



Articles by College of Natural and Applied Sciences Faculty

2013

Electrocatalytic oxidation of propranol using microwave synthesized graphene decorated with gold nanoparticles and single walled carbon nanotubes

Geoffrey Manani
MSU Graduate Student

Matthew Morris

Steven Caudle
MSU Undergraduate

Adam K. Wanekaya
Missouri State University

Amos Mugweru

Follow this and additional works at: <https://bearworks.missouristate.edu/articles-cnas>

Recommended Citation

Manani, Geoffrey, Mathew Morris, Steven Caudle, Adam Wanekaya, and Amos Mugweru. "Electrocatalytic Oxidation of Propranol Using Microwave Synthesized Graphene Decorated with Gold Nanoparticles and Single Walled Carbon Nanotubes." *Chemistry and Materials Research* 3, no. 11 (2013): 39-49.

This article or document was made available through BearWorks, the institutional repository of Missouri State University. The work contained in it may be protected by copyright and require permission of the copyright holder for reuse or redistribution.

For more information, please contact [BearWorks@library.missouristate.edu](mailto: BearWorks@library.missouristate.edu).

Electrocatalytic oxidation of propranolol using microwave synthesized graphene decorated with gold nanoparticles and single walled carbon nanotubes

Geoffrey Manani², Mathew Morris¹, Steven Caudle², Adam Wanekaya² and Amos Mugweru^{1*}

1. Department of Chemistry and Biochemistry, Rowan University, 201 Mullica Hill Road Glassboro, NJ 08028, USA

2. Department of Chemistry, Missouri State University, 901 South National Ave, Springfield, MO 65897, USA

*Email of the corresponding author: mugweru@rowan.edu

Abstract

Graphene-gold -single walled carbon nanotubes nanocomposites (AuNPs/GN-SWCNT) were synthesized through a simple one-step process, and were used to modify working electrode sensing platform. The nanocomposites were characterized using X-ray Diffraction (XRD), Scanning Electron Microscope (SEM), energy dispersive spectroscopy (EDX), cyclic voltammetry and electrochemical impedance spectroscopy. The nanocomposite material after immobilization on glassy carbon electrode showed excellent catalytic properties towards propranolol. The electrocatalytic effect for oxidation of propranolol was reflected by a significant increase of the peak current with a significant shift in peak potential toward lower oxidation potential as compared with the unmodified electrode. The detection limit for propranolol was found to be $0.04 \times 10^{-6} \mu\text{A}/\mu\text{M}$ of propranolol with linear correlation coefficient $R^2 = 0.996$

Keywords: Propranolol, Gold nanoparticle, Reduced Graphene, Carbon nanotubes Cyclic Voltammetry, Amperometry.

1. Introduction

Propranolol (1-iso-propylamino-3-naphthoxy-propan-2-ol) is a non-selective β -blocker derived from β -adrenergic antagonists.(Ammon, et al., 1977) It is a successful β -blocker used in the treatment of hypertension, anxiety, panic attacks, convulsions and angina pectoris.(Crowther and Smith, 1968) Propranolol is an amphipathic molecule with the (R)-(+)-enantiomer interacting and stabilizing cellular membranes while the β -adrenergic blocking activity resides in the (S)-(-)-enantiomer.(Stoschitzky, et al., 1995) This drug has a high affinity for binding plasma proteins including the most abundant protein in blood, serum albumin (Zahra, et al., 2006) which comprises 60% of the total albumin.(Hu, et al., 2006) The efficacy of many drugs is known to change once they bind to serum albumin hence many promising new drugs can be rendered ineffective because of their affinity for the plasma proteins.(Carter and Ho, 1994) As a result, drug level analysis in a blood sample can be complex due to hindrances from drug-protein binding. Thus, sensitive methods for analysis of drugs especially in complex samples such as blood are desirable.

Many methods have been explored for detection of propranolol including solid phase micro-extraction(Mullett, et al., 2001) capillary electrophoresis(Zhu, et al., 1999), spectroscopy(Gotardo, et al., 2008; Gowda, et al., 2002; Idowu, et al., 2004) and high-performance liquid-chromatography(Das Gupta, 1985). Problems encountered using chromatographic methods include the need for derivatisation, time-consuming extraction procedures, expensive instrumentation and running costs. Electrochemistry is a useful technique to investigate properties of drugs especially those that are electro-active. The technique has attracted more attentions because of its quick response, high sensitivity and potential for miniaturization. Many papers are starting to show up in the literatures that use electrochemistry in drug analysis.(Goyal, et al., 2006) However, for propranolol PRO, only a few papers in the literature are available that deal with electrochemical detection.(Deng, et al., 2011; Zhang, et al., 2009) Few materials have so far been tested for use in analysis of this drug.

Materials such as Gold nanoparticles (GNP's) immobilized on electrodes have electro-catalytic properties that is influenced by particle size distribution.(Shipway, et al., 2000) On the other hand, graphene, a single-atom-thick planar sheet of sp^2 -bonded carbon atoms perfectly arranged in a honeycomb lattice show extraordinary structural properties.(Allen, et al., 2009; Craciun, et al., 2011; Singh, et al., 2011) Graphene can improve performance of biosensors through enhanced adsorption of analytes.(Pruneanu, et al., 2011; Wu, et al., 2010) Graphene can also enhance performance by increasing the signal-to-noise ratio, loading of the recognition molecule, as well as provide large surface area for adsorption analyte.(Xie, et al., 2009) Due to these advantages, graphene based biosensors have been used for detection of saccharides(Huang, et al., 2010), proteins (Mao, et al., 2010), and

glucose.(Zhou, et al., 2008)

Recently, reports of reduced graphene oxide (RGO) electrode decorated with gold nanoparticles yielded important materials useful for electrochemical detection of biological molecules.(Du, et al., 2010) These metal nanoparticles and graphitic carbon nanostructures that may also include carbon nanotubes (CNTs) are receiving considerable research attention due to their potential as hybrid hetero-structures with combined synergistic material properties.(Ding, et al., 2012) These functional hybrids have potential applications in catalysis due to the high surface area of both building blocks and extremely reactive surface of metal nano-crystals (Shan, et al., 2010; Yu and Dai, 2010) and in chemical sensing.(Kan, et al., 2011)

Hybrid materials such as nanoparticle-decorated carbon nanotubes can be synthesized using microwave energy in solvents. In most cases the thermal reduction-deposition of metal ions is triggered by the dielectric heating of the solvent.(Bai, et al., 2006; Guo, et al., 2010; Wang, et al., 2009) In this manuscript, a chloroaurate solution in presence of both graphene and single walled carbon nanotubes was reduced in a one step process through microwave irradiation resulting in gold nanoparticle-decorated graphene. The nano-composites synthesized in this method were investigated in an attempt to develop a simple and reliable method for their use in the determination of PRO. The enhanced electrochemical performances of the graphene composites were demonstrated in the cyclic voltammogram, and the usefulness of the graphene–Au-SWCNT material as biosensor was proven by detecting PRO with improved sensitivity.

2. Experimental

2.1. Chemicals Reagents and Instruments

Hydrogen tetrachloroaurate hydrate ($\text{HAuCl}_4 \cdot 3\text{H}_2\text{O}$), 99% was purchased from Alfa Aesar, Graphite oxide was purchased from Advanced Chemical Materials (Medford, MA), Propranolol was obtained from Enzo Life Sciences. Single walled carbon nanotubes (SWCNT) were from sigma Aldrich. All other reagents and chemicals were of reagent grade. Electron Microscopy images were recorded on a FEI Quanta 200 Field Emission SEM with EDS System.

2.2 Synthesis of Au-SWCNT-Graphene

Low-dimensional sp^2 carbon nanomaterials such as CNTs and graphene are excellent microwave absorbers due to their electrical conductivity. In this work, 90 mg of SWNT and 180 mg of graphite oxide were dispersed by ultrasonication (30 min) in 50 ml of DI water, after adding 5mL of $\text{HAuCl}_4 \cdot 3\text{H}_2\text{O}$ solution. The solution was then transferred to a standard 10 mL quartz vial for the microwave reactor (CEM Mars). The vial was then sealed with a septum, placed inside the reactor cavity, and further capped with a stainless steel pressurized top. The solution was then irradiated with microwaves at 800 W for 5 min at 200°C . After reaction, the septum was removed from the quartz vial and the product washed with DI water and dried at 60°C .

2.3. Electrochemistry and Electrode preparation

2.0 mg graphene–Au-SWCNT synthesized according to the procedure above and 1 ml of DMF containing 20 mg of nafion were thoroughly mixed to form slurry. A GCE with a diameter of 3mm was polished with alumina slurry, and then washed ultrasonically in distilled water and ethanol for 2 min, respectively. The electrode was then fabricated by casting 10 μL of the nano-composite solution on the well-polished GCE and dried in air. Cyclic voltammetry (CV) and Amperometry were performed with a computer-controlled electrochemical workstation (CHI 660C, USA) with ohmic drop 98% compensated. A three electrode system was used with platinum wire as counter electrode and Ag/AgCl as reference electrode (Bio-analytical, systems USA). Glassy carbon electrode with immobilized Au-SWCNT-Graphene was used as the working electrode. Both CV and amperometry were carried out in 20 mM phosphate buffer pH 7.0.

3. Results and discussions

X-ray diffraction Analysis

Synthesis of hybrid materials containing grapheme and carbon nanotubes have previously been reported (Bai, et al., 2006; Zhang, et al., 2010). Here, graphene oxide was mixed with SWCNT in presence of gold solution and then irradiated with microwave energy. X-ray diffraction patterns of the resulting nano-composites were compared against data base of known materials where applicable.

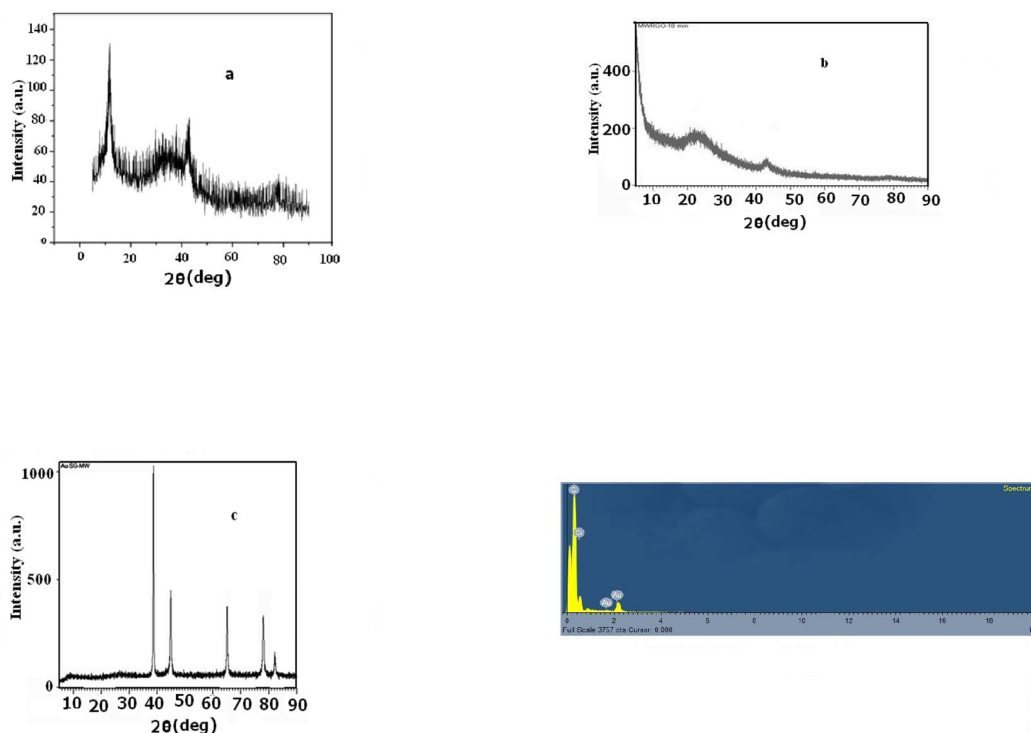


Fig. 1 XRD of (a) Graphite oxide (b) Reduced graphene (c) Graphene–Au–SWCNT nanoparticles (d) EDX of graphene–Au–SWCNT nanoparticles.

Synthesis of hybrid materials containing graphene and carbon nanotubes have previously been reported (Bai, et al., 2006; Zhang, et al., 2010). Here, graphene oxide was mixed with SWCNT in presence of gold solution and then irradiated with microwave energy. X-ray diffraction patterns of the resulting nano-composites were compared against data base of known materials where applicable. The typical XRD patterns of graphene oxide and reduced graphene are shown in figure 1a and figure 1b. As displayed in figure 1a, the most intensive peak of GO at around $2\theta = 11.1^\circ$ corresponds to the (001) feature diffraction peak, and the interlayer spacing (0.8 nm) was much larger than that of pristine graphite (0.34 nm) due to the introduction of oxygen-containing functional groups on the graphite sheets. Reduced graphene oxide as shown figure 1b, has a new broad diffraction peak (d-spacing 3.7 Å at $2\theta = 24.0^\circ$), which is closer to the typical (002) diffraction peak of graphite (d-spacing 3.35 Å at $2\theta = 26.6^\circ$). Microwave irradiation used caused exfoliation and reduction of graphene oxide. This facile and efficient process provided a straightforward method to generate graphene from graphene oxide. In the process, reduction of the gold ions also took place on the graphene surface producing gold nanoparticles supported on the reduced or partially reduced graphene oxide as shown in figure 1c. This reaction occurred resulting in incorporation of gold on the graphene surface. Well defined crystalline peaks corresponding of gold were visible as shown in figure 1c. In addition, we also find from the X-ray diffraction that the gold nanoparticles adopt the well known fcc structure even when combined with graphene and carbon nanotubes. EDX verified the presence of gold in graphene–Au–SWCNT (Figure 1d). Results show presence of presence of Au, C and Cr on the surface. Cr emanated from the wafer .

3.1 Scanning Electron Microscopy Analysis

The surface morphology of graphene–Au–SWCNT, material used to modify the working electrode is important as it affects the sensing performance of the electrode. Figure 2a and 2b shows the SEM image of graphene–Au–SWCNT at two different locations. The 3D structure of graphene was clearly visible with gold nanoparticles

evenly distributed on the surface of graphene. The gold nanoparticles formed on the 3D graphene surface showed average diameter of 20 nm. With the high surface area of nanoparticles coupled with three dimensional conductive of graphene and carbon nanotubes, enhanced electronic transmission rate was expected. Microwave radiation is easily absorbed by carbon materials such as SWCNT, and graphene causing rapid localized heating. The local heating of the carbon substrates (SWCNT, and graphene) caused nearby $\text{HAuCl}_4 \cdot 3\text{H}_2\text{O}$ to afford the near instantaneous formation of gold nanoparticles, decorating the graphene and SWCNT within minutes of microwave exposure.

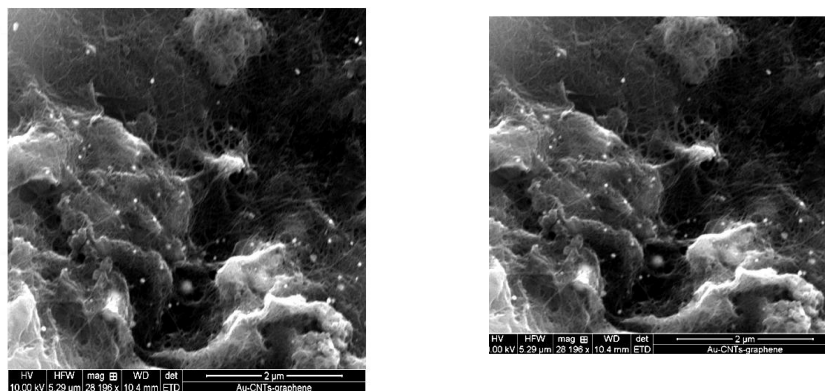


Fig. 2 SEM of gold nanoparticles supported on graphene and SWCNT (two different locations)

A closer look at figure 2 reveals that the dispersity of Au NPs is relatively homogeneous without aggregation, and exists on the top of the graphene sheets as well as in the interlayers, meaning that the Au NPs are assembled with graphene sheets uniformly during the solvent evaporation. It is possible to alter the density of the Au NPs on the graphene sheets by controlling the concentration of Au NP solution. This method of synthesis also avoids byproducts or impurities that may be present by the chemical based synthesis methods.(Xu, et al., 2013).

3.2 Electrochemical impedance spectroscopy

Conducting surfaces including surfaces modified with nanomaterials change the double layer capacitance as well as the electron transfer resistance of the corresponding electrode. The changes introduced through surface modification can be monitored by obtaining the electrochemical impedance spectroscopy (EIS) of the surfaces. (Erdem, et al., 2012) EIS is a technique developed some time back(Metters, et al., 2011; Randviir and Banks, 2013) but has recently been gaining attention in electrochemical research, especially in the field of bio-sensing.

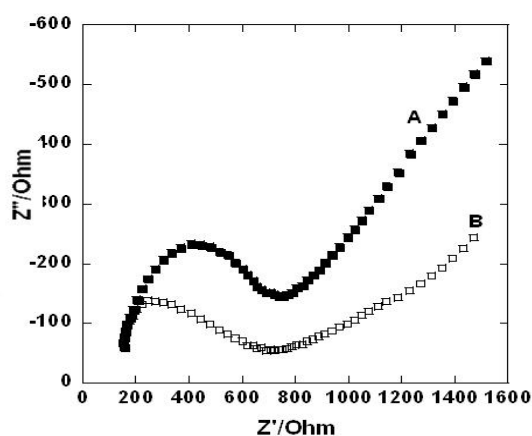


Fig. 3 Electrochemical impedance spectroscopy: (a) bare GCE, (b) 3D-AuNPs/GN/GCE

EIS was used in this work to mainly characterize electrodes surfaces modified with graphene–Au–SWCNT. The Electrochemical impedance studies were carried out in 5 mM $\text{Fe}(\text{CN})_6^{3-}/\text{Fe}(\text{CN})_6^{4-}$ in phosphate buffer solution. Figure 3 shows the Nyquist plot (Z' versus Z'') of bare GCE and GCE coated with graphene–Au–SWCNT nanocomposites. The Randles equivalent circuit model used to fit the data is also shown with R_s being the electrolyte resistance, R_{ct} is the charge resistance, C_{dl} is the double layer resistance and Z_w is the Warburg impedance. The semicircle diameter at higher frequencies in the Nyquist diagram reflects the interfacial electron transfer resistance (R_{ct}) which controls the electron transfer kinetics of $\text{K}_3[\text{Fe}(\text{CN})_6]/\text{K}_4[\text{Fe}(\text{CN})_6]$ at the electrode surface. It can be seen that EIS of the bare GCE is (figure 3a) composed of a large semicircle and a straight line featuring a diffusion limiting step of the $\text{K}_3[\text{Fe}(\text{CN})_6]/\text{K}_4[\text{Fe}(\text{CN})_6]$ processes. After GCE is modified with graphene–Au–SWCNT, the semicircle diameter obviously decreases (figure 3b), meaning that graphene–Au–SWCNT facilitates the electron transfer.

3.3 Electrochemical characteristic of propranolol on Au-SWCNT-Graphene

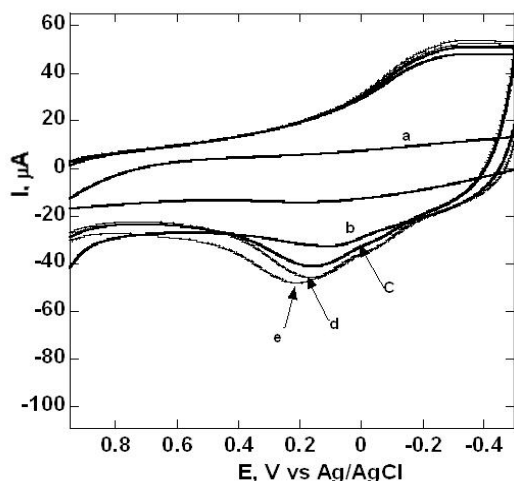


Fig. 4 Cyclic voltammograms of GN-AuNP-SWCNT-GCG (a) phosphate buffer solution (b) Buffer containing (2 μM propranolol (c) 4μM of propranolol (d) 8μM propranolol and (e) 10μM of propranolol.

In order to investigate the electrochemical behaviors of the graphene–Au-SWCNT material, CV measurements were carried out with those composite films as a working electrode. Cyclic voltammetry (CV) is a useful electrochemical characterization technique, it is able to qualitatively evaluate oxygen-related functionalities on CNTs/graphene(Barisci, et al., 2000) including surface reactions due to different metal–carbon nanostructures.(Sheng, et al., 2011) CV measurements of graphene-Au-SWCNT in PRO drug were obtained to evaluate the electrochemical oxidation catalysis by the hybrid material

Enzymatic oxidation of propranolol is known to yield a hydroxyl group (Fantuzzi, et al., 2011) but electrochemical oxidation may yield a hydroxyl group as well as a secondary amine group.(Bishop and Hussein, 1984; Radi, et al., 2004) In electrochemical oxidation, two electrons are involved.

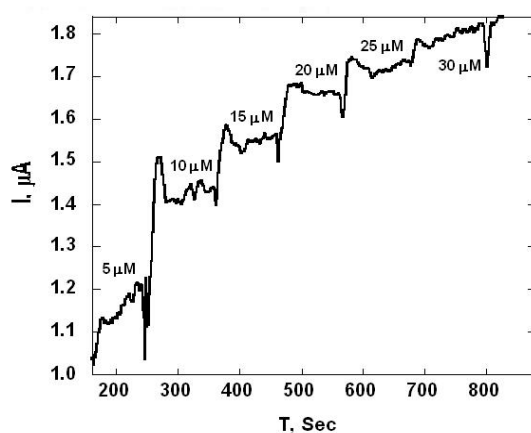


Figure 5. Chronoamperogram of a glassy carbon electrode coated with graphene–Au-SWCNT in 20 mM phosphate buffer pH 7.0 with continuous addition of PRO. The electrode was kept at +0.2 V versus Ag/AgCl reference electrode.

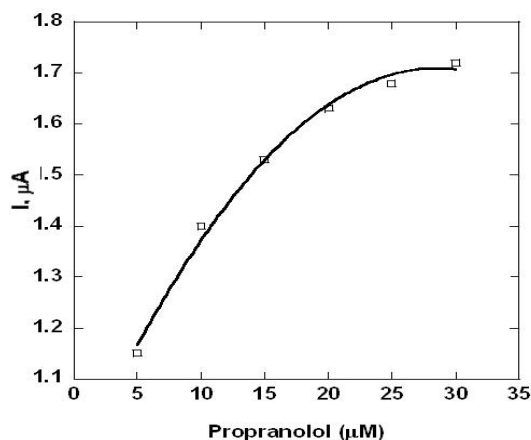
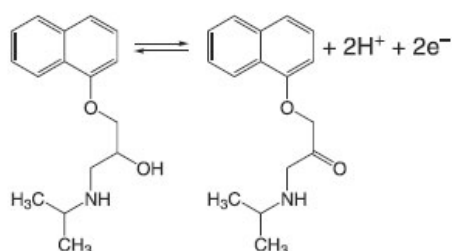


Fig. 6

Calibration curve of PRO obtained from Amperometry.

Figure 4 shows cyclic voltammograms obtained in 20 mM phosphate buffer using a glassy carbon electrode modified with graphene–Au–SWCNT. Figure 4 (Voltammogram a) represent bare glassy carbon electrode in buffer solution. The featureless voltammogram does not change even in presence of PRO at the potential window of 0.9V to -0.5V versus Ag/AgCl electrode. Glassy carbon electrode modified with graphene–Au–SWCNT shows a cyclic voltammogram with an oxidation peak around 0.2V vs Ag/AgCl and a reduction peak around -0.2 V Vs Ag/AgCl electrode. All the voltammograms were obtained at 50 mV/s scan rate in 20 mM pH 7.0 phosphate buffers. Oxidation of PRO on this electrodes resulted in an oxidation peak increase as shown in figure 4. Among the four solutions analyzed, 10μM of PRO solution yielded the highest oxidation current while 2 μM, solution yielded the least current. Recently published works indicate that PRO can be oxidized at higher potentials using other materials.(Chen, et al., 2013)

Direct oxidation of PRO on a glassy carbon electrode resulted in weak oxidation peaks at around 0.156 V and reduction peaks at 0.098 V versus. (Baranowska and Koper, 2011) The scheme for PRO oxidation is given in scheme 1 below



Schematic 1: Representation of propranolol oxidation mechanism

Figure 5 shows amperometric voltammogram of graphene–Au–SWCNT in phosphate buffer solution with the working electrode maintained at 0.2 V vs Ag/AgCl electrode. In this technique, the buffer was first placed in the electrolyte cell and PRO solution was continuously added while monitoring the peak current. 10 μL of 1mM PRO solution was drawn using a syringe and injected in the buffer solution. The solution was continuously stirred. The peak current increased upon injection of PRO. When the current stabilized, the process was repeated

to obtain the voltammogram (figure 5). Propranolol concentration in the cell was re-calculated each time after injection. We observe that each addition results in a step like increase in current indicating that this material is responding to PRO addition. Addition of the analyte was commenced after 160 seconds of system stabilization. At about 700 seconds the step increase was much smaller signifying that saturation had occurred. The electro-catalysis of graphene has been widely reported towards sensing various analytes.(Kim, et al., 2010) Graphene material with its whole volume exposed to electrode surface plus other catalytic nanoparticles maximizes the catalytic effect. Graphene is also highly conductive material that may enhance the electron transfer.

The only difference between bare GCE and graphene–Au-SWCNT is that the presence of highly conductive Graphene and SWCNT leads to a substantial increase of peak current of PRO.

The enhanced catalytic effect of a graphene–Au-SWCNT modified electrode may be attributed to π – π stacking interaction between PRO and the sp^2 hybridized carbon in graphene, making electron transfer possible. Furthermore, gold nanoparticles, may also–enhance electron tunneling on the nano-structured surface. These results imply that the synergistic effect of Au NP with the reduced graphene is demonstrated in terms of electrochemical response

The results from amperometry analysis indicate the occurrence of the Michaelis–Menten type mechanism (figure 6). At low concentration (below $15\mu\text{M}$), the peak current varies in a linear manner with PRO concentrations. At above $15\mu\text{M}$ the peak current gradually becomes independent at more elevated PRO concentrations. This observation provides a crucial mechanistic indicator that the PRO oxidation indeed follows Michaelis–Menten kinetics. However, there could be some other possibilities, such as the adsorption of PRO also leading the current to reach a plateau at high concentrations.

4.0 Conclusions

We have established that a mixture of $\text{HAuCl}_4 \cdot 3\text{H}_2\text{O}$ and SWCNTs and graphene using microwave irradiation in a single step resulted in formation of a hybrid material (graphene–Au-SWCNT). Gold was reduced using microwave irradiation in preparation of gold nanoparticle on graphene. During the conversion, SWCNT acted as the supporting substrate for the templated formation of gold nanoparticles from the $\text{HAuCl}_4 \cdot 3\text{H}_2\text{O}$ decomposition. Gold-carbon hybrids were efficiently used for the electrocatalytic oxidation of PRO. An important advantage of the method is that no further product purification was needed except for drying. The nanocomposite material after immobilization on glassy carbon electrode showed excellent catalytic properties towards PRO. The electrocatalytic effect for oxidation of PRO was reflected by a significant increase of the peak current with a significant shift in peak potential toward lower oxidation potential (500 mV), compared with the unmodified electrode. The detection limit for propranolol was found to be $0.04 \times 10^{-6} \mu\text{A}/\mu\text{M}$.

Acknowledgements:

The authors would like to thank Dr. Sassikal, Jyorthirmayee Sassidharan Nair for her helpful suggestions.

References

- Allen, M.J., Tung, V.C. & Kaner, R.B. (2009) Honeycomb Carbon: A Review of Graphene. *Chem. Rev.* American Chemical Society, pp. 132-145.
- Ammon, H.L., Howe, D.-B., Erhardt, W.D., Balsamo, A., Macchia, B., Macchia, F. & Keefe, W.E. (1977) The crystal structures of dichloroisoproterenol, propranolol and propranolol hydrochloride, *Acta Crystallographica Section B*, 33, 21-29.
- Bai, J., Xu, Z. & Zheng, Y. (2006) Microwave-polyol Process for Functionalizing Carbon Nanotubes with SnO and CeO Coating, *Chemistry Letters*, 35, 96-97.
- Baranowska, I. & Koper, M. (2011) Electrochemical behavior of Propranolol and its major metabolites, 4'-hydroxypropranolol and 4'-hydroxypropranolol Sulfate, on glassy carbon electrode, *Journal of the Brazilian Chemical Society*, 22, 1601-1609.
- Barisci, J.N., Wallace, G.G. & Baughman, R.H. (2000) Electrochemical Characterization of Single-Walled Carbon Nanotube Electrodes, *Journal of The Electrochemical Society*, 147, 4580-4583.
- Bishop, E. & Hussein, W. (1984) Electroanalytical studies of beta-adrenergic blocking agents; N-isopropylethanolamine derivatives; procainamide, *Analyst*, 109, 65-71.
- Carter, D.C. & Ho, J.X. (1994) Structure of serum albumin, *Advances in Protein Chemistry*, 45, 153-203.
- Chen, L., Li, K., Zhu, H., Meng, L., Chen, J., Li, M. & Zhu, Z. (2013) A chiral electrochemical sensor for propranolol based on multi-walled carbon nanotubes/ionic liquids nanocomposite, *Talanta*, 105, 250-254.
- Craciun, M.F., Russo, S., Yamamoto, M. & Tarucha, S. (2011) Tuneable electronic properties in graphene, *Nano*

- Today*, 6, 42-60.
- Crowther, A.F. & Smith, L.H. (1968) Beta-adrenergic blocking agents. II. Propranolol and related 3-amino-1-naphthoxy-2-propanols, *Journal of Medicinal Chemistry*, 11, 1009-1013.
- Das Gupta, V. (1985) Quantitation of propranolol hydrochloride in pharmaceutical dosage forms by high-performance liquid chromatography, *Drug Development and Industrial Pharmacy*, 11, 1931-1937.
- Deng, B., Yin, H., Liu, Y. & Ning, X. (2011) Pharmacokinetics of Propranolol Hydrochlorid in Human Urine by Capillary Electrophoresis Coupled with Electrochemiluminescence, *Analytical Sciences*, 27, 55-59.
- Ding, M., Tang, Y. & Star, A. (2012) Understanding Interfaces in Metal–Graphitic Hybrid Nanostructures, *The Journal of Physical Chemistry Letters*, 4, 147-160.
- Du, M., Yang, T. & Jiao, K. (2010) Immobilization-free direct electrochemical detection for DNA specific sequences based on electrochemically converted gold nanoparticles/graphene composite film, *Journal of Materials Chemistry*, 20, 9253-9260.
- Erdem, A., Muti, M., Karadeniz, H., Congur, G. & Canavar, E. (2012) Electrochemical monitoring of indicator-free DNA hybridization by carbon nanotubes–chitosan modified disposable graphite sensors, *Colloids and Surfaces B: Biointerfaces*, 95, 222-228.
- Fantuzzi, A., Mak, L.H., Capria, E., Dodhia, V., Panicco, P., Collins, S. & Gilardi, G. (2011) A New Standardized Electrochemical Array for Drug Metabolic Profiling with Human Cytochromes P450, *Analytical Chemistry*, 83, 3831-3839.
- Gotardo, M.A., Tognolli, J.O., Pezza, H.R. & Pezza, L. (2008) Detection of propranolol in pharmaceutical formulations by diffuse reflectance spectroscopy, *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, 69, 1103-1109.
- Gowda, B.G., Seetharamappa, J. & Melwanki, M.B. (2002) Indirect spectrophotometric determination of propranolol hydrochloride and piroxicam in pure and pharmaceutical formulations, *Analytical Sciences*, 18, 671-674.
- Goyal, R.N., Gupta, V.K., Oyama, M. & Bachheti, N. (2006) Differential pulse voltammetric determination of atenolol in pharmaceutical formulations and urine using nanogold modified indium tin oxide electrode, *Electrochemistry Communications*, 8, 65-70.
- Guo, S., Wen, D., Zhai, Y., Dong, S. & Wang, E. (2010) Platinum Nanoparticle Ensemble-on-Graphene Hybrid Nanosheet: One-Pot, Rapid Synthesis, and Used as New Electrode Material for Electrochemical Sensing, *ACS Nano*, 4, 3959-3968.
- Hu, Y.-J., Liu, Y., Sun, T.-Q., Bai, A.-M., Lü, J.-Q. & Pi, Z.-B. (2006) Binding of anti-inflammatory drug cromolyn sodium to bovine serum albumin, *International Journal of Biological Macromolecules*, 39, 280-285.
- Huang, Y., Dong, X., Shi, Y., Li, C.M., Li, L.-J. & Chen, P. (2010) Nanoelectronic biosensors based on CVD grown graphene, *Nanoscale*, 2, 1485-1488.
- Idowu, O.S., Adegoke, O.A. & Olaniyi, A.A. (2004) Colorimetric assay of propranolol tablets by derivatization: Novel application of diazotized 4-amino-3,5-dinitrobenzoic acid (ADBA), *Journal of AOAC International*, 87, 573-578.
- Kan, L., Xu, Z. & Gao, C. (2011) General avenue to individually dispersed graphene oxide-based two-dimensional molecular brushes by free radical polymerization, *Macromolecules*, 44, 444-452.
- Kim, Y.-R., Bong, S., Kang, Y.-J., Yang, Y., Mahajan, R.K., Kim, J.S. & Kim, H. (2010) Electrochemical detection of dopamine in the presence of ascorbic acid using graphene modified electrodes, *Biosensors and Bioelectronics*, 25, 2366-2369.
- Mao, S., Lu, G., Yu, K., Bo, Z. & Chen, J. (2010) Specific Protein Detection Using Thermally Reduced Graphene Oxide Sheet Decorated with Gold Nanoparticle-Antibody Conjugates, *Advanced Materials*, 22, 3521-3526.
- Metters, J.P., Kadara, R.O. & Banks, C.E. (2011) New directions in screen printed electroanalytical sensors: an overview of recent developments, *Analyst*, 136, 1067-1076.
- Mullett, W.M., Martin, P. & Pawliszyn, J. (2001) In-tube molecularly imprinted polymer solid-phase microextraction for the selective determination of propranolol, *Analytical Chemistry*, 73, 2383-2389.
- Nath, A., Chechersky, V., Ramanujachary, K.V., Butterick, J.I., Robert, Lofland, S. & Preite, S. (2006) Emission Mossbauer studies of the magnetoresistive compound, La_{0.7}Sr_{0.3}MnO₃, *Solid State Communications*, 138, 224-228.
- Pruneanu, S., Pogacean, F., Biris, A.R., Ardelean, S., Canpean, V., Blanita, G., Dervishi, E. & Biris, A.S. (2011) Novel Graphene-Gold Nanoparticle Modified Electrodes for the High Sensitivity Electrochemical Spectroscopy Detection and Analysis of Carbamazepine, *The Journal of Physical Chemistry C*, 115,

- 23387-23394.
- Radi, A., Wassel, A.A. & El Ries, M.A. (2004) Adsorptive behaviour and voltammetric analysis of propranolol at carbon paste electrode, *Chemia Analytyczna*, 49, 51-58.
- Randviir, E.P. & Banks, C.E. (2013) Electrochemical impedance spectroscopy: an overview of bioanalytical applications, *Analytical Methods*, 5, 1098-1115.
- Shan, C., Yang, H., Han, D., Zhang, Q., Ivaska, A. & Niu, L. (2010) Graphene/AuNPs/chitosan nanocomposites film for glucose biosensing, *Biosensors and Bioelectronics*, 25, 1070-1074.
- Sheng, W., Woo Lee, S., Crumlin, E.J., Chen, S. & Shao-Horn, Y. (2011) Synthesis, Activity and Durability of Pt Nanoparticles Supported on Multi-walled Carbon Nanotubes for Oxygen Reduction, *Journal of The Electrochemical Society*, 158, B1398-B1404.
- Shipway, A.N., Katz, E. & Willner, I. (2000) Nanoparticle arrays on surfaces for electronic, optical, and sensor applications, *ChemPhysChem*, 1, 18-52.
- Singh, V., Joung, D., Zhai, L., Das, S., Khondaker, S.I. & Seal, S. (2011) Graphene based materials: Past, present and future, *Progress in Materials Science*, 56, 1178-1271.
- Stoschitzky, K., Lindner, W. & Kiowski, W. (1995) Stereoselective vascular effects of the (R)- and (S)-enantiomers of propranolol and atenolol, *Journal of Cardiovascular Pharmacology*, 25, 268-272.
- Wang, S., Jiang, S.P., White, T.J., Guo, J. & Wang, X. (2009) Electrocatalytic Activity and Interconnectivity of Pt Nanoparticles on Multiwalled Carbon Nanotubes for Fuel Cells, *The Journal of Physical Chemistry C*, 113, 18935-18945.
- Wu, L., Chu, H.S., Koh, W.S. & Li, E.P. (2010) Highly sensitive graphene biosensors based on surface plasmon resonance, *Opt. Express*, 18, 14395-14400.
- Xie, L., Ling, X., Fang, Y., Zhang, J. & Liu, Z. (2009) Graphene as a Substrate To Suppress Fluorescence in Resonance Raman Spectroscopy, *Journal of the American Chemical Society*, 131, 9890-9891.
- Xu, M.-Q., Wu, J.-F. & Zhao, G.-C. (2013) Direct Electrochemistry of Hemoglobin at a Graphene Gold Nanoparticle Composite Film for Nitric Oxide Biosensing, *Sensors*, 13, 7492-7504.
- Yu, D. & Dai, L. (2010) Self-assembled graphene/carbon nanotube hybrid films for supercapacitors, *Journal of Physical Chemistry Letters*, 1, 467-470.
- Zahra, R., Ahmad, R., Ali Asghar, M.S., Ali, A. & Soghra, K. (2006) A study of the interaction between propranolol and NSAIDs in protein binding by gel filtration method, *Indian Journal of Clinical Biochemistry*, 21, 121-125.
- Zhang, M., Lei, D., Yin, X., Chen, L., Li, Q., Wang, Y. & Wang, T. (2010) Magnetite/graphene composites: microwave irradiation synthesis and enhanced cycling and rate performances for lithium ion batteries, *Journal of Materials Chemistry*, 20, 5538-5543.
- Zhang, Z.-X., Zhang, X.-W. & Zhang, S.-S. (2009) Heart-cut capillary electrophoresis for drug analysis in mouse blood with electrochemical detection, *Analytical Biochemistry*, 387, 171-177.
- Zhou, M., Shang, L., Li, B., Huang, L. & Dong, S. (2008) Highly ordered mesoporous carbons as electrode material for the construction of electrochemical dehydrogenase- and oxidase-based biosensors, *Biosensors and Bioelectronics*, 24, 442-447.
- Zhu, X., Ding, Y., Lin, B., Jakob, A. & Koppenhoefer, B. (1999) Study of enantioselective interactions between chiral drugs and serum albumin by capillary electrophoresis, *Electrophoresis*, 20, 1869-1877.