Journal of Materials and Environmental Science
ISSN : 2028-2508
CODEN : JMESCN

J. Mater. Environ. Sci., 2021, Volume 12, Issue 01, Page 128-136

http://www.jmaterenvironsci.com

Electrochemical behavior of methocarbamol on platinum electrode by cyclic voltammetry

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Received 15 Nov 2020,
Revised 29 Jan 2020,
Accepted 30 Jan 2021

Keywords
- ✓ *Cyclic voltammetry,*
- ✓ *Methocarbamol,*
- ✓ *Preparative electrolysis*
- ✓ *LC/MS*
- ✓ *Differential pulse voltammetry*

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Abstract

The electrochemical behavior of methocarbamol was investigated in semi organic media using a platinum electrode. A detailed study by cyclic voltammetry and potentiostatic electrolysis were carried out for better understanding of its anodic oxidation process. The effect of scan rate on current and potential showed that methocarbamol is electroactive with an irreversible peak located at Ep =1.44 V /ECS and demonstrated that the electrode process was controlled by diffusion. Thus, the number of exchanged electrons during oxidation process, the standard redox potential and the standard rate constant were determined. In addition, the liquid chromatography–mass spectrometry and Fourier-transform infrared spectroscopy analysis of preparative electrolysis solution showed that guaifenesin is the major oxidation product of methocarbamol and permitted to propose its oxidative mechanical reaction. Furthermore, differential pulse voltammetry on platinum electrode permits the selective determination of methocarbamol. According to the XTP 90-210 standard the limit of detection and the limit of quantification were determined and are respectively equal to 0.4 µg/mL and 3.3 µg/ mL.

1.Introduction

Methocarbamol (MET) also named 2-hydroxy-3-(2-methoxyphenoxy) propyl carbamate is a central muscle relaxant used to relax muscles and relieve pain and discomfort caused by strains, sprains, and other muscle injuries [1-5]. Methocarbamol is deriving of carbamate of guaifenesin and its chemical structure is represented in Figure 1. Several methods were reported in the literature proposing fast and reliable techniques for the determination of methocarbamol in different matrices such as chromatographic techniques [6-13]. To our knowledge, no electrochemical studies related to the anodic oxidation of methocarbamol was investigated. However, electrochemical methods have proved to be very sensitive for the determination of organic molecules that undergo oxidation and reduction reaction including drugs and related pharmaceuticals molecules [14-17]. Indeed, the advantage of electrochemical techniques is due to their simplicity, low cost and relatively short analysis time when compared to another techniques organic compounds [18-23]. For these reasons, the first part of this work aims to attend a deeper understanding of voltammetric behaviour of methocarbamol in aprotic medium using cyclic voltammetry. In the second part, results obtained from preparative electrolysis, after liquid

chromatography mass spectrometry and FTIR analysis were performed in order to propose a mechanistic scheme of its anodic oxidation and finally, an application of electrochemical study of methocarbamol by differential pulse voltammetry (DPV) was performed in order to highlight the applicability of this work.

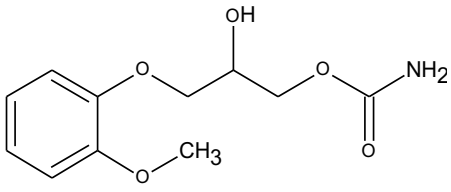

Figure. 1. Chemical structure of methocarbamol

2.Materials and Methods:

2.1. Electrochemical

The electrochemical measurements were made in semi-organic media (water/acetonitrile) in the presence of lithium perchlorate ($LiClO_4$) 0.1M as the supporting electrolyte. Volta lab 80 analyser purchased by radiometer was used to perform voltammetric study. The working electrode was a 2 mm diameter platinum disk. The exhaustive electrolyses were carried out at a constant potential located on the first wave using a PTJ 35-2 potentiostat and an IG5 integrator both from Tacussel. The separated cell was equipped with a platinum grid (4 cm^2) and a platinum wire respectively as the working and the auxiliary electrode. The reference was a saturated calomel electrode (SCE).

2.2. LC/MS analysis

The electrolysis solution was analysed using liquid chromatography equipped with a C-18 column type Symmetry ® Waters (150 mm × 4.6 mm and 5 µm particle size) at 40°C. The mobile phase was 60 % acetonitrile, 40% phosphate buffer pH=8. The mass spectrometric analysis is performed with an Agilent 1100 MSD triple-quadrupole in the electrospray positive mode. Nitrogen is the nebulizer and the collision gas. The analysis parameters are fixed as follows: T = 400°C; gas flow: 12 L/min; nebulizer gas pressure: 50 psi; capillary voltage: 5000 V; corona current: 4 µA

2.3. Chemical

Methocarbamol (MET) also named 2-hydroxy-3-(2-methoxyphenoxy) propyl carbamate, lithium perchlorate, used as supporting electrolyte, and guaifesein were purchased from Fluka. Acetonitrile and water with HPLC quality were purchased from Panreac.

3.Results and discussion

3.1 Voltammetric study of methocarbamol

To elucidate the electrode reaction of MET, a cyclic voltammogram at platinum electrode was recorded at 310^{-3}M concentration on semi organic medium. Figure 2 exhibits one well defined anodic peak located at the potential (E= 1.44 V /SCE) with no reduction peak in the reverse scan suggesting that the irreversible nature of electrode reaction.

3.1. Effect of scan rate variation

Relationship between peak current and scan rate can give us more information involving electrochemical oxidation mechanism. Thus, the voltammetric behaviour of MET at different scan rate between 20 to 100 $mV.s^{-1}$ was studied. Figure 3 illustrates all corresponding voltammograms.

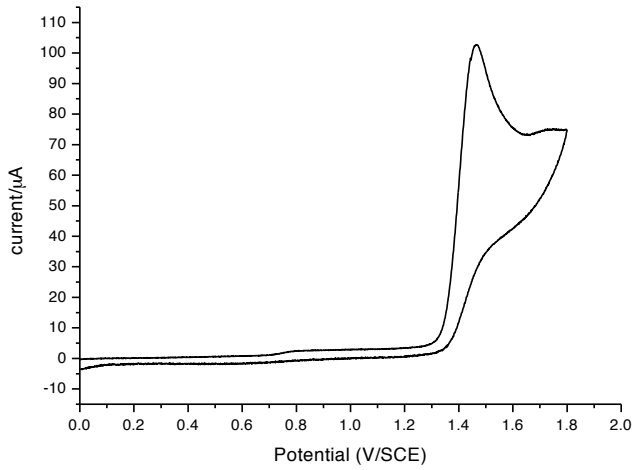

Figure. 2. Oxidation voltammogram of methocarbamol in 50% ACN-50% water, $LiClO_4$(0.1M), C = 3 mM, v =100mV.s^{-1}, platinum disk (ϕ= 2 mm).

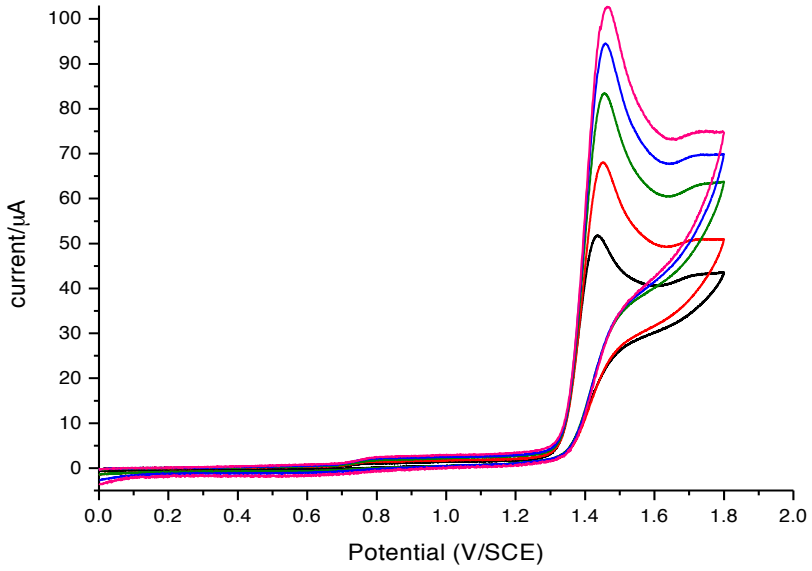

Figure. 3. Oxidation voltammograms of MET in 50% ACN-50% water, LiClO4 (0.1M), C = 3 mM, v = 20, 40, 60, 80,100 mV s^{-1}, platinum disk (ϕ= 2 mm).

The examination of Figure 3 shows that when scan rate increase, current increase and the peak potential shift to more anodic values. The plot Ip as a function as $v^{1/2}$ was performed and illustrated in Figure. 4. Indeed, a good linear relationship between peak current and the square root of scan rate was obtained. The corresponding equation is Ip = 9.33 $v^{1/2}$ + 0.3002 with R^2=0.997. The value of the slope equal to 0.933 was very close to the theoretically expected value obtained when the electrode process was controlled by diffusion [24-28].

Based on the literature, for an irreversible electrode process, the potential peak can be defined by the following equation:

$$\mathbf{Ep = E_0 + (2.0303RT/\alpha\, nF)\ log\ (RTk_0/\alpha\, nF) + (2.303RT/\alpha\, nF)\ log\ v}$$

where α is the transfer coefficient, k_0 the standard rate constant of the reaction, n the number of electrons, ν the scan rate and E_0 is the standard redox potential, T=298 K, R=8.314 J mol^{-1} K^{-1} and F= 96480 $C.mol^{-1}$ [29-30]. Thus, α.n value can be determined through the slope of curve of Ep as function as log ν illustrated in Figure 5.

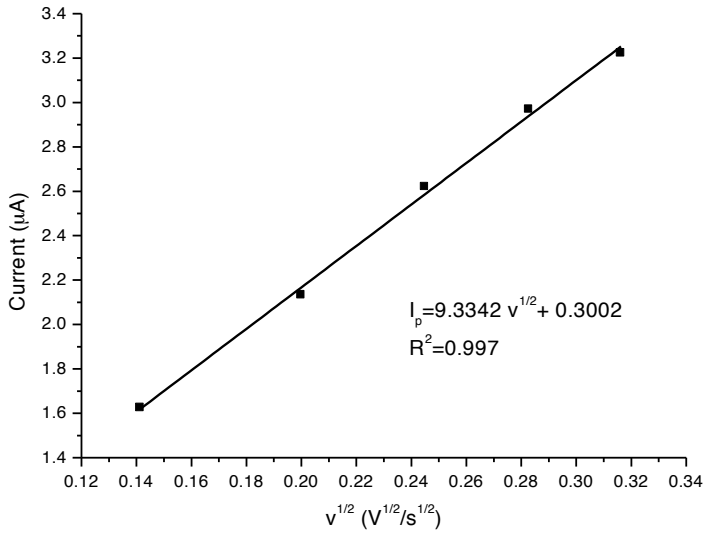

Figure 4. Dependence of peak current in the square root of scan rate or scan rate

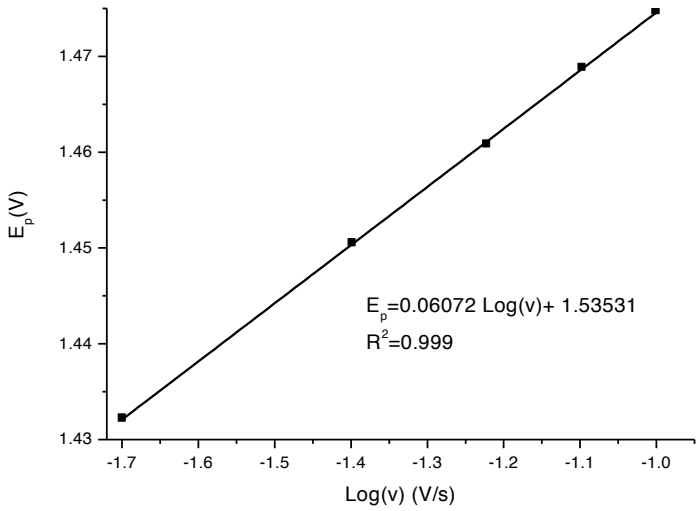

Figure 5. Linear relation between peak potential and logarithm of scan rate.

The examination of Figure 5 shows that the slope value is 0.06072 V and after equation 1 resolution αn was determined to be 0.974. Moreover, α is supposed to be 0.5 when total irreversibility electrode process was obtained [31-32]. Thus, the number of electrons involving during the electrochemical oxidation was calculated to be 1.948 ≈ 2. The same result, concerning electronic stoichiometry, was obtained by comparison between the peak current and that related ferrocene, a reference compound which is characterized by a monoelectronic reversible peak and whose diffusion coefficient is comparable with the methocarbamol. In the other hand, after determination of E_0 value obtained by extrapolation of the plot of Ep as a function as log v to vertical axis at v=0 from the interception of the above plot [33-34]. The value of standard rate constant k_0 was calculated to be 228 s^{-1}.

3.2. preparative electrolysis

To get more information about MET oxidation products, preparative electrolysis was conducted at a constant potential located on the first wave. Electrolysis was stopped after the passage of a quantity of electricity equal to 2F/mol to avoid the complication of the mechanism by possible reactions of products formed. Liquid chromatography mass spectrophotometry and FTIR analysis were performed to identify electrolysis products.

Obtained results lead that the major oxidation product (P1) of MET is 3-(o-Methoxyphenoxy)-1,2-propanediol also named guaifenesin. In fact, the comparison between reference and electrolysis chromatograms indicate that the peak related to the MET was eluted at t_R =5.55 min retention time disappear completely and a new peak appears at t_R = 4.31 min with high intensity. The P1 retention time suggests that this compound is more polar than MET in accordance with the retention mechanism on reversed phases [35]. This peak is probably due to the elimination of the carbamic acid. The proposed chemical structure was confirmed by the FTIR analysis. Indeed, the comparison between FTIR spectrum of reference and electrolysis solutions (Figure.6) shows that a wide and intense band located between 3200-3600 cm^{-1} appears in electrolysis solutions. This band can be attributed to the elongation of the OH bonds indicating an increase in the number of OH groups. We also noted that the band located around 1650 cm^{-1} becomes more intense. This result can be explaining, referred to the IR tables, as the elongation of the conjugated carbonyl functions.

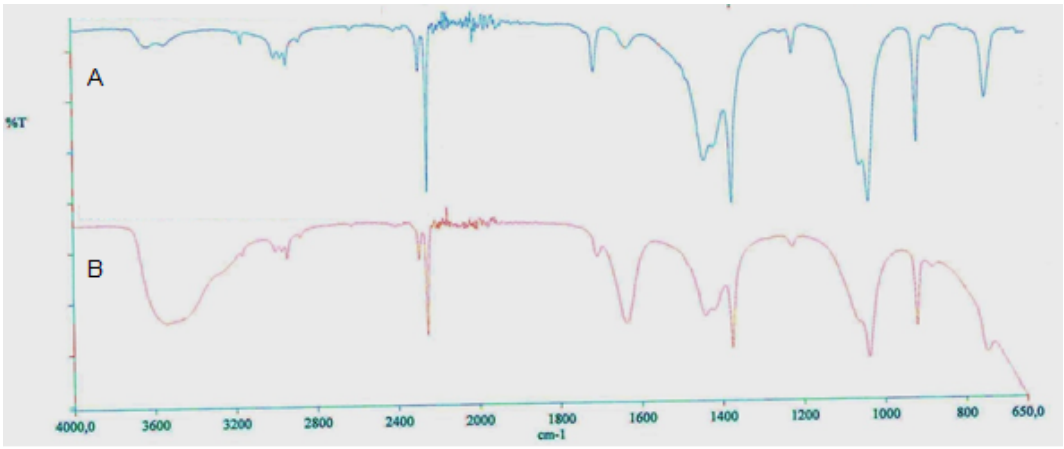

Figure 6. (A) FTIR spectra of methocarbamol and (B) FTIR spectra of electrolysis solution.

Finally, based on obtained results, the mechanistic scheme of methocarbamol oxidation on platinum electrode was proposed in Figure 7.

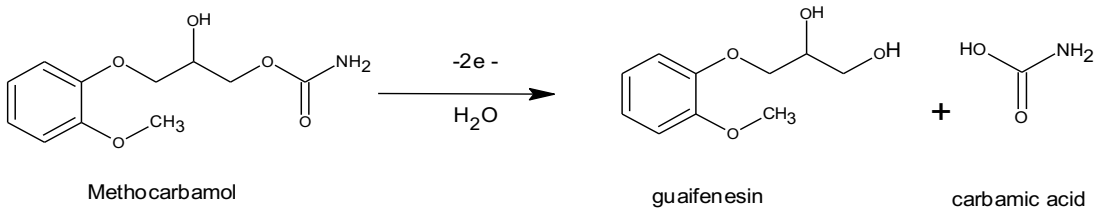

Figure 7. Mechanism of the anodic oxidation of Methocarbamol

3.3. Analytical application

In order to develop a voltammetric methodology for determining the drug, we selected the differential pulse voltammetry mode (DPV), since the peaks were sharper and better defined than those obtained by cyclic voltammetry, with lower background current. A typical DPV for methocarbamol concentration ranging between 10 and 60 µg. mL^{-1} is reported on Figure. 8.

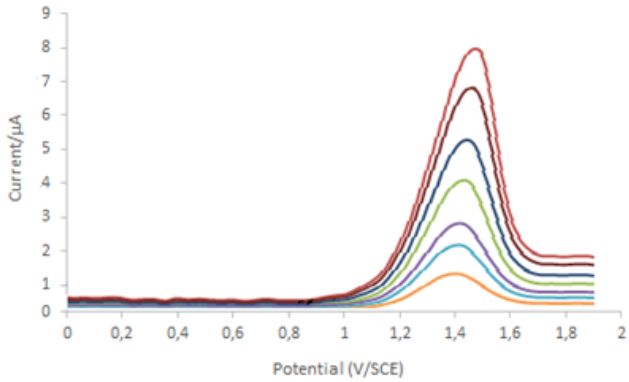

Figure 8. Differential pulse voltammograms of methocarbamol in 50% ACN-50% water, LiClO4 (0.1M), platinum disk (ϕ= 2 mm); scan rate: 5mVs^{-1}; pulse amplitude = 50mV; pulse width: 20 ms. C = 1 − 7 µg/mL.

3.3.1. Linearity study

Linearity was evaluated by representing the variation of current with standard concentrations in semi organic media using DPV in Figure 9. Curve was represented by straight line equation Ip = 0.1116 C - 0.08, with $R^2 = 0.998$. The tests concerning the homogeneity of variances, the intercept, the existence of a significant slope led to the conclusion that the method is linear.

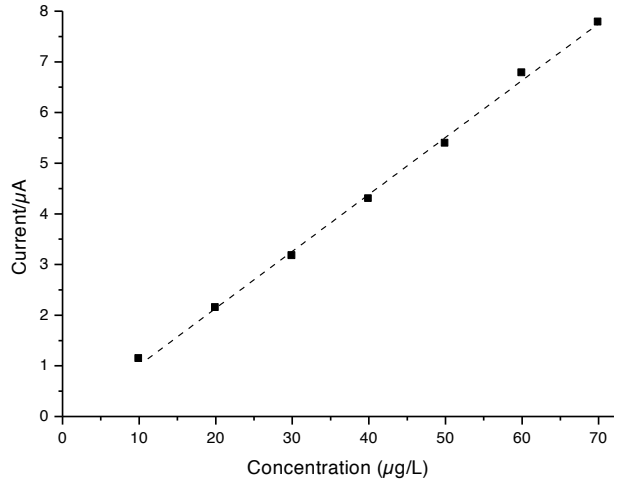

Figure 9. Linear relation between peak potential and concentration.

3.3.2. Limit of detection and limit of quantification

The limit of detection is the smallest amount or concentration of analyte in the sample that can be reliably distinguished from zero. In practice, this is the lowest concentration that can be detected, but not necessarily quantified. In our study, the limit of detection and the limit of quantification of methocarbamol using differential pulse voltammetry were determined and are respectively equal to 0.4 µg/mL and 3.3 µg/ mL. All results were obtained according to the XTP 90-210 standard.

3.3.3. Selectivity of DPV method

A mixture of methocarbamol and guaifasein at the same concentration was prepared and then analyzed by differential pulse voltammetry (Figure 10). Examination of obtained voltammogram highlights evidence two well separated peaks: one located at a potential of 1.44 V / ECS corresponding to the MET and the other located at E = 0.9 V / ECS relative to the guaifasein. This result proved that DPV technique is selective and can be used to determine MET in different matrices containing the guaifasein.

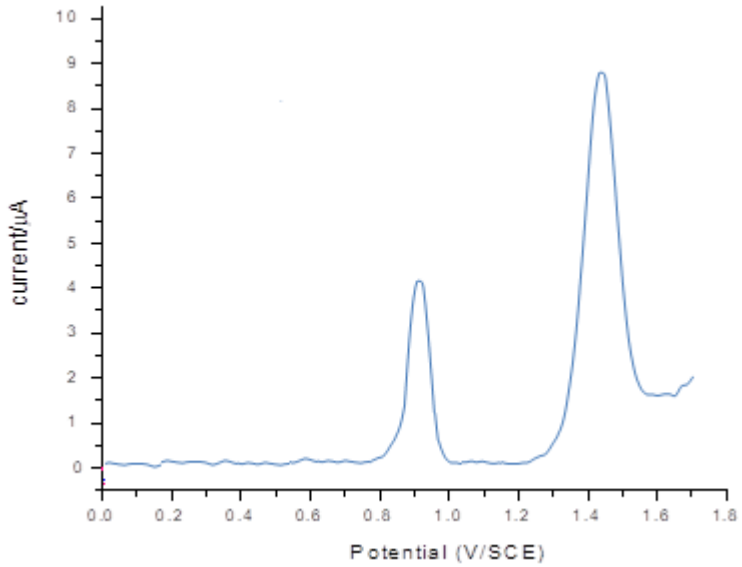

Figure. 10. Differential pulse voltammogram of MET (C = 60 ppm) and guaifenesin (C = 60 ppm) in 50% ACN-50% water, LiClO4 (0.1M), platinum disk (ϕ= 2 mm); scan rate: 5mVs^{-1}; pulse amplitude =50mV; pulse width: 20 ms.

Conclusion

The electrochemical behaviour of methocarbamol was investigated in semi organic media on platinum electrode. Cyclic voltammetry results indicate that methocarbamol is electroactive with an irreversible peak. The number of exchanged electrons during oxidation process, the standard redox potential and the standard rate constant were determined. A detailed study carried out by potentiostatic electrolysis shows that the major oxidation product is guaifenesin. Thus, a mechanistic scheme of methocarbamol oxidation on platinum electrode was proposed. Furthermore, this electrochemical study shows that differential pulse voltammetry is effective in the selective determination of methocarbamol in the presence of guaifasein. The corresponding limits of detection and quantification were determined according to the XTP 90-210 standard.

Acknowledgments : This research study has been achieved through financial contribution of Tunisian Higher Education and Scientific Research Ministry.

References

[1] S. Alessiseverini, R.T. Coutts, F. Jamali, F.M. Pasutto, High-performance liquid chromatographic analysis of methocarbamol enantiomers in biological fluids. *J. Chromatogr* 582 (1992) 173–179. doi:10.1016/0378-4347(92)80316-i.

[2] E. F. Elkady. Simultaneous determination of diclofenac potassium and methocarbamol in ternary mixture with guaifenesin by reversed phase liquid chromatography. *Talanta*, 82 (2010) 1604-1607. doi: 10.1016/j.talanta.2010.07.024.

[3] W. J. Chang, Muscle Relaxants for Acute and Chronic Pain. *Phys Med Rehabil Clin N Am* 31, (2020) 245-254. doi: 10.1016/j.pmr.2020.01.005.

[4] M. B. Gholivand, M. Khodadadian, M. Rationally designed molecularly imprinted polymers for selective extraction of methocarbamol from human plasma. *Talanta,* 85 (2011)1680-1688. doi: 10.1016/j.talanta.2011.06.066.

[5] M. Ghoneim, H. S. El-Desoky. Electrochemical determination of methocarbamol on a montmorillonite-Ca modified carbon paste electrode in formulation and human blood. *Bioelectrochemistry*. 79 (2010) 241–247. doi: 10.1016/j.bioelechem.2010.06.005.

[6] W. Zha, Z. Zhu. Determination of methocarbamol concentration in human plasma by high performance liquid chromatography–tandem mass spectrometry. *J. Chromatogra B*. 878, (2010) 831–835. doi: 10.1016/j.jchromb.2010.01.025.

[7] H. M. Mohamed, M. T. Lamie, Analytical eco-scale for assessing the greenness of developed RP-HPLC method used for simultaneous analysis of combined antihypertensive medications, *J. AOAC. Int*. 99 (2016) 1260–1265. doi: 10.5740/jaoacint.16-0124.

[8] T. Prabha, A. Caroline Grace, B. Nivethitha, M. Jagadeeshwaran, T. Sivakumar. Method Development, Validation and Degradation Studies of Methocarbamol from Methocarbamol Injection. *Int. J. Pharm. Sci. Rev. Res,* 50 (2018) 169-174.

[9] N.P. Patel, M. Hinge, Development and validation of UV spectroscopic method for simultaneous estimation of methocarbamol and diclofenac sodium in injection dosage form, *WJPPS* 5 (2016) 1625–1636.

[10] W. Zha, Z. Zhu. Determination of methocarbamol concentration in human plasma by high performance liquid chromatography–tandem mass spectrometry. *J. Chromatogra B*. 878 (2010) 831–835. doi: 10.1016/j.jchromb.2010.01.025

[11] J. Fischer, J. González-Martín, P. Lochyński, H. Dejmková, K. Schwarzová-Pecková, M. Vega, Voltammetric study of triazole antifungal agent terconazole on sp^3 and sp^2 carbon-based electrode materials. *J. Electroanal. Chem.* 869 (2020) 114054-114061. doi: 10.1016/j.jelechem.2020.114054.

[12] P. Qiushi, Z. Yajuan, D. Rui, Z. Wen, P. Qianrong, Y. Min. Simultaneous Determination of Methocarbamol and Ibuprofen in the Presence of Five Related Impurities by Reversed Phase Liquid Chromatography. *Anal. Chem. Lett.*, 7 (2017) 623- 631. doi:10.1080/22297928.2017.1385419.

[13] A. Zaouak, F. Matoussi, M. Dachraoui, Electrochemical Study of Diphenyl Ether Derivatives*, Int. J. Electrochem.* (2011). ID 904570 doi:10.4061/2011/904570.

[14] H. Farsam, E. Souri, N. Gharavi. A New HPLC Technique for the Separation of Methocarbamol Enantiomers. *J. Pharm. Pharmacol*. 51 (1999) 873–875. doi:10.1211/0022357991773096.

[15] A. Zaouak, F. Matoussi, M. Dachraoui. Investigation of the anodic oxidation of aryloxy propionic acid derivatives in acetonitrile. *J. Mater. Environ. Sci*. 6 (2015) 138-145.

[16] C.P. Andrieux, P. Hapiot, J.M. Saveant, Fast kinetics by means of direct and indirect electrochemical techniques. *Chem. Rev.* 90 (1990) 723-738 doi:10.1021/cr00103a003.

[17] S. A. E. A. Mohamed, F. F. Belal. A micellar HPLC method for simultaneous determination of methocarbamol in three different tablets using single run; application to human plasma and evaluation of the method greenness. *Microchem. J.* 148 (2019) 262- 269. doi: 10.1016/j.microc.2019.04.079

[18] C. P. Andrieux, A. Merz, J.M. Saveant, Dissociative electron transfer. Autocatalysis and kinetic characteristics of the electrochemical reductive cleavage of the carbon halogen bond in alkyl halides giving rise to stable radicals and carbanions. *J. Am. Chem. Soc*. 107 (1985) 6097-6103 doi:10.1021/ja00307a045

[19] G. Kim, C.M. Kim, J. Jeong, H. J. Woo, S.H Kwon, H. Yang. Simple electrochemical method for monitoring the time-dependent dissolution behavior of layers deposited by atomic layer deposition. *J. Electroanal. Chem*. 877 (2020) 114550-114556. doi:10.1016/j.jelechem.2020.114550.

[20] Lima, C. D., Couto, R. A. S., Arantes, L. C., Marinho, P. A., Pimentel, D. M., Quinaz, M. B., Dos Santos, W. T. P. Electrochemical detection of the synthetic cathinone 3,4-methylenedioxypyrovalerone using carbon screen-printed electrodes: a fast, simple and sensitive screening method for forensic samples. *Electrochim. Acta*, 354 (2020) 136728. doi: 10.1016/j.electacta.2020.136728

[21] M.R. Montoya, E. Morales I. Giraldez, R.E. Brito, J.M.R. Mellado, Electrochemical oxidation of isothiazolinone biocides and their interaction with cysteine. *Electrochim. Acta*. 337 (2020) 135770 doi:10.1016/j.electacta.2020.135770

[23] A.F.B. de Andrade, S.K. Mamo, J. Gonzalez-Rodriguez, Rapid screening method for new psychoactive substances of forensic interest: electrochemistry and analytical determination of phenethylamines derivatives (NBOMe) via cyclic and differential pulse voltammetry, *Anal. Chem.* 89 (2017) 1452-1458. doi: 10.1021/acs.analchem.6b02426

[24] W.T.P. Dos Santos, R.G. Compton. Simple method to detect the stimulant modafinil in authentic saliva using a carbon-nanotube screen-printed electrode with adsorptive stripping voltammetry, *Sensor Actuat. B-Chem*. 285 (2019) 137-144 doi:10.1016/j.snb.2019.01.047

[25] M. Y. Díaz-Cardenas, M. G. Valladares-Cisneros, C. Menchaca-Campos, S. Lagunas-Rivera, J. G. Gonzalez-Rodríguez, J. Uruchurtu-Chavarín. Electrochemical and chemical quantum studies of a natural alkaloid compound: Boldine, as green corrosion behaviour on carbon steel and Copper in sulfuric acid. *J. Mater. Environ. Sci*., 10 (2019) 1011-1024.

[26] E. Lamy, L. Nadjo, J.M. Saveant, Standard potential and kinetic parameters of the electrochemical reduction of carbon dioxide in dimethylformamide. *J. Electroanal. Chem*. 78 (1977) 403-407. doi:10.1016/s0022-0728(77)80143-5

[27] B. M. Amrutha, J. G. Manjunatha, S. Aarti Bhatt, N. Hareesha. Electrochemical Analysis of Evans Blue by Surfactant Modified Carbon Nanotube Paste Electrode, *J. Mater. Environ. Sci.* 10 (2019) 668-667.

[28] E. Chrzescijanska, E. Wudarska, E. Kusmierek, J. Rynkowski, Study of acetylsalicylic acid electroreduction behavior at platinum electrode. *J. Electroanal. Chem*. 713 (2014) 17–21. doi: 10.1016/j.jelechem.2013.11.015.

[29] P.T. Kissinger, W. H. Heineman, Laboratory Techniques in Electroanalytical Chemistry, second ed. (1996), Marcel Dekker, New York.

[30] A. K. Timbola, C. D, Souza, C. Soldi, M. G. Pizzolatti, A.Spinelli, Electro-oxidation of rutin in the presence of p-toluenesulfinic acid, *J. Appl. Electrochem*. 37 (2007) 617–624. doi:10.1007/s10800-007-9292-6.

[31] D. L. Shekappa, A.B. Teradale, N. U. Shrishail, T. N. Sharanappa, Electrochemical Oxidation and Determination of Methocarbamol at Multi-walled carbon nanotubes-modified glassy carbon electrode. *Anal. Bioanal. Electrochem*. 8 (2016) 304-317.

[32] E. Laviron, General expression of the linear potential sweep voltammogram in the case of diffusion less electrochemical systems. *J. Electroanal. Chem. Interf. Electr*. 101 (1979) 19–28. doi.:10.1016/S0022-0728(79)80075-3

[33] Y. Wu, X. Ji, S. Hu, Studies on electrochemical oxidation of azithromycin and its interaction with bovine serum albumin. *Bioelectrochemistry*. 64 (2004) 91–97. doi:10.1016/s1567-5394(04)00176-8

[34] Y. M. Zhang, W. You, Z. N. Gao, T. L. Yang. Electrochemical Behaviors of Methocarbamol at an Acetylene Black-Ionic Liquid Modified Carbon Paste Electrode and its Electrochemical Determination. *Croat. Chem. Acta,* 86 (2013) 309. doi:10.5562/cca2094.

[35] A. Vailaya, C. Horvath, Retention in reversed-phase chromatography: Partition or adsorption. *J. Chromatogr A*. 829 (1998) 1-27. doi:10.1016/s0021-9673(98)00727-4.