Nanomaterials-Based Biosensors for Detection of Glucose

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Abstract: It is well known that glucose is a common and significant substance in the human body. Therefore, it is quite important to detect glucose in the human body. This work will summarize some nanomaterials that have been successfully used for glucose biosensors as well as some other promising nanomaterials. And some nanomaterials will be used in combination to achieve better results.

1. Introduction

Glucose is important to the body because it provides energy. People eat carbohydrates and break them down by enzymes in the body to obtain glucose. After glucose is broken down, it will be transported to the whole body with the blood circulation [1]. As one of the main energy sources, glucose can help people maintain physiological functions, such as controlling body temperature and heartbeat and physiological processes. But too much glucose can also reflect some health problems of the body, such as diabetes and obesity, or too little blood sugar can also lead to some problems, such as hypoglycemia [2].

Therefore, detection of glucose is very important to monitor health. Based on the structure of glucose, its strong reducibility makes it easy to detect. However, due to the cross reaction of reducing agents in the reduction method to result in false values, the aromatic compounds used in the condensation method have strong corrosively and toxicity, and the enzyme method is relatively more accurate and cheaper, even if it cannot be directly applied to urine detection. People need a new method to detect glucose, which is nanomaterials. Various nanomaterials have been employed to construct glucose biosensors due to their large specific surface area, excellent physical and chemical properties and improved the performances of as-prepared glucose biosensors [3], as shown in Figure 1.

Nanomaterials is an advanced area of research that allows to produce a wide class of materials, including particulate materials with at least one dimension of less than 100 nanometers (nm). The researchers found that the size of a substance influences its physicochemical properties. Then the importance of nanoparticulate materials were realized and have attracted considerable interest because of their unique properties. For example, its “adjustability”, scientists can fine tune the properties of substances by changing the size of particles, including melting point, fluorescence, conductivity, magnetic capability and chemical reactivity. And the surface area of nanomaterials is very high. Higher surface area can help them better contact and collision probability with substances, which can greatly speed up the reaction rate. This makes it have the potential to be a good catalyst. Nowadays, many kinds of nanomaterials have been used in biosensor research and the recent popular nanomaterials. And the devices need more improved sensitivity and selectivity, more rapid response time, and lower cost [4].

Since 1981, due to the characteristics of nanomaterials, scientists have introduced them into the field of biosensors. This improves the sensitivity and other analytical characteristics of the biosensor. Among many nanomaterials, gold nanoparticles (AuNPs), carbon nanotubes (CNTs), graphene (GR) and photonic crystals (PCS) are widely used in the field of biosensors because of their high stability, excellent biocompatibility, high surface energy and strong signal amplification effect [5].

In this article, the performance of nanomaterials-based biosensors for detection of glucose will be present, as well as their own advantages and disadvantages in the sensor field.

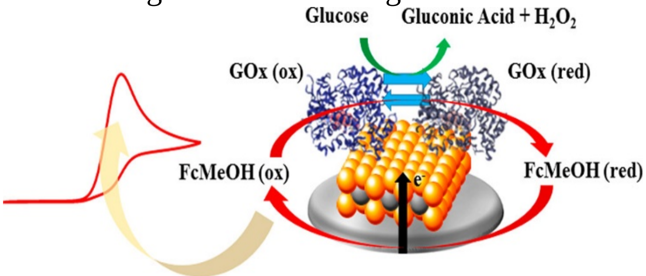

Figure 1. Schematic Representation Illustrating for the developed biosensing method [3].

2. Application of Carbon Nanotubes

Carbon nanotubes (CNTs) are the most used nanomaterials in glucose biosensors. Carbon nanotube is a kind of seamless cylindrical tube, which is composed of many small carbon rings and six carbon atoms. These small carbon rings form GR plates. According to the layered structure of GR plate, carbon nanotubes can be divided into two categories: single wall carbon nanotubes (SWCNTs) and multi wall carbon nanotubes (MWCNTs) with multiple rolling GR layers [7]. Since GOx produces hydrogen peroxide in the presence of glucose, hydrogen peroxide is detected in the biosensor by connecting electrodes. Carbon nanotubes and reduced graphene oxide (RGO) nanosheets will try to construct glucose biosensors together with gold nanowire arrays. It has been proved to be a good substrate for the preparation of glucose biosensors. At the same time, combined with the prepared glucose biosensor, the glucose concentration was determined by microfluidic injection analysis [8]. As shown in Figure 2, a review of Förster resonance energy transfer (FRET)-based biosensors using nanomaterials as sensing probes was present for analysis of target.

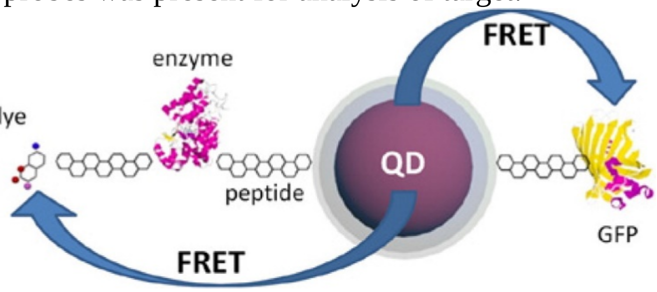

Figure 2. Schematic illustration for the developed biosensing method [7].

Therefore, what are the reasons for using RGO and CNT. It is a very promising electrode material for supercapacitors. Firstly, experiments show that the appropriate addition of carbon nanotubes can effectively improve the capacitance and cycle performance. Secondly, flexible all solid-state asymmetric supercapacitors based on RGO, and carbon nanotube electrodes were prepared, and showed the same capacitive electrochemical properties under bending conditions. Third, it can turn on a light-emitting diode, which means its feasibility in practical application. In addition, RGO and CNT composites were prepared by a simple one-step hydrothermal method [9].

Although enzyme glucose biosensors have been widely used, the efficiency of enzyme glucose biosensors will be affected due to the solidification of proteins on carbon nanotubes. In order to compensate for the low efficiency caused by protein solidification, signal amplification can be realized by crosslinking additional enzymes with CNT. However, this has no significant effect on the sensitivity of carbon nanotube enzyme glucose sensor. The biggest problem of carbon nanotube enzyme glucose sensor is that it is easy to become extremely unstable over time [7]. Another nanomaterial AuNPs can be added to enhance signal amplification. In order to solve this problem, AuNP MWCNT biosensor was prepared. The sensor based on AuNP MWCNT can display the same value as the automatic glucose analyzer when detecting the glucose level in human blood samples [10]. However, when sucrose, fructose and other sugar molecules exist in the sample, AuNP MWCNT shows a negative reaction under the optimized conditions, and multi-step synthesis is still needed. In order to solve this multi-step problem, scientists led by sun tried to use ionic solution to realize one-step rapid reaction of non-enzymatic glucose sensor. The detection limit of ion solution for multi walled carbon nanotubes is 0.89 μm. However, after 30 days of development, the response decreased by only about 5%.

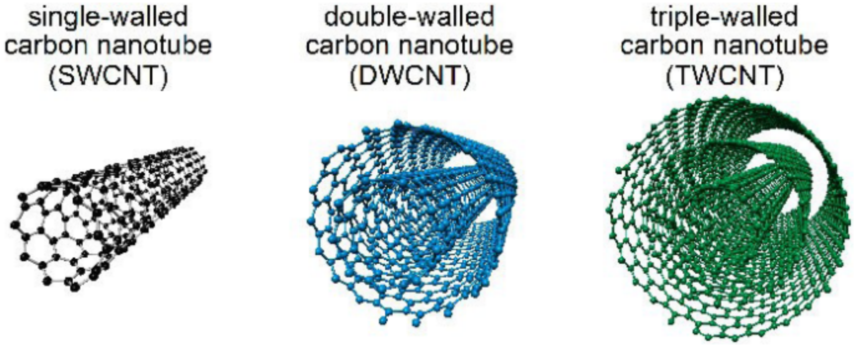

Figure 3. Schematic illustration for the developed biosensing method [8].

Different structures of CNTs have been synthesized, as shown in Figure 3. Scientists soon developed CNT sensors based on the field of electrochemistry. Due to its large aspect ratio, CNT has a larger surface area, which not only strengthens the transmission of heterogeneous charges, but also enhances the docking point of biometrics. And CNT also has good conductivity and charge transfer. Moreover, some metal impurities in CNT can also increase its electrocatalytic performance. The glucose sensor developed based on the above characteristics, such as SWCNT, has good performance. SWCNT can detect glucose at concentrations as low as 1.441 MA/dl. Moreover, the structure of CNT can make it work under negative voltage and can eliminate the electrochemical signal of oxidized blood disruptors, such as uric acid, in normal voltage. Similarly, the multi wall MWCNT with high density also made a breakthrough in the field of solidified enzyme, which retained 86.7% of the initial enzyme activity. Such characteristics also enable CNTs to combine well with metal nanoparticles. Combining with metal particles can effectively reduce interference and bring lower detection limit. Another version of SWCNT created using Pt nanospheres is more sensitive and can detect glucose levels in blood. These electrochemical biosensors can also detect saliva and tears, creating a development space for noninvasive glucose detection. The carbon nanotube electrode modified with [1,1-binaphthyl]-4,4-diol can be used for the simultaneous detection of dopamine, folic acid and uric acid. Adding [1,1-binaphthyl]-4,4-diol to the paste electrode can improve the sensitivity of the electrode. The detection limits of dopamine, uric acid and folic acid were 0.49 mmol/L, 4.2 mmol/L and 7.69 mmol/L, respectively. Multilayer carbon nanotubes and gold nanorods composite modified glassy carbon electrode can be used for electrocatalytic oxidation and detection of L-cysteine. The electrode oxidizes L-cysteine at very low potential, and other normal interfering mercaptan compounds such as cysteine, glutathione and N-acetylcysteine will not be oxidized. The sensor has the advantages of good stability, fast response time, large catalytic constant, wide linear response range and low detection limit [11,12,13]. In addition, as shown in Figure 4, CNTs also were modified by different types of nanomaterials.

Pregnancy associated plasma protein is an enzyme detected in prenatal screening to determine whether the fetus has Down syndrome. A novel electrochemical immunosensor for competitive detection of PAPP-A in serum was developed. The glassy carbon electrode was modified with single wall carbon nanotube/chitosan complex, and then coated with PAPP-A. After washing, the electrode was incubated with streptavidin alkaline phosphatase and then electrochemically tested. In order to detect human carcinoembryonic antigen, Park et al. modified the glassy carbon electrode by multi-layer drop coating/electrodeposition assembly of redox graphite, multi wall carbon nanotubes and prussian blue nanoparticles. The assembly contains anchored gold nanoparticles that can immobilize carcinoembryonic antigen antibodies. The electrode and the redox graphene Prussian blue five-layer electrode have the best performance, high selectivity, and the immobilized detection limit is 60 pg/ml.

The label-free detection of thrombin can be realized by immobilizing thrombin binding aptamer on single wall carbon nanotube modified glassy carbon electrode. The linear range of the electrode is 10-100 nmol/L and the detection limit is 10 nmol/L. There is a sensitive nanostructured immunoelectrode for the electrochemical detection of dengue virus NS1 protein. The method is to deposit a layer of carbon nanotubes on a glassy carbon electrode, and then attach polypropylene to its surface. The electrochemical properties of sensor immunoassay are indirect, which is produced by the combination of hydrogen peroxide or peroxidase with NS1 antibody. The linear range of the sensor is 0.1~2.5 μG/ml, the detection limit is 0.035 μg/ml [14].

3. Application of Gold Nanoparticles

Another very common nanomaterial in the field of biosensors is AuNPs. Its unique performance makes it particularly popular in the development of optical and electrochemical sensors. Because of its biocompatibility, optical and electronic properties and relatively simple production and modification, it is loved by scientists. An optical phenomenon in which light radiation of a specific wavelength causes electronic oscillations in a conveyor belt. These oscillating electrons are called resonance surface plasmon. The change of oscillation frequency will lead to the visible color change of AuNP. At the same time, AuNPs have a strong transduction platform through refractive index detection. This characteristic is conducive to high sensitivity biosensors and can also reach the detection limit at the single molecule level. In addition to its excellent optical properties, it can also transfer electrons between various electroactive biological species and electrodes, which is suitable for oxidoreductase biosensors.

In classical electrochemical enzyme induction, detectable molecules must diffuse into the solution, resulting in non-negligible electrode loss, and AuNP can transfer electrons involved in redox reaction to the reaction center close to the enzyme. Wilner et al. recombined GOx on the surface through AuNP and fad to improve enzyme contact. Moreover, 1.4 nm AuNP can functionalize fad, and the composite composed of fad, AuNP and GOx is installed on the gold electrode, reflecting the role of AuNP as a conductive carrier in enzyme arrangement. AuNP, PQQ and GDH can also form composite materials. Compared with the previous composite materials, the efficient wiring of this composite material leads to higher conversion rate between drinking electrodes. This characteristic makes the biosensor made of composite materials with AuNP, PQQ and GDH as raw materials minimize the influence of nonspecific oxidation disruptors, because the oxidation of glucose is not affected by oxygen under the action of the material. At the same time, Wilner also uses AuCl4- and H2O2 produced by the enzyme to catalyze the growth of AuNP, which increases the absorbance of AuNP, so that people can develop biosensors based on H2O2 and develop new fields and applications. In addition to the enzyme field, another humorous printing technology can say that AuNP is evenly distributed on the carbon electrode, which enables the mass production of AuNP based biosensors.

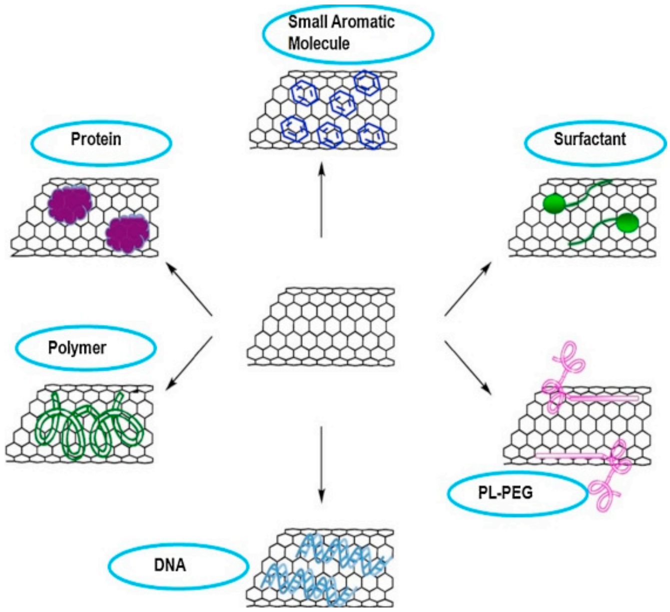

Figure 4. CNTs modification using different types of nanomaterials. [10].

In order to verify the possibility of this technology, many different ink formulations have been tested to find the best formulation and printing parameters. In the early development of this technology, it was found that high printing force may cause the ink containing AuNP to spread too much, and low printing force will cause ink spots on the electrode. At the same time, the evaporation rate of ink is as important as the polymer content. Too fast evaporation will lead to a large loss of AuNP, and too much polymer will reduce the distribution of AuNP on the carbon surface and become uneven because of the increase of ink viscosity.After many attempts, now people have basically mastered a stable ink formula, and because the surface area and volume ratio of AuNP particles are very large, it is suitable for most high-sensitivity biosensors. In the field of glucose sensing, AuNP can provide a biocompatible environment for enzymes such as GOx. This increases the response of the electrode to glucose addition. The technology is still immature, and the detection of glucose is only one of its potential applications [15].

4. Application of Graphene

Graphene is a composite carbon nano material composed of single atom two-dimensional SP sheets. It has high thermal conductivity and conductivity and has excellent tensile strength. Its defect sites in C-C lattice are conductive to heterogeneous charge transport, which makes it very suitable for curing in electrochemical metal decoration and immobilization of biometrics. Its biggest feature is that it can measure potentially measuring glucose is the environment. Because graphene is produced for cell mobilization. From the test of mouse fibroblasts, graphene shows that it has good adhesion and differentiation [16]. Therefore, it is feasible to detect glucose by cell solidification on graphene or graphene oxide. In the study of graphene, scientists found that it has quite or even better research prospects than CNT.

Kang et al. Etched graphene from graphite sulfuric acid, nitric acid and potassium chlorate, and coated the mixture on the glass carbon electrode to obtain a graphene-based glucose sensor. Recently, chemical vapor deposition (CVD) has been applied to graphene nanosheets on silicon substrate surface and applied to glucose sensing. After electrochemical deposition, platinum metal particles silenced on graphene nanosheets were re deposited with GOx doped conductive polymer. Isomorphism changes the current pulse size of click nanoparticles, and the size, density and morphology of platinum nanoparticles have changed to a certain extent. The glucose sensor based on this has a lower detection limit (5.40×10^{-3} mg/dl) and a wider linear sensing range (0.1801-900.7795 mg/dl) [6]. Such a wide linear sensing range makes it conducive to detect glucose in blood, tears, urine and other multi serum samples, and even become the development space of noninvasive sensing.

In In this section, we describe a glucose biosensor based on zirconium dioxide (ZrO_2) and gold nanoparticles with good electrical conductivity and biocompatibility. Zirconium dioxide and gold nanoparticles were synthesized as a novel material for glucose biosensor, which is biocompatible and has a large surface area to immobilize more glucose oxidase. In addition, the conductivity of the sensor was increased when ZrO_2 and gold nanoparticles were compounded together. The glucose biosensor based on this design has a good detection range and low detection limit, and a fast response time [17].

5. Conclusion

As a conclusion, nanomaterials can help us better detect glucose. The sensitivity of some electro-optical reactions and enzyme oxidation reactions to the sensor is strengthened, which makes its detection limit lower and has more room for development. At the same time, the use of CNT and graphene gradually makes nondestructive glucose detection possible and brings more convenience to people's life. Moreover, not only these nanomaterials listed in this paper, but also many nanomaterials have also contributed to the development of glucose biosensors. At the same time, more other methods, such as colorimetry, also make the field of glucose biosensor full of development space. In the future, people will pay more attention to the combined use of nanomaterials, to combine a variety of characteristics and maximize the function. Glucose sensor is unknown. People also hope to apply it in the field of cancer diagnosis, hoping that relatively low-cost nanomaterials can bring people better medical conditions.

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