

Sensors constructed from carbon nanomaterials and their applications

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Abstract. Diabetes is a growing disease, with patient morbidity and mortality increasing every year. Since diabetes is associated with short- and long-term health problems, it has become extremely important to detect and effectively treat diabetes. Many research institutes and healthcare organizations are leaning towards the use of cost-effective biosensors to monitor the body's blood glucose standards and provide accurate health diagnosis. Biosensors help in accurate diabetes diagnosis and monitoring for effective treatment and management. Based on the recent advances in nanotechnology, a variety of glucose biosensors made of carbon nanomaterials have been developed, and such sensors are a key factor for diabetes diagnosis and treatment, with better performance and sensitivity for better detection of the disease and tracking of the response to treatment. Thus, this research illustrates the significant advances in nanotechnology-based biosensors for medical applications and the potential of carbon nanomaterials for good applications in medical testing.

Keywords: Carbon Nanomaterials, Biosensors, Application.

1. Introduction

Over the past decade, various sensing devices have been used to analyze human metabolites, it can detect the healthy condition of people, the most widely used are electrochemical sensors because of their advantages such as low cost, selectivity, sensitivity, and fast detection speed. According to combining carbon and other polymer nanomaterials, can improve the effect of the sensor. In this era, many diseases threaten the lives of human beings throughout the world. Just like COVID-19 in recent years, the danger to a person is enormous, and in severe cases, it can cause respiratory failure or even organ failure leading to death. Most of these diseases have a high mortality rate, similar to diabetes, cancer and Alzheimer's disease (AD), which is increasing in the number of patients and deaths year by year, and this is a disease with high morbidity and mortality which carries symptoms of slow and non-healing wounds about patients. Globally, it costs approximately \$500 billion per year to treat diabetes.

Diabetes is a metabolic disease caused by high blood sugar that jeopardizes human health and has infected more than 420 million people in the world. This disease causes elevated glucose levels in the blood. High levels of glucose can cause stroke, kidney disease and more. Therefore, early detection of glucose levels is a very important issue. In addition, AD is a chronic, progressive developmental neurodegenerative disease. It occurs mostly in older people and can make them become demented. And there is no way to fully treat this disease with current technology. For people with diabetes, the use of accurate, fast and stable sensors to monitor blood sugar levels in the patient's body is paramount. There

are many ways to diagnose diabetes, and most of the traditional diagnostic techniques are glucose analyzers, which take blood from a pricked finger, but there is a lot of uncertainty because the value of each measurement can only show the situation at the time of the measurement. Detection by CT scanning is costly. According centrifugation, enzymes, and chromatography reduce the quality of the test because it relies on the person himself to observe and measure data, which is not sufficiently accurate, stable, and efficient. Amperometric detection by electrochemical sensors is the most widely used because it improves the estimation of blood glucose levels. However, the use of nanotechnology to diagnose and treat diabetic patients is a new alternative method because it has the advantages of effectiveness, high sensitivity, high selectivity, and fast detection speed. Biosensors are based on receptors to analyze the process used to detect sensor measurement and detection.

Early researchers and scientists have attempted to solve this problem about diagnosing type 1 diabetes by using nanotechnology to develop contrast agents, improving the efficacy of insulin therapy by implanting glucose-detecting sensors into patients, and using nanotechnology to increase glucose response. Carbon nanomaterials (CNMs) could help scientists find a new approach that is safer and has fewer side effects. The materials are specialized to transmitting metallic nanoparticles, small molecules and peptides to treat diabetes. Based on the unique properties of carbon nanomaterials, it can at just the right number of drugs to the patient, reducing the side effects of drugs and preventing patients from developing drug resistance. However, its biggest drawback is that it is expensive to produce. There are many different types of carbon nanomaterials, including graphene, graphene oxide, reduced graphene oxide, and other carbon materials that contain unique chemical properties. In these materials, graphene has good properties in the field of science.

The complexity of the structure of carbon nanomaterials gives them a great advantage in medicine, and graphene nanomaterials (GNMs) have the advantages of greater surface-to-volume ratio, better electrical and thermal conductivity, greater sensitivity and selectivity, and they can operate under harsh conditions and are well suited for doping, loading and capping properties of active molecules. However, graphene has drawbacks such as low quantity and hydrophobicity, which limit its application in biosensors. Graphene oxide and reduced graphene oxide solve this problem because of the enhanced hydrophilicity of their graphene layers and high conductivity makes it easier to use. In addition, one-dimensional carbon nanotubes are also used in biosensors as a material with a special structure, due to its special properties, and it is able to monitor the process of biomolecular interactions. Because of carbon nanomaterials have one of the characteristics is large surface area, so it allows for greater filling capacity as well as large mass transport of reactants, which has the effect of enhancing the signal. In addition, single-walled carbon nanotubes (SWCNTs), which have been widely used in biosensors in recent years, it consists of multilayers of concentric single-walled graphene cylinders linked together by van der Waals forces. In terms of chemical properties, due to their large surface area, they can immobilize a larger number of enzymes and expand the reaction area between the enzyme and the substrate, which improves the conductivity, as well as the signal response of the sensor. However, the insolubility of such carbon nanotubes makes them ineffective in practical applications. Therefore, this review describes the role of different types of carbon nanomaterials in the treatment and monitoring of diabetes and diabetes-related diseases, as well as their applications.

2. Carbon nanomaterials

Much attention has been paid to carbon nanomaterials in the last decade, especially fullerenes (OD), graphene, carbon nanotubes, and carbon dots (CDs). Due to the very small size of the carbon nanostructures, which is approximately between 1 nm and 1 μm , so these materials are well suited for use as nanocarriers and nanocapsules. Fullerenes were discovered in 1985 by Kroto's group. and won the Nobel Prize in Chemistry in 1996 [1]. Fullerene is a hollow molecule composed entirely of carbon and can be categorized as C_{20} , C_{60} , C_{70} , depends on the total number of carbon atoms, the smallest fullerenes is C_{20} . The shape is usually as spherical, elliptical. C_{60} is the most widely used, the structure is spherical with 60 carbon atoms highly symmetrical and arranged in hexagonal and pentagonal shapes.

In addition to this, the synthesis of carbon nanotubes was initially achieved by the utilisation of the arc discharge evaporation process in the year 1991 [2]. In total, there are two categories of carbon nanotubes, SWCNTs and multi-walled carbon nanotubes (MWCNTs) [2]. When compared to multi-walled carbon nanotubes, single-walled carbon nanotubes have a greater aspect ratio, length-to-diameter ratio, and superior homogeneity. It has better mechanical properties, electrical and thermal conductivity. In terms of dynamics, the density is only 1/6 of steel, yet the tensile strength is 100 times more than that of steel. And because MWCNTs are smaller in size, they have a greater length to diameter ratio. Carbon nanotubes can also be categorized into armchair, serrated and chiral based on their structural features. But there is not enough data about the medical applications of carbon nanomaterials for the treatment of diabetes. Carbon nanofibers have analogous structure and characteristics with carbon nanomaterials, and have the advantages of easy production, low cost, and good functionality, and their high conductivity make the electrons transfers more easily so thus can improves the sensitivity of biosensors. In addition to this, carbon nanofibers can be easily synthesized as electrodes for biosensors, and electrodes fabricated through carbon nanomaterials have large surface area ratios, allowing the large number of nanoparticles uniformly distributed on the surface.

3. Enzymatic and non-enzymatic carbon nanomaterials for electrochemical biosensors

Due to the number of diabetic patients yearly increase in the world, there is a need to follow the trend to develop a glucose biosensor capable of rapid detection. Glucose sensors utilize the highly specific and catalytic nature of enzymes to achieve concentration monitoring of the molecule by using enzymes as sensitive progenitors of biosensors, in simple terms, converts biological events to electrical signals. In measure the glucose, either enzymatic or non-enzymatic methods can be used. Glucose sensors that use an enzyme base use glucose oxidase (GOx), while glucose sensors that use a non-enzymatic base use electrocatalytic activity [3]. According to the difference about the electron transfer mechanism, enzyme-based glucose biosensors can be divided into three methods [4]. The first method is based on the use of oxygen molecules as electron acceptors, the immobilization of glucose oxidase on the surface of the electrodes, the method of hydrogen peroxide, and the determination of the reduction of oxygen or the method of hydrogen peroxide to indirectly determine the glucose content. But the disadvantage of this method is limited by oxygen. The second method is to use electron-conducting medium instead of oxygen as electron acceptors, which can quickly carry out redox reactions, the disadvantage is that the electron medium is easy to diffuse out of the enzyme layer into the substrate solution, this will destabilize the sensor. A final approach is direct immobilization of enzymes on modified electrodes for electron transfer, this makes the sensor more sensitive and has better selectivity, but the transmission rate is limited.

Non-enzyme-based biosensors for direct oxidation of glucose at the electrode containing an electrocatalysis center. Through widely research carbon nanofibers can be used as substrates for non-enzymatic biosensors and perform well. Through composites composed of nanofibers, nanosheets, nanorods, nanoribbon, nanowires and nanotubes have been used by researchers in the construction of biosensors. Considering how quickly glucose biosensors are becoming, the foundation of third-generation glucose biosensors is the idea that by promoting the transfer of glucose oxidase cofactors and electrodes, the electron transfer path can be shortened. Nevertheless, achieving electron transport between the electrode and the redox centre in GOx is a challenge due to its unique structure. Over the past two decades, carbon nanomaterials have attracted much attention for their excellent physical, chemical and electrical properties. Due to their unique shapes with larger surface-to-volume ratios that enable most of the atoms to storm the surface, such materials can be used as electrode modifiers to accelerate the transfer of electrons and thus improve the performance of sensing [5].

4. Glucose levels by fluorescence

Glucose testing has an important role in pharmaceuticals, especially for the treatment of diabetic patients, for identification of glucose is an important basis. Glucose is a chronic hyperglycemia, so it is extremely important to detect and control the glucose region. There are many ways to detect glucose levels,

electrochemical methods of detection, blood tests. But detecting glucose level by blood test is not a good method recognized by most people. Therefore, fluorescence assays have been developed, which have the advantage is more sensitive than other assays, non-invasive as well as the expected lifetime of the fluorescence upgrades is available, in addition the fluorescence reverberation method can be functionalized. However, when the glucose signal is converted to fluorescence flag, the position of glucose fluorescence is unexpected.

To solve this problem, a biomolecule equipped with a sensor and recognizing glucose is needed [6]. Nanomaterials with fluorescent motility can perfectly convert glucose signals into fluorescent flag sensors, especially in terms of fluorescence lifetime. Moreover, nanomaterials have the advantage of high performance in the detection of glucose on cells. The nanobiosensing of fluorescent materials with respect to glucose depends on the subsequent use of the instrument, when used as a glucose assay, the release of the fluorescent color will affects the fluorescence lifetime. In different studies, it can also be used to catalyze oxidation reactions, such as hydrogen peroxide being used as glucose to change its fluorescence.

5. Applications

5.1. Glucose biosensor made of carbon nanotubes

A catalyst was synthesised comprising of carbon nanotubes, 2,2,6,6-tetramethylpiperidine 1-oxyl, polyacrylic acid, polyethylenimine, and GOx. It shows good sensitivity and the linear range is 1-10 mmol [7]. A graphene-based hybrid glucose biosensor was presented, whereby the film is constructed using GOx, and the prepared hybrid biosensor has good sensitivity (26.5 $\mu\text{A}/\text{mMcm}$), while the linear dynamic range is 0.5 to 13.5 mol [8]. The sensitivity of multiwall carbon nanotubes is 9.36 $\mu\text{A}/\mu\text{mol}$ and the linear range is 0.1-2.5 μmol [9].

Direct implantation of carbon nanotubes resulted in the development of saliva-based glucose detecting electrodes on fluorine doped tin oxide coated glass substrates. Subsequently, the immobilisation of GOx is achieved by the use of polyethylenimine, which facilitates the electrostatic force. Due to the three-dimensional uniqueness of carbon nanotubes, a highly conductive layer can be formed on the FTO substrate to accelerate the electron transfer. GOx can be immobilized on the electrode without binding, increasing the contact surface and the reaction efficiency. So far, applications for this glucose biosensor (prepared by growing carbon nanotubes directly on the substrate) have not yet been developed. The sensors prepared by this method have the advantages of large surface area and high electrical conductivity, this effectively quickens the transport of GOx's electrons at the electrode.

5.2. Fluorescent probe

In addition, the fluorescent probes employed in this study are characterised by their water solubility, selectivity, and sensitivity involved the examination of molybdenum disulphide quantum dots (MoS_2 QDs) by the utilisation of H_2O_2 -mediated fluorescence bursting. A straightforward hydrothermal technique was used to create molybdenum disulphide quantum dots, and it has the advantages of high stability, high quantum yield and bright blue fluorescence. Glucose oxidizes to form H_2O_2 , and the fluorescent quantum dots of MoS_2 can be selectively quenched by H_2O_2 , thus MoS_2 QDs can be used to quantitatively detect glucose. In order to prove the photoluminescence quenching of MoS_2 , examine the MoS_2 QDs' photoluminescence in GOx, pure glucose, and the combination of these two molecules. It was found that the fluorescence intensity of MoS_2 QDs remains unchanged when only glucose or GOx was available, but when a glucose-containing mixture was added, the fluorescence intensity will decrease. The findings indicated that the quantum dots composed of MoS_2 QDs experienced quenching as a result of the presence of H_2O_2 , which was created during the glucose oxidation process catalysed by GOx (Figure 1a), and the fluorescence focus kept shrinking by the increase of the amount of glucose, indicating that the additional H_2O_2 was obtained by glucose immobilization (Figure 1b). And there is a significant positive correlation between the state of glucose and the fluorescence decrease (Figure 1c).

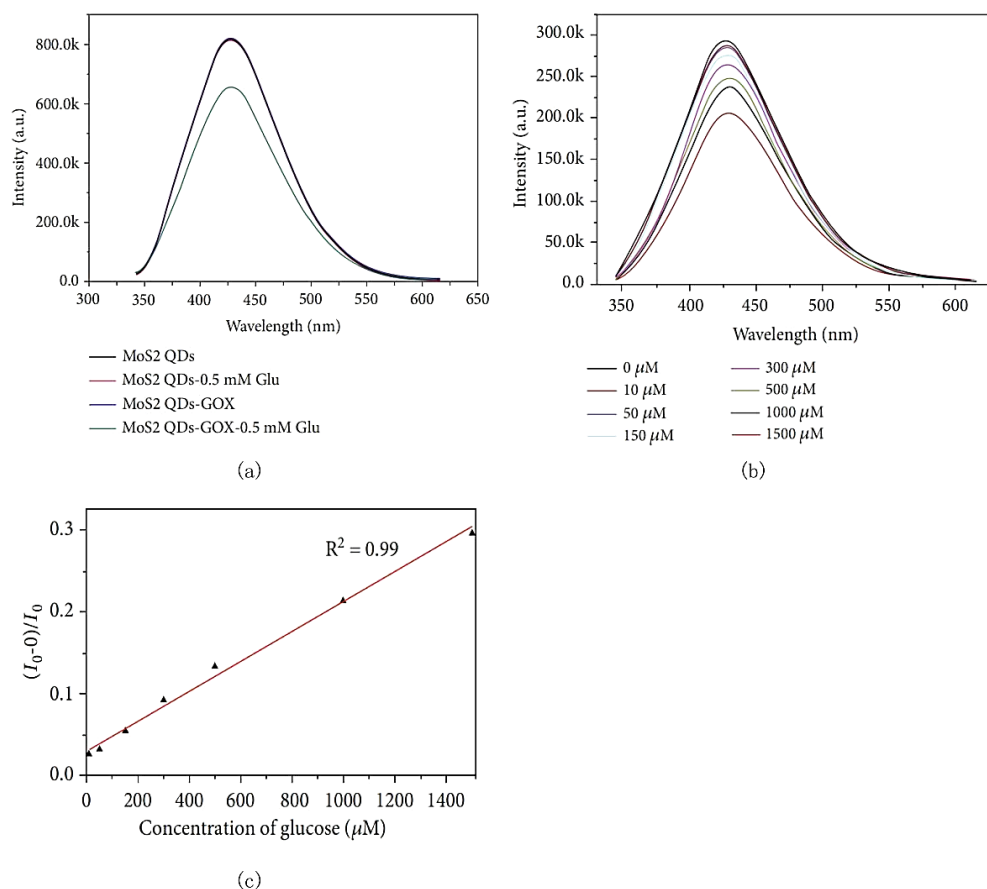


Figure 1. Performance of fluorescence detection methods based on MoS₂ QDs. (a) MoS₂ QDs photoluminescence spectrum. (b) Photoluminescence spectrum of MoS₂ QDs contain GOx solution at a concentration of 0.2 mg/mL. (c) The relationship between quenching ability and dextrose concentration [10].

6. Conclusion

Diabetes mellitus is a metabolic disorder characterised by hyperglycemia, resulting in widespread organ damage and dysfunction. Testing for diabetes mellitus involves measuring the blood glucose level in the patient's body. In the past, people usually used blood glucose meters to measure this, but this is an unstable measurement method. There is a need to develop a non-invasive, real-time and favorable sensor for glucose detection. Nanotechnology is an advanced method, in different types of nanoparticles, carbon nanoparticles are more effectively used in medical sensors. CNMs are favorable in electrical and physical properties for their development in biosensors. By synthesizing CNMs with specific sensing elements, biosensors with high sensitivity and specificity can be fabricated, and all these advantages have contributed to the rapid development of biosensors in many applications, including disease diagnosis and food safety. Therefore, this paper reviews the use of CNMs for the development of a variety of glucose biosensors for diseases such as diabetes.

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