



UNIVERSITI PUTRA MALAYSIA

***SIMULTANEOUS ELECTROCHEMICAL DETECTION OF URIC ACID,
DOPAMINE AND ASCORBIC ACID USING
POLY (3,4-ETHYLENEDIOXYTHIOPHENE)/REDUCED
GRAPHENE OXIDE/MANGANESE DIOXIDE***

NURULKHALILAH BINTI TUKIMIN

FS 2018 57



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By

NURULKHALILAH BINTI TUKIMIN

**Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in
Fulfilment of the Requirement for the Degree of Master of Science**

November 2017

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Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfilment of the requirement for the degree of Master of Science

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By

NURULKHALILAH BINTI TUKIMIN

November 2017

Chairman: Assoc. Prof. Yusran Sulaiman, PhD
Faculty: Science

The coexistence of uric acid (UA), ascorbic acid (AA) and dopamine (DA) in human body system is difficult to be measured due to their close oxidation potentials. The abnormal level of these analytes in human body would lead to various diseases. In order to solve this problems, poly(3,4-ethylenedioxythiophene)/reduced graphene oxide electrode (PrGO) and manganese dioxide deposited on PrGO (PrGO/MnO₂) composites were prepared using cyclic voltammetry for UA detection in the presence of AA and simultaneous detection of UA, AA and DA, respectively. The PrGO and PrGO/MnO₂ composites showed an improved electrocatalytic activity towards the oxidation of analytes in pH 6.0 (0.1 M PBS). The PrGO/MnO₂ electrode was able to detect UA, AA and DA simultaneously while, PrGO composite was only able to detect UA in the presence of AA, indicating PrGO/MnO₂ composite has better catalytic activity than PrGO composite which lead to the current increased and good peak potential separation (ΔE_p) of each analyte. The limit of detection and sensitivity of PrGO for the detection of UA are 0.19 μM (S/N = 3) and 0.01 $\mu\text{A}/\mu\text{M}$, respectively in the range of 1-300 μM . The PrGO/MnO₂ electrode has detection limits towards UA, AA and DA with the values of 0.05, 1.00 and 0.02 μM with a linear response of 1-800, 0.03-45 and 0.3-80 μM , respectively. The ΔE_p values of AA-DA, AA-UA and DA-UA were 166, 312 and 146 mV, respectively. Both sensors also showed an excellent reproducibility and repeatability towards the analytes.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia
sebagai memenuhi keperluan untuk ijazah Master Sains

**PENGESANAN ELEKTROKIMIA SERENTAK TERHADAP
ASID URIK, DOPAMINA DAN ASID ASKORBİK MENGGUNAKAN
POLI (3,4-ETILENADIOKSITIOFENA)/
GRAFİN OKSIDA TERTURUN/MANGAN DIOKSIDA**

Oleh

NURULKHALILAH BINTI TUKIMIN

November 2017

Pengerusi: Professor Madya Yusran Sulaiman, PhD

Fakulti: Sains

Kehadiran asid urik (UA), asid askorbik (AA) dan dopamina (DA) di dalam sistem tubuh badan manusia agak sukar untuk di kenalpasti kerana keupayaan pengoksidaan mereka adalah lebih kurang sama. Tahap tidak normal kehadiran ketiga-tiga analit ini di dalam tubuh badan manusia boleh menyebabkan pelbagai penyakit. Bagi menyelesaikan masalah ini, poli(3,4etilenadioksitiofena)/grafin oksida terturun (PrGO) dan mangan dioksida yang didepositkan di atas komposit PrGO (PrGO/MnO₂) masing-masing telah dihasilkan menggunakan voltammetri berkitar untuk mengesan UA dengan kehadiran AA dan juga untuk pengesanan serentak terhadap UA, AA dan DA. Komposit PrGO dan PrGO/MnO₂ menunjukkan pencapaian aktiviti elektrokatalitik terhadap pengoksidaan analit di dalam pH 6.0 (0.1 M PBS). Elektrod PrGO/MnO₂ dapat mengesan UA, AA dan DA secara serentak manakala, komposit PrGO hanya dapat mengesan UA dengan kehadiran AA sahaja kerana komposit PrGO/MnO₂ mempunyai aktiviti pemangkin yang lebih baik berbanding komposit PrGO yang membawa kepada peningkatan arus dan pemisahan puncak keupayaan (ΔE_p) yang baik untuk setiap analit. Had pengesanan dan kepekaan PrGO terhadap UA masing-masing adalah 0.19 μM (S/N = 3) dan 0.01 $\mu\text{A}/\mu\text{M}$ dalam julat 1-300 μM . Elektrod PrGO/MnO₂ mempunyai had pengesanan terhadap UA, AA dan DA masing-masing mempunyai nilai 0.05, 1.00 dan 0.02 μM dengan tindak balas linear 1-800, 0.03-45 dan 0.3-80 μM . Nilai ΔE_p AA-DA, AA-UA dan DA-UA adalah 166, 312 dan 146 mV. Kedua-dua alat pengesanan mempunyai kebolehasihan dan kebole hulangan yang cemerlang.

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I certify that a Thesis Examination Committee has met on 28 November 2017 to conduct the final examination of Nurulkhalilah binti Tukimin on her thesis entitled "Simultaneous Electrochemical Detection of Uric Acid, Dopamine And Ascorbic Acid using Poly(3,4- Ethylenedioxythiophene)/ Reduced Graphene Oxide/Manganese Dioxide" in accordance with the Universities and University Colleges Act 1971 and the Constitution of the Universiti Putra Malaysia [P.U.(A) 106] 15 March 1998. The Committee recommends that the student be awarded the Master of Science.

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LIST OF SYMBOLS

Symbol	Meaning	Usual unit
A	area of electrode	cm^2
C	concentration	mol cm^{-3}
E	electrode potential	V
E_p	peak potential	V
ΔE_p	peak potential separation	V
I	current	A
I_{pa}	anodic peak current	A
R_{ct}	charge transfer resistance	Ω
v	scan rate	V s^{-1}
t	time	s
n	number of electrons	-
D	diffusion coefficient	$\text{cm}^2 \text{s}^{-1}$
Z'	real impedance	Ω
Z''	imaginary impedance	Ω

LIST OF ABBREVIATIONS

A	ampere
μ A	microampere
mA	milliampere
AA	ascorbic acid
ac	alternating current
BPPF6	1-butylpyridinium hexafluorophosphate
CNS	central nervous system
CPs	conducting polymers
CSHM	chitosan/silica sol-gel hybrid membranes
CT	catechol
CV	cyclic voltammetry
2D	two-dimensional
DA	dopamine
DHB	3,4-dihydroxybenzaldehyde
DPV	differential pulse voltammetry
EASA	electrochemical active surface area
EG	exfoliated graphite
EIS	electrochemical impedance spectroscopy
FESEM	field emission scanning electron microscopy
FIA	flow injection analysis
FTIR	Fourier transform infrared
FTO	fluorine doped tin oxide
GCE	glassy carbon electrode
GO	graphene oxide

GOx	glucose oxidase
Hz	hertz
kHz	kilohertz
HQ	hydroquinone
IL	carbon ionic liquid
LOD	limit of detection
LSV	linear sweep voltammetry
cm	centimeter
M	molar
μ M	micromolar
mM	millimolar
nM	nanomolar
MNC	mesoporous nitrogen rich carbonaceous
MO	metal oxide
MPs	metal nanoparticles
MTNCPE	TiO ₂ nanoparticle carbon paste
MWCNT	multi walled carbon nanotube
NP	nanoparticle
OCP	open circuit potentials
PANI	polyaniline
PANI/GO	polyaniline/graphene oxide
PBS	phosphate buffer solution
Pd/CNFs	palladium loaded with carbon nanofibers
PEDOT	poly(3,4-ethylenedioxythiophene)
ppm	parts per million
PPy	polypyrrole

PPy/rGO	polypyrrole/reduced graphene oxide
PrGO	poly (3,4-ethylenedioxythiophene/ reduced graphene oxide
PrGO/MnO ₂	poly(3,4-ethylenedioxythiophene)/reduced graphene oxide/manganese dioxide
Pt	platinum
Pt/GE	platinum/graphene
rGO	reduced graphene oxide
RSD	relative standard deviation
S/N	signal of ratio
SnO ₂ /GN	SnO ₂ /graphene nanocomposite
SOF	silica optical fibers
UA	uric acid
V	volts
mV	millivolt
XPS	X-ray photoelectron spectroscopy
XRD	X-ray diffraction

CHAPTER 1

INTRODUCTION

1.1 Background of study

Uric acid (UA) exists in bio-fluids in the form of urine and blood in human body. It is a protein metabolism desecrates which presents a large amount in certain foods that may cause some harms because humans do not have any enzyme to break down the uric acid (Oda *et al.*, 2002). Thus, uric acid will accumulate and contribute to gout sickness or kidney stones. Gout is one of the diseases where uric acid crystals are formed in the joints which cause an aching inflammatory response (Rock *et al.*, 2013). Based on Desideri *et al.*, (2014), the normal range of UA in urine is about 2.4 - 6.0 mg/dL (14.3 - 35.7 μM). Therefore, the detection of UA (Figure 1.1) becomes necessary to prevent from abnormal levels of UA occurred in the body which can be related to other kinds of diseases such as hypertension, metabolic syndrome and kidney injury (Soltani *et al.*, 2013).

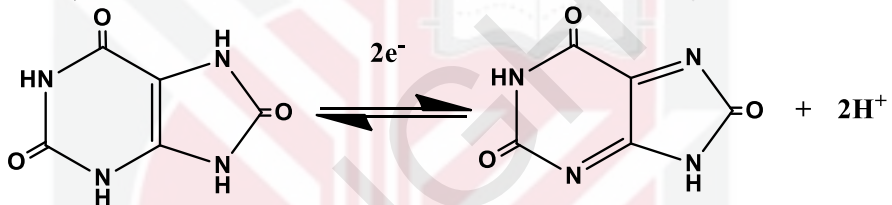


Figure 1.1: Chemical reaction of uric acid (UA)

While, dopamine (DA) as shown in Figure 1.2 presents as an essential neurotransmitter or known as chemical messengers having a crucial function in the central nervous system (CNS) of human which serves as an emotion control and hormonal balance (Thomas, 1997). When the level of DA is decline, it will cause to nervous system diseases, such as Parkinson's disease and schizophrenia (Sansuk *et al.*, 2012). Thus, the detection of DA is crucial to control the hormonal balance in the human body and prevent from aforementioned kind of diseases occurred and maintaining the normal level in human body as shown in table 1.1.

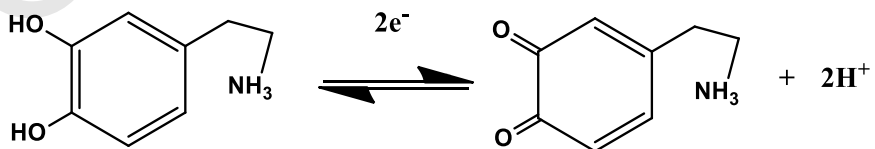


Figure 1.2: Chemical reaction of dopamine (DA)

Table 1.1: The normal range of DA in human body (Gardner and Shoback, 2011)

Ages	Dopamine contain
4-6 years	95-221 $\mu\text{g/day}$
7-12 years	76-371 $\mu\text{g/day}$
13-17 years	137-393 $\mu\text{g/day}$
18-69 years	77-324 $\mu\text{g/day}$
70 years and older	56-272 $\mu\text{g/day}$

Furthermore, ascorbic acid (AA) as shown in Figure 1.3 is an influential antioxidant which naturally exists in vegetable products and also presence in citrus fruits like oranges, lemons, grapefruit, and limes. High quantity of oxidative molecules contained in the human body could damage human cells and lead to severe diseases (Jones, 2006) such as cancer, heart disease, muscle degeneration and many other health problems. The normal range of AA in children and adult is about 2 – 400 mg/dL (11 μM – 2.3 mM) and 2-2,000 mg/dL (11 μM – 11 mM), respectively (Joint, 2002, Levine *et al.*, 1999). Moreover, being over exposure under the sun could also cause human skin cell to be oxidized and create the free-radicals. Thus, the antioxidant is needed in the human body in order to stop this cellular oxidation chain reaction phenomenon by neutralizing the free radicals. Antioxidants are commonly used to cure and prevent from infertility, scurvy, hepatic disease, common cold and mental illnesses (Du *et al.*, 2014). However, it is important to control the level of AA-contain in the human body from getting other side effects due to over consume for example urinary oxalate arises (Davis *et al.*, 1994) and glycosylation of proteins (Davie *et al.*, 1992, Khatami *et al.*, 1988).

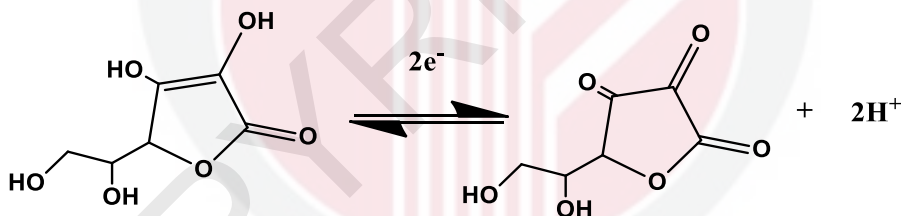


Figure 1.3: Chemical reaction of ascorbic acid (AA)

Recently, many research related in the field of applied science focusing on the electrochemical sensors. The electrochemical sensors have high sensitivity towards electro-active molecules. As different electro-active molecules can be reduced or oxidized at different potential values, electrochemical sensors are able to determine the potential of redox reaction of the molecules and it has high effective towards molecule which is able to be used in biofluids and has good limit of detection for small volume of analyte content (D’Orazio, 2003, Wilson, 2005). An electrochemical sensor is a device with integrated self-contained which is able to provide quantitative information using receptor which is in direct contact with the transduction element (Thévenot *et al.*, 2001). Thus, the human interest and the world market demand to have devices that are able to do a simple and effective detection of the concentration of UA, DA and AA in the samples. The technique of detection for an electrochemical sensor is determined by the reaction which produces a potential (potentiometric), measurable current

(amperometric), or by the changes of the conductivity of an intermediate (conductometric) among the electrodes (Chaubey and Malhotra, 2002). As an electrochemical sensor which applying three-electrode system, it consists of a working, reference and a counter electrode as shown in Figure 1.4. Commonly, the reference electrode is made of Ag/AgCl and in order to maintain the potential, it is kept in the Cl⁻ ion by immersing in salt solution either potassium or sodium chloride solution. A connection to the electrolytic solution is provided by the counter electrode while, working electrode act as transduction component in the biological sample. Thus, current is connected to the working electrode or transducer in order to give a signal information towards the detection of electro-active molecules (analytes) such as hydroxylamine (Wu *et al.*, 2014), glucose (Batchelor-McAuley *et al.*, 2008, Hui *et al.*, 2015), nitrite (Nie *et al.*, 2013), DNA (Lim *et al.*, 2010), dopamine (Ensafi *et al.*, 2010a, Si *et al.*, 2011, Wang *et al.*, 2014a, Zhang *et al.*, 2003, Zhou *et al.*, 2014), ascorbic acid (Ensafi *et al.*, 2010a, Wang *et al.*, 2014a) and uric acid (Ensafi *et al.*, 2010a, Wang *et al.*, 2014a, Zhou *et al.*, 2014).

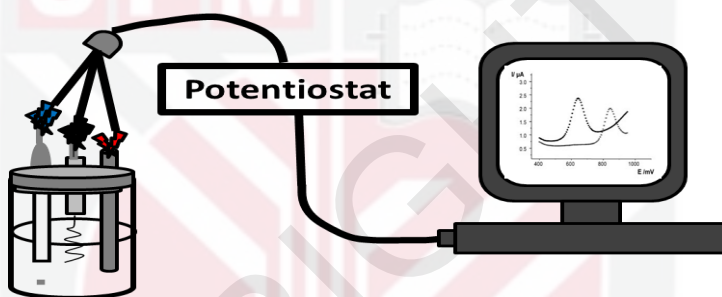


Figure 1.4: Three-electrode system of electrochemical sensor

Many studies concerned on the simultaneous sensing of UA, AA and DA because of these three compounds composed together in human living systems. Their presence in the human body must be controlled in order to keep alarm their abnormal concentration levels which may lead to certain disease (Adams, 1976, Arrigoni and De Tullio, 2002, Wightman *et al.*, 1988). These three compounds have similar electrochemical properties which complicate the identification of their oxidation potential that often overlapped and foul the electrodes besides; these compounds are also easily oxidized (Adams, 1976, Gao and Huang, 1998). Thus, the interest towards modification of electrochemical sensors for simultaneous determination of these three compounds using varieties of materials from conducting polymers (Hui *et al.*, 2015, Manurung *et al.*, 2012, Zhou *et al.*, 2015), graphene-based (Choi *et al.*, 2012, Du *et al.*, 2013) and metal oxide-based (Puangjan *et al.*, 2016, Sriramprabha *et al.*, 2015, Wu *et al.*, 2009) is considered significant in order to have better sensitivity, limit of detection and selectivity.

1.2 Problem statements

The abnormal level of UA, AA and DA in the human body could lead to certain diseases such as kidney injury, scurvy and insomnia, respectively (Arrigoni and De

Tullio, 2002, Rock *et al.*, 2013, Wightman *et al.*, 1988). In order to control and manage the level of these compounds containing in the human body, researchers have developed sensor platforms to determine these three compounds. However, UA, AA and DA are electro-active compounds that have similar electrochemical properties, have more than one isomer which could be formed during the detection, their oxidation potential often overlapped, could foul the electrodes and they are easily oxidized (Adams, 1976, Gao and Huang, 1998). These factors complicate their individual electrochemical identification and lead to the difficulty to measure them accurately.

The detection of DA in the presence of UA has been performed by Wang *et al.* (2014c). Thus, in this work PrGO and PrGO/MnO₂ modified electrodes was fabricated for detection of UA in the presence of AA and simultaneous detection of UA, DA and AA, respectively using electrochemical techniques. The PrGO and PrGO/MnO₂ modified electrodes possesses good properties for electrochemical sensing which increase the peak current and exhibited well-separated oxidation peaks of the analytes.

1.3 Objectives

1. To prepare poly (3,4-ethylenedioxythiophene)/reduced graphene oxide (PrGO) and poly(3,4-ethylenedioxythiophene)/reduced grapheme oxide/manganese dioxide (PrGO/MnO₂) films as sensor platforms using cyclic voltammetry technique.
2. To investigate the sensor performance of PrGO film towards detection of uric acid in the presence of ascorbic acid.
3. To evaluate the sensor performance of PrGO/MnO₂ film towards simultaneous detection of uric acid, ascorbic acid and dopamine.

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