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Original Article

Characterization of Enzymatic Glucose Biosensors Based on A Glassy Carbon Electrode Modified with MoS_2 Nanorods

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Abstract: In this work, molybdenum disulfide (MoS_2) nanorods (NRs) were prepared by a simple hydrothermal method. A sensitive electrochemical glucose biosensor was developed based on the immobilization of glucose oxidase (GOx) on MoS_2 NRs modified glassy carbon electrode (GCE). The SnO_2 NRs were characterized by X-ray diffraction (XRD), scanning electron microscopy (SEM), transmission electron microscopy (TEM), and energy dispersive X-ray spectroscopy (EDS). SnO_2 NRs have large specific area and can load large amounts of GOx molecules. The cyclic voltammetry (CV) of GOx/MoS_2 NR/GCE exhibited a linear relationship between the peak current density of CV with glucose concentration in the range of 3.0 mM to 7.0 mM with the limit of detection (LOD) of 3.0 mM and high sensitivity of 5.46×10^{-4} mA.mM. The parameters affecting the oxidation current density such as pH, temperature, GOx concentration were also investigated. This study demonstrates the feasibility of realizing inexpensive, reliable, and highly effective performance glucose biosensors using MoS_2 nanorods.

Keywords: MoS_2 nanorods, biosensor, glucose, enzyme, electrochemical signal.

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1. Introduction

The measurement of glucose is very important in textile industry, food analysis, environmental monitoring, and medical diagnosis, especially early diagnosis of diabetes in human [1]. Since the first report on the enzyme electrode in 1962 [2], the research field of electrochemical glucose biosensor has grown and developed remarkably due to its high sensitivity, fast analysis speed, high selectivity, easy operation and low cost [3]. Glucose oxidase (GOx) can identify glucose molecules quickly and accurately even in complicated system [4]. Blood glucose level has been determined by electrochemical biosensors, especially enzyme-based amperometric glucose biosensor [5]. It is proved that modification of electrode with nanomaterials is an effective method to overcome the long distance between the redox-active cofactor and the electrode surface [6] and to lower the oxidation/reduction voltage of H_2O_2 liberated enzymatically at the solid electrode [7]. Many kinds of nanomaterials have been used to promote the electron transfer between the enzyme and the electrode, including zinc oxide (ZnO) nanostructures [8-10], Co_3O_4 nanoparticles [11], graphene [12], graphene/Fe_2O_3 [13], gold nanoparticles [14, 15], silver nanoparticles [16], copper oxide (CuO) [17], carbon nanotubes [18], etc. They can improve the immobilization process between the enzyme and the electrode or the electrocatalytic activity towards glucose. Nanostructures establish an electrical connectors between the electrode and the redox center which improve electron transfer [19, 20]. These pioneering studies of Willner group motivated the using nanostructures as the components of biosensors [1, 21, 22]. In amperometric glucose biosensor, glucose oxidase (GOx) was immobilized between two membrane layers, so that only glucose molecules reached the enzyme layer. Glucose was oxidized in the presence of glucose oxidase to become gluconic acid and by-product hydrogen peroxide [21]:

$$C_6H_{12}O_6 + O_2 + H_2O \xrightarrow{\text{Glucose oxidase}} C_6H_{12}O_7 + H_2O_2 \quad (1)$$

An enzyme electrode for glucose determination is based on the detection of liberated hydrogen peroxide during the enzymatic reaction.

$$H_2O_2 \rightarrow O_2 + 2H^+ + 2e^- \quad (2)$$

Hydrogen peroxide (H_2O_2) was decomposed into oxygen and amperometrically detected at the glassy carbon electrode surface. The glucose can be determined by monitoring the oxidation current at constant potential [1].

In 2015, Wu et al., transferred nanoporous gold onto a clean glassy carbon electrode surface (GCE) and later immersed into glucose oxidase (GOx) solution for enzyme immobilization which provided a good interface between the enzyme and the GCE. The resulting GOx/Au/GCE could detect the low concentration of glucose (1.02 μM) [23]. In 2017, Parlak et al., synthesized Au nanoparticles (5 nm diameter) on two-dimensional MoS_2 nanosheets then mixed with glucose oxidase enzyme for electrochemical glucose biosensors [24]. Two-dimensional MoS_2 have been also used for the immobilization of other biomolecules such as carcinoembryonic antigen (CEA) [25], hepatitis B e antigen (HBeAg) [26], MicroRNA (miRNA) [27], etc. The recent literatures of enzymatic glucose biosensors based on different nanostructures such as zinc oxide nanoparticles on graphene – carbon nanotube [28], graphene – polyethyleneimine – gold nanoparticles [29], Fe_3O_4 nanoparticles – polyvinyl alcohol composite [30], Au-Ni coaxial nanorod array [31], chitosan-reduded graphene oxide-Au nanoparticles hybrid [32], Au/MoS_2 nanofilm [33], MnO_2 nanowires [1], graphene/Fe_2O_3 nanowires [13] and so on have been reported. Glucose sensors based on metals or metal oxide nanostructures offer enhanced electroactive surface area and superior sensitivity [21].

The bulk MoS_2 is a semiconducting material with indirect bandgap of 1.2 eV [34] and has wide applications in electronics, optics, mechanics and electrochemistry [35-38]. Over the last decade, MoS_2

has gained great attention in biosensing field due to its promising properties such as chemical stability, high electrocatalytic activity, high surface to volume ratio, nontoxicity, biocompatibility and simple fabrication [22, 33, 39-42]. Various shaped MoS_2 nanostructures, such as flower [42, 43], nanosheet [24, 44, 45], nanorod [46], nanocube [38], nanowire [47] and nanoparticle [37] have been fabricated using physical and chemical methods. Up to now, many studies on different MoS_2 nanostructures for determination of glucose have been published [24, 33, 40-42]. It has been well demonstrated that morphology and size of nanostructures also play an important role in the property of the glucose biosensor [38, 47]. Two-dimensional (2D) layered MoS_2 has been widely employed as biosensor due to its high specific surface area, good biocompatibility, structural stability and large junction area with electrode for enzyme immobilization [42, 48-50]. To our best knowledge, MoS_2 nanorods based glucose biosensors have not been developed. In fact, MoS_2 nanorods have some unique properties comparing to other nanostructures such as nanosheets, nanocubes, quantum dots, nanoparticles. Nanorods facilitate the charge transport along one-dimensional electronic pathway and the diffusion of electrolyte through the space between neighboring nanorods. The biomolecules can stabilize their binding with the nanorods used as the electrode materials [51, 52].

In this work, MoS_2 nanorods were synthesized by a simple hydrothermal route from Na_2MoO_4, $H_4W_{12}SiO_{40}$ and C_2H_5NS. Then MoS_2 NRs were exploited to modify glassy carbon electrode for the immobilization of enzyme to measure glucose. The large surface area of MoS_2 NRs facilitates the electron transfer from electrode surface to glucose oxidase (GOx). The cyclic voltammetry (CV) technique was used to investigate the performance of the built biosensor. The obtained results showed a promising electrode material for the fabrication of excellent glucose biosensor in clinical diagnostics.

2. Experimental

2.1. Chemical Reagents

Potassium hexacyanoferrate (III) $K_3Fe(CN)_6$, phosphate buffer saline (PBS, 0.1 M, pH 7), absolute ethanol (C_2H_5OH), acetone (CH_3COCH_3), glucose ($C_6H_{12}O_6$) were purchased from Beijing Chemical Reagent (China). Molybdic acid sodium salt dehydrates ($Na_2MoO_4.2H_2O$), thioacetamide (C_2H_5NS), silicotungstic acid ($H_4W_{12}SiO_{40}$), glucose oxidase (GOx) were supplied by Sigma Aldrich. All reagents in this work were of analytical grade and applied as received without further refinement. Deionized water (DI) was used to prepare all aqueous solutions and clean glassware.

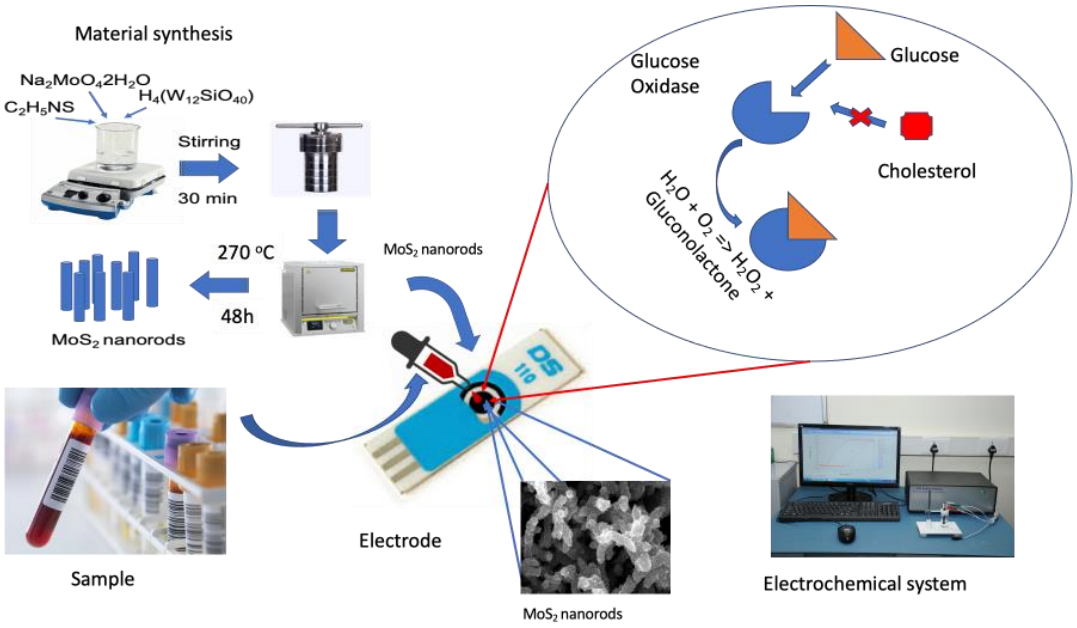
2.2. MoS_2 Nanorods Synthesis

3 mM Na_2MoO_4, 2 mM $H_4W_{12}SiO_{40}$ and 5 mM C_2H_5NS were formulated into a 30 ml of distilled water under magnetic stirring for 30 minutes to form a homogeneous solution that was transferred into a Teflon-lined stainless-steel autoclave of 80% capacity of the total volume. The autoclave was sealed and heated at 270 °C for 48 h. After cooling down to room temperature naturally, the precipitate was filtered and washed with deionized water and ethanol several times to remove ions remained in the final product, and finally it was dried in a vacuum oven at 60 °C for 4 h.

2.3. Preparation of the Modified Electrode

The glassy carbon electrode (GCE) was used as working electrode in the biosensors. The dispersed MoS_2 nanorods on the electrode were prepared as follows: 2 mg of the obtained MoS_2 nanorods powder was added to 1 ml of acetone for 3 h at room temperature to form a homogeneous dispersion in an

ultrasonic bath. The enzyme solution was prepared by dissolving GOx (15 mg/ml) in PBS solution (0.1 M, pH 7). 10 μl of GOx solution was dissolved in 100 μl MoS_2/acetone solution. Subsequently, the prepared material was dropped onto the working area of GCE, then, 5 μl of glutaraldehyde was piped onto cross linking of matrix for 6 h. Finally, the electrode was washed with DI water several times to remove unimmobilized enzyme. The modified electrode was noted as GOx/MoS_2-NR/GCE which was stored at 4 °C in dry condition until use. The schematic of glucose biosensor fabrication is illustrated in Scheme 1.



Scheme 1. The schematic drawing of glucose biosensor fabrication.

2.4. Instrumentation

The morphology of MoS_2 nanorods was observed through scanning electron microscopy (SEM, Hitachi S4800) operated at 5 kV and transmission electron microscope (TEM, JEOL JEM-2100) with a working voltage of 200 kV. The crystalline structure was analyzed by an X-ray diffractometer (XRD, Bruker D8 Advance) with Cu-K_α radiation (wavelength of 0.15418 nm), employing a scanning rate of 0.02°/s and 2θ range from 10 to 70°. The elemental composition of MoS_2 was investigated by using energy dispersive X-ray spectroscopy (EDS) in a Hitachi SU 8020 at an accelerating voltage of 200 kV.

2.5. Electrochemical Measurements for GOx/MoS_2-NR/GCE

Electrochemical experiments were carried out on an IM6-impedance analyzer in PBS solution containing 5 mM $K_3Fe(CN)_6$ as a redox probe using a conventional three-electrode cell. The GOx/MoS_2-NR/electrode was connected to the test and sense probes. The counter electrode and reference electrode were a platinum wire and Ag/AgCl, respectively. The working potential ranges from – 1.0 V to 0.0 V with a scanning rate of 100 mV/s. The difference in the current density was considered as the signal produced by the interaction between GOx and glucose.

3. Results and Discussion

3.1. Characterizations

The morphology of MoS_2 was characterized by SEM image as displayed in Fig. 1a. As can be observed, the obtained MoS_2 displays nanorod-shaped structure and uniform appearance with the diameter of about 100 nm and the length of about 500 nm, which consist of many small particles agglomerated on the surface. This structure could offer a large specific surface area resulting to a big number of immobilization positions and reaction sites for glucose molecules. After the immobilization of GOx on MoS_2 modified electrode, the TEM image of GOx/MoS_2 (Fig. 1c) shows the different morphology in comparison with single MoS_2 nanorods, which indicates the successful modification of GOx on the surface of MoS_2 nanorods. It can be seen that no other elements existed in EDS spectroscopy (Fig. 1b) except Mo and S elements. Additionally, the peaks quantification indicated the atomic ratio of S/Mo was appropriately 1.68, which was close to stoichiometric MoS_2.

A typical XRD pattern of the as-synthesized MoS_2 nanorods was shown in Fig. 1d determining the phase structure of the MoS_2. It was observed that all the diffraction peaks at 2θ value of 14.2°, 33°, 39.9°, 59.1° and 62.1° are ascribed to (002), (100), (103), (110) and (008) planes of MoS_2 which can be exactly indexed to the hexagonal phase (JCPDS card No. 37-1492). The diffraction intensity of samples is sharp, which indicated that the hexagonal MoS_2 with a large crystallinity was formed.

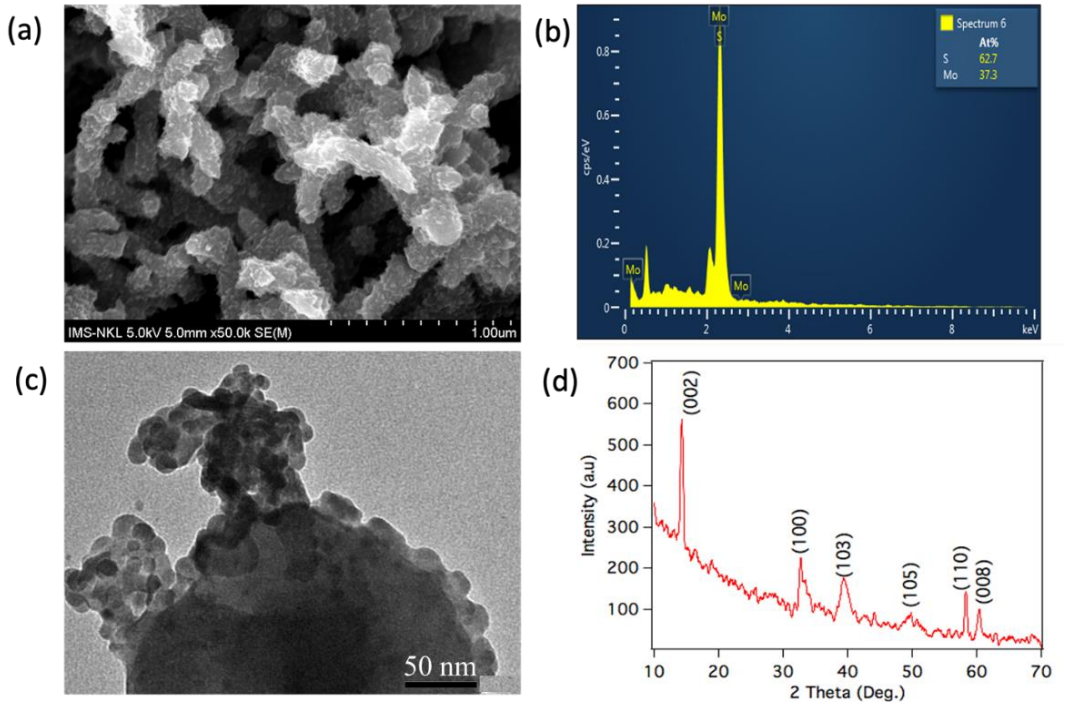


Figure 1. (a) SEM image, (b) EDS spectrum, (c) TEM image, (d) XRD pattern of MoS_2 NR.

3.2. Electrochemical Behaviors of the Fabricated Glucose Biosensor

Fig. 2 shows the CVs of modified electrodes in phosphate buffer saline (PBS, 0.1 M, pH 7) with and without glucose in potential ranging from - 1.0 V to + 0.0 V at a scan rate of 100 mV/s. The CV curves

show a pair of weak and well-defined redox peaks at -0.4 and -0.2 V, indicating that MoS_2 effectively facilitate direct electron transfer of GOx and electrode surface, which may result from large specific surface of MoS_2 nanorods. It is noticeable that the MoS_2-NR/GCE (Fig. 2b) displayed lower oxidation current peak than that of bare GCE (Fig. 2a). Because the MoS_2 surface contains excess negative charges that pushed the negatively charged redox species away from the electrode and resulted in a decreased current density [53]. When GOx was immobilized on the MoS_2 modified electrode (Fig. 2c), the current density decreased significantly, which could to an extent be attributed to non-conductive property of enzyme that impedes the transfer of electrons of the redox species [1, 12]. Compared to MoS_2-NR/GCE electrode, the cathodic peak of GOx/MoS_2-NR/GCE moved to a more positive potential and the anodic peak moved to a more negative potential and, which indicated a quasi-reversible electrochemical reaction process. The electrochemical reaction at GOx/MoS_2-NR/GCE was a typical diffusion-controlled electron-transfer process. The obtained results indicated that GOx was attached successfully onto MoS_2 modified glassy carbon electrode.

Furthermore, to evaluate the sensing performance of bioelectrode, the electroanalytical characterization of GOx/MoS_2-NR/GCE was studied by immersing of electrode in cell containing 0.1M PBS solution with presence of 3.0 mM glucose. As presented in Fig. 2d, upon the addition of 3.0 mM glucose, oxidation peak current density increased compared to one in the absence of glucose. This can be explained as following:

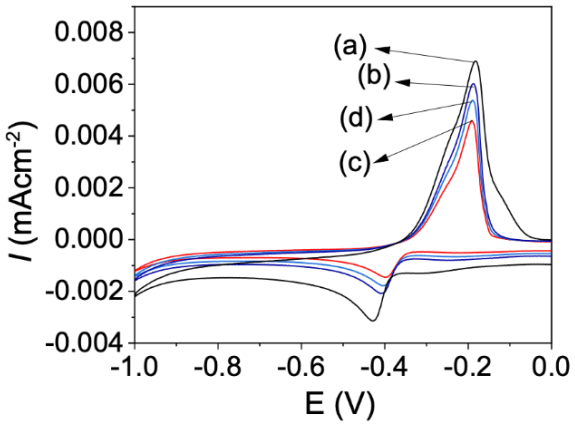


Figure 2. Cyclic voltammogram of (a) bare GCE, (b) MoS_2-NR/GCE, (c) GOx/MoS_2-NR/GCE, (d) GOx/MoS_2-NR/GCE in 0.1 M PBS (pH 7) containing 3.0 mM glucose at a scan rate of 100 mV/s.

When immersing GOx/MoS_2-NR/GCE in PBS solution containing glucose, the biocatalytic reaction between GOx and glucose happened, leading to the reduction of GOx(FAD) to GOx(FADH2) [10] (Eq. 3):

$$\mathrm{GOx(FAD)} + \mathrm{Glucose} \rightarrow \mathrm{GOx(FADH2)} + \mathrm{gluconoloactone} \quad (3)$$

where FAD is flavin adenine dinucleotide. Then, flavin reoxidation combines with dissolved oxygen to produce flavin oxidase and release electrons [9], which results in the increase of oxidation current (Eq. 4):

$$\mathrm{GOx(FADH2)} + \mathrm{O_2} \rightarrow \mathrm{GOx(FAD)} + 2\mathrm{H^+} + 2\mathrm{e^-} \quad (4)$$

CV curves of GOx/MoS_2-NR/GCE used to determine glucose at different concentrations from 3.0 mM to 7.0 mM in phosphate buffer saline (0.1 M, pH 7) at a scan rate of 100 mV/s is illustrated in

Fig. 3a. It was observed that the electrocatalytic current increased proportionally with increasing concentration of glucose.

Fig. 3b shows that the current responses of GOx/MoS_2-NR/GCE increases linearly with the increase of glucose concentration ranging from 3 to 7 mM. The linear regression equation was $I = 0.004 + 5.46 \times 10^{-4} C$, where *I* represents the peak current density of CV (mA/cm^2) and C represents the concentration of glucose (mM). The relation coefficient of 0.9946, a sensitivity of 5.46×10^{-4} mA.mM and a detection limit of 3.0 mM were calculated from the slope of the calibration curve. The GOx/MoS_2-NR/GCE demonstrated much higher sensitivity and wider linear range comparing with other nanomaterials based biosensor reported previously [7, 9].

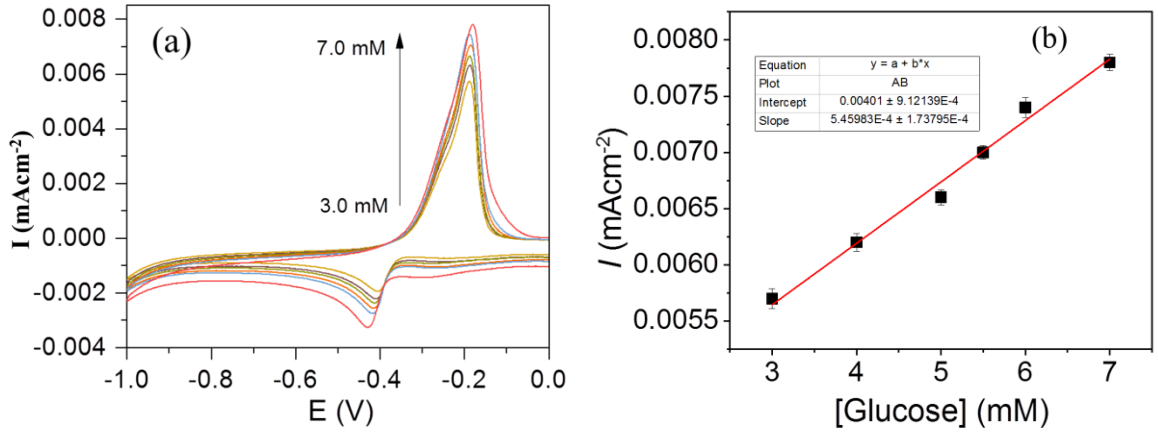


Figure 3. (a) Cyclic voltammogram curves of GOx/MoS_2-NR/GCE biosensor in 0.1 M phosphate buffer saline (pH 7) with different glucose concentrations from 3.0 to 7.0 mM at a scan rate of 100 mV/s; (b) The calibration curve of CV peaks against concentration of glucose.

3.3. Optimization of the Parameters for Glucose Biosensor Performance

The influence of the pH value on the electrochemical behavior of the GOx/MoS_2 NR/GCE was examined in Fig. 4a. The voltammetric behavior of GOx/MoS_2-NR/GCE toward 3.0 mM glucose was investigated in the pH range between 3.0 and 12.0. When the pH value increases from 3 to 7, the oxidation currents increased and reached the maximum value at pH 7.0. Further increasing of pH values resulted in the decrease in the oxidation currents, suggesting the optimal solution pH for the immobilization of GOx. The decrease in current response at higher pH value is possible due to decreased bioactivity of the loaded enzyme molecules [8]. Therefore, pH 7.0 was chosen as the optimal pH value for subsequent measurements in 0.1 M phosphate buffer saline.

Effect of the amount of GOx enzyme on surface of electrode on oxidation current response was also studied in this work. Amount of enzyme was changed from 1.0 mg/ml to 8.0 mg/ml. As illustrated in Fig. 4b, electrode response increased from 6.3 to 8.7 μA/cm^2 when the enzyme concentration increased from 1.0 to 5.0 mg/ml because number of free glucose molecules catalyzed by GOx was raised. Further increase in GOx concentration decreased the oxidation current response because the enzymatic molecules did not take part in glucose oxidation process [54].

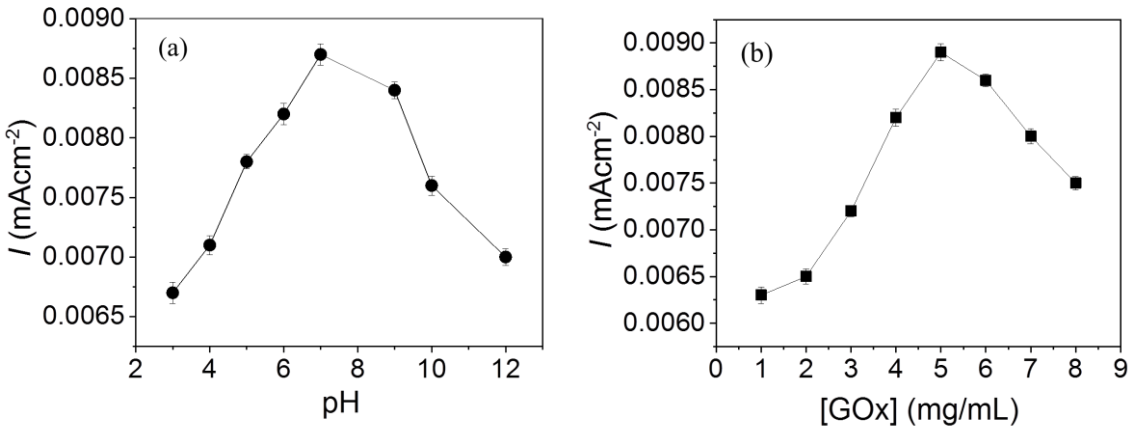


Figure 4. (a) The plot of the oxidation peak current against the pH in PBS solution containing 3.0 mM glucose at scan rate 100 mV/s; (b) Effect of GOx concentration from 1 to 8 mg/ml on the oxidation current response at scan rate of 100 mV/s.

Effecting of temperature on the oxidation current response was investigated in range of 25-60 °C as illustrated in Fig. 5. Oxidation current density gradually increased with the temperature increment from 25 to 45 °C due to the enhanced enzyme activity, then decreased at higher temperature because the enzyme transformed and lost its activity [4, 5]. Obviously, MoS_2 nanostructure greatly promoted the direct electron transfer between GOx and electrode surface, thus showed better performance with high sensitivity in comparison with other types of glucose biosensors reported in recent literatures [13, 28, 55].

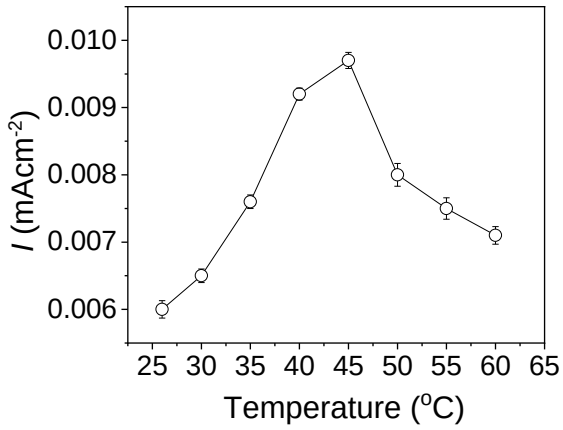


Figure 5. Effect of temperature on the oxidation current density at scan rate of 100 mV/s.

4. Conclusion

In summary, MoS_2 nanorods based biosensors have been developed for glucose detection. The obtained results showed that GOx/MoS_2-NR/GCE electrodes have enhanced the performance of glucose biosensor. These electrodes exhibited a linear range of 3.0 – 7.0 μM and the detection limit of 3.0 μM

which was ascribed to the large surface area of MoS_2 nanorods and catalytic effect of GOx. The excellent performance of GOx/MoS_2-NR/GCE endows it to be a promising biosensor for glucose detection.

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