

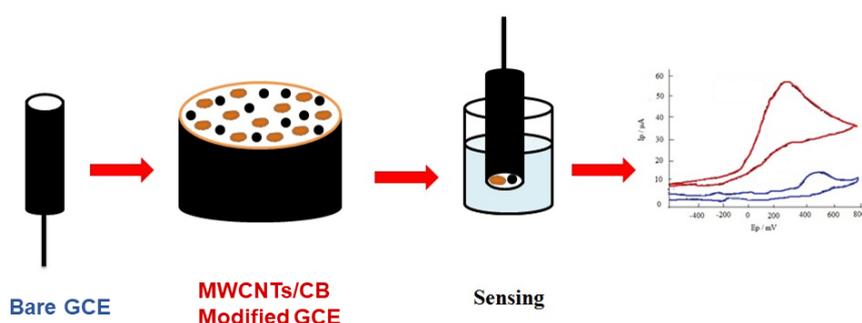
ARTICLE

Voltammetric Assessment of 8-Oxoguanine at a Nano-Structured Carbon Materials Based Modified Glassy Carbon Electrode

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In this study, we have investigated the voltammetric behavior of 8-Oxoguanine on a Multi walled carbon nanotubes / Carbon black modified glassy carbon electrode. The voltammetric oxidation of 8-Oxoguanine on modified electrode was electro-catalytic in nature. The voltammetric oxidation of the substrate was a pH dependent

reversible process. Using cyclic voltammetry, a method for the determination of 8-Oxoguanine was developed. At a pH of 7.4 in phosphate buffer solution, the concentration of 8-Oxoguanine was linear from 30 to 100 μM . The detection limit and quantification limit of 8.38 μM and 27.95 μM were obtained from calibration graph, respectively. The modified electrode shows good recovery and reproducibility with relative standard deviation of 2.12%. The inter-day and intra-day assays were also studied.

Keywords: DNA damage, 8-Oxoguanine, voltammetry, modified electrode, nanomaterials

INTRODUCTION

Some of the genetic diseases like tumors were caused by the damage of DNA. One has to investigate the mechanism with which the diseases occur once the damage of DNA happens that causes genetic information change, so that we can find the root cause and prevention measures of these diseases. Therefore, it is very much needed to develop methods for the analysis of damaged DNA molecules which will act as tools for these types of investigations. The main challenge is that, in presence of large quantities of normal bases, it is very difficult to analyze adducts which are present in very low amounts. Very high amount of 8-Oxoguanine were detected in the tissues of urine and lungs of smokers,¹ also in patients body fluid suffering from cancer, chronic hepatitis, diabetes, and deceases related to aging.² Therefore, the method developed to detect them should be highly sensitive and selective in nature.

Cite: Hegde, R. N.; Vishwanatha, P.; Nandibewoor, S. T. Voltammetric Assessment of 8-Oxoguanine at a Nano-Structured Carbon Materials Based Modified Glassy Carbon Electrode. *Braz. J. Anal. Chem.*, 2022, 9 (37), pp 84-93. <http://dx.doi.org/10.30744/brjac.2179-3425.AR-20-2022>

Submitted 21 March 2022, Resubmitted 26 May 2022, Accepted 09 June 2022, Available online 27 June 2022.

One of the major common DNA lesions obtained from reactive oxygen species is 8-Oxoguanine whose structural formula is shown in Figure 1. There were many reports on the detection of 8-Oxoguanine using conventional methods such as high performance liquid chromatography with electrochemical detection^{3,4,5} and gas chromatography with mass spectroscopy.^{6,7}

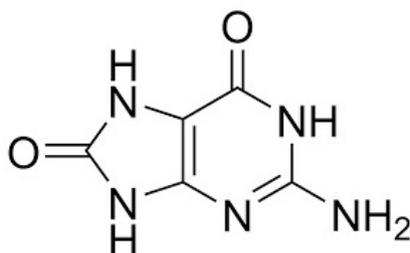


Figure 1. Structure of 8-Oxoguanine.

Electrochemical sensors are becoming a very attractive method to monitor concentration of many drug molecules in analytical field. The remarkable significance of nanomaterials and nanoparticles in recent years has attracted many researchers in the area of developing sensors.^{8,9,10} Especially, nanomaterials synthesized from carbon have attracted many research scientists after their discovery. Among them, carbon nanotubes, fullerenes, graphene and carbon dots have gained much attention in the field of development of electrochemical sensors for detection of variety of molecules. Carbon nanotubes are one-dimensional nanomaterials of hollow tubular shape consisting of carbon atoms in hexagonal shape.¹¹ Based on arrangements of the graphene cylinders in them, carbon nanotubes were classified into single walled carbon nanotubes (SWCNTs) and multi walled carbon nanotubes (MWCNTs). Even though both show electrochemical properties like conductivity,¹² catalytic activity,¹³ stability¹⁴ and biocompatibility,¹⁵ multi walled carbon nanotubes are extremely active than the single walled carbon nanotubes since earlier one contains hole-like defects during its formation. Carbon black (CB), a nanomaterial having low cost shows excellent electrochemical properties. Because of the presence of defective sites, it can also be a good choice for the development of electrochemical sensors.¹⁶ Because of all these properties, we have tried to develop a voltammetric sensor for the detection of 8-Oxoguanine.

There are few reports on electrochemical oxidation and determination of 8-Oxoguanine. In the year 2000, there was an attempt to study the electrochemical oxidation on a glassy carbon electrode.¹⁷ There was a method described for detection of 8-Oxoguanine along with uric acid.¹⁸ The differential pulse voltammetry was used in a wide pH range. The gold electrode was used by Ferapontova to study electrochemistry of guanine and 8-Oxoguanine.¹⁹ They used cyclic voltammetry for the kinetic analysis of oxidation and found that it was a quasi-reversible in nature. There were use of pretreated boron doped diamond electrodes,²⁰ screen printed electrodes,²¹ edge plane pyrolytic graphite electrode modified with SWCNTs,²² edge plane pyrolytic graphite electrode modified with SWCNTs and AuNPs,²³ SWCNTs modified GCE,²⁴ MWCNTs modified GCE,²⁵ rGO-MWCNTs modified GCE,²⁶ sulphur doped rGO modified GCE,²⁷ PtNF-GO modified GCE,²⁸ and screen-printed carbon electrodes modified with carboxy-functionalized multi walled carbon nanotubes²⁹ were also used for the voltammetric study. Recently there was a comprehensive review on sensing of 8-Oxoguanine.³⁰ But the voltammetric behavior of 8-Oxoguanine was not reported yet on a glassy carbon electrode modified with multi walled carbon nano tubes / carbon black. Therefore, we have undertaken the title study since there is a scope for construction of new nano-composite electrodes and use them to determine 8-Oxoguanine.

MATERIALS AND METHODS

Chemicals

All chemicals used are of analytical grade. Multi-walled carbon nanotubes (O.D. x L of 7-15 nm x 0.5-10 μm), 8-Oxoguanine (in amber glass vial) and Carbon black (CB) were obtained from Sigma-Aldrich. The required amount of the substrate was weighed accurately to prepare stock solution and nitrogen gas was flushed gently to remove any oxygen so that premature oxidation of 8-Oxoguanine can be avoided. 0.1 M monobasic sodium phosphate and 0.1 M dibasic sodium phosphate trihydrate were employed to obtain the phosphate buffer solutions (PBS). Doubly distilled water was used to prepare all the solutions which are used in this study.

Instrumentation

Voltammetric runs were recorded on a MARUTEK Potentiostat (Bangalore, India), which has a usual three-electrode cell. Three electrodes were used in the cell: a glassy carbon electrode (unmodified and modified) acting as a working electrode, a Pt wire acting as a counter and a Ag/AgCl serving as a reference electrode. All the potentials in this paper were recorded and given against the Ag/AgCl reference electrode (3 M KCl). The pH of the solutions employed were determined using a pH meter.

MWCNTs/CB modified electrode preparation

2 mg of MWCNTs and CB each was dispersed in 10 mL acetonitrile and agitated in an ultrasonicator to get a stable suspension of MWCNTs/CB. On a polishing cloth, the GCE (unmodified and modified) was polished carefully using α -alumina slurry, and subsequently washed thoroughly with distilled water. Thus, obtained clean GCE was drop coated with 5 μL of MWCNTs/CB suspension already prepared and dried in open atmosphere.

By employing $\text{K}_3\text{Fe}(\text{CN})_6$ (1.0 mM) as a redox probe at different scan rates, the electroactive surface area of bare and modified GCE were computed. The Randles–Sevcik equation for a reversible process was used:

$$I_p = (2.69 \times 10^5) n^{3/2} A D_R^{1/2} C_0 \nu^{1/2} \quad \text{Randles–Sevcik equation}$$

where I_p is the anodic peak current, n is the number of electrons transferred, A is the electrode surface area, D_R is diffusion coefficient, ν is the scan rate and C_0 is the concentration of $\text{K}_3\text{Fe}(\text{CN})_6$.

The values of n and D are 1 and $7.6 \times 10^{-6} \text{ cm}^2 \text{ s}^{-1}$ for 1.0 mM $\text{K}_3\text{Fe}(\text{CN})_6$ with 0.1 M KCl as electrolyte. Using slope of the graph of I_p against $\nu^{1/2}$, the electroactive areas of bare and modified electrodes were computed. For the modified electrode, the area was 0.1424 cm^2 and for bare electrode, 0.04326 cm^2 . From this, we can conclude that the electroactive area has been increased remarkably after modification.

Analytical procedure

The GCE (unmodified and modified) was swept between -600 and 800 mV till stable voltammograms were obtained in PBS (pH 7.4). Then the electrodes were kept in a cell which contains requisite concentration of the substrate and buffer solution. In open circuit, with accumulation time of 300 s and waiting for 20 s, cyclic voltammograms were recorded at a scan rate of 50 mVs^{-1} by sweeping the potential between -600 and 800 mV. All the determinations were recorded at room temperature of $26 \pm 0.2 \text{ }^\circ\text{C}$.

RESULTS AND DISCUSSION

Voltammetric performance of 8-Oxoguanine

Figure 2 shows cyclic voltammograms recorded for 8-Oxoguanine on a bare GCE and GCE modified with MWCNTs/CB. On the bare GCE, oxidation peak was at about 452 mV (Figure 2a), which was a bit weak and broader. On the MWCNTs/CB modified GCE, the oxidation peak was present at about 282 mV

(Figure 2e), which was sharper and stronger than earlier with significant increase in peak current and remarkable decrease in peak potential. The cause for the improved performance of MWCNTs/CB modified GCE may be due to the unique properties of nano-dimensional materials like high aspect ratio, high surface area, and electro-catalytic activity. No oxidation peak was recorded with this modified electrode in buffer solution of pH 7.4, but the background current becomes larger, because the nano-materials used were increasing the surface area.

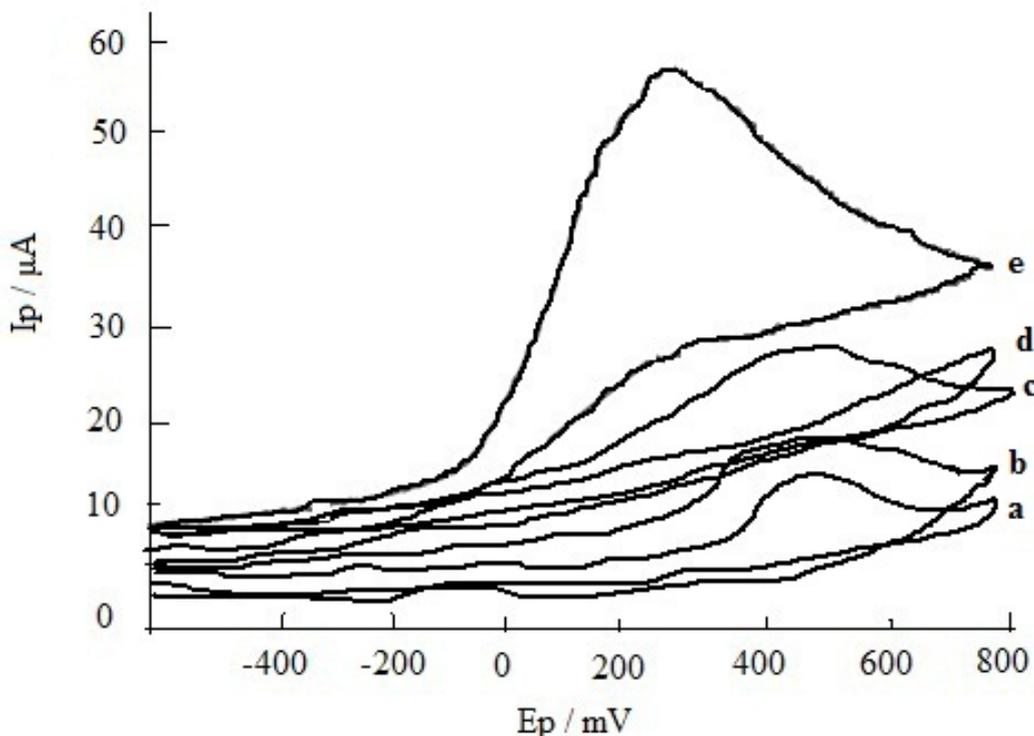


Figure 2. Cyclic voltammogram recorded for 3×10^{-4} M of 8-Oxoguanine at pH 7.4 in 0.1 M PBS (a) at bare GCE, (b) at CB modified GCE, (c) at MWCNTs modified GCE, (e) at MWCNTs/CB modified GCE and (d) Blank CV of MWCNTs/CB modified GCE.

Effect of quantity of MWCNTs/CB

The influence of the amount of MWCNTs/CB on oxidation peak current was studied. Highest peak current was obtained when $5 \mu\text{l}$ of MWCNTs/CB suspension was used for drop coating. But when the amount of suspension is less than $5 \mu\text{l}$, there is little decrease in peak current. This may be due to the fewer amounts of nanomaterials present, which results in the less current. But when suspension volume is more than $5 \mu\text{l}$, the film becomes thick and the conductivity of this film reduces those results in low peak current. Hence, $5 \mu\text{l}$ of MWCNTs/CB suspension was employed in the further investigation.

Effect of pH

The pH of the reaction medium plays vital role especially for the reactions which occur on an electrode. The influence of pH on the peak current of the title reaction was studied using CV. Using PBS, the pH of the reaction medium was altered in the range between 5.8–8.0. The study indicated that, the peak potential was moved to lesser positive values as pH of solution increased. The physiological pH of 7.4 was used for further studies.

Effect of scan rate

From the correlation among the peak current and scan rate, some valuable information can be obtained including the mechanism with which the reaction was occurring. Hence, the effect of scan rate on oxidation of 8-Oxoguanine was investigated at dissimilar scan rates from 10 to 100 mVs^{-1} (Figure 3). The peak current increased linearly with scan rate. The following equation was obtained $I_p = 10.2 v + 14$; $R^2 = 0.997$ as shown in Figure 4 which is the plot of peak current values against the scan rate. There was a linear relationship observed among $\log I_p$ and $\log v$ and the plot yields the equation $\log I_p = 0.505 \log v + 1.309$; $R^2 = 0.985$, whose slope value is near to the theoretical value of 0.5, which indicates electro-oxidation was a diffusion-controlled process¹⁷ (Figure 5). As scan rate was raised, the peak potential values moved to more and more positive values. A linear graph was obtained after plotting peak potential against logarithm of scan rate with following equation $E_p = 224.8 + 19.2 \log v$; $R^2 = 0.997$ (Figure 6).

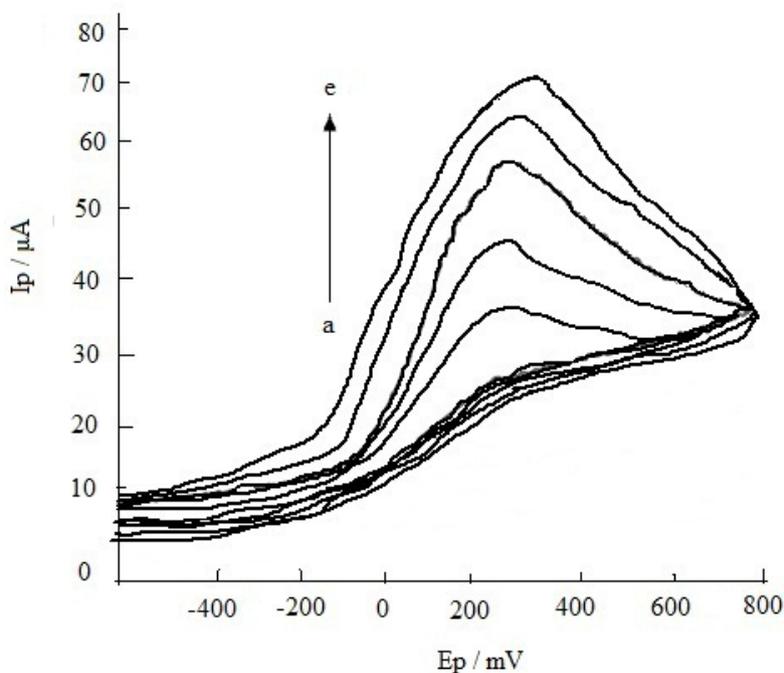


Figure 3. Cyclic voltammograms recorded for 3×10^{-4} M of 8-Oxoguanine at pH 7.4 in 0.1 M PBS with scan rates of (a) 10, (b) 20, (c) 50, (d) 70 and (e) 100 mVs^{-1} at MWCNTs/CB modified GCE.

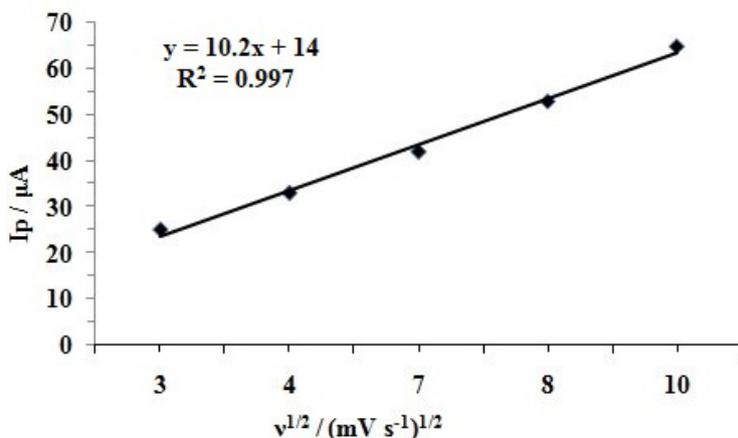


Figure 4. Graph of peak current versus square root of scan rate.

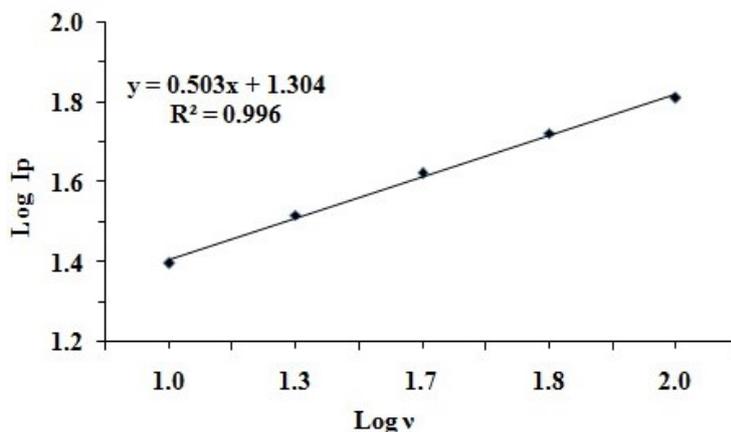


Figure 5. Plot of peak current logarithm to base 10 against scan rate logarithm to base 10.

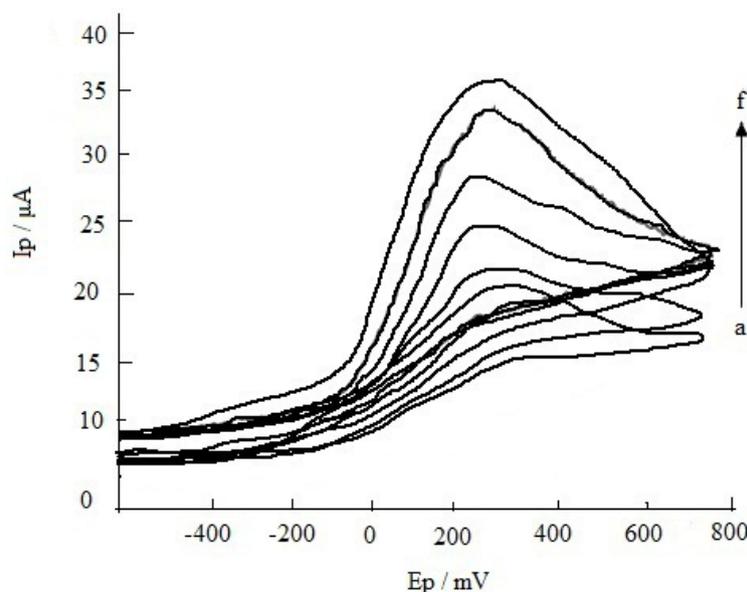


Figure 6. Cyclic voltammograms of 8-Oxoguanine at pH 7.4 in 0.1 M PBS at (a) 30, (b) 40, (c) 50, (d) 70, (e) 85 and (f) 100 μM at MWCNTs/CB modified GCE.

Calibration curve

We tried to develop a voltammetric method for assessment of the drug, for which cyclic voltammetry was used. At a physiological pH of 7.4 in PBS solution, cyclic voltammograms were recorded by increasing the concentration of 8-Oxoguanine. The recorded voltammograms showed that with raise in amount of 8-Oxoguanine, the anodic peak current raised accordingly, which is shown in Figure 6. Using the best possible environment as described above, a calibration graph was obtained for 8-Oxoguanine from 30 to 100 μM (Figure 7). The straight-line equation from calibration graph was $I_p (\mu\text{A}) = 0.266 + 4.4 C$; $R^2 = 0.998$ (C is in μM). It was observed that, divergence from linearity for the solution with higher amount of the substrate, owing to the adsorption of substrate or its product after oxidation at the surface of the electrode. The detection limit and quantification limit obtained were 8.38 μM and 27.95 μM , respectively. The detection limit and quantification limit were calculated by the equations: Detection limit = $3s/m$ and Quantification limit = $10 s/m$. The obtained results were compared with those already reported and were given in Table I.

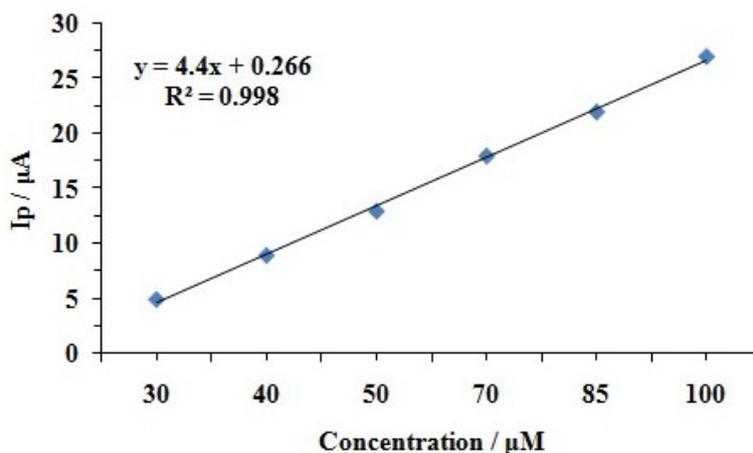


Figure 7. Graph of peak current versus concentration of 8-Oxoguanine.

Table I. Comparison of voltammetric detection of 8-Oxoguanine at carbon electrode modified with various nanomaterials

Electrode	Electrode modifier	Method	Linear range (M)	LOD	Ref.
EPPGE	SWCNTs	SWV	$3 \times 10^{-11} - 7.5 \times 10^{-11}$	1×10^{-11}	22
EPPGE	SWCNTs/AuNPs	SWV	$1 \times 10^{-11} - 1 \times 10^{-8}$	5×10^{-12}	23
GCE	SWCNTs	LSV	$2.9 \times 10^{-9} - 8.7 \times 10^{-5}$	1.0×10^{-9}	24
GCE	MWCNTs	CV	$5.6 \times 10^{-8} - 1.6 \times 10^{-5}$	0.2×10^{-9}	25
GCE	rGO-MWCNTs	SWV	$3-75 \times 10^{-6}$	35×10^{-9}	26
GCE	Sulphur-doped rGO	DPV	$2 \times 10^{-9} - 20$	1×10^{-9}	27
GCE	PtNF-GO	DPV	$0.7 \times 10^{-9} - 2 \times 10^{-6}$	25×10^{-6}	28
SPCE	MWCNTs-COOH	DPV	$0.3 \times 10^{-6} - 2.4 \times 10^{-4}$	0.57×10^{-6}	29
GCE	MWCNTs/CB	CV	$30 \times 10^{-6} - 100 \times 10^{-6}$	8.38×10^{-6}	This work

EPPGE edge plane pyrolytic graphite electrode, SWCNTs single-walled carbon nanotubes, MWCNTs multi-walled carbon nanotubes, AuNPs gold nanoparticles, rGO reduced graphene oxide, GO graphene oxide, SPCE screen-printed carbon electrode, CB carbon black, SWV square wave voltammetry, LSV linear sweep voltammetry, CV cyclic voltammetry, DPV differential pulse voltammetry.

Reproducibility

The reproducibility of the modified electrode was studied as follows. The voltammograms were recorded for 50 μM 8-Oxoguanine using modified electrode which was renewed every time for every numerous hours within a day, and it was found Relative Standard Deviation (RSD) of 2.12% for the peak current for 10 number of measurements. If the temperature was unchanged, then the reproducibility between days was similar to that of within a day. But the electrode has to be modified again after each reading, due to the adsorption of oxidation product.

Intra-day and Inter-day assay

In order to verify the accuracy and precision of the method, the assay of 8-Oxoguanine was done for inter-day and intra-day. This was done at three concentration levels: at high concentration level of 120 μM , medium concentration level of 60 μM and low concentration of 20 μM of 8-Oxoguanine. Voltammograms were recorded once in a day ($n = 5$) during four consecutive days for the inter-day assay and under identical conditions at the same concentrations ($n = 5$) for four times in a day to calculate assay in a day.

The accuracy values obtained for the intra-day assay were 101.68%, 100.23% and 99.84% for high, medium and low concentration levels, respectively (Table II). The average precision values were in the range of 5 to 10% in intra-day as tabulated in Table II. The accuracy values of 100.62%, 99.76% and 101.83% were obtained for high, medium and low concentrations, respectively in a day. In a day, the average precision values were in the range of 4-11% (Table II). The accuracy and precision values obtained were within $\pm 15\%$. Therefore, the obtained values for intra-day and in a day are within acceptable limits.³¹

Table II. Data obtained for the assay of 8-Oxoguanine for intra-day and in a day

Concentration (μM)	Concentration determined (μM)	Recovery (%)	Accuracy (%)	Precision (RSD%)
Intra-day				
120	120.24 \pm 0.31	100.2	101.68	5.43
60	59.87 \pm 0.52	99.7	100.23	10.04
20	20.42 \pm 0.24	102.1	99.84	7.52
Inter-day				
120	120.31 \pm 0.18	100.2	100.62	10.87
60	60.15 \pm 0.09	100.3	99.76	4.13
20	19.74 \pm 0.65	98.7	101.83	6.57

CONCLUSION

In the present effort, a glassy carbon electrode modified using multi-walled carbon nanotubes/carbon black has been effectively constructed to study voltammetric oxidation of 8-Oxoguanine in PBS. The nanomaterials used have shown electro-catalytic activity during electro-oxidation of 8-Oxoguanine, with improvement in the anodic peak current due to the special properties exhibited by the nanomaterials. For the assessment, the anodic peak at about 282 mV was used and the linear range using calibration graph was also determined. This voltammetric sensor can be employed for voltammetric assessment of 8-Oxoguanine with good reproducibility and recovery. This work adds a new modified electrode to voltammetric field.

Conflicts of interest

The authors declare that there is no conflict of interest.

Acknowledgments

The authors are grateful to the Karnataka Science and Technology Academy, Government of Karnataka, Bengaluru, India, for the financial support.

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