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Review

Designing Nanocomposite-Based Electrochemical Biosensors for Diabetes Mellitus Detection: A Review

Xiang Guo,*[,†] Jiaxin Wang,[†] Jinyan Bu,[†] Huichao Zhang,[†] Muhammad Arshad,[†] Ayesha Kanwal,[†] Muhammad K. Majeed,* Wu-Xing Chen, Kuldeep K Saxena, and Xinghui Liu*

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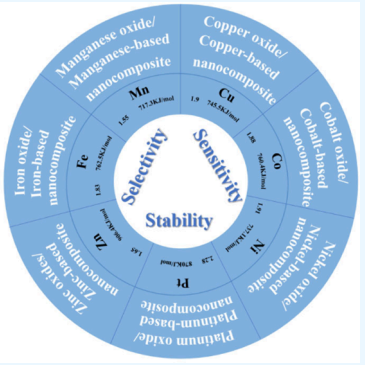
ABSTRACT: This review will unveil the development of a new generation of electrochemical sensors utilizing a transition-metal-oxide-based nanocomposite with varying morphology. There has been considerable discussion on the role of transition metal oxide-based nanocomposite, including iron, nickel, copper, cobalt, zinc, platinum, manganese, conducting polymers, and their composites, in electrochemical and biosensing applications. Utilizing these materials to detect glucose and hydrogen peroxide selectively and sensitively with the correct chemical functionalization is possible. These transition metals and their oxide nanoparticles offer a potential method for electrode modification in sensors. Nanotechnology has made it feasible to develop nanostructured materials for glucose and H_2O_2 biosensor applications. Highly sensitive and selective biosensors with a low detection limit can detect biomolecules at nanomolar to picomolar (10^{-9} to 10^{-12} molar) concentrations to assess physiological and metabolic parameters. By mixing carbon-based materials (graphene oxide) with inorganic nanoparticles, nanocomposite biosensor devices with increased sensitivity can be made using semiconducting nanoparticles, quantum dots, organic polymers, and biomolecules.



1. INTRODUCTION

Diabetes mellitus, one of the most prevalent and deadly diseases, is a chronic metabolic illness that affects millions of individuals worldwide. According to 2019 IDF data, China, India, and the United States of America are the three countries with the largest number of diabetic patients with 116.4 million, 77 million, and 31 million, respectively. As of 2021, the number of diabetic patients worldwide has reached 529 million. It is estimated that by 2050, the number of diabetic patients worldwide will reach 1.31 billion. China and India continue to bear the highest burden of diabetes. By 2050, the number of diabetics is anticipated to rise from 422 million to 642 million. Accurate and stringent blood glucose monitoring is necessary for optimal diabetic management. With such high demand, analytical instruments for blood glucose measurement are projected to account for 85% of the biosensor market. Diabetes mellitus is a hereditary disease. The group of disorders characterized by an elevated blood sugar level is heterogeneous. People with diabetes enable blood sugar metabolism in their blood due to glucose passing into the urine. Diabetes causes insufficient kidneys, lower limbs, heart disease amputation, and blindness in adults. Diabetes mellitus has two types: insulin-dependent diabetes (type 1, IDDM) and non-insulin-dependent diabetes mellitus (type 2, NIDDM). Type 1 is referred to as juvenile diabetes because of a pancreatic insulin hormone deficiency that is separated from the pancreatic beta-cell. It is a congenital disability. Sometimes, a viral infection activates the T-cells of the immune system and destroys the beta cells. As a result, insulin is not produced, so patients is treated with exogenous insulin for survival.[1] Polymorphisms and genetic diseases (type 1 in general) of diabetes are present in the short-arm of chromosome 11. Diabetes type 2 disease is non-insulin-dependent and more common than type 1. Currently, worldwide, 90% of diabetes patients are type 2. In type 2 diabetes, a person fails to respond to insulin and cannot take glucose from the blood. These individuals produce endogenous insulin. In obese populations and after age 40, it is more common. Diabetes also develops environmental factors early. Before 25 years of age, 2−5% of diabetes happen. It is called young people's maturity diabetes (MODY). MODY is an autosomal dominant trait. MODY is 50% caused by changes in the glucokinase gene. Glucokinase is an enzyme that is present in the pancreas and responsible for the conversion of glucose to glucose 6-phosphate.

MODY can be caused by a mutation in the other four genes that encode pancreatic development and insulin expression transcription factors. However, these MODY genes do not play

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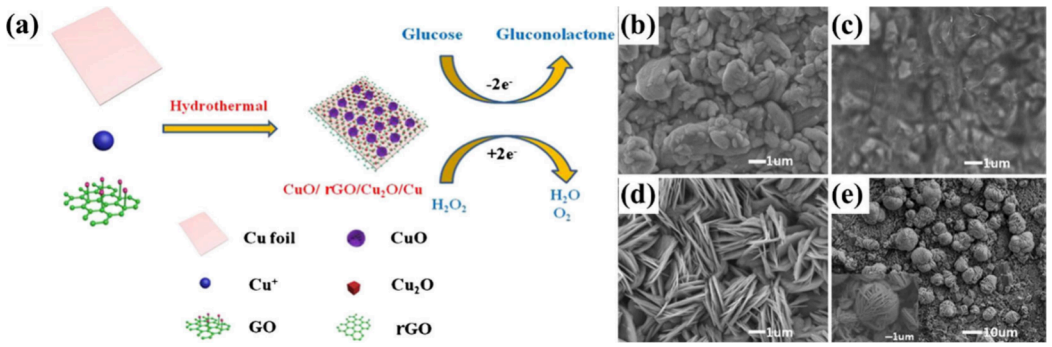

Figure 1. (a) Schematic representation for the production and electrochemical testing of the CuO/rGO and Cu_2O/Cu electrode, (b) FESEM images of CuO/Cu, (c) rGO/Cu_2O/Cu, (d) CuO/Cu_2O/Cu, (e) CuO/rGO/Cu_2O/Cu, Inset: 3D hierarchical spherical CuO Reproduced with permission from ref 22. Copyright 2017 Springer-Verlag Wien.

an essential role in adult-onset type 2.[2] The food sector, fuel cells, the environment, and the pharmaceutical industries benefit from quantitative glucose measurement .[3,4] Detection of H_2O_2 and $C_6H_{12}O_6$ is essential in enterprise and clinical applications in the food industries. Glucose and hydrogen peroxide concentrations are crucial in our bodies because both act as oxidizing agents. In diabetes, glucose levels decrease and increase because of a lack of insulin. The pancreatic islets of Langerhans beta cells synthesize insulin.[5] Nanomaterials are very important in industry because they have been used in many fields, such as medicine, plastics, ceramics, and the food industry, to detect poisonous chemicals. They determine diverse biological chemicals, like glucose, H_2O_2, uric acid, and dopamine.[6−8] Nanocomposite materials are also utilized in electric biosensors. Hydrogen peroxide is vital in many industries such as food, pharmaceuticals, plastics, and medicine.

H_2O_2 is the byproduct of numerous oxidase enzymes, including glucose oxidase and cholesterol oxidase.[7−9] The product of glucose oxidation is hydrogen peroxide. The hydrogen peroxide level in our organism causes several disorders, such as cancer and renal insufficiency.[10] Increasing the glucose level in our body causes the symptoms of diabetes, so for this purpose, a very accurate, low-cost, low-limit detection, sensitive, long-term stability, and nonenzymatic electrochemical biosensor has been synthesized for the detection of $C_6H_{12}O_6$ and H_2O_2. Noninvasion electrochemically detection of $C_6H_{12}O_6$ and H_2O_2 is very accurate compared to the enzymatic electrochemically biosensor.[11] Enzymes are proteins and are very specific. They are susceptible to temperature, pH, and heat. Enzymes denature quickly if a minor temperature, pH, or heat change occurs. It is challenging to transport and has no long-term stability. Therefore, nonenzymatic electrochemical sensing of $C_6H_{12}O_6$ and H_2O_2 is accurate and suitable because they are easy to transport and handle.[12−14]

Early detection and diagnosis of illness is a possible application for electrochemical biosensor platforms because of their simple production, cheap cost, and excellent biocompatibility.[15,16] New surface changes, microfabrication methods, and nanomaterials can be used to create sensitive and selective electrochemical biological sensor systems.[17] Platforms based on electrochemical biosensors offer potential uses in the early detection and diagnosis of illness.[18] This review focuses on applying metal and metal oxide nanocomposites in the biosensor. Various types of nanocomposite-based biosensors have been investigated in that regard. Key biosensor categories were electrical, flexible, and biosensors of the field.[16] This work highlights the most recent advances in the design of sensing and biosensor systems based on functional nanomaterials. The performance of several biosensors is thanks to their superior electrical, mechanical, thermal, and biological characteristics.[19]

2. TRANSITION METAL/METAL OXIDE FOR BIOSENSORS

2.1. Copper Oxide/Copper-Based Nanocomposite.

The copper oxide nanocomposite presents potential and stability in the detection and H_2O_2 of $C_6H_{12}O_6$. Copper oxide is a semiconductor-type transition metal oxide with a tiny energy gap of only 1.2 eV. Copper oxide shows great characterization with low cost, high specificity, and nontoxicity.[20] The graphene is mixed with other heteroatoms of metal oxide (copper, cobalt, nickel, manganese, platinum, and zinc). The advantages of these nanostructured-based materials are enhanced surface area and sensitivity. Additionally, when nanostructured materials are doped in carbon-based materials, metal (metal oxide) hybridization shows excellent electrolytic behavior and efficiently enhances selectivity, conductivity, and low-limit detection. Furthermore, it increases the conduction path of electricity of electrons and improves the ability to transfer quickly to detect H_2O_2 of $C_6H_{12}O_6$. Reduce graphene oxide is functionalized with copper oxide. It shows excellent efficiency toward seeing H_2O_2 of $C_6H_{12}O_6$. The trouble is that Cu's nanostructure is always exploited in an alkaline solution. So, first, researchers transformed Cu into a $Cu(OH)_2$ nanostructure by electrochemical oxidation in an alkaline solution. However, it is not good electrochemically conducting to apply glucose and hydrogen peroxide, so when they operationalized with the reduced graphene oxide, they showed excellent stability, sensitivity, low limit detection, conductivity, and thermally stability.[21] Unique Cu/CNCs were synthesized by thermolysis of a simple Cu/CMS (HKUST-1) structure generated by the nanosphere of 3D-KNCs for the detection of nonenzymatic sensing, employed in different techniques, and are closely packed on the 3D dimensional nephritis stem-driven macroporous carbon (3D-KSCs). Thermo-logical procedures for nonenzymatic detection of $C_6H_{12}O_6$ and H_2O_2, which were less costly and extremely easy to handle, were introduced in history. People have created Cu nanospheres/porous carbon/3D-KSCs with a broad linear range of 15.84 μM to 5.62 mM, low limit detection of 4.8 μM, and high sensitivity of 28.67 μA mM^{-1} cm^{-2}. The electrode was functional and showed great intention toward the electro-

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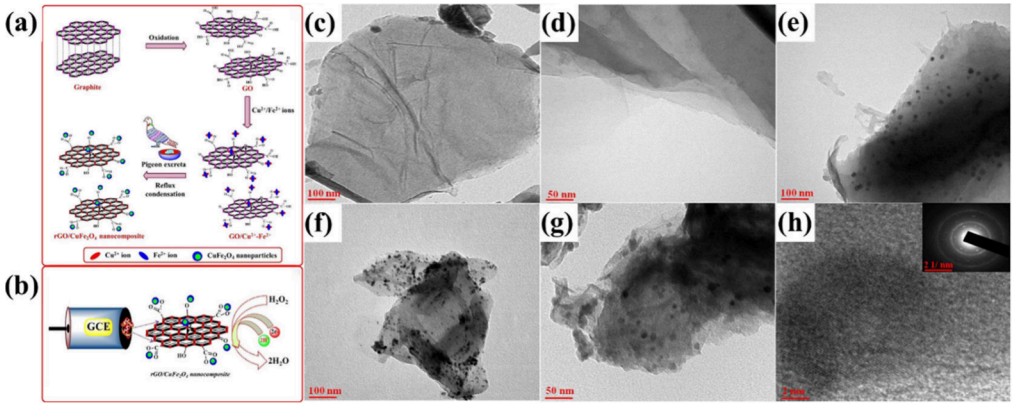

Figure 2. (a) Illustrative scheme for nanocomposite rGO/$CuFe_2O_4$ nanocomposites, (b) rGO/$CuFe_2$/GCE electrocatalytic reduction of H_2O_2, (c, d) TEM images of rGO, (e) rGO/Cu, and (f-h) rGO/$CuFe_2O_4$ nanostructures, (inset of h) corresponding SAED pattern. Reproduced with permission from ref 27. Copyright 2017 American Chemical Society.

catalytic activity of glucose oxidation.[21] The hydrothermal and in situ deposited technique is utilized to make a Cu nanocomposite and subsequent deposit on copper foil (Figure 1). Three types of nanocomposite involvements (rGO/Cu_2O, Cu_2O/Cu, and CuO/rGO). A typical reaction occurs between graphene and copper. Graphene carries a positive and copper contains a negative charge so that the electrostatic force of attraction is present in them so that they show excellent efficiency toward the application of biosensing H_2O_2 of $C_6H_{12}O_6$ mutant foil amperometric detection, indicating glucose decreasing (0.65 V vs. SCE) and H_2O_2 (0.3 V) amperometric detection. 0.1 M NaOH detective glucose <0.5 μM to 8.3 mM, and pH = 7 sensory sensing to H_2O_2 sensation is 366.2 $\mu AmM^{-1}cm^{-2}$, the limit is 0.05 μM, the linear range of the detection <0.5 μM to 9.7 mM, and the response time is 0.8s.[22]

In this article, eco-friendly chemicals (green chemicals) are used by researchers for the detection of $C_6H_{12}O_6$ and H_2O_2 based on the graphite electrode functionalized with copper oxide fabricated with reduced graphene oxide (CuNps/rGO-PGE). They showed great sensitivity, straightforwardness, fastness, low cost, and low limit detection because the nanosized copper particle shows much less value than the other group and shows excellent efficiency toward applying robust sensing. Copper oxide nanoparticles operationalized with the reduced graphene oxide show excellent stability, CuO/NP/rGO-PGE sensitivity shows great efficiency and stability in alkaline solution, and cyclic voltammetry shows the great electrocatalytic activity of glucose. The low limits of the [4760 (±3.2) μA mM^{-1} cm^{-2}] and [0.091 (±0.003) μM)] were detected by the amperometric method.[23] The growth of CuO nanoneedles in the presence of moderate circumstances in graphene quantum dots (GQDs/CuOs) graphene nanocomposites (GQds/CuO). GQDs/CuO nanocomposites were manufactured to create a blue solution in the presence of H_2O_2 and are utilized to simulate the oxidization of (TBM) 3,3,5,5-tetramethylbenzidine as a highly productive peroxidase. This technique shows that the generation of OH radicals indicates the nature of the peroxidase-like activity of GQDs/CuO nanocomposites. GQDs/CuO nanocomposites effectively enhance the absorbance at 650 nm for detecting hydrogen peroxide in the wide linear range of 0.5−10 μM and a limit of detection (LOD) of 0.17 μM. It is practical, accurate, efficient, cheapest, selective, and sensitive. The GQD/CuO catalytic reaction and enzyme glucose oxidation with glucose oxidase is amended by a technique for detecting $C_6H_{12}O_6$ in the blood from a wide linear range of 2 to 100 μM with low-limit detection.[24] Detection of $C_6H_{12}O_6$, a novel transition metal, is used, which is Cu-sulfide fabricated with reduced graphene oxide, which shows excellent stability and sensitivity toward the oxidation of glucose. Based on the nonenzymatic detection of $C_6H_{12}O_6$, which has a compassionate and stable sensitivity, MoS_2-rGO is more efficient than Cu_xS-rGO's wide linear range of 2−6330 μM and LOD 0.6 μM. The highly productive sensor offers an efficient response in $C_6H_{12}O_6$ detection for human serum of 97.2% and 101.2% was produced. These easy and high-efficiency approaches may be utilized to synthesize using electrochemical sensors and electrocatalysis by using functionalized multiple metals sulfide composites.[25] Electrochemical methods to prepare copper nanoparticles are eco-friendly, low-cost, and highly sensitive. Copper nanoparticles have received great attention in nanoscience technology because they are thermally stable and have good conductivity. Different methods are used to prepare copper nanoparticles, such as hydrothermal, precipitation, etc. In the preceding study, many people employed stabilizing agents. For example, Karthikeyan and C synthesized CuNPs, such as organic, inorganic, bimolecular, surfactant, and other biopolymers, to boost copper nanoparticle stability. A highly sensitive and stable nanocomposite was created for $C_6H_{12}O_6$ detection in rGO/Histidine-CuNPs/GCE. This sensor has an optimum linear response to Hydrogen peroxide of 1 μM to 5 mM with a low detection limit of 75 nm. The most significant thing in nanocomposite development is that the sensors that are selective and sensitive to H_2O_2 are very low-cost, readily available, eco-friendly, and easy to manufacture.[26] Green chemistry is also of great importance for the application of biosensing. The researcher used a significantly stabilized and eco-friendly pigeon excreta as a reducing agent for detecting H_2O_2, they synthesized ($CuFe_2O_4$) functionalized with reduced graphene oxide (Figure 2). Due to the spherical shape of the ($CuFe_2O_4$), it uniformly absorbs the reduced graphene oxide, which shows great sensitivity and conductivity. rGO/$CuFe_2O_4$ nanocomposite was produced in a preprepared form, with high sensitivity at 265.57 $\mu AmM^{-1}cm^{-2}$, a low detection limit of 0.35 μM, and a wide linear range between 1 μM to 11 mM, toward Hydrogen peroxide. The modified structure has shown a significant effect on the sensing of H_2O_2. These features not only discuss selectivity, stability, and nonenzymatic sensing tools, but also provide information

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about eco-friendly nanocomposites and the assessment of H_2O_2 concentration in the human serum sample.[27]

To detect $C_6H_{12}O_6$ and H_2O_2, researchers synthesized nonporous (np-PtCu) via a step dealloying method under mild conditions. Then, they fabricated a glassy carbon electrode that showed excellent efficiency in sensing $C_6H_{12}O_6$ and H_2O_2 toward the neutral pH. Screening H_2O_2 assay demonstrates a high working voltage of 0.7 V, a significant linear range of (0.01 to 1.7 mM), low limits detection of 0.1 μM, and a high reversible hydrogen electrode. This technique is unsuitable for the availability concentration of dopamine, acetaminophen, and ascorbic acid.[28] The researcher developed a bimetallic copper oxide-gold nanoalloy for the colorimeter detection of $C_6H_{12}O_6$ and H_2O_2. When CuO-Au nanoalloys were added to the solution containing DPBF and H_2O_2, the productivity of ROS was at a very high rate (0.1092 min^{-1}). The absorption peak of DPBF at 430 nm decreased, showing ROS generation. The CuO-Au nanoalloys were estimated for their colorimetric detection of $C_6H_{12}O_6$. The show great LOD for the $C_6H_{12}O_6$ was evaluated to be 6.75 μM. The sensing of $C_6H_{12}O_6$ occurred in two steps and under various pH conditions; the first step is the $C_6H_{12}O_6$ oxidation, which takes place at pH = 7.4 at 37 °C. Researchers provided the optimum condition for CuO-Au nanoalloys peroxidase-like activity at room temperature at pH = 4 at room temperature.[29] Researchers are striving to build a highly sensitive, selective $C_6H_{12}O_6$ and H_2O_2 detector, and it is incredibly essential to both the healthcare and food industries, so they were able to synthesize nonenzymatic electrochemical sensing utilizing CuO nanorods for $C_6H_{12}O_6$ and H_2O_2 sensing. The CuO-based nanorods demonstrate a high sensitivity for ~1319 μA mM^{-1} cm^{-2}, a linear 5−825 μM glucose-sensing range. The sensing of H_2O_2 in a linear range of 0.25−18.75 mM is ~84.89 $\mu AmM^{-1}cm^{-2}$ and shows the same electrode's remarkable selectivity toward the H_2O_2. Cu−O nanocomposite displays various sensitivities and selectivity.[30] Development of ultrasensitive and ultra-selective sensors golden-copper alloy nanoparticles (Au−Cu alloy NPs) for the sensing of nonenzymatic $C_6H_{12}O_6$ and (H_2O_2), Au−Cu−NPs have branched nanostructures that are an electrochemical catalyst (Figure 3). The series of Au−Cu−NPs are generated using a reduction process with different ratios of metal. The morphology of the AUC/NPs is varied by changing the AU content in the synthesis reaction from highly branched structures (nanourchin, nanobramble, nanostar, nanocrystal). Cu-rich/Au−Cu nanobramble and Au-rich/Au−Cu nanostar show selective electrocatalysis conductors for H_2O_2 electro-oxidative behavior.

With a linear operating range of 0.25 to 10 mM, the Au−Cu nanobramble sensor has considerable potential in glucose detection. This sensor has a sensitivity of 339.35 μA $mM^{-1}cm^{-2}$, adequate selectivity, and a reasonable stability detection limit (LOD) of 16.62 μM. Furthermore, the Au−Cu nanostar sensor has outstanding electrochemical reactions for H_2O_2 reduction with remarkable selectivity, reproducibility, and a fast duration of response of around 2−3s. The H_2O_2 linear range is 0.05 to 10 mM, with LOD and 10.93 μM and 133.74 μA; given the synergistic surface structure and atomic composition effects, Au−Cu alloys are a successful nano-catalyst for the sensing of both $C_6H_{12}O_6$ and H_2O_2.[31]

2.2. Cobalt Oxide/Cobalt-Based Nanocomposite. Cobalt is a semiconductive p-type. It is built upon nanoparticles and is widely applicable in lithium batteries, biosensors, and magnetic materials. Various techniques are

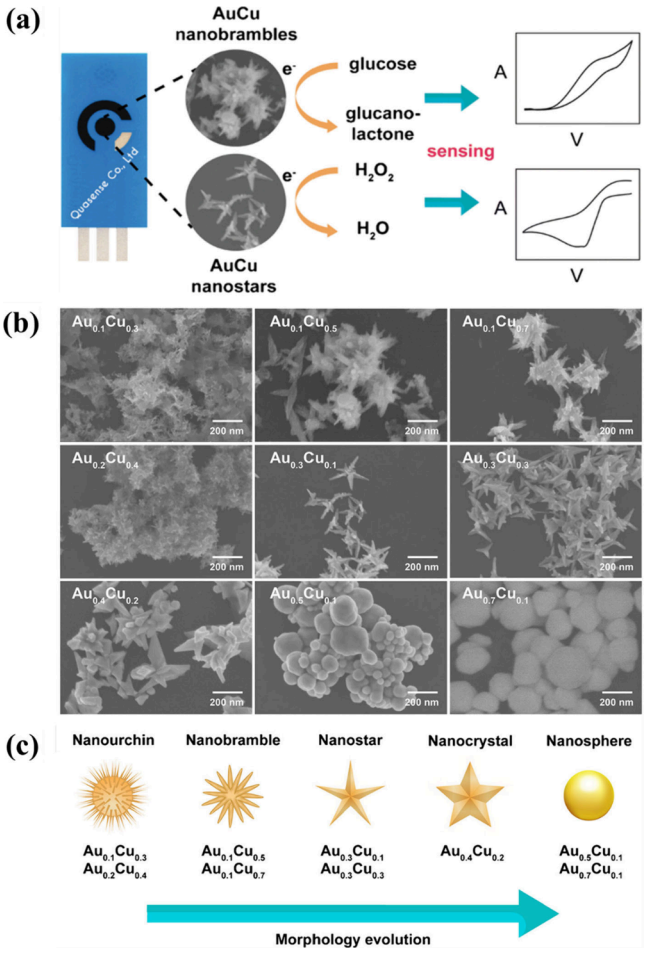

Figure 3. Schematic depiction of Au−Cu alloy glucose and H_2O_2 sensing mechanism, (b) SEM images of Au_xCu_y alloy NPs with different volumes of Au and Cu precursors in the reaction mixture, and (c) schematic diagram showing a morphology evolution of Au_xCu_y alloy NPs as a function of Au precursor. Reproduced with permission from ref 31. Copyright 2020 Springer-Verlag GmbH Austria, part of Springer Nature.

accessible for cobalt oxide synthesis, such as sol−gel, hydrothermal technique, heat decomposition processes, and reflux techniques.[32] The spinal-shaped crystal structure of CoO has many functional applications, such as heterogeneous catalysis, electrochemical devices, biosensors, and magnetic materials. The hydrothermal method is the most efficient method for preparing CoO because the crystal of the cobalt oxide shows great magnetic properties and the optical and supercapacitance properties of cobalt oxide.[33] For enhancement of the activity of electrochemical properties of the biosensor, reduced graphene oxide is operationalized with cobalt oxide, which is more reliable, low cost, susceptible, and incredibly efficient and then modified on the glassy carbon electrode. They show more efficiency toward the application of sense. The electrochemical performance of rGO/Co_3O_4 nanoparticles has been assessed for glucose detection by cyclic voltammetry without enzymes (CV). With a short reaction time of low limit detection of 3.6 nM, there was an excellent sensitivity to glucose with 5s LOD. The capability of the sensor to detect glucose in the actual test showed its potential utility for rapid and precise diagnosis of daily glucose.[34] Glucose detection and hydrogen peroxide development are highly

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effective. It is a highly active catalyst electrode offering broad surfaces and a straightforward evaluation of target molecules.

This article examined efficient (Co_3N-NW/TM) synthesis as a catalytic electrode for glucose oxidation occurring in an alkaline solution. After electrochemical testing of the Co_3N-NW/TM shows excellent nonenzymatic sensing of $C_6H_{12}O_6$ and H_2O_2. High sensitivity, with a range between 0.1 μM and 2.5 mM, and a low detection limit of 50 nM has been produced by detecting glucose with reasonable stability and productiveness of 3325.6 μA mM^{-1} cm^{-2}. The satisfactory sensitivity of 139.9 μA mM^{-1} cm^{-2} using an amperometric technique indicates a linear distance of 2 μM to 28 mM and a low limit detection of 1 μM (S/N= 3). Sensing H_2O_2, application is beneficial for determining different biomolecules and checking the $C_6H_{12}O_6$ and H_2O_2 in human blood serum.[35] By combining two metals (bimetallic) at 25-butaoxidase-like activities are increased owing to a strong redox cycling effect between the Co(III)/Co(II) and Cu(II) pairs due to the bridging ligand, 2,4,6-tri(4-carboxyphenyl)-1,3,5-triazine with Cu(II) and Co(II) ions. Enzymatic sensing of the H_2O_2 fluorometric method was used, which shows low limit detection of 0.33 μM.[36]

Zhao et al. synthesized copper(II)/cobalt(II) organic gel with enhanced peroxidase-like activity for the fluorometric determination of glucose and H_2O_2 (Figure 4).[37] The resulting metal−organic gel (MOG) shows enhanced peroxidase-like activity, most likely due to the synergetic redox cycling between the Co(III)/Co(II) and Cu(II)/Cu(I) pairs. The MOG can catalyze the reaction of H_2O_2 with terephthalic acid (TPA), producing a blue fluorescence product with the maximum excitation/emission at 315/446 nm. This study may open a new avenue to design and synthesize nanomaterial-based biomimetic catalysts with multiple metals synergistically enhanced catalytic activity for potential applications in biocatalysis, bioassays, and nanobiomedicine.

Multiple illnesses can be caused by an abnormal quantity of (H_2O_2) in blood plasma and cells. A sensitive and selective technique for monitoring H_2O_2 is therefore needed. A hydrogen peroxide-detection platform based on a nanocomposite of cobalt oxyhydroxide (Co-OOH) and reduced graphene oxide (rGO) was developed in the current study. Soft chemistry was used to create CoOOH nanoflakes assembled on the surface of rGO. Chemistry was used to establish Co-OOH nanoflakes, which were subsequently constructed on the surface of rGO. When it came to H_2O_2 detection, the nanocomposite showed an outstanding electrochemical performance. As a result, the LOD was 0.01 μM for the linear ranges of 6−200 and 200−1500 μA mM^{-1} cm^{-2}. Compared to zero-dimensional nanoparticles, CoOOH nanoflakes had more exposed catalytic active sites, while rGO had excellent conductivity, which together had a synergistic impact. With outstanding results, H_2O_2 was detected in human blood and HeLa cells using the nanocomposite.[38] Graphene oxide encapsulated cobalt oxide polyhedrons (3DGO−Co_3O_4PHs), and cobalt oxide polyhedrons were produced by hydrothermal means for the susceptible detection of hydrogen peroxide (H_2O_2). To confirm the structure and shape of Co_3O_4, elemental, diffraction, and electrochemical investigations were done. In addition to its outstanding electrocatalytic activity, the composite has a wide electrochemical area and a roughened surface due to the excellent synergy between the Co_3O_4/PHs and the GO. Physiological, metabolic, pharmacological, and therapeutic uses of H_2O_2 need the creation of susceptible

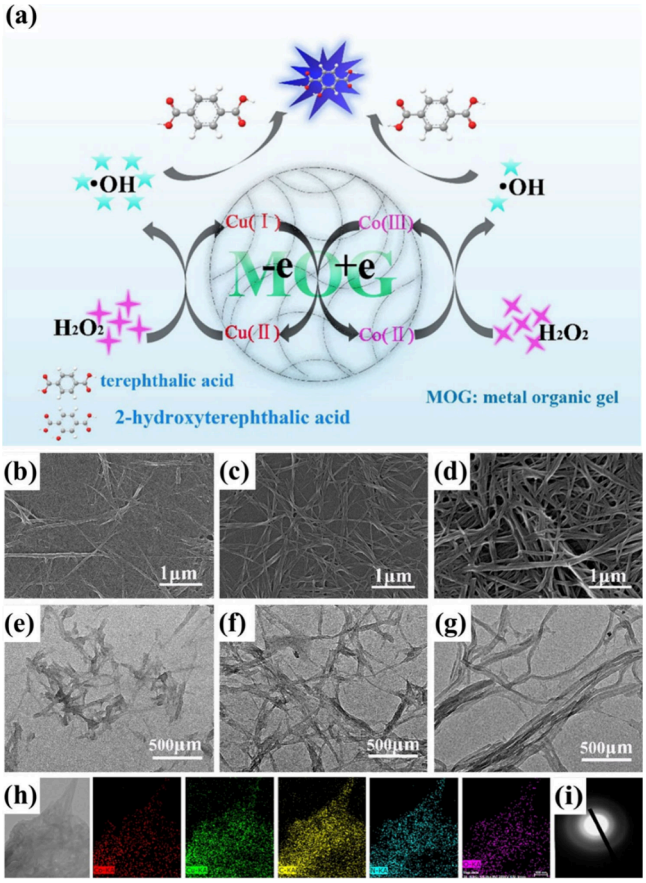

Figure 4. (a) Possible mechanism for $Cu_{0.5}/Co_{0.5}$-MOG as an artificial enzyme, (b−d) SEM images of Cu-MOG, $Cu_{0.5}/Co_{0.5}$-MOG and Co-MOG, (e-g) the corresponding TEM images; (h) TEM and elemental mapping images of $Cu_{0.5}/Co_{0.5}$-MOG for Co, Cu, C, N and O, and (i) SAED pattern of $Cu_{0.5}/Co_{0.5}$-MOG. Reproduced with permission from ref 37. Copyright 2019 Springer-Verlag GmbH Austria, part of Springer Nature.

sensors. An assay for H_2O_2 that is fast, sensitive, selective, repeatable, and durable was disclosed by using a 3D GO−Co_3O_4/PHs modified electrode with an LOD of 15 nM; the sensor is more sensitive than sensors that have been previously reported. Real-time analysis of commercially available contact lenses and disinfection cleaning solutions was demonstrated without preparation.[39] After spraying Co_3O_4 and MoS_2 micropowders at room temperature in a vacuum chamber, the nanocomposites were deposited on titanium sheets. The H_2O_2 in 0.1 M NaOH was detected using Co_3O_4−MoS_2/NCs/Ti electrodes instead of enzymes. X-ray photoelectron spectroscopy indicated an increased synergy between cobalt-based active sites and MoS_2 species. Titanium-modified electrodes with Co_3O_4−MoS_2/NCs showed excellent selectivity for H_2O_2-oxidation in NaOH at 0.1 M concentrations. The electrodes' sensitivity reached a high of 3000 μA mM^{-1} cm^{-2} at a Co_3O_4 content of 75%.[40]

Graphene oxide, cobalt oxide, and horseradish peroxidase (HRP/GO-Co_3O_4) were synthesized in a Nafion matrix and applied to a glassy carbon electrode (GCE). Using cyclic voltammetry and DC potential amperometry at a working potential of 0.57 V (vs Ag/AgCl) at pH 7.0, the modified electrode's reaction to H_2O_2 was studied. A LOD of 2 mM and a response time of the 20s are all included. A significant percent recovery value of H_2O_2 in a hair color solution was

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used to test the efficacy of the sensor for routine analysis.[41] A high-performance trifunctional catalyst, Co_3O_4 nanoparticles linked to nitrogen-doped reduced graphene oxide (Co_3O_4/N-rGO), is utilized for oxygen reduction reaction (ORR), oxygen evolution reaction (OER), and hydrogen peroxide (H_2O_2) detection, as shown in Figure 5. The electrocatalytic activity of

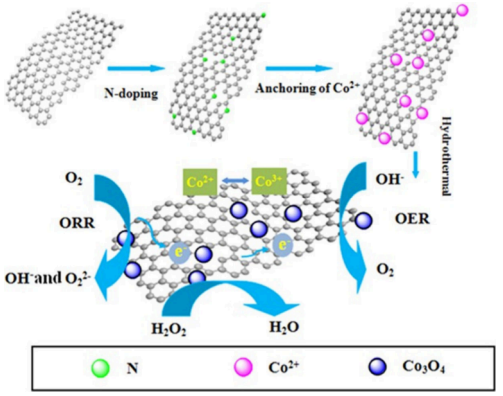

Figure 5. (a) Schematic illustration of the synthesis of Co_3O_4/N-rGO. Reproduced with permission from ref 42. Copyright 2017 Springer Nature.

Co_3O_4/N-rGO for hydrogen peroxide reduction was investigated by using cyclic voltammetry, linear sweep voltammetry, and chronoamperometry. Its linear response ranges from 0.5 to 17.5 mM, and its LOD is 0.01 mM when H_2O_2 is reduced at 0.6 V. Due to its vigorous ORR activity, Co_3O_4/rGO or nitrogen-doped reduced graphene oxide (N-rGO) has minimal catalytic activity. With an ORR peak potential of 0.26 V (compared to Ag/AgCl) and many-electron transfer numbers of 3.4, the Co_3O_4/N-rGO hybrid exhibits satisfactory catalytic activity but better stability to Pt/C in alkaline solutions.[42]

A new binary ZnO−CoO nanocomposite (ZnO−CoO/rGO) was effectively produced using an easy and inexpensive two-step method. On a glassy carbon electrode, the resulting ZnO-CoO/rGO hybrids with excellent electrical conductivity and numerous active sites may be adjusted to detect glucose and H_2O_2 simultaneously. It has a wide linear range of glucose (10 μM to 11.205 mM) and H_2O_2 (25 μM to 11.1 mM), and it has a sensitivity of 168.7 $\mu AmM^{-1}cm^{-2}$ for H_2O_2 and a range of 25A mM to 11.1 mM. The LOD is 1.3 and 0.44 μM for the oxidation of glucose and the reduction of H_2O_2. Regarding detecting glucose oxidation and hydrogen peroxide reduction, LOD are 1.33 μM and 0.44 μM, respectively. In addition, the ZnO−CoO/rGO hybrid's exceptional selectivity, long-term stability, and excellent repeatability make them a potential choice for practical applications.[43] These nanoparticles of CoFe on nitrogen-doped graphene were used to create a novel enzymeless sensor for hydrogen peroxide (H_2O_2). The hydrothermal reaction from graphene oxide synthesizes coFe-layered double hydroxides (CoFe/LDHs). In the end, CoFe/LDHs/GO pyrolysis under NH_3 results in CoFe/NGR. The electrocatalytic activity of CoFe nanoparticles is substantially enhanced by supporting them on the NGR because of the high electric conductivity of NGR. A nonenzymatic detection of H_2O_2 can be achieved by combining CoFe with NGR. Its electrocatalytic activity toward H_2O_2 is higher than that of unsupported CoFe nanoparticles, with a high sensitivity of 435.7 $\mu AmM^{-1}cm^{-2}$ and an LOD of 0.28 μM to reduce H_2O_2.[44] Rearchers used EDTA as the chelating agent to synthesize porous (CoHCF-NSp's) (50 nm in size). This is owing to CoHCF's fast nucleation, which is enhanced by increasing the EDTA concentration and 60 °C heating of the EDTA complex. A significant improvement in electrochemical characteristics was achieved by synthesizing porous nanospheres with a high surface area and pore volume. For the construction a susceptible H_2O_2 sensor, porous CoHCF-were NSp was utilized. Using the CoHCF nanospheres, screen-printed sensors demonstrated a linear response of 0.002−1.13 mM, with a LOD of 2.1 μM. Sensitivity was measured at 329 $\mu A\ mM^{-1}\ cm^{-2}$, significantly higher than most previously mentioned H_2O_2 sensors. A study of the manufactured sensors revealed that they were stable at room temperature. It was determined that the sensors successfully tested real-world samples (lake, river water, and soft drink).[45] By borohydride reduction techniques without stabilizers, MWCNT-supported Ag, Co, and Ag−Co alloy nanocatalysts were produced at various metal loadings to gain improved hydrogen peroxide sensitivity. Glassy carbon electrode (GCE) was modified with Ag/MWCNT, Co/MWCNT, and Ag−Co/MWCNT alloy nanoparticles for electrochemical studies by using cyclic voltammetry (CV) and differential pulse voltammetry (DPV). In 0.1 M phosphate-buffered solution, Ag−Co/MWCNT/GCE showed the best performance in the electrochemical oxidation of H_2O_2 (PBS). For Ag−Co/MWCNT/GCE, the sensitivity and LOD values were 57.14 $\mu A\ cm^{-2}\ mM^{-1}$ and 0.74 μM, respectively. The value of Ag/MWCNT/GCE is 41.66 $\mu A\ cm^{-2}\ mM^{-1}$, while for Co/MWCNT/GCE, it is 13.88 $\mu A\ cm^{-2}\ mM^{-1}$. It was anticipated that the LOD values for Ag and Co were 1.84 and 3.3 μM for MWCNT and GCE, respectively.[46] For electrochemical detection of H_2O_2, Co_3O_4 was produced using a simple hydrothermal and calcination process. Co_3O_4 is combined with cypress leaves, loofah sponge, and pine needles to increase its electrochemical performance. According to the electrochemical tests, the Co_3O_4/loofah sponge-derived carbon composite demonstrated greater electrochemical activity toward H_2O_2 than the other two composites. Using Co_3O_4/loofah sponge-derived carbon, the sensor's linear range was from 5.00 μM to 11.40 mM with a 47.83 $\mu AmM^{-1}cm^{-2}$ sensitivity and a 1.50 μM (S/N = 3) LOD. As a result, this new nonenzymatic sensor can be used to detect H_2O_2.[47]

2.3. Nickel Oxide/Nickel-Based Nanocomposite. Nickel nanoparticles (NiNPs)-decorated electrochemically reduced graphene oxide (ERGO) nanocomposite (NiNPs/ERGO) was fabricated on an indium−tin-oxide electrode using a facile one-pot electrochemical approach for highly sensitive detection of glucose.[48] Nickel shows excellent sensitivity and a highly stable performance instead of bare-reduced graphene oxide. researchers synthesized low-cost, stable, and sensitive materials that detect the level of glucose and hydrogen peroxide (NiMn-LDH/GO). NiMn-LDH/GO nanocomposite shows excellent attention toward the sensitivity for the oxidation of glucoseand show reduction toward the H_2O_2 as well as LOD of 1.2 μM and 4.4 μM, for the sensing of glucose the linear ranges occupied the four fits of rage the peas of magnitude from 2 μM to 3.386 mM with a correlation coefficient of 0.998. That is why it is suitable for sensing other sugar-like substances (mannitol, erythritol, sucrose). The nonenzymatic rapid senor of glucose and hydrogen peroxide (reach ready-state in less than 10 s) show excellent stability and reproducibility, which encourage the development of highly developed explore of

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multiple layered based nanomaterial in the application of electrochemical sensors.[49]

$$(OH)_2 + OH^- \rightarrow NiOOH + H_2O + e^- \quad (1)$$

$$NiOOH + \text{glucose} \rightarrow Ni(OH)_2 + \text{glucolactone} \quad (2)$$

A dendritic core−shell copper−nickel alloy/metal oxide on nickel foam (Cu−Ni/NF) electrode for nonenzymatic $C_6H_{12}O_6$ sensing has been produced using a simple electrodeposition approach followed by oxidation in NaOH solution. Using a binder-free electrode, direct electrodeposition enhances electron transfer and the dendritic shape increases $C_6H_{12}O_6$ diffusion while providing adequate active sites necessary for glucose electrocatalysis. As a result of the synergistic effect generated by the metallic core and the bimetallic oxide shell, the unique core−shell structure enhances glucose oxidation catalysis. Therefore, the Cu−Ni/NF electrode has a high sensitivity of 11.34 mA mM^{-1} cm^{-2}, a LOD of 2 μM (S/N = 3), and a wide linear range of 1−600 μM for $C_6H_{12}O_6$ sensing all of which are impressive.[50]

2.4. Platinum Oxide/Platinum-Based Nanocomposite. Various physicochemical characterization approaches were used to examine Pt/g-C_3N_4 and ZnO, showing that the biosensor has an extremely high reaction speed, a wide linear range of 0.25 to 110 mM, a limit of detection of 0.1 mM, and a low applied potential of 3.34 μA mM cm^{-2} with high sensitivity. The reaction time is quick (5 s vs Ag/AgCl), which is a major benefit of this biosensor. Additionally, the sensor can be reused 4 times in full blood without a loss of activity, helping to reduce strip costs.[51] A mesoporous (HI-ePt) platinum electrodeposition was found to be a good amperometric sensor for detecting H_2O_2 over a wide range of concentrations based on a hexagonal (HI) lyotropic fluid. It demonstrated good reproducibility, high accuracy, and high measurement precision. Mesoporous microelectrodes maintain the rapid mass transfer rate of conventional microelectrodes while significantly increasing their catalytic activity due to their high real area. This novel combination outperforms previous amperometric hydrogen peroxide sensors in terms of quality and quantity.[52]

The unique electrical properties of nanowires require their efficient integration as functional materials on signal transduction platforms. This work presents a novel method for assembling gold and platinum alloys on microelectrode devices with H_2O_2 detection capabilities. The alloy nanowires were electrodeposited by applying alternating current to the microelectrodes. The nanowires were characterized and found to exhibit a typical single-phase alloy structure, a highly uniform bimetallic compound morphology, and precise control. These alloy nanowires displayed electrocatalytic activity for detecting H_2O_2 with excellent sensitivity, a limit of detection of 1.5 mM, and a fast response time. The synergistic effect of the bimetallic binding sites in the hydrogen peroxide-responsive mechanism is also discussed, which has significant implications for designing functional nanowires as sensor materials for a wide range of applications.[53] A minimal amount of hydrogen peroxide (H_2O_2) is required for various industrial and biological applications. Electrochemical sensors utilizing platinum (Pt) provide excellent sensing capabilities. Given the high cost of Pt, it is beneficial to develop high-performance H_2O_2 sensors with a reduced Pt mass loading. Researchers have implemented an ultralow mass loading technique for Pt nanoparticles on high surface areas using cathodic polarization treatment. Without Pt precursors in the electrolytes, Pt can be released from a Pt-mesh anode through multiple cyclic voltammetric (CV) cycles, then migrate via the electrolyte to anchor as nanoparticles with small size distribution on the rGO−CNT hybrid. The Pt mass loading can be precisely controlled by adjusting the number of CV cycles. The optimal hybrid obtained after 3000 CV cycles contains approximately 4.8 wt % of Pt nanoparticles measuring around 3−6 nm in size. The morphological and physicochemical characteristics of the Pt/rGO−CNT hybrids were evaluated to understand the relationship between their synthetic structure and sensitivity. The porous carbon hybrid comprises nanosheets of reduced graphene oxide (rGO) interconnected with carbon nanotubes.

The hybrid H_2O_2 sensor exhibits superior performance with a low detection limit of 1 μM, linear detection ranges up to 15 mM, and high sensitivity of 2027 μA mM cm^{-2} compared to the Pt/rGO−CNT, which is one of the best Pt/carbon-based materials reported recently. These sensors demonstrate excellent H_2O_2 detection capabilities and can detect traces of H_2O_2 in milk and juice samples, even below the permissible residue limits. This sensor technology shows promise for practical applications in food processing.[54] A nanostructured catalyst with peroxidase activity is introduced, consisting of graphene nanotubes filled with platinum nanoparticles doped with nickel and nitrogen. Initially, Ni-doped nitrogen-rich (Ni/NGT) and Pt-doped graphene nanotubes were refluxed to create a supermolecular assembly. Subsequently, a two-stage process involving pyrolysis and leaching resulted in the formation of nanostructured tubes for the Pt-doped catalyst synthesis. The biocompatibility of this nanostructure was exceptional, and it exhibited high efficiency when coupled with glucose oxidase (GOx). The glucose concentration range is linear from 43 pm to 220 μM, the LOD is 1 pM, and the quantification limit is 3.4 pM with strong replicability (<3%). A visual microfluidic test on paper was also developed with an analytical range of 0.1−50 mM. It is easy and quick enough to make glucose testing at home helpful. The method for glucose measurement in tear and saliva samples was effectively implemented.[55] Much work has been paid to colorimetric glucose detection with enzyme imitation nanoparticles (NPs). However, Many NPs do not have good resolution stability, leading to decreased color changes in substrate color detection. High cationic density macromolecules may be adequate stabilization candidates from NPs. Researchers developed platinum-stabilized polyethylene NPS (Ptn-PEI/NPS) for Glucose colorimetric sensing. In this system, the nanoparticles of platinum employed were tiny (3.21 to 3.70 nm) and narrow. The hydrodynamic dimensions of Pt50−PI/NPs were slightly positive and showed good stability within 1 week. Pt50-PEI/NPs-catalyzed 3,3,5-tetramethylbenzidine (TMB), which generates the peroxidase-like property of Pt50-PEI/NPS. In the H_2O_2 presence, the TMB is blue oxidized (OxTMB). This reaction was optimally conditioned by pH 4.0 at 30 °C. Furthermore, Pt50-PEI/NPS were employed to measure a linear concentration range with a detection maximum of 4.2 μM from 10 to 5000 μM. For instance, our approach measured the glucose levels in the saliva for 0.15 mM. The great stability of Pt50-PEI/NPs improves good accessibility and, hence, outstanding catalytic properties of the active core of Pt-NPs. This proven technology has significant potential to be used for other glucose-detecting applications.[56] Huge attention has been given to the extremely sensible detection of $C_6H_{12}O_6$

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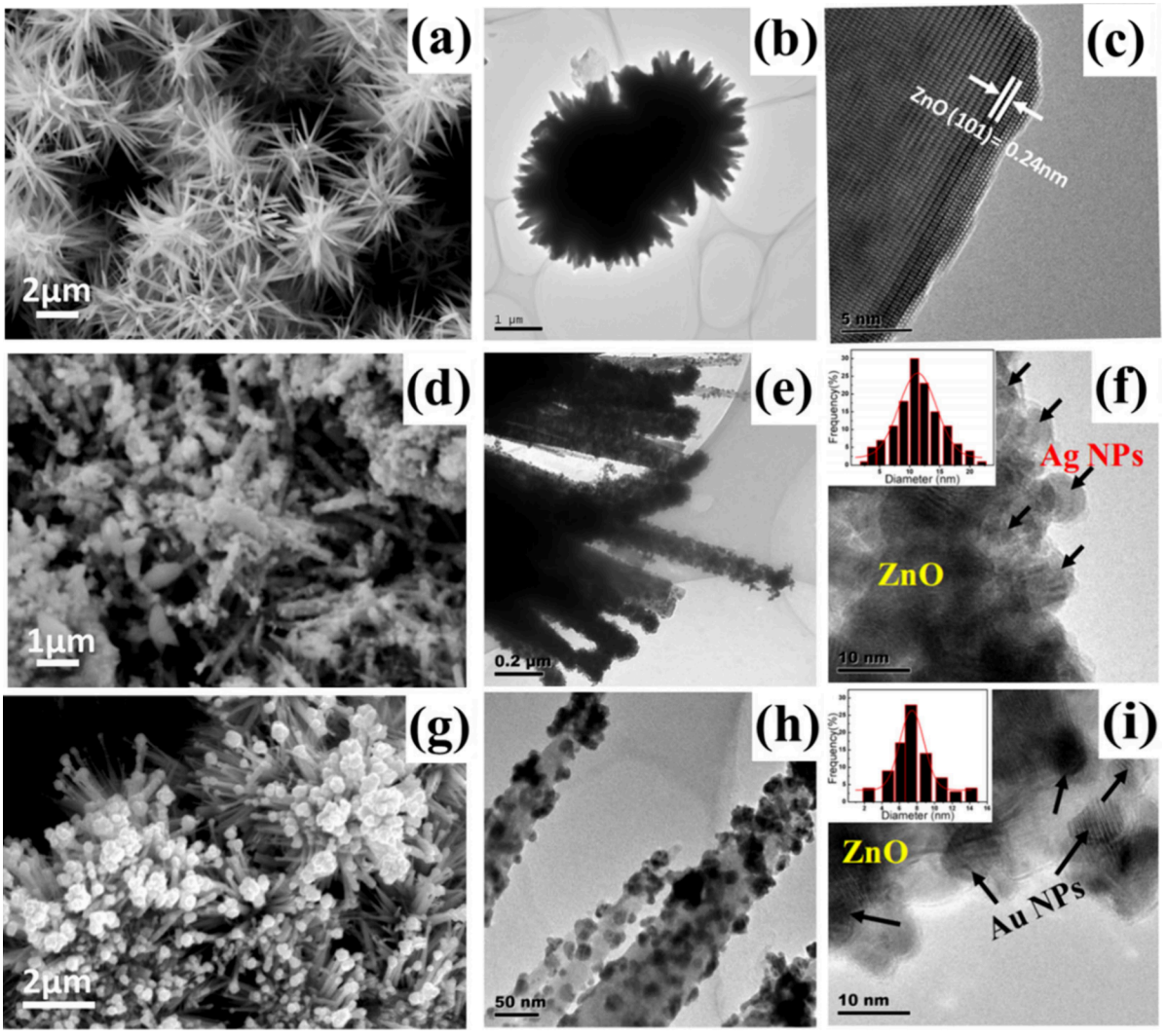

Figure 6. FESEM image of (a) pure ZnO, (d) Ag−ZnO, and (g) Au-ZnO nanoflowers; TEM image of (b) pure ZnO nanoflowers, (e) Ag−ZnO, (h) Au-ZnO. (c) HRTEM image b, corresponding high-magnification image of (f) Ag−ZnO, and (i) Au−ZnO. Inset in (f) and (i) is the size distribution of Ag and Au NPs dispersed on the pure ZnO surface. Reproduced with permission from ref 61. Copyright 2016 Springer Science +Business Media Dordrecht.

based on the peroxidase characteristics of nanoclusters. In that study, Pt-PCRP (Potassium Tetrachloroplatinate and PCRP Potassium) stabilized platinum nanoclusters were manufactured using a green technique. The ultrasmall dimensions of nanoclusters (Pt-NCs) were 1.26 ± 0.34 nm. Pt-PCRP-NCs were 29.7 nm hydrodynamically, with a zeta potential of −12.0 mV. Pt-PCRP-NCs showed high biocompatibility with HeLa cells and Red Blood cells. Pt- PCRP-NCs have also catalyzed a breakdown of the H_2O_2 to create −OH, which is further oxidized colorless by 3,3,5,5-tetramethylbenzidine (TMB), which shows a peroxidase-like characteristic, to blue oxidized by 3,3,5,5- tetramethylbenzidine (OxTMB). Most significantly, the high-selectivity and low-detection limits for the colorimetric approach for glucose detection using Pt-PCRP-NCs were 0.38 μM. PtPCRP-NCs have been employed to accurately detect glucose in human serum, saliva, and sweat. The technique has been established. They offer strong potential for future glucose applications in clinical diagnostics for the created ultrasmall and biocompatible Pt-PCRP-NC.[57] A new electrochemical detection platform was built based on dewdrop-like platinum nanoparticles adorned with silver nanocomposites (AgNFs-Pt@BSA), which were manufactured by the replacement reaction from chloroplatinic acid with AgNFs. As predicted, the final result of the AgNFs-Pt/BSA nanocompound resulted in strong electron conductivity due to the metallic structures of AgNFs with large areas; Pt nanocomponents positively improved the electrocatalytic activity toward (H_2O_2). Bovine serum coated with AgNFs-Pt offered several functional groups, such as bovine serum albumin (BSA) (especially NH_2). Inspired by these properties, we created an outstanding glucose biosensor through glutaraldehyde (AgNFs-Pt/BSA/GA/GO/D) via cross-linking glucose oxidase with AgNFs-Pt/BSA. The linear glucose range from 1 to 14 mM, with a LOD threshold of 0.3 mM at a noise signal, shows linear high electrochemical responses. In addition, attractive selectivity, high reproducibility, and sustainable stability have led to promising analytical effectiveness in detecting glucose in human serum samples manufactured by electrochemical sensors. All the pleasing results gave a significant forward and prospective orientation for the future clinical uses of human blood glucose detection.[58] The creation of ultrasmall platinum nanoparticles is required

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for the sensitive detection of glucose in complex media without enzyme interference. Colorimetric glucose detection with Zwitterionic Dendrimer-encapsulated platinum nanoparticles (Ptn-G5MC/NPs) has been studied for its high sensitivity and precision. Poly(amidoamine) dendrimers of generation 5 comprising maleic anhydride and cysteamine were first generated via surface modification of zwitterion dendrimers (G5MC).

For Ptn-G5MC, the average estimated diameters (n = 50, 110, and 165) of Pt nanoparticles were (1.64 0.22), (2.09 0.24), and (2.98 0.29) nm, respectively. In addition, there was no apparent cytotoxicity against HUVEC cells and HeLa cells in different pH and fibrinogen solutions. In addition, Ptn-G5MC NPs could create blue-oxidized TMB (oxTMB), suggesting its peroxidase-like property, by catalyzing 3,3,5,5-tetramethylbenzidine/TMB with H_2O_2. This colorimetric technique was also employed for high-sensitivity and high-selectivity glucose detection. A linear range of 652 nm absorbed glucose concentration from 7 to 1380 mM and an LOD of 2.8 mM were observed. Furthermore, proteins were not changed by the relative activity of the Ptn-G5MC-NPs. The ultrasmall size of Pt-NPs and the high strength of the Pt55-G5MC-NPs in complicated means are ascribed to those improved features. The glucose level in saliva was determined to be 0.18 mM as a valid sample. The suggested glucose sensor might have successful applications in biocatalysis and bioassays for glucose detection.[59]

2.5. Zinc Oxide/Zinc-Based Nanocomposite. Synthesizing the nanocomposites of metal oxide deposited on the nanotubes in multiple walls (MWCNT) is a highly effective and accessible approach for H_2O_2 and glucose detection. Zinc oxide hexagonal nanorods were also synthesized by probe sonication and fictionalized with MWCNT-cellulose nanocrystals (MWCNT-CNC) for the first time in the literature. With the help of bath sonication, Researchers also prepared stable hemin biocomposites for the ultrasensitive electrochemical detection of H_2O_2.

Figure 6 shows various ways of characterization research confirmed the existence of native hemine in the MWCNT-CNC/ZnO-NR nanocomposite. The modified electrode MWCNT-CNC/ZnO-NR/Hemin exhibits excellent attention to 2.3-fold with an improved reduction potential for electrocatalytic activity (−0.2) to H_2O_2 sensing. Electrodes have a high response (−0.2 V versus Ag/AgCl) in the linear concentration of H_2O_2, ranging from 4183.3 μM to 4.0 μM.[60] With the help of the coprecipitation method, Muhammad Hussain et al. have synthesized zinc oxide nanostructure fabrication with the Au 8 nm and Ag 15 nm nanoparticles functionalized by the hydrothermal processes. Different characterizations show the activity of noble metals with zinc oxide nanoflowers. The photocatalytic activity of Au−ZnO, and Ag−ZnO composites improved as the deficiency increased. Therefore, ZnO-funded Au nanoparticles show very efficient sensing of hydrogen peroxide at low limits of detection of 2.5 μM due to efficient catalytic activity and stability of the Au nanoparticles (S/N = 3, with a wide range of 1 to 20 μM, have high levels of strength and sensitivity of 50.8 $\mu A \mu m^{-1} cm^{-2}$, with fast responses of <3 s and stability as compared to pure zinc oxide. All the noble metals functionalized with zinc oxide powerfully respond to the nonenzymatic, eco-friendly detection of different biomolecules.[61]

Glucose detection has become increasingly important. This study offered a new glucose sensor to manufacture electrodes based on nanocomposite-modified graphene/zinc oxide nanocomposite Ni foam (G-ZnO/Ni). The G-ZnO/Ni foam electrode electricity was assessed using cyclic voltammetry (CV) and amperometry analysis. To reduce glucose within the linear range of 50−1000 μM and with a correlation rate of 0.986, the produced electrode displayed great electrocatalytic activity. Ni foam sensor was adjusted with a sensitivity of 1635.52 $\mu A\ mM^{-1}\ cm^{-2}$ in graphene/zinc oxide. It improves the electrochemical performance of glucose and is promising in glucose applications with high-sensitivity detection. In this article, the hybrid electrode was utilized on a current-response nonenzymatic glucose sensor of the single-wall carbon nanorod (SWCNT)/Cu_2O/ZnO nanorods (NRs)/ graph was examined concerning the functional channel generation process. There were four processes to synthesize the hybrid electrode.[62] The graphene was first created by chemical vapor deposition (CVD), followed by wet transmission to a transparent glass of indium oxide (ITO). Second, the graphene/ITO glass was spotted in a zinc oxide (ZnO) seed layer, and the hydrothermal process eventually produced ZnO NRs. Third, ZnO NRs were electrochemically encased in cuprous oxide (Cu_2O). Fourthly, the SWCNTs with a surfactant Nafion were deposited onto the Cu_2O surface. Sensitivity has increased significantly from 0.6 to 11.1 mm. The determination coefficient had increased from 0.9766 to 0.9923 by addition to the functional chain mechanism SWCNTs/Cu_2O without graphene, all of which have been shown to increase significantly, from 11.2 to 289.8 $\mu A\ mM^{-1}\ cm^{-2}$, linear distance, the sensitivity from 289.8 to 466.1 $\mu A\ mM^{-1}\ cm^{-2}$ at minor concentrations when the graphene was introduced to the functional channel electrode.[63]

The interest in mixed transition metal oxides has been expanding in catalysts and electrocatalysts. As shown in Figure 7, the $ZnMn_2O_4$ microspheres were easily manufactured using

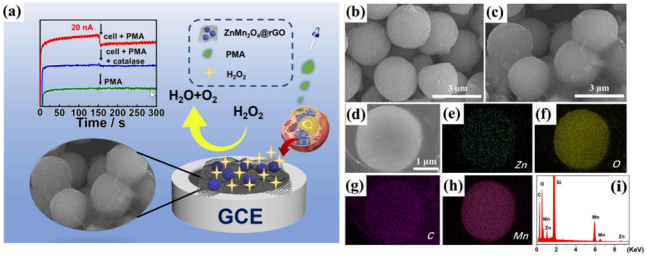

Figure 7. (a) Schematic diagram of the significant steps for the synthesis of $ZnMn_2O_4$@rGO, (b) SEM image of $ZnMn_2O_4$, (c) SEM image of $ZnMn_2O_4$@rGO, (d−h) elemental mapping images of $ZnMn_2O_4$@rGO and corresponding elemental mapping images of Zn, O, C, and Mn, and (i) EDS spectrum. Reproduced with permission from ref 64. Copyright 2019 American Chemical Society.

the solvothermal method in reduced graphene oxide-wrappings ($ZnMn_2O_4$/rGO). The $ZnMn_2O_4$/rGO produced was used as a promising electrocatalyst for hydrogen peroxide reduction (H_2O_2).

In a broad range of concentrations of 0.03−6000 μM with a LOD of 0.012 μM, $ZnMn_2O_4$/rGO glassy carbon electrode ($ZnMn_2O_4$/rGO/GCE) displayed a linear detection for H_2O_2. The biosensor has been assessed to measure H_2O_2, which can be produced by human breast cancer cells (MCF-7).[64]

A novel biocompatible electrode is presented to alleviate the failings of quick, direct glucose-biosensing equipment in laboratory studies. Nano-ZnO was sputtered into a precovered

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conductive layer of fluorinated tin oxide (FTO) via a reactive direct current magnetron sputter technique. To develop the efficient medium for the immobilization of covalent glucose oxidase enzyme (GOx) through cyanuric chloride (GOx/nano-ZnO/PVA/FTO) spin-coated poly(vinyl alcohol) (PVA), optimum instrumental deposition conditions were employed. Field emission scanning electron microscopy and electrochemical impedance spectroscopy were used to evaluate the morphology of the redesigned electrode. $I-V$ measurements showed an excellent glucose detection sensitivity (0.041 mA/mM) between 0.2−20 mM and a 2.0 μM limit. These show that the biodevices have tremendous potential to track the number of biological fluid biocompounds with great precision, selectivity, and accurate analysis. Most sorts of real-time analysis may be permitted due to the quick reaction time of the GOx/nano-ZnO/PVA/FTO biosensor < 3 s.[65] A single-pot synthesis of ficin (a cystenic proteolytic POx activity enzyme), zinc(II), and 2-methylimidazole was developed into an enzyme-metal organic frame (MOF) composite with a saucer-like shape. The composites had 2.5 times more catalytic activity than free Ficin and a better affinity for the substrate. This was used to design a colorimetric glucose assessment. Adding glucose oxidase causes H_2O_2 to become blue, which can be detected at 652 nm and then oxidized by ficin. The LOD of the test was 0.12 μM, and its selectivity was excellent. It has been effectively employed in diluted serum samples to determine glucose.[66]

Recently, H_2O_2 nonenzymatically colorimetric nitride (g-C_3N_4) was studied as a peroxidase-like catalyst. In this work, researchers devised a soft template approach for dope zinc ions in mesoporous graphitic carbon-nitride (Zn-mpg-C_3N_4) thin nanosheets supporting a simple, cheap, and eco-friendly hydrogen bond. Different characterization procedures determined that the morphology and content of produced samples.PEG-1500 has benefited from improving porosity and the surface area of g-C_3N_4, while zinc charge has increased electrical characteristics in the context of g-C_3N_4. The catalytic activity of samples such as peroxidase was studied and comparable by a colorimetric technique based on developing the blue reaction mix between 3, 3, 5, and 5-tetramethylbenzidine and the hydrogen peroxide (H_2O_2). Compared with natural HRP, g-C_3N_4, and mpg-C_3N_4, the as-made 10% Zn-mpg-C_3N_4 had more significant peroxidase activity. The thin structure, higher-specific surface area, excellent electron transfer capability, expanded band space, and greater responsible separation of the catalyst using the doping modification of the direct zinc ions were the cause of this improved peroxidase-like activity. Applying kinetics from Michaelis−Menten, the steady-state kinetics mechanism was examined, and the reaction followed the mechanism of a ting pong. This exceptional catalytic activity allowed us to detect H_2O_2 by designing a quick and easy colorimetric sensing process. In the optimal condition, a linear range are 10−2000 μM (R_2 = 0.9981), LOD is 1 μM, glucose limits is 1.4 μM, and H_2O_2 detection limits is 3.0 μM. Given the benefits of the created sensor compared with earlier approaches, such as simple and easy operation, economical efficiency, environmentally friendly, naked-eyed observations, and speedy responses, the developed sensor has enormous potential.[67] Hydrogen peroxide (H_2O_2 is regarded as very harmful and may cause illnesses such as Alzheimer's, Parkinson's, cardiovascular, tumors, and cancer at higher levels of human body concentration. H_2O_2 detection in human blood serum is, therefore, increasingly needed. A zinc-oxide-poly(vinyl alcohol) (ZnO-PVA) nanocomposite as a nanointerface was used to construct an electrochemical sensor. The bioelectrode manufactured from Au/ZnO-PVA/CAT/Chitosan exhibits a redox peak with −0.408 and 0.259 V for anodic and cathodic peak potential for Fe(III), Fe(II), and H_2O_2:1/2 O_2 redox pairs. A linear range was created with a sensitivity of 210.49 μA μM^{-1} cm^{-2}, a response < 1 s, an LOD of 9.13 nM, and a quantification limit of 30.13 nM.

A Michaelis−Menten constant (KM 0.39 μM and dry stability of 93% up to 20 days) has been shown in the bioelectrode. The biosensor produced was used effectively for determining H_2O_2 levels in human blood serum samples.[68] The H_2O_2 is a byproduct of some metabolic processes, and its overproducing in live cells can lead to the formation of cancer and many illnesses through enzymes like glucose oxidase (GOx), cholesterol oxidase (ChoOx), and other means. H_2O_2, thus, is very important in determining illnesses, industries, and health strategies for the environment. Researchers generated ZnO−CuO nanofibers using an electrospinning approach for enzyme-free electrochemical H_2O_2 sensing. In phosphate-buffered saline (PBS), the sensory characteristics of the carbon paste electrode (CPE) adapted for the detection of H_2O_2, at pH 7.4, with ZnO (0.3 wt %)/CuO (0.7 wt %) nanofibers, were examined. In addition to modified electrodes for H_2O_2, the ZnO_3−CuO_7 nanofiber had the lowest load-transferred resistance and the best electrocatalytic performance. (CV) and the mechanics for the electrochemical reaction of H_2O_2 on the surface of the optimized electrode were also explored in the scan rate and H_2O_2 concentration effect of the reduction procedure. Chronoamperometry was calculated by 1.65×10^{-5} cm^2 s^{-1} and 6×10^3 cm^3 mol^{-1} s^{-1}, respectively, for diffusions of H_2O_2 and the catalytic rate constants. In addition, amperometric H_2O_2 detection has been achieved with a low 2.4 μM LOD and a wide linear range of 3 to 530 μM. Meanwhile, there was no discernible reaction to biomolecules such as ascorbic acid, uric acid, dopamine, and glucose from the optimized electrode. The findings showed that the modified electrode was an H_2O_2 biosensor with increased repeatability and stability, showing high sensitivity and selectivity.[69] A new gold composite-based electrochemical sensor (AuNP/ZnO/NTs) was developed and used as a nonenzymatic (H_2O_2) sensor The biomineralization Strategy for ZnO-NTs was established with the use of silk fibroin fibers (SFFs), and the ZnO-NTs thereby gained SFF's benefits, such as mechanical stability, the flexibility of biomimetic shape, and biocompatibility. Using the electrostatic absorption of AuNPs on the surface of ZnO-NTs, AuNPs/ZnO-NTs were further developed to catalyze the decrease in H_2O_2. The work capacity was 0.05 V, much more significant than in the literature, which shows excellent anti-interference capability in the actual application. The catalytic current was linearly proportional in the concentration range of 1 μM-3.0 mM with a sensitivity of 1336.7 μA mM^{-1} cm^{-2}. It was calculated that the LOD was 0.1 μM (S/N = 3). The electronic property and strong electron transport capabilities of the structure of AuNPs/ZnO-NTs have been linked to this sensitivity. In addition, the results of H_2O_2 were shown in actual samples to be acceptable to the conventional titration of the end-results of H_2O_2 were shown in actual samples to be acceptable to the traditional titration of the permanganate potassium and demonstrated the potential for employment in actual detections as the appropriate sensor. Permanganate potassium demonstrated the potential for actual

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detections as the appropriate sensor.[70] The glassy-carbon electrode, with nanoparticles inserted in the ZnO/NDO-NDCS/GOx carbon sheets, has been constructed to provide a novel, highly selective, sensitive, and stable enzyme glucose sensor. First, a simple hydrothermal procedure generated ZnO/NDCS. ZnO NPs, nitrogen, and carbon precursors were Zn powder, aqueous ammonia, and peach extract. The manufactured biosensor GCE/ZnO-NDCS/GOx was 231.7 μA mM^{-1} cm^{-2} with good replicable sensitivity. A wide linear range of 0.2 to 12 mM with an R^2 coefficient of correlation = 0.998 and a LOD of 6.3 μM was shown, based on the S/N ratio = 3. The GCE/ZnO-NDCS/GOx biosensor is acceptably stable and selective and has been used to monitor human blood serum glucose quantity. In additional applications in the solar cell and Optoelectronics sector, the generated ZnO/NDCS nanocomposite can be beneficial. These positive findings propose a simple and practical approach to obtaining the enzyme glucose sensor electrode material.[71]

The production of vertically aligned zinc oxide nanorods on a steel foil (ZnO/SSNs) with a typical household microwave oven is described as a simple and speedy microwave-aided hydrothermal approach in this study. ZnO-NRs were studied by the morphology, microstructure, or properties of electrochemical measurements and (SEM), X-ray diffraction (XRD). The ZnO nanorods were generated with an increasing density as the repeated heating periods and concentrations rose. $ZnCr_2O_4$ and $ZnFe_2O_4$ were identified as having extensive absorption in the visible region during hydrothermal development of the ZnO materials in the nanorods ZnO. Photocurrent measurements indicate the maximum current density, which may be utilized as a photoelectron (PEC) sensor, using ZnO-NRs photo electrodes manufactured at concentrations of 0.05 M and repetitive 8 times. The ZnO-NRs were utilized as a PEC sensor to detect glucose and H_2O_2 under visible light irradiation. With a broad linear range (2−100 μM and 0.1−100 μM, respectively), high PEC sensor sensors demonstrate great photosensitivity to glucose and hydrogen peroxide with a LOD (3.14−0.27 μM). Still, PEC sensors fail to react to the glucose and H_2O_2 changes without light irradiation.[72]

A vertically produced zinc oxide nanorod (NR) sensor based on the functionality of the Fe_2O_3 ferrous oxide is studied. A sol−gel and a hydrothermal growth technique were employed to produce well-aligned and high-density ZnONRs using an FTO/glass substrate. The dip-coating method changed the as-crowned ZnO NRs surface with Fe_2O_3. Nafion membrane layer covered the immobilized surface. The manufactured glucose sensor was evaluated using 3 electrode stations in a solution in a phosphate buffer at room temperature, where the ZnO NRs/Fe_2O_3−Nafion membrane was utilized as counter and the reference electrodes, the platinum plate, and silver−silver chloride. A high sensitiveness in the order of 0.052 μAcm^{-2} (mg/dL), a low detection limit of around 0.95 mM, an intense and rapid reaction time of ∼1 s, and a linear response to changes at glucose levels from 100 to 400 mg/dL were showed in the suggested nonenzymatic and modified glucose sensor. The sensor's linear amperometric response covers the physiological and clinical interest in diabetes patients with glucose levels. After several measurements, the instrument worked accurately and reproducibly. The glucose sensor proposed will be utilized for clinical in vivo glucose surveillance.[73]

Based on polyethylene-Au nanoparticles-zinc protoporphyrin, a new electrochemical biosensor for sensitive hydrogen peroxide (H_2O_2) was created (PEI-AuNPs-ZnPP). PEI-AuNPs- ZnPP has been developed with the help of carboxylic coupling of ZnPP with PEI-AuNP amino. To analyze PEI-AuNPs-ZnPP production, this method exhibited a strong sensitivity for H_2O_2 detection under optimum circumstances and a LOD of 0.0861pM. In addition, this biosensor can effectively be used in human serum samples to monitor H_2O_2. These results indicated that in complex biological samples, PEI-AuNPs-ZnPP might be a promising option for H_2O_2 detection.[74]

2.6. Iron Oxide/Iron-Based Nanocomposite. For glucose and hydrogen peroxide nonenzymatic detection, researchers synthesized a low-cost, efficient, selective, sensitive biosensor developed of nanodots of indium tin oxide for which the block copolymer method was used. Then they fabricated it on the glassy carbon electrode, which showed more electrical conductivity, high efficiency, high surface area to volume ratio, thermally stability, as well as high sensitivity and linear from 2.5×10^{-3} to 6.5 mM with a sensitivity 191.6 μA mM^{-1} cm^{-2} and low limit detection was 1.1×10^{-3} mM. Various characterization techniques, CV, and amperometric methods are used to check the selectivity and sensitivity toward the application of biosensors.[75] A highly particular frame synthesized using the hydrothermal method produced mesoporous carbon (OMC) for glucose detection and hydrogen peroxide from the porphyrinic iron-organic frame (pFeMOF). Fe (III) enhances the electrochemical signals, conductivity, selectivity, stabilization, and sensitivity of the peroxidase pFeMOF, powerfully and more stable coordinates with the porphyria porphyrized groups. The linear range of H_2O_2 electrocatalytic reduction is between 0.5 and 70.5 μM with a high level of sensitivity of 67.54 μA mM^{-1}.[76]

Researchers have synthesized a simple, efficient, low-cost graphitic carbon nitride (g-C_3N_4)/iron oxide-copper nanosheet from restacking for the nonenzymatic sensing of $C_6H_{12}O_6$ and H_2O_2. The C_3N_4/Fe_2O_3−Cu biosensor shows a glucose detection limit of 0.3 mM in the linear range of 0.6 μM to 2.0 mM.[77] The sensor exhibits good chemical activity, catalytic efficiency, low cost, and thermal stability. To achieve high sensitivity for detecting $C_6H_{12}O_6$ and H_2O_2, researchers synthesized a very sensitive biosensor using iron−carbon (Fe/C) magnetic nanotubes prepared via the direct cracking method under an inert atmosphere. The sensor utilizes a peroxidase substrate, N-diethyl-p-phenylenediamine sulfate, which catalyzes the oxidation of peroxidase to produce a purple color product. This sensor exhibits good conductivity, efficiency, and stability in sensing glucose and hydrogen peroxide, with a linear response range from 10 nM to 0.2 mM H_2O_2 and a detection limit of 1.5 nM.[78]

Figure 8a shows the catalytic oxidation of tetramethylbenzidine (TMB) by Fe-*g*-C_3N_4 in the presence of H_2O_2 for the detection of glucose. Fe-doped g-C_3N_4 (Fe-gC_3N_4) was prepared in contrast to g-C_3N_4 because its large surface of iron contains mesopores, cracks, mesopores, and a small bandgap, and high folding is present in the structure of iron, as shown in Figure 8b, c. Thus, Fe-*g*-C_3N_4 shows higher peroxidase activity, which changes color as a substrate utilized as. After optimization of this method, researchers have obtained a wide linear range for the sensing of H_2O_2 from 0.005 to 400 μM (R^2 = 0.9971) with a LOD of 0.005 μM, and the colorimetric detection of glucose was also determined with a linear range of 1−1000 μM (R^2 = 0.9996) and a LOD of 0.5

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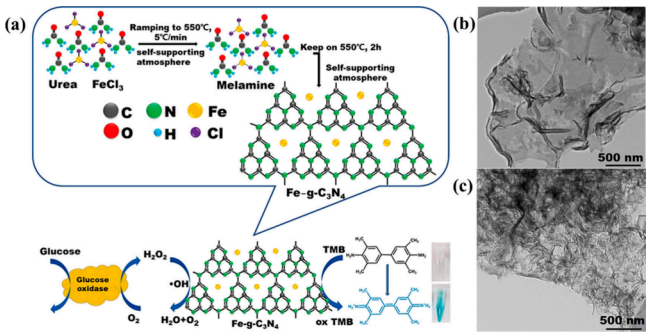

Figure 8. (a) Schematic illustration of the preparation and formation of Fe-*g*-C_3N_4 and (b, c) TEM image of Fe-*g*-C_3N_4. Reproduced with permission from ref 79. Copyright 2019 American Chemical Society.

μM. It is also valuable for the sensing of H_2O_2 in milk and human serum.[79]

2.7. Manganese Oxide/Manganese-Based Nanocomposite. A unique nanocomposite (Cu_2O/MnO_2) was synthesized using the reflux method to enhance this material. Researchers modified the surface of the glassy carbon electrode to enhance the detection of hydrogen peroxide and glucose and evaluated the stability and sensitivity of the nanocomposite material. The material was characterized by SEM, TEM, X-ray diffraction, and FTIR, showing a strong response for detecting hydrogen peroxide and glucose. The nanocomposite material exhibited an excellent detection limit of 63 nM (S/N = 3) with a fast time response of 0.56 s^{-1} for electron transfer. The sensitivity of the biosensor was high at 256.33 μA mM^{-1} cm^{-2}, and it had a wide linear detection range from 0.5 μM to 20 mM. The biosensor also showed excellent stability (DI response 15%, n = 100), reproducibility (3.55% RSD, n = 10), and repeatability (1.25% RSD, n = 10). Overall, the synthesized material demonstrated great economy, high sensitivity, low detection limit, and high stability for detecting glucose and hydrogen peroxide.[80]

The amperometric detection of $C_6H_{12}O_6$ and H_2O_2 was achieved using an eco-friendly and highly compatible method developed through cyclic voltammetry, demonstrating excellent efficiency and stability. The sensor showed remarkable sensitivity and performance across a wide linear range from 2.0 $\times$ 10^{-6} to 5.0 $\times$ 10^{-3} M using a MnO_2/unzipped SWCNT/GCE-based nanocomposite. It exhibited a detection limit of 0.31 $\times$ 10^{-6} M (10.7 ppb) with a correlation coefficient of 0.9822 under physiological pH conditions (pH 7.4).[81] By using two different metal oxide, researchers synthesized a unique nanocomposite Mn_3O_4–$MnCo_2O_4$ by facile solvothermal precipitation method by using carbon nanotube as a surrender (sacrificial) platform for the detection of $C_6H_{12}O_6$ and H_2O_2. It shows excellent sensing toward detecting glucose and hydrogen peroxide in a wide linear range of 0.1–1274.3 μM and an LOD of 0.020 μM (S/N = 3). Biosensors aimed to determine the H_2O_2 level in milk and bovine serum samples, which show remarkable selectivity and efficient stability.[82] Wu et al. have used a readily available pencil graphite material coating with manganese oxide (MnO/PE), and its efficiency has increased for detecting $C_6H_{12}O_6$ and H_2O_2. Synthesized material characterized using different techniques, XRD, X-rays, SEM, and TEM, show excellent efficiency linear concentration range was 0.056–1.41 mM, with a high sensitivity of 2.19 μAmM^{-1} and show LOD is 18.3 μM.[83] By using a very efficient and easily handled hydrothermal method used for the synthesis of nanocomposite MnO_2-GNSs/GCE and the enhancement of the conductivity fabricated by the facile drop-coating procedure was used for the detection of H_2O_2 and $C_6H_{12}O_6$ compared to the bare GCE GNSs/GCE and c-MnO_2/GNSs/GCE, MnO_2-GNSs/GCE which show the low efficiency and conductivity toward the biosensing. A linear current response of H_2O_2 in the concentration range of 0.5–350 μM (R^2 = 0.998) with a high sensitivity of 422.10 μA mM^{-1} cm^{-2} with LOD of 0.19 μM (S/N = 3) obtained efficient result after testing accurate sample.[84] The enzyme sensing of glucose and hydrogen peroxide was assessed by using a colorimetric approach. Human serum albumin-model nanosheets MnO_2 as oxidase mimics as activity, therefore researchers manufacture a very efficient, fast, sensitive, and selective nanocomposite based on HAS-modified MnO_2 nanosheets with LODs from 0.56 μM to 0.32 μM, with a linear range from 0.5 μM to 50 μM LOD.[85] Built using metal-oxide architecture, applications in optoelectronics, energy converters, and electrical sensors have been widely extended. In this work, the $MnOMn_3O_4$ microparticles, olive-like heterostructured, wrapped in reduced graphene oxide (MnO-Mn_3O_4/rGO), were manufactured by easy solvothermal calcination processes and due to the combination of superior electrical rGO conductivity and the synergistic impact of MNO and Mn_3O_4, the as-synthesized MnO–Mn_3O_4/rGO had a robust catalytic effect on H_2O_2 electroreduction. An extensive linear range of 0.004–17 mM, a low detection maximum of 0.1 μM, and a high sensitivity of 274.15 μA mM^{-1} cm^{-2} were achieved using the modified glassy carbon electrode from MnO-Mn_3O_3/rGO. The sensor presented remarkable selectivity and efficient stability. The biosensor was successfully used to detect H_2O_2, which shows its promise of possible applications for useful electrochemical sensors in tomato sauce with a satisfactory recovery.[86]

The semiconductor-based heterostructure can modify the characteristics of the materials and fulfill their potential use by using the required compositions and morphologies. There are, however, few examples of the heteronanorods in a single material of metal oxide with diverse valencies. Researchers had successfully combined a hydrothermal (MnOx nanorod) method, a wet chemical process (for composites), a thermal–thermal process (for heterostructures), and X-ray diffraction to show the formation process. This method also produces the Mn_3O_4–MnO_2 heteronanorods/graphic nanocomposite (MM- HNRS/GS), as shown in Figure 9.

Electrochemical studies indicated that, compared to its components, the composite exhibits a more positive onset potential and higher limit current and kinetic current densities due to the synergistic effect between Mn_3O_4 and rGO. The transferred electron number in the ORR catalyzed by the Mn_3O_4/rGO composite is close to 4, which suggests that the composite catalyzed ORR proceeds along a highly efficient path. In addition, the composite showed high tolerance to methanol crossover and better stability than a commercial Pt/C catalyst.[87]

Electrochemical findings demonstrate a surprising synergistic effect and considerably improved electrocatalytic activity in reducing H_2O_2 based on Mn_3O_4 and MnO_2. MM-HNRS/GS offers excellent sensor performance for the nonenzymatic and noble metal-free detection of H_2O_2, including fast amperometric response (in 3 s), high sensitivity (1,443 μA mM^{-1} cm^{-2}), and low detection limit (0.16 μM) (S/N = 3). They took advantage of heteronanorods' electroreduction, high

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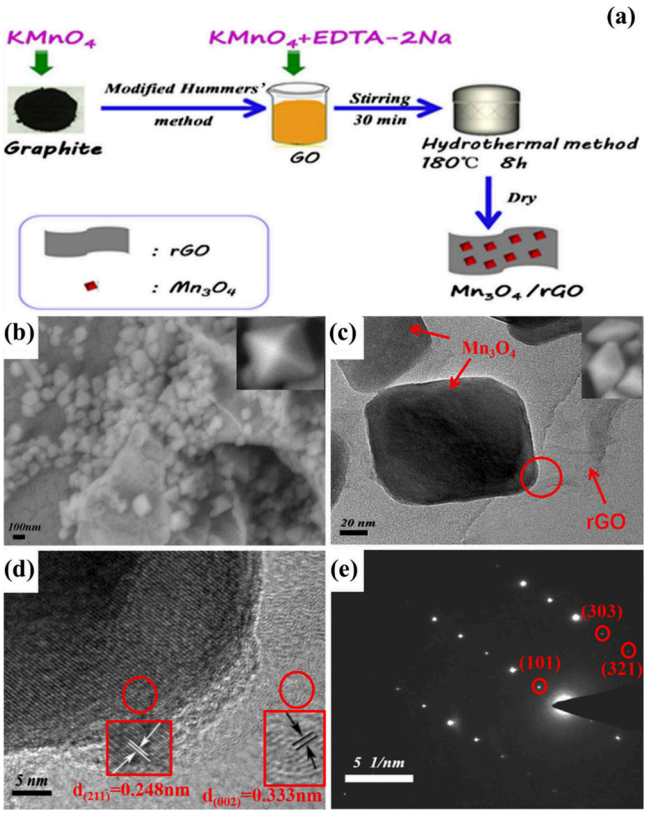

Figure 9. (a) Schematic showing the preparation of the Mn_3O_4/rGO composite, (b) SEM, (c) TEM images of the Mn_3O_4/rGO composite, (d) HREM image of the Mn_3O_4/rGO composite, and (e) associated selected-area electron diffraction (SAED) pattern. Reproduced with permission from ref 86. Copyright 2018 Springer-Verlag GmbH Germany, part of Springer Nature.

conductivity, and large-scale GS area. Furthermore, high selectivity, reproductiveness, and stability are attained.[87] By hydrothermal reduction of graphene nanosheets (GNSs) with manganese dioxide (MnO_2), the authors created a new composite of manganese dioxide and graphene nanosheets (MnO_2-GNSs). An electrochemical sensor based on nonenzymatic Hydrogen peroxide (H_2O_2) was detected using a MnO_2-GNSs composite. MnO_2-GNSs composite modified glassy carbon electrode (MnO_2-GNSs/GCE) electrochemical characteristics were studied by using cyclic voltammetry (CV), electrochemical impedance spectroscopy (EIS), and amperometry (AM). As a result of the MnO_2 particle catalytic ability and the conductivity of GNSs, the constructed sensor showed electrocatalytic solid activity for the oxidation of H_2O_2. Amperometric response to H_2O_2 was linear in the optimal circumstances across the range 0.5−350 M, with a LOD of 0.19 (S/N = 3) and high sensitivities of 422.20 A mM^{-1} cm^{-2} (S/N = 3). On MnO_2-GNSs/GCE, H_2O_2 in antiseptic solution had a percent recovery range of 96.50% to 101.22% with a relative standard deviation (RSD) of 1.48% to 4.47% because of their high reproducibility, anti-interference, and repeatability, the developed MnO_2-GNSs/GCE might be a viable platform for the practical detection of H_2O_2.

3. FUTURE PERSPECTIVES AND CONCLUSION

There have been numerous attempts at developing an ultrasensitive glucose sensor free of interference from other electroactive species, but none of them have proven successful. When nanotechnology was introduced, molecular-level control of sensing devices was somewhat conceivable. Enzymatic glucose sensors may be susceptible to interference from other biomolecules because they rely on the catalytic action of enzymes, which can lead to a lack of specificity in their response to particular glucose concentrations. Additionally, the stability of these sensors can decrease over time and due to changes in environmental conditions, as the activity of the enzymes can be affected. Continuous and nonenzymatic glucose sensing utilizing a more reliable and sensitive glucose sensor continues to be required by diabetic patients in hospitals today. Metal-oxide nanoparticles have attracted scientists' attention because of their vast surface-to-volume ratios and high IEP values in the expectation of more stable, sensitive, but less interfering free glycemic monitoring systems. Although protein enzymes denature during immobilization or detection procedures, a metal-oxide nonenzymatic glucose sensor does not lose sensitivity. This study has reviewed the most often utilized electrochemical techniques and metal oxides for glucose biosensors. For electrolyte substances for glucose sensing, ZnO has shown high sensitivity and selectivity for glucose monitoring. Due to its ability to directly electro-oxide glucose without enzyme immobilization, the nanostructured CuO-modified electrode lowers the cost of sensor manufacture and increases its performance. As a result of its low working potential, a CuO nanostructure-modified electrode demonstrated the best level of sensitivity and the lowest LOD compared to other metal oxide-based $C_6H_{12}O_6$ sensors. Different metal oxides, such as nickel and magnesium oxide, are also possible as glucose sensors. In human blood, in addition to glucose, there are many electroactive substances that can interfere with measurement results during the detection process of an electrochemical glucose sensor. Under the operating voltage of the electrochemical sensor, these substances can also be oxidized, generating current signals similar to those of glucose oxidation, which thus affect the selectivity and sensitivity of the sensor and causes interference. Metal oxides possess characteristics, such as low cost, diversity, biocompatibility, stability, ease of preparation, and functionalization. However, the main obstacles to the commercialization of metal oxide-based nonenzymatic glucose sensors are their lower electrical conductivity and catalytic activity. There are still numerous benefits to glucose sensing based on new metal-oxide nanoparticles, even though it requires additional academic and technological investigations before it can be commercialized. Since diabetes incidence is increasing, Researchers will continue to be interested in glucose sensors. The theoretical and practical information obtained by studying metal-oxide nanostructured $C_6H_{12}O_6$ sensors will be expanded to the whole biosensor industry.

AUTHOR INFORMATION

Corresponding Authors

Xiang Guo − *Science and Technology on Aerospace Chemical Power Laboratory, Laboratory of Emergency Safety and Rescue Technology, Hubei Institute of Aerospace Chemotechnology, Xiangyang 441003, China*; Email: guoxiang@casc42.cn

Muhammad K. Majeed − *Department of Materials Science and Engineering, The University of Texas at Arlington, 76019 Arlington, Texas, United States*; orcid.org/0000-0001-5259-6270; Email: kashifmajeed96@gmail.com

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Xinghui Liu − *Science and Technology on Aerospace Chemical Power Laboratory, Laboratory of Emergency Safety and Rescue Technology, Hubei Institute of Aerospace Chemotechnology, Xiangyang 441003, China;* orcid.org/0000-0001-7744-1400; Email: liuxinghui119@gmail.com

Authors

Jiaxin Wang − *Science and Technology on Aerospace Chemical Power Laboratory, Laboratory of Emergency Safety and Rescue Technology, Hubei Institute of Aerospace Chemotechnology, Xiangyang 441003, China*

Jinyan Bu − *Science and Technology on Aerospace Chemical Power Laboratory, Laboratory of Emergency Safety and Rescue Technology, Hubei Institute of Aerospace Chemotechnology, Xiangyang 441003, China*

Huichao Zhang − *Science and Technology on Aerospace Chemical Power Laboratory, Laboratory of Emergency Safety and Rescue Technology, Hubei Institute of Aerospace Chemotechnology, Xiangyang 441003, China*

Muhammad Arshad − *Department of Chemistry, National Sun Yat-sen University, Kaohsiung 80424, Taiwan China; CAS Key Laboratory for Biomedical Effects of Nanomaterials and Nanosafety, National Center for Nanoscience and Technology (NCNST), Beijing 100190, China*

Ayesha Kanwal − *Department of Chemistry, IRCBM, COSMAT University Islamabad, Lahore campus 54000 Lahore, Pakistan*

Wu-Xing Chen − *Institute of Environmental Engineering, National Sun Yat-Sen University, 80424 Kaohsiung, Taiwan*

Kuldeep K Saxena − *Division of Research and Development, Lovely Professional University, 144411 Phagwara, India*

Complete contact information is available at: https://pubs.acs.org/10.1021/acsomega.4c02540

Author Contributions

†X.G. and J.W. contributed equally.

Notes

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