THINK INDIA Journal

ISSN:0971-1260
Vol-22-Issue-16-August-2019

Carbon-Based Nanotheranostics

Pallavi Nayak[1], Manvendra Singh[1], Vijay Mishra[1]*

[1]School of Pharmaceutical Sciences, Lovely Professional University, Phagwara (Punjab), India- 144411

***Corresponding author**

Dr. Vijay Mishra

School of Pharmaceutical Sciences,

Lovely Professional University, Phagwara, (Punjab), India

Email: vijaymishra2@gmail.com

Abstract

Carbon-based nanomaterials comprise nanotubes of carbon, nanodiamonds, graphenes and their derivatives, carbon dots, and fullerenes. Because of their extraordinary chemical, thermal, electric, optical, mechanical characteristics and special structural dimensions, these materials gained attention in different areas, including the biomedical field. Recently, the attention has been on cell and tissue imaging and the availability of therapeutic drugs for cancer diagnosis and the reconstruction of tissues. The wide-range one-photon property, ease functionalization and biocompatibility of carbon-based nanomaterials have allowed them eligible imaging agents for tumor diagnosis. This study reflects on the recent discovery of different imaging techniques of carbon-based nanomaterials and explores potential and effective therapeutic and clinical methods to treat various diseases, including cancer.

Keywords: Carbon-based nanomaterials, Carbon nanotubes, Functionalization, Graphene quantum dots

1. Introduction

On a regular basis, carbon-based nanomaterials (CBNs) become attractive nanomaterials in science and technology [1-3]. Because of the presence of numerous carbon allotropes, beginning with very well-known allotropic forms like diamond, graphite, amorphous carbon, to newly discovered propitious fullerene, graphene quantum dots (GQDs), graphene oxide (GO), and carbon nanotubes (CNTs), the CBNs have recently been considered worthy of treasure. Each carbon family member has some irrepressible characteristics and has been extensively utilized in various biomedical applications along with the delivery of a drug, imaging, biosensing, cancer therapy, tissue engineering, and diagnosis. CBN's specific optical characteristics, i.e. strong photostability, tunable narrow range of emissions and intrinsic

ISSN:0971-1260
Vol-22-Issue-16-August-2019

fluorescence, enable their possible use within cell and tissue imaging and diagnosis. By altering the surface with functional groups like epoxy, carboxyl acid and hydroxyl can optimize its properties. Furthermore, altering their surfaces with the above functional group helps their properties to be controlled [4].

2. Carbon-based nanomaterials

Carbon-based nanomaterials (CBNs) have in the past few decades shown enormous effect in the field of biomedical science with their abilities to supply therapeutic molecules and analyze cells and tissues required to cure and treat diseased and toxic tissues (Fig.1).

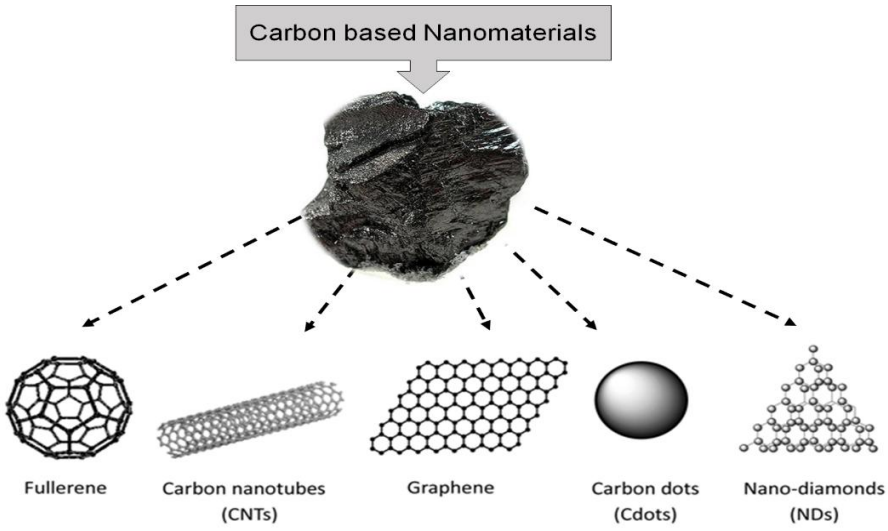

Fig.1. Different carbon-based nanomaterials

2.1 Carbon nanotubes

Nanotubes of carbon are typically fabricated by arc discharge or graphite chemical vapours [5-7]. These are cylindrical structured and have a broad range of optical and electrical and optical characteristics, both because of the sp^2 carbon and also for their tunable physical properties. Based on cylindrical graphene sheets CNTs are categorized as single-wall carbon nanotubes (SWCNTs) and multi-wall carbon nanotubes (MWCNTs). The size range of SWCNTs and MWCNTs vary between 0.4 and 2.5 nm. The multi-layered CNTs provide various physical phénomènes and functionalities with a combination of 2D crystal and different optical, mechanical and electrical properties, which is associated with van der Waal forces [8].

2.2 Carbon dots

The C-dots of less than 10 nm in diameter are discrete spherical particles. The composition of the sp^2 hybridized is a mixture of oxygen in the form of many members of the oxygen, for example, carboxyl (-COOH), aldehyde (-CHO) and hydroxyl (-OH). Therefore, C-dots reflect

ISSN:0971-1260
Vol-22-Issue-16-August-2019

well-organized, broad-aspect carbon atoms, with strong chemical and thermal stabilities, large surfaces and improved drug-carrying capacity in contrast to large particles, such as quantum dots [9,10]. The distribution of anticancer drugs can also be provided by C-dots. Traditional chemotherapy can suppress and remove tumours, but can adversely affect healthy tissue. The use of nontoxic C dots via targeted drug delivery can be resolved. As an alternative to Q-dots, C-dots have low cytotoxicity and good photostability, which is widely utilized for diagnostics.

2.3 Graphene

Graphene is a 2-layer sp^2-bonded 2-dimension carbon surface with several excellent chemical and physical characteristics. Graphene has been studied broadly in many diverse areas since its discovery in 2004. Different graphene-based biosensors were manufactured to detect highly sensitive biomolecules by using the interesting optical, chemical, and electrical properties of graphene [11-13]. The poly-aromatic surface structure of graphene has an ultra-high surface area that can be charged easily using the *p-p* stacking of aromatic drug molecules for pharmaceutical drug delivery applications.

2.4 Fullerenes

Fullerenes, also known as Buckyballs or Buckminsterfullerenes, are allotropes of the nanomaterial's carbon group [14,15]. Fullerenes have a structure of sp^2 carbons with special chemical and physical properties and a highly symmetrical cage of various sizes (C_{60}, C_{76}, etc). The synthesized composition contains C_{60} as the most abundant fullerene. An extensive study was performed on the fullerenes with carbon nanotubes and a broader area of science and technology of nanoscale materials has been created since the development of graphene in 2004. While fullerenes and carbon nanotubes have an indistinguishable diameter range, the materials are still intended to demonstrate a variety of sizes and structures. Fullerenes and carbon nanotubes are commonly known to be zero- and one-dimensional materials; these have different implications for structures and properties.

2.5 Nanodiamond

The field of biomedical engineering was also attracted by nanodiamond in the past years [17]. Nanodiamonds are most frequently detonated and synthesize by high-energy graphite treatment and are less than 10 nm. Its physical properties are identical to bulk diamonds, such as fluorescence and photoluminescence, and they are biocompatible. In contrast to other CBNs, tetrahedral carbon clusters of sp^3 are mostly NDs. However, the surface of nanodiamonds is operating for colloidal stability with different functional groups or sp^2

ISSN:0971-1260
Vol-22-Issue-16-August-2019

carbon that allows the chemical modification of a targeted drug, gene delivery and the labeling of the tissue.

3. Theranostics applications of CBN

One of the several medicinal systems currently being investigated is the theranostic, which incorporates both therapy and diagnosis. A major benefit from the enormous aspect ratio and surface area present in the use of carbon nanomaterials in heat treatments is the use of multiple copies of theranostic engines like ligands and various polymers to enhance biocompatibility and water solubility, as well as imaging labels. Table 1 provides an overview of several representative studies of combined CBN theranostics.

3.1 Photothermal Therapy (PTT)

Functional fullerenes like polyhydroxy fullerenes (PHF) can produce thermal energy up to their ignition temperature when exposed to low-intensity NIR light (10 W/cm^2) [19]. NonInvasive treatment of cancer has also been evaluated for this fascinating property of functionalized fullerenes [20]. Tumors subsequently treated with PHF nanoparticles and exposed to 785 nm lasers during a two-hour period reduced their cross-sectional region by 32%, compared with no significant tumor-size changes in the test mice [21]. For these PHFs, such rapid tumor-shrinking observed in 2 hours compared to days needed for gold nanostructures requires further study and potential use in the ablation of photothermal tumors of these functional fullerenes.

3.2 Photodynamic Therapy (PDT)

Fullerenes are able to generate reactive oxygen species when exposed to harmless visible light [22]. Clinical applications for tumor theranostic therapies are beneficial for the photodynamics properties, can only attain the water solubility, specific targeting, and ideal molecular size after sufficient surface functionalization. Recently, the covalent conjugation of various terminal structures and molecular weights in PEG chains has been reported for the photodynamic anti-tumor role of C_{60}. The strongest suppression of the in vivo tumor growth exhibited by C_{60} when it combined with methyl-terminated PEG with the largest molecular weight and with the largest circular half-life.

3.3 Gene Treatment

In addition to conventional methods including radiation therapy, chemotherapy, and surgery, gene therapy is a possible alternative to cancer treatments. For gene transmission, viral and non-viral vectors are popular. Viral vectors are often immunogenic and cause inflammation.

ISSN:0971-1260
Vol-22-Issue-16-August-2019

Nonviral vectors are often less effective because they cannot pass through the nuclear membrane easily [24].

Table 1. Application of various carbon-based nanomaterials for different cancer treatment

Carbon-based nanomaterials	Imaging modality	Cell lines	Application	References
MWCNTs	_	PANC-1	Pancreatic cancer	25
C_{60}	MRI	_	Cancer theranostic	26
SWCNTs	_	4T1	Chemo-photothermal therapy	27
Graphene-based quantum dots	Fluorescence imaging	_	Breast cancer therapy	28
Gd-encapsulated graphene carbon	_	SSC-7	Photodynamic therapy	29
Carbon-based quantum dots	Optical imaging	_	Chemotherapy	30
GQDs		SW620, HCT116	Radiotherapy	31

4. Recent studies on carbon-based nanomaterials for cancer therapy

Badea et al. developed pemetrexed (Pm) and quercetin (Q) loaded MWCNTs to study anti-tumor behavior. The dynamic light scattering (DLS) procedure analyzed the mean nanoparticular dimension and, the nanosystems' physical stability was measured by an electro-kinetic potency (ζ). The release of Pm and Q in two different pHs (5.5 and 7.5) from nanosystems showed the release of both compounds is based on a Fickian diffusion mechanism. The anti-tumor potential of MWCNT-Pm-Q was demonstrated by substantial changes in cell morphology in pancreatic cells, with a reduction in cell viability below 60% at dose 25, 20 and 2 μg/mL of MWCNTs, Pm and Q, respectively after 24 h. Furthermore, the pancreas has shown a high level of ROS, increased MWCNT burden and increased lysosome at doses above 25 μg/mL of MWCNTs, 20 μg/mL of PM and 2 μg/mL of Q as compared to nanosystems with a single drug [32].

A novel type of fluoresce nanozyme has been developed by Guo et al. to identify and treat cancer cells. They were manufactured using a facial co-precipitation method for the fabrication of ferrous phosphate-carbon dots ($Fe_3(PO_4)_2 \cdot 8H_2O$-CD), then further modified on

ISSN:0971-1260
Vol-22-Issue-16-August-2019

the surface by folic acid (FA) to attain $Fe_3(PO_4)_2 \cdot 8H_2O$-CDs-FA hybrid nanoflowers (hNF) for final use. In-vitro investigation shows that the hNFs have led to improved cytotoxicity of HeLa, even at low doses of ascorbic acid or H_2O_2, while no obvious harm was reported to normal cells with the same treatment that confirmed that selective cancer cell killing by hNFs was possible [33].

Lu et al., fabricated low toxic, biostable and water-soluble SWNTs with great efficiency in photothermal conversion. Dye-conjugated SWCNTs bind with antibodies which can prompt them precisely targeted at pancreas tumors for the imaging of dyes with cytotoxic PTT. The PTT offers safe and impressive therapies with limited adverse effects and thus a positive approach to cancer treatment [34].

5. Different aspects of CBNs for imaging

5.1 Magnetic Resonance Imaging (MRI)

For MRI applications, the fullerenes themselves are free of any required paramagnetic properties. Metallofullerene was made to encapsulate the Gd^{3+} paramagnetic ions for MRI applications, which results in a highly stable structure, not only maintaining Gd^{3+} properties, but also avoiding leakage in vivo, in order to minimize possible toxics [36].

5.2 Photoacoustic Imaging

Photoacoustic (PA) imaging is a noninvasive technique focused on the use of ultrasounds produced by a laser, combining visual and ultrasound functions [4]. PA Imaging has recently become an effective imaging strategy to focus on low-energy (visible and NIR laser light) absorption to support high-band ultrasound waves. PA imaging frequently combines with PTT to increase tumor irradiation and tumor targeting.

5.3 Fluorescence imaging.

Down-conversion fluorescence is a common type of fluorescence found in photoluminescence. Cristal defects and doping elements (n and o) are related to different colors in CBN [37]. Organic dye and metal dots have primarily been used in single-photon cell labeling, microsurgery, and imaging however low-energy fluorescence photons are emitted after high-energy fluorescence photons have been consumed. In clinical applications, the application of high energy photons has some disadvantages like auto fluorescence of samples, low penetration depth, and cell damage.

5.4 Raman imaging

Photostability, high spatial resolution, multiplex ability, and high sensitivity is the technique of Raman imaging. The typical Raman fingerprint specimens distinguish most structural

ISSN:0971-1260
Vol-22-Issue-16-August-2019

bonds of CBN. Raman technology relies on the unique vibrating elastic photo mode, allowing the signal-noise ratio, higher photo-stability and resolution of Raman signals than fluorescent signals. Raman has therefore rapidly emerged as a possible replacement for investigating CBN and its cell imaging [38-40].

6. Conclusion

In the past decade, research and applications over biomedicine of carbon nanomaterials have made significant progress that can help scientists to decode and improve the diagnosis and treatment of a number of diseases including cancer, biological phenomena, and their source and perspective. Because carbon nanomaterials play an important role in possible biomedical uses like cancer theranostics, their exposure to the general public is simultaneously increased and will attract a great deal of attention with respect to safety and health problems.

The majority of studies with carbon nanomaterials based on various approaches, because it is still primary research in the field. Only a few studies have been reported until the date for the progress of theranostic nanoplatforms. Some usable carbon nanomaterials are developed in animal models as stable and well-tolerated, which greatly encourages more study and understanding of the activities of carcinogenic theranostics in the carcinogenic material in vivo.

7. References

1. Maiti D, Tong X, Mou X, Yang K. Carbon-Based Nanomaterials for Biomedical Applications: A Recent Study. Frontiers in Pharmacology. 2018;9.
2. Zhang J, Zhang J, Li W, Chen R, Zhang Z, Zhang W, Tang Y, Chen X, Liu G, Lee CS. Degradable hollow mesoporous silicon/carbon nanoparticles for photoacoustic imaging-guided highly effective chemo-thermal tumor therapy in vitro and in vivo. Theranostics. 2017;7(12):3007.
3. Lin G, Mi P, Chu C, Zhang J, Liu G. Inorganic nanocarriers overcoming multidrug resistance for cancer theranostics. Advanced Science. 2016 Nov;3(11):1600134.
4. Patel KD, Singh RK, Kim HW. Carbon-based nanomaterials as an emerging platform for theranostics. Materials Horizons. 2019;6(3):434-69.
5. Cha C, Shin SR, Annabi N, Dokmeci MR, Khademhosseini A. Carbon-based nanomaterials: multifunctional materials for biomedical engineering. ACS Nano. 2013 Apr 5;7(4):2891-7.
6. Iijima S, Ichihashi T. Single-shell carbon nanotubes of 1-nm diameter. nature. 1993 Jun;363(6430):603.

ISSN:0971-1260
Vol-22-Issue-16-August-2019

7. Dresselhaus G, Riichiro S. Physical properties of carbon nanotubes. World scientific; 1998 Jul 22.
8. Zhbanov AI, Pogorelov EG, Chang YC. Van der Waals interaction between two crossed carbon nanotubes. ACS Nano. 2010 Sep 23;4(10):5937-45.
9. Mishra V, Patil A, Thakur S, Kesharwani P. Carbon dots: emerging theranostic nanoarchitectures. Drug discovery today. 2018 Jun 1;23(6):1219-32.
10. Zuo P, Lu X, Sun Z, Guo Y, He H. A review on syntheses, properties, characterization and bioanalytical applications of fluorescent carbon dots. Microchimica Acta. 2016 Feb 1;183(2):519-42.
11. Zhou M, Zhai Y, Dong S. Electrochemical sensing and biosensing platform based on chemically reduced graphene oxide. Analytical Chemistry. 2009 Jun 12;81(14):5603-13.
12. Tang LA, Wang J, Loh KP. Graphene-based SELDI probe with ultrahigh extraction and sensitivity for DNA oligomer. Journal of the American Chemical Society. 2010 Jul 27;132(32):10976-7.
13. Dang Q, Lu S, Yu S, Sun P, Yuan Z. Silk fibroin/montmorillonite nanocomposites: effect of pH on the conformational transition and clay dispersion. Biomacromolecules. 2010 May 28;11(7):1796-801.
14. Zhang X, Ma Y, Fu S, Zhang A. Facile Synthesis of Water-Soluble Fullerene (C60) Nanoparticles via Mussel-Inspired Chemistry as Efficient Antioxidants. Nanomaterials. 2019 Dec;9(12):1647.
15. Kokubo K, Sato N, Sakurai H. Colloidal Gold Nanoparticles Stabilized By Hydroxylated Fullerenes. InMeeting Abstracts 2017 Apr 15 (No. 13, pp. 851-851). The Electrochemical Society.
16. Mochalin VN, Shenderova O, Ho D, Gogotsi Y. The properties and applications of nanodiamonds. Nature nanotechnology. 2012 Jan;7(1):11.
17. Nayak TR, Zhang Y, Cai W. Cancer theranostics with carbon-based nanoplatforms. In Cancer Theranostics 2014 Jan 1 (pp. 347-361). Academic Press.
18. Janib SM, Moses AS, MacKay JA. Imaging and drug delivery using theranostic nanoparticles. Advanced drug delivery reviews. 2010 Aug 30;62(11):1052-63.
19. Krishna V, Singh A, Sharma P, Iwakuma N, Wang Q, Zhang Q, Knapik J, Jiang H, Grobmyer SR, Koopman B, Moudgil B. Polyhydroxy fullerenes for non-invasive cancer imaging and therapy. Small. 2010 Oct 18;6(20):2236-41.

ISSN:0971-1260
Vol-22-Issue-16-August-2019

20. Chen Z, Ma L, Liu Y, Chen C. Applications of functionalized fullerenes in tumor theranostics. Theranostics. 2012;2(3):238.
21. Huang L, Terakawa M, Zhiyentayev T, Huang YY, Sawayama Y, Jahnke A, et al. Innovative cationic fullerenes as broad-spectrum light-activated antimicrobials. Nanomedicine 2010;6(3):442-52.
22. Liu J, Tabata Y. Photodynamic antitumor activity of fullerene modified with poly(ethylene glycol) with different molecular weights and terminal structures. J Biomater Sci Polym Ed 2011;22:297-312.
23. Mintzer MA, Simanek EE. Nonviral vectors for gene delivery. Chem Rev 2009;109(2):259-302.
24. Mocan T, Matea CT, Cojocaru I, Ilie I, Tabaran FA, Zaharie F, Iancu C, Bartos D, Mocan L. Photothermal treatment of human pancreatic cancer using PEGylated multi-walled carbon nanotubes induces apoptosis by triggering mitochondrial membrane depolarization mechanism. Journal of Cancer. 2014;5(8):679.
25. Shi J, Wang L, Gao J, Liu Y, Zhang J, Ma R, Liu R, Zhang Z. A fullerene-based multi-functional nanoplatform for cancer theranostic applications. Biomaterials. 2014 Jul 1;35(22):5771-84.
26. Yang J, Su H, Sun W, Cai J, Liu S, Chai Y, Zhang C. Dual chemodrug-loaded single-walled carbon nanohorns for multimodal imaging-guided chemo-photothermal therapy of tumors and lung metastases. Theranostics. 2018;8(7):1966.
27. De S, Patra K, Ghosh D, Dutta K, Dey A, Sarkar G, Maiti J, Basu A, Rana D, Chattopadhyay D. Tailoring the efficacy of multifunctional biopolymeric graphene oxide quantum dot-based nanomaterial as Nanocargo in Cancer therapeutic application. ACS Biomaterials Science & Engineering. 2018 Jan 30;4(2):514-31.
28. Chen H, Qiu Y, Ding D, Lin H, Sun W, Wang GD, Huang W, Zhang W, Lee D, Liu G, Xie J. Gadolinium-encapsulated graphene carbon nanotheranostics for imaging-guided photodynamic therapy. Advanced Materials. 2018 Sep;30(36):1802748.
29. Singh RK, Patel KD, Mahapatra C, Kang MS, Kim HW. C-dot generated bioactive organosilica nanospheres in theranostics: multicolor luminescent and photothermal properties combined with drug delivery capacity. ACS applied materials & interfaces. 2016 Sep 6;8(37):24433-44.

ISSN:0971-1260
Vol-22-Issue-16-August-2019

30. Ruan J, Wang Y, Li F, Jia R, Zhou G, Shao C, Zhu L, Cui M, Yang DP, Ge S. Graphene quantum dots for radiotherapy. ACS Applied Materials & Interfaces. 2018 Mar 15;10(17):14342-55.
31. Badea N, Craciun MM, Dragomir AS, Balas M, Dinischiotu A, Nistor C, Gavan C, Ionita D. Systems based on carbon nanotubes with potential in cancer therapy. Materials Chemistry and Physics. 2019 Nov 8:122435.
32. Guo J, Wang Y, Zhao M. Target-directed functionalized ferrous phosphate-carbon dots fluorescent nanostructures as peroxidase mimetics for cancer cell detection and ROS-mediated therapy. Sensors and Actuators B: Chemical. 2019 Jun 26:126739.
33. Lu GH, Shang WT, Deng H, Han ZY, Hu M, Liang XY, Fang CH, Zhu XH, Fan YF, Tian J. Targeting carbon nanotubes based on IGF-1R for photothermal therapy of orthotopic pancreatic cancer guided by optical imaging. Biomaterials. 2019 Mar 1;195:13-22.
34. Matshitse R, Managa M, Nyokong T. The modulation of the photophysical and photodynamic therapy activities of a phthalocyanine by detonation nanodiamonds: Comparison with graphene quantum dots and carbon nanodots. Diamond and Related Materials. 2019 Nov 9:107617.
35. Mody VV, Nounou MI, Bikram M. Novel nanomedicine-based MRI contrast agents for gynecological malignancies. Advanced Drug Delivery Reviews. 2009 Aug 10;61(10):795-807.
36. Liu M, Xu Y, Niu F, Gooding JJ, Liu J. Carbon quantum dots directly generated from electrochemical oxidation of graphite electrodes in alkaline alcohols and the applications for specific ferric ion detection and cell imaging. Analyst. 2016;141(9):2657-64.
37. Zhang Z, Wang M, Gao D, Luo D, Liu Q, Yang J, Li Y. Targeted Raman imaging of cells using graphene oxide-based hybrids. Langmuir. 2016 Sep 30;32(40):10253-8.
38. Niu JJ, Schrlau MG, Friedman G, Gogotsi Y. Carbon nanotube-tipped endoscope for in situ intracellular surface-enhanced raman spectroscopy. Small. 2011 Feb 18;7(4):540-5.
39. Sharma H, Agarwal DC, Shukla AK, Avasthi DK, Vankar VD. Surface-enhanced Raman scattering and fluorescence emission of gold nanoparticle-multiwalled carbon nanotube hybrids. Journal of Raman Spectroscopy. 2013 Jan;44(1):12-20.
40. Balasubramanian K, Zuccaro L, Kern K. Tunable enhancement of raman scattering in graphene-nanoparticle hybrids. Advanced Functional Materials. 2014 Oct;24(40):6348-58.

