.09	0.25	0.27 ± 0.03
Rumatin (Noel) Tablet	0.6437	–	0.5	0.49 ± 0.01
Xeroflam (Helios) Tablet	1.0312	–	0.5	0.47 ± 0.05
Muscle relaxants				
Duodil (Duphar) Tablet	0.6377	–	0.3	0.204 ± 0.009
Parafon (Ethnor) Tablet	0.6257	–	0.3	0.244 ± 0.003
Expectorants, Cough-suppressants, Mucolytics and Decongestant's				
Cinaryl (Themis) Tablet	0.5019	–	0.4	0.43 ± 0.02
Coldol (Borachem) Tablet	0.6199	–	0.5	0.517 ± 0.005
Contac-CC (Eskayef) Tablet	0.7035	–	0.45	0.455 ± 0.001
Paracodrate (H.Jules) Tablet	0.5777	–	0.325	0.30 ± 0.02
Ralcidin (Rallis) Tablet	0.4179	–	0.3	0.296 ± 0.006
Seumol-Plus (Blue Shield) Tablet	0.65	–	0.5	0.48 ± 0.01
Sinarest (Centaur) Tablet	0.6747	–	0.5	0.52 ± 0.02
Vicks Action 500 (Proctor & Gamble) Tablet	0.7502	–	0.5	0.52 ± 0.01
Vikoryl (Alembic) Tablet	0.6203	–	0.5	0.420 ± 0.007

3.2. Internal standard addition method in perchloric acid medium

Polarographic internal standard addition method in 0.14 M $HClO_4$ - 0.008 % Gelatin medium can also be applied satisfactorily to the determination of paracetamol present in synthetic sample at a R.P.E. Fig. 3 (a) and (b) shows graphic representation of the internal standard addition method of evaluation. The determination error is ±2.1% with a standard deviation of ± 0.002.

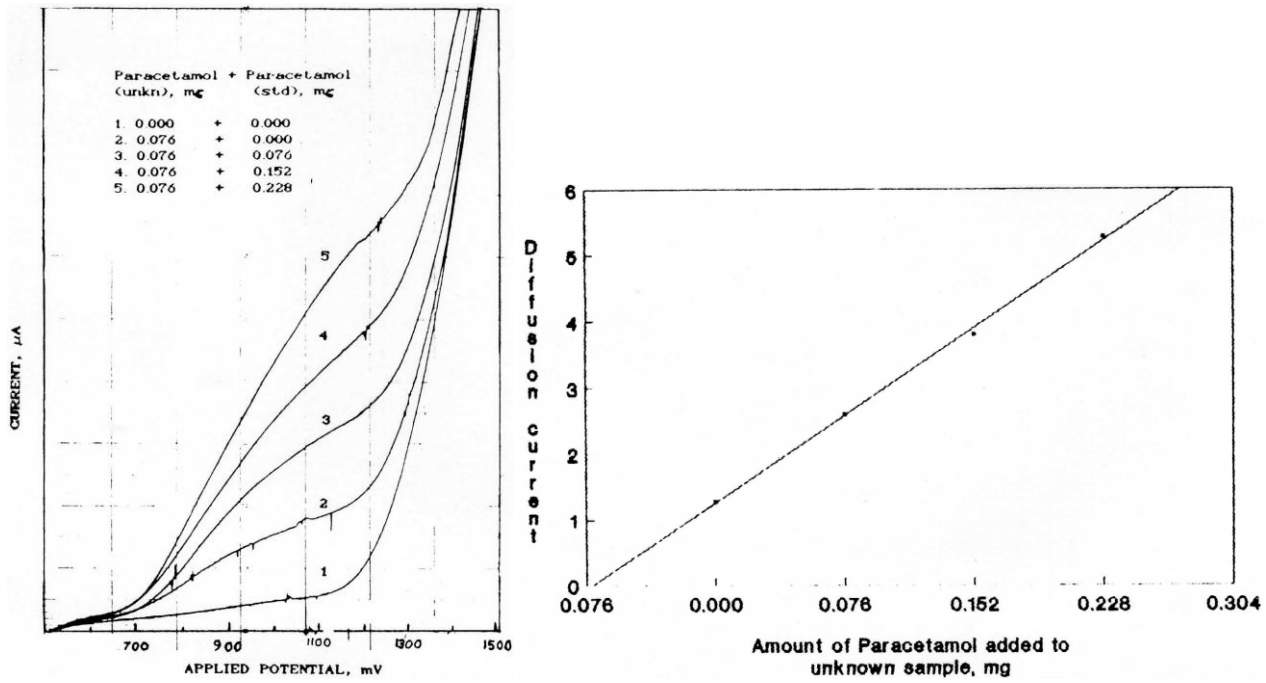

Fig. 3: (a) Polarographic determination of Paracetamol in synthetic samples by internal standard addition method in 0.1 M $HClO_4$ & 0.008 % Gelatin; (b) Plot of diffusion current as a function of amount of paracetamol added to synthetic sample in 0.1 M $HClO_4$& 0.008 % Gelatin

4. Conclusion

The results of polarographic determination of paracetamol from synthetic and medicinal samples by calibration and internal standard addition methods are in good agreement with the quoted values. The method is precise as indicated by low values of standard deviations.The oxidation of paracetamol at rotating platinum electrode is irreversible.

5. References

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