Journal of Advanced Chemical Sciences 2(4) (2016) 369–372

ISSN: 2394-5311

Contents List available at JACS Directory

Journal of Advanced Chemical Sciences

journal homepage: www.jacsdirectory.com/jacs

Simultaneous Electrochemical Determination of Paracetamol and Ibuprofen at The Glassy Carbon Electrode

E. Suresh[1], K. Sundaram[1], B. Kavitha[2], S. Maria Rayappan[3], N. Senthil Kumar[3,*]

[1]*Department of Chemistry, Karpagam University, Karpagam Academy of Higher Education, Coimbatore – 641 021, Tamil Nadu, India.*
[2]*Department of Chemistry, Sri Ranganathar Institute of Engineering and Technology, Coimbatore – 641 110, Tamil Nadu, India.*
[3]*Department of Chemistry, Arignar Anna Government Arts College, Cheyyar – 604 407, Tamil Nadu, India.*

ARTICLE DETAILS

Article history:
Received 12 August 2016
Accepted 30 August 2016
Available online 02 September 2016

Keywords:
Paracetamol
Ibuprofen
Voltammetry
Simultaneous Detection
Pharmaceutical

ABSTRACT

The aim of this investigation is to develop an analytical method for the simultaneous estimation of Paracetamol and ibuprofen in commercial tablets using differential pulse stripping voltammetric (DPSV) and square wave stripping voltammetric (SWSV) techniques. The effect of supporting electrolyte, pH and scan rate on voltammetric response of paracetamol with ibuprofen was studied and the optimum experimental conditions were derived. Linear response of peak currents on the concentration in the range between 300 and 700 ppb, good repeatability (RSD of 2.4% for SWSV and 2.7% for DPSV of seven successive measurements) and the detection limit of 200 ppb for DPSV and 100 ppb for SWSV were observed. The method was validated for accuracy, precision and specificity. The practical analytical utility of proposed method was successfully demonstrated by determination of both drugs in pharmaceutical formulations (tablets) with results in a close statistical agreement to those declared by manufactures.

1. Introduction

Paracetamol, para-(N-acetyl-4-aminophenol) is widely used as analgesic and anti-pyretic [1]. It is mainly used as an alternative to aspirin for relief of mild pain and antipyresis. Paracetamol is as an active ingredient in pharmaceutical preparations. Paracetamol can cause serious or fatal adverse effects when taken in overdose; the liver conjugation becomes inundated, causing paracetamol to be metabolised by an alternative pathway.

Ibuprofen (IBU) is a non-steroidal anti-inflammatory drug, it works by reducing hormones that cause inflammation and body pain. It is used for the relief of symptoms of arthritis, fever, primary dysmenorrhea, and as an analgesic. The World Health Organization includes ibuprofen in its "Essential Drugs List"; a list of minimal medical needs for a basic health care system. However, Ibuprofen can increase risk of fatal heart attack or stroke, especially if it is used for long term or taken in high doses.

Identification and quantification of these drugs is of paramount importance, since an overdose of these drugs can cause adverse effects. Simultaneous determination of paracetamol and ibuprofen using derivatives of the ratio spectra method was reported [2, 3]. Ibuprofen in film coated tablets of different strengths has been determined using different spectrophotometric methods [4]. A limited number of spectrophotometric methods applicable to these samples are based on derivative (first and second-order) UV spectroscopy [5]. The determination of Ibuprofen in biological fluids by LC–UV or LC–MS was reported and validated over the 10–1000 ng/mL range [6]. The extensive literature survey revealed that numbers of methods are reported for the detection of individual drugs and combinations using UV and HPLC methods [7-9]. Electrochemical methods, such as differential pulse polarography (DPP), stripping voltammetry (SV), differential pulse voltammetry (DPV) and square-wave voltammetry (SWV) have been widely applied for the determination of pharmaceuticals [10–21]. However, the simultaneous electrochemical estimation of both drugs in combined dosage forms was not reported so far.

The aim of the present work is to develop simple, precise and accurate electrochemical method for the simultaneous determination of paracetamol and ibuprofen in pharmaceutical formulations.

2. Experimental Methods

All electrochemical measurements were performed using CH Instruments Electrochemical Workstation (CHI 650C). Typically, three-electrode cell was used for electrochemical measurements. Glassy carbon (GC) was used as working electrode. GC electrode was pre-treated by mechanical polishing over a velvet micro-cloth with an alumina suspension. Ag/AgCl and platinum wire were used as reference and counter electrodes, respectively. Potentials notified in the present work are against Ag/AgCl. The electrochemical measurements were performed by purging nitrogen in the electrochemical cell (15-mL capacity) containing analyte for 15 minutes under constant stirring. All electrochemical experiments were performed at 25 °C inside the Faraday cage in order to minimize the contribution of background noise to the analytical signal.

Paracetamol and ibuprofen were purchased from Merck (AR grade). Stock solution of ibuprofen and paracetamol was prepared with aqueous ethanol. Deionised water was used for all the preparations and measurements. The morphology of the electrode surface was examined by Nanosurf Easy scan 2 AFM under the following conditions. Scan direction – up, time/line – 206 ms, tip voltage -1.0 V, vibration frequency – 169.969 KHz, Measurement environment – air and operating mode – dynamic force.

3. Results and Discussion

3.1 Effect of pH

Cyclic voltammograms of paracetamol and ibuprofen were recorded at various pHs between 1.0 and 13.0 at scan rate of 100 mVs^{-1}. The cyclic voltammetric response at different pHs revealed the electroactive nature of both drugs. Two oxidation and one reduction peaks were observed in all pHs. The influence of pH on the oxidation and reduction of the compounds were studied. Fig. 1 and Fig. 2 show the effect of pH on the peak potential and peak current values, respectively. Variation of peak

*Corresponding Author
Email Address: nsk.nagai@gmail.com (N. senthil kumar)

Cite this Article as: E. Suresh, K. Sundaram, B. Kavitha, S. Maria Rayappan, N. Senthil Kumar, Simultaneous electrochemical determination of paracetamol and ibuprofen at the glassy carbon electrode, J. Adv. Chem. Sci. 2(4) (2016) 369–372.

current with pHs resulted in a parabolic curve. Maximum peak current for oxidation was observed at pH 1.0. This may be due to the faster electron transfer rate at acidic pH and this indicates that the rate of the reaction is controlled only by electron transfer. From the study, it is concluded that pH 1.0 is the optimum pH for the electrochemical process and further studies were performed at this pH.

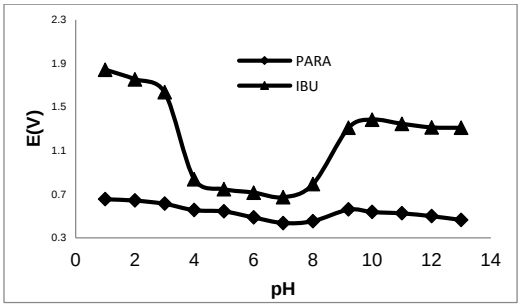

Fig. 1 Plot of peak potential vs pH

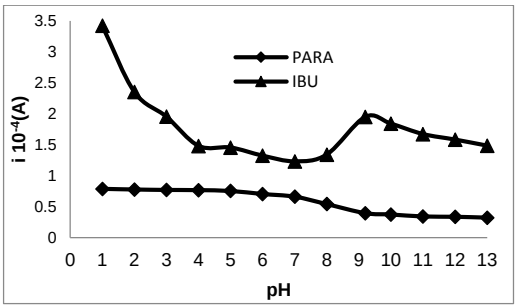

Fig. 2 Plot of peak current vs pH

3.2 Voltammetric Studies

The cyclic voltammetric behaviour of paracetamol and ibuprofen in 0.1 M H_2SO_4 + 50% aqueous methanol (pH 1.0) was studied at the GC electrode. Two anodic and one small reduction peaks were observed in the potential range from 0 to 2 V, Fig. 3. The anodic peak observed around 0.739 V is accounted for the oxidation of paracetamol and 1.825 V for the oxidation of ibuprofen.

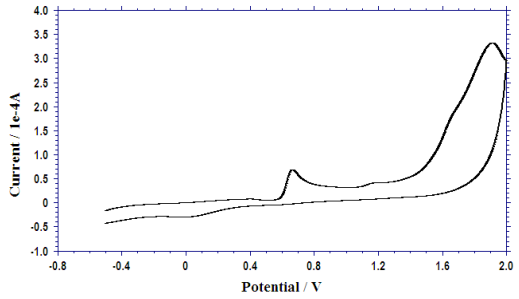

Fig. 3 Cyclic voltammetric response of paracetamol and ibuprofen (300 ppm) at GC electrode (pH 1.0; scan rate: 100 mVs^{-1})

The effect of scan rate on the peak current and peak potential was studied. The scan rate was varied between 25 and 500 mVs^{-1}. The peak current increases with increase in scan rate (Figs. 4 and 5). A linear correlation was obtained between peak currents and the square root of scan rate. This indicates that the nature of redox process at the GC electrode is controlled by diffusion (Fig. 4). The log i_p vs log scan rate (Fig. 5) exhibited linearity with a slope of 0.3561. The effect of peak potential with scan rate is shown in Fig. 6. The peak potential values shifted anodically with increase in scan rate. By using E_p vs log ν plot, α value was calculated and found to be 0.244.

The effect of change in concentration of the analytes was studied by changing the concentration from 100 to 500 ppm at a scan rate of 100 mVs^{-1}, Fig. 7. The peak current showed linearity with varying concentrations and resulted in a good correlation (r^2 = 0.992).

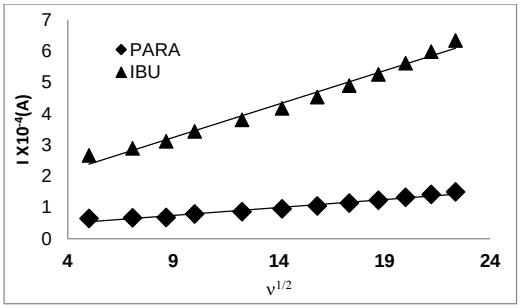

Fig. 4 Plot of peak current vs square root of scan rate

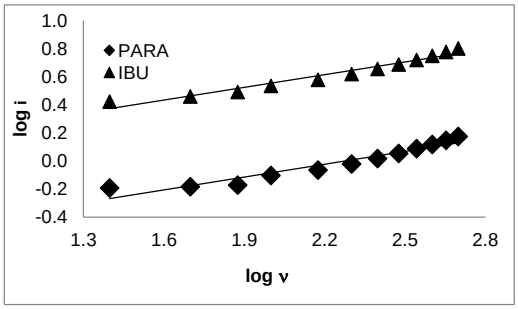

Fig. 5 Plot of log peak current vs log scan rate

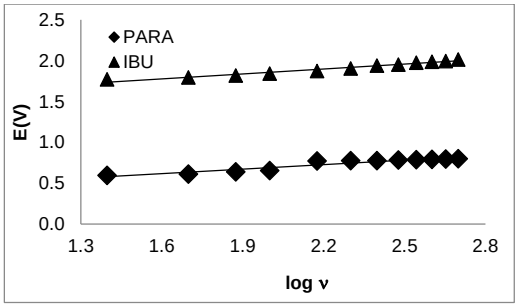

Fig. 6 Plot of potential vs log scan rate

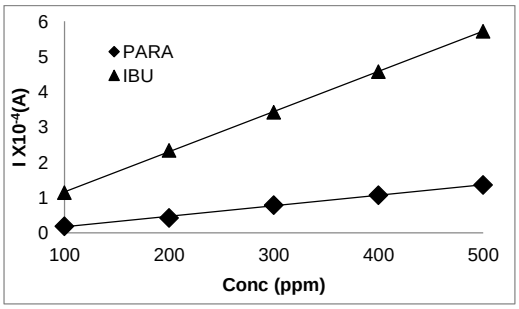

Fig. 7 Plot of peak current vs concentration of paracetamol and ibuprofen

3.3 Stripping Voltammetry

3.3.1 Differential Pulse Stripping Voltammetry (DSPV)

Stripping voltammetry is a very sensitive method for the analysis of trace concentrations of electro active species in solution. The advantages of stripping voltammetry include sensitivity (ppb) and short analysis time (tens of minutes). Adsorptive stripping voltammetry involves two steps; first step is the accumulation of analyte on the electrode surface and the second step involves stripping. It was expected that paracetamol and ibuprofen would adsorb on the electrode during the accumulation step and strip off easily in the following stripping step. The stripping voltammetric studies of both the drugs were done at GC electrode in ethanol medium (pH 1.0). The drugs exhibited excellent stripping voltammetric signal. AFM image of paracetamol and ibuprofen adsorbed on GC surface is shown in Fig. 8. Small granular like structures are seen on the electrode surface. A systematic study of various instrumental parameters that affect the stripping response was carried out with 300 ppb concentration of drugs.

The instrumental parameters such as accumulation potential, initial scan potential, deposition potential, pulse amplitude, pulse increment, pulse width, and pulses were optimized to get sensitive response and is tabulated in Table 1.

Cite this Article as: E. Suresh, K. Sundaram, B. Kavitha, S. Maria Rayappan, N. Senthil Kumar, Simultaneous electrochemical determination of paracetamol and ibuprofen at the glassy carbon electrode, J. Adv. Chem. Sci. 2(4) (2016) 369–372.

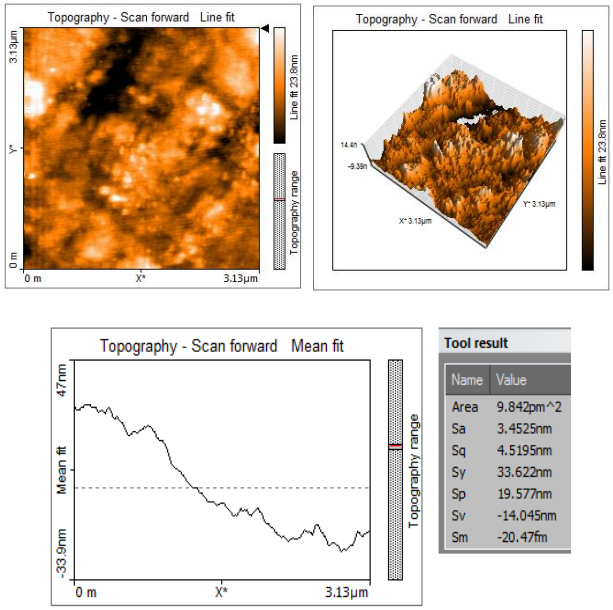

Fig. 8 AFM images of paracetamol and ibuprofen adsorbed on the GC electrode surface

Table 1 Optimum parameters condition of stripping voltammetry of paracetamol and ibuprofen at glassy carbon electrode at pH 1.0

Parameters	DPSV Range examined	DPSV Optimized value	SWSV Range examined	SWSV Optimized value
Accumulation potential (V)	0.2 to 1.5	0.6	-0.3 to 1.6	0.4
Deposit time (sec)	5 to 75	15	15 to 75	30
Initial scan potential (V)	-0.1 to 0.5	0	-0.1 to 0.3	0
Pulse height (V)	0.025 to 0.15	0.1	-	-
Pulse width (msec)	25 to 150	100	-	-
Pulse period (sec)	2 to 10	6		
Scan rate (mV/sec)	20 to 80	60	-	-
Square wave amplitude (mV)	-	-	20 to 70	40
Frequency (Hz)	-	-	10 to 100	50
Scan increment (mV)	2 to 20	6	2 to 20	2
Stirring rate (rpm)	50 to 250	200	50 to 250	250
Rest period (Sec)	2 to 10	5	2 to 10	5

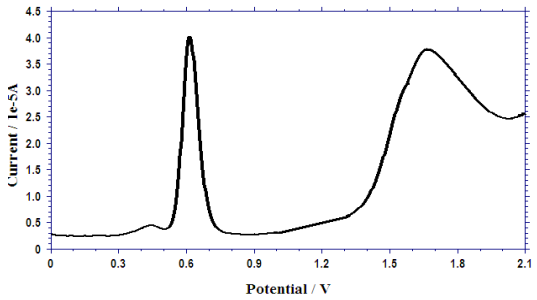

Fig. 9 Differential pulse stripping voltammogram recorded in the electrolyte medium containing Paracetamol and Ibuprofen at the GC electrode under optimum condition

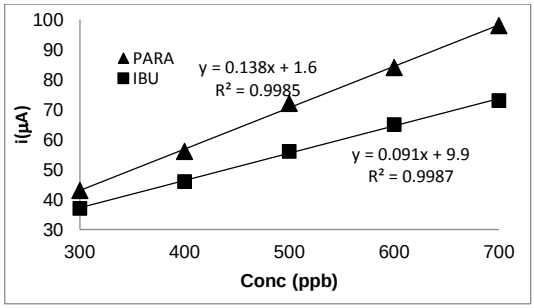

Fig. 10 Calibration plot of DPSV

Under optimum experimental conditions, the influence of concentration on the stripping signal was studied. The experimental results showed that the peak current increased with the increase in concentration of drugs. A representative differential stripping voltammogram is shown in Fig. 9. A calibration curve was made, which indicates the linear dependence of peak current with concentrations between 300 and 700 ppb, Fig. 10. The lower limit of detection was found to be 200 ppb. High reproducibility of the stripping signal (R.S.D. of 2.7%) was observed for 7 repetitive measurements at a concentration level of 300 ppb.

3.3.2 Square Wave Stripping Voltammetry (SWSV)

Square wave stripping voltammetry was carried out in pH 1.0 and the parameters which affect the stripping signals were optimized as follows.

Effect of accumulation potential was studied by varying from -0.3 to 1.6 V. Maximum current was observed at 0.4 V. Considerable responses were observed when the initial scanning potential is fixed at 0 V. Hence 0 V was fixed as optimum value for initial scan potential. Step potentials were varied from 2 to 10 mV and the deposition time between 15 and 75 s. The optimum values were found to be 2 mV and 30 s, respectively. Effect of square wave amplitude on the peak signal was studied by varying from 20 to 70 mV. Square wave amplitude of 40 mV was chosen as optimum. The effect of scanning frequency on the peak current value was varied from 10 to 100Hz and 50 Hz was fixed as suitable frequency. The optimum experimental conditions for SWSV are presented in Table 1.

Representative square wave stripping voltammogram is shown in Fig. 11 and the calibration plot of peak current vs. concentration derived from the stripping voltammograms is presented in Fig. 12. The electrode shows linearity for the current response to the concentration in the range between 300 and 700 ppb. The reproducibility of the stripping signal was ascertained in terms of relative standard deviation for five measurements carried out at a concentration level of 300 ppb and found to be 2.4 %.

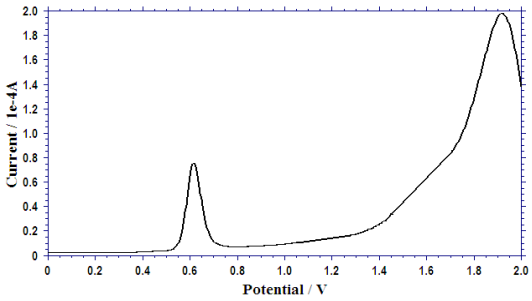

Fig. 11 Square wave stripping voltammogram recorded in the electrolyte medium containing paracetamol and ibuprofen at the GC electrode under optimum condition

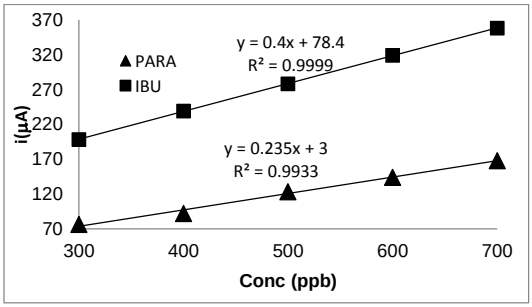

Fig. 12 Calibration plot of SWSV

3.3.3 Determination of Drugs in Pharmaceutical Samples

The applicability of the proposed analytical method for practical purpose was assessed by determination of paracetamol and ibuprofen in various tablets and injection samples under the optimized conditions. Stock solution was prepared by dissolving the tablets and was subsequently diluted without any pretreatment. Table 2 presents the results for the detection of Paracetamol and Ibuprofen in pharmaceutical drugs. The results are satisfactory and agree with value determined reported by the manufacture.

Table 2 The amount of compounds determined by SWSV at GC electrode

Brand name	Company name	Tablets (mg)		Experimental value (mg)		% of RSD	
		PARA	IBU	PARA	IBU	PARA	IBU
Abufen-C	Shinto Biotec	500	400	475	392	1.6	2.2
Actimol-F	Pharmed	500	400	489	391	1.1	2.7
Brupal	Geno	500	400	474	395	2.5	1.9
Combiflam	Sanofi Aventis	325	400	320	389	1.4	2.5
Bumol	Radisun LS	500	400	488	396	2.3	2.1

Cite this Article as: E. Suresh, K. Sundaram, B. Kavitha, S. Maria Rayappan, N. Senthil Kumar, Simultaneous electrochemical determination of paracetamol and ibuprofen at the glassy carbon electrode, J. Adv. Chem. Sci. 2(4) (2016) 369–372.

4. Conclusion

A simple electro analytical method for the simultaneous estimation of paracetamol and ibuprofen is proposed. Proposed analytical technique is simple and rapid in comparison with other analytical methods used for the determination of drugs. The methodology adopted in the present investigation can be conveniently extended to other pharmaceutical drugs.

References

[1] Z. Yasmeen, T. Mamatha, H. Farheen, H.K. Qureshi, Dissolution method development and validation for combination of ibuprofen and paracetamol tablets, Asian J. Pharm. Clin. Res. 6 (2013)164-168.

[2] Y.M. Issa, S.I.M. Zayed, I.H.I. Habib, Simultaneous determination of ibuprofen and paracetamol using derivatives of the ratio spectra method, Arabian J. Chem. 4 (2011) 259-263.

[3] V.D. Hoang, D.T. Ha Ly, N.H. Tho, H.M. Thi Nguyen, UV Spectrophotometric simultaneous determination of paracetamol and ibuprofen in combined tablets by derivative and wavelet transforms, Sci. World J. 2014 (2014) 13-26.

[4] A.A. Wahbi, E. Hassan, D. Hamdy, E. Khamis, M. Barary, Spectrophotometric methods for the determination of ibuprofen in tablets, Pak. J. Pharm. Sci. 18 (2005) 1-6.

[5] S. Sunaric, M. Petkovic, M. Denic, S. Mitic, A. Pavlovic, Determination of ibuprofen in combined dosage forms and cream by direct UV spectrophotometry after solid-phase extraction, Acta Pol. Pharm. 70 (2013) 403-411.

[6] L. Andrade, T. Pekol, A. Grenier, A. Awad, Validation of LC–MS-MS methods for the determination of ibuprofen in miniature swine plasma and synovial fluid, Recent Develop. LC Column Technol. 29 (2011) 10-17.

[7] S.L. Narasimha, G. Nishant, P. Balakrishna, Development and validation of a RP-HPLC for simultaneous determination of ibuprofen and paracetamol in solid dosage forms: Application to dissolution studies, Int. J. Res. Pharm. Sci. 2 (2011) 331-337.

[8] R.S. Joshi, N.S. Pawar, S. Sameer Katiyar, B. Devendra Zope, et al, Development and validation of UV spectrophotometric method for simultaneous estimation of paracetamol and ibuprofen in pure and tablet dosage form, Pelagia Res. Library Der Pharm. Sinica. 2 (2011) 164-171.

[9] G. Riddhi, M. Rajashree, S. Pankaj, Development and validation of sprctrophotometric methods for simultaneous estimation of ibuprofen and paracetamol in soft gelatin capsules by simultaneous equation method, Int. J. Chem. Technol. Res. 2 (2010) 1881-1885.

[10] A. Lakshmi, G. Gopu, S. Thanikaikarasan, T. Mahalingam, P. Alvarez, et al, Electroanalysis of diazepam on nanosize conducting poly (3-methylthiophene) modified glassy carbon electrode, J. New Mat. Electrochem. Sys.17 (2014) 185-190.

[11] A. Lakshmi, C. Vedhi, Synthesis and characterization of poly (3-hexylthiophene) and used as modified electrode for determination of antidepressants in pharmaceutical formulations and urine samples, J. Electrochem. Soc.160 (2013) H1-H6.

[12] A. Lakshmi, J. Anandha Raj, G. Gopu, P. Arumugam, C. Vedhi, Electrochemical, electrochromic behaviour and effects of supporting electrolyte on nano-thin film of poly (3,4-ethylenedioxy thiophene), Electrochim. Acta 92 (2013) 452-459.

[13] M. Sikkander, C. Vedhi, P. Manisankar, Cyclic voltammetric determination of 1, 4-Dihydro pyridine drugs using MWCNTs modified glassy carbon electrode, Der Chem. Sinica 3 (2012) 413-420.

[14] M. Sikkander, C. Vedhi, P. Manisankar, Electro chemical stripping studies of amlodipine using mwcnt modified glassy carbon electrode, Chem. Mat. Res. 1 (2011) 1-7.

[15] M. Sikkander, C. Vedhi, P. Manisankar, Utilization of sodium montmorillonite clay for enhanced electrochemical sensing of amlodipine, Ind. J. Chem. 55 A (2016) 571-575.

[16] G. Gopu, B. Muralidharan, C. Vedhi, P. Manisankar, Determination of three analgesics in pharmaceutical and urine sample on nano poly (3, 4-ethylenedioxythiophene) modified electrode, Ionics 18 (2012) 231-239.

[17] G. Gopu, P. Manisankar, B. Muralidharan, C. Vedhi, Stripping voltammetric determination of analgesics in their pharmaceuticals using nano-riboflavin-modified glassy carbon electrode, Inter. J. Electrochem. 2011 (2011) 1-11.

[18] B. Muralidharan, G. Gopu, C. Vedhi, P. Manisankar, Determination of analgesics in pharmaceutical formulations and urine samples using nano polypyrrole modified glassy carbon electrode, J. Appl. Electrochem. 39 (2010) 1117-1184.

[19] B. Muralidharan, G. Gopu, C. Vedhi, P. Manisankar, Voltammetric determination of analgesics and urine using a montmorillonite modified electrode, Appl. Clay Sci. 42 (2008) 206-213.

[20] C.L. Athota, R.K. Valluri, N.R. Gollapalli, Chemical speciation of divalent metal complexes of L-aspartic acid in propylene glycol-water mixtures, J. Adv. Electrochem. 1 (2015) 5-8.

[21] G. Singh, S. Rani, Determination of promethazine in various pharmaceutical samples using promethazine selective poly(vinyl chloride) membrane electrode, J. Adv. Electrochem. 2 (2016) 42-44.

Cite this Article as: E. Suresh, K. Sundaram, B. Kavitha, S. Maria Rayappan, N. Senthil Kumar, Simultaneous electrochemical determination of paracetamol and ibuprofen at the glassy carbon electrode, J. Adv. Chem. Sci. 2(4) (2016) 369–372.