UDK 631:544.774

Use of Carbon Nanotubes in Medicine

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Key words: carbon nanotube, repairing, regenerative, scaffold, virus, lung cancer, tumor, drug delivery

The outstanding physical properties of carbon nanotubes (CNTs), e.g. their mechanical and chemical durability as well as thermal and electrical conductivity allow for the use of CNTs in many applications. CNTs were discovered about two decades ago [18]. They show a unique structure that can be envisioned as a graphene sheet rolled into tubular structure. CNTs can be either single-walled (i.e., SWCNT) or multi-walled (i.e., MWCNT) depending on the number of a concentric graphitic layers. The diameter is typically 1-10 nm for SWCNTs whereas it can be varied from 1 to over 100 nm for MWCNTs. The length of CNTs can also be varied in a broad range from several nm to over 1 mm. The aspect ratio (length vs. diameter) of CNTs can be larger than $\sim 10^6$. CNTs are one of the materials with the highest known mechanical strength. The intrinsic tensile strength and Young's modulus can reach 1 TPa. Depending on the rolling angle of a graphene sheet (i.e., chirality), CNTs can be either semiconducting or metallic [18]. In their metallic form, CNTs show a very high electrical conductivity with the capability of carrying electrical current over 50 times greater than typical metals. The electrical properties of CNTs are also potentially relevant to biomedical applications. MWCNTs are much less toxic than SWCNTs because of the differences in diameter and surface chemistry

Semiconductor sensors many promising for medical applications of exhaled by the organism gases are developed in Yerevan State University (Department of Physics of semiconductors and microelectronics and semiconductor research center and the nanotechnology) in Armenia. Acetone, ammonia, ethanol, hydrogen peroxide, nitrogen oxides nanosensors should be mentioned among them. Warfare chemical sensors were investigated in framework of the NATO grant. Independent testing of chemical warfare and smoke sensors in the USA and Czech Republic were shown promise of their use. In particular, large attention is given to sensors made from metal oxides doped carbon nanotubes [2-8], which have high sensitivity and other excellent characteristics.

Nowadays, exhaled breath is considered a diagnostic tool for disease and underlying health conditions [9, 10]. The large experience in YSU in the field of gas semiconductor detectors allows us to intensive work in this field. For example, we have now the first samples of diabetes detectors which measure the acetone level in an organism [11, 12]. So, CNTs an ideal candidate material for a new class of molecular sensors. Carbon nanotubes (CNTs) are widely used for the detection of various gases (including in the human body) and in dentistry, virology and cardiology.

One of the most active research fields in modern biomedical engineering and clinical practice is the repair and regeneration of hard tissues in the human body such as bone and teeth. Traditional materials that serve as scaffolds in clinical applications include naturally-derived collagen, chitosan, and different synthetic polymers. Of course, it is desirable for the scaffold to be biocompatible and able to control the proliferation and differentiation of cells into the required lineage and structure. The good mechanical strength, flexibility, and lightweight make CNTs ideal materials for use as reinforcement of engineered composites. Today CNTs are used in functional scaffolds for repairing and regenerative purposes [17].

Inorganic composite-based MWCNT hybrid membranes coated with copper(I) oxide, titanium(IV) oxide, and iron(III) oxide nanoparticles were investigated in the removal of viruses (bacteriophages) from contaminated water [25] and used as virus adsorbents.

Injectable polymer/CNT composites are being used today for enhancing cardiomyocyte proliferation and function [22], and cardiac differentiation of stem cells [23]. Electrically conductive CNTs can be used in composite scaffolds as synthetic cell culture platforms for enhanced differentiation of human mesenchymal stem cells (hMSCs). Through analysis of fiber morphology, elastic modulus and conductivity, it was established that scaffold properties are affected by the inclusion of CNTs and can be tailored for specific applications. CNTs-based scaffolds have been recently found to support the *in vitro* growth of cardiac cells: in particular, their ability to improve cardiomyocytes proliferation, maturation, and electrical behavior are making CNTs extremely attractive for the development and exploitation of interfaces able to impact cardiac cells physiology and function.

CNTs are used now as new nanocarriers for drug delivery. Researchers have recently applied CNTs to diagnose and treat cancers such as lung, breast, prostate, liver, colon, etc. [29]. Besides, quantum dots, gold, and magnetic nanoparticles were a series of nanomaterials that could be utilized to detect cancers [13]. The methods a chemotherapy, radiation therapy, and various medications are used for detection of different cancers (for example, lung cancer [30]). These methods were not highly effective due to the non-targeted and damaging of healthy tissues such as hair follicles. Based on these approaches, damage in the cell cycle, break in the double strands of DNA, inflammatory responses, tissue fibrosis, etc., will have occurred. On the other hand, there were a series of treatment obstacles; low stability, solid solubility in water, and cell resistance to treatment in the chemotherapy method.

Tumor-targeting has many difficulties even with using the specific antibodies to bind to cancer cells; pulmonary tumors are among the invincible types of cancer, on which the researchers work to solve this issue.

In fact, CNTs are made in five ways, which are described as arc discharge, laser ablation, chemical vapor deposition, flame synthesis, and silane solution methods. Also, CNTs are purified in three ways as air oxidation, sonication, and acid refluxing. On the other hand, the CNTs are a fascinating substance that can be employed to bind proteins, peptides, nucleic acids, and various drugs. Furthermore, CNTs have a high potential for drug delivery due to their tubular and fiber-like structure. The usable techniques to evaluate the CNTs and drugs with each other were collected as transmission electron microscopy (TEM), scanning electron microscopy (SEM), Raman spectroscopy, Fourier transforms infrared spectroscopy (FTIR), and X-ray diffraction (XRD), etc.

Consider below the pulmonary toxicity assessment of CNTs. CNTs could quickly enter the lungs through the respiratory tract and then rapidly enter and affect the nervous, lymphatic, and circulatory systems, leading to toxic effects. [19]. The main reasons of these toxic effects can be durability, the amount of residual oxygen reactive metal, and size. By removing the residual metals and selecting appropriate dimensions, the CNTs can be safe in drug transmission. The smaller sizes were with less toxicity; furthermore, the concentration of metal impurities such as iron did not contribute to toxicity [21]. Indeed, the greater the curvature, the less damage occurred to the cells. Due to the high structural similarity of CNTs with asbestos, which is usually used, similar physiological effects on the human bronchial epithelial cells are shown. In humans exposed to the CNTs, they could induce lung and pleural lesions, inflammation, pleural fibrosis, and lung tumors. The stiffness, hardness, length, width, and CNT longevity are five factors that could induce a harmful effect.

The too lowest dose of MWCNTs could induce pulmonary fibrosis. Also, MWCNTs, like asbestos, could alter the expression of several genes and cell survival and proliferation [17]. The CNT produced the least toxicity compare with asbestos [26]. On the other side, functional CNT showed less toxicity with higher activity toward CNT without functionalization. The safe applied dose of CNTs was not yet finally determined [32]. Also, researchers can reduce (rule) the toxic effects by choosing the appropriate dimensions (shorter length and higher width), more curved nanotubes, and using the functionalized form [24]. Moreover, the MWCNT was used more efficiently due to less toxicity toward SWCNT. On the other side, there were significant contrasts in using the nanotubes which induced tumor growth and tumor suppressor protein.

Using CNTs in lung cancer treatment is very promising. Generally, lung cancer's clinical manifestations include fatigue, coughing, wheezing, pain in the chest, the brevity of breath, swallowing hardness, anxiety, and yellow fingers.

Also, a lung cancer diagnosis is possible with helping 4 methods with the names of radiological, non-radiological imaging such as MRI, endoscopic, and biochemical methods [35]. In usual, diagnosis, type, and degree of lung cancer are performed by CT scan imaging. [31, 32]. But, unfortunately, too low-dose CT scans may bring false-positive answers about having lung cancer [16]. Today, the biomarkers of both protein and genetic modifications are known for lung cancer.

Numerous biosensors were studied to bind to these biomarkers for non-invasive detection [20]. The sensor array of CNTs has demonstrated a discrepancy between the healthy and the patient respiratory sample in the volatile organic components (VOC). Therefore, the detection of VOCs and tumor markers by breath analysis with helping CNT is a modern and studied method. [9, 10, 35]. The sensors identify different biomarkers due to the solubility, polarity, and chemical associations, especially for tuberculosis disease [27]. The design of an electronic nose with CNTs to delete the VOC of lung cancer patients was an inexpensive and rapid method. Water, methanol, isopropanol, ethanol, acetone, 2-butanone, and propanol were found as polar vapors lung cancer biomarkers. The CNTs, doped with platinum, can detect styrene and benzene vapors that existed in the exhale of lung cancer patients. This sensitivity was very low in natural nanotubes.

SWCNTs decorated with Pd, Pt, Ru, or Rh elements could also be used to detect toluene gas as an indicator of lung cancer. A research, conducted in [1], stated that a biosensor created by CNT covered with Rh catalyzer can distinguish and absorb C_6H_7N, and C_6H_6 in the exhaled air of lung cancer patients [34]. Another scheme used to enhance lung cancer detection was preparing a combination of SWCNT and chitosan [14]. Due to the differences in nicotinic acetylcholine receptors in normal and small cells of lung cancer, the nanotube-based electrode sensor for the quantitative electrophysiological monitoring of a no adherent cell has been demonstrated [33].

Conclusion

CNTs could quickly enter the lungs or other tumors through the respiratory tract and then rapidly enter and affect the nervous, lymphatic, and circulatory systems. CNTs have a high potential for drug delivery due to their tubular and fiber-like structure. The CNTs can be safe in drug transmission. The treatment with CNT was much more effective and more successful than the traditional treatments for this cancer. The smaller sizes were with less toxicity; furthermore, the concentration of metal impurities such as iron did not contribute to toxicity. Using the functionalization, nanotubes with a longer length, more width, and greater curvature partially can be done with lower toxicity. MWCNTs functionalized with chitosan had less toxicity for healthy cells and more anti-tumor effect were confirmed.

So. carbon nanotubes (CNTs) are used now for effective drug delivery and toxicities of tumor cells without the damage of healthy ones. The collection of studies summarized in [29, 30] includes the dose of CNTs, duration, method of induction, etc., to achieve the most controlled conditions for human studies.

Accepted 03.03.21

Использование углеродных нанотрубок в медицине

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Углеродные нанотрубки (УНТ) широко используются для детектирования различных газов (в том числе в организме человек) в стоматологии, вирусологии и кардиологии. УНТ могут быстро попасть через дыхательные пути в легкие или опухоли, а затем быстро проникнуть и воздействовать на нервную, лимфатическую и кровеносную системы. УНТ обладают высоким потенциалом доставки лекарств из-за их трубчатой и волокнистой структуры. Лечение УНТ намного более эффективнее и успешнее, чем традиционные методы лечения рака легких. Меньшие размеры имели меньшую токсичность; кроме того, концентрация металлических примесей, таких как железо, не влияет на токсичность. Используя функционализацию, нанотрубки с большей длиной, большей шириной и большей кривизной частично могут быть получены с меньшей токсичностью. Многостеночные УНТ, функционализированные хитозаном, обладали меньшей токсичностью для здоровых клеток, был подтвержден больший противоопухолевый эффект. Углеродные нанотрубки теперь используются для эффективной доставки лекарств и с меньшей токсичностью в опухолевые клетки без повреждения здоровых клеток.

Ածխածնային նանոխողովակների օգտագործումը բժշկության մեջ

Վ.Մ.Հարությունյան

Ածխածնային նանոխողովակները (ԱՆԽ) լայնորեն օգտագործվում են ատամնաբուժության, վիրուսաբանության և սրտաբանության մեջ տարբեր գազերի (այդ թվում ՝ մարդու մարմնում) հայտնաբերման համար: Ածխածնային նանոխողովակները (ԱՆԽ) շնչառական տրակտի միջոցով կարող են արագ մուտք գործել թոքեր կամ այլ ուռուցքներ, այնուհետև արագ թափանցել և ազդել նյարդային, ավշային և շրջանառու համակարգերի վրա: ԱՆԽ-ներն ունեն գլանային և թելքավոր կառուցվածքի բարձր թմրանյութերի մատակարարման ներուժ: ԱՆԽ-ները կարող են անվտանգ լինել դեղեր տեղափոխելիս: ԱՆԽ–ներով բուժումը շատ ավելի արդյունավետ և հաջող է անցնում, քան այս

քաղցկեղի ավանդական բուժումն է: Ավելի փոքր չափերն ավելի քիչ թունավորություն ունեին: Բացի այդ, երկաթի նման մետաղական խառնուրդների կոնցենտրացիան չի ազդում թունավորության վրա: Ֆունկցիոնալացման միջոցով ավելի մեծ երկարությամբ, ավելի լայնությամբ և ավելի մեծ կորությամբ նանոխողովակներ մասամբ կարելի է ձեռք բերել ավելի քիչ թունավորությամբ: Խիտոսանով ֆունկցիոնալացված բազմապատային ԱՆԽ-ներն ավելի քիչ թունավորություն ունեին առողջ բջիջների համար, և հաստատվեց ավելի մեծ հակաուռուցքային էֆեկտ: Այնպես որ ԱՆԽ-ներն այժմ արդյունավետ օգտագործվում են դեղորայքի առաքման ուռուցքային բջիջների համար՝ առանց թունավորության և առողջությանը վնասելու:

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