Electro-analysis of the drugs in solid dosage form at platinum and gold electrodes

Waqar Hussein, Edmond Bishop[1] and Dilshad Waqar[2]
Dow College of Pharmacy, Dow University of Health Sciences, Karachi, Pakistan
[1]Department of Chemistry, Exeter University, Stocker Road, Exteter, England
[2]Department of Chemistry, Karachi University, Karachi, Pakistan

Abstract: Voltammetric analysis at platinum and gold rotating disc electrode (RDE) in 0.1 mol l^{-1} sulphuric acid has been applied for the determination of the active ingredient in solid dosage form. Non zero intercept in the limiting current versus concentration plot was proportionally good to excellent for the solid dosage form and is free from interference from adsorption on the electrodes. All of the dosage forms proved amenable to rapid voltammetric determination with a means standard deviation of 1.2

Keyword: Rotating disc electrode voltammetry; Solid dosage form; active drug determination.

INTRODUCTION

Voltammetry in one of the important electrochemical method use for the analysis of drug substances. It is based on oxidative and reductive electrolysis at an electrode surface controlled by charge transfer and the rate at which species diffuse from the solution to the electrode (ie mass transfer). The change in current at the electrode is proportional to the concentration of the electroactive material and is monitored as a function of the applied potential. Hence voltammetry is the study of such current in which the current voltage characteristics depend on the rate of the electrode reaction. The technique is versatile for both qualitative and quantitative analysis to be perform simultaneously on a wide Varity of sample and yields information on single or diverse electroactive species in the same sample. It has a wide linear dynamic range and produces reproducible and easily interpretable results for the determination of the drugs. The parameters for voltammetric analyses of drugs or electroactive substances are based on the redox properties of the organic molecule. The proper choice of the supporting electrolyte, the control of pH and choice of working electrode are important consideration in the development of an accurate and precise analytical method. The theoretical background of voltammetry has been dealt in detail (Bengi and Sibel 2007, Adam 1969).

Various analytical methods are used for the analysis of drug substances. Rapid voltammetric determination of the active drugs in dosage form has been evaluated using high precession rotating disc electrode voltammetry in the natural clinical environment of aqueous media. A systematic investigation of the solid dosage form listed in table 1 is described. Despite a knowledge of their participation in biological electron transfer systems little has been published on electroanalytical method of these drugs (Bengi and Sibel, 2007). Anodic oxidation of dothiepin in nonaqueous media is reported as one electron step with the formation of a cation radical (Elliathy and Volke 1978). Cyclic voltammetry of imipramine in acetonitrite showed transfer of more then two electrons (Butkiewics 1972). The determination of imipramine and desipramine by electrospray ionization (Jafari *et al*., 2011) and by striping differential pulse voltammetry at glassy carbon electrode is also reported (Galeano-Diaz *et al*., 2011). Direct oxidation of cholpromanzine at platiumn and gold electrode in 2-6 mol l^{-1} and 0.1 mol l^{-1} sulphuric acid has been reported (Merkle and Discher, 1964; Kabasakalian and Mc Glotten, 1959) to give two waves and one wave in 0.5 mol l^{-1} sulphuric acid. No third wave has previously been reported and the presence of chloride obscures the interpretation of the electrode process.

Voltammetric determination of propranolol (Irena and Marta, 2011), levodopa (Ali *et al*., 2010), methyldopa (Carmen *et al*., 2007), electrocatalytic measurement of levodaopa (Halimeh *et al*., 2009) electrosensitive technique for oxprenolol (Matsui *et al*., 2007) and spectrophotomery for dothiepin and spectrochemical determination of chlorpromazine (Danicla and lueno, 2005) (Hisham *et al*., 2006) has been reported. Example from the literature on the determination of these drugs are: Fluorimetry (Black *et al*., 1965) spectrophotometery (Elzeany *et al*., 2003), GLC (Hackett and Dusci, 1979), HPLC (Pritchard *et al*., 1979), TLC (Ching-Erhlin *et al*., 1996), radioimmunoassay (Kawashima *et al*., 1976) and GC-MS (Ehrsson 1976), Procainamide has been determined polarographically (Pierre-Masturi and Jacques, 1985) and voltammetry with solvent polymeric membrane ion sensors (Ortuno *et al*., 2007) as well as by other methods but the common method of assay is HPLC (Karimi *et al*., 2011). The object of the present study is to present the application of voltammeteric method for the determination of some drugs in solid dosage form and comparison of results with the British Pharmacopoeia methods.

**Corresponding author:* e-mail: drwaqarhussein@yahoo.com

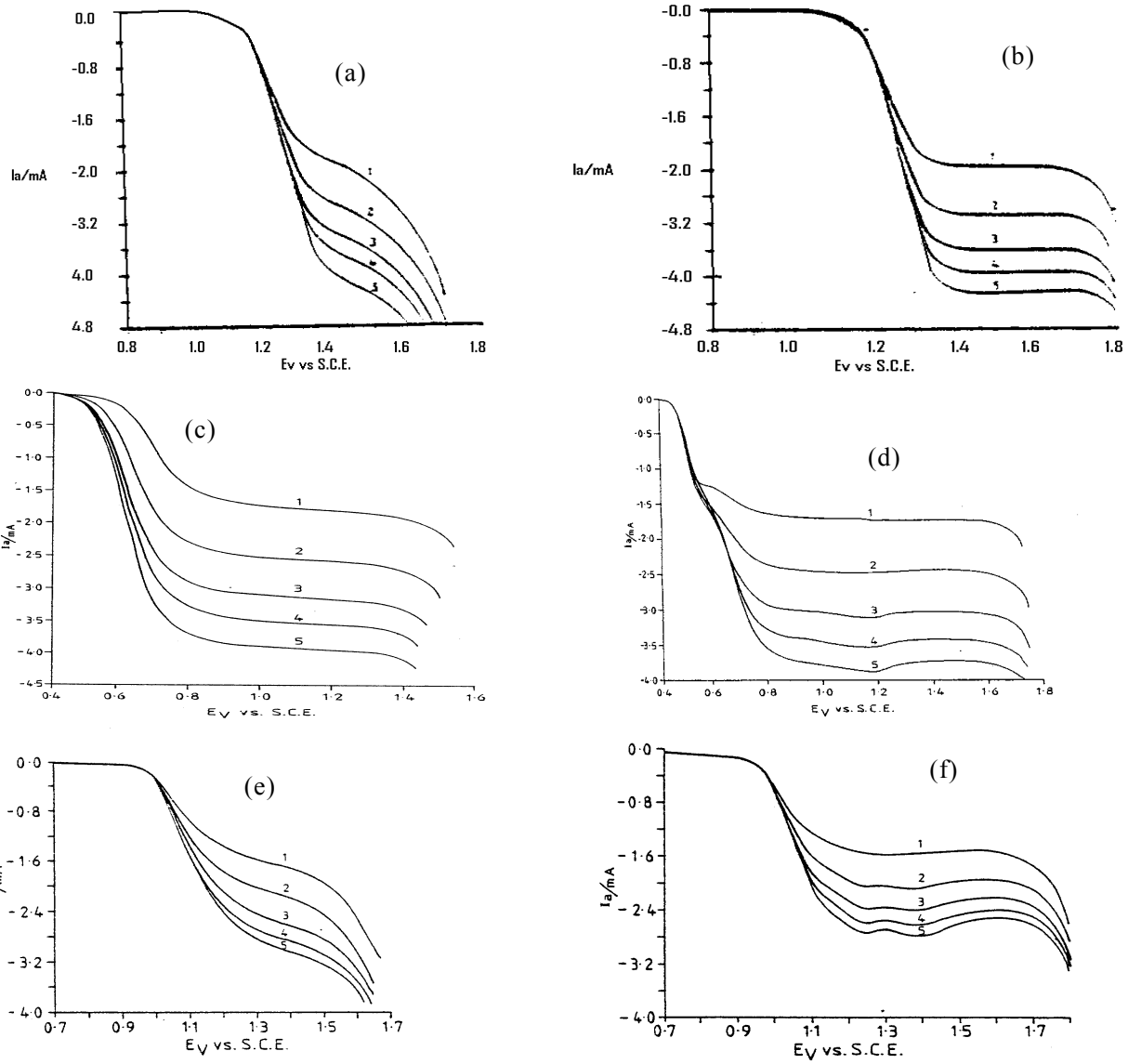

Fig. 1: Anodic Voltammogram of the drug in tablet in 0.1 mol l^{-1} sulphuric acid electrode area 0.503 cm^2, rotation speed 10, 20, 30, 40 and 50 Hz scan speed 5mVs^{-1}(a) Oxprenolol at platinum (b) at gold (c) L-dopa at platinum (d) at gold (e) Procainamide at platinum (f) at gold.

MATERIALS AND METHODS

The glassware, rotating electrode assembly and its associated electronics, electrode activation, other apparatus and solution manipulation and deoxygenation and general procedure for voltammetry has been described (Bishop and Hussein, 1984). The samples of dosage form and pure drugs were supplied of drug standard by the manufacturer named in table 1. These were stored under protection from light and handled under nitrogen. The samples mainly in their hydrochloride form were of drug standard grade and converted to sulphate as previously described (Bishop and Hussein, 1984). The normal voltammetric scan speed was 5mVs^{-1} and the geometric area of the electrode was 0.503 cm^2.

Solutions of dosage form for voltammetric study

According to British Pharmacopeia (2003), a sample of 20 tablets of each formulation was weighed and crushed to fine powder. A quantity of the powder equivalent to one tablet active ingredient (as specified for each formulation) was taken and dissolved in 20 ml water and shaken well to ensure complete solubility of the drug. The solution was filtered in 50 ml volumetric flask. The residue and filter paper was washed with a small amount of water to transfer the dissolved drug. 5 ml 1 mol l^{-1} sulphuric acid was added, the solution was shaken and then sufficient water was added to make upto 50 ml. the solution was transferred to a thermostate cell for voltammetric determination. The active compounds were also examined in citrate and phosphate buffers. Current-potential curve

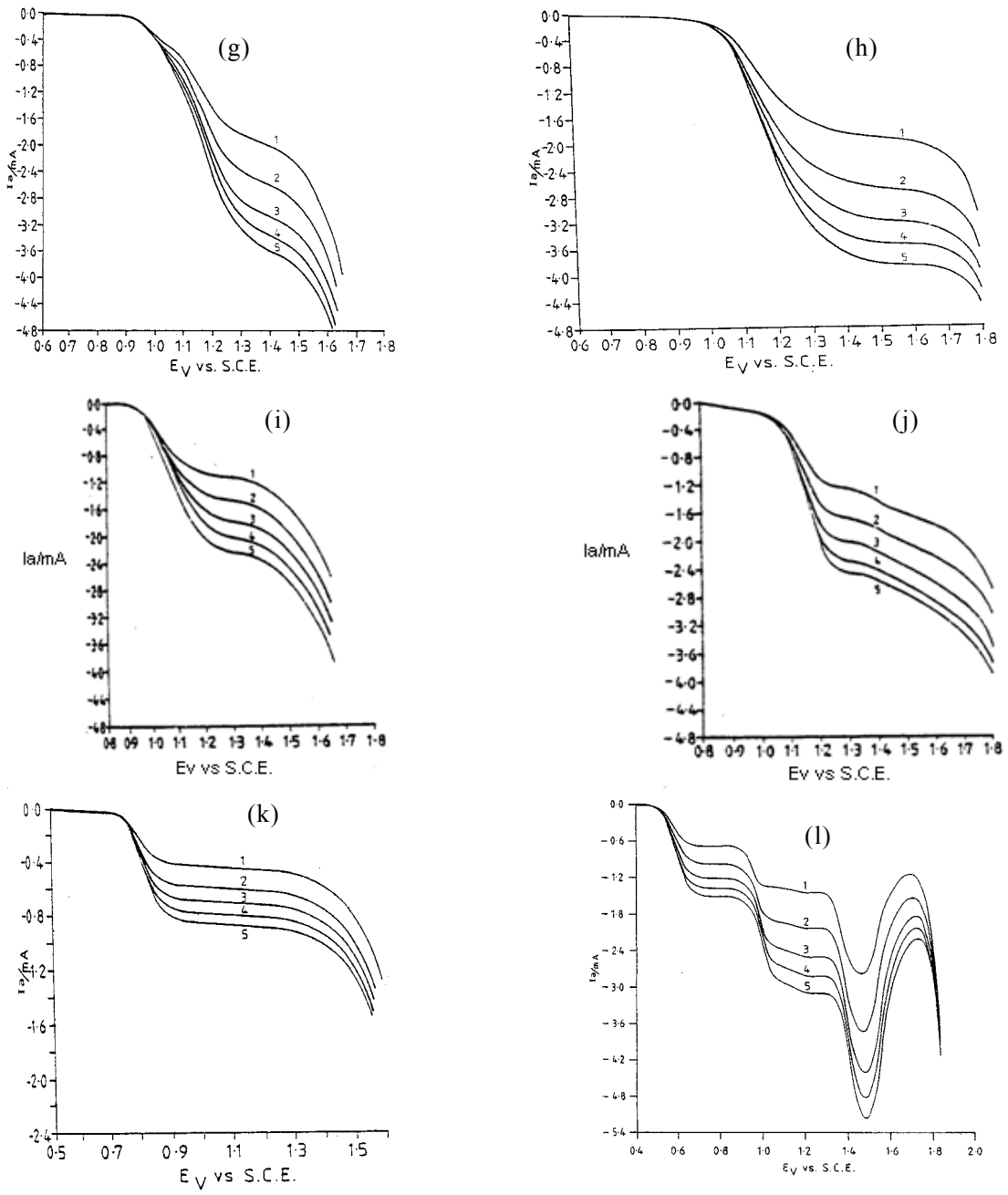

Fig. 2: Anodic Voltammogram of the drug in tablet in 0.1 mol l^{-1} sulphuric acid electrode area 0.503 cm^2, rotation speed 10, 20, 30, 40 and 50 Hz scan speed 5mVs^{-1} (g) Propranolol at platinum (h) at gold (i) Dothiepin at platinum (j) at gold (k) Imipramine at Platinum (l) Chlorpromazine at gold (second wave limiting current is used).

for each dosage form were recorded at 25^0C as described (Bishop and Hussein, 1984).

Limitation of Voltammetric Method

1. Voltammetry is widely used method due to its remarkable detectability, experimental simplicity and low cost for the analysis of pharmaceutical compounds and biological sample with detection limit 10^{-7}M.
2. In recent advances the instrument can be made computerized processing for analytical data.
3. The performance of the voltammetric technique is strongly affected by the working electrode surface hence activation of the electrode is essential to renew the surface that enhance the diffusion process.
4. The increasing popularity of voltammetric technique at solid disc electrode can be attributed to the fact that the

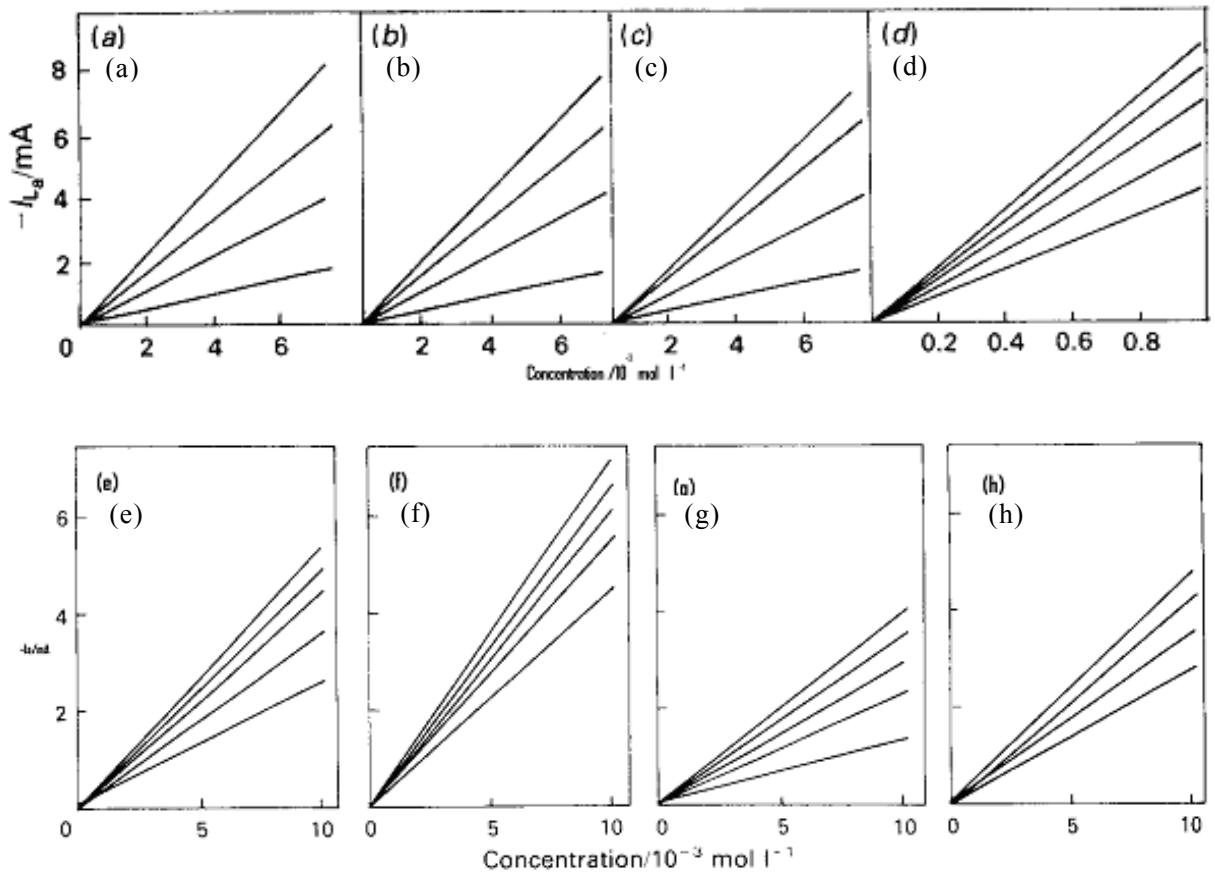

Fig. 3: Calibration plots of limiting current against concentration (a) Oxprenolol at platinum (b) at gold (c) Methyl dopa at platinum (d) Desipramine at gold (e) Propranolol at platinum (f) L-dopa at gold G(g) Procainamide at platinum (h) Dothiepin at platinum for nominal concentration of 2, 5, 8 and 10x10^{-3} mol l^{-1} with increasing frequency 10, 20, 30, 40 and 50 Hz.

oxidation of organic molecules can not be studied by mercury electrode due to its limited anodic potential range.

5. In voltammetry the choice of solvent is an essential aspect, least number of complication occur if measurement can be made in aqueous media with adequate buffering be provided to avoid change in pH and resultant change in electrochemical system.
6. Dilute supporting electrolyte 10^{-1} or 10^{-2} mol dm^3 shows exceptionally good result in concentrated solutions a decrease of diffusion coefficient takes place due to increase in viscosity.

RESULTS

Application of voltammetric method

Voltammetric study of each pure drug listed in table 1 in 0.1 mol l^{-1} sulphuric acid has been performed in detail by scanning the voltammogram at different rotation speeds, (10, 20, 30, 40 and 50 Hzs) of platinum and gold electrodes. The kinetic study and analytical validity of the system has been described earlier (Bishop and Hussein, 1984). To appraise the reliability of rapid determination a series of four solutions of each of these pure drug was prepared and voltammograms were scanned at rotation speeds 10,20, 30, 40 and 50 Hz. The measurement of the limiting current was made at each five rotation and calibration curves for the individual pure drugs were constructed some are presented in fig. 3. The voltammograms of the drug in each solid dosage form were recorded in 0.1 mol l^{-1} sulphuric acid at 10,20,30,40 and 50Hz on both electrodes. Figs. 1 and 2 produce identical voltammetric curves as reported for pure drugs (Bishop and Hussein, 1984).

The content of active ingredient in one tablet was determined by measuring the limiting current of anodic voltammetric curve of dosage form at 50 Hz rotation speed and calculation of the concentration from the slope and intercept of the respective calibration graph. The calibration results of various dosage form at platinum and gold electrodes are given in table 3 and 4 with relative standard deviation is just under 2% less than 10 min being required for each drug measurement. Assay of dosage

Table 1: details of tablet formulations used in the investigation

Proprietary Name	Generic Name	Content mg/tablet	Batch No	Manufacturer
Trasicor	Oxprenolol HCl	20	F 213	Ciba Laboratories
Tofranil	Impipramine HCl	25	3632	Geigy Pharmaceuticals
Pertofran	Desipramine HCl	25	P10001/5019	Geigy Pharmaceuticals
Inderal	Propranolol HCl	40	510	Imperial Chemical Industry
Prothiaden	Dothiepin HCl	75	5KK	Boots Company Limited
Largactil	Chlorpromazine HCl	100	NM2158	May & Baker Limited
Aldomet	Methylodpa	125	21070	Merck Sharp & Dohme Ltd.
Pronestyl	Procainamide HCl	250	CONIHO 38	Squibb & Sons Limited
Brocadopa	Levodopa	500	0064	Brocades Great Britain

Table 2: voltammetric charactersistics of the drug in tablets

Drug in Tablet	Platinum Electrode			Gold Electrode		
	Wave used	E½ V	Limitings* Current,(I_L) mA	Wave used	E½ V	Limitings* Current, mA
1. Oxprenolol HCl	Single	1.12	1.24	Single	1.14	1.28
2. Imipramine HCl	Single	0.81	1.30	Single	0.83	1.33
3. Desipramine HCl	Single	0.81	1.10	Single	0.82	1.15
4. Propranolol HCl	Second	1.12	1.87	Second	1.15	1.95
5. Dothiepin HCl	Single	1.08	2.05	Single	1.15	2.28
6. Chlorpromazine HCl	Single	0.59	1.57	Single	0.59	1.64
7. Methyldopa	Single	0.62	2.66	Single	0.64	2.77
8. Procainamide HCl	Single	1.0	2.30	Single	1.05	2.37
9. Levodopa	Single	0.65	3.70	Single	0.69	3.72

*IL represents to the concentration of compound in the solution used for measurement.

Table 3: data for the voltammetric assay of the drug in tablets at platinum electrodes

Drug in Tablets	Declared	Content (mg/Tablet)		B.P. ± % Limits *
		Found Mean± S.D.	Recovery %	
1. Oxprenolol HCl	20	19.7 ± 0.7	98.5	92.5 – 107.5
2. Imipramine HCl	25	25.4 ± 0.3	101.6	92.5 – 107.5
3. Desipramine HCl	25	24.8 ± 0.1	99.2	92.5 – 107.5
4. Propranolol HCl	40	40.5 ± 0.5	101.2	95.0 – 105.0
5. Dothiepin HCl	75	74.1 ± 0.6	98.8	92.5 – 107.5
6. Chlorpromazine HCl	100	97. 3± 0.5	97.3	92.5 – 107.5
7. Methyldopa	125	123.9 ± 1.0	99.1	95.0 – 105.0
8. Procainamide HCl	250	250.0 ± 0.3	100.0	95.0 – 105.0
9. Levodopa	500	496.9 ± 1.2	99.4	95.0– 105.0

* British Pharmacopoeia (2003)

form presented no difficulty.

The Voltammetric characteristics of the medicinal compounds in tablets used in this investigation are given in table 2, which are identical to the pure drugs as reported (Bishop and Hussein, 1984). The Voltammetric assay results for the individual tablets at platinum and gold electrodes are reported in table 3 and table 4, respectively. The percentage recovery of the labelled amount, obtained for the two electrodes, indicates that the activity of both electrodes is almost the same under identical experimental conditions and equally reliable results can be obtained from the use of either electrode. The obtained results were verified by British Pharmacopoeia (B.P., 2003) methods i.e. spectrophotometric/titrimetric. Calibration curves of individual pure drug were prepared with four different concentrated solutions and with their measured absorbance the drug in one tablet was determined by measuring the absorbance for particular drug solution from the slope of the

Table 4: data for the voltammetric assay of the drug in tablets at gold electrodes

Drug in Tablets	Declared	Content (mg/Tablet)		B.P. ± % Limits *
		Found Mean± S.D.	Recovery%	
1. Oxprenolol HCl	20	20.5 ± 0.4	102.5	92.5-107.5
2. Imipramine HCl	25	24.5 ± 0.2	98.0	92.5-107.5
3. Desipramine HCl	25	24.8 ± 0.1	99.2	92.5-107.5
4. Propranolol HCl	40	39.7 ± 0.4	99.2	95.0-105.0
5. Dothiepin HCl	75	74.1 ± 0.6	99.8	92.5-107.5
6. Chlorpromazine HCl	100	97. 3± 0.5	97.3	92.5-107.5
7. Methyldopa	125	123.9 ± 1.0	99.1	95.0-105.0
8. Procainamide HCl	250	249.5 ± 0.3	99.8	95.0-105.0
9. Levodopa	500	496.9 ± 1.2	99.4	95.0-105.0

*British Pharmacopoeia (2003)

Table 5: Assay of Tablet s Content According to British Pharmacopeia

Drug in Tablet	Content Mg/tablet	Content Mg/tablet	
		Found Mean±SD	Recovery%
Oxprenolol	20	19.80 ± 0.6	98.6
Imipramine	25	24.75 ± 0.3	99.5
Desipramine	25	24.85 ± 0.2	99.8
Propranolol	40	39.65 ± 0.6	97.6
Chlorpromazine	100	100.15 ± 0.4	101.05
Methyl-dopa	125	124.90 ± 0.7	99.90
Procainamide	250	250.05 ± 1.0	101.8
Levo-dopa	500	497.02 ± 0.8	98.7
Dothiepin or Dosulepin	75	74.4 ± 1.1	97.7

Table 6: Precision and accuracy of the assay methods

Drug in Tablets	Voltammetric Assay				B.P Assay*	
	Pt Electrode		Au Electrode			
	R.S.D.** %	R.E. *** %	R.S.D. %	R.E. %	R.S.D. %	R.E. %
1. Oxprenolol HCl	2.5	-1.5	2.0	+2.5	1.5	+2.0
2. Imipramine HCl	1.2	+1.6	0.8	+2.0	1.2	-1.2
3. Desipramine HCl	0.4	-0.8	0.4	-0.8	0.8	-2.4
4. Propranolol HCl	1.2	+1.2	1.0	-0.7	1.5	+2.2
5. Dothiepin HCl	0.8	-1.2	0.8	-1.2	0.5	-0.9
6. Chlorpromazine HCl	0.5	-0.7	0.5	-2.7	0.2	+0.9
7. Methyldopa	0.8	-0.9	0.8	-0.9	0.4	-0.5
8. Procainamide HCl	0.0	0.0	0.1	-0.2	0.2	-0.4
9. Levodopa	0.2	-0.6	0.2	-0.6	0.1	-0.3

*British Pharmacopoeia (2003), **Relative Standard Deviation, ***Relative error

respective calibration graph. The calibration results and titrimetric finding are reported in table 5.

DISCUSSION

The assay values lie well within the B.P. limits specified for the individual compounds. The results of the assay carried out by the B.P. methods show that all the values are with the specified limits. The two methods may be compared on the basis of their relative precision and accuracy. The relative standard deviation for the voltammetric method and the B.P. method range from 0.0 to 2.5 (platinum electrodes) and 0.1 to 2.0 (gold electrode). The relative standard error for these methods is ±2.5% table 6. Thus within the experimental limitation the voltammetric method appears to be as good as the B.P. method. It does not involve any pretreatment of the sample and is sufficiently sensitive, rapid and reliable for the assay of medicinal agents in pharmaceutical dosage forms.

On the basis of the comparison made between the voltammetric and B.P. methods, it may be concluded that electrochemical methods such as voltammetry could be successfully applied to the assay of pharmaceutical compounds having electro-oxidisible or electro-reducible characteristics. A few applications of polarographic determination are reported in the United States Pharmacopoeia while so far none of these methods is included in the British Pharmacopoeia. With suitable development of the technique, its adaptation for pharmaceutical purposes and evaluation of the effect of commonly used excipients, it would be worthwhile to incorporate voltammetric methods in the British Pharmacopoeia as useful rapid and reliable alternative methods.

Influence of pH on Electroanalytical Performance

Hydrogen ions are involved in the redox reaction on organic compounds. The solution pH and viscosity can influence the course of the electrochemical reaction as well as the potential at which it occurs. Alternation of pH often results in a change in the reaction product. The half wave potentials for organic compounds are marked by pH dependent (Bishop 1975). An electrode process consuming or producing hydrogen ions will tend to alter the pH of the solution at the electrode surface unless the solution is well buffered marked change in pH can occur in the surface film as the electrolysis proceeds.

These changes will affect the oxidation and reduction potential of the reaction and lead to drawn out poorly defined wave. When the electrode process is altered by the pH nonlinearity in the diffusion current concentration relationship must be expected. The organic compounds electrolysis requires good buffering for reproduceable results (Bishop 1975).

The citrate and phosphate buffer exerted specific influence on electrode and electrode processes. The charge transfer rate constant for the back ground reaction decreased with increasing pH but charge transfer coefficient is little effected (Bishop and Hussein, 1984). In the present study for both platinum and gold electrodes the best performance was observed in 0.1 mol 1 sulphuric acid. Variation in half wave potential wave height and wave suppression differed from compound to compound, but not fresh wave appeared. In general the quality of the voltammogram deteriorated on increasing the pH (Bishop and Hussein 1984). In view of the electrochemical behaviour of the compounds studied, 0.1 mol l^{-1} sulphuric acid has proved to be the best medium for analytical work. No reliable results were obtained for the electrochemical behavior of drugs in citrate and phosphate buffers. It appears that the best performance is achieved under strongly acidic medium pH 1.0 (Bishop and Hussein 1984).

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