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Mini Review

The Recent progress of Graphene-Based Nanomaterials in Biomedical Applications

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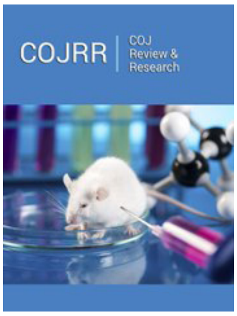

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Abstract

Graphene-Based Nanomaterials (GBNs) exhibit unique physicochemical properties (such as: large planar area, high electrical conductivity, thermal stability, incredible strength, remarkable biocompatibility, ease of functionalization, and excellent ability to quench fluorescence) that lead to many potential applications. Due to the unique properties of graphene-based nanomaterials, biomedical applications of graphene-based nanomaterials have attracted considerable interest in the last few years. In this mini review, we present an overview of current advances in applications of graphene in biomedical applications with focus on drug/gene delivery, antibacterial activity, biosensing, bioimaging, cancer therapy, with a brief discussion on the challenges and perspectives for future research in this field.

Keywords: Graphene, Biomedical application; Drug delivery; Biosensing; Bioimaging

Introduction

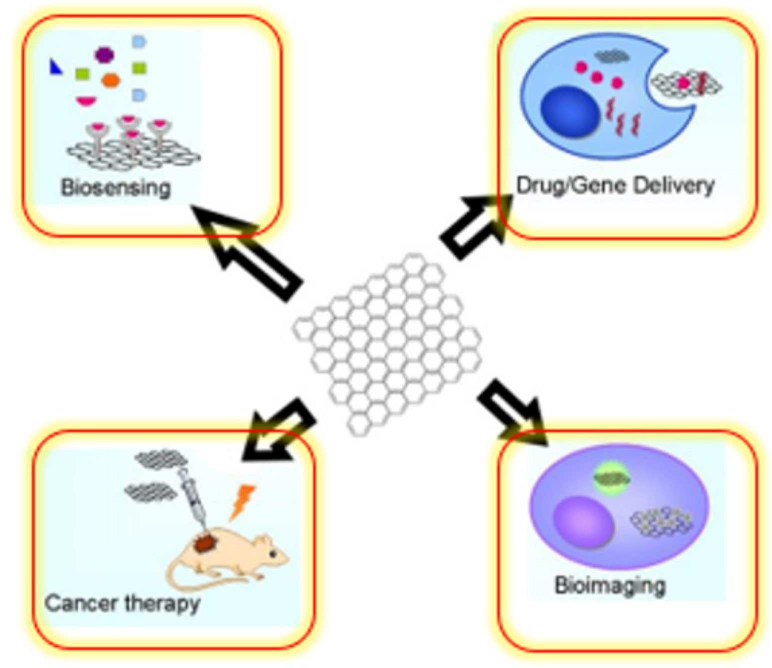

Figure 1: Biosensing, drug/gene delivery, cancer therapy and bioimaging.

Graphene is an amazing new material. It was discovered in 2004 and it consists of carbon atoms arranged in a perfect hexagonal lattice (Figure 1). Another structure of carbon is graphite. Where the carbon atoms are laid out and stacked up in sheets. If you separate out just one atomic layer of graphite, this is graphene. Figure 2 shows a schematic representation of chemical structures of Graphene-Based Nanomaterials (GBNs) including graphene, Graphene Oxide (GO) and reduced Graphene Oxide (rGO) [1]. Because graphene is only one atom thick, it has some amazing properties. It's fantastically strong, very light, extremely flexible. And it conducts electricity and heat better than almost any other materials. Graphene has a high surface area, and this enables a lot more drugs to be loaded onto its surface. This could potentially reduce the side effects of associated with the current cancer treatment. Graphene also has a high acidity in terms of chemistry, pretty much anything can be attached onto its surface enabling a specific and precise targeting for drug delivery.

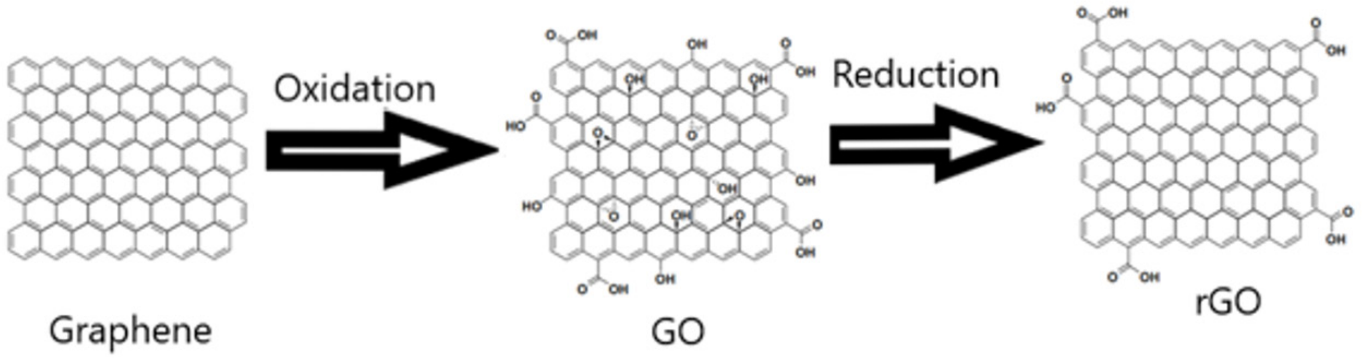

Figure 2: Schematic representation of structures of graphene, GO and rGO.

Graphene displays numerous of tremendous properties such as high electrical conductivity, thermal stability, and incredible strength. All these properties could be used for biomedical application and therefore makes graphene a very attractive material. Indeed, applications can now be envisioned outside the body, such as healing sensors, and inside the body, such as drug delivery and potentially changing cell behavior [2-4]. Graphene is an excellent material for sensors applications because every atom of graphene is exposed to its environment and can detect changes in its surroundings. It can be used to detect chemicals and toxic gases, even biological agents like drugs in our body. Specifically, the high sensitivity of graphene makes it talented to detect one molecule of gas that adsorbed on its surface, Moreover, graphene can be used for sensing stresses, strains and structural components. This mini review, present an overview of current advances in applications of graphene in biomedical applications.

Biomedical Applications of GBNs

Drug/gene delivery

To safely achieve the desired therapeutic effect, while having fewer side effects on healthy tissues, Drug Delivery Systems (DDS) have been used to transport therapeutic drugs in the body as needed. Chemotherapy drugs often have drastic side effects on non-targeted tissues due to its poor solubility and lack of selectivity in drug localization into tumor [5]. Recently, several nano-sized drug carriers have been investigated by nanotechnology techniques [6]. Graphene-Based Nanomaterials (GBNs) have been widely investigated as nano-carriers in the field of nanomedicine, such as drug/gene delivery systems due to appropriate high surface area, high acidity, biocompatibility, and easiness of surface functionalization [7,8]. A list of some investigated anticancer chemotherapeutics delivered using nanosheets of GBN derivatives loaded via physical absorption or chemical conjugation was provided Shim et al. [1]. This list includes anthracycline antibiotics, quinolone alkaloids, taxanes, platinum complexes, nitrosourea compounds, pyrimidine analogs, polyphenolic compounds, quinone compounds and other chemotherapeutics [1]. A delivery of mixed anticancer drugs by functional GO was further investigated by Zhang et al. [9]. In this work, two anticancer drugs, including Doxorubicin (DOX) and Camptothecin (CPT), were loaded onto the Folic Acid-conjugated Nanoscale Graphene Oxide (NGO (FA-NGO)) by means of л–л stacking and hydrophobic interactions. Their results revealed that FA-NGO loaded with the two anticancer drugs showed extraordinarily higher cytotoxicity against target cells compared to NGO loaded with only a single drug.

Antibacterial activity

Many recent studies have demonstrated that GBNs exhibits promising antibacterial properties [10]. Tu et al. [11] showed that the outer and inner membranes of *E. coli* being degraded by pristine graphene nanosheets and reduced their viability. Li et al. [12] studied the antibacterial activity of monolayer graphene films on Cu, Ge, and SiO_2. The study revealed that graphene films on Ge and especially on Cu surprisingly inhibited the growth of *S. aureus* and *E. coli* Pham et al. [13] found that variable bactericidal efficiency of *P. aeruginosa* and *S. aureus* was exhibited by pristine graphene nanosheets.

Biosensors and bioimaging

GBNs can be used for biosensing and bioimaging due to their distinct properties, such as a high electrical conductivity (up to 6000S/cm), a large planar area (theoretically 2630m^2/g for single-layer graphene), an excellent ability to quench fluorescence, ease of functionalization, and optical properties [14]. Small molecules such as glucose, nicotinamide, dinucleotide adenine, adenine triphosphate, hydrogen peroxide, estrogen was detected by GBNs biosensors [15-17]. In addition, macromolecules, such as biomarkers to diagnose the disease, were detected by GBNs biosensors. Several studies showed that the nanocomposites of GBNs with metal nanoparticles, auxiliary biomolecules (chitosan), and bioenzyme (horseradish peroxidase) catalyze glucose enzymatic reaction with high efficiency for electrochemical sensing due to their enhanced electronic and synergistic compositions [18-20]. An enzyme-immobilization matrix based on GO was reported Zhang et al. [21]. Their results illustrated that enzyme immobilization on GO sheets can take place readily without use of any cross-linking reagents or additional surface modification. GO has a large specific surface area and is abundant in oxygen-containing groups, therefore an enzyme can be bound to its surface through a condensation reaction between the terminal amino groups of the enzyme and the carboxyl groups on GO. More notably, enzymes retain their structural integrity and biological activity when they are bonded to GO [22]. Graphene was used as both a modification material and a carrier for establishing a better immunosensor by Liu et al. [23]. A simple sonication-induced nano-assembly generation method was used to fabricate a hybrid system of AuNP/poly (diallyldimethylammonium chloride)-PDDA/GO immunosensor [23]. This system showed great sensitivity, with a detection limit of 0.05ng/ml. A fluorescence immunosensor for pathogen detection was developed by Jung et al. [24]. The gold nanoparticles (AuNPs), which act as energy acceptors, were linked to a secondary antibody through a 100-mer ssDNA molecule. The AuNPs on the GO surface quenched the fluorescence.

GO has been explored for bioimaging, due to its unique properties, such as biocompatibility, ready cellular uptake, flexible chemical modifications, and optical properties. A functionalized graphene was utilized as an *in vitro* and *in vivo* imaging probe by introducing fluorescent molecules to GO [2]. Besides fluorescence imaging, Magnetic Resonance Imaging (MRI) is also a powerful *in vivo* and non-invasive imaging technique that has been widely used in clinical practice [25]. Chen W et al. [26] have used aminodextran coated Fe_3O_4 nanoparticles immobilized onto GO, to enhance the biocompatibility and the cellular MRI. Their results showed that the Fe_3O_4 -GO composites exhibited significantly enhanced cellular MRI signal compared with isolated Fe_3O_4 nanoparticles.

Cancer therapy

Over the past decade, the usage of nanomaterials for cancer treatment has been a popular research focus. Nanomaterials, such as Graphene-Based Nanomaterials (GBNs), have been used for cancer cell imaging, chemotherapeutic drug targeting, chemotherapy, photothermal therapy, and photodynamic therapy. Phototherapy, including Photothermal Therapy (PTT) and Photodynamic Therapy (PDT), can control disease by specific light irradiation [2]. Recently, the concept of targeted nanoparticles in cancer therapy and *in vivo* biocompatibility of graphene-based nanomaterials were summarized by Sharma et al. [27]. They have provided a comprehensive review of detail chemistry and properties of GO and provide of functionalized GO and GO-metal nanoparticle composites in nanomedicine involving anticancer drug delivery and cancer treatment [27]. Hyaluronic Acid (HA)-Modified Nanographene (NGO) composite was synthesized for the targeted delivery of epirubicin by Jung et al. [28]. Their results showed that NGO–HA–epirubicin combination can be effectively applied for the treatment of tumours overexpressing HA receptors. Furthermore, innovative redox-responsive nanocarrier system based on GO–HA was synthesized by Liu et al. [29]. They have synthesized HA–SS–NH_2 complex via the reaction of activated HA with cystamine dihydrochloride containing disulfide bonds (SS) [29]. The NGO–SS–HA complex showed specific binding to cancer cells and exhibited redox-responsive cargo release in tumor cells overexpressing GSH.

Summary and Future Perspectives

It is apparent that the unique structures of Graphene-Based Nanomaterials (GBNs) and its fascinating properties and functionalization have raised a great interest and provided more routes for the research and development in their applications in biomedical area in recent years. Surface-functionalized GO has become a popular nanocarrier, specifically for targeted drug delivery systems and cancer therapy. We have selectively reviewed the rapid and exciting advances in the biomedical applications of GBNs with focus on drug/gene delivery, antibacterial activity, biosensing, bioimaging, cancer therapy, made in the last few years. This trend, we believe, will continue, and even speed up in the years to come. In summary, graphene and its derivatives emerge as a novel nanomaterial platform for biomedical applications, yet we believe that it's worth to have more effective studies in computational simulations of GBNs need to be examine for the efficacy of GBNs in clinical trials.

References

1. Shim G, Kim MG, Park JY, Oh YK (2016) Graphene-based nanosheets for delivery of chemotherapeutics and biological drugs. Adv Drug Deliver Rev 105(Pt B): 205-227.
2. Yang Y, Asiri AM, Tang Z, Du D, Lin Y (2013) Graphene based materials for biomedical applications. Mater Today 16(10): 365-373.
3. Shareena TPD, McShan D, Dasmahapatra AK, Tchounwou PB (2018) A review on graphene-based nanomaterials in biomedical applications and risks in environment and health. Nano-Micro Lett 10(3): 53.
4. Banerjee AN (2018) Graphene and its derivatives as biomedical materials: future prospects and challenges. Interface Focus 8(3): 20170056.
5. Li C, Wang J, Wang Y, Gao H, Wei G, et al. (2019) Recent progress in drug delivery. Acta Pharm Sin B 9(6): 1145-1162.
6. Hoseini-Ghahfarokhi M, Mirkiani S, Mozaffari N, Abdolahi Sadatlu MA, Ghasemi A, et al. (2020) Applications of graphene and graphene oxide in smart drug/gene delivery: Is the world still flat? Int J Nanomedicine 15: 9469-9496.
7. Goenka S, Sant V, Sant S (2014) Graphene-based nanomaterials for drug delivery and tissue engineering. J Controlled Release. 173: 75-88.
8. Lu CH, Yang HH, Zhu CL, Chen X, Chen GN (2009) A graphene platform for sensing biomolecules. Angewandte Chemie Int Ed Engl 48(26): 4785-4787.

9. Zhang L, Xia J, Zhao Q, Liu L, Zhang Z (2010) Functional graphene oxide as a nanocarrier for controlled loading and targeted delivery of mixed anticancer drugs. Small 6(4): 537-544.

10. Kumar P, Huo P, Zhang R, Liu B (2019) Antibacterial properties of graphene-based nanomaterials. Nanomaterials (Basel) 9(5): 737.

11. Tu Y, Lv M, Xiu P, Huynh T, Zhang M, et al. (2013) Destructive extraction of phospholipids from *Escherichia coli* membranes by graphene nanosheets. Nat Nanotechnol 8(8): 594-601.

12. Li J, Wang G, Zhu H, Zhang M, Zheng X, et al. (2014) Antibacterial activity of large-area monolayer graphene film manipulated by charge transfer. Sci Rep 4: 4359.

13. Pham VT, Truong VK, Quinn MD, Notley SM, Guo Y, et al. (2015) Graphene induces formation of pores that kill spherical and rod-shaped bacteria. ACS Nano 9(8): 8458-8467.

14. Du D, Yang Y, Lin Y (2012) Graphene-based materials for biosensing and bioimaging. MRS Bulletin 37(12):1290-1296.

15. Jana A, Scheer E, Polarz S (2017) Synthesis of graphene-transition metal oxide hybrid nanoparticles and their application in various fields. Beilstein J Nanotechnol 8: 688-714.

16. Lin J, Chen X, Huang P (2016) Graphene-based nanomaterials for bioimaging. Adv Drug Deliver Rev 105(Part B): 242-254.

17. Wu P, Qian Y, Du P, Zhang H, Cai C (2012) Facile synthesis of nitrogen-doped graphene for measuring the releasing process of hydrogen peroxide from living cells. J Mater Chem 22(13): 6402-6412.

18. Lin D, Wu J, Ju H, Yan F (2014) Nanogold/mesoporous carbon foam-mediated silver enhancement for graphene-enhanced electrochemical immunosensing of carcinoembryonic antigen. Biosens Bioelectron 52: 153-158.

19. Nguyen KT, Zhao Y (2014) Integrated graphene/nanoparticle hybrids for biological and electronic applications. Nanoscale 6(12): 6245-6266.

20. Tian J, Huang T, Wang P, Lu L (2015) God/hrp bienzyme synergistic catalysis in a 2-D graphene framework for glucose biosensing. J Electrochem Soc 162(12): B319-B325.

21. Zhang JL, Zhang F, Yang HJ, Huang XL, Liu H, et al. (2010) Graphene oxide as a matrix for enzyme immobilization. Langmuir 26(9): 6083-6085.

22. Pumera M, Scipioni R, Iwai H, Ohno T, Miyahara Y, et al. (2009) A mechanism of adsorption of beta-nicotinamide adenine dinucleotide on graphene sheets: experiment and theory. Chem Eur J 15(41): 10851-10856.

23. Liu K, Zhang JJ, Wang C, Zhu JJ (2011) Graphene-assisted dual amplification strategy for the fabrication of sensitive amperometric immunosensor. Biosens Bioelectron 26(8): 3627-3632.

24. Jung JH, Cheon DS, Liu F, Lee KB, Seo TS (2010) A graphene oxide based immuno-biosensor for pathogen detection. Angew Chem Int Ed Engl 49(33): 5708-5711.

25. Pohlmann A, Cantow K, Hentschel J, Arakelyan K, Ladwig M, et al. (2013) Linking non-invasive parametric MRI with invasive physiological measurements (MR-PHYSIOL): towards a hybrid and integrated approach for investigation of acute kidney injury in rats. Acta Physiol 207(4): 673-689.

26. Chen W, Yi P, Zhang Y, Zhang L, Deng Z, et al. (2011) Composites of aminodextran-coated Fe3O4 nanoparticles and graphene oxide for cellular magnetic resonance imaging. ACS Appl Mater Interfaces 3(10): 4085-4091.

27. Sharma H, Mondal S (2020) Functionalized graphene oxide for chemotherapeutic drug delivery and cancer treatment: A promising material in nanomedicine. Int J Mol Sci 21(17): 6280.

28. Jung HS, Lee MY, Kong WH, Do IH, Hahn SK (2014) Nano graphene oxide–hyaluronic acid conjugate for target specific cancer drug delivery. RSC Adv 4: 14197-14200.

29. Liu J, Zhang D, Lian S, Zheng J, Li B, et al. (2018) Redox-responsive hyaluronic acid-functionalized graphene oxide nanosheets for targeted delivery of water-insoluble cancer drugs. Int J Nanomed 13: 7457-7472.