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Synthesis of Graphene Oxide Electrode for Paracetamol Analysis by Cyclic Voltammetry

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In this study, graphene oxide was made by using improved method of Hummer for paracetamol detection by cyclic voltammetry. The main reason for using graphene oxide electrode for paracetamol detection is the conductive nature of graphene oxide. The cathodic current peak in the graphene oxide electrode has a more sensitive value than the carbon paste electrode. Paracetamol detection of cyclic voltammetric detection has several factors used to accurately detect paracetamol. Factors that can affect the electrode composition, the pH of the solution, the deposition time and the scan rate. In this study, paracetamol detection using graphene oxide electrode has the optimum electrode composition in the ratio of graphene oxide with paraffin 8:2. The pH of optimum solution for detection of paracetamol is 6, 5-second deposition time and scan rate 200 mV/s. Graphene oxide electrode has a detection limit of up to 0.494 ppm or 0.00327 mM (3.27 μM) with recovery 99.615 %. The proposed sensor shows good selectivity, sensitivity, stable repetition and precision.

Keywords: Graphene oxide, Cyclic voltammetry, Paracetamol.

INTRODUCTION

Acetaminophen or paracetamol (PA) is a very important drug because it is widely used for analgesics and antipyretics [1]. In the application of the determination of levels of paracetamol in the pharmaceutical world is very important, because the overdose of paracetamol can cause hepatic necrosis and other poisoning effects. Throughout 2010 there were 4,300 emergency room calls triggered by febrifuge drugs. Most are paracetamol has 3000 cases, while the rest is ibuprofen has 1,300. Cases of paracetamol overdose in children is always there at least once a month, there is a liver damage, from mild to severe [2]. In such phenomena it takes excellent techniques and equipment for paracetamol detection. So far, various techniques have been used to detect paracetamol such as HPLC [3], mass spectrometry [4] and spectrophotometry [5].

The advantage of cyclic voltammetry is to provide sufficient information about the thermodynamics of the redox process, in the kinetics of heterogeneous electron transfer reactions and chemical reactions such as rapid adsorption. In particular, it can locate the rapid redox potential of electroactive species. The voltammetric instruments in use using multiple electrodes include working electrodes, comparative electrodes and auxiliary electrodes. The study of this modified electrode is the working electrode of this matter because the working electrode plays an important role in the oxidation-reduction process directly with the sample. One of the most commonly used electrode is the carbon paste electrode. Carbon is one of the materials that can be used as a working electrode in the field of electroanalis. This is because the carbon electrodes have a fairly wide range of potentials, good electrical conductivity, chemical inert, easy to obtain, relatively low-cost and can be used as sensor applications [6]. In the manufacturing of a carbon paste electrode using paraffin as an adhesive, where paraffin forms the physical interaction with carbon and paraffin has insulator properties so it will be able to inhibit the electron transfer process.

Based on the nature of the paraffin isolator it requires a material that has better conductivity and larger surface area than the carbon. A material having a better conductivity than carbon with paraffin is a graphene oxide material with paraffin. Graphene oxide is a derivative of a sheet-shaped carbon allotrope. Graphene oxide has a conductivity value of 5000 W/mK [7] with a surface area of 2630 m^2/g [8] while the carbon has a conductivity of 25-470 W/mK with a surface area of 1000-2000 m^2/g [9,10]. In Huang *et al*. [11], the difference in conductivity values between graphene/paraffin and graphene oxide/

paraffin was 0.488 (W/mK) and 0.506 (W/mK), respectively. This indicates that graphene oxide material is a good material for the manufacture of working electrodes on voltammetry.

In this study, graphene oxide electrode showed good paracetamol reduction peak. The proposed sensor showing high sensitivity, selectivity with stable repetition and reproducibility. The electrode has an excellent limit of dectection for paracetamol detection and good and practical detection in testing of commercially available samples.

EXPERIMENTAL

Zinc powder, potassium permanganate, hydrochloric acid 37 % p.a, hydrogen peroxide 30 %, sulfuric acid 96 % v/v p.a, phosphoric acid 85 % v/v p.a, aquademineral water, ethanol 96 % v/v p.a, disodium hydrogen phosphate p.a (Na_2HPO_4), sodium dihydrogen phosphate dehydrate ($NaH_2PO_4 \cdot 2H_2O$), potassium chloride were of analytical grades (Merck) and paracetamol pharmaceutical grade. Graphite pencil faber-castel 2B and paraffin oil (Merck) were used to prepare carbon pastes.

Synthesis of graphene oxide: Graphene oxide were prepared by improved hummer method [12,13] and characterized (FTIR, PSA, XRD and SEM). For the reduction of graphene oxide, this suspension in purified water (50 mg/50 mL) was added to 0.6 g of a zinc powder with 20 mL of hydrochloric acid 37 %. After being stirred for 1 h, the solution was cooled down. Subsequently, it was centrifuged and the precipitates were washed with deionized water and then dried at 60 °C in oven for 24 h.

All the electrochemical measurements were performed using a 797 VA Computrace. A three-electrode cell was used at 25 ± 1 °C. An Ag/AgCl (KCl, Sat.) electrode, a platinum wire and a carbon paste electrode modified by graphene oxide were used as reference, auxiliary and working electrodes respectively. Fisherbrand accumet AE150 pH Benchtop Meter was used for pH measurements.

Preparation of electrode: To obtain the best conditions in the preparation of graphene oxide/paraffin oil, we applied various ratio of graphene oxide and paraffin oil (5:5; 6:4; 7:5; 7.5; 2.5; 8:2). The maximum peak current intensity of paracetamol could be obtained in the optimum condition. The graphene oxide/paraffin was prepared by mixing graphene oxide and paraffin oil using a mortar and pestle until a uniform paste was prepared. This paste was then packed into the end of a glass tube (about 15 cm long and 2.5 mm i.d.). A copper wire inserted into the carbon paste provided an electrical contact. When necessary, a new surface was obtained by pushing an excess of the paste out of the tube and polishing it with a weighing paper.

RESULTS AND DISCUSSION

Graphene oxide electrode composition: The electrode composition was made with some variation between graphene oxide and paraffin oil in several comparisons to find out the working electrode composition which gave the best results for paracetamol analysis. The method on voltammetry used to determine the optimum composition of the working electrode using cyclic voltammetry. The optimum composition of the working electrode was obtained by comparing the voltammogram generated from several compositions, selected electrodes having high peak oxidation and narrow reduction reactions.

Paracetamol measurements at pH 6 with a concentration of 50 ppm were performed at a potential difference range of -2 to 1 volt with a scan rate of 100 mV/s. In the results of this study, the values of Ip_c and Ip_a from each electrode composition ratio have an increase in each comparison. This increase corresponds to the nature of the material used for the manufacture of electrodes, graphene oxide is conductor while the paraffin is an insulator.

In this study, the optimum electrode composition was obtained at 80 % graphene oxide and 20 % paraffin oil composition. This is because the 8:2 graphene oxide electrode has the largest Ip_c in comparison of the other electrode (Fig. 1). The working electrode of graphene oxide with paraffin oil has a peak of the paracetamol reduction reaction at a potential difference of -1.0657. Voltamogram of the working electrode graphene oxide with paraffin oil of various compositions is shown in Fig. 1 processed in originpro 8.5.

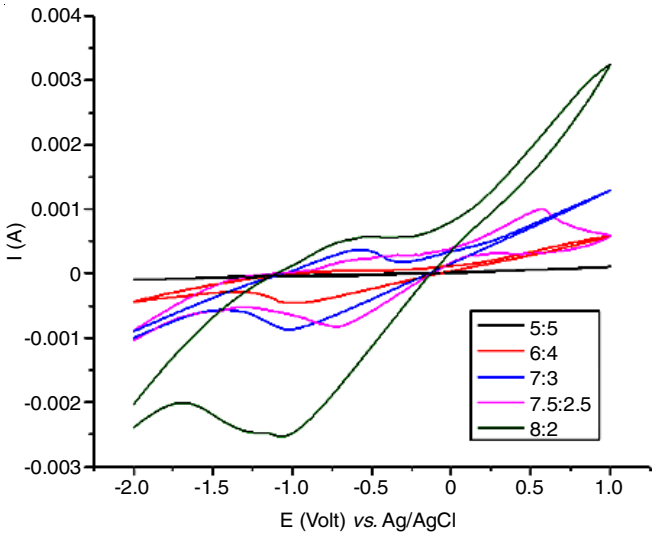

Fig. 1. Cyclic voltammogram of a 0.1 M phosphate buffer solution (pH = 6.0) containing 50 ppm of paracetamol and 5000 ppm potassium chloride at various composite graphene oxides. In all the cases, the scane rate is 100 mV s^{-1}

Optimum pH: On measurement of paracetamol using voltammetric method influenced by pH [14]. This is because on the surface of the graphene oxide electrode, the paracetamol is oxidized to produce H^+ which can affect the pH of the solution. The changes in pH may affect the reduction potential of paracetamol. It can also influence the relationship between the diffusion current to the concentration to be nonlinear. Selection of pH variation based on pKa from acidic paracetamol. Measurement of the mixed solution at a potential difference of -2 to 1 volt with a 10 s deposition time and scan rate of 0.1 V/s. The results obtained from the cyclic voltammetric measurements were processed using originpro 8.5 so that a voltammogram was produced (Fig. 2).

In the voltammogram, Fig. 2 shows that the graphene oxide electrode is capable of oxidizing paracetamol to N-acetyl-*para*-quinoneimine and reducing N-acetyl-*para*-quinone imine to paracetamol characterized by a peak at the anode and cathode. The oxidation reaction of the parasetamol is shown in Fig. 3.

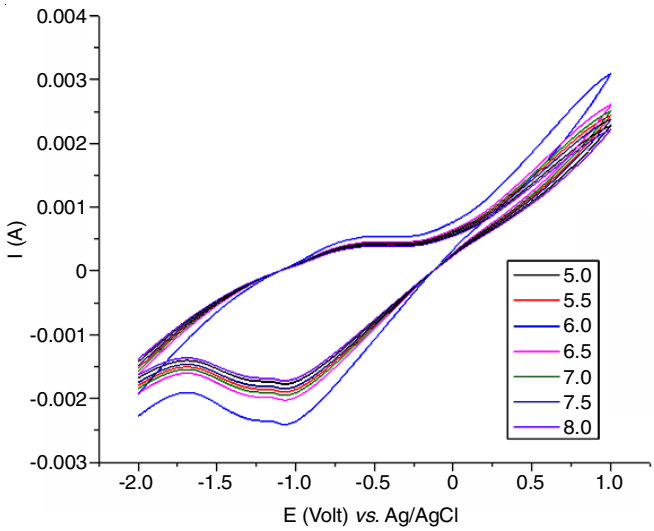

Fig. 2. Cyclic voltammogram at graphene oxide in 0.1 M phosphate buffer solution (pH = 6.0) at a different pHs containing 50 ppm of paracetamol and 5000 ppm potassium chloride. In all the cases, the scane rate is 100 mV s^{-1}

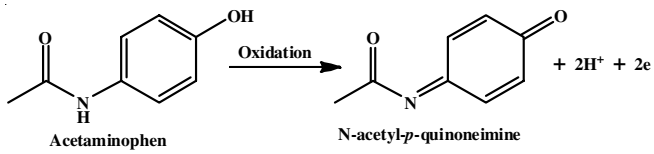

Fig. 3. Oxidation reaction of paracetamol on the surface of the graphene oxide electrode

The result of the voltammogram (Fig. 2) shows at pH 6 the paracetamol has the lagerst oxidation and reduction. The amount of oxidation and reduction is indicated by the large reducing and oxidation current values compared to the others.

Optimum deposition time: The deposition time is the time which takes the analyte to settle on the surface of graphene oxide electrode. The effect of deposition time can be observed by measuring the flow of paracetamol on graphene oxide electrode.

Fig. 4 shows that the deposition time of paracetamol is 5 seconds. The results obtained in this study have the same value

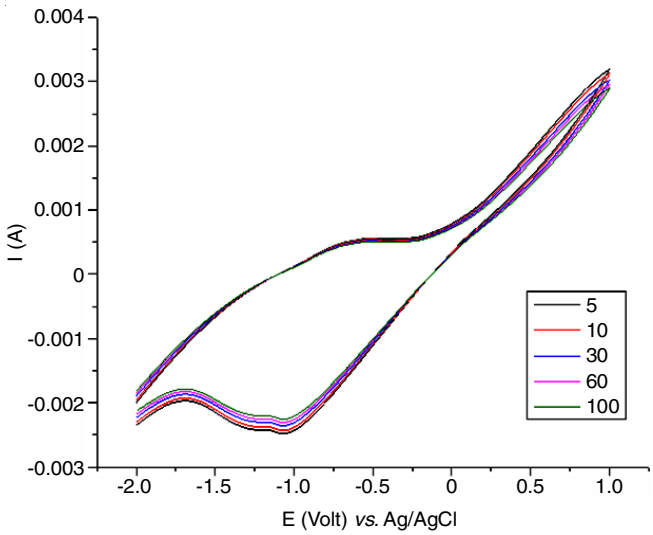

Fig. 4. Voltamogram of paracetamol 50 ppm in pH 6 buffer phosphate at scan rate of 0.1 V s^{-1} with various deposition time

in the reported by Cheemalapati *et al*. [15]. In graphene oxide electrode with a ratio of 8:2, has a 5 s deposition time for paracetamol analyte used for further measurement.

Optimum scan rate: The optimum scan rate measurement is done by manipulating scan rates ranging from 100, 200, 300, 400 and 500 mV/s. In a voltammetric cell there were mixed solutions of 10 mL of 50 ppm paracetamol solution, 10 mL of 5000 ppm KCl solution and 5 mL of buffer phosphate solution. Measurements were carried out by cyclic voltammetry with a 5 s deposition time using a graphene oxide electrode of 8:2. The result of measurement on voltammetry is processed using originpro 8.5 which produces voltammogram in Fig. 5.

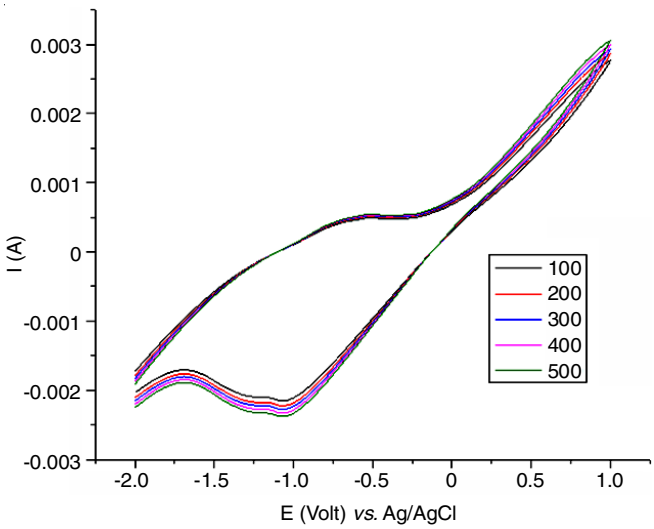

Fig. 5. Cyclic voltamogram at graphene oxide in 0. 1 M phosphate buffer solution (pH = 6.0) at a different scan rates. The scan rates from inner to outer are: 100 to 500 mV s^{-1}. The solution contains 50 ppm of paracetamol and 5000 ppm potassium chlor idea. In all the cases, the scan rate is 100 mV s^{-1}

The voltamogram of scan rate indicates that the greater the scan rate the oxidation peak current and its reduction increased. In this study, we observed an increase in scan rate with peak current by making a graph between $V^{1/2}$ with the oxidation peak current which gives a linear relationship. The linearity indicates that electron transfer of paracetamol solution at the surface of graphene oxide electrode is controlled by diffusion.

Anodic peak current rise is particularly noticeable at 100-200 mV/s which is significant compared to the other scan rate increases. It shows that 200 mV/s is the optimum scan rate used for further measurements.

At the scan rate can also be searched the type of mechanism that occurs on the electrode surface by a comparison between Ip_a with Ip_c. In this study, Ip_c comparison between Ip_a with $Ip_c < 1$ shows a reversible electrochemical reaction mechanism followed by an irreversible (quasi reversible) reaction.

Electrocatalytic oxidation of paracetamol at graphene oxide electrode: The standard solutions used for calibration are 10, 20, 30, 40 and 50 ppm. Measurement for standard calibration with 5 s deposition time, scan rate 200 mV/s at potential -2 to 1 Volt by cyclic voltammetry. In a voltammetric cell, it was charged

TABLE-1
COMPARISON OF THE ANALYTICAL PERFORMANCE OF THE PROPOSED ELECTRODE WITH PREVIOUSLY REPORTED GRAPHENE OXIDE MODIFIED ELECTRODES FOR PARACETAMOL

Modified electrode	LOD[a] (μmol L^{-1})	LR[b] (μmol L^{-1})	Ref.
Graphene oxide[c]	3.270	151070.34-755351.68	This work
MWCNT[d]/graphene oxide	0.050	0.5-400	[16]
Graphene	0.032	0.1-20	[17]

with a mixture of 10 mL solution each of 10, 20, 30, 40 and 50 ppm, 10 mL KCl concentrations of 50-100 times and 5 mL of phosphate buffer pH 6. The voltametric measurement was treated using Originpro 8.5 which is shown in Fig. 6.

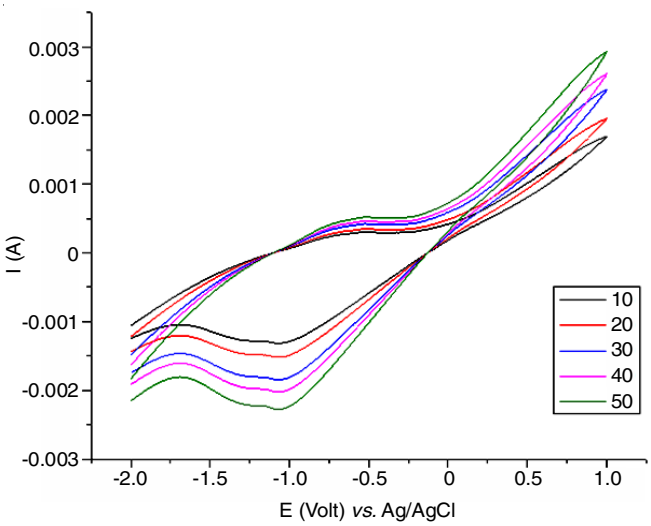

Fig. 6. Paracetamol voltamogram with a concentration of 10-50 ppm in phosphate buffer solution pH 6 with a 5 s deposition time and a scan rate of 200 mV/s

The graph of the relationship between the concentration of standard solution of paracetamol with the cathodic peak (Fig. 6) gives the eqn. 1 with regression $R^2 = 0.9908$.

$$y = -2{,}43005 \times 10^{-5}\, x - 0.00107 \quad (1)$$

The linear eqn. 1 used to determine the concentration of paracetamol in the industrial production-lowering drug.

Recovery and detection limit: The determination of per cent recovery was performed to test the accuracy of paracetamol identification with graphene oxide electrode. The determination of percent recovery is done by re-measuring the standard solution of paracetamol, then the measured current is included in the linear regression eqn. 1. The concentration obtained is compared with the actual concentration of paracetamol. Per cent recovery is calculated by using the eqn. 2.

$$\text{Recovery (\%)} = \frac{\text{Concentration obtained}}{\text{Real concentration}} \times 100 \quad (2)$$

The average per cent recovery result for the measurement of paracetamol with graphene oxide electrode with a ratio of 8:2 was 99.6157 %. Good recovery results show graphene oxide electrodes that are made sensitive to paracetamol samples.

The detection limit is used to determine whether the targeted compound being analyzed is in a sample that is measured or undetectable. Therefore, the detection limit is the lowest limit of paracetamol concentration that can be detected by the created graphene oxide electrode. The detection limit shows the degree of sensitivity of the graphene oxide electrode, the lower the detection limit the better the sensitivity to the sample. In the calculation results obtained a low detection limit is 0.494 ppm. That is, the graphene oxide electrode that has been made has a sensitivity to paracetamol to a concentration of 0.494 ppm (0.00327 mM or 3.27 μM).

Real sample analysis: To evaluate the feasibility of the proposed sensor, the selective of paracetamol in real samples is highly requisite. The analytical performance of the proposed electrode was investigated in pharmaceutical results and the HPLC results are summarized in Table-2. The good recovery results of spiked samples of paracetamol in tablets validating that this proposed graphene oxide electrode could be used for the effective paracetamol in both pharmaceutical samples.

TABLE-2
PARACETAMOL IN PHARMACEUTICAL SAMPLES

Sample	Detected at electrode	Detected at HPLC
1	82.53	78.99
2	81.23	79.12
3	81.86	80.20

Conclusion

In conclusions, graphene oxide electrodes shows good linear relationship with paracetamol concentrations in the range from 10 to 50 ppm and the detection limits was 0.494 ppm. Moreover, graphene oxide electrode exhibited good stability and high reproducibility in cyclic voltammetry determination. The utility of the proposed sensor was evaluated by sensing paracetamol in pharmaceutical samples with good recovery results.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

REFERENCES

1. X. Chen, J. Zhu, Q. Xi and W. Yang, *Sens. Actuators B: Chem.*, **161**, 648 (2012); https://doi.org/10.1016/j.snb.2011.10.085.
2. P.R. May, Ph.D. Thesis, Relationship Knowledge and Parents Attitude Parents Behavior in Provision of Heat-Lowering Drugs (Antipyretics) in Infants Age (0-1 Year), University of Muhammadiyah Malang, Malang, Indonesia (2012).
3. J.M. Wilson, J.T. Slattery, A.J. Forte and S.D. Nelson, *J. Chromatogr. B Biomed. Sci. Appl.*, **227**, 453 (1982); https://doi.org/10.1016/S0378-4347(00)80398-9.
4. H.Ch. Curtius, M. Wolfensberger, B. Steinmann, U. Redweik and J. Siegfried, *J. Chromatogr. A*, **99**, 529 (1974); https://doi.org/10.1016/S0021-9673(00)90882-3.
5. M. Maminski, M. Olejniczak, M. Chudy, A. Dybko and Z. Brzózka, *Anal. Chim. Acta*, **540**, 153 (2005); https://doi.org/10.1016/j.aca.2004.09.011.

6. M.A. Tri, Master Thesis, Modification of Glassy Carbon and Graphite by Iridium Oxide Electrodeposition Technique for Application as Mercury Sensor Electrode, Department of Chemistry. Fakultas Matematika dan Ilmu Pengetahuan Alam, Universitas Indonesia, Jawa Barat, Indonesia (2006).
7. A.A. Balandin, S. Ghosh, W.Z. Bao, I. Calizo, D. Teweldebrhan, F. Miao and C.N. Lau, *Nano Lett.*, **8**, 902 (2008); https://doi.org/10.1021/nl0731872.
8. M.D. Stoller, S.J. Park, Y.W. Zhu, J.H. An and R.S. Ruoff, *Nano Lett.*, **8**, 3498 (2008); https://doi.org/10.1021/nl802558y.
9. L. Marcinauskas, R. Kezelis, Z. Kavaliauskas, A. Zunda and M. Milieska, *Roman. J. Phys*., **62**, 605 (2017).
10. Q. Jiang, M.Z. Qu, G.M. Zhou, B.L. Zhang and Z.L. Yu, *Mater. Lett.*, **57**, 988 (2002); https://doi.org/10.1016/S0167-577X(02)00911-4.
11. Y.-R. Huang, P.-H. Chuang and C.-L. Chen, *Int. J. Heat Mass Transfer*, **91**, 45 (2015); https://doi.org/10.1016/j.ijheatmasstransfer.2015.07.110.
12. D.C. Marcano, D.V. Kosynkin, J.M. Berlin, A. Sinitskii, Z. Sun, A. Slesarev, L.B. Alemany, W. Lu and J.M. Tour, *ACS Nano*, **4**, 4806 (2010); https://doi.org/10.1021/nn1006368.
13. L.T. Sutayasa and I.G.M. Sanjaya, *UNESA J. Chem.*, 23-27 (2016).
14. D.A. Skoog, D.M. West, J.F. Holler and S.R. Crouch, Fundamentals of Analytical Chemistry, David Harris, Belmont: USA, edn 8 (2004).
15. S. Cheemalapati, S. Palanisamy and S.M. Chen, *Int. J. Electrochem. Sci*., **8**, 3953 (2013).
16. S. Cheemalapati, S. Palanisamy, V. Mani and S.-M. Chen, *Talanta*, **117**, 297 (2013); https://doi.org/10.1016/j.talanta.2013.08.041.
17. X. Kang, J. Wang, H. Wu, J. Liu, I.A. Aksay and Y. Lin, *Talanta*, **81**, 754 (2010); https://doi.org/10.1016/j.talanta.2010.01.009.