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APPLICATIONS OF NANOTECHNOLOGY

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ABSTRACT

Cancer is the most common malignancy disease and leading cause of death. However, chemotherapy using anticancer drugs has many drawbacks like poor water solubility, poor bioavailability, rapid relapse, non-specific selectivity, development of drug resistance and side effects on normal tissues. Thus, in recent years, great efforts have been done on nanotechnology that will release drugs in response to stimuli. Graphene quantum dots based nanotechnology has gained much attention as compared with other nanocarriers in research applications and biomedical fields due to their unique physicochemical properties such as bioimaging, drug delivery and biomarker sensors for early detection of disease. GQDs serve as an ideal candidate for loading hydrophobic anticancer drugs due to their unique properties such as single atomic layer with small lateral size and oxygen-rich functional groups at the edges. Also, it acts as a nanocarrier for various chemotherapeutic agents and has good stability in vivo. This review article discusses potential applications of graphene quantum dots as nanocarrier for targeted and controlled release of anticancer drugs. Also, it shows the ability of GQDs as a good nanotechnology drug delivery system to be easily functionalized for used as an imaging platform and targeted multimodal treatment.

Keywords : Nanotechnology; Graphene quantum dots; Drug carriers; Nanocarriers; Nanoparticles.

Introduction

Cancer, one of the most common and leading causes of death today, has become an important public health risk among mankind. More than ten million people are diagnosed with cancer disease annually. At the start, cancer is a localized disease and then spread to distant sites in the body and thus makes it incurable. In general, cancer develops via multistage carcinogenesis process involving cellular physiological systems such as cell signaling and apoptosis and makes it incomprehensible and highly complex disease. Cancer has caused more than 8.2 million deaths and approximately 14.1 million new cases in 2012 and may reach over 25 million new cases in the next two decades indicating the leading cause of death worldwide. The morbidity and mortality of cancer have increased tremendously and created attention for reducing the influence of disease by developing different treatment strategies[1-2]. Patients detected with early-stage cancer may have many treatment options[3]. Thus, early diagnosis is important for reducing the mortality of breast cancer and broadens treatment options. The primary clinical treatment for cancer includes gene therapy, hormone therapy, active surveillance, nano-medicines, surgery, radiation therapy, and chemotherapy[4-5]. Chemotherapy is the main and most widely used treatment for cancer that has spread or metastasized. However, the chemotherapy using anticancer drugs have many disadvantages such as adverse side effects on normal tissues[6-7], poor water solubility, low bioavailability, rapid relapse, development of drug resistance during prolonged treatment and nonspecific selectivity[8]. Therefore, the effectiveness of chemotherapy is limited by its various side effects such as cardiotoxicity and hematotoxicity

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because they not only kill cancer cells that grow and divide but also cause damage to healthy tissues and cells in the body[9-10].

The ideal drug delivery system for cancer should have solubility and stability under physiological conditions and dispersion through the vascular system to ensure interactions with the tumor sites and be selective and specific to cancer cells. To achieve these objectives, significant efforts have been concentrated on novel drug delivery systems i.e. nanotechnology for improving the delivery of anticancer drugs to the site of action[11-12]. Nanotechnology is the science and technology of nanoscale which is about 1-100 nm. Nanotechnology has emerged as a promising tool to reduce the side effects of earlier cancer chemotherapy and improve the therapeutic effectiveness of cancer chemotherapy. The drug carriers used in nanotechnology have the capability of accumulating in tumors through the blood vessels and decrease the chemical-induced damage to the healthy cells. Moreover, drug carriers used in nanotechnology are characterized by their means of functionalization for incorporation with fluorescent markers for simultaneous imaging and diagnosis therapy. Thus, nanotechnology approach is critical in addressing the challenges of cancer adaptation and heterogeneity[13-15].

Researchers have formulated various nanotechnologies for the treatment of cancer which has shown tremendous potential with interesting characteristics and observations. Currently, a wide range of nanotechnology drug delivery systems has been developed including nanoparticles[16-17], nanogels[18], liposomes[19], polymer micelles[20-21] and dendrimers[22] which have improved the water solubility of the anticancer drugs and achieved the specific targeting of the anticancer drugs to the tumor site. However, nanotechnology drug delivery system has shown promising opportunities and characteristics such as improved drug targeting, efficacy, and loading in cancer treatment. Various nanotechnology platforms such as nanoparticles, carbon nanotubes, nanoshells, liposomes, and super-paramagnetic based nanoparticles have increased antitumor efficacy and safety profile. Therefore, applications of nanotechnology have been widely utilized in the biomedical field as drug delivery vehicle, biosensor, and imaging probe.

Applications of Nanotechnology

The application of nanotechnology has received outstanding demand over the last decade for the treatment of cancer. Engineering nanomaterials for cancer diagnosis and treatment have shown the strength for revolutionizing the cancer therapy by developing new theranostic nanotechnologies for simultaneous imaging and therapy. Nowadays, the recent cancer research is going on developing drug targeted nanotechnology having the ability to overcome the mechanisms of drug resistance and achieving more efficient selective drug delivery with minimum damage to normal tissues. Due to the small size and large surface area, nanotechnology show increased bioavailability and ability to cross human cell membrane enhancing the biodistribution of anticancer drugs. The cellular uptake of nanotechnologies for targeting cancer cells is mainly influenced by tumor microenvironment and pH which affects nanoparticle-cell interactions. Thus, poorly soluble anticancer drugs can be dispersed in nanotherapeutic formulation improving the drug solubility, and stability, maintaining the chemotherapeutic effect, minimizing their toxicity and providing site-specific targeting. Further, fluorescent material due to they're nanosize allows simultaneous detection and treatment of cancer cells and make them a suitable platform for cancer chemotherapy.

The control of drug release is important in medicine and therefore, it has received increasing interest in recent years. The features such as inertness and drug loading capacity are the prime factors for nanotechnology based drug delivery systems. However, organizing the drug release profile by keeping the drug dose at a required level for a long time prevents the side effects of the drug. Further, this would increase the time interval and accelerate the treatment process. The important pre-requisites of an ideal drug delivery vehicle includes safety, easy fabrication, and thermodynamic and pH stability. Among various carriers for drug delivery, nanotechnology has shown more advantages as drug carriers as compared with others. Moreover, the recognition of cancer cells over healthy cells is the most important and primary challenging goal in anticancer chemotherapy. For this, graphene quantum dots are the most widely used fluorescent nanocarrier for cancer targeting.

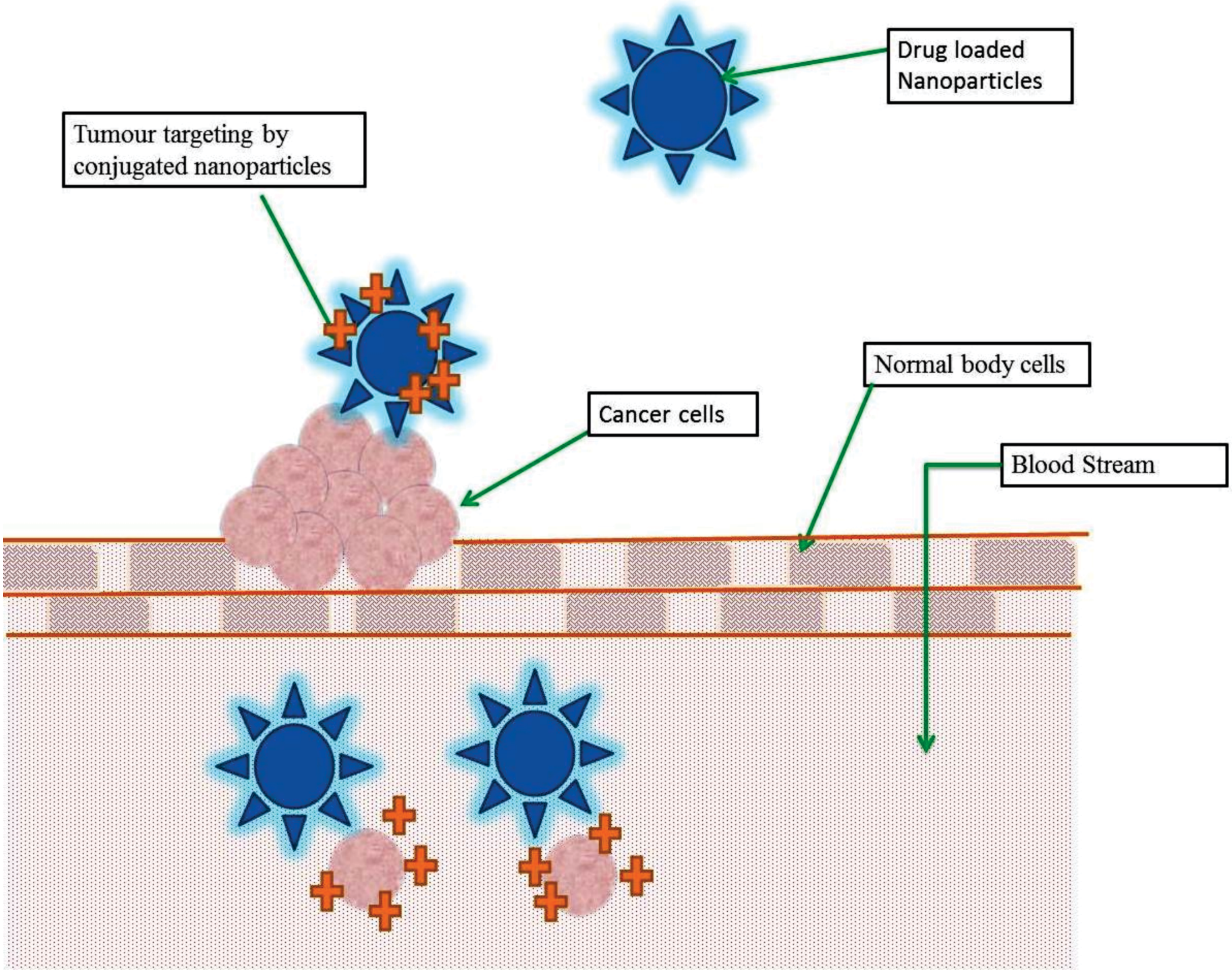

Fig.1-Applications of Nanotechnology for Selective Tumor Targeting

Graphene quantum dots (GQDs)

Graphene is a two dimensional single-atom carbon material that was reported for the first time in 2004 and has attracted great interest because of its novel physical properties such as high surface area, carrier transport mobility, excellent mechanical strength, and superior mechanical flexibility. GQDs have a size in the range of 3-20 nm and are zero-dimensional materials consisting of graphene sheets.

The fluorescence property of GQDs originates from quantum confinement and edge effects make them an ideal platform for the traceable delivery of chemotherapeutic drugs into cancer cells without involving additional fluorescent. GQDs based nanotechnology is capable of functioning as an anticancer drug carrier and a signaler for indicating drug delivery, release and response at different stages by providing distinct fluorescence signals. Firstly, the high specific surface area and biocompatibility properties of GQDs indicate their capability to load drugs with lower toxicity. Another important feature of GQD due to their photoluminescence (PL) property is that the delivery complex could be visualized without modifying them with other marker dyes.

Synthesis of GQDS

In general, GQDs are synthesized by multistep synthetic and preparatory process ensuring their biocompatibility and solubility. The synthesis methods of GQDs are classified into two categories: top down and bottom down methods. In top down method, cutting down of large graphene sheets such as carbon nanotubes, carbon fibers or graphite into small pieces of graphene sheets are most suitable for mass production. Most top down methods are unsatisfactory due to requirements of critical synthesis procedures, special equipment, low QY and difficulty in controlling the size of products which affect the PL performance in the application of photovoltaic and optoelectronic and so on. Bottom up method requires small molecules as starting materials for GQDs buildup and are appropriate for controlling the size of GQDs but require multistep organic reactions and purification at each step. This method is based on carbonizing some special organic precursors via thermal treatment and allowing accurate control over morphology, size distribution and lattice dimensions of products. Thus, some suitable molecular precursors are selected with or without mild surface passivators to synthesize luminescent GQDs using one-step hydrothermal pathway. Top down approaches are illustrated as nanolithography technique, acidic oxidation, hydrothermal microwave assisted, selective plasma oxidation and chemical exfoliation methods have been widely used to synthesize GQDs. Bottom up methods using oxygen-containing aromatic compounds as starting materials polymerized under ultraviolet irradiation method, fullerenes as starting materials through ruthenium catalyzed cage opening, carbonization as starting materials through microwave-assisted hydrothermal method, hydrogen peroxide and expanded graphite as starting materials in a one-step solvothermal method, oxidization, carbonization and reduction successively have been utilized to prepare GQDs recently. On the basis of these two methods, GQDs with particular physicochemical properties can be prepared for different applications. Compared with both methods, bottom up methods are effective for production and result in higher QY, higher FL efficiency. GQDs can also be prepared from food additive citric acid under microwave irradiation conditions.

CONCLUSION

The application of nanotechnology has received outstanding demand over the last decade for the treatment of cancer. Engineering the nanotechnology DDS for cancer diagnosis and treatment have shown the strength for revolutionizing the cancer therapy by developing new theranostic nanotherapeutics for simultaneous imaging and therapy. Nowadays, the recent cancer research is going on developing drug targeted Nanotechnology DDS having the ability to overcome the mechanisms of drug resistance and achieving more efficient selective drug delivery with minimum damage to normal tissues. Due to the small size and large surface area, nanotechnology show increased bioavailability and ability to cross human cell membrane enhancing the biodistribution of anticancer drugs. Further, fluorescent material due to they're nanosize allows simultaneous detection and treatment of cancer cells and make them a suitable platform for cancer chemotherapy.

References :

1. Jemal, A., Miller, K.D., Ma, J., Siegel, R.L., Fedewa, S.A., Islami, F., Devesa, S.S. and Thun, M.J., 2018. Higher lung cancer incidence in young women than young men in the United States. New England Journal of Medicine, 378(21), pp.1999-2009.
2. Jemal, A. and Fedewa, S.A., 2017. Lung cancer screening with low-dose computed tomography in the United States—2010 to 2015. JAMA oncology, 3(9), pp.1278-1281.
3. Davidson, A., Chia, S., Olson, R., Nichol, A., Speers, C., Coldman, A.J., Bajdik, C., Woods, R. and Tyldesley, S., 2013. Stage, treatment and outcomes for patients with breast cancer in British Columbia in 2002: a population-based cohort study. CMAJ open, 1(4), p.E134.
4. Ferrari, M., 2005. Cancer nanotechnology: opportunities and challenges. Nature reviews cancer, 5(3), p.161.

5. Siegel, R.L., Miller, K.D. and Jemal, A., 2015. Cancer statistics, 2015. CA: a cancer journal for clinicians, 65(1), pp.5-29.
6. Erttmann, R., Erb, N., Steinhoff, A. and Landbeck, G., 1988. Pharmacokinetics of doxorubicin in man: dose and schedule dependence. Journal of cancer research and clinical oncology, 114(5), pp.509-513.
7. Wang, S., Konorev, E.A., Kotamraju, S., Joseph, J., Kalivendi, S. and Kalyanaraman, B., 2004. Doxorubicin induces apoptosis in normal and tumor cells via distinctly different mechanisms intermediacy of H2O2-and p53-dependent pathways. Journal of Biological Chemistry, 279(24), pp.25535-25543.
8. Tian, J., Luo, Y., Huang, L., Feng, Y., Ju, H. and Yu, B.Y., 2016. Pegylated folate and peptide-decorated graphene oxide nanovehicle for in vivo targeted delivery of anticancer drugs and therapeutic self-monitoring. Biosensors and Bioelectronics, 80, pp.519-524.
9. Lu, W., Singh, A.K., Khan, S.A., Senapati, D., Yu, H. and Ray, P.C., 2010. Gold nano-popcorn-based targeted diagnosis, nanotherapy treatment, and in situ monitoring of photothermal therapy response of prostate cancer cells using surface-enhanced Raman spectroscopy. Journal of the American Chemical Society, 132(51), pp.18103-18114.
10. Ardeshirpour, Y., Chernomordik, V., Hassan, M., Zielinski, R., Capala, J. and Gandjbakhche, A., 2014. In vivo fluorescence lifetime imaging for monitoring the efficacy of the cancer treatment. Clinical Cancer Research, 20(13), pp.3531-3539.
11. Davis, M.E., Chen, Z. and Shin, D.M., 2010. Nanoparticle therapeutics: an emerging treatment modality for cancer. In Nanoscience And Technology: A Collection of Reviews from Nature Journals (pp. 239-250).
12. Diamantis, N. and Banerji, U., 2016. Antibody-drug conjugates—an emerging class of cancer treatment. British journal of cancer, 114(4), p.362.
13. Barreto, J.A., O'Malley, W., Kubeil, M., Graham, B., Stephan, H. and Spiccia, L., 2011. Nanomaterials: applications in cancer imaging and therapy. Advanced materials, 23(12), pp.H18-H40.
14. Xie, J., Lee, S. and Chen, X., 2010. Nanoparticle-based theranostic agents. Advanced drug delivery reviews, 62(11), pp.1064-1079.
15. Sahoo, S.K., Misra, R. and Parveen, S., 2017. Nanoparticles: a boon to drug delivery, therapeutics, diagnostics and imaging. In Nanomedicine in Cancer (pp. 73-124). Pan Stanford.
16. Podsiadlo, P., Sinani, V.A., Bahng, J.H., Kam, N.W.S., Lee, J. and Kotov, N.A., 2008. Gold nanoparticles enhance the anti-leukemia action of a 6-mercaptopurine chemotherapeutic agent. Langmuir, 24(2), pp.568-574.
17. Yu, M., Jambhrunkar, S., Thorn, P., Chen, J., Gu, W. and Yu, C., 2013. Hyaluronic acid modified mesoporous silica nanoparticles for targeted drug delivery to CD44-overexpressing cancer cells. Nanoscale, 5(1), pp.178-183.
18. Gonc¸alves, M., Maciel, D., Capelo, D., Xiao, S., Sun, W., Shi, X., Rodrigues, J., Tomás, H. and Li, Y., 2014. Dendrimer-assisted formation of fluorescent nanogels for drug delivery and intracellular imaging. Biomacromolecules, 15(2), pp.492-499.
19. Ogawara, K.I., Un, K., Minato, K., Tanaka, K.I., Higaki, K. and Kimura, T., 2008. Determinants for in vivo anti-tumor effects of PEG liposomal doxorubicin: importance of vascular permeability within tumors. International journal of pharmaceutics, 359(1-2), pp.234-240.
20. Cheng, J., Teply, B.A., Sherifi, I., Sung, J., Luther, G., Gu, F.X., Levy-Nissenbaum, E., Radovic-Moreno, A.F., Langer, R. and Farokhzad, O.C., 2007. Formulation of functionalized PLGA–PEG nanoparticles for in vivo targeted drug delivery. Biomaterials, 28(5), pp.869-876.
21. Song, S., Chen, F., Qi, H., Li, F., Xin, T., Xu, J., Ye, T., Sheng, N., Yang, X. and Pan, W., 2014. Multifunctional tumor-targeting nanocarriers based on hyaluronic acid-mediated and pH-

sensitive properties for efficient delivery of docetaxel. Pharmaceutical research, 31(4), pp.1032-1045.
22. Wang, Y., Guo, R., Cao, X., Shen, M. and Shi, X., 2011. Encapsulation of 2-methoxyestradiol within multifunctional poly (amidoamine) dendrimers for targeted cancer therapy. Biomaterials, 32(12), pp.3322-3329.

List of Abbreviations

GQDs- Graphene quantum dots
PL- Photoluminescence
FL- Fluorescence
QY- Quantum yield
DDS- Drug delivery system
2D- Two dimensional

Figures

Fig.1- Applications of nanotechnology for Selective Tumor Targeting