Combining Sensors and Nanoparticles Could Improve Medication Application

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Abstract. More and more scientists are becoming aware of the enormous potential of nanoneedle biosensors as biosensors and nanotechnology advance. Biosensors made of nanoneedles exhibit exceptional sensitivity and specificity. It is a device that integrates nanotechnology and biotechnology that uses chemistry and optics as a detection and analysis mechanism for molecules. As the primary component of the sensor, nanoneedles will be essential in the process of detecting molecules and nanomaterials are the fundamental building blocks that enable nanoneedles to reach their full potential. Nanomaterials are extremely small. They differ from regular materials in terms of their chemical and physical characteristics, and these unique qualities help them interact with molecules effectively. Nanomaterials come in many different forms, such as nanowires, nanotubes, and nanoporous substances. Scientists have been able to make further advancements in the design and use of nanobiosensors thanks to the utilization of these materials and the growth of nanotechnology. This paper's goal is to detail the use of various nanomaterials in nanobiosensors and to emphasize how these materials can enhance the functionality of the sensors.

Keywords: nanotechnology, sensitivity, nanomaterials, nanoporous.

1. Introduction

In the area of medical monitoring, biosensors are used in a highly diverse range of applications. It can find and examine biomarkers to support real-time diagnosis by clinicians [1]. Biosensors can also be utilized during the medication development process. It can result in a more accurate assessment of the drug's relationship to the target molecule. Researchers have been attempting to investigate and apply more sophisticated and stable nanomaterials for the design and development of nanoneedle biosensors for decades in an effort to increase the performance and stability of sensors. An essential link between enzyme and non-enzyme biosensors is nanomaterials [2]. Because of their enormous specific surface area and nanoscale size, which enable a greater number of enzymes to be immobilized on the surface, they interact with biomolecules more effectively and produce a stronger signal [2].

The instrument's sensitivity and selectivity have been greatly enhanced by metal nanoparticles and metal oxide nanomaterials. Metal nanostructures made of gold, silver, and copper are the most prevalent [1]. Numerous researchers have been interested in them and have used their unique optical characteristics and outstanding electrical conductivity to create sensors for material detection. Many metal oxides, including zinc oxide and titanium dioxide, are semiconducting, which means they have distinct optical and electrical properties. They can be utilized to chemically detect sensors and deliver targeted drug delivery in biomedicine. They are frequently paired with electrochemical sensors and frequently utilized in biomedical in vivo and in vitro tests because of their broad application possibilities. Because carbon exists in a variety of allotropes, including carbon nanotubes, graphene, carbon quantum dots, and nanodiamonds, the nanostructure of these materials is diverse [1, 3]. Nanostructure variations result in varied properties and uses for them in various devices. Polymer nanomaterials and biological nanomaterials have good compatibility with living things. Some bionanomaterials are composed of biomolecules like proteins and nucleic acids [1].

These days, a variety of nanomaterials have been integrated with a number of biomedical devices and successfully used in this industry. However, they also encounter various issues at the same time. For instance, minor processing differences may have an impact on the characteristics of nanomaterials during preparation, leading to variable performance. By reading and summarizing pertinent literature,

this study examines the use of several types of nanomaterials in biosensors and how they relate to the medical industry.

2. In biosensors, noble metal nanoparticles have special characteristics.

Noble metal nanoparticles have a lot of potential for use in sensors. By amplifying the signal in accordance with particular electrochemical characteristics, they increase sensitivity and selectivity. Noble metal nanoparticles and nanocomposites have been widely used by scientists as the primary building blocks in the design of biosensors for clinical care, drug delivery, and cancer therapy [3]. Gold nanoparticles (AuNPs) are one of the several noble metals that scientists are particularly interested in. The two primary forms of gold nanoparticles are depicted in Figure 1, and spherical nanoparticles are one of the most intriguing shapes [4].

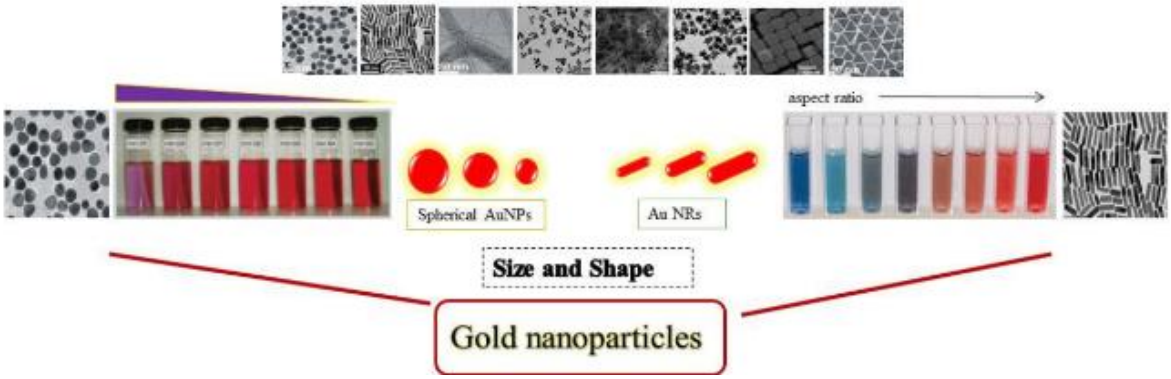


Figure 1. Gold nanoparticles can be divided into AuNPs and AuNRs according to size and shape [4].

2.1. AuNPs can be used in several types of biosensors.

The most representative example of noble metal nanoparticles is gold nanoparticles. Its diameter typically falls between 1 and 100 nanometers. 1D AuNPs (nanorods and nanotubes), 2D AuNPs (gold nanoplates), and 3D AuNPs (nanopillars) are the three categories that can be separated based on size [4]. The optical characteristics of metal nanoparticles at various sizes are depicted in Figure 2. Due to its special optical characteristics, AuNPs are a very useful chemical therapeutic agent in clinical medicine. The assays were carried out on spherical AuNPs in aqueous solution by the researchers. The nucleus size steadily expanded from 1 nm to 100 nm during the measuring process, and the absorbance peak gradually increased from 500 nm to 550 nm. The outcomes demonstrate that the spherical AuNPs' colors shift from orange to red to purple in that order [4]. This demonstrates how the color of gold nanoparticles will be directly impacted by changes in particle size.

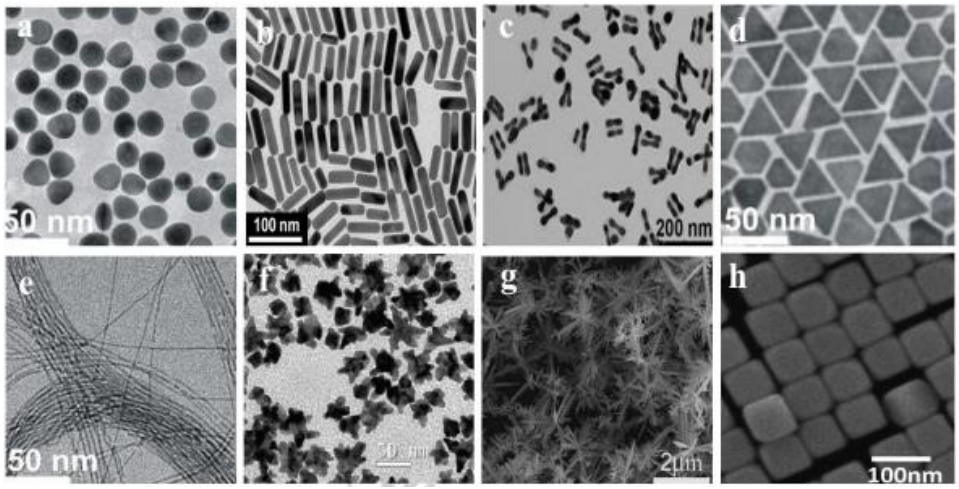


Figure 2. Different sized and shaped nanoparticles have inherent optical characteristics [4].

AuNPs are prepared using a variety of techniques, including physical, chemical, and biological ones. Gamma radiation, microwave radiation, or UV radiation are frequently used in physical procedures to create gold nanoparticles. Particles having a diameter of 5 to 40 nm can have their purity increased by gamma radiation. AuNPs are produced by heating or photochemical reduction under the influence of microwave radiation. UV radiation serves as the primary reducing agent for the creation of nano-gold. Researchers frequently utilize citrate and sodium borohydride as reducing agents in chemical synthesis techniques. The Brust-schiff rin technique, which uses the interaction of thiols with gold to protect AuNPs, was created and put out by researchers in 1994. In the presence of alkylthiols, sodium borohydride reduced AuCl4 to yield nanoparticles with a diameter of 1-3 nm. On the other hand, the primary sources for biosynthesis are chemical molecules found in plants, bacteria, fungi, algae, and viruses.

There are numerous uses for AuNPs in people's daily lives. Based on their unique characteristics, Figure 3 illustrates the relationships between nanoparticles and several sectors. Photodynamic therapy and photothermal therapy are two methods in which AuNPs are mainly used for treatment. Photodynamic therapy is mainly involved in neoplastic diseases and infectious diseases [4]. Based on the energy of the photosensitizer, it produces singlet oxygen and causes necrosis in tumor cells. In photothermal therapy, heat is produced by absorbing visible or infrared light. Malignant tumors are destroyed when temperatures are raised due to increased heat.

AuNPs are crucial for the delivery of medicines. It functions as a nanocarrier and transports different medications (such as proteins and chemotherapeutic agents) thanks to its biocompatibility, controlled dispersion, non-toxicity, and high surface area.

Additionally, one of the primaries uses for AuNPs is biosensing, and various types of sensors utilize various AuNPs characteristics. For instance, the aggregation of AuNPs causes color shifts in colorimetric sensors. Because AuNPs are fluorescent, fluorescent-based sensors can be created. Based on the optical characteristics of AuNPs, the surface plasmon resonance sensor was developed [4].

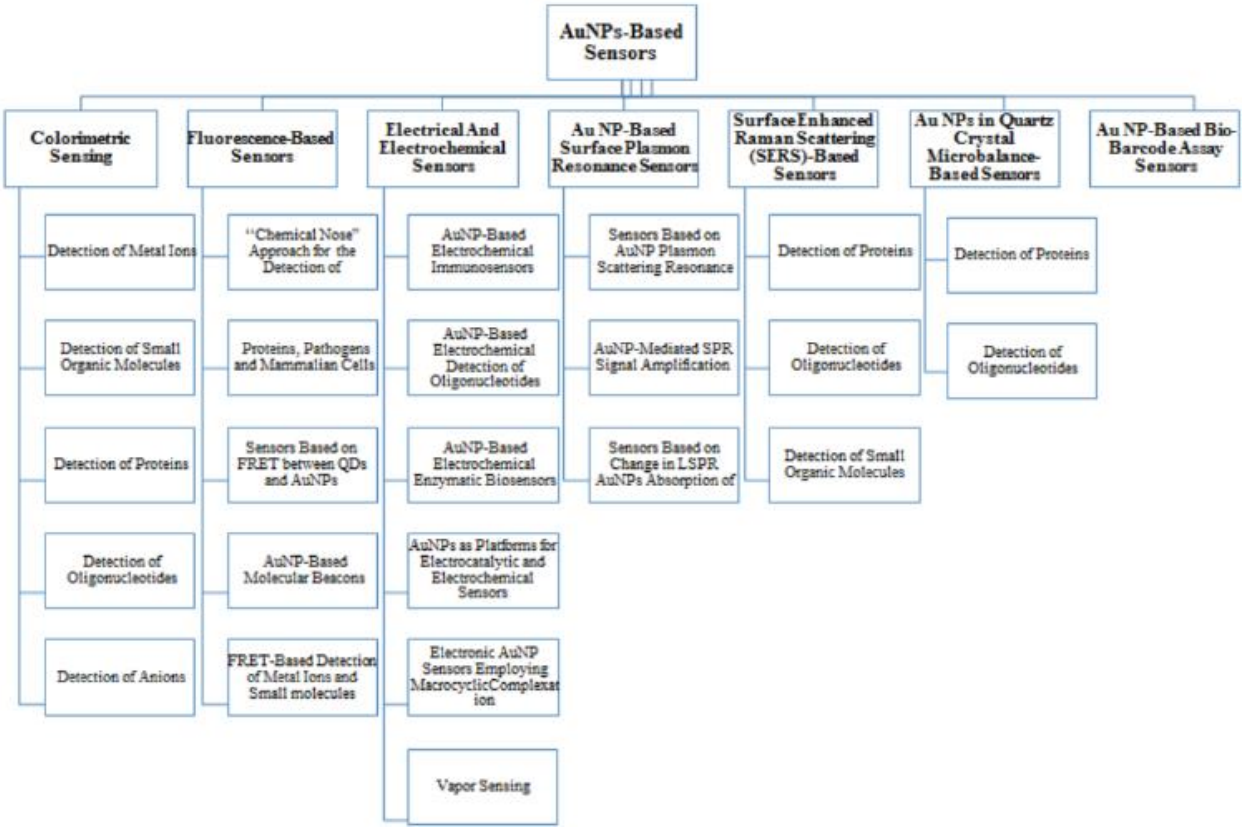


Figure 3. How sensors made with particular nanoparticle physical or chemical properties are used in a variety of industries [4].

3. The potential for metal oxides as nanomaterials is enormous.

Tiny metal and oxygen atoms combine to form metal oxide nanomaterials. In addition to having the characteristics of conventional metal oxides, they also have a variety of unique electrical and chemical properties due to their nanoscale size. Modern technology is frequently integrated with metal oxide nanoparticles to make products that are widely used in people's daily lives. They will include environmental improvements, biosensors, and solar cells. Researchers have discovered that ZnO nanoparticles have a lot of potential in biomedical applications. Large-area fulcrums present in ZnO nanostructures can aid in the immobilization of enzymes. When redox enzymes are transported to the current collector, the ZnO nanostructures offer a direct conduit for electrons. Hydrogen peroxide biosensors are where ZnO nanostructures are mostly used [5].

3.1. Precision is required for hydrogen peroxide biosensor detection levels.

In reaction to cytokines and growth factors, hydrogen peroxide is crucial for redesigning mammalian blood arteries and activating the cells therein. However, overly high hydrogen peroxide concentrations can harm cells by inducing oxidative stress. As a result, the experimenter must control the chemical substance's concentration with extreme precision. There are several different ways to detect hydrogen peroxide, including titration, chromatography, fluorescence, and electrochemical methods [5]. These techniques provide substantially more accurate hydrogen peroxide determination. The basic components of hydrogen peroxide sensors during detection and quantification are enzymes. In most cases, researchers use horseradish peroxidase (HRP) to catalyze hydrogen peroxide to provide a signal that can be electrical or optical and be quantified.

3.1.1. Biological activity of HRP is stabilized by multi-forked ZnO nanostructures.

Enzyme biosensors have strong selectivity and sensitivity as an advantage, but they also clearly have drawbacks. Its cost is very high, and its performance will be unstable due to environmental conditions. Yang and other researchers created and suggested multi-forked ZnO nanostructures to address these issues. It is a nanorod structure created on a surface that resembles a sheet. On the foundation of this multi-forked glassy carbon electrode, the experimenters further developed a new enzyme biosensor. They discovered that the multi-forked nanostructure effectively maintains the biological activity of HRP while producing a low-quality transport barrier in enzymes and solution [5].

3.1.2. Waxberry-like ZnO coupled with electron transfer molecules.

The waxberry-like ZnO structure is another useful substance for immobilizing HPR. It is frequently used by researchers as an electron transfer agent in biosensors to increase effectiveness. Its surface is honeycomb-shaped and contains a large number of pores. High defect density and a sizable surface area are its characteristics. The study's analysis of the honeycomb structure revealed there are many nanoscale holes. The nanosheets are connected to create these holes. Each nanosheet has an average thickness of roughly 20 nm, and the pore is hundreds of nanometers in size [5]. As a result, the protein may easily adhere to the surface of the cavity and enter the cavity, enabling a more precise detection of hydrogen peroxide.

Whether ZnO is waxberry-shaped or has several forks, they all aid in the binding of proteins and the activity of enzymes. Figure 4 illustrates the electrode preparation procedure base on these two configurations [5].

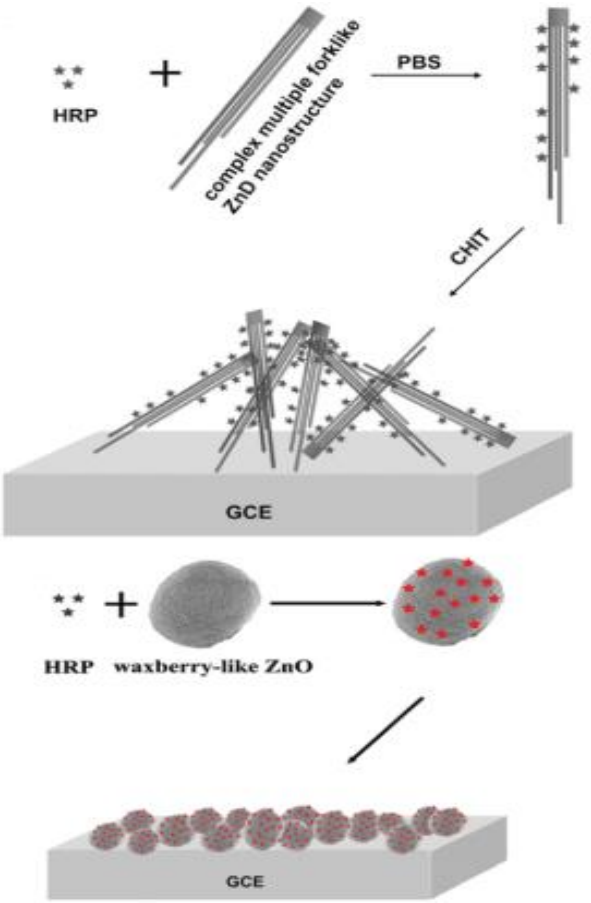


Figure 4. The electrode preparation in Multi-forked ZnO and Waxberry ZnO [5].

3.2. The ability of glucose surface adsorption will regulate electrochemical kinetics.

Glucose biosensors are mainly used in patients with diabetes since glucose metabolism disorders are mostly brought on by excessive blood sugar and a lack of insulin. Around 350 million people worldwide have diabetes, which is an extremely huge figure. To measure glucose levels, researchers have employed a variety of methods including liquid chromatography and spectroscopy. The glucose biosensor is made in a relatively simple manner compared to other sensors, and it also offers the benefits of strong stability and quick response. Three types of glucose oxidase-based reactions are shown in Figure 5: 1. natural oxygen as cofactor; 2. a synthetic electron acceptor acting as a redox acceptor; and 3. direct electron transfer in glucose oxidase and electrodes [5].

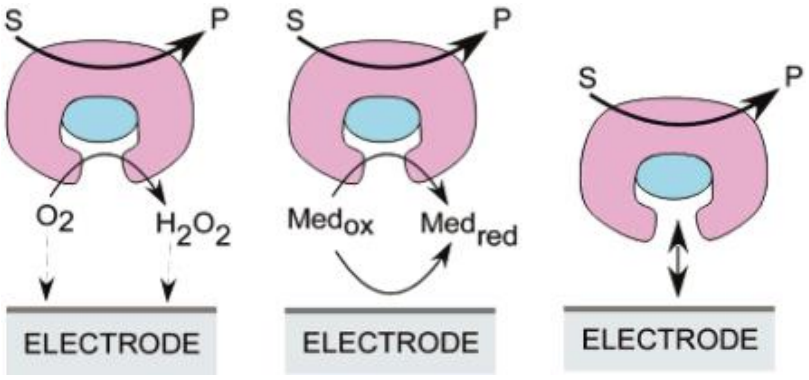


Figure 5. Three forms based on glucose oxidase [5].

The immobilization of glucose oxidase in the biosensor mostly depends on its physical adsorption capability, as opposed to the immobilization of catalase in the biosensor. Additionally, the electrode's morphology and form will have an impact on how much material can be absorbed by it. CuO is a non-toxic and affordable semiconductor. It also has a lot of potential to act as a catalyst in many

different disciplines. Therefore, the researchers decided to utilize it this time as the material for the glucose sensor. They set up a second set of trials without glucose as a control. In the other group, adding CuO into Nafion to raise the surface of the GC electrodes. In the series of tests, Figure 6 demonstrates that the current response of glucose oxidation is relatively weak in the absence of glucose but becomes stronger as the concentration of glucose rises [6]. This suggests that the electrochemical kinetics are influenced by the glucose molecules' ability to adsorb on surfaces.

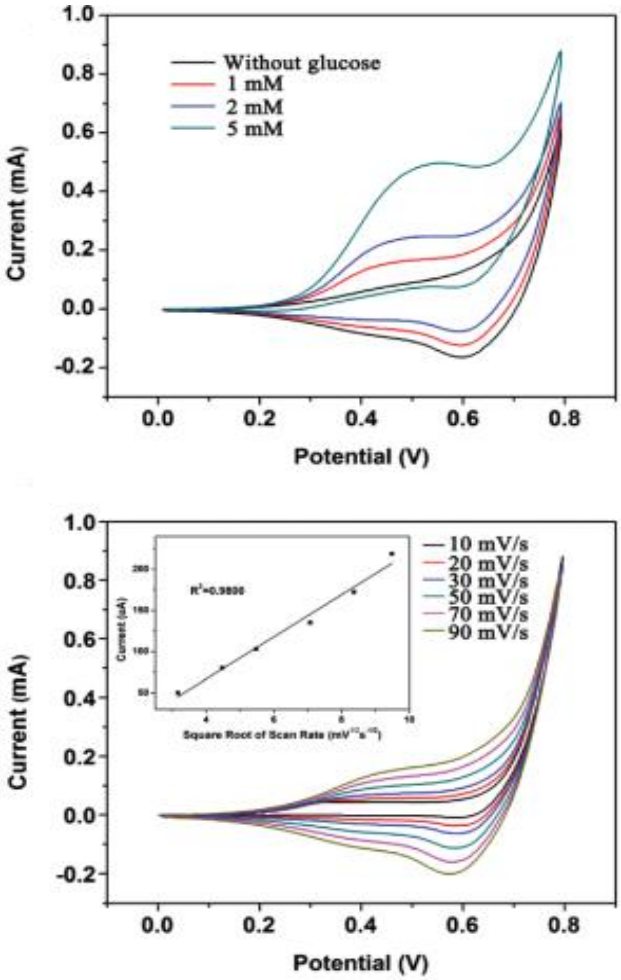


Figure 6. Cyclic voltammetry curve comparison between the two experimental groups [6].

4. Sensor sensitivity could be increased even more via nanocomposites.

Metal and metal oxide nanostructures each offer distinct qualities and benefits, but they also both have drawbacks. Researchers strive to blend various elements and chemicals in the two from a microscopic perspective. This is done to enable new chemicals to produce certain positive qualities and advantages in addition to their respective advantages. In response to the global spread of COVID-19 in recent years, researchers have created a SERS biosensor consisting of a nanocomposite substance called Fe_3O_4 and Au. They develop as a result of the electrostatic interaction between negatively charged colloidal Au and positively charged amino functional groups. Fe_3O_4 microspheres can be made of Fe_3O_4 nanoparticles. It is a sphere with outstanding monodisperse and a particle size of 150 nm. By detecting the virus's signals during the procedure, they are able to catch and isolate the virus in the swab. Their range of applications is equally enormous. For instance, using Fe_3O_4-Au nanocomposites can remove urea in urine and detect adenosine. Additionally, the researchers will mix a few mature SERS bases with Fe_3O_4-Au nanocomposites to improve the performance of SERS sensors [7]. In the course of the detection process, this will increase the sensitivity of SERS to the specificity of target molecules.

It is important to note that the experimenter will amend the nanocomposite substance using the specific protein His-ACE2 in order to get the target molecule before spotting and isolating the virus. His-ACE2 was added to the nanocomposite after which a 2-hour incubation period was followed by numerous washings to lower the amount of ACE2 in the final result [7].

5. Different arrangement structures can be found in carbon nanomaterials.

The primary component of carbon nanomaterials is carbon. Carbon nanomaterials have gotten more and more attention as synthesis and assembly technology has continued to advance. Carbon nanotubes (CNTs), graphene, and fullerenes are the three primary subgroups of carbon nanomaterials [1]. They are the carbon allotropes, which means their structural arrangement will differ slightly. There will therefore be some variations in their characteristics and areas of application.

5.1. Gas sensors can be used with carbon nanotubes (CNTs).

CNTS are excellent one-dimensional materials. Both electrical strength and thermal conductivity are outstanding. The walls of the carbon are made of sheets of graphene, while the interior is hollow structure. Depending on the quantity of graphene sheets, CNTS can be split into single-wall and multi-wall varieties. The sidewall's function is to enhance the CNT sensor's sensitivity and selectivity. The aligned carbon nanotubes are subsequently joined by van der Waals forces to create a stacked structure [8].

CNTs can be made using a number of techniques, such as chemical vapor deposition (CVD), vacuum filtering, in-situ chemical reduction etc. The uniformity and controllability of the films produced by CVD are a benefit. However, because CVD must be carried out at a very high temperature (more than 800 degrees Celsius), some devices may be impacted. The usage of filter paper is limited in the vacuum filtering process, despite its relatively straightforward operation. The yield of the film can be increased by using the in-situ chemical reduction process; however the product's quality isn't very good [9]. Each preparation technique currently has some drawbacks. However, the utilization of CNTs in real-world applications is growing.

Researchers Dai and colleagues decided to use semiconducting single-walled carbon nanotubes (S-SWNTs) for additional research on gas sensors based on the electrical characteristics of CNTs [10]. They initially made an S-SWNT act like a p-type transistor by connecting its two ends with two metals. Next, nitrogen dioxide (NO_2) and ammonia (NH_3) were used to test the sensor's electrical response. The conductance of gas molecules in a SWNT device is depicted in Figure 7 [10].

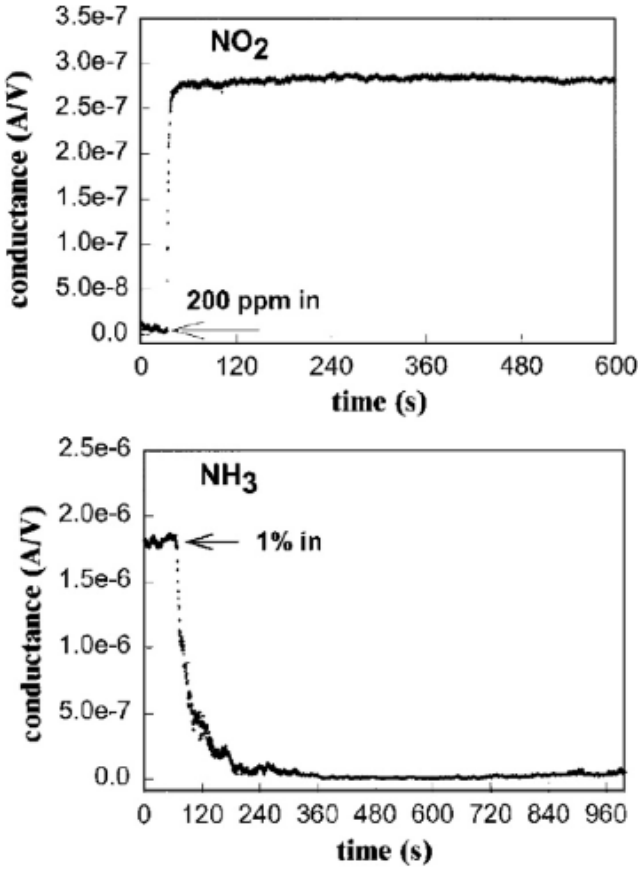


Figure 7. The conductivity of CNTs decreases when they are exposed to NH_3 because their valence bands leave the Fermi level. However, the depleted samples exposure to NO_2 shifts the Fermi level toward the valence band, increasing conductivity [10].

5.2. An oxidant can convert graphene to graphene oxide.

Graphene is a two-dimensional substance, unlike the configuration of CNTs. It is the most stable form of carbon at room temperature. It also possesses exceptional mechanical strength and electrical conductivity. Its structure is a hexagonal honeycomb with sp2 bonding in each layer. Conceptually, folding them could result in the formation of fullerenes and CNTs. Scientists have conducted a number of talks on the production and processing of graphite during the past few decades, including the subject of "graphite oxide" [11]. Under highly oxidative conditions, they exposed graphite to hydrophilic functional groups, resulting in hydrocolloids of graphene oxide flakes. Partial graphene oxide can be reduced to create reduced graphene oxide.

Compared to regular graphene, graphene oxide is easier to manufacture and greater in size. But due to the abundance of oxygen-containing functional groups on its sheets, graphene oxide has a more intricate structure. Additionally, graphene oxide has aliphatic (oxidized) and benzene ring (unoxidized) domains [12]. The experimenter can compare the sizes of two zones based on the level and distribution of oxidation. Different with the procedure used to create CNTs, the early creation of graphite oxide frequently results in the production of toxic gases including NO_2 and N_2O_4. Moreover, the oxidant has strong oxidizing properties when exposed to concentrated sulfuric acid and carries a considerable risk of explosion when coming into touch with organic material. K_2FeO_4 and HSO_4 were used by scientist Peng to create graphene oxide at room temperature, which is a relatively risk-free process. Shen selected benzoyl peroxide as the preparation's raw material [12]. Although the reaction time needed for this manufacturing process is quite quick, benzoyl peroxide still is an unstable and chemical. When the reaction temperature is too high, there is a threat of explosion. The reagents and reaction settings that researchers chose for the manufacture of graphene oxide are listed in Table 1 [12].

Table 1. Reagent choice and reaction conditions each have unique properties [12].

Scientists	Reagent	Reaction time	Reaction temperature	Characteristics
Brodie	KClO3, HNO3	3-4 h	60	The first method
Staudenmaier		96 h	RT	
Hummers	KClO3, HNO3, H2SO4	20 h	RT	Only using HNO3
David	HNO3	<2 h	35	Reaction time is short
Eigler	KMnO4, NaNO3, H2SO4	16 h	10	High quality RGO
Peng	KMnO4, NaNO3, H2SO4 K2FeO4, HSO4	1 h	RT	No heavy metal manganese pollution
Marcano	H2SO4, H3PO4, KMnO4	12 h	50	Low toxicity
Panwar	H2SO4, H3PO4, KMnO4, HNO3	3 h	50	High yield
Shen	Benzoyl peroxide	10 min	110	No liquid

The creation of graphene oxide still has several flaws as of right now. However, by using it and graphene in related sectors and studying how they interact and react with one another, researchers have been able to further enhance the functional qualities of graphene surface composites.

5.3. Functionalized fullerenes can improve the efficiency of charge transport in sensors.

In zero-dimensional form, fullerenes are present in people's daily lives. It occurs in a variety of shapes and sizes, and it contains anything from 30 to 3000 atoms of carbon. The most typical fullerene structure is C60. Due to the characteristics of fullerenes, scientists frequently create mixtures using fullerenes as acceptors and polymers as donors for use in the production of solar cells [13]. This is due to their high power conversion efficiency and ability to be deposited in solution.

Fullerenes can be used in biosensors thanks to their functionalization. It serves as a bridge between the electrodes and the sensor's sensing location. The researchers suggested functionalizing fullerenes with various kinds of chemicals in order to boost usefulness in biosensors. The two types of functionalized fullerenes are outer helical and regular polyhedral. Regular polyhedral is where the molecule is imprisoned inside the cage, whereas outer helical is where the substituents are put outside the cage. Researchers discovered that compared to the inner layer, the outside layer of metal functional groups connected to the carbon cage is more varied and open to fullerene species. The researchers also discovered that the combination of gold nanoparticles and fullerenols could further enhance the performance of the biosensor [14].

6. Conclusion

The use of pharmaceuticals in the realm of medicine has been transformed by modern nanotechnology. Endless possibilities for drug administration and therapy arise from the combination of cutting-edge sensing technologies with nanoscale particles for increased effectiveness and sensitivity. The great sensitivity and selectivity of sensor allows for more precise monitoring of environmental changes and biological markers while detecting chemicals. Additionally, the treatment plan is more customized. Combining the two technologies will increase drug delivery accuracy and further cut down on side effects, allowing doctors to choose from a wider range of medications for treatment options and giving patients more reason to be hopeful.

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