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Carbon Nanomaterials as a Potential Agents for Induction of Apoptosis In Cancerous Tissue

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Abstract

Cancerous condition is the result of abnormal physiological and cellular mechanisms that develop in an individual. The cells prone to cancer exhibit complexed behavioral abnormalities and disobedience to the normal cellular signaling pathways. Benign and malignant cancers show different proliferative behavior depending on the type of cells, their location, and functions. The cancerous tissues have increased vascular supply and a lower ratio of the rate of conversion of oxy-hemoglobin to deoxy-hemoglobin. In tissues, like the dense radiographic breast, show some morphological changes in the cell organelles like nuclei. The carbon nanoparticles act as suitable agents for carrying antiviral drugs, antibiotics, anticancer drugs, agents for imaging, and thermal ablation. Further, considering the multifaceted features, carbon nanomaterials can be a potential agent to induce apoptosis in the cancerous tissue that might help to restrict its growth. All these intentions need careful examinations, applications at laboratory, clinical, and mass-scale production, keeping in mind the environmental, judicial aspects, and human tendencies of maximizing their benefits. This short review is an effort to evaluate the potentials of carbon nanomaterials that can induce apoptosis in cancer tissue.

Keywords: Apoptosis; Biocompatibility; Biodistribution; Cancer Biomarkers; Cancerous Tissue; Carbon Nanomaterials

Cancer and their Physicopathological Features

The cells prone to cancer exhibit complexed behavioral abnormalities and disobedience to the normal cellular signaling pathways. Benign and malignant cancers show different proliferative behavior depending on the type of cells, their location, and function. The cancerous tissues have increased vascular supply and a lower ratio of the rate of conversion of oxy-hemoglobin to deoxy-hemoglobin. The non-invasive diffuse optical tomography and the diffuse correlation spectroscopy techniques help predict the comparative physiopathological biomarkers in cancerous and normal healthy tissues.

There is a direct correlation between the size and the scale or rate of cellular biosynthesis while the cellular geometry and shape relate with the cell organelles and the ambient environment. The metabolites that promote growth and growth inhibitor, and cell cycle activator (cln3) and inhibitor (whi5) also play significant role in maintaining the shape and size of the cell. The cancerous cells show morphogenesis that is different than the normal cellular morphogenesis. The cancerous issues, like dense radiographic breast,

show some morphological changes in the cell organelles and nucleus. Harmful impacts on cells include cellular and nuclear abnormalities such as pleomorphism, anisokayrosis, anaplasia, micro and macro nuclei, hyperchromacia, coarse chromatin pattern, chromatin bridges, irregular nuclear membrane etc. These are the result of changed morphology of the affected cell caused due to physiopathological status of cancerous cell. The disrupted inter and intra cellular communication, unlimited, fast and continuous cell proliferation, higher degree of avoidance of apoptosis, pronounced angiogenesis, and metastasis, are common in cancerous tissue. There is o-glycans protein molecules coated with sugar molecules; these act as sensors for the cells. The sugar molecules are present as long and complex chains in the case of normal cells but in the case of cancerous cells these chains are shorter and simple. This is the result of faulty position of the related enzymes, thereby, causing changes in the surface proteins of cancerous cells. Consequently, this feature enhances the growth of the cancer cells/tissues [1-3]. The telomerase enzyme increases the telomeres, and plays an important role in enhancing the life span of cancerous cells but in the case of normal cells its reduction with each cell division results in the cellular death. The physiology and the pathology of cancerous tissue relates with formation of reactive oxygen species via multiple cellular processes like communicating signaling process, pathological oxidation of DNA, lipids, proteins, cellular stress [4-7].

The specific genes and the signaling pathways correlate with two prime steps of metastasis, namely, annexation from the principle cancerous tissue, and growth at the incidental site. The phenotype traits and the dynamics related to metastatic process are under the influence of elaborate system with specific biophysical aspects. The related genomic and investigatory pathways that have quantitative and cellular physical phenotypic attributions play significant roles during metastasis. As metastasis advances, its components face many impediments because of molecular, extracellular matrices concerning the topology, varied degree of stiffness of ambient tissues, fluid with specific shear and compressive forces. To subjugate these odds, the cancerous cells and other components change the cellular processes like surface receptor expression, recognition of components of cytoskeleton, and directional polarity; these reflect on the fluctuation in the phenotype. The ability to recognize and evaluate mechanical and phenotypic modifications of such transitions will facilitate the overall concept of development of clinical and diagnostic as well as therapeutic aspects, further, the behavior of physical and molecular biomarkers related to cancerous cells and tissue within the ambient environment [8,9].

Tumor and cancerous tissues have different metabolic mechanism as compared to normal tissues. These exhibit three basic physiological features namely morphogenesis, neurogenesis, and angiogenesis. The cancerous molecular mechanism takes over the normal molecular mechanism of the normal tissue. Under these conditions the cancer tissue becomes capable of avoiding apoptosis and becomes immortal. The specific cancerous tissues produce biomolecules which act as biomarkers and are useful clinical and therapeutic applications (mentioned in the following Table 1) [10,11].

Biomolecule	Name of the Cancerous Tissue
Light chain antibody of immunoglobin G (IgG)	Present in urine of multiple myeloma patients
Bence-Jones proteins	Present in serum of myeloma, leukaemia, lymphoma, Waldenstrom's macroglobulinemia
Amylase	Present in Serum in cancer patient
h-chorionic gonadotropin (hCG)	Choriocarcinoma
Catecholamines	Pheochromocytoma and neuroblastoma
Acid phosphatase	Prostate cancer
Alkaline phosphatase	Bone tumour

Table 1: Cancerous Tissue.

Apoptosis

Under normal physiological conditions, the worn out, unwanted cells, cell that become dysfunctioning, and target cells receive apoptosis inducing signals. The proteolytic caspases get activated which dismantle the cytoskeleton that leads to the shrinkage of cell and degradation of cell organelles. The cell membrane develops bud like structures called blebs. The cell membrane develops blebs because the proteins of cytoskeleton undergo uncoupling; this process is zeiosis. The process of uncoupling of protein reduces the amount of ATP via oxidation of fuels. The cytoplasm starts becoming dense and the cell organelles get closer to each other. The nucleus exhibits pyknosis i.e., chromatin condenses and appears as compact patches and move to the periphery of the nucleus, this stage is the hall mark of apoptosis. The DNA of the cell undergoing apoptosis exhibits karyorrhexis- a process in which DNA becomes fragmented and loses continuity resulting in the splitting of DNA into discrete chromatin bodies; these bodies distribute irregularly throughout the cytoplasm. (Karyorrhexis- a term has Greek origin, and it means karyon=kernel or seed or nucleus and rhexis=bursting). During the process of apoptosis the DNA appears like a ladder, this phase is DNA laddering and it is

the common feature. One of the reasons for this phase is deprivation of nutrition. The DNA Laddering is seen during karyorrhexis. The endonucleases result in fragmentation of DNA. These fragments arrange in a specific pattern at regular intervals in a specific pattern that resembles ladder, and conveniently observed during agar gel electrophoresis. The membrane of cell organelles, like mitochondria, specifically becomes more permeable to cytochrome-C. This facilitates its distribution in cytosol and causes imbalance in oxidative phosphorylation, electron transfer system and activation of caspase cascade. Dysfunctioned, worn out, aged, irreparable and unwanted cells when undergo apoptosis, shrink, do not swell or exhibit inflammation, and isolate from the neighboring healthy cell without causing any damage or clinical impact. Overall, cells undergoing apoptosis disintegrate and develop apoptotic bodies. The rates of cell disintegration and splitting are very high and even the rate of cell clearing and clearance of apoptotic cells from biosystem is high [13].

There are extrinsic and intrinsic parameters that induce cellular apoptosis. Generally, toxins, hormones, growth factors, cytokines, and nitric oxide act as extrinsic inducers. These inducers are able to move across cell membrane or change the structure and functions of the components of cell membrane. These changes in the cell membrane help their entry in the target cell. The physicochemical cellular stress inducers initiate intracellular inducers which either bind with glycocorticoids and nuclear receptors, elevate temperature, viral infection, increased intracellular concentration of Ca^{++}, damaged cell membrane, extrinsic inducers like radiation, state of deprived nutrition, hypoxia, activate the regulatory protein system of cell membrane and induce apoptosis after reaching interior of the cell. There are two major regulatory modes, first is mitochondrial regulatory mode and in the second mode there is an increase in the concentration of Ca^{++} and calpin-non-lysosomal cysteine protease. These regulatory functionalities succeed in initiating the apoptosis [13-19].

Role of Carbon Nanoparticles during the Induction of Cellular Apoptosis

The carbon nanomaterials are available as hollow tubes, spherical and elliptical or sheet shapes, and other modified convenient forms as per the suitability for specific biomedical applications. These nanomaterials exhibit a high degree of biocompatibility and biodistribution. The concerned amendments incorporate attachment of carboxyl or ammonium group, noncovalent functionalization like van der Waals, π-π, and hydrophobic and hydrophilic interactions; the hollow carbon nanomaterials can be filled with different drugs or biomolecular cargo and delivered to the desired target sites. These specially coated nanovehicles deliver their goods at a particular site [20,21].

When murine macrophages cell line (RAW 264.7 cells) are exposed to acid treated multiwalled carbon nanotubes (aci-MWCNTs) and taurine functionalized multiwalled carbon nanotubes (tau-MWCNTs) (with concentration 0, 5, 20, 40, 80 μg/ml and duration 12 or 24 h, respectively) induce mild cellular viability and increased degree of the cellular apoptosis but the extent of cellular phagocytosis declines. During the elevated extent of apoptosis scavenger receptors (SR) and caspase-9 play significant role. Among the two functionalized MWCNTs, tau-MWCNTs show relatively weaker impact on the apoptosis in the experimental cell line [22]. Purified multiwalled carbon nanotubes (40, 200, and 400 μg/ml and control-tween-80 +0.9% saline) cause great damage to DNA and induce apoptosis and major loss of cellular viability among normal human dermal fibroblast cells. Although the multiwalled carbon nanotubes behave in toxic manner but their suitable monitoring can be useful in risk assessment aspects [23]. Single walled carbon nanotube and multiwalled carbon nanotubes (concentrations 50 μg/ml and 400 μg/ml for 24, 48, and 72 h exposure) cause time dependent apoptosis in the experimental cells [24]. This aspect can be exploited to induce apoptosis in cancer cells.

Fullerene, carbon nanoparticles exhibit antiviral, antibacterial, antioxidant, anticancer abilities. These carbon nanoparticles also impact immune response of an individual and scavenge reactive oxygen species [25]. The hydroxylated fullernols (derivative from linoleic acid under auto-oxidation condition) show higher rate of scavenging radical species in comparison to β-carotene. If butyl group replaces one hydrogen atom in compound-42 or N-methyl group in compound-45, the apoptotic ability of pyrrolidinium fullerene elevates in the VF-Ba/F3 cells (Ba/F3 cell are murine interleukin-3 dependent pro-B cell line, these are suitable for the investigation related to kinases and kinases inhibitors) Castro, et al. [26]. Although, the mechanisms related to the kinetics and scavenging of fullerene are obscure but there are very chances that their antioxidative and anticancerous abilities can be of importance during remedial aspects of cancer.

Graphene is one of the carbon nanomaterials that show variety of features in its indigenous and combined form. The pristine graphene as nanomaterial is cytophilic towards fibroblast and inflict toxic impacts to HeLa cells. This reflects on the behavior of graphene with respect to the type and nature of the interacting cells. The intracellular uptake of graphene oxide (with concentration less than 20 μg/ml) dysfunctions cell organelles like lysosomes, mitochondria, endoplasmic reticulum and nucleus [20,27]. The cellular up take of graphene oxide as it is hydrophilic in comparison to the reduced graphene oxide. After internalization hydrophilic

graphene oxide elevates ROS production in the presence of NADPH oxidase, changes antioxidant state, gene regulation, repair of DNA and apoptosis while these impacts get declined in the case of reduced graphene oxide [20,28].

Conclusion and Perspectives

Carbon nanomaterials are biocompatible that have appropriate biodispersibility. These are suitable vehicle for antiviral drugs, antibiotics, anticancer drugs, agents for imaging, and thermal ablation. These nanomaterials also deliver their cargo to the set target. Diversified studies on the cancer related biomarkers and carbon nanomaterials open a vast horizon in the field of clinical and therapeutic applications. Although, much has been done in these aspects, still there is a need to delve and ponder for the betterment of man-kind.

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References

1. Gill DJ, Tham KM, Chia J, Wang SC, Steentoft C, et al. (2013) Initiation of GalNAc-type O-glycosylation in the endoplasmic reticulum promotes cancer cell invasiveness. Proceedings of National Academy of Science, USA 110(34): E3152-E3161.

2. Bard F, Chia J (2017) Comment on the GalNAc-T Activation Pathway (GALA) is not a general mechanism for regulating mucin-type O-glycosylation, PLoS one 12(7).

3. Burchell JM, Beatson R, Graham R, Taylor-Papadimitriou J, Tajadura-Ortega V (2018) O-linked mucin-type glycosylation in breast cancer. Biochem Soc Trans 46(4): 779-788.

4. Lahir YK (2015) Lipid oxidation: Biochemical, biological and biophysical aspects. Global Journal of Biosciences and Biotechnology 4(3): 224-233.

5. Lahir YK (2016) Effects of nanomaterials on oxidation stress and protein oxidation in biological system: Biochemical and Biological aspects. Advances in Clinical Toxicology 1(1).

6. Lahir YK, Chitre AV, Dongre PM (2016) Some biophysical and biochemical interactions of nanomaterials on protein oxidation in biological system. Rep Opinion 8(7): 66-71.

7. Luisetto M, Almukhtar N, Ahmadabadi BN, Hamid GA, Mashori GR, et al. (2019) Endogenus toxicology: Modern physio-pathological aspects and relationship with new therapeutic strategies, an integrative discipline incorporating concepts from different research discipline like Biochemistry, Pharmacology and Toxicology. Archives of Cancer Science and Therapy.

8. Wirtz D, Konstantopoulos K, Searson PC (2011) The physics of cancer: the role of physical interactions and mechanical forces in metastasis, Nature reviews. Cancer 11(7): 512-522.

9. Moore NM, Nagahara LA (2014) Physical Biology in Cancer-1: Cellular physics of cancer metastasis. American Journal of Physiology: Cell Physiology 306(2): C78-C79.

10. Geho DH, Bandle RW, Clair T, Liotta LA (2005) Physiological mechanisms of tumor-cell- invasion and migration. Journal of Physiology 20: 194-120.

11. Kamal HFM, Al-Amodi HSB (2016) Cancer biomarkers, chapter in Role of biomarkers in medicine, (Eds) Wang M, et al. open access Intech open, London.

12. Zamzami N, Kroemer G (1999) Apoptosis: Condensed matter in cell death. Nature 401(127): 127-128.

13. Lahir YK (2012) Apoptosis-A Biological Phenomenon. Biochemistry and Cell Arch 12(2): 237-248

14. Kumar C (1998) Robbins Pathologic bases of diseases. SW Saunders Co Philadelphia.

15. Chiarugi A, Moskowitz MA (2002) PARP-a preparatory of apoptotic cell death? Science 297: 259-263.

16. Popov SG, Mill VR, Bernardi J (2002) Lethal toxin of Bacillus anthracis causes apoptosis of macrophages. Biochemistry Biophysics Research Communications 293: 349-355.

17. BrSne B (2003) Nitrogen oxide: No apoptosis or turning it on? Cell Death Differ 10: 864-869.

18. Lodish H, Berk A, Matsudaira P, Kaiser CA, Krieger M, et al. (2004) Molecular cell Biology, Freeman WH and Co, New York.

19. Mark P, Chau SL (2003) Calcium orchestrates apoptosis. Nature Cell Biology 5: 1041-1043.

20. Lahir YK (2019) Graphene and graphene based

nanomaterials are suitable for drug delivery, Chapter in Applications of Targeted Nano-Drugs and Delivery Systems, (Eds) Mohapatra S, et al. Elsevier; 50 Hampshire Street, Cambridge, MA 02139; Elsevier Publication, pp: 157-190.

21. Lahir YK**,** Avti P (2020) Nanomaterials and their interactive behavior with biomolecules, cells, and tissues: (Bentham Books) Bentham Science Publishers, Pvt. Ltd., 80 Robinson Road, #02-00, Singapore 068898, Singapore.

22. Wang X, Guo J, Chen T, Nie H, Wang H, et al. (2012) Multi-walled carbon nanotubes induce apoptosis via mitochondrial pathway and scavenger receptor. Toxicology *in vitro* 26(6): 799-806.

23. Patlolla A, Knighten B, Tchounwou P (2010) Multi-walled carbon nanotubes induce cytotoxicity, genotoxicity and apoptosis in normal human dermal fibroblast cells, Ethnicity and Disease. Winter 20(1 Suppl 1): S1-65-72.

24. Kavosi A, Hosseini SGN, Madani S, Khalighfard S, Khodayri H, et al. (2018) The toxicity and therapeutic effects of single-and multi-wall carbon nanotubes on mice breast cancer. Scientific Reports 8: 8375.

25. Lahir YK (2017) Impacts of fullerene on biological system, Clinical Immunology. Endocrinology and Metabolic Drugs 4(1): 48-57.

26. Castro E, Garcia AH, Zavala G, Echegoyen L (2017) Fullerenes in Biology and Medicine. Journal of materials chemistry B 5(32): 6523-6535.

27. Chowdhury AKMRH, Tab B, Venkatakrishna K (2017) Fibroblast-cytophilic and HeLa cytotoxic dual functions carbon nanoribbon network platform. ACS Applied Mater Interfaces, 9(3): 19662-196676.

28. Chatterjee N, Eom HJ, Choi J (2014) A system toxicology approach to the surface functionality Control of δ-cell interaction, Biomaterials 35(4): 1109-1127.