

Review Article

Carbon Nanotubes in Biosensing Systems

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Chettinad Health City Medical Journal 2020 9(2): 117 - 123

DOI: [https://doi.org/10.36503/chcmj9\(2\)-07](https://doi.org/10.36503/chcmj9(2)-07)

Abstract

In the rapidly developing world, it is very much necessary to make use of sensors and analytical devices for various applications. As nanotechnology is grabbing global attention, developing biosensors with the use of nanoparticles (Nps) is one of the trending topics among research communities. Owing to the properties such as high stability, sensitivity and selectivity carbon nano tubes (CNT) is found as one of the promising candidates for the fabrication of biosensors. From various research results, it is clear that both the single walled CNT and multi walled CNT are used as bio-sensing element. In this context, this short review consolidates the working principle, target analytes and other applications of CNT in a detailed manner.

Key words : Carbon nano tube, biosensor; target analytes, applications.

Overview

Nanotechnology and its products are gaining interests all over the world. Owing to the size depended properties of nanoparticles (Nps), they are utilized by various industries to manufacture commercial products of interest.¹ As Nps have higher sensitivity promoted through large active sites they receive high interest by research communities for the fabrication of diagnostic tools especially sensors.² Existing technologies and detecting devices are highly expensive and requires sophisticated environment.³ So, there is a need to develop facile detecting devices to sense the target analytes with higher sensitivity and selectivity. A biosensor usually works by emitting signal when an analyte comes in contact with the sensing element. When an analyte comes into contact, the transducer converts the biological response into electrical signal.⁴ Owing to the large surface area of Nps, a very small quantity of analyte is required to trigger the signal and therefore, the sensitivity of the biosensor is enhanced.⁵ Further, nano biosensors require only a small quantity of sample for analysis which is a major advantage where the nanosensors out-performs bulk sensor types. Even though, there are many Nps such as magnetite Nps, palladium Nps, silver Nps, zinc oxide Nps, cobalt ferrite Nps, etc. that can be utilized for bio-sensing applications, the high electronic conductivity, high active surface area and mechanical durability of carbon nano tubes (CNT) make it an absolute candidate for the fabrication of

bio-sensors.⁶ Owing to large active surface area, CNT possess high surface to volume ratio which further enhances the sensitivity towards target analyte.⁷ CNTs are one-dimensional manmade allotropes of carbon.⁸ It is a tube-like structure with sp² hybridized C-C bond resembling cylindrically folded graphene sheets.⁹ Depending on the number of sheets on the outer wall, CNTs are categorised into single walled CNT (SWCNT) and multi walled CNT (MWCNT).¹⁰ The SWCNT poses an uncomplicated surface chemistry with a single layer of sheet constitute the wall whereas for MWCNT they have two or more sheets present at the wall.

CNT as bio-sensing system

The CNTs grab the attention of researchers due to their interesting electronic properties i.e. it is a highly conductive material. Owing to the high electrical conductivity, a small change in its surrounding environment can drastically affect its conductivity.¹¹ Scientists make use of this phenomenon to detect the presence of target analyte. For selective sensing of target analyte, the CNTs are usually functionalized with complimentary anti-bodies.¹² There are many types of biosensors fabricated using CNT which are summarized in Table 1.

Based on the fabricated biosensor with the help of CNT, different bio-molecules can be detected which are discussed in detail.

Sl. No.	Type of biosensor	Role of CNT
1	Electrochemical biosensors ¹³	CNT accelerates electron transfer
2	Optical biosensors ¹⁴	MWCNT found to enhance the electron transfer
3	Colorimetric biosensor ¹⁵	Enhanced the sensitivity
4	Electronic biosensor ¹⁶	Improved sensitivity by promoting the electron transfer
5	Piezoelectric biosensor ¹⁷	When CNT incorporated over the Pb(ZrTi)O ₃ membrane, the sensitivity is found to be enhanced
6	Gravimetric biosensor ¹⁸	The resonators using CNT as top electrode showed a higher frequency change
7	Pyroelectric biosensor ¹⁹	The pyro voltage is found to enhanced with temperature by the addition of the MWCNTs

Table 1: Types of biosensors developed making use of CNT

Biosensor for the detection of bacteria

Staphylococcus enterotoxins are a major group of toxins which cause about many types of illness especially food-borne diseases which may contaminate eatables such as meats, dairy, salad, bakery products etc., so, it is important to check and assure the quality of the eatables to prevent from infections caused by them. Bhardwaj et al.²⁰ developed paper based electrochemical biosensors using SWCNT for the detection of *Staphylococcus aureus* (*S. aureus*) which is responsible for major types of food borne diseases. The SWCNTs are conjugated with antibodies by N-(3-dimethylaminopropyl) - N'-ethyl-carbodiimide hydrochloride / N-hydroxysuccinimide. When a milk sample with *S. aureus* contamination is subjected to detection using this sensor by differential pulse voltammetry electrochemical characterisation, changes in the current peak is observed owing to the antigen-antibody interaction. The fabricated biosensor has a detection limit of 13 CFU mL⁻¹. Likewise, Yang et al.²¹ fabricated an optical immunosensor for sensing Staphylococcal Enterotoxin B (SEB) in food. CNT is functionalized with anti-SEB antibodies by electrostatic adsorption; the complex is fixed over the polycarbonate film. The introduction of CNT improves the detection limit more than 6 times.

Biosensor for the detection of glucose

It is important to maintain the sugar level in the body in order to prevent the risks of diabetes and heart diseases. Therefore, it is very important to detect the sugar level in human body. Zhou et al.²² wrapped SWCNT with chitosan molecules which can act as bio-electrochemical sensor for glucose detection. These sensors catalyse the glucose and detect their presence. The biocompatibility of chitosan molecules and the electric properties of the carbon nanotubes together contribute to the development of highly sensitive, highly selective and a reproduc-

ible glucose detector. Similarly, a highly stable MWCNT based electrochemical sensor was fabricated for glucose detection by Wang et al.²³ The sensitivity towards glucose was appreciable in different applied potentials (+0.65 V and +0.45 V). Their stability along with the storage also was durable. It was suggested that the high stability was due to the immobilized enzymes along with the carboxylic acid groups on nanotubes surface. This was due to the open ends of the nanotubes which allowed the enzymes inside the hollow cavity.

Biosensor for the detection of hydrogen peroxide

In the present situation, there is a need to develop a rapid detecting biosensor for H₂O₂ analysis. Too much exposure to hydrogen peroxide may cause tissue damage and gastrointestinal irritation with several adverse effects. An amperometric biosensor was fabricated by horseradish peroxidase in aormosil composite doped with ferrocene monocarboxylic acid-bovine serum albumin conjugate and MWCNT by Tripathi et al.²⁴ The fabricated biosensor displays excellent conductivity owing to the presence of MWCNT where the ferrocene was responsible for the electron transfer. The results proved that the sensor was capable of performing good biosensing activity.

Similarly, H₂O₂ detection was facilitated by incorporating CNT on a graphene paper and preparing an electrochemical biosensor by Yimin sun et al.²⁵ This improved the mechanical strength and surface roughness of the paper followed by decorating the paper with Pt nanoparticles. Their electrochemical sensing properties towards H₂O₂ were impressive and can be very well used for analysing H₂O₂ secreted by cells.

Biosensor for the detection of herbicide

Many research procedures are carried out to detect the presence of herbicides in the water sources. The DNA/MWCNTs-CHIT/PGE electrodes were fabricated by Ensafi et al.²⁶ to detect amitrole in water resource and soil. This electrode can be used to trace the amitrole concentration which contaminates the water sources. This voltammetric detection was found to be fast, simple, sensitive, selective and cost effective for tracing amitrole.

All plastic biosensor was developed using SWNT as an active element for detecting 2,4-dichlorophenoxy acetic acid (2,4-D) herbicides by Wijaya et al.²⁷ This was a simple, cost-effective and label free technique was developed that can detect 500 fM levels of herbicide in soil sample. Likewise, there are many biosensors fabricated using CNT for different applications which are provided as Table 2.

Other applications of CNT

Other than biosensing applications, the CNT is utilized in wide range of applications due to their unique physicochemical properties. It can be used in drug delivery, gene delivery, tissue engineering, osteoproduktive material, etc. Some of the applications are tabulated in Table 3.

Conclusion

From the various research outcomes, it has been understood that the stability, electrical conductivity and high surface area of CNTs make them suitable for successful bio-detection of various analytes such as pathogens, bio molecules etc. Also, it is clear that for selectivity and sensitivity CNTs are functionalized with suitable molecules which are contrary to the target analytes. Further, the surface modified CNTs can be used for many other applications especially for drug delivery and gene delivery. Although there are too many advantages in using

Sl. No.	Biosensor	Target analyte
1	Maltose biosensor based on α -glucosidase and pyranose oxidase immobilised CNT ²⁸	Maltose
2	Titanium dioxide nanotube arrays ²⁹	Hydrogen peroxide
3	Iron -phthalocyanine functionalised MWNT based biosensor ³⁰	Hydrogen peroxide
4	CNT-Polyethylene amine functionalised ionic liquid thin films ³¹	Glucose
5	Poly cyclodextrin and CNT composite electrochemical biosensor ³²	Glucose
6	Magnetic nanoparticles based MWCNT biosensor ³³	Catechol
7	Specific biosensor using CNT functionalised with gold nanoparticles ³⁴	Antigen-antibody binding event
8	MWCNTs/ graphene oxide/ pyrogallol biosensor ³⁵	Omeprazole
9	ZnO-MWCNT hybrid nanocomposite ³⁶	Urea
10	Titanium dioxide/CNT nanocomposite based electrode ³⁷	Cancer cells
11	Hyaluronic acid dispersed CNT ³⁸	NADH
12	Poly brilliant cresyl blue-CNT modified electrode ³⁹	NADH
13	ds DNA decorated Fe ₂ O ₃ /SnO ₂ -chitosan modified MWCNT ⁴⁰	Doxorubicin
14	Platinum electrode modified MWCNT ⁴¹	Doxorubicin, anthracycline
15	Magnetite nanoparticles based MWCNT ⁴²	Nucleotide
16	Electrochemical CNT sensor ⁴³	DNA
17	Nitrogen doped MWCNT ⁴⁴	Paracetamol
18	Conductive polymer MWCNT based sensor ⁴⁵	Paracetamol
19	Chitosan modified CNT sensor ⁴⁶	Glutamate
20	poly amidoamine dendrimer-encapsulated platinum nanoparticles modified MWCNT ⁴⁷	Glutamate

Table 2: Carbon nanotubes-based biosensors and their target analytes

Sl. No.	Biosensor	Application	Significance
1	SWCNT modified with chitosan ⁴⁸	Delivering doxorubicin for liver cancer	The treatment was highly efficient than using free doxorubicin
2	CNT conjugated with chitooligosaccharide ⁴⁹	Delivering gliotoxin for cervical cancer	More effective due to controlled drug release
3	CNT-liposome conjugate ⁵⁰	For delivering anticancer drugs	Improved therapeutic index with high drug loading capacity and less toxicity.
4	Magnetic MWCNT ⁵¹	For delivering chemotherapeutic drugs for cancer	High drug loading capacity and highly selective.
5	Multifunctional polymer coated CNT ⁵²	Drug delivery	Decrease the toxicity and increase therapeutic efficacy.
6	Polyamidoamine based MWCNT ⁵³	Gene delivery	Stability (upto six months)
7	Phospholipid based CNT ⁵⁴	Gene delivery	Ability to effectively condense plasmid DNA.
8	MWNT-polycaprolactone composite scaffold ⁵⁵	Tissue engineering	MWNTs improved the mechanical property.
9	Chitosan-MWNT composite/hydroxy apatite nanocomposite ⁵⁶	Bone tissue engineering	Good mechanical strength was observed.
10	Polyurethane based scaffolds incorporated with MWNTs and zinc oxide nanoparticles ⁵⁷	Bone tissue engineering	Promote osteogenic differentiation of pre-osteoblast cells.

Table 3: Other applications of carbon nanotubes

CNTs, there are some limitations that push them back. However, many researches are being performed to overcome the current limitations and challenges faced with the CNTs for the betterment of futuristic demand.

Acknowledgement

The authors would like to thank the Management of Chettinad Academy of Research and Education, Kelambakkam for providing facilities to complete this work.

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