



Analytical study on certain leached components from plastic and metallic packages

A Thesis

Presented for the partial fulfillment of
Master Degree in Pharmaceutical Sciences
(Pharmaceutical Analytical Chemistry)

By

Ola Moataz Ahmed Mohamed

B.Sc. in Pharmaceutical Sciences 2013

Department of Pharmaceutical Analytical Chemistry

Faculty of Pharmacy

Ain Shams University

Under Supervision of

Prof. Dr. Amira Mabrouk El-Kosasy

Professor of Pharmaceutical Analytical Chemistry

Faculty of Pharmacy, Ain Shams University

The Late Associate Prof. Dr. Omar Abd El-Aziz Ghonim

Associate Professor of Pharmaceutical Analytical Chemistry

Faculty of Pharmacy, Ain Shams University

Associate Prof. Dr. Miriam Farid Ayad

Associate Professor of Pharmaceutical Analytical Chemistry

Faculty of Pharmacy, Ain Shams University

Pharmaceutical Analytical Chemistry Department

Faculty of Pharmacy - Ain Shams University

2018

Approval Sheet

**Title of the Master Degree Thesis in Pharmaceutical Sciences
(Pharmaceutical Analytical Chemistry)**

**Analytical study on certain leached components
from plastic and metallic packages**

Name of the candidate :

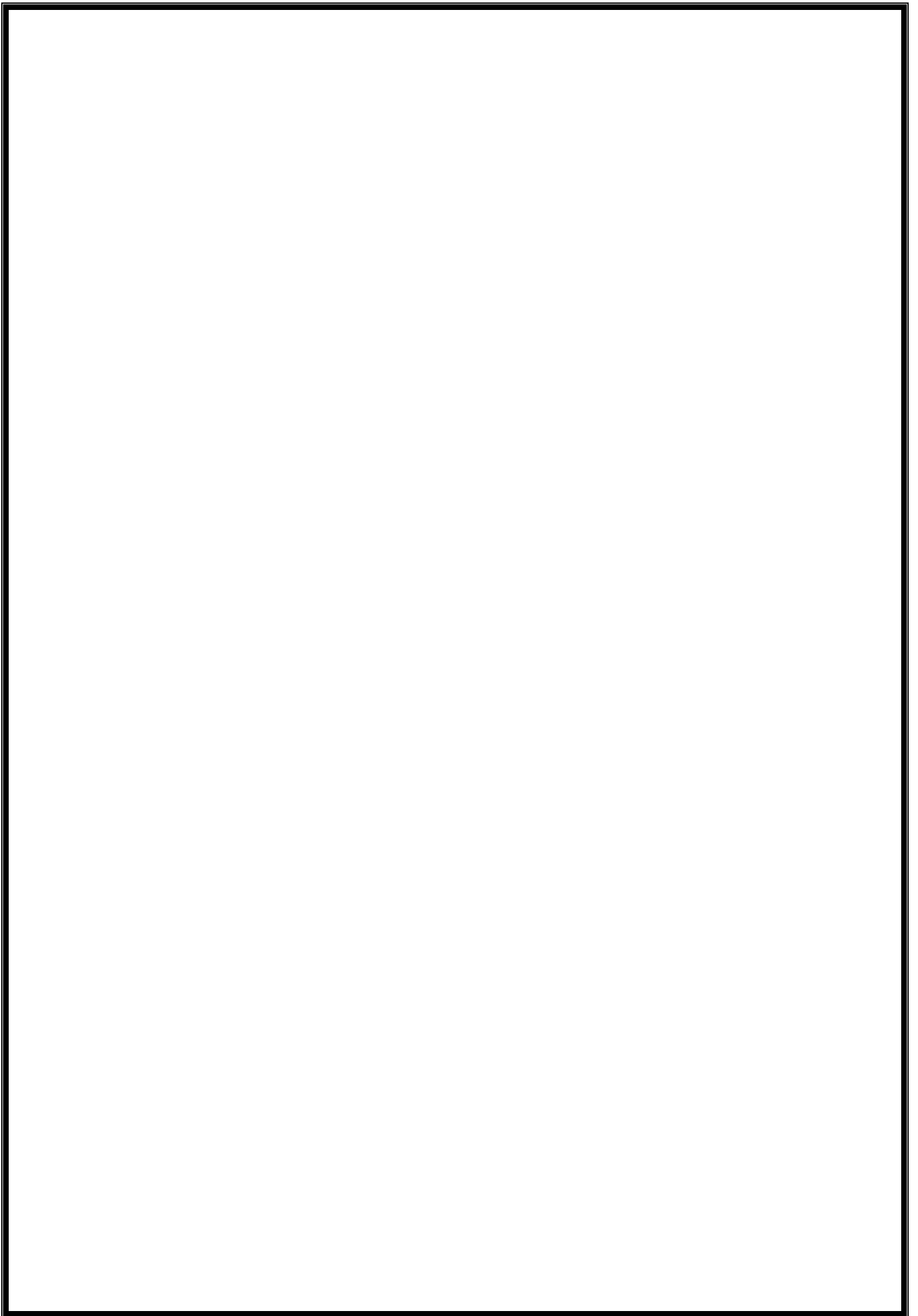
Ola Moataz Ahmed Mohamed

Submitted to:

Department of Pharmaceutical Analytical Chemistry, Faculty of Pharmacy,
Ain Shams University, 2018

Committee in Charge:

- 1. Prof. Dr. Fathallah Fathallah Belal.....**
Professor of Pharmaceutical Analytical Chemistry, Faculty of Pharmacy,
Mansoura University.
- 2. Prof. Dr. Mohie Mohammed Khaled Sharaf El Din.....**
Professor of Pharmaceutical Analytical Chemistry, Faculty of Pharmacy,
Mansoura University.
- 3. Prof. Dr. Amira Mabrouk El-Kosasy.....**
Professor of Pharmaceutical Analytical Chemistry, Faculty of Pharmacy,
Ain Shams University.
- 4. Associate Prof. Dr. Miriam Farid Ayad.....**
Associate Professor of Pharmaceutical Analytical Chemistry, Faculty of
Pharmacy, Ain Shams University.



ACKNOWLEDGEMENTS

*All thanks and gratitude to **Allah** for giving me the strength to finish this thesis and for guiding and supporting me throughout my life.*

*I would like to express my sincere gratitude and deep appreciation to my thesis advisor **Prof. Dr. Amira Mabrouk El-Kosasy**, Professor of Pharmaceutical Analytical Chemistry, Faculty of Pharmacy, Ain Shams University for her valuable scientific guidance, patience, continuous support and encouragement during the whole time of my work.*

*I would like to offer special thanks to **Dr. Omar Abd El-Aziz Ali Ghonim**, Associate Professor of Pharmaceutical Analytical Chemistry, Faculty of Pharmacy, Ain Shams University, who, although no longer with us, continues to inspire by his example and dedication to the students he served over the course of his career.*

*My profound thanks to **Dr. Miriam Farid Ayad**, Associate Professor of Pharmaceutical Analytical Chemistry, Faculty of Pharmacy, Ain Shams University for being my source of motivation, and for her close and continuous supervision. The door to her office was always open whenever I ran into a trouble spot or had a question about my research or writing.*

*I am deeply indebted to **Dr. Hassan Hendawy**, Associate Professor of Pharmaceutical Analytical Chemistry, National Organization for Drug Control and Research (NODCAR) for his effort, time and patience. He taught me a lot and guided me throughout the whole work. His selfless time and care were sometimes all that kept me going.*

I also wish to thank all my colleagues in the Department of Pharmaceutical Analytical Chemistry for their untiring help and friendly cooperation.

To my mother, father, my sister Raghda and my brother Ahmed, my beloved husband Marwan without your passionate support and help I could not have conducted this work successfully.

Thank you very much, everyone!

Ola Moataz

Table of Contents

Table of Contents.....	i
List of figures	ix
List of tables	xvii
Preface	xxiii
Summary	xxv
Part I: General Introduction	1
I.1. Food Contact Materials	2
I.2. Classification of possible leaching components from food contact materials (FCMs)	4
I.3. Migrants under analytical investigation in this thesis.....	9
I.3.1. The role of these migrants in food packaging manufacture.....	9
I.3.2. Potential health hazards associated with exposure to these migrants from food packaging materials	10
I.3.3. Global legislation and limits for these migrants	11
Part II: Literature review.....	13
II.1.The Studied Compounds	14
II.1.A. Bisphenol A (BPA)	14
II.1.A.1. Chemical properties	14
II.1.A.2. Physical Properties.....	14
II.1.B. Bisphenol-A-diglycidyl ether (BADGE)	15
II.1.B.1. Chemical Properties	15

II.1.B.2. Physical Properties.....	15
II.1.C. Bisphenol-A bis (3-chloro-2-hydroxypropyl) ether (BADGE·2HCl)	16
II.1.C.1. Chemical Properties	16
II.1.C.2. Physical Properties	16
II.1.D. Bisphenol-A-(2,3-dihydroxypropyl) glycidyl ether (BADGE·H ₂ O).....	17
II.1.D.1. Chemical Properties	17
II.1.D.2. Physical Properties	17
II.1.E. Bisphenol-A-(3-chloro-2-hydroxypropyl)(2,3- dihydroxypropyl) ether (BADGE·HCl·H ₂ O)	18
II.1.E.1. Chemical Properties	18
II.1.E.2. Physical Properties.....	18
II.2. Methods of Analysis	19
II.2.1. Methods of Analysis of Bisphenol A.....	19
II.2.2. Methods of Analysis of Bisphenol -A- diglycidyl ether and its reaction products.....	69
Part III: Novel carbonaceous and carbon nanotubes-based electrodes for determination of Bisphenol A in bottled water and canned food samples using differential pulse voltammetry	79
III.1. Introduction.....	80
III.2. Experimental	83
III.3. Results and Discussion.....	92

III.4. Conclusion	101
Part IV: Chemometrics-assisted methods for simultaneous determination of Bisphenol -A- diglycidyl ether and its reaction products	127
Section A: Chemometrics-assisted simultaneous voltammetric determination of Bisphenol -A- diglycidyl ether and its reaction products in bottled water and canned food samples	128
IV.A.1. Introduction	129
IV.A.2. Experimental.....	131
IV.A.3. Results and Discussion	135
IV.A.4. Conclusion.....	142
Section B: Chemometrics-assisted spectrophotometric methods for simultaneous determination of Bisphenol -A- diglycidyl ether and its reaction products in canned food samples	169
IV.B.1. Introduction	170
IV.B.2. Experimental.....	172
IV.B.3. Results and Discussion	175
IV.B.4. Conclusion.....	179

Part V: High-performance liquid chromatographic method for simultaneous determination of Bisphenol-A-diglycidyl ether and some of its reaction products in canned foods using photodiode array detector.....	196
V.1. Introduction	197
V.2. Experimental.....	198
V.3. Results and Discussion	207
V.4. Conclusion.....	213
Part VI: General Discussion.....	235
References	253
ملخص الرسالة.....	أ

List of Abbreviations

ANOVA	Analysis of variance
APCI	Atmospheric pressure chemical ionization
AuNPs	Gold nanoparticles
β-CDP	β-cyclodextrin polymer
BADGE	Bisphenol -A- diglycidyl ether
BADGE·2HCl	Bisphenol A bis(3-chloro-2-hydroxypropyl)ether
BADGE·H₂O	Bisphenol-A-(2,3-dihydroxypropyl) glycidyl ether
BADGE·HCl·H₂O	Bisphenol-A-(3-chloro-2-hydroxypropyl) (2,3-dihydroxypropyl)ether
BFDGE	Bisphenol-F-diglycidyl ether
BP	Biphenol
BPA	Bisphenol A
BPAF	Bisphenol AF
BPAP	Bisphenol AP
BPB	Bisphenol B
BPE	Bisphenol E
BPF	Bisphenol F
BPP	Bisphenol P

BPS	Bisphenol S
BPZ	Bisphenol Z
B-R buffer	Britton-Robinson buffer
CC	Chronocoulometry
C-dots	Carbon dots
CE	Capillary electrophoresis
CL	Chemiluminescence
CPE	Carbon paste electrode
CV	Cyclic voltammetry
CZE	Capillary zone electrophoresis
DAD	Diode array detection
DPV	Differential pulse voltammetry
ECL	Electrochemiluminescence
EDC	Endocrine disruptor chemical
EI	Electron ionization
ESI	Electrospray ionization
EU	European Union
FCMs	Food contact materials
FI-CL	Flow injection Chemiluminescence method
GC	Gas chromatography
GCE	Glassy carbon electrode

HPLC	High-performance liquid chromatography
HRP	Horseradish peroxidase enzyme
ICH	International Conference on Harmonization
IUPAC	International Union of Pure and Applied Chemistry
LC	Liquid chromatography
LOD	Limit of detection
LOQ	Limit of quantitation
LVs	Latent variables
MEKC	Micellar electrokinetic chromatography
MIF	Molecular imprinted film
MIP	Molecular imprinted polymer
MS	Mass spectrometry
MS/MS	Tandem mass spectrometry
MWCNTs	Mutli-walled carbon nanotubes
NA	Not Available
p=0.05	The probability of results in 95%
PCR	Principal component regression
PDA	Photodiode array
PGE	Pencil graphite electrode
PLS	Partial least squares

R%	Recovery percent
r	Correlation coefficient
RSD	Relative standard deviation
% RSD	Percentage relative standard deviation
SCF	Scientific Committee on Food
SD	Standard deviation
SMLs	Specific migration limits
SWCNTs	Single-walled carbon nanotubes
SWV	Square wave voltammetry
TBBPA	Tetrabromobisphenol A
TCBPA	Tetrachlorobisphenol A
TD-GC-MS	Thermal desorption gas chromatography mass spectrometry
t-test	Student “t” test
UHPLC	Ultra high-performance liquid chromatography
UPLC	Ultra performance liquid chromatography
UV	Ultraviolet

List of figures

Figure [1]: SEM images of (a) Carbon paste electrode (CPE), (b) Disposable pencil graphite electrode (PGE), (c) Single-walled carbon nanotube (SWCNTs) and (d) Multi-walled carbon nanotubes (MWCNTs).	102
Figure [2]: Cyclic voltammogram of $60.877 \mu\text{g mL}^{-1}$ BPA at pH=7 using CPE with scan rate= 100 mV s^{-1} , anodic peak at 666 mV.....	103
Figure [3]: Cyclic voltammogram of $0.35 \mu\text{g mL}^{-1}$ BPA at pH=7 using PGE with scan rate= 100 mV s^{-1} , anodic peak at 607 mV.....	103
Figure [4]: Cyclic voltammogram of $3.9 \mu\text{g mL}^{-1}$ BPA at pH=7 using SWCNTs with scan rate= 100 mV s^{-1} , anodic peak at 617 mV.....	104
Figure [5]: Cyclic voltammogram of $3.9 \mu\text{g mL}^{-1}$ BPA at pH=7 using MWCNTs with scan rate= 100 mV s^{-1} , anodic peak at 620 mV.....	104
Figure [6]: The effect of pH on the peak current (I_{pa}) and peak potential (E_{pa}) of BPA at CPE using DPV.	105
Figure [7]: The effect of pH on the peak current (I_{pa}) and peak potential (E_{pa}) of BPA at PGE using DPV.	105
Figure [8]: The effect of pH on the peak current (I_{pa}) and peak potential (E_{pa}) of BPA at SWCNTs using DPV.	106
Figure [9]: The effect of pH on the peak current (I_{pa}) and peak potential (E_{pa}) of BPA at MWCNTs using DPV.	106
Figure [10]: Relation between I_{pa} (μA) and $v^{1/2}$ for oxidation of BPA at CPE.....	107
Figure [11]: Relation between I_{pa} (μA) and $v^{1/2}$ for oxidation of BPA at PGE.....	107
Figure [12]: Relation between I_{pa} (μA) and $v^{1/2}$ for oxidation of BPA at SWCNTs.	108

Figure [13]: Relation between I_{pa} (μA) and $v^{1/2}$ for oxidation of BPA at MWCNTs.	108
Figure [14]: Relation between $\log I_{pa}$ (μA) and $\log v$ ($mV s^{-1}$) for oxidation of BPA at CPE.	109
Figure [15]: Relation between $\log I_{pa}$ (μA) and $\log v$ ($mV s^{-1}$) for oxidation of BPA at PGE.	109
Figure [16]: Relation between $\log I_{pa}$ (μA) and $\log v$ ($mV s^{-1}$) for oxidation of BPA at SWCNTs.	110
Figure [17]: Relation between $\log I_{pa}$ (μA) and $\log v$ ($mV s^{-1}$) for oxidation of BPA at MWCNTs.	110
Figure [18]: Relation between E_{pa} (V) and $\ln v$ for oxidation of BPA at CPE.	111
Figure [19]: Relation between E_{pa} (V) and $\ln v$ for oxidation of BPA at PGE.	111
Figure [20]: Relation between E_{pa} (V) and $\ln v$ for oxidation of BPA at SWCNTs.	112
Figure [21]: Relation between E_{pa} (V) and $\ln v$ for oxidation of BPA at MWCNTs.	112
Figure [22]: The proposed oxidation mechanism of BPA at the developed electrodes.	113
Figure [23]: DPV voltammograms of BPA over concentration range from 1.81 to 6.43 $\mu g mL^{-1}$ (pH=7), peak at 505 mV at CPE.	114
Figure [24]: DPV voltammograms of BPA over concentration range from 0.18 to 0.94 $\mu g mL^{-1}$ (pH=7), peak at 554 mV at PGE.	114
Figure [25]: DPV voltammograms of BPA over concentration range from 2.03 to 4.91 $\mu g mL^{-1}$ (pH=7), peak at 520 mV at SWCNTs in 15 mL buffer solution.	115

Figure [26]: DPV voltammograms of BPA over concentration range from 0.91 to 4.91 $\mu\text{g mL}^{-1}$ (pH=7), peak at 530 mV at MWCNTs in 15 mL buffer solution.	115
Figure [27]: Calibration curve of BPA (1.81-6.43 $\mu\text{g mL}^{-1}$), pH=7 using DPV at CPE.	116
Figure [28]: Calibration curve of BPA (0.18-0.94 $\mu\text{g mL}^{-1}$), pH=7 using DPV at disposable PGE.	116
Figure [29]: Calibration curve of BPA (2.03-4.91 $\mu\text{g mL}^{-1}$) using DPV at SWCNTs in 15 mL buffer solution (pH=7).	117
Figure [30]: Calibration curve of BPA (0.91-4.91 $\mu\text{g mL}^{-1}$) using DPV at MWCNTs in 15 mL buffer solution (pH=7).	117
Figure [31]: Overlapped peaks in DPV mode of the same concentration (3.10 $\mu\text{g mL}^{-1}$) of BADGE, BADGE $\cdot$ 2HCl, BADGE $\cdot$ HCl $\cdot$ H $_2$ O and BADGE $\cdot$ H $_2$ O using PGE at pH=12.	143
Figure [32]: The effect of pH on the peak current (I_{pa}) and peak potential (E_{pa}) of BADGE at PGE using DPV.	143
Figure [33]: The effect of pH on the peak current (I_{pa}) and peak potential (E_{pa}) of BADGE $\cdot$ 2HCl at PGE using DPV.	144
Figure [34]: The effect of pH on the peak current (I_{pa}) and peak potential (E_{pa}) of BADGE $\cdot$ HCl $\cdot$ H $_2$ O at PGE using DPV.	144
Figure [35]: The effect of pH on the peak current (I_{pa}) and peak potential (E_{pa}) of BADGE $\cdot$ H $_2$ O at PGE using DPV.	145
Figure [36]: Relation between I_{pa} (μA) and $v^{1/2}$ for oxidation of BADGE at PGE.	145
Figure [37]: Relation between I_{pa} (μA) and $v^{1/2}$ for oxidation of BADGE $\cdot$ 2HCl at PGE.	146