REVIEW

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Carbon nanotubes for cancer therapy and neurodegenerative diseases

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Abstract

Our review summarizes the latest approaches regarding a new class of nanomaterials – carbon nanotubes (CNTs) –, which are promising candidates in different areas of nanomedicine. This paper discusses the main applications of CNTs in the repair of injured nerves and also as delivery systems for cancer therapy in difficult to reach anatomic sites. In terms of neurological applications, we focus on neural interface, neural stimulation, microelectrodes, and differentiation of stem cell into neural cells. Also, we highlight the *in vitro* and *in vivo* applications of CNTs-mediated cancer therapy and we will explain why CNTs are used for the treatment of difficult tumors.

Keywords: carbon nanotubes, biomedical application, neuroregeneration, cancer therapy.

Introduction

Carbon nanotubes (CNTs) were first discovered in 1990 by Iijima [1] using arc-discharge evaporation method and the obtained structures were called multi-walled carbon nanotubes. After two years, Iijima & Ichihashi [2] and Bethune *et al.* [3] obtained single-walls carbon nanotubes by the same route of producing multi-walled CNTs, but adding some metal particles to the carbon electrodes. The 1D structure of CNTs is made of graphene sheets organized in cylindrical shapes to form a tube. Depending on the number of the layers, CNTs can be single-walled nanotubes (SWCNT) consisting of a single graphene sheet rolled up into a tubular structure or multi-walled CNTs (MWCNT) that consists of two or multiple concentric sheets.

Because of their unique electrical, thermal, optical, and mechanical properties as well as their biological (such as surface specificity) properties, CNTs are currently studied in many research and applicative areas, such as field emission [4–6], sensors [7, 8], energy storage [9–11] and nanomedicine. On the biomedical field, CNTs are widely used in the development of biosensors with different sensitivity for the detection of several biological molecules, such as DNA [12], proteins [13, 14] different eukaryotic cells, microorganisms [15, 16], but also in drug delivery [17, 18], cancer therapy [19, 20], and in the development of functional scaffolds and neural prosthesis [21, 22].

In recent years, nerve regeneration and functional recovery represent a major issue in the therapeutic field of injured neurons. Until recently autografts, allografts and xenografts were used for nerve regeneration, but they present numerous disadvantages such as low availability and high rates of immunological rejection. Therefore, the development of artificial nerve prosthesis represents a recent interest field for biomedical applications [23]. Some specific properties such as feasibility, mechanical, electrical and conduction properties, as well as their nano-structured morphology CNTs are proposed as promising candidates for the fabrication of neural scaffolds.

CNTs also offer many possibilities for the development of the next generation of efficient therapeutic agents utilized for cancer therapy. Their features, especially the high surface area to volume ratio and unusual form, which allows the incorporation of specific amounts of chemotherapeutic drugs and the ability to cross the cell membranes, recommend CNTs as appropriate shuttles for the therapy of difficult to treat cancer.

This review highlights and discusses in the first section the current information about the use of CNTs in neurology and treatment of severe neurodegenerative disorders. Then, in the second section, we will focus on the advantages of CNTs nanosystems for cancer therapy.

Application of carbon nanotubes in neurology

Currently, neurological diseases affect a large percentage of the world's population. Due to their properties such as excellent mechanical, electrical conductive capacity, conduction properties and their nanostructure and dimension, which are similar to neurites, ion channels and elements of the neuronal cytoskeleton, CNTs are proposed as promising candidates for neurological applications. Currently, the neurological applications of CNTs include electrical interfaces for neuronal simulation and recording, platforms to promote neuronal survival, differentiation, growth and performance. CNTs have the ability to promote neurite extension and the development of neuronal electrical features [23].

Neuronal differentiation

Several authors have studied the influence of CNTs on stem cells differentiation, such as human embryonic stem cells that have a great potential to be used on the fields of regenerative medicine such as cell replacement therapy, tissue or organ transplantation. Thanks to the

pluripotent nature of these cells [24–26] they can easily differentiate into neuronal cells, and this property recommend mesenchymal stem cells (MSCs) as promising candidates for central nervous systems repair. Additional properties to support this idea are: (*i*) the rapid development and expansion *in vitro* [27], (*ii*) the ability to respond to nerve growth factors by changing the phenotype and (*iii*) the ability to acquire a number of properties characteristic to sympathetic neurons [28].

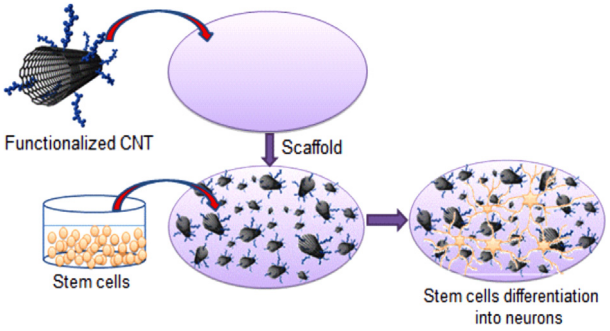

Figure 1 – ***Schematic representation of stem cell differentiation into neurons.***

The first *in vitro* study that indicates the neuronal growth was published by Mattson *et al.* [29]. They demonstrated the ability of MWCNT to support long-term neuronal survival of cultured embryonic rat hippocampal neurons and to provide a permissive substrate for neurite outgrowth. Studies demonstrated also the influence of functionalized CNTs on the modulation of neuronal behavior. The functionalization of MWCNTs with 4-hydroxynonenal has improved the construction of elaborated neurite arborisation by increasing the length and branching distance.

Jin *et al.* [23] evaluated the influences of PLCL (poly L-lactic acid-co-caprolactone) nanofibrous scaffolds coated with MWCNTs on neuronal growth *in vitro* on rat dorsal root ganglia neurons (DRG). They investigated the effect of coated MWCNTs on the expression of FAK (focal adhesive kinase), which is a protein that plays an important role in neurite extension and elongation. After nine days of incubation, it was found that the neurites developed on the CNT-coated PLCL were significantly longer. Their results also revealed that CNT-coated PLCL induce a stronger signal, which means that FAK expression is significantly improved.

Chen & Hsiue [30] investigated the neural differentiation of human bone marrow mesenchymal stem cells after their development on carboxylated MWCNT films deposited onto a collagen coated polystyrene. It has been shown that the proliferation rate of the cells grown on this substrate was slower than of the control group, maybe due the non-arranged structure of CNTS on the scaffold. Also, it has been demonstrated that carboxylated MWCNTs promote the expression of several neural-associated genes while bone associated genes are inhibited when the cells were cultured on this substrate. Due to their properties to promote protein adsorption on the surface, CNTs can promote the adsorption of upregulated neural growth factors to provide an appropriate environment for long-term neural differentiation.

Studies made on the growth and differentiation of human SH-SY5Y cells using functionalized MWCNTs dispersed in a poly-L-lactic acid (PLLA) matrix also revealed a better cell development and differentiation on modified CNTs [31]. The MWCNTs were functionalized with diazonium salt of 4-methoxyaniline. The results demonstrated that CNT–PLLA scaffolds support cell adhesion and differentiation better than PLLA alone. Synthetic peptides L1 and LINGO1 were further developed to mimic the neural environment and studies revealed that these molecules improve neuronal differentiation and can be efficiently used for the functionalization of neural regeneration scaffolds. When the scaffold and the peptides were put together, it was found that the cell proliferation and viability are not altered; moreover, the length of neurite is significantly improved in the case of this system. These data lead to the idea that these scaffolding systems can be applied for supporting neuronal cell growth and differentiation.

Lee *et al.* [32] showed the influences of MWCNTs dispersed in a 3D collagen hydrogels matrix on the differentiation of mesenchymal stem cells in neuronal cells. MWCNTs were first functionalized with carboxyl groups and then with ethylenediamine in the presence of 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide. The collagen solution and CNTs were homogenized to make the composite hydrogel and the MSCs were added in this system in gelation stage. It have been show that cell proliferation rate was improved proportionally with the concentration of CNTs up to 1 wt%, but a high concentration (2 wt%) proved an opposite effect, by fast decreasing cell proliferative potential, maybe because CNTs can incorporate in the water-filled channels loosely bound to the collagen fibers. Also, same authors demonstrated that this composite is effective for the expression of significant levels of neural phenotypes because after investigating the level of bIII tubulin and GAP43 (antibodies specific for neural cells) they found that expression of GAP43 was also significantly upregulated during culture in CNT-collagen hydrogels, that means a neural differentiation of MSC cells [32].

Recording neural activity by using carbon microelectrodes

Microelectrodes developed for neural recording and simulation currently represent valuable research tools to describe the biophysical aspects of the central nervous system and also to treat certain neural disorders. In recent years, among possible materials considered for the manufacture of electrodes are mentioned: platinum [33–35], gold [36, 37], glassy carbon [38, 39], TiN [40, 41] and iridium oxide [42, 43]. Although they are characterized by good impedance characteristics, the main disadvantage is the lack of long-term stability. New nanomaterials, such as carbon nanotubes can improve this problem.

Yen *et al.* [44] evaluated the success of amino-functionalized MWCNTs to promote the neuronal cell growth on the surface of the electrode for extracellular recording. To form the carboxylic groups for subsequent functionalization with 1,4-diaminobutane (0.2 wt%, 1 wt%, 2 wt%, and 3 wt%) MWCNTs were treated with H_2O plasma. Using the X-ray photoelectron apectroscopy (XPS) method, they proved that the highest quantities of amino-groups occur to the sample functionalized with 2% 1,4-

diaminobutane. A good recording electrode for nerve tissue must have low impedance, around the frequency for neural activity, which is about 1 kHz. Compared with other samples, the one functionalized with 2 wt% revealed the lowest value of the impedance which is 0.19 kΩ/mm^2. The interfacial impedance per unit area measured by EIS (electrochemical impedance spectroscopy) for all samples indicate an increase value of 14.1 F/mm^2 (corresponding to the sample treated with 0.2 wt%) to 22 F/mm^2 (corresponding to the sample treated with 2 wt%). These results indicate that amino-functionalized MWCNTs with 2 wt% can provide better sensitivity and facilitate their application for neural recording. The biocompatibility test of neural electrode for neuronal and glial cells indicate that these cells can adhere well on the surface of 2 wt% amino-functionalized MWCNTs without the need of PLL coating due to their positive charge induced by amine groups which facilitate the adhesion and growth of neuronal cells.

Zhou *et al.* [45] studied methods of stability improvement of microelectrodes by coating a platinum microelectrode with a composite film formed by MWCNTs doped with poly(3,4-ethylenedioxythiophene) (PEDOT). Composite film was electrodeposited onto platinum microelectrodes in galvanic and potentiostatic mode. In terms of morphology, it was observed that the film deposition mode had a significant effect on the thickness of the film. Films deposited by potentiostatic mode showed a trend of transverse growth and the diameter of the film reached 215±4 μm. In contrast, the film deposited by galvanostatic mode showed a trend of longitudinal growth and the diameter of the film was 80±3 μm, and it revealed a 3D cone morphology, which may shorten the distance between the neuron and the electrode. They studied also the electrochemical impedance for the two samples in comparison with platinum microelectrode at 1 kHz and found that a decreased from 51±3 to 3.3±0.2 mC/cm^2 for PEDOT/MWCNTs deposited by potentiostatic mode and 2.2± 0.1 mC/cm^2 for PEDOT/MWCNTs deposited by galvanostatic mode. The results showed PEDOT/MWCNTs deposited by galvanostatic mode presented the highest charge injection – Q_{inj} limit due to their porous microstructure and lower diffusion impedance. It has also been showed that these microelectrodes are biocompatible with PC12 cells, as well as the of PEDOT/MWCNT coatings.

Carretero *et al.* [46] investigated the influences of nanostructutred iridium oxide (IrOx)-SWCNTs on increasing charge capacity in neural system. IrOx–CNT films were synthesized in the form of coatings by dynamic electrodeposition. It was demonstrated that CNTs are present in the oxide structure. CV curves have a semi-rectangular shape characteristic of capacitive behavior, but the charge is substantially faradaic, involving the reversible Ir^{3+}/Ir^{4+} couple. Biocompatibility was tested on cortical neurons obtained from mice and the results showed a full compatibility of the IrOx–CNT substrate for the growing and differentiation of neuronal cells.

CNTs for neural interface

Due to specific CNTs properties such as electrical conductivity, nanotopographical and biochemical features, it has been concluded that these nanosystems can mediate neural modulation. Results suggested that CNTs may have synergistic effects on peripheral nerve regeneration when interfaced with an intraluminar structured scaffold. Current research on the field is mostly based on *in vitro* studies, few *in vivo* data to prove the functions of CNTs interfaces biomaterials in nerve damage models being available [47].

Han *et al.* [26] demonstrated *in vivo* functions of amino-functionalized carbon nanotubes onto the surface of aligned phosphate glass microfiber scaffolds in the regeneration of transected rat sciatic nerve, followed by wrapping onto a poly(L/D-lactic acid) (PLDLA) monofiber, then embedding within a three-dimensional porous PLDLA tube. The biocompatibility of this scaffold was measured on PC12 cells and the results show an excellent cellular viability. Next, researchers investigated neurite outgrowth behavior of DRG primary neurons on the CNT-phosphate glass microfibers (PGFs) and on the PGFs. It was demonstrated that neurites extended directionally on the microfiber substrates and this extension was much higher on the CNT-PGFs than on the plain PGFs, but the branch numbers per DRG did not differ significantly between the two samples. Also, the number of attached DRG at three days was greater on the CNT–PGFs than on the PGFs. *In vivo* implantation into transected stumps to fill a 10 mm gap after complete transection of the sciatic nerve of a rat demonstrated that SMI312 positive axons are able to cross the implantable scaffold and the number of S100-positive Schwann cells along the axons was significantly increased when CNT–PGFs was used.

CNTs for neural stimulation

Chronic neural stimulation of electrically responsive tissue such as brain, heart and skeletal muscle, is utilized in neural prostheses to modify, restore or bypass a vagal nerve, retinal and cochlear implants, spinal cord and deep brain by sensing or delivering electrical pulses by neural electrodes. Currently, the most used neural electrodes are made from gold, platinum, iridium, titanium and stainless steel.

Luo *et al.* [48] evaluated the properties for chronic stimulation of poly (3,4-ethylenedioxythiophene) (PEDOT) doped with MWCNTs electrochemically deposited on Pt microelectrodes. After stimulation, it can be seen that the bare Pt electrode exhibited a higher voltage than the PEDOT/MWCNTs coated electrode and the average charge injection limit was 2.5±0.1 mC/cm^2.

Researchers demonstrated also the stability of this electrode during prolonged and aggressive electrical stimulations. After cell seeding on the PEDOT/CNTs substrate it was shown that neural networks were well established, which indicate a healthy neuronal growth on this substrate.

Kolarcik *et al.* [49] obtained a functional coating by using conductive polymer poly(3,4-ethylenedioxythiophene) (PEDOT) and MWCNTs on the electrode surface and doped the system with dexamethasone. Authors used a dual microelectrode (platinum/iridium) and obtained two samples – the first consisting of simple coating of microelectrode with PEDOT/CNT and the second consisting of coatings based on PEDOT/CNTs/dexamethasone. Both samples indicated significantly lower impedance

in vitro across all frequencies. *In vivo*, the electrode performance tests revealed that without stimulation, there were no significant differences in impedance between the samples; with stimulation the impedance of PEDOT/CNT-coated was 65.3±6.8 kΩ and for PEDOT/CNT/dexamethasone-coated was 58.4±7.3 kΩ (significantly lower than the impedance for non-coated electrode (86.5±6.9 kΩ). This decrease in impedance can be attributed to the release of dexamethasone, which could reduce tissue inflammation and hence influence the impedance value. Measurement of inflammatory response was also reduced for PEDOT/CNT-coated electrodes in comparison to uncoated electrodes. Using these electrodes, it can be observed a significantly reduced neuronal damage or death compared with uncoated electrodes.

David-Pur *et al.* [50] developed a flexible electrode for neural stimulation made exclusively from CNTs. The impedance value measured for CNT electrode was 55 kΩ. It has been show that a performance of this product is similar to that of the rigid CNT electrodes, except that it is flexible. Embryonic chick retina derived cells were used to test extracellular neuronal stimulation with this electrode. Stimulation was made using a low electrical field (4 μA), the electrical response being typical for pre-synaptic cells activation. DC capacitance values of the all CNT range with two flexible MEA (micro-electrode-array) presented in this study is well within this $mFcm^{-2}$. Researchers demonstrated also that CNT can be used both *in vivo* and *in vitro* long-term experimentation without delamination of the coatings and the formation of material cracks.

Application of carbon nanotubes in cancer therapy

Carbon nanotubes represent an outstanding choice for anti-cancer therapy due to their advantages over the classical treatment, including high capacity to encapsulate drugs, possess cell membrane penetrability, and have enhanced cellular uptake.

Over the time, a large number of carbon nanotubes-based systems have been designed in order to reduce the drug toxicity and improve the efficiency of the encapsulated drug.

Although carbon nanotubes represent an effective alternative to the use of chemotherapy, pristine CNTs shows low dispersion in aqueous media and high tendency of agglomeration. These problems can be resolved by surface functionalization by non-covalent or covalent strategies [51].

The efficacy of functionalized carbon nanotubes in cancer therapy has been demonstrated over the time by numerous studies by using cancer models such as mice [51], human breast cells [52] and cancer cells grown in fetal bovine serum [53].

Kim *et al.* [52] studied the viability patterns of breast cancer cells in the presence of carbon nanotubes-taxol-embedded polycaprolactone microspheres. The treatment of MCF-7 human breast cancer cells with various taxol-loaded microspheres for three days led to a typical dose-dependent inhibitory effect on cell viability. Also, the *in vitro* tests showed that the encapsulated taxol was continuously released over a 60-day period.

Carbon nanotubes carboxylated and chemical functionalized with 2-hydroxyethylmethacryate (HEMA) and N-vinylpyrrolidone (NVP) used by Abbaszadeh *et al.* [53] revealed a destruction of cancer cells higher than 70% and a damage over normal cells of about 20%.

Doxorubicin (DOX) functionalized SWCNTs were used for targeted therapy of SMMC-7721 liver cancer *in vitro* and *in vivo* by Meng *et al.* [54] and Ji *et al.* [51]. Both studies [51, 54] used chitosan functionalized CNTs to deliver DOX to targeted cells. Authors tried to establish if SWCNTs are safe for drug delivery [51] and showed that even apparent toxicity of CNTs has caused significant concerns in the past decade, the presented data are often inconsistent and conflicting. The therapeutic efficiency of SWCNTs–DOX complexes were firstly tested on a SMMC-7721 cell line and after that, *in vivo* on a mouse model. The results indicated that DOX–SWCNTs complexes have a lower cytotoxic effect than free doxorubicin and they are also more efficient. It was demonstrated the tested complexes exhibited superior pharmaceutical efficiency even when they are used in lower doses.

Authors demonstrated that time and dosage significantly influences the efficiency of the system. The *in vivo* tests revealed that the growth rate of tumors decreased at about 72 hours after the injections [51].

Zhou *et al.* [55] investigated the antitumor effects of immunologically modified glycated chitosan (GC)–SWCNT system and demonstrated that the system retained the optical properties of SWCNTs and the immunological properties of GC. The introduction of this system in mice by intratumoral injection has not led to tumor regression, but prolonged the medium survival time of the mice tested. When the system was irradiated by a near-infrared laser, thermal destruction of the tumor cells was induced.

Amine-functionalized SWCNTs polymerized with polyethylenimine (PEI) [56] proved to cross cell membrane and induced cancer cells apoptosis and suppression *in vitro*. Also, they exhibit higher tumor cell growth inhibition without affecting the main organs *in vivo*. The statistical results indicated the using SWCNTs modified with PEI the tumor size is reduced, mainly by cell necrosis, cell lysis and cell fragmentation. Although SWCNT–PEI could induce cell apoptosis, without laser irradiation, apoptotic cell count is lower [56].

It is well known that single-walled carbon nanotubes can be used in combination with near-infrared (NIR) irradiation for the removal of tumor cells. Considering this statement, a targeting system based on SWCNTs and peptide was used by Hashida *et al.* [57] against tumor cells. They evaluated the lethal effect of this system on colon and HepG2 cells and on subcutaneously implanted colon 26 tumor. Both *in vitro* and *in vivo* results showed an induced heat generation and significant damage to cultured colon 26 and HepG2 cells and a significant inhibition of colon 26 growth but not a complete eradication of the tumors.

SWCNTs can be used on colorectal cancer cells. Thus, Lee *et al.* [58] developed a system of PEGylated SWCNTs conjugated with Py38 and functionalized with C225 in order to transport anticancer agents into colon cancer cells. In order to understand the mechanism of carbon nanotubes internalization and drug release behavior

in cell lines, they marked the systems with fluorescent agents (red and green fluorescence) and then observed them under a confocal microscope. Images of confocal microscopy reveled that carbon nanotubes were firstly internalized into the cancer cells and after 24 hours the entire cell was occupied by SWCNT system. After the internalization and drug release, it has been demonstrated that this system exhibit significant toxicity to human colon carcinoma.

Shao *et al.* [59] examined the cell penetration capacity of SWCNTs drug delivery systems to target tumor cells, reduce non-specific toxicity and enhance drug efficacy. They conjugated SWCNTs with tumor-targeting ligands in order to enhance the internalization. *In vitro* tests, using MCF-7 cells, demonstrated that folic acid-conjugated SWCNT showed target specificity and determines a rate of transfection of about 95±3%. *In vivo* assays revealed that after the intravenous injection of SWCNT-lipid-Paclitaxel in female athymic mice inoculated with MCF-7 tumor cells led to tumor regression and inhibition in the human breast tumor xenograft mouse model.

Mohammadi *et al.* [60] delivered siRNA into breast cancer cells using single-walled carbon nanotubes conjugated with piperazine–PEI derivative. They discovered that the carbon nanotube-based system specifically induce apoptosis in more than 20% cancer cells and increase DNA transfection. Additionally, the researchers explained that the enhancement in the DNA transfection level is due to the covalent conjugation of PEI to SWCNTs. Because of their nano-needle structure, they have the ability to translocate directly into cytoplasm of target cells.

Breast cancer cells have been also used by Ogbodu *et al.* [61] to demonstrate for the first time the photodynamic efficiency of zinc phthalocyanine-spermine-single walled carbon nanotube conjugate. Compared with the complex without spermine, which resulted in only 64% decrease in cell viability, the presence of spermine improved the photodynamic therapy effect, with a 97% decrease in cell viability. Moreover, it was demonstrated that the cell viability decreases in an irradiation time and concentration dependent manner.

On the other hand, the *in vitro* cytotoxicity tests on MCF-7 cancer cells showed that the tested complexes were not toxic in the absence of light. In addition, the main subject of another research [62] was monoamino-phthalocyanine–folic acid conjugate adsorbed on single walled carbon nanotubes. Authors of this study investigated the photodynamic effect on melanoma cells and discovered that SWCNTs–folic acid complex had no significant photothermal effect on the cells. The percentage of cell death observed after irradiation was only 23%.

More that cancer therapy, modified carbon nanotubes can be used as a hemostatic dressing with delayed oncostatic action. Nowacki *et al.* [63] used carbon nanotubes for local tumor recurrence prevention after organ sparing surgery. They doped SWCNTs with cisplatin and tested the system on mice with induced renal cancer using adenocarcinoma 786-O cells. These studies demonstrated that SWCNTs filled with cisplatin inhibit cancer recurrence in animal models and can be successfully applied as hemostatic dressings for local tumor prevention.

Carboxylated-MWCNTs seems to be an optimal choice for the development of drug delivery systems for targeted delivery of drugs on cancer cells, without damaging normal cells or with minimal damage. To sustain this affirmation, Cao *et al.* [64] used MWCNTs modified with hyaluronic acid for the targeted delivery of doxorubicin to HeLa and L929 cells. In this case, the release of doxorubicin and efficiency of the DDS (drug delivery system) was pH-dependent because of the interaction between DOX and MWCNTs, with a faster release rate under acidic conditions.

Also, carboxylated-MWCNTs conjugated with an anti-HER2 antibody [65] were used to investigate the utility of the system in photothermal therapy of breast cancer and it was discovered that breast cancer cells destruction was influenced by the concentration of functionalized MWCNTs, the incubation of cells with 20, respectively 40 ppm leading to 65% and 79% breast cancer cells destruction.

In order to understand the interaction between carboxylated carbon nanotubes and anticancer agents, carboxylated multi-walled carbon nanotubes were loaded with epirubicin hydrochloride (EPI) [66]. The results indicated that the adsorption of EPI on c-MWCNTs was reversible, with a pH-sensitive release behavior.

Multi-walled carbon nanotubes functionalized with mitochondrial-targeting fluorescent rhodamine-110 (MW CNT-Rho) were also used in cancer therapy. Yoong *et al.* [67] demonstrated that the functionalization with a mitochondrial lipophilic cation lead to a mitochondrial MWCNTs-based targeting drug system.

Even if the most studies have been carried out on breast or liver cancer, Rieger *et al.* [20] investigated the potential of carbon nanotubes in bladder cancer treatment. They showed for the first time that multi-walled carbon nanotubes are able to adhere to the urothelium of mouse bladders, without influencing the mucoadhesive properties of the tissue.

To study the effect of carbon nanotubes on gastric cancer cells, Tahermansouri & Ghobadinejad [68] used carboxylated multi-walled carbon nanotubes functionalized with creatinine and aromatic aldehydes. The complexes were tested on both gastric and breast cancer cells and the results indicated that modified MWCNTs have higher toxicity toward gastric cancer cells (about 75%) compared to breast cells (about 51%).

To investigate the effects of carbon nanotubes on the biodistribution of certain compounds, especially platinum-based antitumor drugs (cisplatin, carboplatin and oxaliplatin), which currently are used as first-line chemotherapy for non-small-cell lung cancer and other numerous solid malignancies, Li *et al.* [69] entrapped inside functionalized-multi-walled-CNTs, cisplatin or an inert platinum (IV) complex and intravenously injected the mixture into mice. Their results showed that functionalized MWCNTs enhance the platinum content in almost all tissues without any additional inflammatory reaction or necrosis.

Conclusions and future outlook

Based on these studies, the exceptional nature and the high potential of CNTs in neuroscience are highlighted.

Bioengineering occupy an important position in the design and development of materials with a structure close to that of neural tissue so the cells can adhere, proliferate and grow. Since most methods for obtaining CNTs reported to date rely on metal catalysts and chemical functionalization is essential to improve the biocompatibility and to mitigate the cytotoxicity. Due to the influence of nanotubes on cells viability and cell growth, they can be used as scaffolds in combination with other biomaterials such as biodegradable polymers to guide neural stimulation and regeneration, and default to improve neural activities. Besides that, the advantages offered by CNTs in cancer therapies remain indisputable. However, the full-realization of this great potential still depends on production of biocompatible materials with well-designed efficacy. The progression of current studies indicates that, in the near future, it will be possible to develop CNTs with controlled and optimal *in vivo* characteristics, applicable for human treatment.

Conflict of interests

The authors declare that they have no conflict of interests.

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