ACTA SCIENTIFIC PHARMACOLOGY

Volume 2 Issue 10 October 2021

Research Article

Electrochemical Behavior of Ibuprofen and Its Interaction with Ascorbic Acid Using Square Wave Voltammetry

Abeer Salih Atiya and Noha Mohammed Yahya*

Chemistry Department, College of Education for Girls, Mosul University, Mosul, Iraq

***Corresponding Author:** Noha Mohammed Yahya, Assistant Professor, Chemistry Department, College of Education for Girls, Mosul University, Mosul, Iraq.

Received: August 24, 2021

Published: September 23, 2021

Abstract

Oxygen is necessary for energy production through the electron transfer chain in living system to enable the cell to perform its physiological functions, that can produce free radicals of the type of reactive oxygen species as well as reactive nitrogen species leading to cell damage due to oxidative stress that participates in the side effects of Non-Steroidal Anti-inflammatory drugs (NSAIDs). This contradictory effect of oxygen necessitated the development of an antioxidant such as ascorbic acid to protect cell against oxidation by scavenging and inhibiting the action of free radicals. This research included study the electrochemical behavior of ascorbic acid (AA) as antioxidant, ibuprofen as NSAIDs and their interaction using square wave voltammetry technique (SWV) on the hanging mercury dropping electrode (HMDE) as working electrode, Pt-wire as an auxiliary electrode and Ag/AgCl in Sat. KCl as a reference electrode. Ascorbic acid showed an oxidation peak at +0.125 V in pH 4 of acetate buffer solution. While, Ibuprofen showed Under the same default Condition a reduction peak at 0.0755V. Optimum condition were investigated such as pH, start and end potential, deposition potential, deposition time, equilibrium time, voltage step, amplitude, frequency, the size of the mercury drop and sweep rate. In addition, the interaction between the AA and ibuprofen was evaluated by utilizing the calculation of binding constant. The interaction between Ibuprofen and Ascorbic Acid was investigated by calculating the binding constant.

Keywords: Ibuprofen; Ascorbic Acid; Square Wave Voltammetry; Electrochemical Behavior

Introduction

Ibuprofen based on IUPAC name is RS-2-(4- isobutyl phenyl) propanoic acid (IBP). It is a non-steroidal anti-inflammatory drugs that are pharmacology used as analgesic and anti-pyretic agents [1]. This drug blocks the cyclic enzymes as cyclooxygenase by inhibiting prostaglandin biosynthesis [2]. It is metabolized mostly of 90% in the liver to hydroxy and carboxy metabolites of IBP, with less than 10% excreted in urine and bile as IBP [3]. Otherwise, IBP is not traded or effected on an organized securities exchange and highest-selling drug worldwide, consequently making it the first choice for various short-term non-specific pain indications. High risk consumption of IBP is mainly affected by its moderately weak impacts and low toxicity in humans in comparison with other analgesic and anti-inflammatory drugs [4,5]. Ibuprofen structure shown in figure 1.

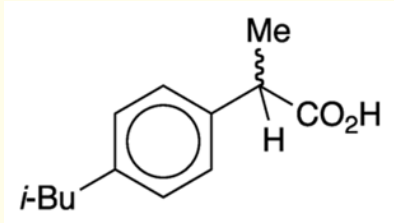

Figure 1: Chemical structure of Ibuprofen.

Currently, electrochemical methods characterize commercially unassuming, time-efficient and comfortable sensitive tool for quantifying various structurally and biologically interesting drugs [4]. So far, the literature review has related to several reports on recognition and quantification of IBP. Despite the useful utilization of conventional bare and chemically modified electrodes, electrochemists are constantly pushed to explore the novel and perspective material platforms as fool-proof electrochemical sensors for detection and determination of IBP and related drugs [5]. The electrochemical response of ibuprofen at the modified surface reveals the irreversible and diffusion electrochemical process. The range of determination was found between 200 ppb, and 400 ppb, the lower limit of detection is 100 ppb through differential pulse voltammetry DPV. The anodic peak was observed at 1.63 V, assigned for the oxidation of ibuprofen, which is not accompanied by corresponding cathodic reduction [6].

Ascorbic acid (AA) or vitamin C is a kind of water soluble vitamin It is important for the formation of growth and repair of bone, skin and muscle. It is also important for the normal function of blood vessels. The action of AA due to its physiological and biochemical properties which are accounted for its work as electron donor [7], in figure 2.

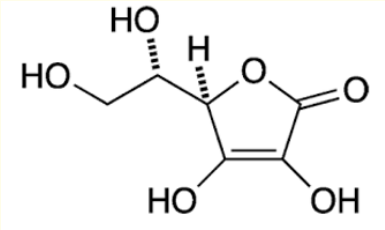

Figure 2: Chemical structure of ascorbic acid.

Hence, vitamin C plays a critical role as antioxidant, to protect cell against damage by free radicals which are produced as by product of normal cell activity and are participate in chemical reaction within the cells [8]. Moreover, through the production of reactive oxygen species, the inflammatory may deplete of antioxidants storage, including vitamin C. Therefore, vitamin C is used in treating inflammatory associated with disease has been considered [9].

Many analytical techniques including titration, chromatography and spectrophotometry were used to determine AA [10]. However, some these techniques have reported disadvantages as a time consuming and others may have low sensitivity [11].

Therefore, the electrochemical methods are employed due to its rapid time consuming, cheap, simplicity, and high sensitivity reach to 10^{-12} M of AA in real samples and in pharmaceutical formulation [12]. Electrochemical determination of AA using electrodes has rather long maintenance. For the investigation of AA by direct electrooxidation some conventional electrodes, such as Hg [13], Au, Pt, and glassy carbon electrode (GCE) has been used. However, the inspection of AA on these electrodes is quite problematic due to the fouling effect on the electrode surface by oxidation. This problem could be solved by modification of the surface of electrode electrochemically as evaluation on unmodified electrodes has some limitations as the overlapping of oxidation potentials could be caused. The problem may be also solved by pulsed laser light treatment, laser pulse irradiation, thermal treatment, dispersion of metal oxides particles on the electrode surface, or by the surface modification by benzoquinone, ferrocene, TCNQ, organosulfur tetrathiafulvalene (TTF), or using 1,1-dimethylferrocene (DMFc) [13].

The aim of this study is to determine the electrochemical behavior of ibuprofen and AA using square wave voltammetry (SWV), then study the interaction between them by calculating the binding constant.

Experimental

Materials and Methods

All reagents and solvents used were obtained from Sigma-Aldrich Germany and Fluka Switzerland company. Ibuprofen and Ascorbic Acid were supplied by the state enterprise for drug industries and medical appliances Samarra-Iraq. The pH of the buffer solutions was measured using pH-meter supplied by company HANNA. Electrochemical measurements were performed using 797 VA Computrace Model supplied by Switzerland Metrohm company [14] by using square wave voltammetry technique (SWV) on the hanging mercury dropping electrode (HMDE) as working electrode, Pt-wire as an auxiliary electrode and Ag/AgCl in Sat. KCl as a reference electrode.

Procedure

The voltametric determination of IBF and AA were carried out in acetate buffer solutions of pH 3,4,5,6, and 7 which prepared from a mixture of 0.2 M of sodium acetate and 0.2 M of acetic acid then

adjusting by 0.1 M of HCl or 0.1M of NaOH to maintain the appropriate pH. Stock solution of IBF was prepared of 10^{-2}M in acetonitrile. Also, stock solution of AA was prepared of 10^{-3}M in distilled water.

Standardization solution 250 ppm of acetate salts of the Cu^{+2}, Cd^{+2}, Zn^{+2}, and Pb^{+2} were prepared in distilled water to calibrate the polarographic analyzer of 797 VA Computrace Metrohm by using SWV technique. The experimental conditions were performed at -1.5V of start potential, +0.25V of end of potential, 0.002V voltage step, 0.02V of amplitude, 50Hz of frequency, 5mmof drop size, and sweep rate of 0.1V/s. The results of polarogram of standardization solution showed in figure 3 [15].

Figure 3: Square wave polarogram of Standardization solution consists of Cu^{+2},Cd^{+2},Zn^{+2}, and Pb^{+2}.

Electrochemical procedure

The electrochemical behavior of $9.9x10^{-5}$M of IBF at HMDE, effect of scan rate in the range between -0.25V to +0.18V, and the influence of pH in the range of 3,4,5,6, and 7 on the peak of potential current of IBF were investigated by applying SWV technique. The effects of voltage step, pulse amplitude, frequency, and drop size were employed to investigate the optimum condition.

The electrochemical behavior of $1.96x10^{-5}$M of AA at HMDE, effect of scan rate in the range between -0.05V to +0.25V, and the influence of pH in the range of 3 - 7 on the peak of potential current of AA were investigated by applying SWV technique. The effects of voltage step, pulse amplitude, frequency, and drop size were employed to investigate the optimum condition.

Results and Discussion

Electrochemical Behavior of Ibuprofen at HMDE

Table 1 presents the polarogram of $9.9x10^{-5}$M of IBF at HMDE in pH4 with scan rate in the range between -0.25V to +0.18V, at default condition of the polarography apparatus.

Parameters	Default Condition Values
Start Potential(V)	-0.25
End Potential(V)	+0.18
Voltage Step(V)	0.002
Amplitude(V)	0.02
Frequency(Hz)	50
Drop size(mm)	5
Sweep rate(V/s)	0.1

Table 1: The values of default condition for $9.9x10^{-5}$ M IBF in pH4 using.

The influence of pH on the reduction wave of IBF was shown in table 2. It was observed an increasing in diffusion current with increasing the value of pH, then the current decreased. The optimum pH was at the value of 5.

pH	Ep(V)	Ip(A)
3	0.0755	7.05×10^{-7}
4	0.0696	2.99×10^{-7}
5	0.0101	2.71×10^{-7}
6	-0.113	1.09×10^{-7}
7	-	-

Table 2: The influence of pH on the potential voltage (Ep) and diffusion current (Ip).

The optimum condition was represented in table 3. Also, the polarogram of SWV of IBF before and after optimum condition was investigated in figure 4.

Parameters	Optimum Condition Values
Start Potential(V)	-0.25
End Potential(V)	+0.18
Voltage Step(V)	0.005
Amplitude(V)	0.03
Frequency(Hz)	50
Drop size(mm)	4
Sweep rate(V/s)	0.25

Table 3: The optimum condition of $9.9x10^{-5}$M of IBF in pH5**.**

Figure 4: SWV Polarogram of 9.9x10^{-5} M of IBF before and after optimum conditions.

In addition, the optimum condition of 1.96x10^{-5} M Ascorbic Acid in pH6 and its polarogram were presented in table 4 and figure 5, respectively.

Parameters	Optimum Condition Values
Start Potential(V)	-0.05
End Potential(V)	0.25+
Voltage Step(V)	0.006
Amplitude(V)	0.02
Frequency(Hz)	50
Drop size(mm)	8
Sweep rate(V/s)	0.3

Table 4: Optimum condition of 1.96x10^{-5} M Ascorbic Acid in pH6.

Figure 5: SWV Polarogram 1.96x10^{-5} M Ascorbic Acid in pH6 before and after optimum condition.

Effect of time on the interaction of IBF and AA

To study the influence of time, SWV Polarogram of 4.98x10^{-5} M of AA interacts with 1x10^{-7}M of IBF in acetate buffer solution of pH7 for 60min. under optimum condition of AA, the results shown in table 5.

Time (Min.)	Ep(V) of Interaction	Ip(A) of Interaction x 10^{-7}
0	0.0215	4.48
5	0.0215	4.12
10	0.0215	4.20
15	0.0215	4.15
20	0.0215	4.12
25	0.0215	4.02
30	0.0215	4.00
35	0.0215	3.95
40	0.0215	3.86
45	0.0215	3.90
50	0.0215	3.80
55	0.0215	3.80
60	0.0215	3.95
S.D		0.188697±

Table 5: Effect of time on the interaction of IBF and AA.

Calculate the binding constant of interaction

In figure 6, Frequent addition of 10^{-7}M of IBF into 4.98x10^{-5}M of AA solution using acetate buffer solution of pH7 was conducting to calculate the binding constant (K) based on the following equation [16,17]:

$$\ln\left(\frac{Ip}{Ip^{\circ}-Ip}\right) = \ln\left(\frac{1}{[Drug]}\right) - \ln K$$

Where, Ip° refers to the current of an oxidation peak of AA, and Ip refers to the current of a reduction peak of IBF.

Conc. of Vit.C(M)	Ep°(V)		Ip°(A) x 10^{-7}	
4.98 x10^{-5}	0.0215		4.37	
Conc. of Ibu. x10^{-7} (M)	Ep(V)	Ip(A) x 10^{-7}	ln(1/[drug])	ln(Ip/(Ip°-Ip)
1	0.0215	4.16	16.118095651	2.9861628225
1.9996	0.0215	4.10	15.4251484504	2.7203202937
2.9991	0.0215	4.01	15.0197833173	2.4104424889
3.9980	0.0156	4.00	14.7323014149	2.3805466345
4.9980	0.0156	3.95	14.5090578185	2.2412161466
5.9960	0.0156	3.95	14.3270030707	2.2412161466
6.9950	0.0156	3.86	14.1729000428	2.0240117367

7.9940	0.0156	3.85	14.0394043907	2.0019996157
8.9920	0.0156	3.60	13.9217603578	1.5422986096
9.99	0.0156	3.57	13.8165110583	1.4957091471
10.987	0.0156	3.52	13.7213828952	1.4209799191
11.985	0.0156	3.50	13.6344397831	1.3920250358
12.983	0.0156	3.44	13.5544548416	1.3080421642
13.980	0.0156	3.43	13.4804679142	1.2944356649
14.977	0.0156	3.43	13.4115799599	1.2944356649
15.974	0.0156	3.34	13.3471332505	1.1764120047
16.971	0.0156	3.33	13.2865896459	1.1637515908
17.967	0.0156	3.31	13.229558909	1.1386792813
18.964	0.0156	3.25	13.1755532059	1.065326311

Table 6: The effect of frequent addition of IBF on the current of oxidation peak of AA.

Figure 6: SWV Polarogram Frequent addition of 10^{-3}M of IBF into $4.98x10^{-5}$M of AA solution using acetate buffer solution of pH7.

The relationship of ln (Ip/ Ip° - Ip) against ln(1/[Drug]), represents in table 6, was obtained straight line with correlation coefficient (R^2= 0.9454) and intercept equal to (-ln K) with negative value of 8.3368 as shown in figure 7.

Figure 7: Relationship of ln (Ip/Ipo - Ip) versus ln(1/[Drug]) of interaction of AA and IBF.

Conclusion

Square wave voltammetry investigation of AA at HMDE against Ag/AgCl in Sat. KCl showed that the oxidation peak potential of +0.0572V with an appropriate peak in pH6 at over the studied range of scan rates, While IBF recorded a reduction peak potential of -0.00809V with an appropriate peak in pH5. From the interaction study, the peak of potential Shift to the value of +0.0215V the scan rate confirmed the irreversibility of the reaction. Furthermore, that shift of peak of potential after optimum condition (from 140mV into the 30mV) indicated the contribution of protons in the oxidation process. Also, the binding constant of AA interaction with IBF illustrated the negative value of K equal to 4.175×10^3.

Acknowledgements

The authors would like to thank the University of Mosul, College of Education for Girls, Department of Chemistry management and staff for all the support during the experimental work stage.

Bibliography

1. R O Day and G G Graham. "Non-steroidal anti-inflammatory drugs (NSAIDs)". *BMJ* 346 (2013).
2. A J Oluwafisayo., *et al*. "Side effects of non-steroidal anti-inflammatory drugs: The experience of patients with musculoskeletal disorders". *American Journal of Public Health Research* 2 (2014): 106-112.
3. Puppala and G A Reddy. "Review on Effects of NSAIDS on Different Systems". *Asian Journal of Pharmaceutical Research and Development* 8.1 (2020): 100-109.
4. D A Shah., *et al*. "Estimation of ibuprofen and famotidine in tablets by second order derivative spectrophotometery method". *Arabian Journal of Chemistry* 10 (2017): S105-S108.
5. H E Ouafy., *et al*. "Determination of Ibuprofen in Tablets and Human Blood Samples: Effect of Clay in Minimizing Overvoltage of Ibuprofen Oxidation". *Chemistry Select* 4.38 (2019): 11282-11287.
6. Švorc I Strežova., *et al*. "An advanced approach for electrochemical sensing of ibuprofen in pharmaceuticals and human urine samples using a bare boron-doped diamond electrode". *Journal of Electroanalytical Chemistry* 822 (2018): 144-152.
7. SA Shahamirifard and M Ghaedi. "Anew electrochemical sensor for simultaneous determination of arbutin and vitamin C based on hydroxyapatite-ZnO-Pd nanoparticles modified carbon paste electrode". *Biosensors and Bioelectronics* 141 (2019): 111474.

8. F Bettazzi., *et al*. "Gold nanoparticles modified graphene platforms for highly sensitive electrochemical detection of vitamin C in infant food and formulae". *Food Chemistry* 344 (2021): 128692.

9. T Tadesse and A Sirgawie. "A comparative study on electrochemical determination of vitamin C in liver and tomato using platinum and glassy carbon electrodes". *Biochemistry and Molecular Biology* 2.3 (2017): 25-36.

10. K Dhara and RM Debiprosad. "Review on nanomaterials-enabled electrochemical sensors for ascorbic acid detection". *Analytical Biochemistry* 586 (2019): 113415.

11. M R Ganjali., *et al*. "Highly sensitive voltammetric sensor for determination of ascorbic acid using graphite screen printed electrode modified with ZnO/Al 2 O 3 nanocomposite". *International Journal of Electrochemical Science* 12 (2017): 3231-3240.

12. A Samide and B Tutunaru. "Interactions between Vitamin C and Nanocolloidal Silver Particles Studied by Cyclic Voltammetry and UV-V is Spectrophotometry". *Electroanalysis* 29.11 (2017): 2498-2506.

13. Z Bitew and M Amare. "Electrochemical determination of ascorbic acid in pharmaceutical tablets using carbon paste electrode". *Infertility* 4 (2019): 5.

14. Ω Metrohm. "797 VA Computrace Software Version 1.3x" Switzerland, Model 797 VA (2009): 42.

15. K Oldham., *et al*. "Electrochemical Scinece and Technology: Fundamentals and Applications". John Wiley and Sons, USA (2012): 380-381.

16. F Jalali and P S Dorraji. "Electrochemical and spectroscopic studies of the interaction between the neuroleptic drug, gabapentin, and DNA". *Journal of Pharmaceutical and Biomedical Analysis* 70 (2012): 598-601.

17. UJ Pandit., *et al*. "Electrochemical and Spectroscopic Evaluation on Interaction of anticancer drug biocalutamide with DNA". *Der Pharma Chemica* 9.1 (2017): 82-88.

Volume 2 Issue 10 October 2021