

Research Progress on Nanomaterial-Based Electrochemical Sensing for Disease Biomarkers

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Abstract: Disease biomarkers serve as crucial indicators for objectively reflecting physiological states and pathological progression, playing a vital role in clinical diagnostics. Electrochemical sensors, with their advantages of simple construction, low cost, and rapid response, have emerged as promising tools with broad applications in clinical diagnosis, biochips, food and drug analysis, and environmental protection. This review systematically examines the application of electrochemical sensors based on diverse nanomaterials—such as graphene, noble metal nanoparticles, carbon nanotubes, quantum dots, and nano-oxides—for the detection of disease biomarkers. Finally, it outlines the research directions and future trends in this field.

Keywords: electrochemical; nanomaterials; biomarkers; disease; sensor

1. Introduction

With the development of the socio-economy, food safety and environmental pollution have become focal concerns. Non-communicable diseases, such as cardiovascular disorders, malignant tumors, and diabetes, induced by these pollutants are on the rise, posing severe threats to human health. Disease biomarkers, when integrated with other diagnostic methods, serve as essential auxiliary tools for the early, sensitive, and accurate assessment and prevention of diseases. The rapid advancement of technology has significantly propelled the development of electrochemical sensors, which are characterized by their simple construction, low cost, and fast response [1].

The emergence of nanomaterials has presented new opportunities to enhance the performance of electrochemical sensors. Commonly used nanomaterials, including graphene [2], carbon nanotubes, gold nanoparticles [3], and quantum dots [4], leverage their unique physicochemical properties to construct high-performance electrochemical sensors, enabling the sensitive detection of disease biomarkers. This paper reviews the construction of electrochemical sensors based on these nanomaterials and predicts their future trends in disease biomarker detection.

2. Electrochemical Sensors Based on Different Nanomaterials

2.1 Graphene Materials

Graphene, a novel two-dimensional nanomaterial composed of sp^2 -hybridized carbon atoms arranged in a honeycomb lattice, has become an ideal conductive material for electrochemical detection systems due to its excellent electrical and thermal conductivity, large specific surface area, wide electrochemical window, strong adsorption capacity, and fast electron mobility. For instance, Samantha et al. synthesized a modified electrode by combining gold nanoparticles, chitosan composite, and graphene, which served as a redox mediator for the highly sensitive detection of carcinoembryonic antigen (CEA) [5]. The adsorption of graphene onto chitosan significantly enhanced electrode conductivity, resulting in a 1.7-fold increase in

sensitivity and a 25-fold decrease in detection limit compared to an unmodified electrode.

2.2 Noble Metal Nanomaterials

Noble metal nanomaterials frequently serve as substrates in the construction of electrochemical sensors. They are typically incorporated through two main approaches: (1) reducing metal oxides to elemental metals under specific conditions via redox reactions, or (2) modifying electrodes with nanocomposite materials containing metal particles. These strategies facilitate electron transfer and enable the immobilization of a large number of antibodies, thereby amplifying the electrochemical signal. A notable example is the covalent interaction between gold (Au) and thiol groups (Au-S bonds), where gold nanoparticles (Au NPs) can be conjugated with various bio-recognition elements to significantly enhance the electrochemical signal.

2.3 Carbon Nanotube Materials

Carbon nanotubes (CNTs) are seamless hollow tubes formed by rolling up sheets of graphite, consisting of carbon hexagons. They are classified into single-walled (SWNTs) and multi-walled (MWNTs) carbon nanotubes based on the number of graphene layers in their rolled structure. CNTs possess unique properties such as rapid charge transfer, good biocompatibility, catalytic activity, and a large specific surface area, leading to the development of numerous CNT-based electrochemical sensors. For example, Zhou et al. employed petal-like CdS-C complexes as electrochemiluminescent materials and fabricated DNAzymes through the reaction of hemin with guanine-rich DNA sequences. The use of DNAzyme-modified gold nanomaterials as probes significantly improved both sensitivity and biocompatibility [6].

2.4 Quantum Dot Materials

Quantum dots (QDs) are a special class of semiconductor nanomaterials or nanocrystals with unique optical, electrical, magnetic, and electrochemical properties. They exhibit high surface activity, small size, and a large specific surface area, allowing them to rapidly respond to subtle external changes. Electrochemical biosensors based on quantum materials are

increasingly attracting attention due to their high sensitivity, excellent selectivity, and fast response speed. HE et al. developed a highly sensitive electrochemical immunoassay for detecting CEA antigen. Experimental results demonstrated a linear detection range of 0.032 to 10 ng/mL and a detection limit as low as 32 pg/mL [7]. Moreover, this sensor showed particularly promising performance in detecting CEA levels in urine samples.

2.5 Nano-Oxide Materials

Nano-oxides are widely utilized in electrochemical biosensors primarily for their excellent biocompatibility and hydrophilicity, which are particularly suitable for the immobilization of biomolecules. These materials facilitate direct electron transfer between the electrode surface and the active sites of biological protein molecules, significantly enhancing both reaction speed and sensitivity. Zinc oxide (ZnO) nano-oxides, for instance, are excellent choices for biomolecule immobilization due to their good biocompatibility, high stability, non-toxicity, and high carrier mobility. In a study by XU et al., an inverse opal structured ZnO nanoparticle electrode was used. A composite of alpha-fetoprotein (AFP), cadmium sulfide quantum dots (CdS), and glucose oxidase (GOD) was formed (AFP-CdS-GOD). Based

on the specific immune competition mechanism between AFP antibodies and this composite, a photoelectrochemical biosensor was fabricated. This sensor exhibited a linear detection range of 0.1 to 500 ng/mL, a detection limit as low as 0.01 ng/mL, along with good stability and anti-interference capabilities [8].

3. Conclusion

Owing to their distinctive properties, including facile surface functionalization, good compatibility, high electrochemical activity, and significant mass and electron transfer capabilities, nanomaterial-based electrochemical biosensors have achieved notable progress across multiple domains. However, the majority of these sensors remain in experimental stages, facing challenges in translating them into practical clinical applications. Current limitations include insufficient sensitivity and stability for detecting complex biological markers, primarily due to the lack of systematic research on miniaturized, high-throughput biosensing at the nanoscale, which hinders their adaptability to diverse biological environments. Despite these challenges, electrochemical biosensors based on nanomaterials are undoubtedly poised to become a major trend in the future of disease biomarker detection.

4. References

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