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EMERGING TECHNOLOGIES FOR URINARY GLUCOSE DETECTION: A MINI-REVIEW OF FUNCTIONALIZED ELECTRODE MATERIALS

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Abstract. The detection of glucose through electrochemical methods in urine has significantly advanced, becoming a prominent and widely accepted approach in healthcare, especially for monitoring diabetes. This approach provides numerous benefits, including non-invasiveness, rapidity and simplicity compared to traditional methods. Therefore, urine glucose monitoring is set to provide a reassuring and comfortable alternative for improving the quality of life of diabetic patients. This review explores the comparative performance of enzymatic and non-enzymatic modified electrodes for glucose detection in urine. Both types of sensors have been enriched with various materials to enhance their electrochemical properties. Enzymatic sensors rely on the specific activity of glucose oxidase, while non-enzymatic sensors use materials such as metal nanoparticles (including gold, cobalt, silver, nickel, etc.), graphene and alloys to detect glucose directly through electrocatalytic mechanisms. The performance of these sensors was assessed based on several factors, including linear range, limit of detection (LoD), response time and stability.

Keywords: *Urine glucose, diabetes mellitus, electrochemical, enzymatic, non-invasive.*

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1. Introduction

Among the leading common glycemic illnesses that impact an abundance of individuals across the globe is diabetes mellitus (Wang *et al*., 2020). The condition presents a substantial danger of early death and can result in severe complications such as cardiac arrest, stroke, renal failure, amputated leg, impairment of vision and neurological disability (WHO, 2016). Diabetes, ranked as the third most prevalent chronic illness, is experiencing a continuous increase in occurrence daily (Panda *et al*., 2021). Hence, it is imperative to regularly monitor the glucose level to decrease the occurrences and complexities associated with diabetes (Azad *et al*., 2022).

Blood and urine biomarkers are effective tools for detecting diabetes (Soltani-Fard *et al*., 2024; Ferreira *et al*., 2021). Blood tests are practical, rapid and sensitive for measuring glucose levels in the body (Obeagu, 2024). Typically, blood glucose screening

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involves using a lancet or needle to obtain the necessary sample (Lee *et al*., 2018). While this method yields accurate results, its drawbacks include high costs, the need for a skilled technician (Wang *et al*., 2022) and the potential for discomfort or infection (Yang *et al*., 2019; Salihu *et al*., 2021). Additionally, patients who experience anxiety about needles may suffer psychological distress, which can lead to fluctuations in glucose levels and ultimately result in inaccurate test outcomes (Cui *et al*., 2023). For these reasons, urine glucose testing presents an appealing alternative to invasive blood sugar monitoring.

Urine, a reliable diagnostic tool for glucose measurement, is collected in a non-invasive manner (Bruen *et al*., 2017). It can effectively detect high glucose levels in the bloodstream through urine analysis, a condition known as glucosuria (Zang *et al*., 2021). When the glucose concentration in urine exceeds 0.8 mM, it confidently indicates the presence of diabetes mellitus (DM) in the individual (Nugba *et al*., 2023). Ordinarily, the human body does not excrete glucose in urine, with levels ranging between 0-15 mg/dL or 0-0.8 mM (Mohammadifar & Choi, 2018). Due to the established correlation between blood and urine glucose concentrations, urine glucose testing is a painless and non-invasive alternative to traditional blood glucose testing. Despite the inherent challenges, these non-invasive methods present significant potential, empowering patients with diabetes to efficiently monitor their glucose levels, giving them more control over their condition (Lee *et al*., 2018). Urine glucose testing serves as a valuable tool not only for diabetes screening but also for supporting diabetic patients, ultimately helping to alleviate medical and economic burdens in areas with limited medical resources or in underdeveloped countries (Wang *et al*., 2022).

Currently, researchers use many methods to detect urine glucose, such as spectrophotometry, colorimetry, chromatography, surface plasmon resonance and electrochemical processes. Among these methods, electrochemical methods attract more attention because they are portable, easy to operate, giving fast response, having high sensitivity and easy to miniaturize (Shakayeva *et al*., 2023).

Electrochemical sensors for glucose determination are generally classified into two primary categories, which are primarily enzymatic and some are free-enzymatic glucose sensors (Hassan *et al*., 2021; Mohamad Nor *et al*., 2022; Govindaraj *et al*., 2023). Enzymatic glucose sensors, particularly those utilizing glucose oxidase, have been widely researched and developed due to their remarkable selectivity and high sensitivity. Regardless, these sensors face limitations regarding long-term stability, as glucose oxidase is susceptible to variations in natural conditions such as pH, temperature, humidity and the presence of interfering substances. Given the identified challenges, it is essential to develop a straightforward glucose sensor that is free from enzymes and demonstrates high sensitivity, exceptional selectivity, rapid response time, low detection limits and the ability for reusability. Non-enzymatic glucose sensors have garnered significant attention as a promising solution to the challenges associated with enzyme-based glucose sensors.

This concise review thoroughly discusses advancements in developing electrochemical sensors for measuring glucose in urine, utilizing both enzymatic and non-enzymatic approaches. We summarize the performance of these sensors from the perspectives of materials, sensing modes and device design, offering valuable insights into the existing technologies for urinary glucose monitoring.

2. Enzymatic detection of urine glucose

Clark and Lyons initially presented the utilization of enzymes in 1962 for the electrochemical identification of glucose. Clark and Lyons (1962) immobilized the glucose oxidase (GOx) enzyme onto the platinum electrode's surface. Based on these findings, GOx is widely used as a glucose sensor because it has catalytic activity and high specificity towards glucose substrates (Hassan *et al*., 2021). The GOx enzyme can oxidize glucose to produce H_2O_2 compounds. These compounds can be detected using electrochemical methods, with the amount of the current being equal to the quantity of glucose in the blood (Lee *et al*., 2018).

In addition to measuring blood glucose levels, urine glucose is frequently employed as a diagnostic tool for diabetes in clinical settings (Wang *et al*., 2022). Extensive research has been conducted on using GOx to determine glucose levels in urine enzymatically.

An enzymatic technique utilizing a sensor composed of a graphene-graphene oxide nanocomposite and glucose oxidase enzyme was employed in a research study to identify glucose in human urine and serum. Notably, the study did not involve using a cross-linker (Wang *et al*., 2019). A nanocomposite of graphene and graphene oxide was utilized as an electrode modifier. The high conductivity of the material allowed for the efficient movement of electrons between the glucose oxidase and the electrode. The assessment of the sensor's functionality was conducted through the implementation of the cyclic voltammetry (CV) approach. Based on the findings, implementing a graphene-graphene oxide nanocomposite provided appropriate enzyme surroundings and enhanced direct electron transfer (DET) on the electrode's surface. The sensor had excellent sensibilities, measuring at 15.85 $\mu A\ mM^{-1}\ cm^{-2}$. It boasted a linear range of 0.1 to 11 mM and a detection limit (LoD) of 20 μM.

A layered composite of glucose oxidase and ascorbate oxidase was employed to modify platinum (Pt) electrodes in another investigation (Go *et al*., 2019) for urinary glucose identification. The fabrication involved creating a chip with three Pt electrodes on a 6-inch quartz wafer using standard semiconductor techniques. Before being coated by the enzyme, the electrode surface was cleaned using acetone, isopropanol and ethyl alcohol to remove any impurities. Subsequently, the immobilization of the glucose oxidase enzyme was carried out on the surface of the electrode and afterward, the platinum-glucose oxidase electrode was covered with an ascorbate oxidase composite. Electrochemical analysis was conducted utilizing the CV methodology. The study showed that the Pt electrode exhibited precise measurements of urinary glucose contents ranging from 0-2000 mg/dL while maintaining excellent linearity and stability.

The researchers developed an innovative electrochemical sensor that utilized paper to detect glucose levels in urine (Mohammadifar *et al*., 2019). This sensor incorporated a single-use paper strip, an amplification circuit and an optical display. The paper strip comprised five electrodes immobilized with the glucose oxidase (GOx) enzyme after being rendered conductive with poly(3,4 ethylenedioxythiopene) polystyrene sulfonate (PEDOT: PSS). The electrodes had been connected to designated indicator circuits activating light-emitting diodes (LEDs) upon reaching predetermined sugar concentrations. This tool could detect glucose in urine at concentrations exceeding 4 mM within less than 2 minutes. The suggested sensor platform exhibited significant promise for monitoring urine glucose levels, demonstrating superior performance to traditional urinary glucose sensors. An illustration of sensor fabrication is presented in Figure 1.

There was an investigation on glucose biosensors using a thermal-based printing method embedded in diapers (Shitanda *et al*., 2022). A three-electrode device was manufactured using a substrate composed of polyethylene terephthalate (PET). The resulting chip underwent modification using the GOx enzyme. Then, a heat transfer system transferred the GOx-modified electrode to the diaper material. CV was the technique employed for conducting electrochemical measurements. The results showed linearity and reproducibility within the 0.1 - 20 mM glucose concentration range. Therefore, this sensor had the potential to be developed commercially to detect urine glucose.

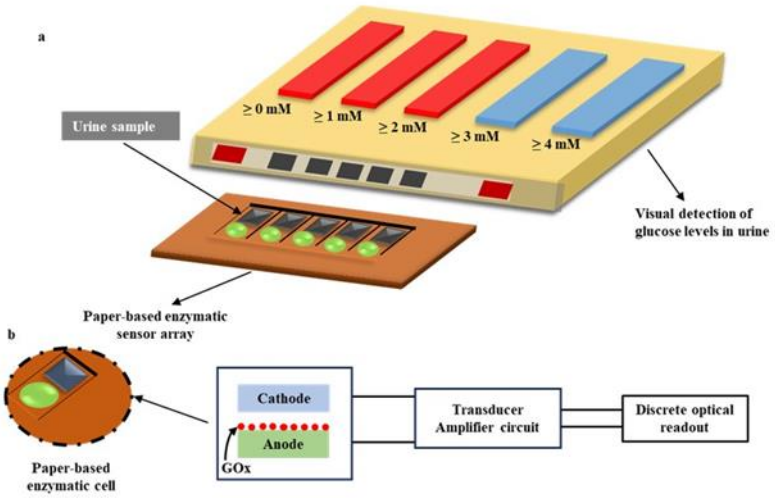

Figure 1. (a) sensor prototype design and (b) procedure for operating sensor

A study successfully demonstrated the modification of bismuth (III) oxide with graphene nanoribbon onto the screen-printed electrode surface (SPCE/GNR/Bi_2O_3). The SPCE/GNR/Bi_2O_3 electrode was employed for glucose identification in blood and urine samples (Đurđić *et al*., 2019). The modified electrode was coated with Nafion after applying the GOx enzyme. CV and amperometric methods assessed the electrochemical response of the modified electrode, demonstrating excellent accuracy, precision and selectivity in determining glucose in the tested samples. The results of the glucose determination indicated that the linear range extended from 0.28 - 1.7 mM, with a LoD of 0.07 mM.

A urine glucose monitoring system that employed an enzymatic biofuel cell (EBFC) system integrated into a diaper was reported (Zang *et al*., 2021). The EBFC system converted biochemical energy from biofuel (urine glucose) into electrical energy through redox reactions. The EBFC biosensor device comprised a biofuel cell, a power management system (PMS) and an LED indicator. The EBFC biosensor was integrated within the absorbent layer of the diaper to produce electrical energy upon coming into touch with urine. The power management system circuit was designed to accumulate energy and trigger the LED indicator upon completion of the energy accumulation process. The LED indicator's flame intensity correlated directly with the urine sample's glucose concentration. The EBFC sensor had been further enhanced with carbon nanotubes (CNT) and gold nanoparticles (AuNP) to improve performance. The EBFC biosensor was produced via screen printing on a PET substrate. The findings demonstrated the high efficacy of the EBFC biosensor device in glucose detection. The

LED brightness frequency was related to glucose intensity (r = 0.994) within the 1-5 mM range and the EBFC biosensor had high selectivity for analytes, as interference tests using uric acid and carbamide demonstrated.

A novel diagnostic tool for glucose detection was developed, employing the enzyme glucose oxidase (GOx) (Xu *et al*., 2019). The platform comprised a nanocomposite composed of multiwall carbon nanotubes (MWCNTs) and an amphiphilic copolymer known as poly(acrylic acid-r-(7-(4-vinyl benzyloxy)-4-methyl coumarin)-r-ethylhexyl acrylate) or PAVE. The GOx@PAVE-CNTs nanocomposites displayed a necklace-shaped structure, with polymer nanoparticles containing GOx functioning as nanobeads and MWCNTs as a continuous string running across the nanobeads. An approach called electrophoretic deposition was utilized to deposit the GOx@PAVE-CNTs nanocomposite onto a glassy carbon electrode (GCE) surface, which resulted in a sensor called GOx@PAVE-CNTs/GCE. The biosensor produced exhibits rapid glucose detection capabilities, boasting a reaction time of under three seconds. The sensor possessed a linear detection range from 1 µM to 5 mM, with a LoD of 0.36 µM. The biosensor had exceptional sensitivity and selectivity. Furthermore, the biosensor GOx@PAVE-CNTs/GCE proved stable and reproducible while employed with human urine and serum specimens.

Nitrogen (N)-doped porous carbon material-based enzymatic biosensor was introduced for monitoring glucose in urine and sugar-containing beverages (Quintero-Jaime *et al*., 2021). Nitrogen-doped carbon compounds were acquired through the thermal processing of polyaniline (PANI), known as PANI thermal treated (PANI TT). The biosensor effectiveness was investigated using the CV method. The biosensor exhibited a high sensitivity in detecting glucose, specifically measuring 23.57 ± 1.77 µA cm^{-2} mM^{-1}. It had a linear detection range of 0.005-5 mM and a LoD of 1 µM. The detection of glucose in urine or samples of commercially available sugar drinks was not adversely affected by the inclusion of uric acid, dopamine, gluconic acid and ascorbic acid.

Table 1. A summary of the efficacy of enzymatic sensors for detecting glucose in urine

Materials	Sensitivity (µA cm^{-2} mM^{-1})	Linear range	LoD	Ref
GOD/GR-GO	15,85	0,1-11 mM	20 µM	(Wang *et al*., 2019)
AOx-GOx-Pt	-	0-2000 mg/dL	-	(Go *et al*., 2019)
PEDOT:PSS-GOx	-	-	4 mM	(Mohammadifar *et al*., 2019)
Chips-GOx-Diaper	-	0,1 – 20 mM	-	(Shitanda *et al*., 2022)
GNR/Bi_2O_3	-	0,28 - 1,7 mM	0,07 mM	(Đurđić *et al*., 2019)
EBFC-CNT-AuNp	-	1-5 mM	-	(Zang *et al*., 2021)
GOx@PAVE-CNTs	-	1 µM - 5 mM	0.36 µM	(Xu *et al*., 2019)
PANI-TT-GOx	23.57±1.77	0,005 - 5 mM	1 µM	(Quintero-Jaime *et al*., 2021)
GOx-PABA-gFET	-	10 µM - 1 mM	4,1 µM	(Fenoy *et al*., 2022)

It had been reported that the detection of urine glucose could be achieved enzymatically by employing a graphene field-effect transistor (gFET) (Fenoy *et al*., 2022). The process involved depositing graphene oxide on an Au-interdigitated electrode (IDE) and reducing it with hydrazine to obtain a graphene field-effect transistor (gFET). The electrode surface of the gFET was modified using a copolymer of poly(3-amino-benzylamine-co-aniline) (PABA) to enable rapid attachment of glucose oxidase (GOx), leading to the creation of GOx-PABA-gFET. The GOx-PABA-gFET biosensor had a sensitivity of -24.9 μA per decade, a rapid response time of 190 s, a LoD of 4.1 μM and a linear range from 10 μM to 1 mM. A summary of the efficacy of enzymatic sensors for detecting glucose in urine is presented in Table 1.

3. Non-enzymatic detection of urine glucose

The limitations of glucose monitoring techniques that rely on enzymes have led to exploring alternative non-enzymatic approaches for detecting glucose (Grochowska *et al*., 2019). The enzymatic system can experience gradual denaturation and instability due to the detrimental effects of humidity and pH. Conversely, non-enzymatic glucose sensors offer numerous benefits including consistent stability, increased sensitivity, cost-effectiveness and quick reaction times (Hernández-Saravia *et al*., 2021; Chu, 2020).

Non-enzymatic sensor development has been attempted with the electrode surface incorporating nanostructured materials such as alloys, carbon nanotubes, metal oxides, magnetic nanoparticles, bimetallic nanomaterials and nanocomposite materials (Shakayeva *et al*., 2023). This sensor utilized an indium tin oxide (ITO) electrode enhanced with gold nanoparticles and boronate affinity for urinary glucose monitoring (Chen *et al*., 2021). The electrochemical sensor used in the experiment was of the sandwich type. It was made up of gold nanoparticles (AuNPs), 3-aminophenyl boronic acid (m-APBA), 4-mercapto benzoic acid (p-MBA) and ferrocene boronic acid (FcBA) or APBA/MBA/AuNPs/ITO sensors. The sensor's efficacy was evaluated on its selectivity, sensitivity and repeatability utilizing three different electrochemical techniques - namely electrochemical impedance spectroscopy (EIS), cyclic voltammetry (CV) and differential pulse voltammetry (DPV). It had a linear detection range of 0.5 – 30 mM and a LoD of 43 μM. The sensor demonstrated exceptional selectivity, sensitivity, stability and reproducibility while measuring glucose levels in urine.

A laser-induced graphene (LIG) sensor with nickel nanoparticle modification (NiNPs-LIG) was also developed to detect urinary glucose (Nugba *et al*., 2023). LIG boasted impressive properties for sensor applications, including excellent electrochemical and surface properties, a high electron transfer rate and a fast, environmentally friendly design. Adding nickel nanoparticles to the LIG enhanced its catalytic activity and overall efficiency. Efficiency measurements were conducted on the NiNPs-LIG sensing device utilizing CV, EIS and chronoamperometry approaches. The findings indicated that the prototype sensor achieved a linear range from 12 μM to 1.5 mM, with a LoD of 0.0152 μM. The designed urine glucose sensor offered promising results with a response time of under 3 seconds and a sensitivity of 5796.18 μA mM^{-1} cm^{-2}. The resulting sensor demonstrated higher dependability for glucose monitoring than commercially available urine glucose sensors.

The Co-MOF and $Co(OH)_2$ were synthesized using the ionothermal method with the aid of ionic liquids to enhance the Co-MOF conductivity (Zhang *et al*., 2020). Co-

MOF/GCE and $Co(OH)_2$/GCE sensors were fabricated by modifying glassy carbon electrodes with Co-MOF and $Co(OH)_2$, respectively, to detect glucose in urine. The Co-MOF/GCE sensor's electrochemical activity was superior to that of the $Co(OH)_2$/GCE sensor, as determined by the CV and amperometric approaches. The designed sensor based on Co-MOF/GCE displayed a wide detection range, from 5 μM to 900 μM, with a LoD of 1.6 μM, indicating its high sensitivity. The sensor also demonstrated excellent selectivity and reproducibility.

A Co/Fe bimetallic catalyst was synthesized and modified with carbon (CoFe/C) to enhance its electrocatalytic activity for detecting glucose in both artificial and human urine (Janyasupab *et al*., 2019). After being modified, the bimetallic catalyst was applied to a glassy carbon electrode. Glucose levels were then measured using CV and DPV methods. The CoFe/C/GCE sensor proved highly effective in detecting glucose levels ranging from 0 to 3 mM in synthetic and human urine samples. Notably, when tested on human urine, the sensor displayed a sensitivity of 59.72 μA mM^{-1} cm^{-2} and a correlation coefficient (R^2) of 0.99.

An investigation was conducted on a platform for measuring glucose concentrations in human urine and serum using NiS nanoclusters dispersed on NiS nanospheres (NC-NiS@NS-NiS) (Arivazhagan *et al*., 2021). The NC-NiS@NS-NiS nanomaterial was then applied onto a nickel foam (NF) substrate to generate NC-NiS@NS-NiS/NF. The fabricated electrode underwent CV and chronoamperometry (CA) procedures to assess its functionality. The sensing platform demonstrated an impressive sensitiveness of 54.6 μA mM^{-1} cm^{-2}, a LoD of 0.0083 μM and a less than 3 seconds response time. It also showed a broad linear range ranging from 20.0 μM to 5.0 mM. The sensor offered also had good selectivity and high reproducibility, leading to a potential way toward designing next-generation sensor platforms.

The detection of urine glucose was accomplished by modifying nanoporous platinum electrodes with Nafion (Pt nanopore/Nafion) (Lee *et al*., 2013). The performance of the Pt nanopore/Nafion sensor was measured using amperometric techniques. The outcomes showed that the detector demonstrated a high level of sensitivity, measuring 0.728 μA mM^{-1} cm^{-2}. It also exhibited a LoD of 10 μM and a wide range of 21.68 mM. Additionally, this sensor detected changes in glucose concentration quickly and returned to normal conditions within 15 seconds.

The suggested glucose sensor was a disposable with a screen-printed carbon electrode (SPCE) decorated utilizing a CuO-IL/rGO nanocomposite. This sensor combined a paper-based device with a potentiostat that could be operated through a smartphone (Janmee *et al*., 2021). The research conducted on the portative glucose sensor, which operated without enzymes and was based on electrochemical principles, showed that it was vulnerable to electrical signals, had a wide linear range and was capable of detecting glucose at low operating potentials with a limit of detection similar to other glucose sensors. By applying chronoamperometry techniques, a linear range of 0.03-7.0 mM was achieved by optimizing the detection potential of +0.4 V for 20 seconds. The device suggested in the study could effectively identify glucose in samples with a LoD of 0.19 μM. Additionally, it could be used without any prior treatment of the samples.

An efficient sonochemical method was utilized to synthesize 2D porous $NiCo_2O_4$ nanosheets to create a glucose sensor without enzymes (Babulal *et al*., 2021). The template material was graphene oxide (GO), while the oxide precursor was a ZIF-67-based Ni-Co MOF. The electrocatalyst, gt-$NiCo_2O_4$NSs, underwent testing utilizing CV

and amperometric techniques to facilitate glucose oxidation at a potential of +0.55 V. The findings suggest that the glucose-sensing ability of the gt-$NiCo_2O_4$ NSs-based sensor exhibited remarkable electrocatalytic properties in detecting glucose. It achieved this with a linear range of 150 nM to 8.86 mM, a low LoD of 7.35 nM and a high sensitivity of 729.72 μA mM^{-1} cm^{-2}.

An amperometric sensor was implemented to identify glucose in the bodily fluids of humans, specifically in blood serum and urine. The sensing device was created by employing thiol-functionalized magnetic nanoparticles (Fe_3O_4-SH) that were decorated with copper (II) oxide honeycombs (CuOHCs) and silver nanoparticles (AgNPs) (Baghayeri *et al*., 2020). The electrode obtained, AgNPs/CuOHCs/Fe_3O_4/GCE, was assessed using CV and EIS methods, revealing a low LoD of 0.015 μM and a linear range spanning from 0.06 to 1000 μM. This sensor was also found to have excellent stability, reproducibility and selectivity when tested under various conditions.

Researchers developed a set of microelectrodes made of carbon nanotubes (CNT μ-ES) for detecting glucose in human urine and serum (Gupta *et al*., 2021). The microsensor series comprised three electrodes: a counter electrode (CE) composed of highly densified carbon nanotube fiber (HD-CNTf), a working electrode (WE) consisting of HD-CNTf that was modified with CuNPs and a quasi-reference electrode (QRE) consisting of HD-CNTf coated with Ag/AgCl and Nafion. The electrochemical efficacy of the microsensor was evaluated by CV and amperometric methods. The findings demonstrated that the microsensor exhibited exceptional stability, consistency and specificity in detecting glucose in urine and serum. It had a LoD of 28 nM, a sensitivity of 1.942 μA mM^{-1} cm^{-2} and a reaction time of 5 seconds.

A coprecipitation method created Au-CuO nanocomposites to determine human urine glucose (Felix *et al*., 2018). The resulting Au-CuO nanocomposite was dripped onto a glassy carbon electrode surface and coated with Nafion. The modified electrode was subjected to the CV technique to assess its electrocatalytic activity as a sensor. The fabricated sensor revealed a remarkable sensitiveness of 3126.76 μA mM^{-1} cm^{-2}, a broad linear range spanning from 5 μM to 650 μM, a rapid reaction time of 3 seconds and a LoD of 1.4 μM. Moreover, this sensor exhibited exceptional selectivity in impurities including dopamine, uric acid and ascorbic acid and was considered stable.

Another non-enzymatic developed from CuO nanodisks for detecting urine glucose had been synthesized using microwaves (Jagadeesan *et al*., 2019). The CuO nanodisks modified the electrode by dripping it directly onto its surface (SPCE/CuO). The SPCE/CuO sensor's capabilities were assessed using the CV method, demonstrating exceptional stability and selectivity. The sensor exhibited potential for detecting glucose, with a sensitivity of 627.3 μA mM^{-1} cm^{-2} and a LoD of 0.2 μM.

Sulfur-doped hollow carbon nano-spheres (NiO@SDHCNSs) were synthesized employing hydrothermal methods and utilized as susceptible non-enzymatic sensing appliances to determine glucose levels in human urine and blood samples (Madhuvilakku *et al*., 2018). The surface of the glassy carbon electrode underwent a modification process utilizing the NiO@SDHCNSs nanocomposite and the efficacy of this modification was then assessed using CV and amperometric techniques. The artificial sensor demonstrated exceptional sensitivity, measuring at 1697 μA mM^{-1} cm^{-2}. It also exhibited a linear range of 0.001-13 mM and a LoD of 0.52 μM. Despite the presence of inhibiting agents, namely dopamine, uric acid and ascorbic acid, it exhibited a remarkable level of specificity.

The surface of glassy carbon (CNH/GCEs) and graphite screen-printed (CNH/GSPEs) electrodes were modified through the Carbon nano horn (CNH)

application (Kachouei *et al*., 2022). Afterward, a bimetallic nickel cobalt sulfide (NiCo-S) was electrodeposited onto each CNH/GCE and CNH/GSPEs. The electrodes made of NiCo-S/CNH/GCEs and NiCo-S/CNH/GSPEs were utilized for detecting glucose concentrations in human biological fluids such as blood serum, urine and saliva. The performance of both sensors in detecting glucose was evaluated using the CV technique. The linear ranges of NiCo-S/CNH/GCEs and NiCo-S/CNH/GSPEs sensors, respectively, were 0.001-4.53 mM and 0.5 -6 mM. They also provided a LoD of 5.6 μM and 35.3 μM, with a sensitivity of 1842 μA mM^{-1} cm^{-2} and 467 μA mM^{-1} cm^{-2}. Additionally, the sensors exhibited good selectivity, stability and repeatability.

A novel sensor had been created for the non-enzyme-based monitoring of human blood and urine glucose levels. The sensor was designed by combining a glassy carbon electrode with a blend of cobalt oxide nanoparticles (Co_3O_4) and reduced graphene oxide (rGO) (Maghsoudi & Mohammadi, 2020). The performance of the suggested sensor, rGO/Co_3O_4/GCE, was determined using the CV technique. The results showed outstanding performance in detecting glucose. The sensor based on modified rGO/Co_3O_4/GCE exhibited a wide linear range between 25 nM and 2 μM. Its response time was 5 minutes, while the detection limit was impressively low, measuring only 3.6 nM. The sensor's repeatability and selectivity were exceptional, as evidenced by the interference value and standard deviation under 5%.

The glucose detection in urine was identified by employing a glassy carbon electrode enhanced with an Ag-CuO nanocomposite (Viswanathan *et al*., 2020). The Ag-CuO nanocomposite was created by modifying the proportion of Ag nanoparticles to CuO. The Ag-CuO composition, with a ratio of 1:2.5, exhibited exceptional performance in glucose oxidation compared to the other evaluated ratios. The assessment of the functionality of the Ag-CuO/GCE sensor was carried out through the application of the CV technique. The suggested sensor can detect glucose within the 5 μM - 30 mM range. It exhibited a sensitivity of 150.17 μA mM^{-1} cm^{-2} and a LoD of 5 μM. This sensor produced excellent selectivity and stability in detecting glucose despite interfering compounds like ascorbic acid, dopamine, sucrose, uric acid and NaCl.

A monitoring system was created to measure human blood serum and urine glucose levels. The system utilized cadmium sulfide (CdS) nanoparticles decorated with MgO-entangled nanosheets (MgOENS) (Ullah *et al*., 2022). The glucose detection capacities of the MgOENS sensor and CdS@MgO sensor were assessed utilizing the CV approach. The MgOENS sensor displayed a sensitivity of 12363 μA mM^{-1} cm^{-2}, a LoD of 0.5 μM, a linear range from 0.0025 to 0.035 mM and a response time of 4 seconds. Conversely, the CdS@MgO sensor had a sensitivity of 28570 μA mM^{-1} cm^{-2}, a LoD of 0.02 μM, a linear range spanning from 1.25 μM to 15 mM and a response time of 2 seconds. The fabricated sensor indicated a considerable level of selectivity towards glucose, even in the presence of other substances that could potentially interfere, such as uric acid, ascorbic acid, sucrose, urea, fructose, cholesterol, L-cysteine and chloride ions. In addition, the sensor exhibited both long-lasting stability and exceptional reproducibility.

An electrochemical sensor that does not depend on enzymes was developed to detect urine glucose. The sensor was created using Au, CuO and MXene V_2CT_x as modifiers (Cui *et al*., 2023). Two different versions of the sensor, Au@CuO/LIG and Au@CuO/V_2CT_x/LIG, were compared for their capacity to identify glucose on laser-induced graphene (LIG) electrodes. The researchers used EIS, CV and chronoamperometry (CA) to evaluate the sensor's effectiveness. The findings indicated that the Au@CuO/LIG sensor had superior effiacy detected urine glucose because it

underwent oxidation faster than the Au@CuO/V_2CT_x/LIG sensor. The detection range of the Au@CuO/LIG sensor was between 0.005 and 5 mM, with a LoD of 1.8 μM. It exhibited a sensitivity of 1.124 x 106 μA mM^{-1} cm^{-2} and a response time of 1.5 seconds, as determined through tests using EIS, CV and CA techniques. This sensor demonstrated both stability and selectivity when detecting glucose in human urine.

A fabrication method for non-enzymatic glucose sensors (NPGs) involving the modification of gold nanoparticles (AuNPs) with laser-etched graphene electrodes (LSGE), denoted as LSGE/AuNPs, was documented (Zhu *et al*., 2021). The AuNPs served as electrocatalysts that were electrodeposited on LSGE. The linear sweep voltammetry (LSV) method was utilized to evaluate the sensor's performance, revealing a LoD of 6.3 μM and a linear range from 10 μM to 10 mM. Furthermore, the developed detector exhibited high sensitivity and specificity towards disruptive substances like urea, L-ascorbic acid, uric acid, dopamine and Na^+ ions. A clear depiction of the fabrication process of LSGE-modified AuNPs can be found in Figure 2.

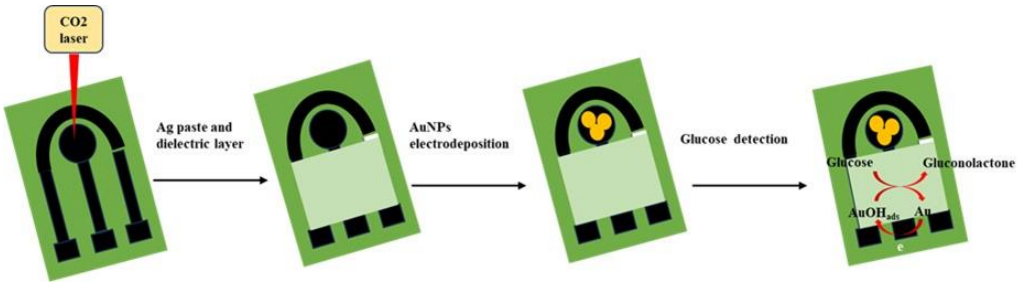

Figure 2. Modified AuNPs fabrication process with LSGE

The identification of glucose in human urine was accomplished by combining multi-walled carbon nanotubes (MWCNTs) with zinc oxide quantum dots (ZnO QDs) nanomaterial components (Vinoth *et al*., 2021). A glassy carbon electrode was coated with ZnO QDs functionalized with MWCNTs; the resulting composite material was denoted as MWCNT/ZnO QDs/GCE. The sensor's electrochemical analysis was conducted using CV, LSV and amperometric techniques. The developed sensor had the following sensitivity, LoD and response time: 9.36 μA per μM per cm squared, a limit of detection of 0.208 μM, linear response ranging from 0.1-2.5 μM and a response time of under 3 seconds. The experimental findings demonstrated that the MWCNT/ZnO QDs/GCE electrochemical sensor exhibited exceptional stability and repeatability. Furthermore, the glucose sensing process remained unaffected by disturbing compounds like sucrose, ascorbic acid, dopamine and uric acid.

The present study utilized a carbon fiber electrode (CFE) for glucose monitoring in human urine. This was achieved by combining MXene Ti_3C_2 with Co_3O_4 nanocubes, resulting in Co_3O_4/MXene@CFE (Manoj *et al*., 2020). The CV approach was utilized to analyze the sensor's electrochemical characteristics. The sensor composed of Co_3O_4/MXene@CFE demonstrated a remarkable sensitivity of 19.3 μA μM^{-1} cm^{-2}, covering a linear range from 0.05 μM to 7.44 mM and achieving a LoD of 10 nM. The sensor's selectivity was assessed while detecting glucose in a finding of affecting chemicals such as ascorbic acid, dopamine, paracetamol, catechol, L-cysteine, resorcinol, uric acid and hydrogen peroxide (H_2O_2). The findings demonstrated that the Co_3O_4/MXene@CFE sensor maintained stability and glucose selectivity over time.

Table 2. The results of evaluating non-enzymatic glucose sensors in detecting urinary glucose

Materials	Sensitivity ($\mu A\ cm^{-2}\ mM^{-1}$)	Linear range	LoD	Ref
APBA/MBA/AuNPs	-	0.5 – 30 mM	43 µM	(Chen *et al*., 2021)
NiNPs-LIG	5796.18	12 µM – 1.5 mM	0.0152 µM	(Nugba *et al*., 2023)
Co-MOF	-	5 µM – 900 µM	1.6 µM	(Zhang *et al*., 2020)
CoFe/C	59.72	0-3 mM	-	(Janyasupab *et al*., 2019)
NC-NiS@ NS-NiS/NF	54.6	20.0 µM - 5.0 mM	0.0083 µM	(Arivazhagan *et al*., 2021)
Pt nanopore/ Nafion	0.728	21.68 mM	10 µM	(Lee *et al*., 2013)
SPCE/CuO-IL/rGO	-	0.03–7.0 mM	0.19 µM	(Janmee *et al*., 2021)
gt-$NiCo_2O_4$NSs	729.72	150 nM – 8.86 mM	7.35 nM	(Babulal *et al*., 2021)
AgNPs/CuOHCs/Fe_3O_4	-	0.06 – 1000 µM	0.015 µM	(Baghayeri *et al*., 2020)
CuNPs/HD-CNT*f*	1.942	-	28 nM	(Gupta *et al*., 2021)
Nf/Au-CuO	3126.76	5 µM–650 µM	1.4 µM	(Felix *et al*., 2018)
SPCE/CuO	627.3	-	0.2 µM	(Jagadeesan *et al*., 2019)
NiO@SDHCNSs	1697	0.001-13 mM	0.52 µM	(Madhuvilakku *et al*., 2018)
NiCo-S/ CNH/GCE	1842	0.001-4.53 mM	5.6 µM	(Kachouei *et al*., 2022)
NiCo-S/CH/GSPEs	467	0.5 – 6.0 mM	35.3 µM	
rGO/Co_3O_4	-	25 nM - 2 µM	3.6 nM	(Maghsoudi & Mohammadi, 2020)
Ago-CuO	150.17	0.005 – 30 mM	5 µM	(Viswanathan *et al*., 2020)
CdS@MgO	28570	1.25 µM – 15 mM	0.02 µM	(Ullah *et al*., 2022)
Au@CuO/ LIG	1.124×10^6	0.005 – 5 mM	1.8 µM	(Cui *et al*., 2023)
LSGE/ AuNPs	-	10 µM - 10 mM	6.3 µM	(Zhu *et al*., 2021)
MWCNT/ ZnO QDs	9.36	0.1-2.5 µM	0.208 µM	(Vinoth *et al*., 2021)
Co_3O_4/MXene@CFE	19.3	0.05 µM – 7.44 mM	10 nM	(Manoj *et al*., 2020)
Zr/CuO MF	$1.250 \times 10^6 \pm$ 0,006	-	0,8 µM	(Chandhana *et al*., 2023)
Cu-MOF	89	0.06 µM – 5 mM	10.5 nM	(Sun *et al*., 2018)

4. Conclusion and perspective

This mini-review examined the latest developments in electrochemical urine glucose sensors with materials that were functionalized both enzymatically and non-enzymatically to obtain probes with good accuracy. Electrochemical enzymatic glucose

detectors have attained extensive commercial use owing to their exceptional attributes of high sensitivity, specificity and prompt response. Nevertheless, these sensors' short shelf life and high production costs limited their applicability. Therefore, these limitations of the enzymatic sensors were overcome by developing non-enzymatic glucose sensors. These sensors used conductive materials such as nano-based materials (nanotubes, bimetal nanomaterials, nanocomposites), metal alloys and metal oxides to modify electrodes. Materials with high conductivity were expected to increase the electron transfer rate, thereby increasing sensor sensitivity. Although many materials have been utilized for urinary glucose sensing systems, advanced exploration regarding the development of new materials is still needed to obtain reliable sensors with low LoD, easy, portable and cost-effective.

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