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CuO Nano Leaves Based Non-Enzymatic Electrochemical Interface for Glucose Sensing

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Abstract
Copper oxide nanoleaves have attracted a lot of interest as potential components for electrochemical glucose sensors. Their distinctive structural features, including as a high surface-to-volume ratio and a customized shape, improve their electrocatalytic activities and increase the sensitivity and selectivity of glucose detection. An overview of the synthesis processes, structural characteristics, and electrochemical capabilities of copper oxide nanoleaves for glucose sensing applications are given in this abstract. Their prospective incorporation into portable and miniaturized sensor platforms is also examined, underlining the important contributions they have made to the field of point-of-care diagnostics and continuous glucose monitoring for diabetics.
Keywords: *CuO Nano leaves, Non-enzymatic Glucose Sensor, Electrochemical Sensor, CV, and Chrono Amperometry.*

1. Introduction
Glucose is the chief source of energy. Due to the chronic medical condition like diabetes the body is unable to properly regulate blood glucose levels. Uncontrolled diabetes can lead to serious complications over time, including heart disease, stroke, slow-healing sores or infections, neuropathy, poor circulation, kidney disease and vision problems. Hence regular glucose level monitoring and managing in the body is much essential to maintain proper diet, medications and Lifestyle.[1] Currently researchers have developed a kind of sensors from advanced materials, to name few, oxide semiconductor, organic semiconductor, field effect type etc [2]. Wherein metal oxides such as Zinc oxide, nickel oxide, Titanium oxide, tungsten oxide, cobalt oxide, Cadmium oxide, tin oxide and copper oxide are best choice in glucose sensors due to their chemical stability, high selectivity, good thermal stability, low cost, biocompatibility, high glucose adsorption, high electron communication features and high transfer kinetics of electrons.[4] But most of the commercial sensing materials based on n-type semiconductors. Compare to the n-type metal oxide sensors, p-type metal oxide sensors has great potential applications.[10] Among various transition metal oxides, p-type semiconductor copper oxide nanoparticles are best suited for non-enzymatic glucose sensors owing to its chelating effect, large active surface area, excellent semiconducting property, low-cost synthesis, and higher electrical conductivity , unique catalytic, optical and electrical properties.[5] Various Copper oxide nanomaterials such as nanocubes, nano flowers nanorods, nanowires, microspheres, thin films etc were used as potential electrode material to fabricate glucose sensors. The CuO nanomaterials are fabricated by various synthetic techniques with different structure morphology using wet chemical precipitation method [3], sol-gel, hydrothermal, green synthesis, flame pyrolysis and biogenic. Among these sonochemical method of synthesis of CuO nanoparticles are best suited. The sonochemical method is a technique that uses ultrasound waves to induce chemical reactions and many advantages over other synthesis methods include its fast reaction kinetics, uniform particle size distribution, and the ability to control the particle size and morphology by adjusting the reaction parameters such as ultrasonic power, reaction time, and precursor

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concentration. In addition, the chemical effects of ultrasound comprise the formation of radicals and the enhancement of apparent reaction rates at ambient temperatures. The variable reaction condition enables us to generate nanomaterials of a much smaller size range and higher surface area than those stated by other fabrication methods [6-7]. Various approaches such as colorimetry, chemiluminescence, electrochemical are reported for the detection of biomolecules. Among this electrochemical approach is advantageous due to high selectivity, high sensitivity, rapid analysis, high accuracy, simple operation and portable device.[8] Herein, we report sonochemical method for synthesis, extensive range of materials characterisation techniques such as Scanning electron microscopy (SEM), Transmission electron microscopy (TEM), X-ray diffraction (XRD), is applied to explore the morphology, surface and electronic structure of the material and sensing applications of new CuO nanomaterial. A non-enzymatic type glucose sensor based on CuO was fabricated to effectively and specifically detect glucose molecule. The fabricated sensor device was employed for glucose sensing properties by varying the glucose concentrations. The transient response and selectivity of fabricated glucose sensor were studied and used to test glucose sensing behaviour, which is suitable for the industrial production. [9]

2. Materials and Methods

Copper nitrate, D-glucose powder and sodium hydroxide were procured from the Merck. The distilled water was used throughout the experiment, was obtained from double distillation unit [11]. The p-XRD of the synthesized CuO nanoleaves were conducted using Bruker instrument. The FT-IR studies of the synthesized CuO nanoleaves were conducted using Shimadzu instrument. The FESEM analysis of CuO nanoleaves were conducted using the Bruker instrument [11-13]. The electrochemical studies were conducted using SP 150 of Biologic make. Three electrode system was used for all electrochemical measurements. Glassy carbon electrode (GCE) was used as working electrode, aqueous Ag/AgCl electrode was used as an reference electrode and Pt wire was used as an counter electrode. 1M NaOH was used as an electrolyte for all electrochemical measurements [14].

2.1.Synthesis of CuO Nano leaves

10ml of 0.01M copper nitrate is prepared in distilled water by adding copper nitrite and sonicated for about 5min then 0.025M 10ml of NaOH solution was added to the above solution. The resultant mixture was ultrasonicated for about 5min and transferred to closed glass bottle and heated to a 80o C on a magnetic stirrer for about 6hr. The dark brown precipitate was obtained. Which is filtered washed with distilled water several times. The final product was dried in a hot air oven at 120O C for about 6hr .

2.2.Fabrication of CuO Nano leaves Modified GCE

The GCE was polished using polishing kit with 0.01, 0.1, and 0.5-micron sized Si and then sonicated in ethanol followed by distilled water. Then the CuO nanoleaves slurry (1 mg/mL) was prepared by dissolving it in distilled water and sonicated for 5 minutes. Then the 100 µL of the slurry was drop casted on to GCE and dried in open air for about 2 hours.

2.3.Analytical Procedure for Glucose Monitoring

The CuO Nano leaves modified GCE was used as working electrode, Ag/AgCl as reference electrode and Pt wire as counter electrode. 5 mL of 1M NaOH solution was used as electrolyte and technique used to monitor glucose was CV. The CV experiment was performed with 100mV Scan rate, for standard solutions of glucose and corresponding calibration graph was plotted and used to monitor glucose from test samples [15].

3. Results and Discussion

3.1.Spectroscopic Characterization of Synthesized CuO Nano leaves

3.1.1. FE-SEM Studies

The morphological features of the as synthesized CuO nanostructures were studied by the FE-SEM technique. The FE-SEM images of CuO nanostructures exhibited nano leaves like morphology under both lower as well as higher magnifications (Figure 1). Furthermore, nanoleaves were grown uniformly in large quantity [16].

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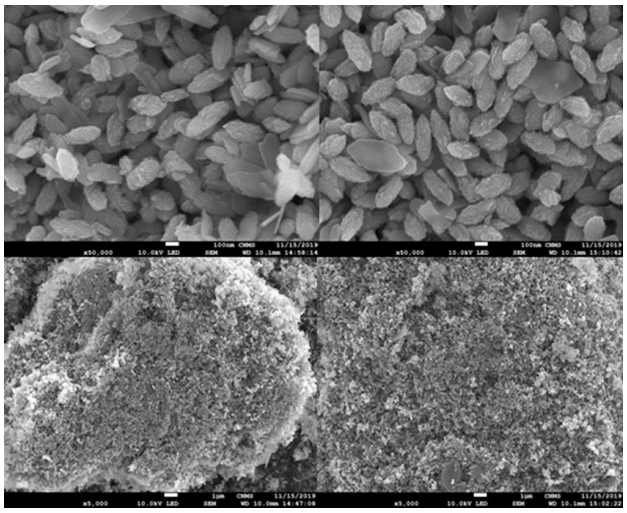

Figure 1 FE-SEM Images of The Cuo Nano Leaves Under Different Magnifications

3.1.2. p-XRD Studies

The crystalline natures of the as synthesized CuO nanoleaves were examined by studying its p-X ray diffraction pattern. The p-XRD pattern of CuO nanoleaves were as given in figure 2. The The p-XRD pattern revealed the monoclinic structure of CuO and indeed it is matching with the JCPDS number 48–1548, indicating single phase monoclinic CuO. Importantly, p-XRD pattern of CuO nanoleaves is free from other major characteristic peaks corresponds to the impurities and other phases.

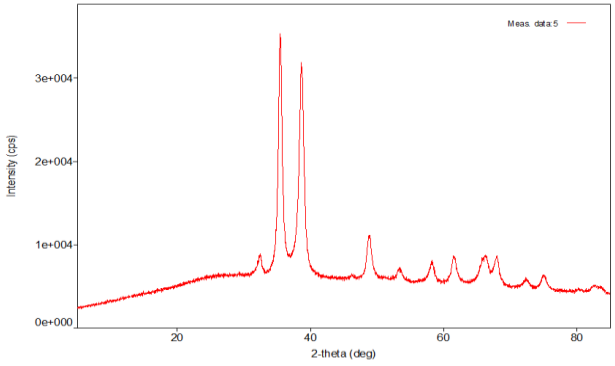

Figure 2 P-XRD Patterns of The as Synthesized Cuo Nano leaves

3.1.3. FT-IR Studies

The FT-IR studies of the as synthesized CuO nanoleaves were conducted. The FT-IR spectra exhibited vibration frequencies at 421 cm-1,521 cm-1, and 598 cm-1 (Figure 3). These three vibration frequencies were attributed to the monocilinc structure of CuO nanoleaves. Furthermore, the vibration frequency cantered at 1630 cm-1 corresponds to the surface adsorbed hydroxyl ions and water molecules (Figure 3).

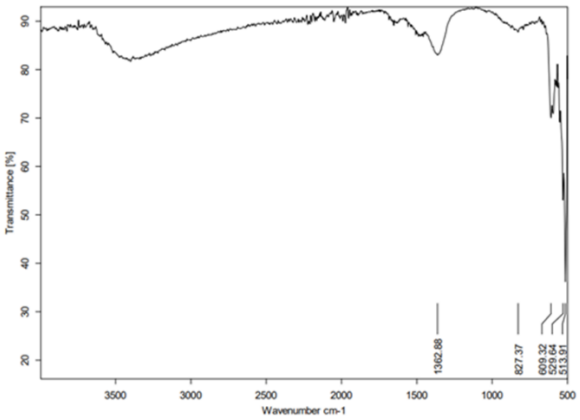

Figure 3 FT-IR Spectrum of The as Synthesized CuO Nano leaves

3.1.4. Electrocatalytic Oxidation of Glucose with CuO Nano leaves Modified GCE

The electrocatalytic oxidation of glucose was examined using bare GCE, CuO Nano leaves modified GCE by Cyclic voltametric technique. The bare GCE, CuO modified GCE didn't exhibit any peaks in the scanned area ranging from 0.2 to 0.8 V in 1M NaOH as electrolyte with scan rate of 100mV (Figure 4 and Figure 6). Interestingly, GCE also didn't exhibit any peak in CV measurements with 0.01mM glucose V in 1M NaOH as electrolyte with scan rate of 100mV when scanned from 0.2 to 0.8 V (Figure 5). This confirms that bare GCE is unable to do the electrocatalytic oxidation of glucose, and can't be used for fabrication of non-enzymatic glucose sensors. The cyclic voltamograms of CuO modified GCE in 1M NaOH doesn't exhibited any peaks (Figure 6); however, CuO nanoleaves modified GCE in 1M NaOH with 0.01mM of glucose exhibited redox peaks around 0.58 V in anodic side and at 0.49V at cathodic side (Figure 7 and Figure 8). The peak at 0.58V in anodic side in figure 7 corresponds to the conversion of Cu (II) to Cu (III) oxidation of glucose to gluconic acid catalysed by the presence of CuO Nano leaves on the GCE. The electrocatalytic oxidation mechanism of glucose in alkaline conditions by CuO is well reported. The

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electrogenerated Cu (III) species, acts as electron mediator, and oxidative Cu(III) species reacts with glucose to yield gluconolactone which on further oxidation finally gives gluconoic acid. The liner increase in current with increase in scan rate (100-600mV s-1) of CVs obtained with CuO nanoleaves modified GCE in 1M NaOH and 0.01mM glucose confirms the surface controlled electrochemical reaction (Figure 9a and Figure 9b). The successive addition of glucose, and measuring the oxidation current at 0.59V using the CuO nanoleaves modified GCE in 1M NaOH found to be linear and this confirms that present sensor system can be used to fabricate non enzymatic glucose biosensor (Figure 10). To demonstrate non enzymatic glucose sensing using the CuO nanoleaves modified GCE, current – time (i-t) response was performed using chronoamperometric technique. The continues addition of glucose with CuO nanoleaves modified GCE, with continuous stirring with rotation speed of 400 rpm (Potential:0.59V, 1M NaOH,glucose:0.01 to 1.0 mM) was shown in figure 11. The CuO nanoleaves modified GCE, exhibited well defined chronoamperometric i-t response for every addition of glucose with in short period of time around 3.5 s. The CV studies as well as chronoaperomtric response of CuO nanoleaves modified GCE towards electrocatalytic oxidation of glucose infers that there is fast electron transfer between the CuO nanoleaves modified GCE and electrolyte interface during successive addition of glucose.

3.1.5. Anti-Interference Studies

Selectivity of the fabricated CuO nanoleaves modified GCE non-enzymatic biosensor was studied by introducing possible interference species in the 1 mM NaOH buffer during CV measurement. Figure 11 shows the current of selectivity measurement with the glucose addition (1 mM) followed by 0.1 mM possible interfering species (i.e. fructose, maltose, sucrose, lactose, dopamine, uric acid, and ascorbic acid) addition and the final 1 mM glucose addition. The CuO nanoleaves modified GCE, responded rapidly after addition of glucose; however, there is no noticeable peak current with addition of interfering species (Figure 12). Additionally, almost same current response was noticed for 0.01 mM glucose addition in the presence of all these interfering species, suggests good selectivity nature of the CuO nanoleaves modified GCE. Hence, the fabricated non-enzymatic biosensor based on CuO nanoleaves modified GCE can serve as a selective electrochemical based non-enzymatic biosensor for glucose detection even in complex medium (i.e., human serum).

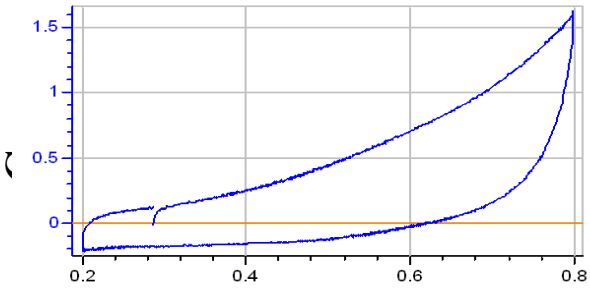

Figure 4 Cyclic Voltamogram Obtained with GCE in 1M NaOH (Scan rate :100mV)

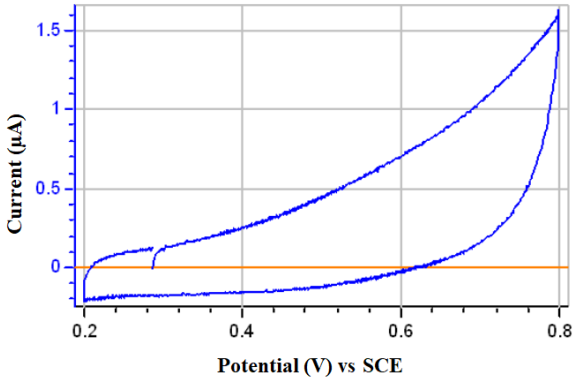

Figure 5 Cyclic Voltamogram Obtained with GCE In 1M NaOh in The Presence Of 0.01 Mm Glucose (Scan rate :100mV)

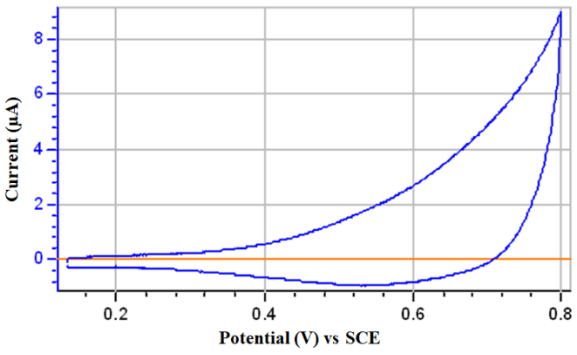

Figure 6 Cyclic Voltamogram Obtained with GCE Modified with Cuo Nano Leaves in 1M NaOH (Scan rate: 100mV)

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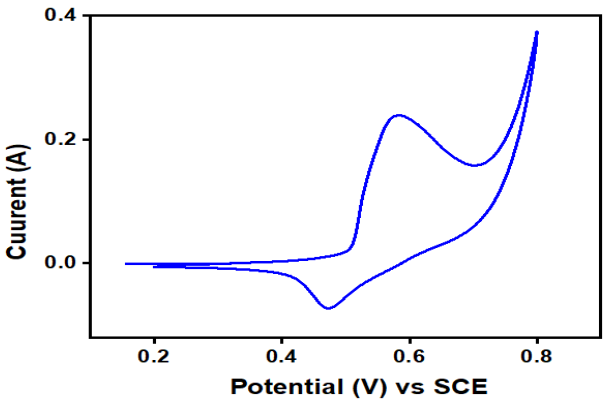


Figure 7 Cyclic Voltamogram Obtained with GCE Modified with CuO Nano Leaves in 0.01mm Glucose (1M NaOh, Scan Rate: 100mv)

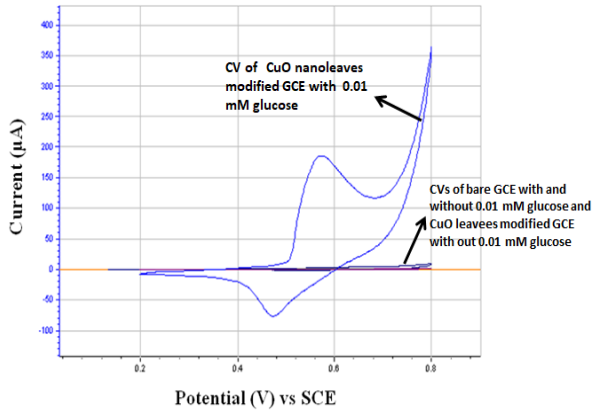
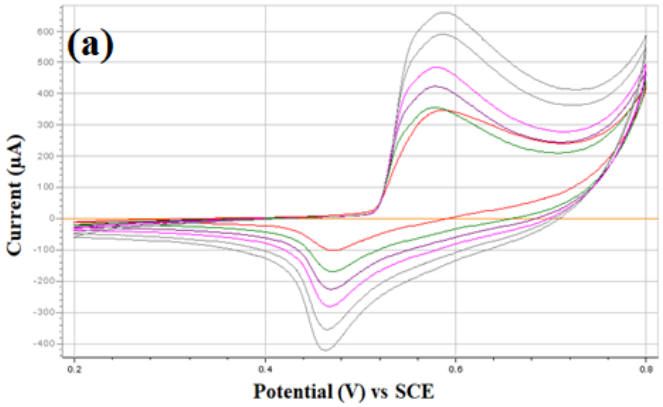


Figure 8 Overlaid Cyclic Voltammogram Obtained with Bare GCE In the Presence & Absence Of 0.01 Mm Glucose, Modified GCE With CuO Nano Leaves in The Presence & Absence Of 0.01 Mm Glucose (Electrolyte 1M NaOh, And Scan Rate :100mv)



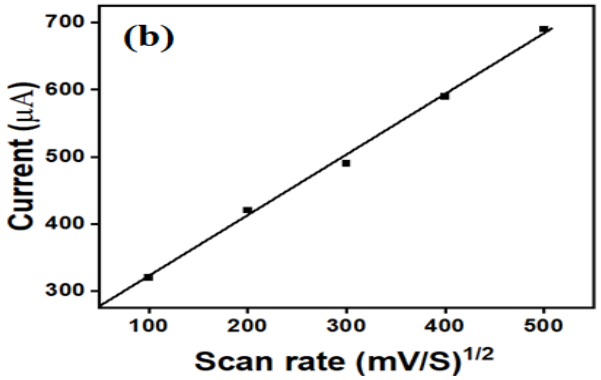


Figure 9 Cyclic Voltammogram Obtained (A) With Modified GCE With CuO Nano leaves in The Presence Of 0.01 Mm Glucose with Different Scan Rates Ranging Fromm 100- 500 Mv (Electrolyte 1M NaOh, And Scan Rate :100mv) (B)Corresponding Calibration Plot

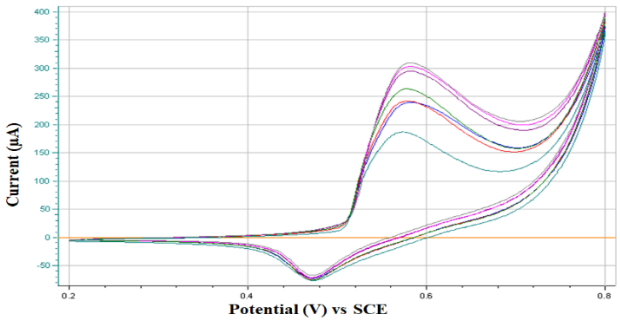


Figure 10 Cyclic Voltamogram Obtained with Modified GCE With CuO Nano leaves in The Presence of Different Concentrations of Glucose (0.01 To 1 Mm) Glucose (Electrolyte 1M NaOh, And Scan Rate :100mv)

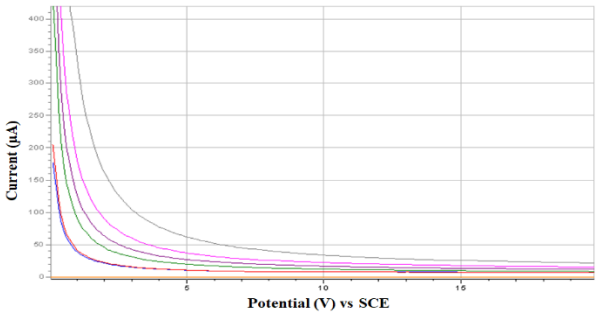


Figure 11 Chronoamperometric Graphs Obtained with Modified GCE With CuO Nano Leaves in The Presence Of 0.01 Mm Glucose with Different Scan Rates Ranging From 100- 600 Mv (Electrolyte 1M NaOh, And Potential:0.58V)

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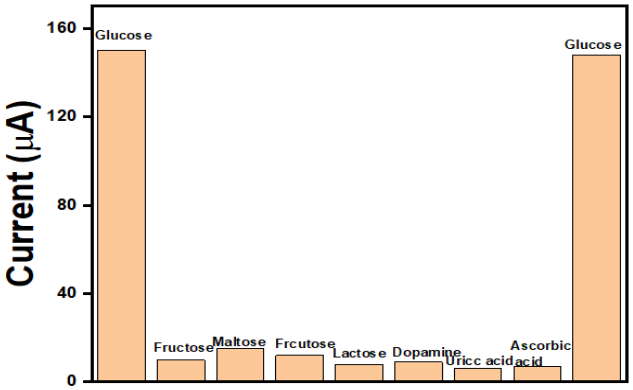

Figure 12 The current densities obtained with modified GCE with CuO nano leaves in the presence of 0.01 mM glucose and other common interferents with CV technique (Electrolyte 1M NaOH, Scan rate:100mV)

3.1.6. Application Studies

The developed non-enzymatic glucose biosensor based on the CuO Nano leaves modified GCE was applied to monitor glucose concentration in human serum samples. The analytical procedure followed for determination of glucose in serum samples was as mention in 2.2 section. The glucose levels of serum samples obtained with our method was well matched with standard clinical method. Furthermore, in order to validate the recoveries, known amount of glucose was spiked with serum samples and total glucose was monitored. The recoveries of spiked samples were found to be more than 99 % (Table-1). This suggests that present sensor can be used to monitor glucose in various biological specimens.

Table 1 Glucose Monitoring in Serum Samples Using Developed Sensor

Sl.No.	Samples	Glucose Originally Found (mM)		Glucose Added (mM)	Total Glucose (mM)		Recovery %	
		Present Method	Standard Method		Present Method	Standard Method	Present Method	Standard Method
1.	Human serum sample1	5.6	5.6	0.5	6.10	6.1	100	100
2.	Human serum sample2	6.8	6.7	1.0	7.82	7.7	98.7	98.7
3.	Human serum sample3	7.2	7.1	2.0	9.2	9.1	100.2	100
4.	Human serum sample4	6.3	6.2	4.0	10.4	10.2	100.9	100
5.	Human serum sample5	4.1	4.0	6.0	10.1	10.0	100	100

Conclusions

In conclusion, we are reporting the and simple hydrothermal method for synthesising CuO nanoleaves in the presence of NaOH. This can be produced in large quantities and can be used for diverse applications. The CuO nanoleaves modified GCE exhibited good electrocatalytic properties for glucose oxidation. The electrocatalytic properties of CuO nanoleaves modified GCE towards glucose oxidation are specific, sensitive and selective. Furthermore, CuO nanoleaves modified GCE was used for monitoring glucose in human serum samples. These results were very consistent with reference to clinical results and further more recovery of glucose in spiked samples is found to be 99 %. These results confirm that present sensor system can be upgraded to biosensor for monitoring glucose in other biological samples like sweet, saliva and tears.

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