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Electrochemical Oxidation of Paracetamol Mediated by Nanoparticles Bismuth Oxide Modified Glassy Carbon Electrode

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Nanoparticles of bismuth oxide (Bi_2O_3) have been mechanically attached on the surface of a glassy carbon electrode. Electrochemical performance of nanoparticles of Bi_2O_3/GC modified electrode shows stable response with enhanced selectivity and sensitivity. Voltammetric determination of the oxidation of paracetamol in 0.1 M KH_2PO_4 electrolyte solution by solid phase voltammetry has shown electrocatalyzing effect. Observation revealed a high peak toward the origin of paracetamol oxidation current, which showed 2.0 times increment as compared to bare GC electrode. The sensitivity under conditions of cyclic voltammetry is significantly dependent on pH and temperature. The variation of scan rate study shows that the system undergoes diffusion-controlled process. Calibration plot reveals linearity from the range 5.0 $x10^{-7}$ to 1.5 $x10^{-3}$M with a correlation coefficient of 0.994. The detection limit was estimated to be 2.0 $x10^{-7}$ M. Based on interference studies, most amino acids have negligibly affected the current response of paracetamol. Practically, nanoparticles of bismuth oxide (Bi_2O_3) modified GC electrode could be used for the determination of parecetamol in blood plasma samples.

Keywords: Nanoparticles Bi_2O_3, modified GCE, paracetamol, cyclic voltammetry

1. INTRODUCTION

Acetaminophenol or paracetamol is one of the most commonly used analgesics in pharmaceutical formulations, for the reduction of fever and also as a painkiller for the relief of mild to moderate pain associated with headache, backache, arthritis and postoperative pain. Acetaminophen is electroactive and voltammetric mechanistic studies for the electrode processes of the acetaminophenol /N-acetyl-p-quinoneimine redox system has been presented [1-7].

Recently, nanoparticle modified electrodes have been proposed for the determination of paracetamol in pharmaceutical preparations including electrodeposition attachment of metal nanoparticles, such as Ru [8], Au [9], Cu [10], in addition C_{60} and CNT based electrodes also show high sensitivity with low detection limit [11-14]. Usually, the modification of the electrode requires a difficult analytical procedure and increases the analysis time although it could be required for a sensitive and selective determination of overdose levels of paracetamol in whole blood or urine [15-16]. Since, bismuth oxide modified electrodes showed electrocatalytic activity for some ascorbic acid compound. Bismuth oxide modified carbon electrode has been also been employed for the determination of heavy metal ions in drinking water, mineral water and urine [17]. Bismuth oxide is known to be an important transition metal oxide due to its characteristic parameters such as energy band gap, and photoconductivity that are suitable for large range applications [18]. The fabrication of chemically modified electrode (CME) has been widely reported to improve sensitivity and selectivity in determining many amino acids, vitamins, drug, DNA and many more in recent years [19-24]. To our knowledge, there is no report in the literature for the enhancement of electrocatalytic oxidation of paracetamol using nanoparticle bismuth oxide modified GC electrode. The characterization of known amount of Bi_2O_3 nanoparticles that could catalyze the oxidation process of paracetamol in 0.1 M KH_2P0_4 electrolyte solution was investigated.

2. EXPERIMENTAL

2.1. Instrumentation and electroanalytical analysis methods

Electrochemical workstations of Bioanalytical System Inc. USA: Model BAS 50W with potentiostat driven by electroanalytical measuring softwares were connected to computer to perform cyclic voltammetry (CV), chronocoulometry (CC) and chronoamperometry (CA). An Ag/AgCl (3 M NaCl) and platinum wire (1mm diameter) were used as a reference and counter electrodes respectively. The working electrode used in this study was 3 mm diameter glassy carbon electrode (GCE). The voltammetric experiments were carried out at 25 ± 2^oC using 0.1 M KH_2P0_4 as supporting electrolyte unless otherwise stated. Solution was degassed with nitrogen for ten minutes prior to recording the voltammogram.

2.2. Chemicals and reagents

Bismuth oxide nanopowdwr (Bi_2O_3) was obtained from Informant advanced materials Company, (US). Paracetamol tablet brand named Tempol from, Pharmaceuticals Ltd in (Malaysia) was used. Deionized water from reverse osmosis (RO) water model Elken (BIO PURE) was used. Unless otherwise specified, the supporting electrolyte was 0.1 M KH_2P0_4 in aqueous media at room temperature. All solutions were deaerated with oxygen-free nitrogen gas for 15 minutes prior to making the measurement.

2.3. Procedures

The pH values of 0.1 M KH_2P0_4, aqueous solution were adjusted using 0.1M KOH or 2M HNO_3.

2.3.1. Preparation of a Bi_2O_3- modified electrode

The solid compound Bismuth oxide (Bi_2O_3) was transferred to the surface of GC electrode as follows: Sample amounts of 1-3 mg of Bi_2O_3 were placed on a coarse grade filter paper. The GC electrode was pressed onto the substance and rubbed over the material, causing some compound to adhere to the electrode surface. The clean glassy carbon surface was renewed after the measurement by polishing with 0.5 µm alumina slurry, followed by ultrasonic cleaning for about 2-3 minutes, rinsing with distilled water.

3. RESULTS AND DISCUSSION

3.1. Enhancement study

The cyclic voltammograms of 0.1 mM paracetamol in 0.1 M KH_2P0_4 showed two folds increase in the oxidation current enhancement of modified GC electrode with nanoparticles of Bi_2O_3 as compared to a bare GC electrode as shown in Fig. 1. The oxidation current enhancement of paracetamol at the Bi_2O_3/GC electrode was caused by the catalytic effect. The oxidation of paracetamol is reversible during CV.

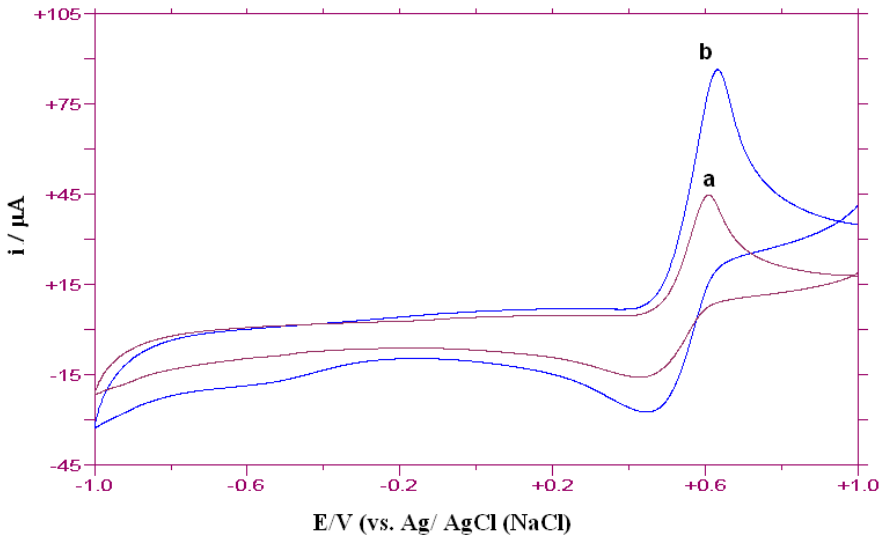


Figure 1. Cyclic voltammograms for oxidation of 0.1 mM paracetamol obtained in 0.1M KH_2P0_4 (pH 4.5), with potential scanning in the positive direction from -1000 to +1000 mV vs Ag/AgCl at a scan rate of 100mV/s at 25°C at (a) bare GC electrode and (b) modified Bi_2O_3/GC

3.2. Effect of pH

The pH was varied from pH 2.0 to 11.0 to determine its effect on the catalytic oxidation of 0.1 mM paracetamol at the Bi_2O_3/GC modified electrode. Fig. 2 shows that the oxidation current of 0.1 mM paracetamol increases with an increase in pH between 3.0 to 8.0 with maximum current enhancement at pH 4.5. The current slowly decreased from pH 4.5 to pH 8.0. As can be seen, the peak potential for paracetamol oxidation varies linearly with pH and is shifted to more negative potentials with increase in pH.

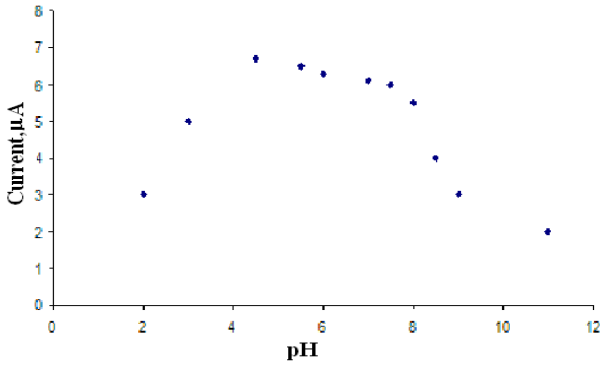


Figure 2. Graph of current flow with varying pH levels for GC electrode modified with modified Bi_2O_3/GC in 0.1 M KH_2P0_4. potential scanning in the positive direction from -1000 to +1000 mV vs Ag/AgCl at a scan rate of 100mV/s

3.3. Effect of temperature

Effect of temperature on the oxidation process of paracetamol was studied. The current increased gradually at the temperature of 20 ^{0}C to 70 ^{0}C. Paracetamol gave a peak response at about 650 mV vs. Ag/AgCl at the bare GC electrode Fig. 3, while the use of Bi_2O_3 nanoparticles modified GC electrode led to an anodic peak at about 540 mV vs. Ag/ AgCl and the peak current increased greatly. The enhanced peak current response is a clear evidence of the catalytic effect of the Bi_2O_3 nanoparticles modified GC electrode towards oxidation of paracetamol. In addition, a shift in the oxidation potential of paracetamol by about 110 mV in the cathodic direction was observed at the modified electrode. The plot of log oxidation current of paracetamol versus reciprocal of temperature was found to be fairly linear as described by 0.9899 R^2. It is also in agreement with thermodynamic expectation of Equations 1 and 2 given below.

$$\sigma = \sigma^0 \text{Exp} (- E_a / RT) \quad (1)$$

$$D = D^\circ \exp (- E_a / RT) \quad (2)$$

Where σ /D are conductivity/diffusion coefficient and σ^0/D° are standard conductivity of the initial diffusibility. However while use at elevated temperature, it can give an increase in current, in practice, application need to be continued close to ambient temperature.

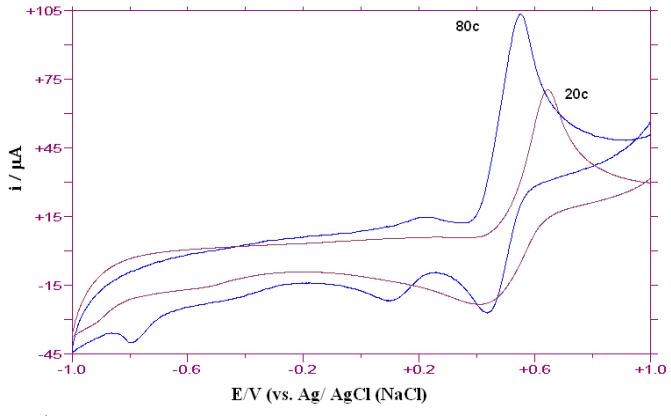


Figure 3. Typical cyclic voltammograms of various temperature 0.1 mM paracetamol at Bi_2O_3 modified GC electrode in 0.1 M KH_2P0_4(pH 4.5), with potential scanning in the positive direction from -1000 to +1000 mV vs Ag/AgCl at a scan rate of 100mV/s.

3.4. Effect of varying paracetamol concentrations

The concentration of standard paracetamol was determined using nanoparticles Bi_2O_3/GC modified electrode. Voltammograms in Fig. 4 show peak current of Paracetamol increases rapidly and linearly with increasing concentration from ($5.0x10^{-7}$ to $1.5x10^{-3}$ mol/L), as described by Equations y = 14.28x+0.23, which showed excellent correlation of 0.994 R^2 value. Based on the slope, m of the linear graph, a good sensitivity response of 14.28 µA/mM was obtained.

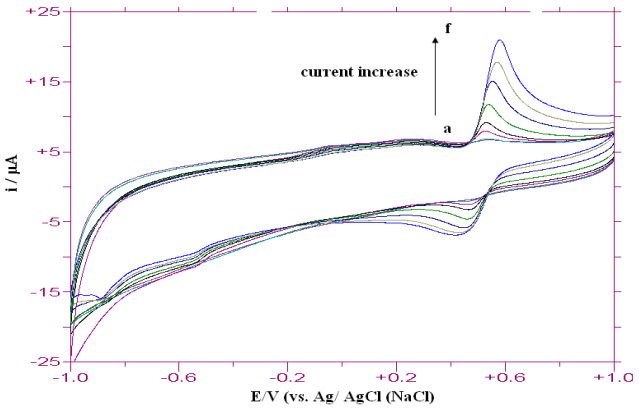


Figure 4. Typical cyclic voltammograms of various paracetamol concentrations in 0.1 M KH_2P0_4,(a 0.5µM, b 0.05mM, c 0.1mM, d 0.5mM, e 1.0mM,f 1.5mM): (y = 14.28x+0.23, R^2= 0.994) at pH 4.5. potential scanning in the positive direction from -1000 to +1000 mV vs Ag/AgCl at a scan rate of 100mV/s .

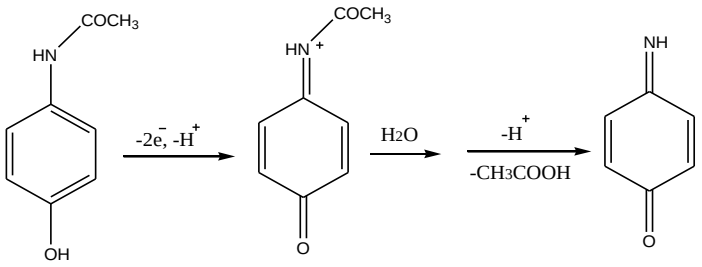
By using the ratio of 3σ/m, where σ is the standard deviation derived from the background noise of 50 date points adjacent to the oxidation peak, a detection limit (DL) of 0.2μM paracetamol was determined. The DL of paracetamol obtained by Bi_2O_3/GCE appears to be comparable and in some cases more superior to that obtained by the reported chemically modified electrode as shown in Table 1.

Table : Comparison of the electrochemical behavior of nanoparticles Bi_2O_3 in detection of Paracetamol with some of the previously reported electrodes.

Electrode	pH	Ep vs. Ag/AgC1(V)	Linear range(M) μ	Detection Limit (μ M)	References
C-Ni/GCE	BR, pH 3	+0.733 (vs. SCE)	7.8-110	-	[1]
Cu-PTTCA/GCE	PBS, pH 7	+0.65	20-5,000	5	[6]
PGE	pH 6.5	+0.492 (vs. SCE)	1-8, 20-100	0.0142	[7]
Nanogold/ITOE	PBS, pH 7.2	+0.830	0.2-1,500	0.18	[9]
Nafion /ROP/GCE	M HClO4	+1.45	50-2500	1.2	[13]
C_{60}/GCE	PBS, pH 7.2	–	50-1,500	50	[14]
VCPTE	PBS, pH 7	-	0.25-5,800	88	[23]
CILE	ABS, pH 4.6	+0.462 (vs. SCE)	1.0-2,000	0.3	[24]
NanoBi_2O_3/GC	pH 4.5	+ 0.61	50-1,500	0.2	This work

3.5. Effect of varying scan rate

The effect of varying scan rates (*v*) on the cyclic voltammograms of 0.1 mM paracetamol using modified Bi_2O_3/GC as working electrode in 0.1 M KH_2P0_4 supporting electrolyte was studied over 5 – 1000 mV/s. Oxidation currents of paracetamol was observed to increase with scan rate due to heterogeneous kinetics. Based on a plot of log (peak current) versus log (scan rate, *v*) for oxidation current of the first cycle, a straight line was obtained fulfilling the equation y = 0.4215x – 0.33 with R^2=0.995 (Fig. 5). A slope of 0.42, which is comparable with theoretical slope of 0.5 for diffusion-controlled process, was obtained. From this study, approximately two protons were transferred in the reaction. Paracetamol oxidation is a two-electron two-proton process in Scheme 1 given below. A conclusion that is consistent with that reported in the literature [24].



(Scheme 1)

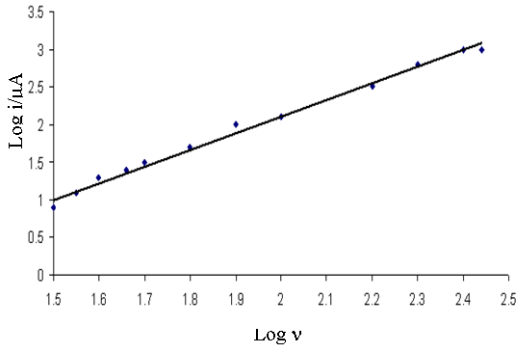


Figure 5. Plot of log Ip_a versus log *v*. Effect of varying scan rates of 0.1 mM paracetamol (y = 0.4215x +0.33, R^2=0.995) using Bi_2O_3/GC electrode in 0.1 M KH_2P0_4 (pH4.5). Potential scanning in the positive direction from -1000 to +1000 mV vs Ag/AgCl at a scan rate rang from 5-1000mV/s.

3.6. Scanning Electron Microscopy

The morphology of the nanostructured of Bi_2O_3/GC electrodes was characterized using scanning electron microscopy (SEM). (a) Before electrolysis and (b) after electrolysis with immersed in 0.1 M KH_2PO_4 electrolyte and an enlargement of 3000 times. (Fig. 6 (a)) shows the change in nanosize of Bi_2O_3 mechanically attached at carbon electrode. Before electrolysis, the morphology of pure Bi_2O_3 nanoparticles reveals a smaller size structure ranging from 120–127 nm (in diameter). After electrolysis, the nanoparticles of Bi_2O_3 increased to size range of 149–159 nm (Fig. 6 (b)) indicating presence of a solid-to-solid conversion process. The detectable difference measured by 28.0±0.3nm may provide a favorable microenvironment for the capture of paracetamol molecules. Stability of the Bi_2O_3 film is evident, as the morphology of the film remains essentially unscathered even after 20 potential cycling.

A B

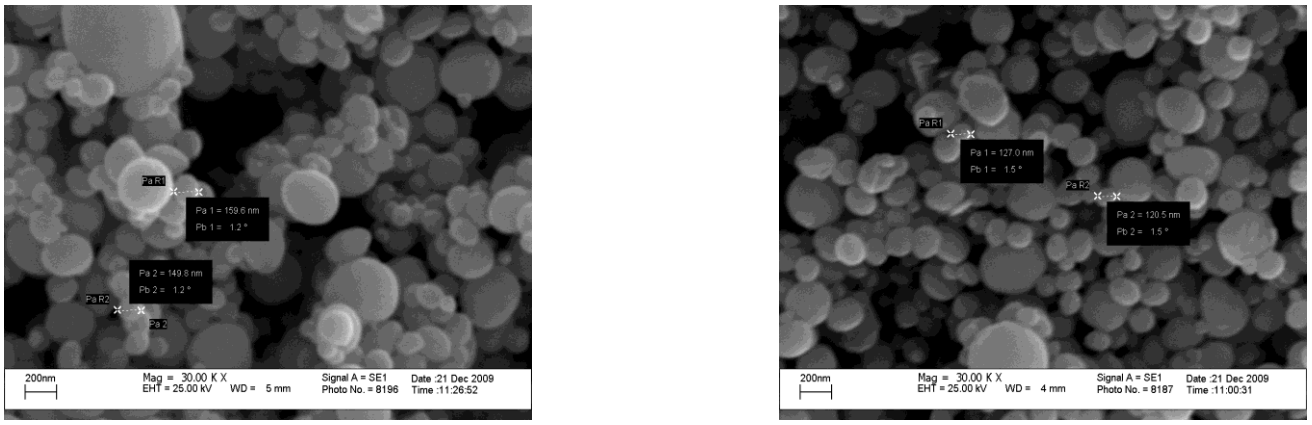


Figure 6. Scanning Electron Microscopy shows the effect of electrolysis (a-before electrolysis; b-after electrolysis) on the morphology of neutral Bi_2O_3 nanoparticles.

3.7. Stability and reproducibility of Bi_2O_3/GC modified electrode

The Bi_2O_3 modified electrode was very stable while kept in 0.1 M KH_2P0_4 solution. Further to examine the stability of the present modified electrode towards the determination of paracetamol using CV for paracetamol was carried out every 1hour interval time. It was found that the oxidation current of paracetamol remains the same with a relative standard deviation of 2.3 % for six times repetitive measurements indicating that this electrode has a good durability and reproducibility.

3.8. Determination of paracetamol in human blood plasma

The recovery results are given in Table 2. The Bi_2O_3 modified electrode was used for determination of paracetamol (Tempol, Malaysia), in human blood plasma samples using 0.1 M KH_2P0_4 solution after the injection of 10 and 20 μM concentration of parecetamol. The reaction showed signals due to the oxidation of parecetamol (Supporting Information, Fig. 4). The observed clear signal for parecetamol and a close to 100% recovery of parecetamol in blood plasma samples. (Table 2) suggested that Bi_2O_3 modified GC electrode could be used for the determination of parecetamol in blood plasma sample.

Table 2. Determination of paracetamol in blood plasma samples using Bi_2O_3 nanoparticles Modified GC electrode.

Human blood serum	Added (□M)	Found (□M)	Recovery
Sample 1	10	10.1	101.0
Sample 2	20	19.99	99.95

4. CONCLUSIONS

The glassy carbon electrode surface modified with nanoparticles Bi_2O_3/GC showed good electrocatalytic response for the oxidation of paracetamol. The oxidation current of paracetamol at Bi_2O_3/GC modified electrode appeared with enhancement of 2 times compared to bare GC electrode. The variation of scan rate study shows that the system undergoes diffusion-controlled process. Calibration plot reveals linearity from the range $5.0x10^{-7}$ to $1.5x10^{-3}$ M with a correlation coefficient of 0.994. The detection limit (3σ) was estimated to be 0.2µM. Based on interference studies, most amino acid under studied the interference examined here do not affect the response of paracetamol at the nanoparticles Bi_2O_3 modified electrode.

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References

1. S.-F.Wang, F. Xie, R. Hu, *Sens. Actuators B* 123 (2007) 495-500
2. S. Christie, M. Leeds, F. Baker, P. Keedy, X. Vadgama, *Anal. Chim. Acta* 272 (1993) 145–150.
3. R.M.D. Carvalho, R.S. Freire, S. Rath, L.T. Kubota,. *J. Pharm. Biomed. Anal*. 34 (2004) 871-878
4. M.E. Bosch, A.J.R. Saˇınchez, F.S. Rojas, *C.J. Pharm. Biomed. Anal*.42 (2006) 291-298
5. N.Wangfuengkanagul, O. Chailapakul. *J. Pharm. Biomed. Anal*. 28 (2002) 841.
6. R. Săndulescu, S. Mirel, R. Oprean *J. Pharm. Biomed*. 23 (2000) 77–87.
7. S. Vijayalatha, H. Gomathi and G. Prabhakara Rao, 33(1994) 101-104
8. E. Asedegbega-Nieto, B. Bachiller-Baezaa, D.G. Kuvshinov, F.R.Garcı. *Carbon* 46 (2008) 1046 – 1052.
9. Santhosh S. Nair, S. Abraham John, *Electrochimica Acta* 54 (2009) 6837–6843
10. Mannan Boopathi , Mi-Sook Won , Yoon-Bo Shima, *Analytica Chimica A*cta 512 (2004) 191–197
11. Pablo Fanjul-Bolado, Pedro José Lamas-Ardisanab, *Analytica Chimica Acta* 638 (2009) 133–138
12. W.T.Tan,A.M.Bond,S.W.Ngooi,E.B.Lim,J.K.Goh, *Analytica Chimica Acta*.491(2003)181-191
13. JM Zen, YS Ting, *Anal Chim Acta* 342 (1997):175–180

14. Rajendra N. Goyal, Sudhanshu P. Singh. *Electrochimica Acta* 51 (2006) 3008–3012
15. R.N. Goyal, V.K. Gupta, M. Oyama, N. Bachheti, *Electrochem. Commun*. 7 (8) (2005) 803–807.
16. S. Zhao, W. Bai, H. Yuan, D. Xiao *Anal. Chim. Acta* 559 (2006) 195- 204
17. R. Pauliukaite, R. Metelka, I. Svancara, A. Krolicka, A. Bobrowski, K. Vytras, E. Norkus, K. Kalcher, *Anal. Bioanal. Chem*. 374 (2002) 1155-1162
18. Lingzhi Li, Bing Yan. *Journal of Alloys and Compounds* 476 (2009) 624–628
19. P.R. Roy, M.S. Saha, T. Okajima, S.-G. Park, A. Fujishima, T. Ohsaka, 51 (2006) 4447-4455
20. T.P. Gujar, V.R. Shinde, C.D. Lokhande, R.S. Mane, S.-H. Han, *Appl.Surf.Sci*. 250(2005) 161-169
21. W.T.Tan, J.K.Goh. *Electroanalysis* 20, (2008) 2447-2453
22. Protiva Rani Roy, Madhu Sudan Saha, Takeyoshi Okajima, Takeo. *Electroanalysis* (2004),16,No.4
23. O. Fatibello-Filho, KO Lupetti , IC Vieira, *Talanta* 55 (2001):685–692
24. Xiaodong ShangGuan & Hongfang Zhang, .*Anal Bioanal Chem* (2008) 391:1049–1055