UNIVERSITI PUTRA MALAYSIA

SURFACE DEPOSITION OF ZINC OXIDE/VANCOMYCIN FOR ENANTIOSELECTIVE ELECTROCHEMICAL SENSING OF PENICILLAMINE ENANTIOMERS

ALVIN LIM TEIK ZHENG

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By

ALVIN LIM TEIK ZHENG

Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfillment of the Requirements for the Degree of Master of Science

January 2018

DEDICATION

I would like to dedicate this thesis to my parents for always guiding me, especially during my troubled times.

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

SURFACE DEPOSITION OF ZINC OXIDE/VANCOMYCIN FOR ENANTIOSELECTIVE ELECTROCHEMICAL SENSING OF PENICILLAMINE ENANTIOMERS

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Chairman : Ruzniza Zawawi, PhD
Faculty : Science

The development of chiral electrochemical sensor in the recognition of Penicillamine (Pen) enantiomer is important for the production of pure enantiomers over racemate in the treatment of an array of diseases. The preparation of the modified electrode was a twofold procedure in which electrodeposition of ZnO was conducted first on the ITO glass substrate. The optimum deposition parameters were at –0.9 V, in a buffer solution of pH 7 at 60 ºC for 900 s based on the cyclic voltammetry (CV) data obtained. The second part of the procedure involved dropcasting Van solution on the surface of the ZnO/ITO modified electrode. Electrochemical impedance spectroscopy (EIS) were carried out to characterize the electrical conductivity of the modified electrodes.. In this study, a novel chiral electrochemical sensor based on ZnO/vancomycin modified indium tin oxide glass substrate (ZnO/Van/ITO) was successfully fabricated and used in the chiral recognition of Pen enantiomers. The results showed that the charge transfer resistance (R_{CT}) is the greatest for ZnO/Van/ITO followed by ZnO/ITO, Van/ITO and bare ITO. Field Emission Scanning Electron Microscopy was carried out to study the surface morphology of the modified electrodes surface.

Different oxidation peak current, I_p of L- and D- Pen were observed in the differential pulse voltammograms (DPV) obtained in the solution containing L- or D-Pen. Under optimum condition, the chiral sensor exhibited good linear response to Pen enantiomers in a linear range of 5 mM to 30 mM with a detection limit of 23.56 mM and 14.73 mM (S/N=3) for the D-Pen and L-Pen respectively. This proposed electrode was shown to exhibit excellent performance in terms of low detection limit and good enantioselectivity for Pen enantiomers. Molecular docking using PyRx was further used to study the computational binding effect of the Van and Pen enantiomers. The

results showed that the binding effect was more prevalent for D-Pen as compared to L-Pen with a value of -2.3 kcal/mol and -2.4 kcal/mol for the D-Pen and L-Pen respectively. The association constant from the experiment, K_D and K_L obtained were 2.314×10^3 and 1.076×10^3 L/mol for the D and L-Pen respectively. The value of K_D was larger compared to K_L indicating that the binding effect is higher between Van/ZnO with D-Pen. The results obtained suggested that this chiral sensor has the ability to discriminate chiral drugs which is useful in pharmaceutical industries.

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

PEMENDAPAN PERMUKAAN ZINK OKSIDA/ VANKOMISIN BAGI PENGESANAN ELEKTROKIMIA ENANTIOPILIHAN BAGI ENANTIOMER PENISILAMINA

Oleh

ALVIN LIM TEIK ZHENG

Januari 2018

Pengerusi : Ruzniza Zawawi, PhD
Fakulti : Sains

Penciptaan sebuah sensor elektrokimia kiral dalam pengesanan enantiomer Penisilamina adalah penting dalam pengeluaran enantiomer asli berbanding racemate dalam merawat pelbagai penyakit. Penyediaan elektrod yang diubahsuai adalah menggunakan dua prosedur. Pertamanya, elektrodeposisi ZnO dijalankan terlebih dahulu pada substrat kaca ITO. Parameter optimum adalah pada -0.9 V, dalam larutan electrolit pH 7 pada 60 ºC selama 900 s berdasarkan data voltammetri kitaran (CV) yang diperolehi. Bahagian kedua prosedur tersebut melibatkan titik tuang Van pada permukaan ZnO/ITO untuk mengubah elektrod tersebut. Pengesan novel elektrokimia kiral menggunakan substrat kaca indium tin oksida (ITO) yang diubahsuai dengan zink oksida dan vankomisin (ZnO / Van / ITO) berjaya direka dan digunakan dalam pengesanan kiral enantiomer penisilamina (Pen). Spektroskopi impedans elektrokimia (EIS) telah dijalankan untuk mengkaji kekonduksian elektrik elektrod yang diubahsuai. Keputusan menunjukkan bahawa rintangan pemindahan caj (R_{CT}) adalah yang paling besar untuk ZnO / Van/ITO diikuti oleh ZnO/ITO, Van/ITO dan ITO. Mikroskopi Elektron Penskanan Pelepasan Medan (FESEM) telah dijalankan untuk mengkaji morfologi permukaan permukaan elektrod yang diubahsuai.

Arus puncak pengoksidaan L-dan D-Pen yang berlainan, Ip, dapat diperhatikan dalam voltamogram pulsa (DPV) yang diperolehi dalam elektrolit yang mengandungi L- atau D-Pen. Dalam keadaan optimum, sensor kiral mempamerkan tindak balas linear yang baik untuk enantiomer Pen dalam julat linear 5 mM hingga 30 mM dengan had pengesanan 23.56 mM dan 14.73 mM (S / N = 3) untuk D-Pen dan L-Pen. Elektrod yang dibina ini menunjukkan prestasi cemerlang dari segi had pengesanan yang rendah dan enantiopilihan yang baik untuk enantiomer Pen. Pengedokan molekular menggunakan perisian PyRx digunakan untuk mengkaji kesan pengikatan komputasi

Van dan enantiomer Pen. Hasilnya menunjukkan bahawa kesan pengikatnya lebih tinggi bagi D-Pen berbanding L-Pen dengan nilai -2.3 kcal / mol dan -2.4 kcal / mol untuk D-Pen dan L-Pen. Pemalar penyekutuan dari eksperimen, K_D dan K_L yang diperolehi masing-masing adalah 2.314×10^3 dan 1.076×10^3 L / mol untuk D dan L-Pen. Nilai K_D lebih besar berbanding K_L menunjukkan bahawa kesan mengikat lebih tinggi antara Van/ZnO dengan D-Pen. Keputusan yang diperolehi mencadangkan bahawa sensor kiral ini mempunyai keupayaan untuk membezakan molekul kiral yang boleh menyumbang dalam industri farmaseutikal.

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I certify that a Thesis Examination Committee has met on 26 January 2018 to conduct the final examination of Alvin Lim Teik Zheng on his thesis entitled "Surface Deposition of Zinc Oxide/Vancomycin for Enantioselective Electrochemical Sensing of Penicillamine Enantiomers" 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.

Members of the Thesis Examination Committee were as follows:

Shahrul Ainliah binti Alang Ahmad, PhD
Senior Lecturer
Faculty of Science
Universiti Putra Malaysia
(Chairman)

Mansor bin Hj Ahmad @ Ayob, PhD
Professor
Faculty of Science
Universiti Putra Malaysia
(Internal Examiner)

Sharifah Mohamad, PhD
Associate Professor
University of Malaya
Malaysia
(External Examiner)

NOR AINI AB. SHUKOR, PhD
Professor and Deputy Dean
School of Graduate Studies
Universiti Putra Malaysia

Date: 26 April 2018

This thesis was submitted to the Senate of the Universiti Putra Malaysia and has been accepted as fulfilment of the requirement for the degree of Master of Science. The members of the Supervisory Committee were as follows:

Ruzniza Zawawi, PhD
Senior Lecturer
Faculty of Science
Universiti Putra Malaysia
(Chairman)

Zulkarnain Zainal, PhD
Professor
Faculty of Science
Universiti Putra Malaysia
(Member)

Ernee Noryana Muhamad, PhD
Senior Lecturer
Faculty of Science
Universiti Putra Malaysia
(Member)

ROBIAH BINTI YUNUS, PhD
Professor and Dean
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Name of Chairman of Supervisory Committee:	Dr.Ruzniza Zawawi

Signature:	______________________
Name of Member of Supervisory Committee:	Professor Dr. Zulkarnain Zainal

Signature:	______________________
Name of Member of Supervisory Committee:	Dr. Ernee Noryana Muhamad

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LIST OF ABBREVIATIONS

Ag/AgCl	Silver-silver chloride reference electrode
CA	Chronoamperometry
CE	Counter Electrode
CME	Chemically Modified Electrode
CNT	Carbon nanotubes
CV	Cyclic voltammogram
DPV	Differential pulse voltammetry
FESEM	Field Emission Scanning Electron Microscopy
GCE	Glassy carbon electrode
Ipa	Anodic peak current
Ipc	Cathodic peak current
ITO	Indium tin oxide
Ox	Oxidation
PBS	Phosphate buffer saline
R2	R-squared
RE	Reference electrode
Red	Reduction
SEM	Scanning electron microscopy
WE	Working electrode
Van	Vancomycin

CHAPTER 1

INTRODUCTION

1.1 General background

The recognition of chiral molecules has been a well-studied subject matter due to their importance to human mankind. It is well known that enantiomers exhibit differing properties in terms of its toxicology, pharmacology and pharmacodynamics even though they possess almost similar molecular structure. The medical and pharmaceutical industries would require pure enantiomer over the racemate in the production of medicines and effective treatments. Chiral recognition and separation of racemic drugs has been an interesting research subject since the introduction of the racemic switch strategy adapted by pharmaceutical industries (Nguyen *et al.,* 2006). Upon comparing affinities, enantiomer exhibiting higher affinity or higher activity is called 'eutomer' while the lower affinity or lesser activity is called 'distomer'(Burke and Henderson, 2002).

There are two known methods in the process of resolving enantiomers which are direct and indirect chiral separation. The indirect chiral separation utilizes derivatization of enantiomers into diastereomers applying optically pure reagent. The process is conducted in this manner as diastereomers differ in their chemical properties in which they can be separated in an achiral environment (Blanco and Valverde, 2003). However, for direct chiral separation method, it is based on labile diastereomers formation with the presence of chiral selector. To date, there are several techniques utilised in chiral analysis, the commonly employed methods are such as spectroscopic methods, high-performance liquid chromatography (HPLC), and electrochemical methods. However, electrochemical methods can be advantageous compared to other techniques due to its simplicity, accuracy, and low material cost. In order to increase sensitivity and selectivity of electrochemical measurements, the implementation of nanomaterials with high surface area and good electrical conductivity such as carbon nanomaterial and metal nanoparticles have been introduced on the surface of the electrode.

Enantioselective sensors have been an effective tool in the monitoring of different interactions of enantiomers, determining purity in chirally pure marketed products and studying toxicological effects of enantiomer. Chiral analysis can be considered a rapidly profound research in the past decade due to its importance in various fields, notably, pharmaceutical and clinical applications due to the potential of different activities and toxicities of drug enantiomers. There are several techniques utilized in chiral analysis, the most common is via spectroscopy methods, high-performance liquid chromatography, and electrochemical methods. The concept of chirality can also been studied in the application of biosensors.

To date, many chiral recognition sensors have been developed that shown to have high sensitivity, selectivity, and compatibility in biological assay. The principal objective of chiral recognition is to construct an effectual chiral selective system, which should have recognition sites for certain chiral enantiomers (Guo *et al.,* 2009). The choice of chiral selector is indeed important to achieve the desired results in chiral analysis. The usage of macrocyclic antibiotics such as glycopeptide, polypeotide and ansamycins as an effective chiral selector reveals a very steady growth of its usage in chiral discrimination of enantiomers (Claudia and Salvatore, 1998).

1.2 Problem Statement

In the current age, the medical and pharmaceutical industries is thriving and require fast and reliable analysis on chiral drugs in which they require pure enantiomer over the racemate in the production of medicines and effective treatments. Nowadays, the commonly used technique in the discrimination of chiral molecules is time consuming and high cost. Electrochemical method has garner wide interest as a reliable technique in chiral analysis. The important research questions that arise revolves around one very important aspect; whether electrochemical determination using vancomycin as the chiral selector of the enantiomer pairs can be a reliable alternative that can provide a substantial data on the discrimination of penicillamine enantiomers.

In this study, the chiral selector employed is vancomycin which is a macrocyclic glycopetide that is proven to successfully discriminate enantiomers in many techniques such as high-performance liquid chromatography (HPLC) and electrochemical methods. The interesting properties of vancomycin containing an array of chiral centre containing functional groups that interacts with the analyte is worth to be explored. Although ZnO is known to be a poor electrochemical compound, it is hoped to understand the capability of ZnO in biosensing capability upon reacting with a macrocyclic glycopeptide for the discrimination of chiral molecules. Since, ZnO is known to exhibit various desirable traits for biosensing such as high catalytic efficiency, strong adsorption capability, and high isoelectric point (IEP; ~9.5) which are suitable for adsorption of certain proteins (e.g. enzymes and antibodies with low IEPs) by electrostatic interaction. Combining the unique properties of Van with ZnO as a hybrid couple is expected to enhance the chiral detection of the enantiomers. To date, there are no published report on the usage of ZnO/Van modified ITO in the chiral analysis of Penicillamine enantiomers. Hence the main goal of the present study was to develop a newly modified electrode based on ZnO/Van/ITO.

The simple experimental design of the nanohybrid electrode is hoped to be a reference for the development of chiral sensor. This will thus give important implications for biosensing, asymmetric syntheses and separation, and understanding the nature of chiral interactions in biological systems. The outcome could hold good application in the fields of electroanalytical chemistry and biosensors. Answers to these puzzling questions will bring significant impact on the understanding of the processes involving chiral molecules in living organism.

1.3 Objectives

The objectives of this study are:

i. To grow the ZnO nanomaterials with well-controlled orientation via electrodeposition technique.
ii. To optimize and characterize the properties of chiral surface composed of ZnO/vancomycin nanohybrid material suitable for enantioselective detection of D- and L- Penicillamine
iii. To evaluate the capability of the prepared nanohybrid-modified electrode in the enantioselective electrochemical sensing of penicillamine enantiomers
iv. To identify the mechanism of the enantioselective electrochemical sensing of penicillamine enantiomers by the nanohybrid matrix using computational method.

REFERENCES

Aini, B.N., Siddiquee, S., Ampon, K., Rodrigues, K.F., Suryani, S., 2015. Development of glucose biosensor based on ZnO nanoparticles film and glucose oxidase-immobilized eggshell membrane. Sens. Bio-Sensing Res. 4, 46–56. https://doi.org/10.1016/j.sbsr.2015.03.004

Ameen, S., Akhtar, M.S., Shin, H.S., 2015. Spindles shaped ZnO modified glassy carbon electrode for the selective monitoring of piperidine. Mater. Lett. 148, 188–191. https://doi.org/10.1016/j.matlet.2015.02.049

Amiri, M., Nekoiean, K., Bezaatpour, A., 2012. Nanomolar determination of penicillamin by using a novel Cobalt/Polyaniline/Carbon Paste Nanocomposite Electrode. Electroanalysis 12–14.

Armstrong, D.W, K.L., Rundlett, Chen, J.R., 1994. Evaluation of the macrocyclic antibiotic vancomycin as a chiral selector for capillary electrophoresisTitle. Chirality 6, 496–509.

Azizi, A., Khelladi, M.R., Mentar, L., Subramaniam, V., 2013. A study on Electrodeposited of Zinc Oxide Nanostructures. Akad. Platf. 559–567.

Bashami, R.M., Hameed, A., Aslam, M., Ismail, I.M.I., Soomro, M.T., 2015. The suitability of ZnO film-coated glassy carbon electrode for the sensitive detection of 4-nitrophenol in aqueous medium. Anal. Methods 7, 1794–1801. https://doi.org/10.1039/c4ay02857k

Batra, N., Tomar, M., Gupta, V., 2015. Biosensors and Bioelectronics ZnO – CuO composite matrix based reagentless biosensor for detection of total cholesterol. Biosens. Bioelectron. 67, 263–271. https://doi.org/10.1016/j.bios.2014.08.029

Blanco, M., Valverde, I., 2003. Choice of chiral selector for enantioseparation by capillary electrophoresis. TrAC - Trends Anal. Chem. 22, 428–439. https://doi.org/10.1016/S0165-9936(03)00705-2

Boatto, G., Nieddu, M., Faedda, M.V., De Caprariis, P., 2003. Enantiomeric separation by HPLC of 1,4-dihydropyridines with vancomycin as chiral selector. Chirality 15, 494–497. https://doi.org/10.1002/chir.10238

Bosa, Z., Coufal, P., Kafkova, Z., 2006. Vancomycin as Chiral Selector for Enantioselective Separation of Selected Profen Nonsteroidal Anti-Inflammatory Drugs in Capillary Liquid Chromatography. Chirality 538, 531–538. https://doi.org/10.1002/chir

Burke, D., Henderson, D.J., 2002. Chirality: A blueprint for the future. Br. J. Anaesth. 88, 563–576. https://doi.org/10.1093/bja/88.4.563

Bushiri, M.J., Gopakumar, V., Vaidyan, V.K., 2012. Structural and surface morphological investigation of formation stages of highly (002) oriented ZnO films on glass substrates by spray pyrolysis method. J. of Optoelectronics and Biomedical Materials. 4, 71–78.

Chekin, F., Raoof, J.B., Bagheri, S., Abd Hamid, S.B., 2012. Fabrication of chitosan-multiwall carbon nanotube nanocomposite containing ferri/ferrocyanide: Application for simultaneous detection of D-penicillamine and tryptophan. J. Chinese Chem. Soc. 59, 1461–1467. https://doi.org/10.1002/jccs.201200138

Chen, Q., Zhou, J., Han, Q., Wang, Y., Fu, Y., 2012. A new chiral electrochemical sensor for the enantioselective recognition of penicillamine enantiomers. J. Solid State Electrochem. 16, 2481–2485. https://doi.org/10.1007/s10008-011-1624-0

Chen, S., Chen, J., Liu, J., Qi, J., Wang, Y., 2016. Enhanced field emission from ZnO nanowire arrays utilizing MgO buffer between seed layer and silicon substrate. Appl. Surf. Sci. 387, 103–108. https://doi.org/10.1016/j.apsusc.2016.06.085

Choi, H., Yoon, H., 2015. Nanostructured Electrode Materials for Electrochemical Capacitor Applications. Nanomaterials 5, 906–936. https://doi.org/10.3390/nano5020906

Claudia, D., Salvatore, F., 1998. Chiral analysis by capillary electrophoresis using antibiotics as chiral selector. J. Chromatogr. A 807, 37–56.

Durst, R.A., Baumner, A.J., Murray, R.W., Buck, R.P., Andrieux, C.P., 1997. Chemically modified electrodes: recommended terminology and definitions. Pure Appl. Chem. 69, 1317.

Ehsan, P., Mohammad Ali, T., Hadi, B., Mehdi, R., 2016. ZnIn2S4 Nanoparticles Modified Carbon Paste Electrode for Voltammetric Determination of Penicillamine. Anal. Bioanal. Electrochem. 8, 803–813.

Ensafi, A.A., Khoddami, E., Rezaei, B., Karimi-Maleh, H., 2010. P-Aminophenol-multiwall carbon nanotubes-TiO2 electrode as a sensor for simultaneous determination of penicillamine and uric acid. Colloids Surfaces B Biointerfaces 81, 42–49. https://doi.org/10.1016/j.colsurfb.2010.06.020

Gholivand, M.B., Shamsipur, M., Dehdashtian, S., Adeh, N.B., 2014. Construction of a sensitive sensor for D-penicillamine using sodium montmorillonite nonoclay as a modifier. J. Electroanal. Chem. 725, 7–11. https://doi.org/10.1016/j.jelechem.2014.04.021

Ghosh, S., Rakshit, A.K., Jain, D., 2007. Electrochemistry II: Voltaic or Galvanic cells.

Girault, H.H., 2005. Analytical and Physical Electrochemistry. EPFL Press.

Gooding, J.J., Lai, L.M.H., Ian, Y.G., 2009. Nanostructured Electrodes with Unique Properties for Biological and Other Applications, in: Chemically Modified Electrode. pp. 1–55.

Guo, H.-S., Kim, J.-M., Chang, S.-M., Kim, W.-S., 2009. Chiral recognition of mandelic acid by L-phenylalanine-modified sensor using quartz crystal microbalance. Biosens. Bioelectron. 24, 2931–2934. https://doi.org/10.1016/j.bios.2009.02.002

Han, B., Liu, X., Xing, X., Chen, N., Xiao, X., Liu, S., Wang, Y., 2016. Sensors and Actuators B : Chemical A high response butanol gas sensor based on ZnO hollow spheres. Sensors Actuators B. Chem. 237, 423–430. https://doi.org/10.1016/j.snb.2016.06.117

Hanukovich, S.P., 2014. Optimization of Zinc Oxide Thin Film Deposition as Part of the p-n Heterojunction for Photovoltaic Applications.

He, M., Zhao, S., Chen, J., 2006. Chiral Separation of Penicillamine Enantiomers by Capillary Electrophoresis and Its Application. Chinese J. Anal. Chem. 34, 655–658. https://doi.org/10.1016/S1872-2040(06)60035-2

Herrero, D., Arias, P.L., Cambra, J.F., Antun, N., 2010. Hydrometallurgical Processes Development for Zinc Oxide Production from Waelz Oxide. Waste and Biomass Valorization 329–337. https://doi.org/10.1007/s12649-010-9033-7

Hills, G.J., Peter, L.M., Scharifker, B.R., Pereira, M.I.D.A.S., 1981. The nucleation and gwoth of two dimensional anodic films under galvanostatic conditions. J. Electroanal. Chem. 124, 247–262.

Hori, S., Suzuki, T., Suzuki, T., Miura, S., Nonomura, S., 2014. Effects of Deposition Temperature on the Electrochemical Deposition of Zinc Oxide Thin Films from a Chloride Solution. Mater. Trans. 55, 728–734. https://doi.org/10.2320/matertrans.M2013386

Illy, B.N., Cruickshank, A.C., Schumann, S., Campo, D., Jones, T.S., Heutz, S., Mclachlan, M.A., Mccomb, D.W., Jason, D., Ryan, M.P., 2011. Electrodeposition of ZnO layers for photovoltaic applications : controlling film thickness and orientation †. J. Mater. Chem. 21, 12949–12957. https://doi.org/10.1039/c1jm11225b

Jafari, M., Tashkhourian, J., Absalan, G., 2017. Electrochemical sensing of D-penicillamine on modified glassy carbon electrode by using a nanocomposite of gold nanoparticles and reduced graphene oxide. J. Iran. Chem. Soc. 2, 1–10.

Karuppiah, C., Palanisamy, S., Chen, S.M., Veeramani, V. Periakaruppan, P., 2014. A novel enzymatic glucose biosensor and sensitive non-enzymatic hydrogen peroxide sensor based on graphene and cobalt oxide nanoparticles composite modified glassy carbon electrode. Sensors Actuators B 450–456.

Kathalingam, A., Kim, M.., Chae, Y.., Rhee, J.., Mahalingam, T., 2009. Studies on Electrochemically Deposited ZnO Thin Films. J. Korean Phys. Soc. 55, 2476. https://doi.org/10.3938/jkps.55.2476

Khelladi, M.R., Mentar, L., Boubatra, M., Azizi, A., 2012. Study of nucleation and growth process of electrochemically synthesized ZnO nanostructures. Mater. Lett. 67, 331–333. https://doi.org/10.1016/j.matlet.2011.09.098

Kounaves, S.P., 1997. Voltammetric techniques, in: Handbook of Instrumental Techniques for Analytical Chemistry. Prentice Hall, Upper Saddle River, NJ, USA.

Kozhukharov, S., Tchaoushev, S., 2011. Perspectives for development and industrial application of spray pyrolysis method, in: Annual Proceeding "Angel Kanchev" University of Rousse. pp. 46–50.

Lamba, R., Umar, A., Mehta, S.K., Kumar, S., 2015. ZnO doped SnO2 nanoparticles heterojunction photo-catalyst for environmental remediation. J. Alloys Compd. 653, 327–333. https://doi.org/10.1016/j.jallcom.2015.08.220

Lee, B., Kang, S., 2006. Properties of ZnO varistor blocks under multiple lightning impulse voltages 6, 844–851. https://doi.org/10.1016/j.cap.2005.03.004

Lee, C., Choi, M., 2016. Effects of the deposition condition on the microstructure and properties of ZnO thin fi lms deposited by metal organic chemical vapor deposition with ultrasonic nebulization. Thin Solid Films 605, 157–162. https://doi.org/10.1016/j.tsf.2015.09.050

Lee, D., 2013. A dual enzyme functionalized nanostructured thulium oxide based interface for biomedical application. Nanoscale 1195–1208. https://doi.org/10.1039/c3nr05043b

Lévy-clément, C., Elias, J., Tena-zaera, R., n.d. 1-D ZnO nanostructures and application to ETA-solar cells. pp. 8–11.

Li, B.L., Luo, J.H., Luo, H.Q., Li, N.B., 2013. A novel strategy for selective determination of d-penicillamine based on molecularly imprinted polypyrrole electrode via the electrochemical oxidation with ferrocyanide. Sensors Actuators, B Chem. 186, 96–102. https://doi.org/10.1016/j.snb.2013.05.091

Li, J., Liu, Z., Lei, E., Zhu, Z., 2011. Effects of potential and temperature on the electrodeposited porous zinc oxide films. J. Wuhan Univ. Technol. Sci. Ed. 26, 47–51. https://doi.org/10.1007/s11595-011-0165-9

Li, S., Li, Y., Chen, Z., Liu, J., Zhang, W., 2012. Post-Treatment of Nanocrystalline SnO 2 Films for Flexible Dye-Sensitized Solar Cells 2012. https://doi.org/10.1155/2012/536810

Liang, Z., Zhang, Q., Jiang, L., Cao, G., 2015. ZnO cathode buffer layers for inverted polymer solar cells. Energy Environ. Sci. 8, 3442–3476. https://doi.org/10.1039/C5EE02510A

Lin, X., Zhu, S., Wang, Q., Xia, Q., Ran, P., Fu, Y., 2016. Chiral recognition of penicillamine enantiomers using hemoglobin and gold nanoparticles functionalized graphite-like carbon nitride nanosheets via electrochemiluminescence. Colloids Surfaces B Biointerfaces 148, 371–376. https://doi.org/10.1016/j.colsurfb.2016.09.013

Liu, W.L., Chang, Y.C., Hsieh, S.H., Chen, W.J., 2013. Effects of anions in electrodeposition baths on morphologies of zinc oxide thin films. Int. J. Electrochem. Sci. 8, 983–990.

Lyons, M.E.G., Keeley, G.P., 2006. The Redox Behaviour of Randomly Dispersed Single Walled Carbon Nanotubes both in the Absence and in the Presence of Adsorbed Glucose Oxidase. Sensors 6, 1791–1826. https://doi.org/10.3390/s6121791

Mahalingam, T., John, V.S., Raja, M., Su, Y.K., Sebastian, P.J., 2005. Electrodeposition and characterization of transparent ZnO thin films. Sol. Energy Mater. Sol. Cells 88, 227–235. https://doi.org/10.1016/j.solmat.2004.06.021

Marie, M., Mandal, S., Manasreh, O., 2015. An Electrochemical Glucose Sensor Based on Zinc Oxide Nanorods. Sensors 15, 18714–18723. https://doi.org/10.3390/s150818714

Mazloum-Ardakani, M., Beitollahi, H., Taleat, Z., Naeimi, H., Taghavinia, N., 2010. Selective voltammetric determination of d-penicillamine in the presence of tryptophan at a modified carbon paste electrode incorporating TiO2 nanoparticles and quinizarine. J. Electroanal. Chem. 644, 1–6. https://doi.org/10.1016/j.jelechem.2010.02.034

Mirrahimi, F., Taher, M.A., Beitollahi, H., Hosseinzadeh, R., 2012. Electrocatalytic and selective determination of d -penicillamine in the presence of tryptophan using a benzoylferrocene-modified carbon nanotube paste electrode. Appl. Organomet. Chem. 26, 194–198. https://doi.org/10.1002/aoc.2838

Modaresinezhad, E., Darbari, S., 2016. Sensors and Actuators B : Chemical Realization of a room-temperature / self-powered humidity sensor , based on ZnO nanosheets. Sensors Actuators B. Chem. 237, 358–366. https://doi.org/10.1016/j.snb.2016.06.097

Nesakumar, N., Sethuraman, S., Krishnan, U.M., Rayappan, J.B.B., 2016. Electrochemical acetylcholinesterase biosensor based on ZnO nanocuboids modified platinum electrode for the detection of carbosulfan in rice. Biosens. Bioelectron. 77, 1070–1077. https://doi.org/10.1016/j.bios.2015.11.010

Nguyen, L.A., He, H., Pham-Huy, C., 2006. Chiral drugs: an overview. Int. J. Biomed. Sci. 2, 85–100.

Nian, B.L., Kwak, J., 2007. A penicillamine biosensor based on tyrosinase immobilized on Nano-Au/ PAMAM dendrimer modified gold electrode. Electroanalysis 19, 2428–2436. https://doi.org/10.1002/elan.200703968

Nikoofar, K., Haghighi, M., Lashanizadegan, M., Ahmadvand, Z., 2015. ZnO nanorods : Efficient and reusable catalysts for the synthesis of substituted imidazoles in water. Integr. Med. Res. 9, 570–578. https://doi.org/10.1016/j.jtusci.2014.12.007

Nkunu, Z.N., Kamau, G.N., Kithure, J.G., Muya, C.N., 2017. Electrochemical Studies of Potassium Ferricyanide in Acetonitrile-Water Media (1 : 1) using Cyclic Voltammetry Method. Int. J. Sci. Res. Innov. Technol. 4, 52–58.

Pandiselvi, K., Thambidurai, S., 2014. Chitosan-ZnO/polyanilne nanocomposite modified glassy carbon electrode for selective detection of dopamine. Int. J. Biol. Macromol. 67, 270–278. https://doi.org/10.1016/j.ijbiomac.2014.03.028

Parthasarathy, S., Nandhini, V., Jeyaprakash, B.G., 2016. Journal of Colloid and Interface Science Improved sensing response of photo activated ZnO thin film for hydrogen peroxide detection. J. Colloid Interface Sci. 482, 81–88. https://doi.org/10.1016/j.jcis.2016.07.066

Peulon, S., Lincot, D., 1996. Cathodic electrodeposition from aqueous solution of dense or open-structured zinc oxide filmstle. Adv. Mater. 8, 166–170.

Pradhan, D., Kumar, M., Ando, Y., Leung, K.T., 2009. Fabrication of ZnO nanospikes and nanopillars on ITO glass by templateless seed-layer-free electrodeposition and their field-emission properties. ACS Appl. Mater. Interfaces 1, 789–796. https://doi.org/10.1021/am800220v

Pradhan, D., Leung, K.T., 2008. Vertical Growth of Two-Dimensional Zinc Oxide Nanostructures on ITO-Coated Glass.pdf. J. Phys. Chem. C 1357–1364.

Prasad, B.E., Kamath, P.V., Ranganath, S., 2012. Electrodeposition of ZnO coatings from aqueous Zn (NO 3) 2 baths : effect of Zn concentration , deposition temperature , and time on orientation. J. Solid State Electrochem. 3715–3722. https://doi.org/10.1007/s10008-012-1804-6

Prună, A., Pullini, D., Mataix, D.B., 2012. Influence of Deposition Potential on Structure of ZnO Nanowires Synthesized in Track-Etched Membranes. J. Electrochem. Soc. 159, 92–98. https://doi.org/10.1149/2.003205jes

Qiong, W., Yiting, H., Mengdan, Z., Xiaochun, H., Lin, X., Nana, W., Huanga, J., Wei, W. and, 2016. Amperometric cholesterol biosensor based on zinc oxide films on a silver nanowire–graphene oxide modified electrode. Anal. Methods 1806–1812.

Raoof, J., Ojani, R., Chekin, F., Hossienzadeh, R., 2007. Carbon Paste Electrode Incorporating 1- [4- (Ferrocenyl Ethynyl) Phenyl] -1-Ethanone for Voltammetric Determination of D-Penicillamine. Int. J. Electrochem. Sci. 2, 848–860.

Raoof, J.B., Ojani, R., Chekin, F., 2007. Electrochemical analysis of D-penicillamine using a carbon paste electrode modified with ferrocene carboxylic acid. Electroanalysis 19, 1883–1889. https://doi.org/10.1002/elan.200703947

Rat'ko, A. a., Stefan, R.-I., van Staden, J. (Koos) F., Aboul-Enein, H.Y., 2004. Enantioselective, potentiometric membrane electrode based on vancomycin. Sensors Actuators B Chem. 99, 539–543. https://doi.org/10.1016/j.snb.2004.01.004

Reyes Tolosa, M.D., Orozco-Messana, J., Lima, a. N.C., Camaratta, R., Pascual, M., Hernandez-Fenollosa, M. a., 2011. Electrochemical Deposition Mechanism for ZnO Nanorods: Diffusion Coefficient and Growth Models. J. Electrochem. Soc. 158, E107. https://doi.org/10.1149/2.020111jes

Salmanipour, A., Taher, M.A., Beitollahi, H., Hosseinzadeh, R., 2013. An electrochemical sensor based on 1-benzyl-4-ferrocenyl-1H-[1,2,3]-triazole/carbon nanotube; Detection of D-penicillamine in the presence of tryptophan. Mater. Sci. Eng. C 33, 3160–3165. https://doi.org/10.1016/j.msec.2013.03.041

Scharifker, B.R., Mostany, J., 2007. Electrochemical Nucleation and Growth, Encyclopedia of Electrochemistry. . Wiley-VCH Verlag GmbH & Co. KGaA.

Shahrokhian, S., Souri, A., Khajehsharifi, H., 2004. Electrocatalytic oxidation of penicillamine at a carbon paste electrode modified with cobalt salophen. J. Electroanal. Chem. 565, 95–101. https://doi.org/10.1016/j.jelechem.2003.09.039

Singh, K., Kaur, A., Umar, A., 2015. A comparison on the performance of zinc oxide and hematite nanoparticles for highly selective and sensitive detection of para-nitrophenol. J. Appl. Electrochem. 253–261. https://doi.org/10.1007/s10800-014-0762-3

Singhal, C., Malhotra, N., Pundir, C.S., Narang, J., 2016. An enzyme free Vitamin C augmented sensing with different ZnO morphologies on SnO 2 / F transparent glass electrode : A comparative study. Mater. Sci. Eng. C 69, 769–779. https://doi.org/10.1016/j.msec.2016.07.012

Soomro, M.Y., Hussain, I., Bano, N., Nur, O., Willander, M., 2012. Piezoelectric power generation from zinc oxide nanowires grown on paper substrate. Phys. status solidi 6, 80–82.

Srivastava, S., Srivastava, A.K., Singh, P., Baranwal, V., Kripal, R., Lee, J., Pandey, A.C., 2015. Synthesis of zinc oxide (ZnO) nanorods and its phenol sensing by dielectric investigation. J. Alloys Compd. 644, 597–601. https://doi.org/10.1016/j.jallcom.2015.04.220

Šulčiute, A., Valatka, E., 2012. Electrodeposition and photoelectrocatalytic activity of ZnO films on AISI 304 type steel. Medziagotyra 18, 318–324. https://doi.org/10.5755/j01.ms.18.4.3089

Tajik, S., Taher, M.A., 2016. Analytical &. Anal. Bioanal. Electrochem. 8, 1000–1011.

Taratula, O., Galoppini, E., Mendelsohn, R., 2009. Stepwise Functionalization of ZnO Nanotips with DNA. Langmuir 25, 2107–2113.

Tena-Zaera, R., Elias, J., Lévy-Clément, C., Bekeny, C., Voss, T., Mora-Seró, I., Bisquert, J., 2008. Influence of the Potassium Chloride Concentration on the Physical Properties of Electrodeposited ZnO Nanowire Arrays. J. Phys. Chem. C 112, 16318–16323. https://doi.org/10.1021/jp804563a

Tereshchenko, A., Bechelany, M., Viter, R., Khranovskyy, V., Smyntyna, V., Starodub, N., Yakimova, R., 2016. Sensors and Actuators B : Chemical Optical biosensors based on ZnO nanostructures : advantages and perspectives . A review. Sensors Actuators B. Chem. 229, 664–677. https://doi.org/10.1016/j.snb.2016.01.099

Tripathy, N., Yasir, M., Sideeq, K., Ahn, M., Khang, G., Hahn, Y., 2016. Hierarchically assembled ZnO nanosheets microspheres for enhanced glucose sensing performances. Ceram. Int. 42,13464–13469. https://doi.org/10.1016/j.ceramint.2016.05.134

Wang, J., 2006. Analytical Electrochemistry, 3rd. ed. John Wiley & Sons, Inc. Publication.

Wang, Y., Han, Q., Zhang, Q., Huang, Y., Guo, L., Fu, Y., 2013a. Chiral recognition of penicillamine enantiomers based on a vancomycin membrane electrode. Anal. Method 5, 5579–5583. https://doi.org/10.1007/s10008-012-1859-4

Wang, Y., Han, Q., Zhang, Q., Huang, Y., Guo, L., Fu, Y., 2013b. Enantioselective recognition of penicillamine enantiomers on bovine serum albumin-modified glassy carbon electrode. J. Solid State Electrochem. 17, 627–633. https://doi.org/10.1007/s10008-012-1859-4

Wang, Y., Zhou, J., Han, Q., Chen, Q., Guo, L., Fu, Y., 2012. Chiral Recognition of Penicillamine Enantiomers Based on DNA-MWNT Complex Modified Electrode. Electroanalysis 24, 1561–1566. https://doi.org/10.1002/elan.201200010

Wangfuengkanagul, N., Chailapakul, O., 2002. Electrochemical analysis of D-penicillamine using a borondoped diamond thin film electrode applied to flow injection system. Talanta 58, 1213–1219. https://doi.org/10.1016/S0039-9140(02)00412-5

Welch, C.M., Compton, R.G., 2010. The use of nanoparticles in electroanalysis: An updated review. Anal. Bioanal. Chem. 396, 241–259. https://doi.org/10.1007/s00216-009-3063-7

Yang, J., Wang, Y., Kong, J., Jia, H., Wang, Z., 2015. Synthesis of ZnO nanosheets via electrodeposition method and their optical properties, growth mechanism. Opt. Mater. (Amst). 46, 179–185. https://doi.org/10.1016/j.optmat.2015.04.016

Yao, G., Zhang, M., Lv, J., Xu, K., Shi, S., Gong, Z., Tao, J., Jiang, X., Yang, L., Cheng, Y., He, G., Chen, X., Sun, Z., 2015. Effects of Electrodeposition Electrolyte Concentration on Microstructure, Optical Properties and Wettability of ZnO Nanorods. J. of Electrochemical Soc. 162, 300–304. https://doi.org/10.1149/2.0881507jes

Zhang, Y., Liu, Y., Yang, Z., Yang, Y., Pang, P., Gao, Y., Hu, Q., 2013. Rapid electrochemical detection of ferulic acid based on a graphene modified glass carbon electrode. Anal. Methods 5, 3834. https://doi.org/10.1039/c3ay40084k

Zhao, Z., Lei, W., Zhang, X., Wang, B., Jiang, H., 2010. ZnO-Based Amperometric Enzyme Biosensors. Sensors 1216–1231. https://doi.org/10.3390/s100201216

Zulkifli, Z., Shinde, S.M., Suguira, T., Kalita, G., 2015. Fabrication of graphene and ZnO nanocones hybrid structure for transparent field emission device. Appl. Surf. Sci. 356, 674–678. https://doi.org/10.1016/j.apsusc.2015.08.157