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Highly sensitive and selective enzyme-free amperometric glucose sensor using a composite from multi-walled carbon nanotubes and cobalt phthalocyanine

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In the present work, a simple and sensitive amperometric enzyme-free glucose sensor was developed at multiwalled carbon nanotubes and cobalt phthalocyanine (MWCNT–CoTsPc) modified electrode. The morphology of the fabricated composite was characterized and confirmed by transmission electron microscopy and UV-Vis spectroscopy. The UV-Vis spectroscopy results confirmed that the MWCNT–CoTsPc composite formed via the strong π–π interaction between CoTsPc and MWCNT. Compared with pristine CoTsPc, the MWCNT–CoTsPc composite modified electrode showed a higher electrocatalytic activity and lower overpotential towards the oxidation of glucose. Amperometric *i-t* technique was used for the determination of glucose. The response of glucose was linear over the concentration ranging from 10 μM to 6.34 mM with the sensitivity of 122.5 μA $mM^{-1}cm^{-2}$. The response time of the sensor was found as 2 s with a limit of detection of 0.14 μM (S/N=3). The fabricated sensor also exhibited its good selectivity in the presence of common interfering species. In addition, the fabricated sensor exhibited its special advantages such as low working potential, good sensitivity along with good repeatability and reproducibility for the determination of glucose.

1. Introduction

Over the past decade, the development of more reliable and sensitive electrochemical sensors for determination of glucose has received much attention owing to its vital role in different areas including clinical diagnostics, fuel cells and food industry[1–7]. The pioneering work of glucose biosensor was proposed by Clark in 1962, the fabrication of electrochemical glucose biosensors using different modifiers has received much attention[8]. The glucose oxidase (GOx) is used as a main electro-catalyst in most of the glucose biosensors due to its high selectivity towards glucose[9]. However, the GOx based glucose biosensors have showed many drawbacks such as short cell lifetime, complicated immobilization procedure, less stable in elevated temperature and pH[10, 11]. To conquer these difficulties, the non-enzymatic or enzyme-free glucose sensors can be used as alternative sensors. Recently, metal nanoparticles, metal oxides and metal alloys have been used extensively for the enzyme-free detection of glucose in alkaline solutions[12–16].Though, these kinds of modified electrodes also showed drawbacks such as low cost and low sensitivity and selectivity[17]. Therefore, the development of a low cost, highly selective, and reliable enzyme-free glucose sensor is still paying much attention in the electroanalytical community.

Over the past two decades, multiwalled carbon nanotubes (MWCNT) has shown a best electrode material in the field of sensor and biosensor application because of its unique mechanical and electronic properties[18, 19]. On the other hand, metallophthalocyanine and metalloporphyrins are belong to the classes of organo-metallic macrocycles, in particular cobalt tetra sulfonated phthalocyanine (CoTsPc) has been well studied and showed an excellent electrocatalytic materials towards several important molecules such as hydrogen peroxide, cysteine, nitrite, nitric oxide and ascorbic acid etc.,[20-21]. Moreover, CoTsPc has also been used as redox mediators for enzyme based glucose sensors[22]. The pristine CoTsPc is not stable on the electrode surface due to their low conductivity along with poor electrochemical activity[23]. Hence the carbon nanomaterials such as single-walled (SWCNTs) or multi-walled carbon nanotubes and graphene have been used with CoTsPc to enhance the electrochemical conductivity and electron transfer of CoTsPc and thus used for many potential applications including electrochemical sensors and biosensors[24–29]. Earlier studies revealed that MWCNTs is an ideal carbon nanomaterial to combine with CoTsPc; more stable on the electrode surface due to the strong π–π interaction between CoTsPc and MWCNTs[30]. The main aim of the present work is utilization of the special properties of the MWCNT–CoTsPc and used as an electro-catalyst for the oxidation of glucose.

In the present work, MWCNT–CoTsPc composite was prepared and applied for the determination of glucose at the first time. It is found that the MWCNT–CoTsPc composite modified electrode showed an excellent electrocatalytic activity towards glucose in alkaline media compared with other modified electrodes (pristine MWCNT and pristine CoTsPc modified electrodes). The fabricated enzyme-free glucose sensor also exhibits its special advantages such as low limit of detection (LOD), wider linear response and fast response for the determination of glucose.

2. Experimental

Materials

MWCNT, CoTsPc and D–Glucose were purchased from Sigma-Aldrich and used as received. The supporting electrolyte used in all the electrochemical studies was 0.1 M NaOH solution, prepared using NaOH with deionised water. Prior to each experiment, all the solutions were deoxygenated with pre-purified N_2 gas for 15 min unless otherwise specified. Double distilled water with conductivity of ≥18 MΩ cm−1 was used for all the experiments. The human blood serum sample was collected from the valley biomedical, Taiwan product & services, Inc. This work was reviewed and approved by the ethics committee of Chang-Gung memorial hospital through the contract no.IRB101-5042A3.

Methods

The electrochemical measurements were carried out using CHI 611A electrochemical work station. Electrochemical studies were performed in a conventional three electrode cell using glassy carbon electrode (GCE) as a working electrode (working area 0.071 cm^2), Ag|AgCl (saturated KCl) as a reference electrode and Pt wire as a counter electrode. Amperometric measurements were performed with analytical rotator AFMSRX (PINE instruments, USA) with a rotating disc electrode (RDE) having working area of 0.24 cm^2. TEM images were taken with JEOL 2000 transmission electron microscope (operating at 200 kV) equipped with an energy dispersive X-ray (EDX) analyzer. UV-Vis spectroscopy studies were performed by U-3300 spectrophotometer. All the electrochemical experiments were performed in deoxygenated 0.1 M NaOH solution.

Preparation of MWCNT-CoTsPc composite modified electrode

For the preparation of MWCNT–CoTsPc composite, the MWCNT (2 mg/mL) and CoTsPc (0.2 mg/mL) aqueous solutions were mixed and ultrsonicated for 3 hours. The resulting residue was washed several times with deionized water to remove the excess of CoTsP*c*. The final composite is denoted as MWCNT-CoTsPc. Prior to modification, the GCE surface was polished with 0.05 µm alumina slurry using a Buehler polishing kit, then washed with deionized water, ultrsonicated for 5 min and allowed to dry at room temperature. Then, about 5 µL of MWCNT–CoTsPc composite was drop casted on the pre-cleaned GCE surface and dried at ambient conditions. The CoTsPc and MWCNT modified GCEs also prepared by the same procedure without MWCNT and CoTsPc.

3. Results and Discussion

Characterization of MWCNT–CoTsPc composite

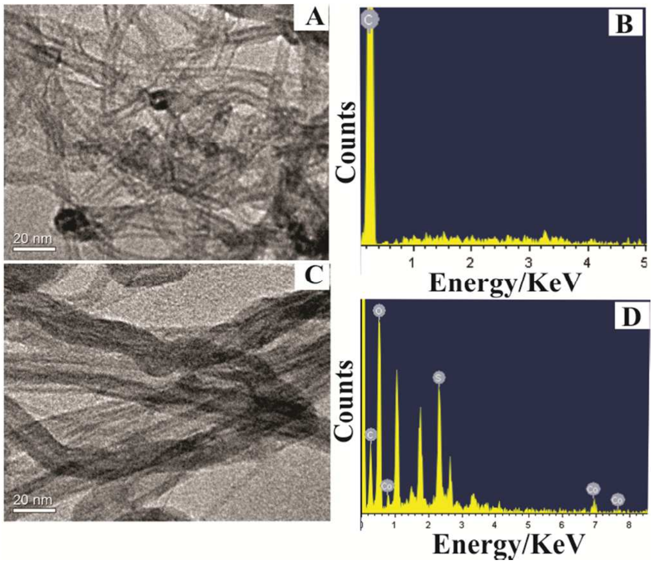

Fig. 1 TEM image of pristine MWCNT (A) and MWCNT–CoTsPc (B). EDX spectra of MWCNT (C) and MWCNT–CoTsPc (D).

TEM image (Fig. 1B) reveals that the CoTsPc is more randomly absorbed onto/into MWCNT networks and the width of the nanotubes before and after the modification with CoTsPc were calculated to be 5 ± 2 and 15 ± 3 nm, respectively. The result reveals that the incorporation of CoTsPc on the MWCNT networks (Fig. 1A). Moreover, the EDX spectrum of MWCNT–CoTsPc (Fig. 1D) portrays the signals for carbon, oxygen, sulphur and cobalt with a weight percentage of 45.95, 35.89, 12.93 and 5.23%, respectively. The EDX spectrum of pristine MWCNT portrays the signal only for carbon and the result confirmed the formation of MWCNT- CoTsPc composite.

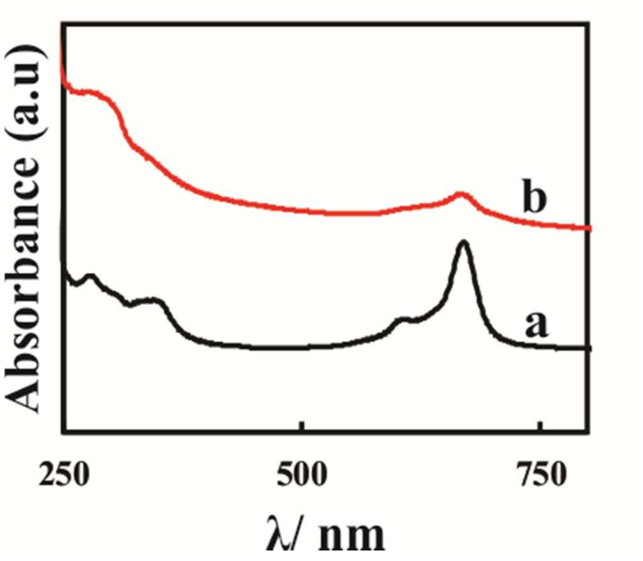

Fig. 2 UV-Visible spectra of CoTsPc (a) and MWCNT–CoTsPc (b).

The UV–Vis spectra used for the confirmation of π–π* interaction between MWCNT and CoTsPc. The **Fig. 2** shows the UV–Vis spectra of CoTsPc (a), MWCNT–CoTsPc (b). The band at 600–710 nm (Q-band) was observed in UV–Vis spectra is due to the allowed π–π* transition for the phthalocyanine. The absorption maxima of pristine CoTsPc is located at 661 and 625 nm. On the other hand, the Q-band of MWCNT–CoTsPc was red shifted (Bathochromic shift) significantly to 654 and 615 nm, due to the electron transfer from the MWCNT to CoTsPc ring. The lowered band gap between highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) is also the possible reason for the red shift of the composite in the UV-Vis spectra.[31] The result reveals the strong intercalation of CoTsPc onto the MWCNT through π–π interaction and resulting in the increase in width of the nanotubes in the composite rather than pristine nanotubes, as supported by the TEM images.

The cyclic voltammetry response of different modified electrodes towards glucose

The cyclic voltammetric response of the different modified electrodes was tested in the presence and absence of glucose in 0.1 M NaOH. Fig. 3 shows the cyclic voltammetric response obtained at GCE electrode modified with CoTsPc (A), MWCNT (B) and MWCNT–CoTsPc (C) in the absence (a) and presence of 1 mM glucose (b) in 0.1 M NaOH at a scan rate of 50 mV s^{-1}. As it can be seen from the Fig. 3C, in the absence of glucose, the MWCNT–CoTsPc modified electrode showed a pair of well-defined redox peak with a formal potential of –0.4789 V and 0.1136 in a NaOH solution, corresponding to Co(I)/Co(II) and Co(II)/Co(III) couples in CoTsPc. Whereas in the presence of 1 mM glucose, a sharp anodic response was observed at an onset potential of 0.178 V along with the Co(II)/Co(III) couples at MWCNT–CoTsPc modified electrode[32]. This is due to the oxidation of glucose to gluconolactone at the modified electrode surface.

On the other hand, CoTsPc and MWCNT modified electrodes showed a broad response to 1 mM glucose with an onset potential of 0.325 and 0.412 V, respectively. The observed current response at the MWCNT–CoTsPc modified electrode for glucose is about 2.8 and 3.6 folds higher than those observed at CoTsPc and MWCNT modified electrodes. Furthermore, the onset potential of MWCNT–CoTsPc modified electrode towards glucose significantly shifted to negative potential (0.198 V) compared with other modified electrodes. The high electrocatalytic activity and lower overpotential of the composite towards glucose is may be due to the strong intercalation of CoTsPc onto/into the MWCNT networks. The results concluded that the MWCNT–CoTsPc composite modified electrode showed a more synergistic effect on the electrocatalytic oxidation to glucose.

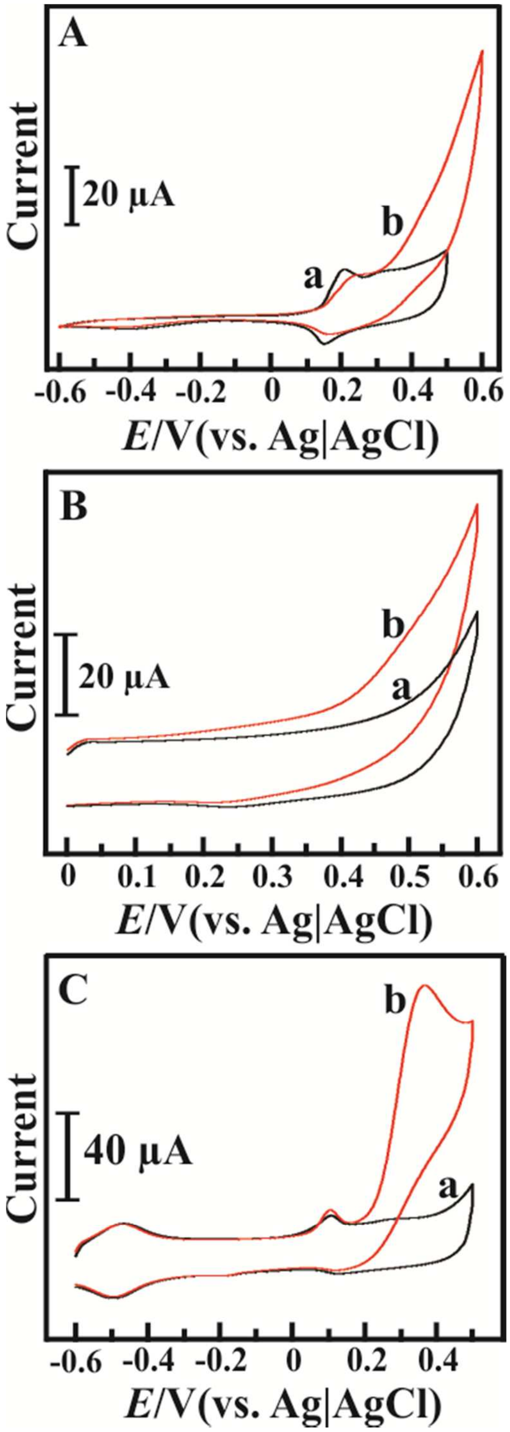

Fig. 3 Cyclic voltammograms obtained at GCE electrode modified with CoTsPc (A), MWCNT (B) and MWCNT–CoTsPc (C) in the absence (a) and presence of 1 mM glucose (b) in 0.1M NaOH at a scan rate of 50 mV s^{-1}.

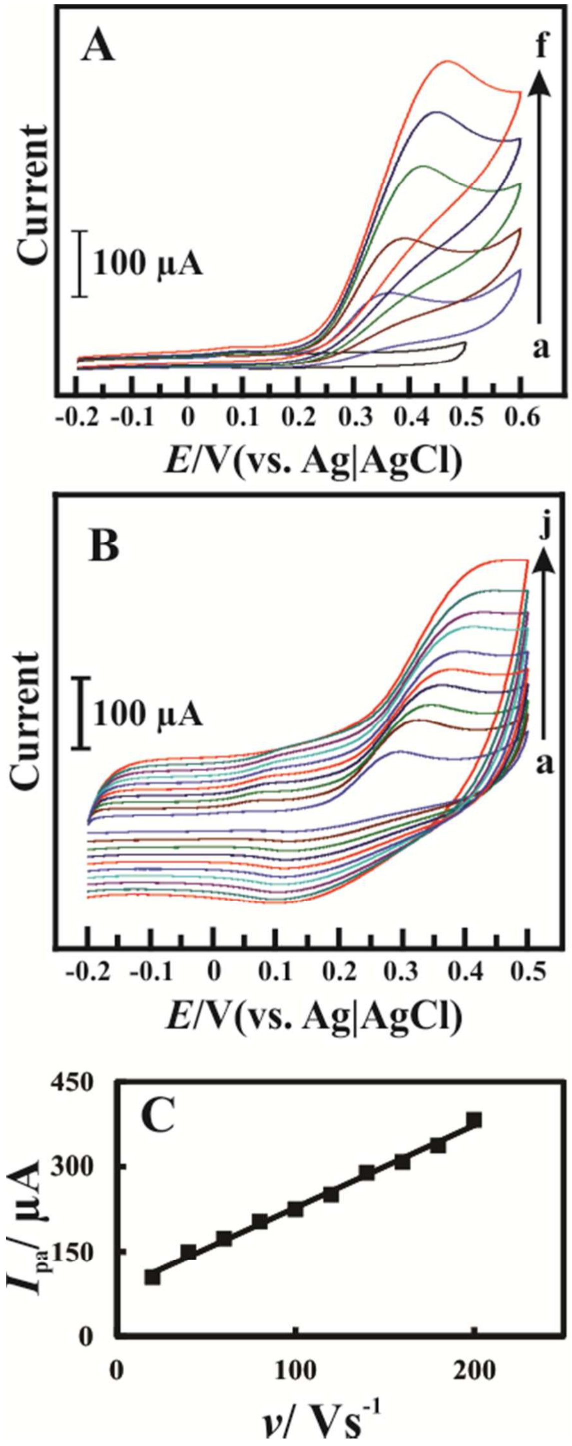

Fig. 4 A) Cyclic voltammograms obtained at MWCNT–CoTsPc/GCE in the absence (a) and presence of each 1 mM glucose addition (b-f) in 0.1M NaOH at a scan rate 50 mV s^{-1}. B) The cyclic voltammetry response of MWCNT–CoTsPc/GCE in 0.1 NaOH containing 1 mM glucose at different scan rates from 0.01 to 0.1 Vs^{-1} (a to j). C) Linear plot for I_{pa} vs. scan rates.

Electro-oxidation of glucose and effect of scan rate

In order to evaluate the electrocatalytic activity of MWCNT–CoTsPc modified GCE towards glucose, the electrochemical oxidation of glucose were carried out by using cyclic voltammetry. Fig. 4A shows the cyclic voltammetry response of MWCNT–CoTsPc modified GCE in the absence (a) and presence of 1–6 mM glucose (b–f) in 0.1 M NaOH. Upon the addition of 1 mM glucose, a sharp oxidation peak was appeared, and further increased with the further addition of glucose. In the absence of glucose, the glucose oxidation peak at 0.4 V does not appear at the composite electrode. Therefore, an increase in anodic peak current at 0.4 V is due to the presence of glucose. The results further confirmed that the MWCNT–CoTsPc modified GCE is a suitable electrode material for the determination of glucose.

The effect of scan rate of the electrocatalytic oxidation of glucose was investigated at MWCNT–CoTsPc modified GCE. Fig. 4B depicts the cyclic voltammetry response of MWCNT–CoTsPc modified GCE in a 0.1 NaOH solution containing 1 mM glucose at different scan rates from 0.01 to 0.1 V s^{-1} (a to j). It can be seen that the anodic peak current response of glucose was found to be proportional to the scan rates from 0.01 to 0.1 V s^{-1} with a correlation coefficient of 0.9944 (Fig. 4C). The result further confirms that the electro-oxidation of glucose at the modified electrode surface is a surface–confined electrochemical process[33].

Amperometric determination of glucose

The effect of the applied potential on the electrocatalytic oxidation of MWCNT–CoTsPc modified electrode to glucose was studied by amperometric *i-t* technique. The electrocatalytic response of the MWCNT–CoTsPc modified electrode was investigated at different applied potentials (0.1–0.3 V) in a 0.1 M NaOH solution containing 100 µM glucose and the results are shown in Fig. 5A. It was found that a sharp and stable amperometric response was observed at 0.3 V and the amperometric signal decrease when the working potential more or less than 0.3 V, hence 0.3 V was chosen as a working potential for the amperometric experiments.

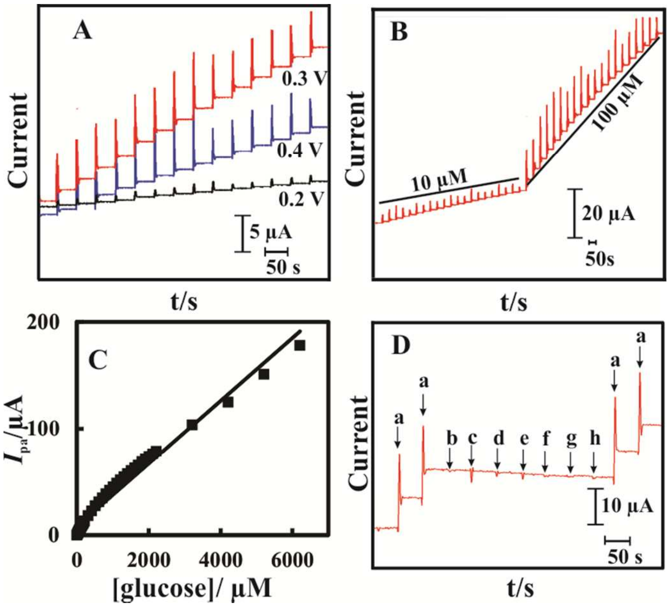

Fig. 5 A) Amperograms obtained at MWCNT–CoTsPc/GCE upon each addition of 100 µM glucose into the constantly stirred 0.1 M NaOH solution at different working potentials. The applied potentials are denoted as; a=0.2 V, b=0.3 V and c=0.4 V. B) An amperometric i-t response of MWCNT–CoTsPc/GCE upon addition of 10 µM and 100 µM glucose into 0.1M NaOH at the applied potential of 0.30 V. C) The corresponding calibration plot for I_{pa} vs. [glucose]. D) In the same conditions, an amperometric i-t response of MWCNT–CoTsPc/GCE upon addition of 1 mM glucose (a) and 0.1 mM concentration of galactose (b), sucrose (c), fructose (c), lactose (d), ascorbic acid (e), uric acid (f) and dopamine (h).

Amperometric technique was further used for the determination of the glucose at the MWCNT–CoTsPc composite modified electrode. Fig. 5B displays the typical amperometric i-t response of MWCNT–CoTsPc composite modified electrode to the successive addition of different concentration glucose into the 0.1 M NaOH solution. The applied potential was held at 0.3 V. It can be seen from Fig. 5B that a well-defined and stable amperometric response was observed for the each addition of 10 µM glucose and it was increased with increase of glucose concentration from 10 to 100 µM. The response time of the sensor was calculated as 2s, which indicates the fast electrocatalytic oxidation of glucose at MWCNT–CoTsPc composite electrode surface. Moreover, the amperometric response current was linear against the concentration glucose in the ranging from 10 µM to 6.34 mM (Fig. 5C). The linear regression equation was found as I_{pa} (µA) = 0.0364x + 9.5473c (µM), $R^2 = 0.9869$. The sensitivity was calculated as 122.5 µA mM^{-1} cm^{-2} with a limit of detection of 0.014 µM (S/N=3). The analytical performances (sensitivity, LOD and applied potential) of our sensors is comparable with previously reported enzyme free glucose sensors using carbon nanotubes, metals and metal nanoparticles modified electrodes and shown in Table 1. The Table 1 is evident that the fabricated MWCNT–CoTsPc glucose sensor exhibits the good performance in more than one category. Furthermore, the fabricated electrode exhibits good linear range and low LOD compared with other previously reported similar glucose sensors.[18, 30–36] However, the sensitivity is quite low compared with metal oxides, alloys and metal hydroxides. The good analytical performance (low detection potential, wider linear response and low LOD) of the MWCNT–CoTsPc modified electrode is owing to the strong π-π stacking interaction between MWCNT and phthalocyanine rings resulting in enhanced electrocatalytic activity towards glucose.

Selectivity of the sensor

The selectivity of the sensor is mandatory in amperometric sensors to further apply for the practical applications. Hence, the electroactive compounds such as dopamine, ascorbic acid, uric acid and other carbohydrate compounds usually co-exist with glucose in human blood and they can easily oxidize at the positive potential. In order to verify the selectivity of the fabricated MWCNT–CoTsPc glucose sensor, amperometric *i-t* was performed in the presence of other potentially active compounds. Fig. 5D shows the amperometric *i-t* response of MWCNT–CoTsPc modified electrode upon addition of 1 mM glucose (a) and 0.1 mM concentrations of galactose (b), sucrose (c), fructose (c), lactose (d), ascorbic acid (e), uric acid (f) and dopamine (h). A well-defined and stable amperometric response was obtained for the addition of 1 mM glucose, indicating the good electrocatalytic behaviour of the fabricated sensor. While the 200 fold excess concentration of interfering species showed a very little response compared with the response to glucose. The result confirmed that the MWCNT–CoTsPc modified electrode is more sensitive and selective to the detection of glucose in the presence of potentially active interfering compounds. The reproducibility (8 measurements) and repeatability (2 electrodes) of the MWCNT–CoTsPc modified electrode for the detection of 1 mM glucose was found with the RSD of 2.6 and 4.2 %, respectively. The result indicates the good precision and accuracy of the fabricated glucose sensor.

Repeatability and reproducibility

The repeatability and reproducibility of the sensor has been assessed by CV. CVs were recorded in 0.1 M NaOH at the scan rate of 50 mVs^{-1} in the presence of 1 mM glucose. The fabricated sensor offered good repeatability with the relative standard deviation (RSD) of 2.39% for 5 successive measurements in a single modified electrode. In addition, the biosensor exhibited good reproducibility with an R.S.D of 2.21% for 5 individual measurements carried out at five different modified electrodes.

Practical application of the sensor

In order to ensure the practical applicability of the developed electrode, the MWCNT–CoTsPc modified electrode was used for the detection of glucose in Human blood serum samples. The Human serum samples collected from the normal and diabetes patients. The serum samples were predetermined by a commercial Tecan Sunrise plate reader and detected values are summarized in Table. 2. We also investigated the glucose concentration in different serum samples by using an amperometric *i-t* method. The experimental conditions are similar as Sec. 3.5. The obtained results are summarized in Table 2. It can be seen from the Table 2 that the good recovery (97.0–102.4%) towards glucose was obtained using the MWCNT–CoTsPc electrode and detected value are in good agreement with the value detected by a commercial Tecan Sunrise plate reader. Hence it can be more suitable material for the detection of glucose in Human serum samples.

4. Conclusions

An amperometric enzyme-free glucose sensor has been developed at the MWCNT/CoTsPc composite modified electrode for the first time. The developed MWCNT/CoTsPc composite electrode exhibited excellent electrooxidation behaviour towards glucose in 0.1 M NaOH. The observed sensitivity of the sensor is about 1.8 and 2.5 folds higher than that of MWCNT and CoTsPc modified electrodes. Moreover, the fabricated enzyme-free glucose sensor showed the good analytical features such as wider linear response (up to 2.21 mM), lower working potential (0.3 V), high sensitivity, low LOD (0.014 µM) and fast amperometric response (2 s) along with good repeatability and reproducibility. In addition, the fabricated sensor also exhibited a good selectivity towards glucose in the presence of excess addition of potentially active interfering species.

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Notes and references

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Table.1 Comparison of the analytical parameters obtained at MWCNT–CoTsPc/GCE with previously reported enzyme free glucose sensors.

Modified electrode	E_{app} (V)[a]	Linear range (mM)	LOD[b] (µM)	Sensitivity (µAµM^{-1} cm^{-2})	Ref.
GOD[c]/Nafion/(LbL)[d]/ABSGR[e]	–0.4	0.1–8	50	17.5	34
GR-CoPc/GOx[c]	0.4	0.01–14.8	1.6	5.09	35
CoPc[f]/SPCE[g]	0.5	0.2–5	–	1.12	22
CoPc–(CoTPP)$_4$[h]	0.4	2–11	10	0.024	36
GOx/TiO2/FePc[i]-CNTs	0.5	0.05–4	30	8.25	37
CoTCAPc[j] SAM-ME-Au[k]	0.6	0.1–25	8.4	0.007	38
FeTMPyP[l]/RGNR[m]	–0.41	0.5–10	–	–	39
PG[n]/OPPyNF[o]/CoPcTS	0.4	0.25–20	100	5.695	40
(Ni-Co)(OH)$_2$	0.47	0.025–3.7	–	0.112	41
CoOOH	0.50	0.03–0.7	10.9	0.967	42
Au/LDH[p]-CNTs-G[q]	0.55	0.01–6.1	1.0	1.98	43
Co$_3$O$_4$	0.2	0.1–12	26.5	0.0458	44
MWCNT–CoTsPc	0.3	0.01–6.210	0.14	0.1225	This Work

[a]E_{app}– applied potential, [b]*LOD* limit of detection, , [c]GOD&GOx– glucose oxidase, [d]*LBL*- layer by layer [e]ABSGR– alcian blue pyridine-tetrasulfonated pthalocyanine Graphene, [f]CoPc–cobalt phthalocyanine, [g]SPCE- screen printed electrode, [h]CoTPP–cobalt(II) phthalocyanine–cobalt(II)tetra(5-phenoxy-10,15,20 triphenylporphyrin),[i]FePc– iron phthalocyanine, [j]CoTCAPc–cobalt tetracarboxylic acid phthalocyanine, [k]SAM-ME – self-assembled monolayer (SAM)–2-mercaptoethanol, [l]FeTMPyP–iron (III) meso-tetrakis(N–methylpyridinum–4–yl) porphyrin, [m]RGNR– reducedgraphene nanoribbons, [n]PG– pencil graphite, [o]OPPyNF– overoxidized PPy nano fiber, [p]LDH–layered double hydroxide, [q]G– graphene.

Table.2 Determination of glucose in normal and diabetes patients' blood serum samples.

Sample	Glucose detected by commercial detector(mM)	Glucose detected by our sensor (mM)	Recovery (%)	RSD
1	5.05	4.92	97.42	3.2
2	4.62	4.58	99.13	3.4
3	5.31	5.44	102.4	3.9
4	6.85	6.72	98.01	4.1
5	7.12	7.23	101.5	4.6
6	6.61	6.46	97.7	4.8

1, 2, 3 – Serum samples from normal patients.4, 5, 6 – Serum samples from diabetes patients.

RSD – Relative standard deviation for three measurements.