

DETERMINATION OF NIFEDIPINE, AMPICILLIN AND PENICILLIN G  
AND THEIR ELECTRO-OXIDATION PRODUCTS BY VOLTAMMETRIC  
TECHNIQUES

MOHD DZUL HAKIM BIN WIRZAL

A thesis submitted in fulfilment of the  
requirements for the award of the degree of  
Doctor of Philosophy (Chemistry)

Faculty of Science  
Universiti Teknologi Malaysia

JANUARY 2016

*SPECIALLY DEDICATED TO,*

*MY MAMA, NUR SYAMSI AHMAD AND MY PAPA, WIRZAL  
MUNCHAK FOR YOUR PRAYERS, WORDS OF ENCOURAGEMENT, LOVE  
AND CARE.*

*MY BROTHERS, SHAREZAL WIRZAL AND AZIZI WIRZAL FOR  
YOUR SUPPORT, CARE AND ENCOURAGEMENT.*

## ACKNOWLEDGEMENT

The experience throughout the process of completing this study has been enriching and meaningful. I would like to take this opportunity to personally expand my appreciation to a few people here.

First and foremost, I would like to thank Prof. Dr. Abdull Rahim Mohd Yusoff for his dedication and commitment in guiding me throughout the process of completing my thesis. Your time, energy, knowledge and invaluable experience have enriched my interest towards research activity. Not forgetting to Prof. Dr. Hadi Nur for his valuable guidance and encouragement.

Secondly, I would like to thank Prof. Dr. Jiří Barek and Prof. Dr. Jiří Zima from Faculty of Science, Charles University, Prague, Czech Republic, for their valuable time, guidance, useful discussion and collaboration to complete my project.

Next, to my labmates in Chemistry Department, Faculty of Science, UTM, (Taufiq, Thana, Akmal, Amin, Faizuan, Azizul, Liyana, Syaza and Azah), my labmates from Lab 112, Chemistry Department, Faculty of Science, Charles University (Dima, Jarca, Romana, Honza, Milan and Hanka), and my good friend, Diyana Nasir for your willingness, availability, encouragement, support, prayers and friendship towards me to complete this project. I would also like to thank to the academic and technical staffs of the Department of Chemistry at both Charles University and UTM especially to Kak Ramlah, Kak Fariza and Kak Zana for their assistance throughout this work.

Above all, I thank God Almighty for His unmerited favour and wonderful grace in guiding every step of my life, and giving me the faith to believe that all things are possible to him who believes.

## ABSTRACT

The study of the electrochemical behaviour of ampicillin (AMP), penicillin G (PG) and nifedipine (NFD) were carried out using three different working electrodes namely hanging mercury drop electrode (HMDE), mercury meniscus modified silver amalgam electrode (m-AgSAE) and boron-doped diamond electrode (BDDE). All measurements were made versus Ag/AgCl (3 M KCl) using cyclic voltammetry (CV), differential pulse voltammetry (DPV) and adsorptive stripping voltammetry (AdSV). Due to the toxicity of mercury, m-AgSAE was constructed as an alternative electrode for HMDE. The DPV determination of NFD were conducted using mixtures of Britton-Robinson (BR) buffer pH 8 with methanol in three different volume/volume ( $v/v$ ) ratios (1:1, 9:1, and 99:1) in the concentration range of 0.2 to 20  $\mu\text{mol/L}$ . The ratio 9:1 was chosen as the optimal ratio for NFD determination. The limit of quantification (LOQ) was 0.12  $\mu\text{mol/L}$  for (HMDE) and 1.2  $\mu\text{mol/L}$  (m-AgSAE). Attempts to increase the sensitivity using AdSV at both electrodes were not successful. For the determination of AMP and PG, the optimal conditions have been performed in Britton-Robinson (BR) buffer in the concentration range of 1 to 9  $\mu\text{mol/L}$  (HMDE) and 10 to 90  $\mu\text{mol/L}$  (m-AgSAE). The limit of detection (LOD) for AMP and PG at HMDE were 0.09 and 0.065  $\mu\text{mol/L}$ , respectively and the LOD for AMP and PG at m-AgSAE were 3.8 and 2.5  $\mu\text{mol/L}$ , respectively. PG also was successfully determined using the BDDE working electrode where PG showed well developed oxidation peak at potential between 800 to 1100 mV vs Ag/AgCl (3 M KCl) in BR buffer. The highest and best developed peak was obtained at pH 4 at a potential of +980 mV vs Ag/AgCl (3 M KCl). Attempts to increase the sensitivity using adsorptive stripping DPV at BDDE were not successful. The LOD and LOQ for PG were 0.23  $\mu\text{mol/L}$  and 1.5  $\mu\text{mol/L}$ , respectively. The practical application of the newly developed method was verified on the determination of NFD, AMP and PG in spiked samples of drinking and river water using optimum conditions. Voltammetry and LC-MS method was used for monitoring the electro-oxidation mechanism of AMP, PG and NFD. The electro-oxidation process was performed in three different mediums of electrolyte which were tap water (pH~6.5) and BR buffer of pH 4 and pH 10, while the electro-oxidation time were set to 15, 30 and 60 minutes. A series of mixed metal oxides (MMO) titanium-based electrodes ( $\text{TiO}_2/\text{Ti}$ ,  $\text{IrO}_2\text{-TiO}_2/\text{Ti}$ ,  $\text{RuO}_2\text{-TiO}_2/\text{Ti}$  and two  $\text{RuO}_2\text{-IrO}_2\text{-TiO}_2/\text{Ti}$  with different ratios of the metal oxide) were used as an anode. AMP, PG and NFD were successfully degraded using electro-oxidation process with the best MMO electrode for the degradation was  $\text{RuO}_2\text{-IrO}_2\text{-TiO}_2/\text{Ti}$  in tap water (pH~6.5) medium. LC-MS analysis was performed to determine the by-product and mechanism of the degradation process of the drugs were proposed.

## ABSTRAK

Kajian sifat elektrokimia ampisilin (AMP), penisilin G (PG) dan nifedipin (NFD) telah dijalankan dengan menggunakan tiga elektrod kerja yang berbeza iaitu elektrod titisan raksa tergantung (HMDE), elektrod perak amalgam terubahsuai meniskus raksa (m-AgSAE) dan elektrod berlian terdopkan boron (BDDE). Semua pengukuran dibuat terhadap Ag/AgCl (3 M KCl) menggunakan voltammetri kitaran (CV), voltammetri denyut pembeza (DPV) dan voltammetri jerapan pelucutan (AdSV). Oleh kerana ketoksikan raksa, m-AgSAE telah dibina sebagai elektrod alternatif untuk HMDE. Penentuan NFD secara DPV telah dilakukan dengan menggunakan campuran larutan penimbal Britton-Robinson (BR) pH 8 dengan metanol dalam tiga nisbah isipadu per isipadu ( $v/v$ ) yang berbeza (1: 1, 9: 1, 99: 1) dalam julat kepekatan 0.2-20  $\mu\text{mol/L}$ . Nisbah 9:1 dipilih sebagai nisbah optimum bagi penentuan NFD. Had kuantitatif (LOQ) bagi NFD ialah 0.12  $\mu\text{mol/L}$  (HMDE) dan 1.2  $\mu\text{mol/L}$  (m-AgSAE). Percubaan untuk meningkatkan kepekaan menggunakan AdSV di kedua-dua elektrod tidak berjaya. Untuk penentuan AMP dan PG, keadaan optimum telah dilakukan dalam larutan penimbal Britton-Robinson (BR) dalam julat kepekatan 1 hingga 9  $\mu\text{mol/L}$  (HMDE) dan 10 hingga 90  $\mu\text{mol/L}$  (m-AgSAE). Had pengesanan (LOD) bagi AMP dan PG di HMDE masing-masing ialah 0.09  $\mu\text{mol/L}$  dan 0.065  $\mu\text{mol/L}$  sementara LOD untuk AMP dan PG di m-AgSAE masing-masing ialah 3.8 and 2.5  $\mu\text{mol/L}$ . PG juga telah berjaya ditentukan dengan menggunakan elektrod kerja BDDE di mana PG menunjukkan puncak pengoksidaan yang baik pada keupayaan antara 800 mV hingga 1100 mV vs Ag/AgCl (3 M KCl) dalam larutan penimbal BR. Puncak voltammogram tertinggi dan terbaik telah diperolehi pada pH 4 pada keupayaan +980 mV vs Ag/AgCl (3 M KCl). Percubaan untuk meningkatkan kepekaan dengan menggunakan jerapan pelucutan DPV di BDDE tidak berjaya. LOD dan LOQ bagi PG masing-masing ialah 0.23  $\mu\text{mol/L}$  dan 1.5  $\mu\text{mol/L}$ . Penggunaan praktis kaedah baharu yang dibangunkan ini telah ditentusahkan bagi penentuan NFD, AMP dan PG yang ditambah ke dalam sampel air minuman dan air sungai menggunakan keadaan optimum. Kaedah voltammetri dan LC-MS telah digunakan untuk memantau mekanisme elektro-pengoksidaan bagi AMP, PG dan NFD. Proses elektro-pengoksidaan telah dilakukan dalam tiga medium elektrolit berbeza iaitu air paip (pH~6.5) dan larutan penimbal BR pada pH 4 dan pH 10, manakala masa elektro-pengoksidaan telah ditetapkan pada 15, 30 dan 60 minit. Elektrod berasaskan titanium bagi satu siri campuran logam oksida (MMO) ( $\text{TiO}_2/\text{Ti}$ ,  $\text{IrO}_2\text{-TiO}_2/\text{Ti}$ ,  $\text{RuO}_2\text{-TiO}_2/\text{Ti}$  dan dua  $\text{RuO}_2\text{-IrO}_2\text{-TiO}_2/\text{Ti}$  dengan nisbah yang berbeza oksida logam) digunakan sebagai anod. AMP, PG dan NFD telah berjaya didegradasi menggunakan proses elektro-pengoksidaan dengan elektrod MMO terbaik untuk degradasi ialah  $\text{RuO}_2\text{-IrO}_2\text{-TiO}_2/\text{Ti}$  dalam medium air paip (pH~6.5). Analisis LC-MS telah dijalankan untuk menentukan hasil sampingan daripada proses degradasi dan mekanisme penguraian dadah bagi AMP, PG dan NFD dicadangkan.

## TABLE OF CONTENTS

CHAPTER	TITLE	PAGE
	<b>DECLARATION</b>	ii
	<b>DEDICATION</b>	iii
	<b>ACKNOWLEDGEMENT</b>	iv
	<b>ABSTRACT</b>	v
	<b>ABSTRAK</b>	vi
	<b>TABLE OF CONTENTS</b>	vii
	<b>LIST OF TABLES</b>	xiii
	<b>LIST OF FIGURES</b>	xvi
	<b>LIST OF ABBREVIATION</b>	xxxiii
	<b>LIST OF SYMBOLS</b>	xxxiv
	<b>LIST OF APPENDIX</b>	xxxv
<b>1</b>	<b>INTRODUCTION</b>	<b>1</b>
	1.1 Background of Study	1
	1.2 Problem Statement	3
	1.3 Research Objectives	4
	1.4 Scope of Research	5
	1.5 Significance of Research	6
	1.6 Research Novelty	7
<b>2</b>	<b>LITERATURE REVIEW</b>	<b>8</b>
	2.1 Occurrence of Pharmaceutical Waste in Water	8
	2.2 Ampicillin	9
	2.3 Penicillin G	10
	2.4 Nifedipine	11

2.5 Determination of Drugs by Various Analytical Methods	12
2.6 Voltammetry	19
2.6.1 Types of Voltammetry	20
2.6.1.1 Cyclic Voltammetry	20
2.6.1.2 Pulse Voltammetry	21
2.6.1.3 Cathodic Stripping Voltammetry	22
2.6.1.4 Square Wave Voltametry	23
2.6.2 Electrochemical Cell & Electrode System	24
2.6.2.1 Working Electrode	26
2.6.2.1.1 Hanging Mercury Drop Electrode	27
2.6.2.1.2 Mercury Meniscus Modified Silver Amalgam Electrode	27
2.6.2.1.3 Boron Doped Diamond Electrode	28
2.6.2.2 Reference Electrode	29
2.6.2.3 Auxiliary Electrode	29
2.6.3 Supporting Electrolyte	29
2.7 Determination of New Emerging Pollutants (NEPs) and target drugs (Penicillin G, Ampicillin and Nifedipine) using Different Working Electrode	30
2.8 Degradation of Drugs using Various Techniques	45
2.8.1 Electrochemical/Oxidation/Degradation Process	52
2.8.1.1 Mixed Metal Oxide Electrode	56
<b>3 EXPERIMENTAL</b>	<b>58</b>
3.1 Chemicals and Reagents	58
3.2 Glassware	58
3.3 Preparation of Solutions	59
3.3.1 Britton Robinson (BR) Buffer	59
3.3.2 Ampicillin Standard Solution	59
3.3.3 Penicillin G Standard Solution	59

3.3.4 Nifedipine Standard Solution	60
3.4 Instrumentations	60
3.4.1 Voltammetry	60
3.4.1.1 Working Electrodes	62
3.4.1.1.1 Hanging Mercury Drop Electrode	62
3.4.1.1.2 Mercury Meniscus Modified Silver Amalgam Electrode	63
3.4.1.1.3 Boron Doped Diamond Electrode	64
3.4.2 Liquid Chromatography-Mass Spectrometry	65
3.5 Voltammetry Procedures	66
3.6 Optimization of Voltammetry Parameters	67
3.6.1 Effect of the pH	67
3.6.2 Effect of Initial Potential	68
3.6.3 Effect of Accumulation Potential	68
3.6.4 Effect of Accumulation Time	68
3.6.5 Calibration	68
3.7 Mixed Metal Oxide (MMO) Electrodes	69
3.8 Electro-oxidation Setup	69
3.9. Electro-oxidation Procedures	70
3.10 Sample Preparation	71
<b>4 DETERMINATION AND ELECTRO-OXIDATION OF NIFEDIPINE</b>	<b>72</b>
4.1 Introduction	72
4.2 Determination of Nifedipine using Voltammetric Technique	73
4.2.1 Voltammetric Behaviour of Nifedipine at HMDE and m-AgSAE	73
4.2.2 Effect of Methanol Concentration	78
4.2.3 Adsorptive Stripping Voltammetry	85



4.2.4	Determination of Nifedipine in Model Samples of Drinking and River Water	85
4.2.5	Interference Study	89
4.3	Electro-oxidation of Nifedipine	90
4.3.1	TiO <sub>2</sub> /Ti Electrode	91
4.3.2	IrO <sub>2</sub> -TiO <sub>2</sub> /Ti and RuO <sub>2</sub> -TiO <sub>2</sub> Electrode	92
4.3.3	RuO <sub>2</sub> -IrO <sub>2</sub> -TiO <sub>2</sub> /Ti Electrodes	94
4.4	LC-MS Determination	96
4.5	Effect of Electrode Composition on Rate of Degradation	103
4.6	Chapter Summary	104
<b>5</b>	<b>DETERMINATION OF AMPICILLIN USING VOLTAMMETRIC TECHNIQUE IN DRINKING AND RIVER WATER SAMPLES</b>	<b>106</b>
5.1	Introduction	106
5.2	Voltammetric Behavior of Ampicillin at HMDE and m-AgSAE	106
5.2.1	Effect of pH	107
5.2.2	Effect of Initial Potential and Accumulation Potential	115
5.2.3	Effect of Accumulation Time	117
5.2.4	Limit of Detection	118
5.2.5	Determination of Ampicillin in Model Sample of Drinking and River Water	120
5.2.6	Interference Study	123
5.3	Electro-oxidation of Ampicillin	124
5.3.1	TiO <sub>2</sub> /Ti Electrode	125
5.3.2	IrO <sub>2</sub> -TiO <sub>2</sub> /Ti and RuO <sub>2</sub> -TiO <sub>2</sub> Electrode	127
5.3.3	RuO <sub>2</sub> -IrO <sub>2</sub> -TiO <sub>2</sub> /Ti Electrodes	129
5.4	LC-MS Determination	131
5.5	Effect of Electrode Composition on Rate of Degradation	138

5.6 Chapter Summary	139
<b>6 PENICILLIN G DETERMINATION AND ITS ELECTRO-OXIDATION USING MMO ELECTRODES</b>	<b>141</b>
6.1 Introduction	141
6.2 Voltammetric Behavior of penicillin G at HMDE and m-AgSAE	141
6.2.1 Effect of pH	142
6.2.2 Effect of Initial Potential and Accumulation Potential	149
6.2.3 Effect of Accumulation Time	151
6.2.4 Limit of Detection	152
6.2.5 Determination of Ampicillin in Model Sample of Drinking and River Water	154
6.3 Voltammetric Behavior of penicillin G at BDDE	157
6.3.1 Effect of pH of Supporting Electrode	157
6.3.2 Electrochemical Behavior Study showing Effect of Initial Potential, Accumulation Potential and Accumulation Time	161
6.3.3 Limit of Detection	163
6.3.4 Determination of Penicillin G in Model Samples of Drinking and River Water	165
6.3.5 Interference Study	167
6.4 Electro-oxidation of Penicillin G	169
6.4.1 TiO <sub>2</sub> /Ti Electrode	170
6.4.2 IrO <sub>2</sub> -TiO <sub>2</sub> /Ti and RuO <sub>2</sub> -TiO <sub>2</sub> Electrode	172
6.4.3 RuO <sub>2</sub> -IrO <sub>2</sub> -TiO <sub>2</sub> /Ti Electrodes	174
6.5 LC-MS Determination	176
6.6 Effect of Electrode Composition on rate of Degradation	182
6.7 Chapter Summary	183

<b>7</b>	<b>CONCLUSIONS AND RECOMMENDATIONS</b>	<b>186</b>
	7.1 Conclusion	186
	7.2 Recommendations for Future Works	190
	<b>REFERENCES</b>	<b>191</b>
	Appendix A	214

## LIST OF TABLES

<b>TABLE NO.</b>	<b>TITLE</b>	<b>PAGE</b>
2.1	Determination of penicillin using various analyses.	14
2.2	Determination of nifedipine using various analyses.	17
2.3	Determination of ampicillin using various analyses.	18
2.4	Determination of new emerging pollutants (NEPs) using Voltammetry at BDDE.	31
2.5	Determination of new emerging pollutants (NEPs) using voltammetry at m-AgSAE.	36
2.6	Determination of new emerging pollutants (NEPs) using voltammetry at HMDE.	38
2.7	Determination of penicillin G and nifedipine using voltammetry.	43
2.8	Degradation of drugs using various techniques.	46
2.9	Degradation of drugs using Electrochemical/oxidation/degradation Method.	54
2.10	Degradation of NEPs using Mixed Metal Oxide (MMO) electrode.	57
3.1	Parameters used for LC-MS analysis	65
3.2	Type of MMO electrodes for electro-oxidation process.	69
4.1	Parameters of calibration lines for nifedipine determination using DPV at HMDE and m-AgSAE.	84

4.2	Parameters of calibration straight lines for the determination of nifedipine at HMDE. Mixtures of sample (river and drinking water): BR buffer pH 8 (9:1).	88
4.3	Parameters of calibration straight lines for the determination of nifedipine at m-AgSAE. Mixtures of sample (river and drinking water): BR buffer pH 8 (9:1).	88
4.4	The exact mass measurements obtained in the TOF mode for molecular ions	97
4.5	Mass Spectral analysis of the proposed metabolites detected during the electro-oxidation of nifedipine using MMO electrodes.	98
4.6	The degradation of nifedipine with different electrode compositions	103
4.7	Summary on the determination of nifedipine using voltammetric technique.	105
4.8	Summary on the degradation of nifedipine using electro-oxidation method	105
5.1	Parameters of calibration lines for ampicillin determination using DPCSV at HMDE and m-AgSAE.	119
5.2	Parameters of calibration straight lines for the determination of ampicillin at HMDE. Mixtures of sample (river and drinking water): BR buffer pH 7 (9:1).	122
5.3	Parameters of calibration straight lines for the determination of ampicillin at m-AgSAE. Mixtures of sample (river and drinking water): BR buffer pH 8 (9:1).	122
5.4	The exact mass measurements obtained in the TOF mode for molecular ions.	132
5.5	Mass Spectral analysis of the proposed metabolites detected during the electro-oxidation of ampicillin using MMO electrodes.	133
5.6	The degradation of ampicillin with different composition of electrodes.	138

<b>5.7</b>	Summary on the determination of ampicillin using voltammetric technique.	140
<b>5.8</b>	Summary on the degradation of ampicillin using electro-oxidation method	140
<b>6.1</b>	Parameters of calibration lines for penicillin G determination using DPCSV at HMDE and m-AgSAE.	153
<b>6.2</b>	Parameters of calibration straight lines for the determination of penicillin G at HMDE. Mixtures of sample (river and drinking water). BR buffer pH 12 (9:1).	156
<b>6.3</b>	Parameters of calibration straight lines for the determination of penicillin G at m-AgSAE. Mixtures of sample (river and drinking water). BR buffer pH 12 (9:1).	156
<b>6.4</b>	Parameters of calibration lines for penicillin G determination using DPV at BDDE.	164
<b>6.5</b>	Parameters of calibration straight lines for the determination of penicillin G at BDDE. Mixtures of sample (river and drinking water). BR buffer pH 4 (9:1).	166
<b>6.6</b>	The exact mass measurements obtained in the TOF mode for molecular ions.	177
<b>6.7</b>	Mass Spectral analysis of the proposed metabolites detected during the electro-oxidation of penicillin G using MMO electrodes	177
<b>6.8</b>	The degradation of penicillin G with different composition of electrodes.	182
<b>6.9</b>	Summary on the determination of penicillin G using voltammetric technique.	184
<b>6.10</b>	Summary on the degradation of penicillin G using electro-oxidation method	185

## LIST OF FIGURES

FIGURE NO.	TITLE	PAGE
1.1	Number of publications with the words ‘new emerging contaminants’ in the title or abstract published since 2006.	2
2.1	Ways Pharmaceuticals enter the environment	9
2.2	Structure of Ampicillin ((2 <i>S</i> ,5 <i>R</i> ,6 <i>R</i> )-6-([(2 <i>R</i> )-2-amino-2-phenylacetyl]amino)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid).	10
2.3	Structure of Penicillin G ((2 <i>S</i> ,5 <i>R</i> ,6 <i>R</i> )-3,3-dimethyl-7-oxo-6-(2-phenylacetamido)-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid).	11
2.4	Structure of 3,5-dimethyl-2,6-dimethyl-4-(2-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate (nifedipine).	12
2.5	Waveform for cyclic voltammetry.	20
2.6	Schematic drawing of applied potential vs. time for differential pulse techniques.	21
2.7	Electrochemical cell for voltammetric analysis: (a) Cross-section side view; (b) Top view of cap.	24
3.1	Voltammetry system from Autolab (Metrohm, Switzerland).	61
3.2	Eco-Tribo Polarograph (Polaro-Sensors, Prague, Czech Republic).	61
3.3	Hanging Mercury Drop Electrode (HMDE) from Metrohm, Switzerland.	62
3.4	Hanging Mercury Drop Electrode (HMDE) from Polaro-Sensors, Prague, Czech Republic.	63

3.5	Laboratory-made m-AgSAE with the disc diameter 0.50 mm (Polaro-Sensors, Prague, Czech Republic).	64
3.6	Boron doped diamond electrode (BDDE) (Widsor Sciencetific Ltd., United Kingdom).	64
3.7	Liquid Chromatography- Mass Spectrometry (LC-MS) from Dionex, USA.	66
3.8	(A) The electro-oxidation setup and (B) The MMO setup in the electro-oxidation process.	70
4.1	DP voltammograms of 100 $\mu\text{mol/L}$ nifedipine at HMDE in BR buffer–MeOH (1:1) medium. The numbers indicate pH of BR-buffer. Reference electrode: Ag/AgCl (3 M KCl).	74
4.2	DP voltammograms of 100 $\mu\text{mol/L}$ nifedipine at m-AgSAE in BR buffer–MeOH (1:1) medium. The numbers indicate pH of BR-buffer. Reference electrode: Ag/AgCl (3 M KCl).	74
4.3	Reduction Schematic for reduction of nifedipine	75
4.4	The dependence of DPV peak potential of nifedipine ( $C_{\text{NFD}} = 100 \mu\text{mol/L}$ ) at HMDE on pH of BR-buffer, DPV measured in a mixture of BR buffer and MeOH (1:1). Reference electrode: Ag/AgCl (3 M KCl).	76
4.5	The dependence of DPV peak potential of nifedipine ( $C_{\text{NFD}} = 100 \mu\text{mol/L}$ ) at m-AgSAE on pH of BR-buffer, DPV measured in a mixture of BR buffer and MeOH (1:1). Reference electrode: Ag/AgCl (3 M KCl).	76
4.6	The dependence of DPV peak current of nifedipine ( $C_{\text{NFD}} = 100 \mu\text{mol/L}$ ) at HMDE on pH of BR-buffer, DPV measured in a mixture of BR buffer and MeOH (1:1). Reference electrode: Ag/AgCl (3 M KCl).	77
4.7	The dependence of DPV peak current of nifedipine ( $C_{\text{NFD}} = 100 \mu\text{mol/L}$ ) at m-AgSAE on pH of BR-buffer, DPV measured in a mixture of BR buffer and MeOH (1:1). Reference electrode: Ag/AgCl (3 M KCl).	77



- 4.8** DP voltammograms of nifedipine at HMDE and in BR-buffer pH 8-MeOH (1:1), ( $C_{NFD}$  (1) 0 (supporting electrolyte), (2) 20, (3) 40, (4) 60, (5) 80, (6) 100 ( $\mu\text{mol/L}$ ). Right: Corresponding calibration straight lines Reference electrode: Ag/AgCl (3 M KCl). 79
- 4.9** DP voltammograms of nifedipine at m-AgSAE in BR-buffer pH 8-MeOH (1:1), ( $C_{NFD}$  (1) 0 (supporting electrolyte), (2) 20, (3) 40, (4) 60, (5) 80, (6) 100 ( $\mu\text{mol/L}$ ). Right: Corresponding calibration straight lines. Reference electrode: Ag/AgCl (3 M KCl). 79
- 4.10** DP voltammograms of nifedipine at HMDE in BR-buffer pH 8-MeOH (1:1), ( $C_{NFD}$  (1) 0 (supporting electrolyte), (2) 2, (3) 4, (4) 6, (5) 8, (6) 10 ( $\mu\text{mol/L}$ ). Right: Calibration straight line. Reference electrode: Ag/AgCl (3 M KCl). 80
- 4.11** DP voltammograms of nifedipine at m-AgSAE in BR-buffer pH 8-MeOH (1:1), ( $C_{NFD}$  (1) 0 (supporting electrolyte), (2) 2, (3) 4, (4) 6, (5) 8, (6) 10 ( $\mu\text{mol/L}$ ). Right: Corresponding calibration straight lines. Reference electrode: Ag/AgCl (3 M KCl). 80
- 4.12** DP voltammograms of nifedipine at HMDE in BR-buffer pH 8-MeOH (9:1), ( $C_{NFD}$  (1) 0 (supporting electrolyte), (2) 20, (3) 40, (4) 60, (5) 80, (6) 100 ( $\mu\text{mol/L}$ ). Right: Corresponding calibration straight lines. Reference electrode: Ag/AgCl (3 M KCl). 81
- 4.13** DP voltammograms of nifedipine at m-AgSAE in BR-buffer pH 8-MeOH (9:1), ( $C_{NFD}$  (1) 0 (supporting electrolyte), (2) 20, (3) 40, (4) 60, (5) 80, (6) 100 ( $\mu\text{mol/L}$ ). Right: Corresponding calibration straight lines. Reference electrode: Ag/AgCl (3 M KCl). 81
- 4.14** DP voltammograms of nifedipine at HMDE in BR-buffer pH 8-MeOH (9:1), ( $C_{NFD}$  (1) 0 (supporting electrolyte), (2) 2, (3) 4, (4) 6, (5) 8, (6) 10 ( $\mu\text{mol/L}$ ). Right: Corresponding calibration straight lines. Reference electrode: Ag/AgCl (3 M KCl). 82

- 4.15** DP voltammograms of nifedipine at m-AgSAE in BR-buffer pH 8-MeOH (9:1), ( $C_{\text{NFD}}$  (1) 0 (supporting electrolyte), (2) 2, (3) 4, (4) 6, (5) 8, (6) 10 ( $\mu\text{mol/L}$ ). Right: Corresponding calibration straight lines. Reference electrode: Ag/AgCl (3 M KCl). 82
- 4.16** DP voltammograms of nifedipine at HMDE in BR-buffer pH 8-MeOH (9:1), ( $C_{\text{NFD}}$  (1) 0 (supporting electrolyte), (2) 0.2, (3) 0.4, (4) 0.6, (5) 0.8, (6) 1.0 ( $\mu\text{mol/L}$ ). Right: Corresponding calibration straight lines. Reference electrode: Ag/AgCl (3 M KCl). 83
- 4.17** DP voltammograms of nifedipine at HMDE in BR-buffer pH 8-MeOH (99:1), ( $C_{\text{NFD}}$  (1) 0 (supporting electrolyte), (2) 2, (3) 4, (4) 6, (5) 8, and (6) 10 ( $\mu\text{mol/L}$ ). Right: Corresponding calibration straight lines. Reference electrode: Ag/AgCl (3 M KCl). 83
- 4.18** DP voltammograms of nifedipine at m-AgSAE in BR-buffer pH 8-MeOH (99:1), ( $C_{\text{NFD}}$  (1) 0 (supporting electrolyte), (2) 2, (3) 4, (4) 6, (5) 8, (6) 10 ( $\mu\text{mol/L}$ ). Right: Corresponding calibration straight lines. Reference electrode: Ag/AgCl (3 M KCl). 84
- 4.19** Adsorptive stripping DP voltammograms of nifedipine with accumulation time (1) 0 sec (2) 10 sec, (3) 30 sec, (4) 60 sec, (5) 90 sec at HMDE in BR buffer pH 8-MeOH (9:1). Concentration of nifedipine = 1  $\mu\text{mol/L}$ . Reference electrode: Ag/AgCl (3 M KCl). 85
- 4.20** DP voltammograms of nifedipine ( $C_{\text{NFD}}$  (1) 0 (supporting electrolyte) (2) 1.8, (3) 3.6, (4) 5.4, (5) 7.2, (6) 9.0 ( $\mu\text{mol/L}$ ) at HMDE in drinking water sample - BR buffer pH 8 (9:1) mixtures. Right: Corresponding calibration straight lines. Reference electrode: Ag/AgCl (3 M KCl). 86
- 4.21** DP voltammogram of nifedipine at HMDE in river sample- BR buffer pH 8 (9:1) mixtures. ( $C_{\text{NFD}}$  (1) 0 (supporting electrolyte) (2) 1.8, (3) 3.6, (4) 5.4, (5) 7.2, (6) 9.0 ( $\mu\text{mol/L}$ ). Right: Corresponding calibration straight lines. Reference electrode: Ag/AgCl (3 M KCl). 86

- 4.22** DP voltammograms of nifedipine ( $C_{\text{NFD}}$ ) (1) 0 (supporting electrolyte) (2) 1.8, (3) 3.6, (4) 5.4, (5) 7.2, (6) 9.0 ( $\mu\text{mol/L}$ ) at m-AgSAE in drinking water sample - BR buffer pH 8 (9:1) mixtures. Right: Corresponding calibration straight lines. Reference electrode: Ag/AgCl (3 M KCl). 87
- 4.23** DP voltammograms of nifedipine ( $C_{\text{NFD}}$ ) (1) 0 (supporting electrolyte) (2) 1.8, (3) 3.6, (4) 5.4, (5) 7.2, (6) 9.0 ( $\mu\text{mol/L}$ ) at m-AgSAE in river water sample - BR buffer pH 8 (9:1) mixtures. Right: Corresponding calibration straight lines. Reference electrode: Ag/AgCl (3 M KCl). 87
- 4.24** Cation and anion interference on nifedipine in drinking and river water sample at HMDE. Reference electrode: Ag/AgCl (3 M KCl). Concentration of cation/anion = 5  $\mu\text{mol/L}$ . 89
- 4.25** Cation and anion interference on nifedipine in drinking and river water sample at m-AgSAE. Reference electrode: Ag/AgCl (3 M KCl). Concentration of cation/anion = 5  $\mu\text{mol/L}$ . 90
- 4.26** Voltammograms for electro-oxidation of nifedipine in (A) pH 4, (B) tap water and (C) pH 10; electro-oxidation time (1) 0 min (2) 15 min (3) 30 min (4) 60 min.  $\text{TiO}_2/\text{Ti}$  electrode as anode; Initial concentration for nifedipine = 10  $\mu\text{mol/L}$ . Working electrode for voltammetry determination: HMDE. Reference electrode: Ag/AgCl (3 M KCl). 91
- 4.27** The percentage of degradation of nifedipine using voltammetry monitoring in (A) pH 4, (B) tap water and (C) pH 10; electro-oxidation time (1) 0 min (2) 15 min (3) 30 min (4) 60 min.  $\text{TiO}_2/\text{Ti}$  electrode as anode; Initial concentration for nifedipine = 10  $\mu\text{mol/L}$ . Working electrode for voltammetry determination: HMDE. Reference electrode: Ag/AgCl (3 M KCl). 92
- 4.28** Voltammograms for electro-oxidation of nifedipine in (A) pH 4, (B) tap water and (C) pH 10; electro-oxidation time (1) 0 min (2) 15 min (3) 30 min (4) 60 min.  $\text{IrO}_2\text{-TiO}_2/\text{Ti}$  electrode as anode; Initial concentration for nifedipine = 10  $\mu\text{mol/L}$ . Working electrode for voltammetry determination: HMDE. Reference electrode: Ag/AgCl (3 M KCl). 93

- 4.29** Voltammograms for electro-oxidation of nifedipine in (A) pH 4, (B) tap water and (C) pH 10; electro-oxidation time (1) 0 min (2) 15 min (3) 30 min (4) 60 min. RuO<sub>2</sub>-TiO<sub>2</sub>/Ti electrode as anode; Initial concentration for nifedipine = 10 µmol/L. Working electrode for voltammetry determination: HMDE. Reference electrode: Ag/AgCl (3 M KCl). 93
- 4.30** The percentage degradation of nifedipine using voltammetry monitoring in (A) pH 4, (B) tap water and (C) pH 10; electro-oxidation time (1) 0 min (2) 15 min (3) 30 min (4) 60 min. (1) IrO<sub>2</sub>-TiO<sub>2</sub>/Ti and (2) RuO<sub>2</sub>-TiO<sub>2</sub>/Ti electrode as anode; Initial concentration for nifedipine = 10 µmol/L. Working electrode for voltammetry determination: HMDE. Reference electrode: Ag/AgCl (3 M KCl). 94
- 4.31** Voltammograms for electro-oxidation of nifedipine in (A) pH 4, (B) tap water and (C) pH 10; electro-oxidation time (1) 0 min (2) 15 min (3) 30 min (4) 60 min. RuO<sub>2</sub>-IrO<sub>2</sub>-TiO<sub>2</sub>/Ti (40:10:50) electrode as anode; Initial concentration for nifedipine = 10 µmol/L. Working electrode for voltammetry determination: HMDE. Reference electrode: Ag/AgCl (3 M KCl). 95
- 4.32** Voltammograms for electro-oxidation of nifedipine in (A) pH 4, (B) tap water and (C) pH 10; electro-oxidation time (1) 0 min (2) 15 min (3) 30 min (4) 60 min. RuO<sub>2</sub>-IrO<sub>2</sub>-TiO<sub>2</sub>/Ti (10:40:50) electrode as anode; Initial concentration for nifedipine = 10 µmol/L. Working electrode for voltammetry determination: HMDE. Reference electrode: Ag/AgCl (3 M KCl). 95
- 4.33** The percentage degradation of nifedipine using voltammetry monitoring in (A) pH 4, (B) tap water and (C) pH 10; electro-oxidation time (1) 0 min (2) 15 min (3) 30 min (4) 60 min. (1) RuO<sub>2</sub>-IrO<sub>2</sub>-TiO<sub>2</sub>/Ti (10:40:50) and (2) RuO<sub>2</sub>-IrO<sub>2</sub>-TiO<sub>2</sub>/Ti (40:10:50) electrode as anode; Initial concentration for nifedipine = 10 µmol/L. Working electrode for voltammetry determination: HMDE. Reference electrode: Ag/AgCl (3 M KCl). 96

4.34	The chromatograms of nifedipine (A) before electro-oxidation (B) after electro-oxidation and (C) overlay between chromatograms (A) and (B).	99
4.35	Mass spectra in product ion scan mode of nifedipine at a 0.1 $\mu\text{mol/L}$ in $\text{ES}^+$ .	100
4.36	Mass spectral profiles of electro-oxidation of nifedipine (A) 5-methoxycarbonyl-2,6-dimethyl-4-phenyl-1,4-dihydropyridine-3-carboxylic acid derivatives (B) 2,6-dimethyl-4-phenyl-1,4-dihydropyridine-3,5-dicarbaldehyde derivative.	101
4.37	A proposed reaction pathway for the electro-oxidation of nifedipine by MMO electrode.	102
5.1	DPCSV of 5 $\mu\text{mol/L}$ ampicillin at HMDE in BR buffer. The numbers indicate pH of BR-buffer. Reference electrode: Ag/AgCl (3 M KCl).	108
5.2	DPCSV of 50 $\mu\text{mol/L}$ ampicillin at m-AgSAE in BR buffer. The numbers indicate pH of BR-buffer. Reference electrode: Ag/AgCl (3 M KCl).	108
5.3	Reduction Schematic of ampicillin.	109
5.4	The dependence of DPCSV peak potential of ampicillin ( $c_{\text{AMP}} = 5 \mu\text{mol/L}$ ) at HMDE on pH of BR-buffer. Reference electrode: Ag/AgCl (3 M KCl).	110
5.5	The dependence of DPCSV peak potential of ampicillin ( $c_{\text{AMP}} = 50 \mu\text{mol/L}$ ) at m-AgSAE on pH of BR-buffer. Reference electrode: Ag/AgCl (3 M KCl).	111
5.6	The dependence of DPCSV peak current of ampicillin ( $c_{\text{AMP}} = 5 \mu\text{mol/L}$ ) at HMDE on pH of BR-buffer. Reference electrode: Ag/AgCl (3 M KCl).	111
5.7	The dependence of DPCSV peak current of ampicillin ( $c_{\text{AMP}} = 50 \mu\text{mol/L}$ ) at m-AgSAE on pH of BR-buffer. Reference electrode: Ag/AgCl (3 M KCl).	112

- 5.8** DPCSV for ampicillin at pH 6 using HMDE, BRB 0.04 M as electrolyte,  $E_i = 0$  mV,  $E_{acc} = 0$  mV,  $t_{acc} = 30$  s, scan rate =  $20$  mVs<sup>-1</sup> where, (1) BR buffer (2) 1 (3) 3 (4) 5  $\mu$ mol/L of ampicillin. Reference electrode: Ag/AgCl (3 M KCl). 112
- 5.9** DPCSV for ampicillin at pH 7 using HMDE, BRB 0.04 M as electrolyte,  $E_i = 0$  mV,  $E_{acc} = 0$  mV,  $t_{acc} = 30$  s, scan rate =  $20$  mVs<sup>-1</sup> where, (1) BR buffer (2) 1 (3) 3 (4) 5  $\mu$ mol/L of ampicillin. Reference electrode: Ag/AgCl (3 M KCl). 113
- 5.10** DPCSV for ampicillin at pH 7 using m-AgSAE, BRB 0.04 M as electrolyte,  $E_i = 0$  mV,  $E_{acc} = 0$  mV,  $t_{acc} = 30$  s, scan rate =  $20$  mVs<sup>-1</sup> where, (1) BR buffer (2) 10 (3) 30 (4) 50  $\mu$ mol/L of ampicillin. Reference electrode: Ag/AgCl (3 M KCl). 113
- 5.11** DPCSV for ampicillin at pH 8 using m-AgSAE, BRB 0.04 M as electrolyte,  $E_i = 0$  mV,  $E_{acc} = 0$  mV,  $t_{acc} = 30$  s, scan rate =  $20$  mVs<sup>-1</sup> where, (1) BR buffer (2) 10 (3) 30 (4) 50  $\mu$ mol/L of ampicillin. Reference electrode: Ag/AgCl (3 M KCl). 114
- 5.12** DPCSV for ampicillin at pH 9 using m-AgSAE, BRB 0.04 M as electrolyte,  $E_i = 0$  mV,  $E_{acc} = 0$  mV,  $t_{acc} = 30$  s, scan rate =  $20$  mVs<sup>-1</sup> where, (1) BR buffer (2) 10 (3) 30 (4) 50  $\mu$ mol/L of ampicillin. Reference electrode: Ag/AgCl (3 M KCl). 114
- 5.13** The effect of initial potential on ampicillin reduction peak at (A) HMDE and (B) m-AgSAE.  $t_{acc} = 30$  s,  $E_{acc} = 0$  mV, scan rate =  $20$  mVs<sup>-1</sup> and BRB 0.04 M as electrolyte. Concentration of ampicillin at HMDE = 5  $\mu$ mol/L, while, 50  $\mu$ mol/L at m-AgSAE. Reference electrode: Ag/AgCl (3 M KCl). 116
- 5.14** The effect of accumulation potential on ampicillin reduction peak at (A) HMDE and (B) m-AgSAE.  $t_{acc} = 30$  s,  $E_i = 0$  mV, scan rate =  $20$  mVs<sup>-1</sup> and BRB 0.04 M as electrolyte. Concentration of ampicillin at HMDE = 5  $\mu$ mol/L, while, 50  $\mu$ mol/L at m-AgSAE. Reference electrode: Ag/AgCl (3 M KCl). 116

- 5.15** The effect of accumulation time on ampicillin reduction peak at (A) HMDE and (B) m-AgSAE.  $E_i = 0$  mV,  $E_{acc} = 0$  mV, scan rate =  $20$  mVs<sup>-1</sup> and BRB  $0.04$  M as electrolyte. Concentration of ampicillin at HMDE =  $5$   $\mu$ mol/L, while,  $50$   $\mu$ mol/L at m-AgSAE. Reference electrode: Ag/AgCl (3 M KCl). 117
- 5.16** Voltammograms for ampicillin at HMDE in BR-buffer pH 7, ( $C_{AMP}$  (1) 0 (supporting electrolyte), (2) 1, (3) 3, (4) 5, (5) 7, (6) 9 ( $\mu$ mol/L). Right: Corresponding calibration straight lines. Reference electrode: Ag/AgCl (3 M KCl). 119
- 5.17** Voltammograms for ampicillin at m-AgSAE in BR-buffer pH 8, ( $C_{AMP}$  (1) 10, (2) 30, (3) 50, (4) 70, (5) 90 (6) 110 ( $\mu$ mol/L). Right: Corresponding calibration straight lines. Reference electrode: Ag/AgCl (3 M KCl). 120
- 5.18** Voltammograms of ampicillin ( $C_{AMP}$  (1) 0 (supporting electrolyte) (2) 0.9, (3) 2.7, (4) 4.5, (5) 6.3, (6) 8.1 ( $\mu$ mol/L) at HMDE in (A) drinking water sample (B) river water sample with mixture of BR buffer pH 7. Reference electrode: Ag/AgCl (3 M KCl). 121
- 5.19** Voltammograms of ampicillin ( $C_{AMP}$  (1) 9, (2) 27, (3) 45, (4) 63, (5) 81 ( $\mu$ mol/L) at m-AgSAE in (A) drinking water sample (B) river water sample with mixture of BR buffer pH 8. Reference electrode: Ag/AgCl (3 M KCl). 121
- 5.20** Cation and anion interference on ampicillin in drinking and river water sample at HMDE. Reference electrode: Ag/AgCl (3 M KCl). Concentration of cation/anion =  $5$   $\mu$ mol/L. 123
- 5.21** Cation and anion interference on ampicillin in drinking and river water sample at m-AgSAE. Reference electrode: Ag/AgCl (3 M KCl). Concentration of cation/anion =  $5$   $\mu$ mol/L. 124

- 5.22** Voltammograms for electro-oxidation of ampicillin in (A) pH 4, (B) tap water and (C) pH 10; electro-oxidation time (1) 0 min (2) 15 min (3) 30 min (4) 60 min. TiO<sub>2</sub>/Ti electrode as anode; Initial concentration for ampicillin = 5 μmol/L. Working electrode for voltammetry determination: HMDE. Reference electrode: Ag/AgCl (3 M KCl). 126
- 5.23** The percentage of degradation of ampicillin using voltammetry monitoring in (A) pH 4, (B) tap water and (C) pH 10; electro-oxidation time (1) 0 min (2) 15 min (3) 30 min (4) 60 min. TiO<sub>2</sub>/Ti electrode as anode; Initial concentration for ampicillin = 5 μmol/L. Working electrode for voltammetry determination: HMDE. Reference electrode: Ag/AgCl (3 M KCl). 126
- 5.24** Voltammograms for electro-oxidation of ampicillin in (A) pH 4, (B) tap water and (C) pH 10; electro-oxidation time (1) 0 min (2) 15 min (3) 30 min (4) 60 min. IrO<sub>2</sub>-TiO<sub>2</sub>/Ti electrode as anode; Initial concentration for ampicillin = 5 μmol/L. Working electrode for voltammetry determination: HMDE. Reference electrode: Ag/AgCl (3 M KCl). 128
- 5.25** Voltammograms for electro-oxidation of ampicillin in (A) pH 4, (B) tap water and (C) pH 10; electro-oxidation time (1) 0 min (2) 15 min (3) 30 min (4) 60 min. RuO<sub>2</sub>-TiO<sub>2</sub>/Ti electrode as anode; Initial concentration for ampicillin = 5 μmol/L. Working electrode for voltammetry determination: HMDE. Reference electrode: Ag/AgCl (3 M KCl). 128
- 5.26** The percentage degradation of ampicillin using voltammetry monitoring in (A) pH 4, (B) tap water and (C) pH 10; electro-oxidation time (1) 0 min (2) 15 min (3) 30 min (4) 60 min. (1) IrO<sub>2</sub>-TiO<sub>2</sub>/Ti and (2) RuO<sub>2</sub>-TiO<sub>2</sub>/Ti electrode as anode; Initial concentration for ampicillin = 5 μmol/L. Working electrode for voltammetry determination: HMDE. Reference electrode: Ag/AgCl (3 M KCl). 129



- 5.27** Voltammograms for electro-oxidation of ampicillin in (A) pH 4, (B) tap water and (C) pH 10; electro-oxidation time (1) 0 min (2) 15 min (3) 30 min (4) 60 min. RuO<sub>2</sub>-IrO<sub>2</sub>-TiO<sub>2</sub>/Ti (40:10:50) electrode as anode; Initial concentration for ampicillin = 5 μmol/L. Working electrode for voltammetry determination: HMDE. Reference electrode: Ag/AgCl (3 M KCl). 130
- 5.28** Voltammograms for electro-oxidation of ampicillin in (A) pH 4, (B) tap water and (C) pH 10; electro-oxidation time (1) 0 min (2) 15 min (3) 30 min (4) 60 min. RuO<sub>2</sub>-IrO<sub>2</sub>-TiO<sub>2</sub>/Ti (10:40:50) electrode as anode; Initial concentration for ampicillin = 5 μmol/L. Working electrode for voltammetry determination: HMDE. Reference electrode: Ag/AgCl (3 M KCl). 130
- 5.29** The percentage degradation of ampicillin using voltammetry monitoring in (A) pH 4, (B) tap water and (C) pH 10; electro-oxidation time (1) 0 min (2) 15 min (3) 30 min (4) 60 min. (1) RuO<sub>2</sub>-IrO<sub>2</sub>-TiO<sub>2</sub>/Ti (40:10:50) and (2) RuO<sub>2</sub>-IrO<sub>2</sub>-TiO<sub>2</sub>/Ti (10:40:50) electrode as anode; Initial concentration for ampicillin = 5 μmol/L. Working electrode for voltammetry determination: HMDE. Reference electrode: Ag/AgCl (3 M KCl). 131
- 5.30** The chromatograms of ampicillin (A) before electro-oxidation (B) after electro-oxidation and (C) overlay between chromatograms (A) and (B). 134
- 5.31** Mass spectra in product ion scan mode of ampicillin at a 0.5 μmol/L in ES<sup>+</sup>. 135
- 5.32** Mass spectral profiles of electro-oxidation of ampicillin (A) N-[(E)-3-ethylhex-3-enyl]-3,3-dimethyl-4-thia-1-azabicyclo[3.2.0]heptan-6-amine (B) 3-[2-[(3,3-dimethyl-4-thia-1-azabicyclo[3.2.0]heptan-6-yl)amino]ethyl]hexanedioic acid. 136
- 5.33** A proposed reaction pathway for the electro-oxidation of ampicillin by MMO electrode. 137
- 6.1** Schematic reduction of Penicillin G. 143

- 6.2** DPCSV of 5  $\mu\text{mol/L}$  penicillin G at HMDE in BR buffer. The numbers indicate pH of BR-buffer. Reference electrode: Ag/AgCl (3 M KCl). 144
- 6.3** DPCSV of 50  $\mu\text{mol/L}$  penicillin G at m-AgSAE in BR buffer. The numbers indicate pH of BR-buffer. Reference electrode: Ag/AgCl (3 M KCl). 145
- 6.4** The dependence of peak potential of penicillin G ( $C_{\text{PG}} = 5 \mu\text{mol/L}$ ) at HMDE on pH of BR-buffer. Reference electrode: Ag/AgCl (3 M KCl). 145
- 6.5** The dependence of peak potential of penicillin G ( $C_{\text{PG}} = 50 \mu\text{mol/L}$ ) at m-AgSAE on pH of BR-buffer. Reference electrode: Ag/AgCl (3 M KCl). 146
- 6.6** The dependence of peak current of penicillin G ( $C_{\text{PG}} = 5 \mu\text{mol/L}$ ) at HMDE on pH of BR-buffer. Reference electrode: Ag/AgCl (3 M KCl). 146
- 6.7** The dependence of peak current of penicillin G ( $C_{\text{PG}} = 50 \mu\text{mol/L}$ ) at m-AgSAE on pH of BR-buffer. Reference electrode: Ag/AgCl (3 M KCl). 147
- 6.8** DPCSV for penicillin G at pH 9 using HMDE, BRB 0.04 M as electrolyte,  $E_i = 0 \text{ mV}$ ,  $E_{\text{acc}} = 0 \text{ mV}$ ,  $t_{\text{acc}} = 30 \text{ s}$ , scan rate =  $20 \text{ mVs}^{-1}$  where, (1) BR buffer (2) 1 (3) 3 (4) 5 ( $\mu\text{mol/L}$ ) of penicillin G. Reference electrode: Ag/AgCl (3 M KCl). 147
- 6.9** DPCSV for penicillin G at pH 10 using HMDE, BRB 0.04 M as electrolyte,  $E_i = 0 \text{ mV}$ ,  $E_{\text{acc}} = 0 \text{ mV}$ ,  $t_{\text{acc}} = 30 \text{ s}$ , scan rate =  $20 \text{ mVs}^{-1}$  where, (1) BR buffer (2) 1 (3) 3 (4) 5 ( $\mu\text{mol/L}$ ) of penicillin G. Reference electrode: Ag/AgCl (3 M KCl). 148
- 6.10** DPCSV for penicillin G at pH 11 using HMDE, BRB 0.04 M as electrolyte,  $E_i = 0 \text{ mV}$ ,  $E_{\text{acc}} = 0 \text{ mV}$ ,  $t_{\text{acc}} = 30 \text{ s}$ , scan rate =  $20 \text{ mVs}^{-1}$  where, (1) BR buffer (2) 1 (3) 3 (4) 5 ( $\mu\text{mol/L}$ ) of penicillin G. Reference electrode: Ag/AgCl (3 M KCl). 148
- 6.11** DPCSV for penicillin G at pH 12 using HMDE, BRB 0.04 M as electrolyte,  $E_i = 0 \text{ mV}$ ,  $E_{\text{acc}} = 0 \text{ mV}$ ,  $t_{\text{acc}} = 30 \text{ s}$ , scan rate =  $20 \text{ mVs}^{-1}$  where, (1) BR buffer (2) 1 (3) 3 (4) 5 ( $\mu\text{mol/L}$ ) of penicillin G. Reference electrode: Ag/AgCl (3 M KCl). 149

- 6.12** The effect of initial potential on penicillin G reduction peak at pH 12 using (A) HMDE and (B) m-AgSAE.  $E_{acc}= 0$  mV,  $t_{acc}= 30$  s, scan rate =  $20$  mVs<sup>-1</sup> and BRB  $0.04$  M as electrolyte. Concentration of penicillin G =  $5$   $\mu$ mol/L (HMDE) and  $50$   $\mu$ mol/L (m-AgSAE). Reference electrode: Ag/AgCl (3 M KCl). 150
- 6.13** The effect of accumulation potential on penicillin G reduction peak at pH 12 using (A) HMDE and (B) m-AgSAE.  $E_i= 0$  mV,  $t_{acc}= 30$  s, scan rate =  $20$  mVs<sup>-1</sup> and BRB  $0.04$  M as electrolyte. Concentration of penicillin G =  $5$   $\mu$ mol/L (HMDE) and  $50$   $\mu$ mol/L (m-AgSAE). Reference electrode: Ag/AgCl (3 M KCl). 150
- 6.14** The effect of accumulation time on penicillin G reduction peak at pH 12 using (A) HMDE and (B) m-AgSAE.  $E_i= 0$  mV,  $E_{acc}= 0$  mV, scan rate =  $20$  mVs<sup>-1</sup> and BRB  $0.04$  M as electrolyte. Concentration of penicillin G =  $5$   $\mu$ mol/L (HMDE) and  $50$   $\mu$ mol/L (m-AgSAE). Reference electrode: Ag/AgCl (3 M KCl). 151
- 6.15** Voltammograms for penicillin G at HMDE in BR-buffer pH 12, ( $c_{PG}$  (1) 0 (supporting electrolyte), (2) 1, (3) 3, (4) 5, (5) 7, (6) 9 ( $\mu$ mol/L). Right: Corresponding calibration straight lines. Reference electrode: Ag/AgCl (3 M KCl). 153
- 6.16** Voltammograms for penicillin G at m-AgSAE in BR-buffer pH 12, ( $c_{PG}$  (1) 0 (supporting electrolyte), (2) 10, (3) 30, (4) 50, (5) 70, (6) 90 ( $\mu$ mol/L). Right: Corresponding calibration straight lines. Reference electrode: Ag/AgCl (3 M KCl). 154
- 6.17** Voltammograms of penicillin G ( $c_{PG}$  (1) 0 (supporting electrolyte) (2) 0.9, (3) 2.7, (4) 4.5, (5) 6.3, (6) 8.1 ( $\mu$ mol/L) at HMDE in (A)drinking water sample (B) river water sample with mixture of BR buffer pH 12 Reference electrode: Ag/AgCl (3 M KCl). 155

- 6.18** Voltammograms of penicillin G ( $c_{PG}$  (1) 0 (supporting electrolyte) (2) 9, (3) 27, (4) 45, (5) 63, (6) 81 ( $\mu\text{mol/L}$ ) at m-AgSAE in (A) drinking water sample (B) river water sample with mixture of BR buffer pH 12. Reference electrode: Ag/AgCl (3 M KCl). 155
- 6.19** Cyclic voltammograms of 500  $\mu\text{mol/L}$  penicillin G at BDDE in BR buffer. The numbers indicate pH of BR-buffer. Reference electrode: Ag/AgCl (3 M KCl). 158
- 6.20** The dependence of CV peak potential of penicillin G ( $c_{PG} = 500 \mu\text{mol/L}$ ) at BDDE on pH of BR-buffer. Reference electrode: Ag/AgCl (3 M KCl). 159
- 6.21** The dependence of CV peak current of penicillin G ( $c_{PG} = 500 \mu\text{mol/L}$ ) at BDDE on pH of BR-buffer. Reference electrode: Ag/AgCl (3 M KCl). 160
- 6.22** Mechanism of electro-oxidation of (A) Penicillin G to (B) Beta-sulfoxide of penicillin G. 160
- 6.23** Effect of initial potential on penicillin G oxidation peak on BDD electrode at BRB pH 4. Scan rate = 50 mV/s. Concentration of penicillin G = 5  $\mu\text{mol/L}$ . Reference electrode: Ag/AgCl (3 M KCl). 162
- 6.24** Effect of accumulation potential on penicillin G oxidation peak on BDD electrode at BRB pH 4. Scan rate = 50 mV/s. Concentration of penicillin G = 5  $\mu\text{mol/L}$ . Reference electrode: Ag/AgCl (3 M KCl). 162
- 6.25** Effect of accumulation time ( $t_{acc}$ ) on 5  $\mu\text{mol/L}$  penicillin G oxidation peak on BDDE in BRB pH 4 with initial potential ( $E_i$ ) = 500 mV and scan rate = 50 mV/s. Reference electrode: Ag/AgCl (3 M KCl). 163
- 6.26** DP voltammogram of penicillin G at BDDE in BR buffer pH 4 (1) 0 (supporting electrolyte) (2) 1 (3) 3 (4) 5 (5) 7 (6) 9 ( $\mu\text{mol/L}$ ) in 0.04 M BRB. Right: Corresponding calibration straight lines. Reference electrode: Ag/AgCl (3 M KCl). 164

- 6.27** DP voltammogram of penicillin G at BDDE in drinking water sample-BR buffer pH 4 (9:1) (1) 0 (supporting electrolyte) (2) 0.9 (3) 2.7 (4) 4.5 (5) 6.3 (6) 8.1 ( $\mu\text{mol/L}$ ) in 0.04 M BRB. Reference electrode: Ag/AgCl (3 M KCl). 165
- 6.28** DP voltammogram of penicillin G at BDDE in river water sample-BR buffer pH 4 (9:1) (1) 0 (supporting electrolyte) (2) 0.9 (3) 2.7 (4) 4.5 (5) 6.3 (6) 8.1 ( $\mu\text{mol/L}$ ) in 0.04 M BRB. Reference electrode: Ag/AgCl (3 M KCl). 166
- 6.29** Cation and anion interference on penicillin G in drinking and river water sample at HMDE. Reference electrode: Ag/AgCl (3 M KCl). Concentration of cation/anion = 5  $\mu\text{mol/L}$ . 167
- 6.30** Cation and anion interference on penicillin G in drinking and river water sample at m-AgSAE. Reference electrode: Ag/AgCl (3 M KCl). Concentration of cation/anion = 5  $\mu\text{mol/L}$ . 168
- 6.31** Cation and anion interference on penicillin G in drinking and river water sample at BDDE. Reference electrode: Ag/AgCl (3 M KCl). Concentration of cation/anion = 5  $\mu\text{mol/L}$ . 168
- 6.32** Voltammograms for electro-oxidation of penicillin G in (A) pH 4, (B) tap water and (C) pH 10; electro-oxidation time (1) 0 min (2) 15 min (3) 30 min (4) 60 min.  $\text{TiO}_2/\text{Ti}$  electrode as anode; Initial concentration for penicillin G = 5  $\mu\text{mol/L}$ . Working electrode for voltammetry determination: HMDE. Reference electrode: Ag/AgCl (3 M KCl). 171
- 6.33** The percentage of degradation of penicillin G using voltammetry monitoring in (A) pH 4, (B) tap water and (C) pH 10; electro-oxidation time (1) 0 min (2) 15 min (3) 30 min (4) 60 min.  $\text{TiO}_2/\text{Ti}$  electrode as anode; Initial concentration for penicillin G = 5  $\mu\text{mol/L}$ . Working electrode for voltammetry determination: HMDE. Reference electrode: Ag/AgCl (3 M KCl). 171

- 6.34** Voltammograms for electro-oxidation of penicillin G in (A) pH 4, (B) tap water and (C) pH 10; electro-oxidation time (1) 0 min (2) 15 min (3) 30 min (4) 60 min. IrO<sub>2</sub>-TiO<sub>2</sub>/Ti electrode as anode; Initial concentration for penicillin G = 5 μmol/L. Working electrode for voltammetry determination: HMDE. Reference electrode: Ag/AgCl (3 M KCl). 172
- 6.35** Voltammograms for electro-oxidation of penicillin G in (A) pH 4, (B) tap water and (C) pH 10; electro-oxidation time (1) 0 min (2) 15 min (3) 30 min (4) 60 min. RuO<sub>2</sub>-TiO<sub>2</sub>/Ti electrode as anode; Initial concentration for penicillin G = 5 μmol/L. Working electrode for voltammetry determination: HMDE. Reference electrode: Ag/AgCl (3 M KCl). 173
- 6.36** The percentage degradation of penicillin G using voltammetry monitoring in (A) pH 4, (B) tap water and (C) pH 10; electro-oxidation time (1) 0 min (2) 15 min (3) 30 min (4) 60 min. (1) IrO<sub>2</sub>-TiO<sub>2</sub>/Ti and (2) RuO<sub>2</sub>-TiO<sub>2</sub>/Ti electrode as anode; Initial concentration for penicillin G = 5 μmol/L. Working electrode for voltammetry determination: HMDE. Reference electrode: Ag/AgCl (3 M KCl). 173
- 6.37** Voltammograms for electro-oxidation of penicillin G in (A) pH 4, (B) tap water and (C) pH 10; electro-oxidation time (1) 0 min (2) 15 min (3) 30 min (4) 60 min. RuO<sub>2</sub>-IrO<sub>2</sub>-TiO<sub>2</sub>/Ti (40:10:50) electrode as anode; Initial concentration for penicillin G = 5 μmol/L. Working electrode for voltammetry determination: HMDE. Reference electrode: Ag/AgCl (3 M KCl). 174
- 6.38** Voltammograms for electro-oxidation of penicillin G in (A) pH 4, (B) tap water and (C) pH 10; electro-oxidation time (1) 0 min (2) 15 min (3) 30 min (4) 60 min. RuO<sub>2</sub>-IrO<sub>2</sub>-TiO<sub>2</sub>/Ti (10:40:50) electrode as anode; Initial concentration for penicillin G = 5 μmol/L. Working electrode for voltammetry determination: HMDE. Reference electrode: Ag/AgCl (3 M KCl). 175

- 6.39** The percentage degradation of penicillin G using voltammetry monitoring in (A) pH 4, (B) tap water and (C) pH 10; electro-oxidation time (1) 0 min (2) 15 min (3) 30 min (4) 60 min. (1) RuO<sub>2</sub>-IrO<sub>2</sub>-TiO<sub>2</sub>/Ti (40:10:50) and (2) RuO<sub>2</sub>-IrO<sub>2</sub>-TiO<sub>2</sub>/Ti (10:40:50) electrode as anode; Initial concentration for penicillin G = 5 μmol/L. Working electrode for voltammetry determination: HMDE. Reference electrode: Ag/AgCl (3 M KCl). 175
- 6.40** The chromatograms of penicillin G (A) before electro-oxidation (B) after electro-oxidation and (C) overlay between chromatograms (A) and (B). 178
- 6.41** Mass spectra in product ion scan mode of penicillin G at a 0.5 μmol/L in ES<sup>+</sup>. 179
- 6.42** Mass spectral profiles of electro-oxidation of penicillin G (A) formaldehyde; 6-[[*(Z)*-hex-4-enyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid (B) formaldehyde; 2-(hydroxymethyl)-3,3-dimethyl-6-[[*(Z)*-3-methylenehex-4-enyl]amino]-4-thia-1-azabicyclo[3.2.0]heptan-7-ol (C) (*Z*)-1-[(7-hydroxy-3,3-dimethyl-4-thia-1-azabicyclo[3.2.0]heptan-6-yl)amino]hex-4-ene-1,3-diol. 180
- 6.43** A proposed reaction pathway for the electro-oxidation of penicillin G by MMO electrode. 181

**LIST OF ABBREVIATIONS**

Ag/Cl	-	Argentum Chloride
AMP	-	Ampicillin
BDDE	-	Boron Doped Diamiond Electrode
BRB	-	Britton Robinson buffer solution
CV	-	Cyclic voltammetry
DPASV	-	Differential pulse anodic stripping voltammetry
DPCSV	-	Differential pulse cathodic stripping voltammetry
DPV	-	Differential pulse voltammetry
DW	-	Deionized water
HMDE	-	Hanging mercury drop electrode
KCl	-	Potassium chloride
LC-MS	-	Liquid chromatography mass spectrometry
LOD	-	Limit of detection
LOQ	-	Limit of quantitative
m-AgSAE	-	Mercury meniscus silver solid amalgam electrode
MeOH	-	Methanol
MMO	-	Mixed metal oxide electrode
NEPs	-	New emerging pollutants
NFD	-	Nifedipine
PG	-	Penicillin G
RSD	-	Relative standard deviation
SD	-	Standard deviation
UV	-	Ultra violet



**LIST OF SYMBOLS**

$\mu\text{M}$	-	micro molar
$\mu\text{m}$	-	micrometer
$\mu\text{mol/L}$	-	micromol per litre
A	-	Ampere
$\text{A/cm}^2$	-	ampere per square centimeters
$\text{cm}^2$	-	Square centimeters
$E_{\text{acc}}$	-	Accumulation potential
$E_i$	-	Initial potential
$E_{\text{reg}}$	-	Regenerated Potential
g	-	Grams
$\text{IrO}_2$	-	Iridium Oxide
$m/z$	-	mass per charge number
min	-	Minutes
mL	-	milliliter
$\text{mm}^2$	-	Square millimeters
$\text{mol/L}$	-	mol per litre
nA	-	nanoampere
$\text{RuO}_2$	-	Ruthenium Oxide
s	-	Second
$t_{\text{acc}}$	-	Accumulation time
$\text{TiO}_2$	-	Titanium Oxide
V	-	Voltage
v/v	-	volume over volume
$\mu\text{L}$	-	microliter
$\Omega\text{ cm}$	-	ohm centimeters

**LIST OF APPENDIX**

<b>APPENDIX NO.</b>	<b>TITLE</b>	<b>PAGE</b>
A	List of Publication and Conferences during PhD Study (2011-2015)	214

## CHAPTER 1

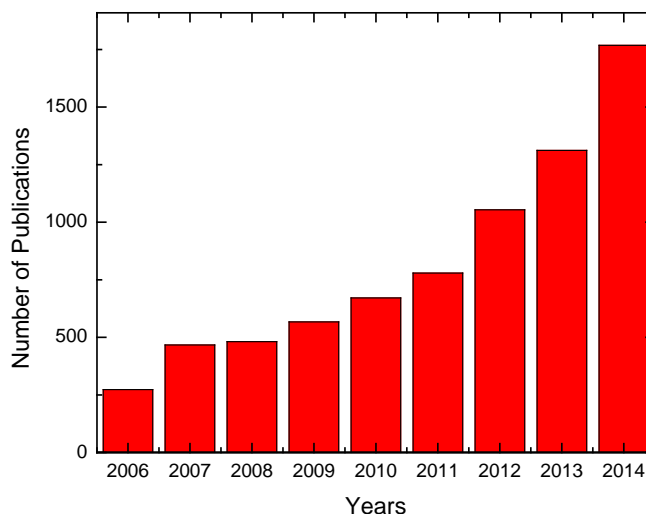
### INTRODUCTION

#### 1.0 Background of Study

In recent years, there has been an increasing concern about the presence of new emerging pollutants (NEPs) such as pesticides, drugs, dyes and endocrine disrupting chemicals (EDCs) waste in the aquatic environment (Deblonde *et al.*, 2011; Rodil *et al.*, 2012; Jiang *et al.*, 2013). These may cause a huge effect in the environment and eventually will affect human health. NEPs had been observed in the sewage water (De la Torre *et al.*, 2012; Peysson and Vulliet, 2013), surface water (Moreno-González *et al.*, 2013; Meffe and de Bustamante, 2014) or even in drinking water (Schriks *et al.*, 2010; Post *et al.*, 2012) and the increasing concern over the risks of NEPs is reflected by a rapid increase in the number of scientific publications (Scopus, ISI journal and web of science) exploring the environmental impacts of NEPs over the past few years (Fig. 1.1).

Among the NEPs, the presence of drugs (antibiotic, anti-depression and hypertension drugs) in the aquatic environment seems to attract researchers due to their unrestricted and widely used in both human and livestock. These drugs enter the environment through many ways such as wastewater affluent, treated sewage, industrial and clinical waste and also via excretion by human and animals (through urine; as inactive polar conjugates). Some of them can disrupt the endocrine system of aquatic animals (Benjamin, *et al.*, 2008 and Pei-Jen *et al.*, 2007). It also can enter the food chain and can increase the risk of cancer in human (Banerjee *et al.*, 2011; Bangalore *et al.*, 2011; Veitonmäki *et al.*, 2013). Antibiotic drugs for example have

several side effects ranging from hypersensitivity reaction (e.g. allergy to penicillin), soft stools or diarrhea to more serious effects such as damage of vital organs (Sørensen *et al.*, 1999; Evaggelopoulos and Samanidou, 2013).



**Figure 1.1:** Number of publications with the words ‘new emerging contaminants’ in the title or abstract published since 2006.

Electroanalytical methods (e.g. voltammetric techniques) are well known as one of the alternative techniques for the determination of metals (Achterberg and Braungardt, 1999; Hwang *et al.*, 2008; Injang *et al.*, 2010; Trindade *et al.*, 2012; Nascimento *et al.*, 2014; Lin *et al.*, 2015) and organic compounds (Zanoni *et al.*, 1997; Guaratini *et al.*, 2001; Guiberteau *et al.*, 2001; Deýlová *et al.*, 2014; Ivandini *et al.*, 2014; Janíková-Bandžuchová *et al.*, 2015). The advantages of the voltammetric techniques are due to its sensitivity, selectivity, simple instrument, easy to operate and low operational costs. The sensitivity of the technique can also be increased by modification of the working electrodes.

The fundamental concept of electrochemistry is basically based on the interface between the measurements of electrical quantities such as current, potential and charge and also their relationship with chemical parameters. There are two types of electro-analytical measurements namely;

- (i) Potentiometry which is a static (zero current) technique in which information about the sample composition is obtained from measurement of potential established across a membrane.
- (ii) Potentiostatic also known as controlled potential that based on the dynamic (non-zero current) situations. The electrode potential is used to drive an electron-transfer reaction and initial the measurement of current. This principle can measure any chemical species that is electro-active, i.e. which can be made to reduce or oxidize.

Electrochemical methods (electro-oxidation, electro-coagulation, electro-flotation, etc.) have gained interest in water treatment for the degradation/removal of NEPs. For example, electro-oxidation has been successfully applied to degrade organic pollutants (Särkkä *et al.*, 2008; Bagastyo *et al.*, 2011; Schaefer *et al.*, 2015). The electro-oxidation of NEPs can be enhanced by using metal oxide (MO) and mixed metal oxides (MMO) electrodes. These electrodes have shown a promising results for several electro-oxidation processes in degradation of NEPs such as drugs (Radjenovic *et al.*, 2011; Sopaj *et al.*, 2015), dyes (Zhou *et al.*, 2011), pesticides (Henych *et al.*, 2015; Madsen *et al.*, 2015) and also other organic compounds (Särkkä *et al.*, 2008; Schaefer *et al.*, 2015). MMO have some advantages include a wide potential window in aqueous and non-aqueous electrolytes, chemical and physical stability and small background, which makes them a popular choice as a new electrode material.

## 1.2 Problem Statement

Currently, several methods are available for the determination of NEPs, but most of these methods need expensive instrumentations, tedious sample preparation and suffer from instrument difficulty due to matrix interference. High performance liquid chromatography (HPLC) for example have a complex design (prior extraction and pre-concentration stage) and also need to combine with other instrument such as

MS-MS in order to obtain lower detection limit. Thus, a new method must be developed to overcome this problem. In the case on electrochemical studies, working electrode such as HMDE was the common and popular working electrodes used in the determination of NEPs. However, due to the toxicity (E.g. HMDE (metallic mercury)), alternative electrodes are searched possibly with performance similar to mercury electrodes but less toxic and more environmentally friendly (“Greener working electrode”).

The interest in NEPs does not only focus on the main compounds but also the degradation or transformational products. Many reports stated that the presence of NEPs in pharmaceutical effluents and surface waters have raised substantial concern in the public and regulatory agencies as it gives potential risk to humans and wildlife. It is important to have an effective primary treatment for the removal/degradation of NEPs from hospital and clinical wastewater to protect the environment. From our literature reviews, a number of methods such as bio-analytical assessments, photo-degradation and activated carbon have been used to overcome this situation. However, most of these methods still do not satisfy the requirements (e.g. need longer time to degrade the compounds). Hence, a new method must be developed in order to reduce and eliminate these chemicals.

### **1.3 Research Objectives**

- 1) To study the electrochemical behavior of selected drugs using voltammetric techniques with three different working electrodes (Hanging mercury drop electrode (HMDE), mercury meniscus silver solid amalgam electrode (m-AgSAE) and boron doped diamond electrode (BDDE)).
- 2) To develop a method for the determination of the drugs utilizing (BDDE and m-AgSAE) as new “Green” working electrode.
- 3) To study and evaluate the efficiency of commercial mixed metal oxide (MMO) electrodes in the electro-oxidation of the selected drugs.

- 4) To apply the developed method for the determination of selected drugs in real samples.

#### **1.4 Scope of Research**

The scope of the study involves the determination and the electro-oxidation of ampicillin, penicillin G and nifedipine. To achieve these, the study was divided into three parts;

1. Part I: The study of the electrochemical behavior of ampicillin, penicillin G and nifedipine using voltammetric technique with hanging mercury drop electrode (HMDE), mercury meniscus modified silver amalgam electrode (m-AgSAE) and boron doped diamond electrode (BDDE) working electrodes.
2. Part II: The employment of the developed method for the determination of ampicillin, penicillin G and nifedipine in real samples (drinking and river water) using HMDE, m-AgSAE and BDDE.
3. Part III: The study of the electro-oxidation of ampicillin, penicillin G and nifedipine using commercial mixed metal oxide electrodes (different in compositions and ratios;  $\text{TiO}_2/\text{Ti}$ ,  $\text{IrO}_2\text{-TiO}_2/\text{Ti}$ ,  $\text{RuO}_2\text{-TiO}_2/\text{Ti}$ ,  $\text{IrO}_2\text{-RuO}_2\text{-TiO}_2/\text{Ti}$ ) and the determination of the degradation (or transformational products) were carried out using voltammetric and LC-MS techniques.

## 1.5 Significance of Research

Due to the increasing fears in the toxicity of mercury, which can cause “mercuriophobia” (Cizek *et al.*, 2007; Fischer *et al.*, 2007; Chorti *et al.*, 2014), a newly developed electrode must be constructed to overcome these crucial problems; resulting in the development of mercury meniscus modified silver amalgam electrode (m-AgSAE). M-AgSAE can be compared with HMDE and it is a suitable alternative electrode for HMDE with less toxicity.

On the other hand, the electrochemical methods for removal of heavy metals in industrial wastewaters are well known. However, the application for the removal/degrade of organic pollutants is quite new. Electrochemical method is seen to be the suitable and simple method for NEPs removal/degrade because of the simultaneous oxidation-reduction process taking place at the electrodes without the need to add in any chemicals and time consuming. Indeed, the electrochemical methods have been suggested as a useful method of removing/degrade harmful NEPs in wastewater and effluent.

Fortunately, the unique properties of MMO (as anode materials) can successfully overcome these problems. MMO electrode has high catalytic activity and also has low oxygen evolution over potential which can make the electrode easily realize oxygen evolution. This research will help to develop a new method for the degradation of ampicillin, penicillin G and nifedipine using electro-oxidation method and to evaluate the effectiveness of MMO electrodes in order to degrade nifedipine, ampicillin and penicillin G.



## 1.6 Research Novelty

The novelty of this research includes:

- a) The method for electrochemical determination of ampicillin, penicillin G and nifedipine mercury meniscus modified silver amalgam electrode (m-AgSAE). The mercury meniscus modified silver amalgam electrode (m-AgSAE) is equally sensitive compared with HMDE (i.e. still having the properties of HMDE) but more “Greener” (less amount of mercury used).
  
- b) A novel method for the removal/degradation of ampicillin, penicillin G and nifedipine using electro-oxidation method with titanium based mixed metal oxide (MMO) as the anode electrode.

## REFERENCES

- Achterberg, E.P. and Braungardt, C. (1999). Stripping voltammetry for the determination of trace metal speciation and in-situ measurements of trace metal distributions in marine waters. *Analytical Chimica Acta*, 400, 381–397.
- Aguilera-ruiz, E., García-pérez, U.M., Garza-galván, M. De, Zambrano-robledo, P., Bermúdez-reyes, B., and Peral, J. (2015). Applied Surface Science Efficiency of  $\text{Cu}_2\text{O}/\text{BiVO}_4$  particles prepared with a new soft procedure on the degradation of dyes under visible-light irradiation. *Applied Surface Science*, 328, 361–367.
- Ahmar, H., Fakhari, A.R., Tabani, H., and Shahsavani, A. (2013). Optimization of electromembrane extraction combined with differential pulse voltammetry using modified screen-printed electrode for the determination of sufentanil. *Electrochimica Acta*, 96, 117–123.
- Ahmed, S., Rasul, M.G., Brown, R., and Hashib, M.A. (2011). Influence of parameters on the heterogeneous photocatalytic degradation of pesticides and phenolic contaminants in wastewater: A short review. *Journal of Environmental Management*, 92, 311–330.
- Alalm, M.G., Tawfik, A., and Ookawara, S. (2015). Degradation of four pharmaceuticals by solar photo-Fenton process: Kinetics and costs estimation. *Journal of Environmental Chemical Engineering*, 3, 46–51.
- Al-Qaim, F.F., Abdullah, M.P., Othman, M.R., Latip, J., and Zakaria, Z. (2014). Multi-residue analytical methodology-based liquid chromatography-time-of-flight-mass spectrometry for the analysis of pharmaceutical residues in surface water and effluents from sewage treatment plants and hospitals. *Journal of chromatography. A*, 1345, 139–53.
- An, J., Li, G., An, T., Song, W., Feng, H., and Lu, Y. (2015). Photocatalytic degradation of three amantadine antiviral drugs as well as their eco-toxicity evolution. *Catalysis Today*, 1–8.

- Bacigalupo, M. a, Meroni, G., Secundo, F., and Lelli, R. (2008). Time-resolved fluoroimmunoassay for quantitative determination of ampicillin in cow milk samples with different fat contents. *Talanta*, 77, 126–30.
- Bagastyo, A.Y., Radjenovic, J., Mu, Y., Rozendal, R. A, Batstone, D.J., and Rabaey, K. (2011). Electrochemical oxidation of reverse osmosis concentrate on mixed metal oxide (MMO) titanium coated electrodes. *Water research*, 45, 4951–9.
- Baghayeri, M., Namadchian, M., Karimi-Maleh, H., and Beitollahi, H. (2013). Determination of nifedipine using nanostructured electrochemical sensor based on simple synthesis of Ag nanoparticles at the surface of glassy carbon electrode: Application to the analysis of some real samples. *Journal of Electroanalytical Chemistry*, 697, 53–59.
- Ballesteros Martín, M.M., Sánchez Pérez, J. a, Casas López, J.L., Oller, I., and Malato Rodríguez, S. (2009). Degradation of a four-pesticide mixture by combined photo-Fenton and biological oxidation. *Water research*, 43, 653–60.
- Bandžuchová, L., Šelešovská, R., Navrátil, T., and Chýlková, J. (2011). Electrochemical behavior of folic acid on mercury meniscus modified silver solid amalgam electrode. *Electrochimica Acta*, 56, 2411–2419.
- Bandžuchová, L., Švorc, L., Sochr, J., Svítková, J., and Chýlková, J. (2013). Voltammetric method for sensitive determination of herbicide picloram in environmental and biological samples using boron-doped diamond film electrode. *Electrochimica Acta*, 111, 242–249.
- Banerjee, Y., Taranikanti, V., and Alriyami, M. (2011). Can antihypertensive drugs increase the risk of cancer? *Trends in molecular medicine*, 17, 175–6; 176–7.
- Bangalore, S., Kumar, S., Kjeldsen, S.E., Makani, H., Grossman, E., Wetterslev, J., Gupta, A.K., Sever, P.S., Gluud, C., and Messerli, F.H. (2011). Antihypertensive drugs and risk of cancer: network meta-analyses and trial sequential analyses of 324,168 participants from randomised trials. *The Lancet. Oncology*, 12, 65–82.
- Baranowska, I., Markowski, P., Gerle, A., and Baranowski, J. (2008). Determination of selected drugs in human urine by differential pulse voltammetry technique. *Bioelectrochemistry (Amsterdam, Netherlands)*, 73, 5–10.
- Barrio Diez-Caballero, R. J., L. Lopez De La Torre, J.F. Arranz Valentin and A. Arranz Garcia (1989). Adsorptive stripping voltammetry for the determination of nifedipine in human serum. *Talanta*, 36, 501–504.

- Belal, F. (2000). Kinetic spectrophotometric determination of ampicillin and amoxicillin in dosage forms. *IL Farmaco*, 55, 680–686.
- Belal, T.S., Mahrous, M.S., Abdel-Khalek, M.M., Daabees, H.G., and Khamis, M.M. (2014). Validated HPTLC method for the simultaneous determination of alfuzosin, terazosin, prazosin, doxazosin and finasteride in pharmaceutical formulations. *Analytical Chemistry Research*, 1, 23–31.
- Benjamin, L. L. T., Hawker, D. W., Muller, J. F., Tremblay, L. A. and Chapman, H. F. (2008). Stir bar sorptive extraction and trace analysis of selected endocrine disruptors in water, biosolids and sludge samples by thermal desorption with gas chromatography–mass spectrometry. *Water Research* 42, 404 – 412.
- Bernalte, E., Marín Sánchez, C., and Pinilla Gil, E. (2011). Determination of mercury in ambient water samples by anodic stripping voltammetry on screen-printed gold electrodes. *Analytica chimica acta*, 689, 60–4.
- Bhattacharjee, A. and Ahmaruzzaman, M. (2015). Journal of Colloid and Interface Science A novel and green process for the production of tin oxide quantum dots and its application as a photocatalyst for the degradation of dyes from aqueous phase. *journal of Colloid and Interface Science*, 448, 130–139.
- Białk-bieli, A., Stepnowski, P., Stolte, S., and Siedlecka, E.M. (2014). Electrochemical degradation of sulfonamides at BDD electrode: Kinetics, reaction pathway and eco-toxicity evaluation. 280, 579–587.
- Bianchi, C.L., Colombo, E., Gatto, S., Stucchi, M., Cerrato, G., Morandi, S., and Capucci, V. (2014). Photocatalytic degradation of dyes in water with micro-sized TiO<sub>2</sub> as powder or coated on porcelain-grès tiles. *Journal of Photochemistry & Photobiology, A: Chemistry*, 280, 27–31.
- Blair, B.D., Crago, J.P., Hedman, C.J., Treguer, R.J.F., Magruder, C., Royer, L.S., and Klaper, R.D. (2013). Evaluation of a model for the removal of pharmaceuticals, personal care products, and hormones from wastewater. *The Science of the total environment*, 444, 515–21.
- Blogoja Jardanoski, V.M. and K.S. (1996). Square wave voltammetry of 1-Benzyl-tetrazole-5-thiol. *Croatica chemica acta*, 69, 37–47.
- Bonfil, Y. and Brand, M. (2000). Trace determination of mercury by anodic stripping voltammetry at the rotating gold electrode. *Analytical Chimica Acta*, 424, 65–76.

- Bourgin, M. (2013) Study of the degradation of pesticides on loaded seeds by ozonation. *Journal of Environmental Chemical Engineering*, 1, 1004–1012.
- Brett, C.M.A., Maria, A., and Brett, C.F.O. (1989). DC anodic stripping voltammetry at mercury thin film electrodes : the shape and position of the stripping peaks at hydrodynamic electrodes. *J. Electroanal. Chem*, 262, 83–95.
- Brigante, M., Emmelin, C., Ferronato, C., Della, M., Previtera, L., Olivier, J., and Chovelon, J. (2007). Effect of positional isomerism on the abiotic degradation of pesticides : Case of m - and p -imazamethabenz-methyl. *Chemosphere*, 68, 464–471.
- Calza, P., Medana, C., Sarro, M., Rosato, V., Aigotti, R., Baiocchi, C., and Minero, C. (2014). Photocatalytic degradation of selected anticancer drugs and identification of their transformation products in water by liquid chromatography-high resolution mass spectrometry. *Journal of chromatography. A*, 1362, 135–44.
- Castro, D., Moreno, M.A., and Lastres, J.L. (2001). First-derivative spectrophotometric and LC determination of nifedipine in Brij ® 96 based oil / water / oil multiple microemulsions on stability studies. *Journal of Pharmaceutical and Biomedical Analysis*, 26 26, 563–572.
- Chellammal, S., Kalaiselvi, P., Ganapathy, P., and Subramanian, G. (2012). Anodic incineration of phthalic anhydride using RuO<sub>2</sub>–IrO<sub>2</sub>–SnO<sub>2</sub>–TiO<sub>2</sub> coated on Ti anode. *Arabian Journal of Chemistry*. Available online 4 May 2012
- Chen, T.-S., Chen, P.-H., and Huang, K.-L. (2014). Electrochemical degradation of N,N-diethyl-m-toluamide on a boron-doped diamond electrode. *Journal of the Taiwan Institute of Chemical Engineers*, 45, 2615–2621.
- Chorti, P., Fischer, J., Vyskocil, V., Economou, A., and Barek, J. (2014). Voltammetric Determination of Insecticide Thiamethoxam on Silver Solid Amalgam Electrode. *Electrochimica Acta*, 140, 5–10.
- Cizek, K., Barek, J., Fischer, J., Peckova, K., and Zima, J. (2007). Voltammetric Determination of 3-Nitrofluoranthene and 3-Aminofluoranthene at Boron Doped Diamond Thin-Film Electrode. *Electroanalysis*, 19, 1295–1299.
- Danhel, A., Shiu, K.K., Yosypchuk, B., Barek, J., Peckova, K., and Vyskocil, V. (2009). The Use of Silver Solid Amalgam Working Electrode for Determination of Nitrophenols by HPLC with Electrochemical Detection. *Electroanalysis*, 21, 303–308.

- Danhel, A., Yosypchuk, B., Vyskocil, V., Zima, J., and Barek, J. (2011). A novel paste electrode based on a silver solid amalgam and an organic pasting liquid. *Journal of Electroanalytical Chemistry*, 656, 218–222.
- Danhel, A., Raindlova, V., Havran, L., Pivonkova, H., Hocek, M., and Fojta, M. (2014). Electrochemical behaviour of 2,4-dinitrophenylhydrazide as multi-redox centre DNA label at mercury meniscus modified silver solid amalgam electrode. *Electrochimica Acta*, 126, 122–131.
- De La Torre, A., Concejero, M., and Martínez, M. (2012). Concentrations and sources of an emerging pollutant, decabromodiphenylethane (DBDPE), in sewage sludge for land application. *Journal of Environmental Sciences*, 24, 558–563.
- De Lima, F., Gozzi, F., Fiorucci, R., Cardoso, C. A. L., Arruda, G.J., and Ferreira, V.S. (2011). Determination of linuron in water and vegetable samples using stripping voltammetry with a carbon paste electrode. *Talanta*, 83, 1763–8.
- De Lima-Neto, P., Correia, A.N., Portela, R.R., Julião, M.D.S., Linhares-Junior, G.F., and De Lima, J.E.S. (2010). Square wave voltammetric determination of nitrofurantoin in pharmaceutical formulations on highly boron-doped diamond electrodes at different boron-doping contents. *Talanta*, 80, 1730–6.
- Deblonde, T., Cossu-Leguille, C., and Hartemann, P. (2011). Emerging pollutants in wastewater: a review of the literature. *International journal of hygiene and environmental health*, 214, 442–8.
- Dejmeková, H., Barek, J., and Zima, J. (2011). Determination of Aminonitrophenols in Hair Dyes Using a Carbon Paste Electrode and a Boron-Doped Diamond Film Electrode – A Comparative Study. *Int. J. Electrochem. Sci.*, 6, 3550–3563.
- Deng, J., Shao, Y., Gao, N., Xia, S., Tan, C., Zhou, S., and Hu, X. (2013). Degradation of the antiepileptic drug carbamazepine upon different UV-based advanced oxidation processes in water. *Chemical Engineering Journal*, 222, 150–158.
- Deýlová, D., Vyskočil, V., and Barek, J. (2014). Voltammetric determination of 2-amino-6-nitrobenzothiazole and 5-nitrobenzimidazole using a silver solid amalgam electrode modified by a microcrystalline natural graphite–polystyrene composite film. *Journal of Electroanalytical Chemistry*, 717-718, 237–242.

- Diao, J., Zhao, G., Li, Y., Huang, J., and Sun, Y. (2013). Carboxylesterase from *Spodoptera Litura*: Immobilization and use for the degradation of pesticides. *Procedia Environmental Sciences*, 18, 610–619.
- Dirany, A., Sirés, I., Oturan, N., and Oturan, M. a. (2010). Electrochemical abatement of the antibiotic sulfamethoxazole from water. *Chemosphere*, 81, 594–602.
- Dorival-García, N., Zafra-Gómez, A., Navalón, A., González, J., and Vílchez, J.L. (2013). Removal of quinolone antibiotics from wastewaters by sorption and biological degradation in laboratory-scale membrane bioreactors. *The Science of the total environment*, 442, 317–28.
- Dorival-García, N., Zafra-Gómez, A., Cantarero, S., Navalón, A., and Vílchez, J.L. (2013). Simultaneous determination of 13 quinolone antibiotic derivatives in wastewater samples using solid phase extraction and ultra performance liquid chromatography–tandem mass spectrometry. *Microchemical Journal*, 106, 323–333.
- Dornellas, R.M., Franchini, R. A. A., Da Silva, A.R., Matos, R.C., and Aucelio, R.Q. (2013). Determination of the fungicide kresoxim-methyl in grape juices using square-wave voltammetry and a boron-doped diamond electrode. *Journal of Electroanalytical Chemistry*, 708, 46–53.
- Dos Santos, L.B.O., Abate, G., and Masini, J.C. (2004). Determination of atrazine using square wave voltammetry with the Hanging Mercury Drop Electrode (HMDE). *Talanta*, 62, 667–74.
- Duwensee, H., Adamovski, M., and Flechsig, G. (2007). Adsorptive stripping voltammetric detection of daunomycin at mercury and bismuth alloy electrodes. *Int. J. Electrochem. Sci.*, 2, 498–507.
- Dzul, M. W., H., Rahim, A., Y. M., Zima, J., and Barek, J. (2015). Voltammetric Determination of Nifedipine at a Hanging Mercury Drop Electrode and a Mercury Meniscus Modified Silver Amalgam Electrode. *Int. J. Electrochem. Sci.*, 10, 4571–4584.
- El-Kafrawy, D.S. and Belal, T.S. (2014). Validated HPTLC method for the simultaneous determination of cinnarizine and dimenhydrinate in their combined dosage form. *Journal of the Association of Arab Universities for Basic and Applied Sciences*. Available online 12 July 2014

- Elmolla, E.S. and Chaudhuri, M. (2010a). Degradation of amoxicillin, ampicillin and cloxacillin antibiotics in aqueous solution by the UV/ZnO photocatalytic process. *Journal of hazardous materials*, 173, 445–9.
- Elmolla, E.S. and Chaudhuri, M. (2010b). Photocatalytic degradation of amoxicillin, ampicillin and cloxacillin antibiotics in aqueous solution using UV/TiO<sub>2</sub> and UV/H<sub>2</sub>O<sub>2</sub>/TiO<sub>2</sub> photocatalysis. *Desalination*, 252, 46–52.
- Evaggelopoulou, E.N. and Samanidou, V.F. (2013). Development and validation of an HPLC method for the determination of six penicillin and three amphenicol antibiotics in gilthead seabream (*Sparus Aurata*) tissue according to the European Union Decision 2002/657/EC. *Food chemistry*, 136, 1322–9.
- Feng, L., Hullebusch, E.D. Van, Rodrigo, M.A., Esposito, G., and Oturan, M.A. (2013). Removal of residual anti-inflammatory and analgesic pharmaceuticals from aqueous systems by electrochemical advanced oxidation processes . A review. *Chemical Engineering Journal*, 228, 944–964.
- Fernández-González, A., Badía, R., and Díaz-García, M.. (2003). Micelle-mediated spectrofluorimetric determination of ampicillin based on metal ion-catalysed hydrolysis. *Analytica Chimica Acta*, 484, 223–231.
- Fischer, J., Vanourkova, L., Danhel, A., Vyskocil, V., Cizek, K., Barek, J., Peckova, K., Yosypchuk, B., and Navratil, T. (2007). Voltammetric Determination of Nitrophenols at a Silver Solid. *Int. J. Electrochem. Sci.*, 2, 226–234.
- Forsman, U.L.F. (1983.) Cathodic stripping voltammetric determination of trace amounts of penicillins. *Analytica Chimica Acta*, 146. 71-86
- Gaichore, R.R. and Srivastava, A.K. (2013). Voltammetric determination of nifedipine using a  $\beta$ -cyclodextrin modified multi-walled carbon nanotube paste electrode. *Sensors and Actuators B: Chemical*, 188, 1328–1337.
- García-gómez, C., Drogui, P., Zaviska, F., Seyhi, B., Gortáres-moroyoqui, P., Buelna, G., and Neira-sáenz, C. (2014). Experimental design methodology applied to electrochemical oxidation of carbamazepine using Ti/PbO<sub>2</sub> and Ti/BDD electrodes. *Journal of Electroanalytical Chemistry*, 732, 1–10.
- Gazy, A., Hassan, E.M., Abdel-Hay, M.H., and Belal, T.S. (2007). Differential pulse cathodic voltammetric determination of floctafenine and metopimazine. *Journal of pharmaceutical and biomedical analysis*, 43, 1535–9.



- Gbylik-Sikorska, M., Posyniak, A., Sniegocki, T., and Zmudzki, J. (2015). Liquid chromatography–tandem mass spectrometry multiclass method for the determination of antibiotics residues in water samples from water supply systems in food-producing animal farms. *Chemosphere*, 119, 8–15.
- Giacomino, A., Abollino, O., Lazzara, M., Malandrino, M., and Mentasti, E. (2011). Determination of As(III) by anodic stripping voltammetry using a lateral gold electrode: experimental conditions, electron transfer and monitoring of electrode surface. *Talanta*, 83, 1428–35.
- Goto, T., Ito, Y., Yamada, S., Matsumoto, H., and Oka, H. (2005). High-throughput analysis of tetracycline and penicillin antibiotics in animal tissues using electrospray tandem mass spectrometry with selected reaction monitoring transition. *Journal of chromatography. A*, 1100, 193–9.
- Gotti, R., Fiori, J., Calleri, E., Temporini, C., Lubda, D., and Massolini, G. (2012). Chiral capillary liquid chromatography based on penicillin G acylase immobilized on monolithic epoxy silica column. *Journal of chromatography. A*, 1234, 45–9.
- Guaratini, C.C.I., Fogg, A.G., Valnice, M., and Zanoni, B. (2001). Assessment of the application of cathodic stripping voltammetry to the analysis of diazo reactive dyes and their hydrolysis products. *Dyes and Pigments*, 50, 211–221.
- Guiberteau, A., Galeano, T., Mora, N., Parrilla, P., and Salinas, F. (2001). Study and determination of the pesticide Imidacloprid by square wave adsorptive stripping voltammetry. *Talanta*, 53, 943–949.
- Guo, M., Xie, X., Jia, J., Liang, Z., Fan, C., and Han, P. (2015). Experimental study and theoretical calculation on the conductivity and stability of praseodymium doped tin oxide electrode. *Electrochimica Acta*, 151, 177–185.
- Haddad, T. and Kümmerer, K. (2014). Characterization of photo-transformation products of the antibiotic drug Ciprofloxacin with liquid chromatography–tandem mass spectrometry in combination with accurate mass determination using an LTQ-Orbitrap. *Chemosphere*, 115, 40–6.
- Hassen, W.M., Abdelghani, A., Vonna, L., Cherif, K., Boussaid, M., and Maaref, M. a. (2007). Electrochemical properties and topology of gold electrodes with adsorbed penicillin G for biosensor applications. *Sensors and Actuators B: Chemical*, 120, 621–627.

- He, X., Mezyk, S.P., Michael, I., Fatta-Kassinos, D., and Dionysiou, D.D. (2014). Degradation kinetics and mechanism of  $\beta$ -lactam antibiotics by the activation of  $\text{H}_2\text{O}_2$  and  $\text{Na}_2\text{S}_2\text{O}_8$  under UV-254nm irradiation. *Journal of hazardous materials*, 279, 375–83.
- Heller, D.N., Smith, M.L., and Chiesa, O.A. (2006). LC/MS/MS measurement of penicillin G in bovine plasma, urine, and biopsy samples taken from kidneys of standing animals. *Journal of chromatography. B, Analytical technologies in the biomedical and life sciences*, 830, 91–9.
- Henych, J., Štengl, V., Slušná, M., Matys Grygar, T., Janoš, P., Kuráň, P., and Štastný, M. (2015). Degradation of organophosphorus pesticide parathion methyl on nanostructured titania-iron mixed oxides. *Applied Surface Science*, 344, 9–16.
- Hsieh, S.-H., Huang, H.-Y., and Lee, S. (2009). Determination of eight penicillin antibiotics in pharmaceuticals, milk and porcine tissues by nano-liquid chromatography. *Journal of chromatography. A*, 1216, 7186–94.
- Huang, C., Gao, J., and Miao, L. (2012). Simultaneous determination of flucloxacillin and ampicillin in human plasma by ultra performance liquid chromatography-tandem mass spectrometry and subsequent application to a clinical study in healthy Chinese volunteers. *Journal of pharmaceutical and biomedical analysis*, 59, 157–61.
- Hwang, G.H., Han, W.K., Park, J.S., and Kang, S.G. (2008). Determination of trace metals by anodic stripping voltammetry using a bismuth-modified carbon nanotube electrode. *Talanta*, 76, 301–8.
- Ibrahim, M.S. (2000). Voltammetric behaviour and determination of the anthracycline antitumor drug nogalamycin. *Analytica Chimica Acta*, 409, 105–112.
- Injang, U., Noyrod, P., Siangproh, W., Dungchai, W., Motomizu, S., and Chailapakul, O. (2010). Determination of trace heavy metals in herbs by sequential injection analysis-anodic stripping voltammetry using screen-printed carbon nanotubes electrodes. *Analytica chimica acta*, 668, 54–60.
- Ishida, M., Kobayashi, K., Awata, N., and Sakamoto, F. (1999). Simple high-performance liquid chromatography determination of ampicillin in human serum using solid-phase extraction disk cartridges. *Journal of Chromatography B*, 727, 245–248.

- Ivandini, T. a., Wicaksono, W.P., Saepudin, E., Rismetov, B., and Einaga, Y. (2014). Anodic stripping voltammetry of gold Nanoparticles at boron-doped diamond Electrodes and Its application in immunochromatographic strip tests. *Talanta*. 134,136-143.
- Jain, R., Yadav, R.K., and Dwivedi, A. (2010). Square-wave adsorptive stripping voltammetric behaviour of entacapone at HMDE and its determination in the presence of surfactants. *Colloids and Surfaces A: Physicochemical and Engineering Aspects*, 359, 25–30.
- Janíková-Bandžuchová, L., Šelešovská, R., Schwarzová-Pecková, K., and Chýlková, J. (2015). Sensitive voltammetric method for rapid determination of pyridine herbicide triclopyr on bare boron-doped diamond electrode. *Electrochimica Acta*, 154, 421–429.
- Jiang, J.-Q., Zhou, Z., and Sharma, V.K. (2013). Occurrence, transportation, monitoring and treatment of emerging micro-pollutants in waste water — A review from global views. *Microchemical Journal*, 110, 292–300.
- Jiranek, I., Peckova, K., Kralova, Z., Moreira, J.C., and Berek, J. (2009). The use of silver solid amalgam electrode for voltammetric and amperometric determination of nitroquinolines. *Electrochimica Acta*, 54, 1939–1947.
- Joseph, S. and Mathew, B. (2015). Microwave-assisted green synthesis of silver nanoparticles and the study on catalytic activity in the degradation of dyes. *Journal of Molecular Liquids*, 204, 184–191.
- Joss, A., Zabczynski, S., Göbel, A., Hoffmann, B., Löffler, D., McArdell, C.S., Ternes, T. a, Thomsen, A., and Siegrist, H. (2006). Biological degradation of pharmaceuticals in municipal wastewater treatment: proposing a classification scheme. *Water research*, 40, 1686–96.
- Junza, a, Amatya, R., Barrón, D., and Barbosa, J. (2011). Comparative study of the LC-MS/MS and UPLC-MS/MS for the multi-residue analysis of quinolones, penicillins and cephalosporins in cow milk, and validation according to the regulation 2002/657/EC. *Journal of chromatography. B, Analytical technologies in the biomedical and life sciences*, 879, 2601–10.
- Katzung, Bertram G. (2007). *Basic and Clinical Pharmacology*, 10<sup>th</sup> edition. New York, NY: McGraw Hill Medical. 733.

- Khan, A.A.P., Mohd, A., Bano, S., Siddiqi, K.S., and Asiri, A.M. (2012). Spectrophotometric methods for the determination of ampicillin by potassium permanganate and 1-chloro-2,4-dinitrobenzene in pharmaceutical preparations. *Arabian Journal of Chemistry*, 2, 225-263.
- Komersova, A., Bartos, M., Kalcher, K., and Vytr, K. (1998). Trace iron determination in aminoisophthalic acid using differential-pulse cathodic stripping voltammetry at carbon paste electrodes. *Journal of Pharmaceutical and Biomedical Analysis*, 16, 1373-1379.
- Kordouli, E., Bourikas, K., Lycourghiotis, A., and Kordulis, C. (2015). The mechanism of azo-dyes adsorption on the titanium dioxide surface and their photocatalytic degradation over samples with various anatase/rutile ratios. *Catalysis Today*, 252, 128-135.
- Ku, P., Skopalová, J., and Lemr, K. (2015). Electrochimica Acta Electrochemical oxidation of fesoterodine and identification of its oxidation products using liquid chromatography and mass spectrometry. *Electrochimica Acta*, 159, 131-139.
- Kumar, S., Singh, S., and Srivastava, V.C. (2014). Electro-Oxidation of Nitrophenol by Ruthenium Oxide Coated Titanium Electrode: Parametric, Kinetic and Mechanistic Study. *Chemical Engineering Journal*. 263, 135-143.
- Kumar, V., Bhutani, H., and Singh, S. (2007). ICH guidance in practice: validated stability-indicating HPLC method for simultaneous determination of ampicillin and cloxacillin in combination drug products. *Journal of pharmaceutical and biomedical analysis*, 43, 769-73.
- Kurbanoglu, S., Gumustas, M., and Ozkan, S. A. (2013). Simultaneous estimation and validation of some binary mixtures of antihypertensive drugs by RP-LC methods using two new generation silica columns. *Journal of pharmaceutical and biomedical analysis*, 72, 198-201.
- Lai, W.W., Lin, H.H., and Lin, A.Y. (2015). TiO<sub>2</sub> photocatalytic degradation and transformation of oxazaphosphorine drugs in an aqueous environment. *Journal of Hazardous Materials*, 287, 133-141.
- Leonardo, W., Azário, M., Roberto, P., Henrique, J., and Santos, Z. (2015). Photocatalytic degradation of drugs by supported titania-based catalysts produced from petrochemical plant residue. *Powder Technology*, 279, 166-172.

- Li, D., Yang, M., Hu, J., Zhang, Y., Chang, H., and Jin, F. (2008). Determination of penicillin G and its degradation products in a penicillin production wastewater treatment plant and the receiving river. *Water research*, 42, 307–17.
- Li, W., Tanumihardja, J., Masuyama, T., and Korshin, G. (2014). Examination of the kinetics of degradation of the antineoplastic drug 5-fluorouracil by chlorine and bromine. *Journal of hazardous materials*, 282, 125–132.
- Lin, H., Li, M., and Mihailovič, D. (2015). Simultaneous Determination of Copper, Lead, and Cadmium Ions at a Mo<sub>6</sub>S<sub>9</sub>-xI<sub>x</sub> Nanowires Modified Glassy Carbon Electrode Using Differential Pulse Anodic Stripping Voltammetry. *Electrochimica Acta*, 154, 184–189.
- Liu, Y., Liu, H., Ma, J., and Li, J. (2012). Preparation and electrochemical properties of Ce-Ru-SnO<sub>2</sub> ternary oxide anode and electrochemical oxidation of nitrophenols. *Journal of hazardous materials*, 213-214, 222–9.
- Lourenço, A.S., Sanches, F. A. C., Magalhães, R.R., Costa, D.J.E., Ribeiro, W.F., Bichinho, K.M., Salazar-Banda, G.R., and Araújo, M.C.U. (2014). Electrochemical oxidation and electroanalytical determination of xylitol at a boron-doped diamond electrode. *Talanta*, 119, 509–16.
- Luo, W., Ang, C.Y.W., and Jr, H.C.T. (1997). Rapid method for the determination of ampicillin residues in animal muscle tissues by high-performance liquid chromatography with fluorescence detection. *Journal of Chromatography B*, 694, 401–407.
- Macarov, C. a, Tong, L., Martínez-Huélamo, M., Hermo, M.P., Chirila, E., Wang, Y.X., Barrón, D., and Barbosa, J. (2012). Multi residue determination of the penicillins regulated by the European Union, in bovine, porcine and chicken muscle, by LC-MS/MS. *Food chemistry*, 135, 2612–21.
- Madsen, H.T., Søggaard, E.G., and Muff, J. (2015). Reduction in energy consumption of electrochemical pesticide degradation through combination with membrane filtration. *Chemical Engineering Journal*, 276, 358–364.
- Mahgoub, H. and Ahmed, F. (1998). UV-spectrophotometric determination of ampicillin sodium and sulbactam sodium in two-component mixtures. *Journal of Pharmaceutical and Biomedical Analysis*, 17, 1273–1278.
- Makgae, M.E., Klink, M.J., and Crouch, A. M. (2008). Performance of sol-gel Titanium Mixed Metal Oxide electrodes for electro-catalytic oxidation of phenol. *Applied Catalysis B: Environmental*, 84, 659–666.

- Mandal, S. and Natarajan, S. (2015). Adsorption and catalytic degradation of organic dyes in water using ZnO/Zn<sub>x</sub>Fe<sub>3-x</sub>O<sub>4</sub> mixed oxides. *Journal of Environmental Chemical Engineering*, 3, 1185–1193.
- Mansour, D., Fourcade, F., Soutrel, I., Hauchard, D., Bellakhal, N., and Amrane, A. (2015). Mineralization of synthetic and industrial pharmaceutical effluent containing trimethoprim by combining electro-Fenton and activated sludge treatment. *Journal of the Taiwan Institute of Chemical Engineers*, 000, 1–10.
- Meffe, R. and De Bustamante, I. (2014). Emerging organic contaminants in surface water and groundwater: a first overview of the situation in Italy. *The Science of the total environment*, 481, 280–95.
- Michalska, K., Pajchel, G., and Tyski, S. (2004). Capillary electrophoresis method for simultaneous determination of penicillin G, procaine and dihydrostreptomycin in veterinary drugs. *Journal of Chromatography B*, 800, 203–209.
- Millar, J A, K. A. McLean, D.J.S. and J.L.R. (1983). The Effect of the Calcium Antagonist Nifedipine on Pressor and Aldosterone Responses to Angiotensin II in Normal Man. *Eur J. Clin. Pharmacol*, 24, 315–321.
- Misra, N.N., Pankaj, S.K., Walsh, T., Regan, F.O., Bourke, P., and Cullen, P.J. (2014). In-package nonthermal plasma degradation of pesticides on fresh produce. *Journal of Hazardous Materials*, 271, 33–40.
- Mitchell, S.M., Ullman, J.L., Teel, A.L., Watts, R.J., and Frear, C. (2013). The effects of the antibiotics ampicillin, florfenicol, sulfamethazine, and tylosin on biogas production and their degradation efficiency during anaerobic digestion. *Bioresource technology*, 149, 244–52.
- Moats, W.A. (1990). Determination of penicillin G in milk by high-performance liquid chromatography with automated liquid chromatographic cleanup. *Journal of Chromatography*, 50, 177–185.
- Mohamed, G.G. (2001). Spectrophotometric determination of ampicillin , dicloxacin , flucloxacillin and amoxicillin antibiotic drugs : ion-pair formation with molybdenum and thiocyanate. *Journal of Pharmaceutical and Biomedical Analysis*, 24, 561–567.

- Moreira, F.C., Garcia-segura, S., Boaventura, R.A.R., Brillas, E., and Vilar, V.J.P. (2014). Applied Catalysis B: Environmental Degradation of the antibiotic trimethoprim by electrochemical advanced oxidation processes using a carbon-PTFE air-diffusion cathode and a boron-doped diamond or platinum anode. *Applied Catalysis B, Environmental*, 160-161, 492–505.
- Moreno-González, R., Campillo, J. A, García, V., and León, V.M. (2013). Seasonal input of regulated and emerging organic pollutants through surface watercourses to a Mediterranean coastal lagoon. *Chemosphere*, 92, 247–57.
- Mumjitha, M. and Raj, V. (2015). Electrochemical synthesis, structural features and photoelectrocatalytic activity of TiO<sub>2</sub>-SiO<sub>2</sub> ceramic coatings on dye degradation. *Materials Science and Engineering: B*, 198, 62–73.
- Muskal, N. and Mandler, D. (2000). The Electrochemistry of Thiol Self-Assembled Monolayers ( SAMs ) on a Hanging Mercury Drop Electrode ( HMDE ). *www.currentseparation.com*, 2, 49–54.
- Muthulingam, S., Lee, I., and Uthirakumar, P. (2015). Journal of Colloid and Interface Science Highly efficient degradation of dyes by carbon quantum dots / N-doped zinc oxide ( CQD / N-ZnO ) photocatalyst and its compatibility on three different commercial dyes under daylight. *Journal of Colloid And Interface Science*, 455, 101–109.
- Naguib, I. a. and Abdelrahman, M.M. (2014). Stability indicating HPTLC method for determination of Metopimazine in pharmaceutical formulation and human plasma. *Beni-Suef University Journal of Basic and Applied Sciences*, 3, 52–62.
- Nascimento, D.S., Insausti, M., Band, B.S.F., and Lemos, S.G. (2014). Simultaneous determination of Cu, Pb, Cd, Ni, Co and Zn in bioethanol fuel by adsorptive stripping voltammetry and multivariate linear regression. *Fuel*, 137, 172–178.
- Ni, Y., Qiu, P., and Kokot, S. (2004a). Simultaneous determination of three organophosphorus pesticides by differential pulse stripping voltammetry and chemometrics. *Analytica Chimica Acta*, 516, 7–17.
- Ni, Y., Qiu, P., and Kokot, S. (2004b). Study of the voltammetric behaviour of maleic hydrazide and its determination at a hanging mercury drop electrode. *Talanta*, 63, 561–5.

- Niksa, M.J. and E.J.R. (2009). Precious metal containing mixed metal oxide (MMO) electrodes have revolutionized the electrochemical industries, especially electroplating and chlorine generation. MMO electrodes have also enabled the development of other electrochemical processes by impr.
- Niopas, I. and Daftsios, A. C. (2003). Determination of nifedipine in human plasma by solid-phase extraction and high-performance liquid chromatography: validation and application to pharmacokinetic studies. *Journal of Pharmaceutical and Biomedical Analysis*, 6, 1213-1218
- Obendorf, D. and Stubauer, G. (1995). Adsorptive stripping voltammetry of nifedipine at a HMDE ; determination of trace levels nifedipine in blood and urine. *Journal of Pharmaceutical and Biomedical Analysis*, 13, 1339–1348.
- Oliveira, R.T.S., Salazar-Banda, G.R., Santos, M.C., Calegari, M. L., Miwa, D.W., Machado, S. A. S., and Avaca, L. A. (2007). Electrochemical oxidation of benzene on boron-doped diamond electrodes. *Chemosphere*, 66, 2152–8.
- Orbeci, C., Untea, I., Nechifor, G., Segneanu, A.E., and Craciun, M.E. (2014). Effect of a modified photo-Fenton procedure on the oxidative degradation of antibiotics in aqueous solutions. *Separation and Purification Technology*, 122, 290–296.
- Passamonti, P., Bartgcci, V., and Pucciarelli, F. (1987). Determination of captopril using adsorptive cathodic differential pulse stripping voltammetry with the hmde. *J. Electroanal. Chem.*, 230230, 99–108.
- Pei-Jen, C., Rosenfeldt, E. J., Kullman, S. W., Hinton, D. E. and Linden, K. G. (2007). Biological assessments of a mixture of endocrine disruptors at environmentally relevant concentrations in water following UV/H<sub>2</sub>O<sub>2</sub> oxidation. *Science of the Total Environment*, 376, 18–26
- Petersen, M. A, Sale, T.C., and Reardon, K.F. (2007). Electrolytic trichloroethene degradation using mixed metal oxide coated titanium mesh electrodes. *Chemosphere*, 67, 1573–81.
- Peterson, J.W., Petrasky, L.J., Seymour, M.D., Burkhart, R.S., and Schuiling, A.B. (2012). Adsorption and breakdown of penicillin antibiotic in the presence of titanium oxide nanoparticles in water. *Chemosphere*, 87, 911–7.



- Peysson, W. and Vulliet, E. (2013). Determination of 136 pharmaceuticals and hormones in sewage sludge using quick, easy, cheap, effective, rugged and safe extraction followed by analysis with liquid chromatography-time-of-flight-mass spectrometry. *Journal of chromatography. A*, 1290, 46–61.
- Pohanka, M., Band'ouchová, H., Vlčková, K., Žd'árová Karasová, J., Kuča, K., Damková, V., Pecková, L., Vitula, F., and Pikula, J. (2011). Square wave voltammetry on screen printed electrodes: comparison to ferric reducing antioxidant power in plasma from model laboratory animal (Grey Partridge) and comparison to standard antioxidants. *Journal of Applied Biomedicine*, 9, 103–109.
- Post, G.B., Cohn, P.D., and Cooper, K.R. (2012). Perfluorooctanoic acid (PFOA), an emerging drinking water contaminant: a critical review of recent literature. *Environmental research*, 116, 93–117.
- Punzi, M., Anbalagan, A., Aragão Börner, R., Svensson, B.-M., Jonstrup, M., and Mattiasson, B. (2015). Degradation of a textile azo dye using biological treatment followed by photo-Fenton oxidation: Evaluation of toxicity and microbial community structure. *Chemical Engineering Journal*, 270, 290–299.
- Quero-Pastor, M., Valenzuela, A., Quiroga, J.M., and Acevedo, A. (2014). Degradation of drugs in water with advanced oxidation processes and ozone. *Journal of environmental management*, 137, 197–203.
- Qureshi, S.Z., Qayoom, T., and Helalet, M.I. (1999). Simultaneous spectrophotometric and volumetric determinations of amoxicillin, ampicillin and cloxacillin in drug formulations: reaction mechanism in the base catalysed hydrolysis followed by oxidation with iodate in dilute acid solution. *Journal of Pharmaceutical and Biomedical Analysis*, 21, 473–482.
- Radi, A. (2003). Determination of pantoprazole by adsorptive stripping voltammetry at carbon paste electrode. *Il Farmaco*, 58, 535–539.
- Radjenovic, J., Escher, B.I., and Rabaey, K. (2011). Electrochemical degradation of the  $\beta$ -blocker metoprolol by Ti/Ru<sub>0.7</sub> Ir<sub>0.3</sub>O<sub>2</sub> and Ti/SnO<sub>2</sub>-Sb electrodes. *Water Research*, 45, 3205–14.
- Ribeiro, F.W.P., Mendonça, G.L.F., Soares, J.E.S., Freire, V.N., De Souza, D., Casciano, P.N.S., De Lima-Neto, P., and Correia, A.N. (2014). Exploiting the Reduction of Haloperidol: Electrochemical and Computational Studies Using Silver Amalgam and HMDE Electrodes. *Electrochimica Acta*, 137, 564–574.

- Rodil, R., Quintana, J.B., Concha-Graña, E., López-Mahía, P., Muniategui-Lorenzo, S., and Prada-Rodríguez, D. (2012). Emerging pollutants in sewage, surface and drinking water in Galicia (NW Spain). *Chemosphere*, 86, 1040–9.
- Rui, Z., Jingguo, W., Jianyu, C.U.I., Lin, H.U., and Kangguo, M.U. (2010). Photocatalytic degradation of pesticide residues with RE<sup>3+</sup>-doped nano-TiO<sub>2</sub>. *Journal of Rare Earths*, 28, 353–356.
- Särkkä, H., Vepsäläinen, M., Pulliainen, M., and Sillanpää, M. (2008). Electrochemical inactivation of paper mill bacteria with mixed metal oxide electrode. *Journal of hazardous materials*, 156, 208–13.
- Sartori, E.R., Medeiros, R.A., Rocha-Filho, R.C., and Fatibello-Filho, O. (2010). Square-wave voltammetric determination of propranolol and atenolol in pharmaceuticals using a boron-doped diamond electrode. *Talanta*, 81, 1418–24.
- Schaefer, C.E., Andaya, C., and Urtiaga, A. (2015). Assessment of disinfection and by-product formation during electrochemical treatment of surface water using a Ti/IrO<sub>2</sub> anode. *Chemical Engineering Journal*, 264, 411–416
- Schriks, M., Heringa, M.B., Van Der Kooi, M.M.E., De Voogt, P., and Van Wezel, A.P. (2010). Toxicological relevance of emerging contaminants for drinking water quality. *Water research*, 44, 461–76.
- Schubert, J.K., Miekisch, W., Fuchs, P., Scherzer, N., Lord, H., Pawliszyn, J., and Mundkowski, R.G. (2007). Determination of antibiotic drug concentrations in circulating human blood by means of solid phase micro-extraction. *Clinica chimica acta; international journal of clinical chemistry*, 386, 57–62.
- Scott R. Hamann, Michael T. Piascik and R. G. McAllister, J. (1986). Aspects of the clinical pharmacology of nifedipine, a dihydropyridine calcium-entry antagonist. *Biopharmaceutics & drug disposition*, 7, 1–10.
- Senturk, Z. A, S.A. Ozkan, Y.O. (1998). Electroanalytical study of nifedipine using activated glassy. *Journal of Pharmaceutical and Biomedical Analysis*, 16, 801–807.
- Šelešovská, R., Bandžuchová, L., Navrátil, T., and Chýlková, J. (2012). Voltammetric determination of leucovorin using silver solid amalgam electrode. *Electrochimica Acta*, 60, 375–383.

- Shaalán, R. A., Belal, T.S., El Yazbi, F. A., and Elonsy, S.M. (2014). Validated HPTLC methods for determination of some selected antihypertensive mixtures in their combined dosage forms. *Bulletin of Faculty of Pharmacy, Cairo University*, 52, 225–237.
- Shah, D. A., Patel, D. V., Mehta, F. A., Chhalotiya, U.K., and Bhatt, K.K. (2014). Development of stability indicating HPTLC Method for the Estimation of Irbesartan and Amlodipine besylate in combination. *Journal of Taibah University for Science*, 2, 177-186.
- Siangproh, W., Ngamukot, P., and Chailapakul, O. (2003). Electrochemical determination of captopril at boron-doped diamond thin film electrode applied to a flow injection system. *Sensors and Actuators B: Chemical*, 91, 60–66.
- Silva, M., Azenha, M.E., Pereira, M.M., Burrows, H.D., Sarakha, M., Forano, C., Ribeiro, M.F., and Fernandes, A. (2010). Applied Catalysis B: Environmental Immobilization of halogenated porphyrins and their copper complexes in MCM-41: Environmentally friendly photocatalysts for the degradation of pesticides. *Applied Catalysis B, Environmental*, 100, 1–9.
- Sivagami, K., Krishna, R.R., and Swaminathan, T. (2014). Photo catalytic degradation of pesticides in immobilized bead photo reactor under solar irradiation. *Solar Energy*, 103, 488–493.
- Sopaj, F., Rodrigo, M. A., Oturan, N., Podvorica, F.I., Pinson, J., and Oturan, M. A. (2015). Influence of the anode materials on the electrochemical oxidation efficiency. Application to oxidative degradation of the pharmaceutical amoxicillin. *Chemical Engineering Journal*, 262, 286–294.
- Sørensen, L.K., Snor, L.K., Elkær, T., and Hansen, H. (1999). Simultaneous determination of seven penicillins in muscle, liver and kidney tissues from cattle and pigs by a multiresidue high-performance liquid chromatographic method. *Journal of Chromatography B*, 734, 307–318.
- Souza, C.D., Braga, O.C., Vieira, I.C., and Spinelli, A. (2008). Electroanalytical determination of sulfadiazine and sulfamethoxazole in pharmaceuticals using a boron-doped diamond electrode. *Sensors and Actuators B: Chemical*, 135, 66–73.
- Steter, J.R., Barros, W.R.P., Lanza, M.R. V, and Motheo, A.J. (2014). Electrochemical and sonoelectrochemical processes applied to amaranth dye degradation. *Chemosphere*, 117, 200–7.

- Sun, H., Yang, H., Huang, W., and Zhang, S. (2015). Immobilization of laccase in a sponge-like hydrogel for enhanced durability in enzymatic degradation of dye pollutants. *Journal of Colloid and Interface Science*, 450, 353–360.
- Svorc, L., Sochr, J., Rievaj, M., Tomčík, P., and Bustin, D. (2012). Voltammetric determination of penicillin V in pharmaceutical formulations and human urine using a boron-doped diamond electrode. *Bioelectrochemistry (Amsterdam, Netherlands)*, 88, 36–41.
- Švorc, L., Cinková, K., Sochr, J., Vojs, M., Michniak, P., and Marton, M. (2014). Sensitive electrochemical determination of amlodipine in pharmaceutical tablets and human urine using a boron-doped diamond electrode. *Journal of Electroanalytical Chemistry*, 728, 86–93.
- Švorc, L., Sochr, J., Tomčík, P., Rievaj, M., and Bustin, D. (2012). Simultaneous determination of paracetamol and penicillin V by square-wave voltammetry at a bare boron-doped diamond electrode. *Electrochimica Acta*, 68, 227–234.
- Švorc, L., Sochr, J., Svítková, J., Rievaj, M., and Bustin, D. (2013). Rapid and sensitive electrochemical determination of codeine in pharmaceutical formulations and human urine using a boron-doped diamond film electrode. *Electrochimica Acta*, 87, 503–510.
- Tajik, S., Taher, M.A., and Beitollahi, H. (2013). Simultaneous determination of droxidopa and carbidopa using a carbon nanotubes paste electrode. *Sensors and Actuators B: Chemical*, 188, 923–930.
- Tantis, I., Bousiakou, L., Frontistis, Z., Mantzavinos, D., Konstantinou, I., Antonopoulou, M., Karikas, G., and Lianos, P. (2015). Photocatalytic and photoelectrocatalytic degradation of the drug omeprazole on nanocrystalline titania films in alkaline media: Effect of applied electrical bias on degradation and transformation products. *Journal of Hazardous Materials*, 294, 57–63.
- Terada, H. and Sakabe, Y. (1985). Simultaneous determination of penicillin G, penicillin V and ampicillin in milk by high-performance. *Journal of Chromatography*, 348, 319–387.
- Ternes, T., (1998). Occurrence of drugs in German sewage treatment plants and rivers. *Water Research*, 32, 3245–3260

- Thomas, A., Ukpoma, O.K., Inman, J. A, Kaul, A.K., Beeson, J.H., and Roberts, K.P. (2008). Quantification of penicillin G during labor and delivery by capillary electrophoresis. *Journal of biochemical and biophysical methods*, 70, 992–8.
- Trindade, J.M., Martiniano, L.C., Gonçalves, V.R. a., Souza, A.G., Marques, A.L.B., Baugis, G.L., Fonseca, T.C.O., Song, C., Zhang, J., and Marques, E.P. (2012). Anodic stripping voltammetry coupled with design of experiments for simultaneous determination of  $Zn^{+2}$ ,  $Cu^{+2}$ ,  $Pb^{+2}$ , and  $Cd^{+2}$  in gasoline. *Fuel*, 91, 26–32.
- Tucker, F.A. (1985). Note Study of nifedipine photodecomposition capillary gas-liquid chromatography in plasma. *Journal of Chromatography*, 342, 193–198.
- Tyszczyk-Rotko, K., Bęczkowska, I., and Nosal-Wiercińska, A. (2014a). Simple, selective and sensitive voltammetric method for the determination of herbicide (paraquat) using a bare boron-doped diamond electrode. *Diamond and Related Materials*, 50, 86–90.
- Tyszczyk-Rotko, K., Bęczkowska, I., Wójciak-Kosior, M., and Sowa, I. (2014b). Simultaneous voltammetric determination of paracetamol and ascorbic acid using a boron-doped diamond electrode modified with Nafion and lead films. *Talanta*, 129, 384–91.
- Urrutia, C., Rubilar, O., Tortella, G.R., and Diez, M.C. (2013). Chemosphere Degradation of pesticide mixture on modified matrix of a biopurification system with alternatives lignocellulosic wastes. *Chemosphere*, 92, 1361–1366.
- Uslu, B., Topal, B.D., and Ozkan, S. A. (2008). Electroanalytical investigation and determination of pefloxacin in pharmaceuticals and serum at boron-doped diamond and glassy carbon electrodes. *Talanta*, 74, 1191–200.
- Vasiliadou, I. A, Molina, R., Martínez, F., and Melero, J. A. (2014). Experimental and modeling study on removal of pharmaceutically active compounds in rotating biological contactors. *Journal of hazardous materials*, 274, 473–82.
- Vasiliadou, I. A., Molina, R., Martínez, F., and Melero, J. A. (2013). Biological removal of pharmaceutical and personal care products by a mixed microbial culture: Sorption, desorption and biodegradation. *Biochemical Engineering Journal*, 81, 108–119.

- Veitonmäki, T., Tammela, T.L.J., Auvinen, A., and Murtola, T.J. (2013). Use of aspirin, but not other non-steroidal anti-inflammatory drugs is associated with decreased prostate cancer risk at the population level. *European journal of cancer (Oxford, England : 1990)*, 49, 938–45.
- Villabona-leal, E.G., López-neira, J.P., Pedraza-avella, J.A., Pérez, E., and Meza, O. (2015). Screening of factors influencing the photocatalytic activity of  $\text{TiO}_2 : \text{Ln}$  (Ln =La, Ce, Pr, Nd, Sm, Eu and Gd) in the degradation of dyes. *Computational Materials Science*, 107, 48–53.
- Waller, D.G., Renwick, A.G., Gruchy, B.S., and George, C.F. (1984). The first pass metabolism of nifedipine in man D. *Br. J. clin. Pharmac.*, 18, 951–954.
- Wang, J. (2006). Analytical Electrochemistry. 3<sup>rd</sup> Edition. A. John Wiley & Sons INC. Publication. New Jersey.
- Wang, Q., Vasilescu, A., Subramanian, P., Vezeanu, A., Andrei, V., Coffinier, Y., Li, M., Boukherroub, R., and Szunerits, S. (2013). Simultaneous electrochemical detection of tryptophan and tyrosine using boron-doped diamond and diamond nanowire electrodes. *Electrochemistry Communications*, 35, 84–87.
- Wang, W., Wu, Q., Wang, Z., Hu, H., and Negishi, N. (2015). Chemosphere Photocatalytic degradation of the antiviral drug Tamiflu by UV-A/ $\text{TiO}_2$ : Kinetics and mechanisms. *Chemosphere*, 131, 41–47.
- Wang, Y.H., Chan, K.Y., Li, X.Y., and So, S.K. (2006). Electrochemical degradation of 4-chlorophenol at nickel-antimony doped tin oxide electrode. *Chemosphere*, 65, 1087–93.
- White, W.B., Turner, J.R., Sica, D., Bisognano, J.D., Calhoun, D. A., Townsend, R.R., Aronow, H.D., Bhatt, D.L., and Bakris, G.L. (2014). Detection, Evaluation, and Treatment of Severe and Resistant Hypertension Proceedings from an American Society of Hypertension Interactive Forum held in Bethesda, Maryland, USA, October 10<sup>th</sup> 2013. *Journal of the American Society of Hypertension*, 8, 743–757.
- Winchester, L.C., Podany, A.T., Baldwin, J.S., Robbins, B.L., and Fletcher, C. V. (2014). Determination of the Rifamycin Antibiotics Rifabutin, Rifampin, Rifapentine and their Major Metabolites in Human Plasma via Simultaneous Extraction Coupled with LC/MS/MS. *Journal of Pharmaceutical and Biomedical Analysis*, 104, 55-61.

- Wu, W., Huang, Z. H., and Lim, T. T. (2014). Recent development of mixed metal oxide anodes for electrochemical oxidation of organic pollutants in water. *Applied Catalysis A: General*, 480, 58–78.
- Xiao, Y., Wang, H.Y., and Han, J. (2005). Simultaneous determination of carvedilol and ampicillin sodium by synchronous fluorimetry. *Spectrochimica acta. Part A, Molecular and biomolecular spectroscopy*, 61, 567–73.
- Yang, X., Zou, R., Huo, F., Cai, D., and Xiao, D. (2009). Preparation and characterization of Ti/SnO<sub>2</sub>-Sb<sub>2</sub>O<sub>3</sub>-Nb<sub>2</sub>O<sub>5</sub>/PbO<sub>2</sub> thin film as electrode material for the degradation of phenol. *Journal of hazardous materials*, 164, 367–73.
- Yardimci, C. and Su, I. (2002). Determination of nifedipine in human plasma by square wave adsorptive stripping voltammetry. *Journal of Pharmaceutical and Biomedical Analysis*, 30, 573–582.
- Yokoyama, Y., Tomatsuri, M., Hayashi, H., Hirai, K., Ono, Y., Yamada, Y., Todoroki, K., Toyo'oka, T., Yamada, H., and Itoh, K. (2014). Simultaneous microdetermination of bosentan, ambrisentan, sildenafil, and tadalafil in plasma using liquid chromatography/tandem mass spectrometry for pediatric patients with pulmonary arterial hypertension. *Journal of pharmaceutical and biomedical analysis*, 89, 227–32.
- Zanoni, M.V.B., Fogg, A.G., Barek, J., and Zima, J. (1997). Electrochemical investigations of reactive dyes ; cathodic stripping voltammetric determination of anthraquinone-based chlorotriazine dyes at a hanging mercury drop electrode. *Analytica Chimica Acta*, 349, 101-109
- Zapardibl, A. (1993). Voltammetric studies of a psychotropic drug with nitro groups . determination of flunitrazepam in urine using HMDE. *Talanta*, 40, 1649–1656.
- Zayed, S.I.M. and Habib, I.H.I. (2005). Adsorptive stripping voltammetric determination of triprolidine hydrochloride in pharmaceutical tablets. *Farmaco (Società chimica italiana : 1989)*, 60, 621–5.
- Zayed, S.I.M. and Issa, Y.M. (2009). Cathodic adsorptive stripping voltammetry of drotaverine hydrochloride and its determination in tablets and human urine by differential pulse voltammetry. *Bioelectrochemistry (Amsterdam, Netherlands)*, 75, 9–12.

- Zendelovska, D., Simeska, S., Sibinovska, O., Kostova, E., Miloševska, K., Jakovski, K., Jovanovska, E., Kikerkov, I., Trojačanec, J., Zafirov, D. (2006). Development of an HPLC method for the determination of nifedipine in human plasma by solid-phase extraction. *Journal of Chromatography B* 1-2, 85-88
- Zhang, C., Liu, L., Wang, J., Rong, F., and Fu, D. (2013a). Electrochemical degradation of ethidium bromide using boron-doped diamond electrode. *Separation and Purification Technology*, 107, 91–101.
- Zhang, H., Zhang, P., Ji, Y., Tian, J., and Du, Z. (2015). Photocatalytic degradation of four non-steroidal anti-inflammatory drugs in water under visible light by P25-TiO<sub>2</sub>/tetraethyl orthosilicate film and determination via ultra performance liquid chromatography electrospray tandem mass spectrometry. *Chemical Engineering Journal*, 262, 1108–1115.
- Zhang, X.-H., Wang, S.-F., and Sun, N.-J. (2004). Direct determination of brucine by square wave voltammetry on 4-amino-2-mercaptopyrimidine self-assembled monolayer gold electrode. *Bioelectrochemistry (Amsterdam, Netherlands)*, 65, 41–6.
- Zhang, Y., Yang, N., Murugananthan, M., and Yoshihara, S. (2013b). Electrochemical degradation of PNP at boron-doped diamond and platinum electrodes. *Journal of hazardous materials*, 244-245, 295–302.
- Zhang, Y.-H., Xu, D., Liu, J.-Q., and Zhao, X.-H. (2014). Enhanced degradation of five organophosphorus pesticides in skimmed milk by lactic acid bacteria and its potential relationship with phosphatase production. *Food chemistry*, 164, 173–8.
- Zhong, Y.S., Ni, Y.N., and Kokot, S. (2012). Application of differential pulse stripping voltammetry and chemometrics for the determination of three antibiotic drugs in food samples. *Chinese Chemical Letters*, 23, 339–342.
- Zhou, M., Särkkä, H., and Sillanpää, M. (2011). A comparative experimental study on methyl orange degradation by electrochemical oxidation on BDD and MMO electrodes. *Separation and Purification Technology*, 78, 290–297.
- Zhu, Y., Moreno, M.L., Porqueras, E., Bourke, E., Bruzzi, A., Aletrari, M., Kanari, P., Partasidou, D., Nienhuis, J., Ferigo, W., Robert, J.L., and Miuer, J.H.M. (1996). Interlaboratory study of the analysis of ampicillin by liquid chromatography. *Journal of Pharmaceutical and Biomedical Analysis*, 14, 1151–1156.