Transactions on Materials, Biotechnology and Life Sciences
ISSN: 2960-1932, eISSN: 2960-2319 | Volume 4
NSCBM 2024

Graphene-Based Nanomaterial and Its Applications as Drug Nanocarrier

Yucong Sun *

Department of Queen Mary University of London Engineering School, Northwestern Polytechnical University, Xi'an, China

* Corresponding Author Email: sycteresa@mail.nwpu.edu.cn

Abstract. Graphene-based nanomaterial can be used in many fields due to its excellent properties. Nowadays, it is widely used in drug delivery systems as nanocarriers due to its unique structure, large surface area, and biocompatibility. It can be more easily combined with other nanoparticles through modification. Cancer is a disease with a high mortality rate. It remains the top rank leading to death for many years. In order to treat cancer, using graphene and its derivatives as nanocarriers to transport medicine has become a popular strategy in recent years. In this review, several features of graphene-based nanomaterials were discussed firstly, which is the reason why graphene can be used as material carriers. Then, the functionalization of graphene materials using both covalent and non covalent methods was emphasized. Besides, specific examples of graphene as nano anti-cancer carriers were introduced. Moreover, the advantages and disadvantages of this kind of material were discussed. Finally, the potential research directions of graphene as a drug carrier in the future were discussed. This work will contribute to promoting the application of graphene based nanomaterials as drug nanocarriers.

Keywords: Graphene-based nanomaterial; drug delivery systems; anticancer nanocarrier.

1. Introduction

Drug delivery Systems (DDSs) are critical to drug therapy. Many drugs have been successfully used in the treatment of disease. Drug delivery technologies can enhance on-target delivery and minimize off-target effects. Traditional medicine delivery methods have a long treatment cycle and is toxic to the non-target area [1]. Therefore, new techniques were explored to improve the DDSs. The development of nanotechnology had a huge impact on the medical field. Plenty of experiments and studies have shown that nanomaterials would help to improve the shortcomings of traditional drug delivery systems. Nanoparticles (NPs) are considered to be useful materials for physiochemical delivery due to their outstanding properties. These nanoparticles exhibit more attachment points on the surface, which makes them move quickly and have good biocompatibility. Besides, the biochemical properties of nanoparticle drug carriers can be greatly released due to the improvements in the permeability of the membrane [2].

Graphene is a nanomaterial with a monolayer of graphite and has a perfect two-dimensional honeycomb structure. Graphene-based nanomaterials have attracted a great number of attentions among the carbon-based materials. The unique structure endows this material with unique physical and chemical properties. Due to the structural differences, many different substances are derived from graphene, such as graphene quantum dots, fullerene, carbon nanosheets, three-dimensional graphite, carbon nanotubes, etc. With the introduction or reduction of oxygen and other functional groups, graphene can form other substances, including graphene oxide (GO), and reduced graphene oxide (rGO) [3].

The modified graphene-based material could provide medications more stable and effectively compared to non-modified graphene. Many investigations have been conducted concerning with the reactive oxygen species (ROS) induction potential, substantial carrier capacity, and simplicity of function. It is proved that modified graphene-based material are suitable options for targeted delivery. Therefore, it is of great significance to explore the application of graphene materials in drug carriers.

This work summarizes the typical properties of graphene and its derivatives. In addition, applications of graphene as drug delivery carriers are also be introduced, especially for anticancer therapy.

2. Features of Graphene-based Material

2.1. Antibacterial Feature

Graphene, which is the toughest and lightest substance, is made of a thin single sheet of carbon atoms arranged in a honeycomb structure. The antibacterial characteristics of graphene have successfully been explained by numerous types of research including oxidative and membrane stress. The graphene is toxic to the bacteria because its ROS deactivates the bacteria's structure. Besides, graphene can remove the electrons from the surface of bacteria, and it has acuate edges which can harm the membranes physically. These all contribute to the antibacterial properties of graphene. In 2010, scientists demonstrated that GO and rGO are also antibacterial. These materials need time and a certain amount of concentration to reveal the antibacterial effect [4]. Besides, the antibacterial properties are proved to be enhanced with relative smaller size and more chemical functional groups. Furthermore, it is illustrated that the generated ROS by GO can produce oxidative stress, which could inhibit the growth of bacteria. This is demonstrated by the high antibacterial activity of the GO-loaded PMMA nanocomposite against E. coli [5].

Numerous functionalization and surface modification have been conducted to increase the antibacterial activity of graphene. Besides, photocatalytic functionalization can also prevent aggregation of graphene and improve antibacterial activity.

2.2. Surface Feature

Many features have made the graphene-based material widely used in various applications, which include the large surface area. The huge surface area makes graphene-based materials easy to absorb other substances like drugs or functional groups. 2D structure of graphene is thought to be made up of σ bonds holding sp^2 hybridization carbon atoms together. Therefore, delocalized electrons can be found within the graphene. Consequently, in a graphene structure, electrons are free to change their position. Since GO has functional groups on the outside of the structure, it shows both hydrophilic and hydrophobic properties. It can absorb chemical molecules at the hydrophobic side since the π–π conjugated system can make the connection with them. At the same time, it can attach to biomolecules such as proteins and other functional groups due to the hydrophilic group on the other side of the surface. rGO has less surface charge, hydrophilicity, and oxygen content than GO. This allows for improvements in optical absorption, electrical conductivity restoration, and a flat area for substance attaching [6].

3. Modification of Graphene-based Nanomaterials as Drug Carriers

It can be known that due to the π–π stacking and high surface area, other functional groups and biomacromolecules can be conjugated on the graphene-based nanomaterials. This phenomenon allows graphene and its derivatives to be used as bioactive agents. Due to the -OH and -COOH groups on the surfaces of GO, other chemical structures are also tending to be adsorbed. Therefore, the needed drugs combined with graphene-based material directly. This process is simple, and it has a relatively higher drug-loading ability. On the other side, it is difficult to regulate the presence and properties of the end products. To enhance the stability of graphene-based materials, functionalized graphene was explored. Among all the methods, covalent and non-covalent processes are the most common way to format functionalized graphene.

3.1. Covalent Modification Methods

The modification of chemotherapy medications with graphene-based material will improve the bio-distribution and refine extravasation volume. The time of blood flow in the vessels would be

prolonged. In addition, an additional definite method of drug transport could be proposed. Moreover, chemosensitizer could also be produced. This modified graphene-based material exhibit numerous advantages [7]. One of the most comprehensive techniques for functionalizing graphene-based nanomaterial is covalent modification, which typically involves the introduction of groups containing oxygen and double bonds. One effective covalent modification technique is amidation. Besides, GO sheets can also be grafted with polymers via nucleophilic substitution, such as PEG, PVA, and PEI. This can enhance the hydrophilicity of graphene-based material, promote dispersibility for drug delivery [8]. Another technique for covalent modification is the free radical reaction. Furthermore, adding epoxy groups or using certain materials can also be used for covalent formation.

3.2. Non-Covalent Modification Methods

Graphene-based material can also be modified by using non-covalent techniques. The non-covalent modification process can increase the dispersion stability of graphene by using π–π stacking and hydrogen bonding. It can also use chemical agents that attach to the ionic atoms to fabricate the nanomaterial. Non-covalent surface alteration is opposed to the covalent adjustment method. It can guarantee that the structure of graphene-based materials is preserved. The most commonly used non-covalent modification pathway is the interaction between π-π bonds. By using the π-π interaction, modified groups are evenly distributed over the graphene surface in the epoxy solution. Strong cross-linking occurs between them. Both organic and inorganic components will be adsorbed by this type of interaction. Besides, other non-covalent modifications are also widely used. For example, polyelectrolytes can be absorbed on the surface of GO by electrostatic forces due to the presence of carboxyl groups. Chitosan-functionalized GO has been employed as the carrier of 5-fluorouracil and ibuprofen [9]. Doxorubicin (DOX) has also been placed onto graphene nanosheets which are functionalized with gelatin via the physisorption approach [10].

4. Applications for Graphene-based Nanomaterials as the Nanocarriers of the Anti-cancer Drugs

Cancer is a major cause of human mortality, even though tremendous progress in customized therapy have been made. The development of nanocarriers that can transport anticancer medications specifically and efficiently is one of the strategies that is now gaining a lot of attention. Graphene-based materials exhibit great potential as nanocarriers in this regard because they present high biocompatibility and capacity in loading drugs. The following examples introduce the applications of graphene-based nanomaterials in different kinds of anticancer drug delivery systems.

Graphene-based material functionalized with PEG is widely used in anticancer medication delivery methods. PEG-decorated GO was reported by Liu et al. as a useful agent that can deliver anticancer medications effectively [11]. By attaching PEG with graphene, the biocompatibility of this material was enhanced. Moreover, the effective duration of the drug is improved. This effect is achieved by using noncovalent connections to transport hydrophobic anticancer drugs. When compared to free medicines, this compound demonstrated greater cellular absorption and anticancer activity. It is reported that fabricating the rGO using the phospholipid-based amphiphilic polymer contribute to the transfection of small interfering RNA (siRNA). Compared to free small interfering RNA, the produced nanocarrier could distribute the RNA without enzymatic degradation. The altered GO might also be used as a nanocarrier to introduce siRNA into cells. The presence of the siRNA gene decreased the growth of the tumor. As a result, it is recommended to use this nanosystem to deliver the genes and stop the desired gene expression.

Graphene-based materials can also be used for targeted drug delivery. Targeting agents are affixed to nanocarriers as part of the design process. After being modified, the graphene-based material can be used to deliver therapeutic agents. Ashjaran et al. have designed a fluorouracil loaded graphene oxide nanohybrid (GO/NHs) [12]. This functionalized material was used as a nanocarrier and its relevant properties were tested in MCF7 breast cancer cells, such as cytotoxicity and apoptosis. The result of

those tests demonstrated that GO/NHs is biocompatible. The dose of fluorouracil could be reduced without affecting its efficacy. This implies that GO/NHs may be employed as a medication delivery nanocarrier for the therapy of breast cancer. It is also an effective delivery method by mediating HN-1 on graphene oxide nanomaterial through hydrogen bonding and π-π bonding. It can be used to deliver doxorubicin to target and cure oral squamous cell carcinoma [13]. The used doxorubicin had higher uptake and aggressiveness in OSCC cells, compared to the unused NGO-based doxorubicin. Fabricating hyaluronic acid (HA) with GO and then targeting it into cancer cells is another application. Coloading paclitaxel (Ptx) and doxorubicin onto GO with HA functionality (GO-HA) resulted in a drug delivery system that can inhibit cancer cells effectively [14]. A different targeted drug delivery technique called DA-nGO was developed based on dopamine (DA) functionalization. The anticancer medication methotrexate can be delivered to the target cells effectively when it is prepared with the help of this material.

5. Conclusion

The drug delivery system has been greatly improved with the modification of graphene. Graphene can be formatted with other functional groups due to the honeycomb structure and π–π stacking. Complex substances can be delivered through the modification of graphene. This expands the use of graphene-based nanomaterial. These materials can be used in anticancer drug delivery which provides a more effective way for target treatment. In this work, several features of graphene and its derivatives were discussed. Covalent and non-covalent fabrication methods are highlighted. In addition, the method which they can been used in the cancer-curing is also provided. Although graphene-based materials have lots of advantages, there are also some limitations. The cytotoxicity of the graphene-based material should be further investigated in the future. Improving the safety of graphene as a drug carrier will contribute to its clinical application.

References

[1] Afzal O, Altamimi ASA, Nadeem MS, Alzarea SI, Almalki WH, Tariq A, Mubeen B, Murtaza BN, Iftikhar S, Riaz N, Kazmi I. Nanoparticles in Drug Delivery: From History to Therapeutic Applications. Nanomaterials, 2022, 12(24): 4494-4521

[2] Jampilek J, Kralova K. Advances in Drug Delivery Nanosystems Using Graphene-Based Materials and Carbon Nanotubes. Materials, 2021, 14(5): 1059-1099

[3] Jeong, W.Y., Choi, H.E. and Kim, K.S. Graphene-based nanomaterials as drug delivery carriers. Multifaceted Biomedical Applications of Graphene. Advances in Experimental Medicine and Biology, 2022, 1351:109-124.

[4] Gungordu Er S, Edirisinghe M, Tabish TA. Graphene-Based Nanocomposites as Antibacterial, Antiviral and Antifungal Agents. Adv Healthc Mater. 2023, 12(6): 2201523.

[5] Matharu RK, Tabish TA, Trakoolwilaiwan T, Mansfield J, Moger J, Wu T, Lourenço C, Chen B, Ciric L, Parkin IP, Edirisinghe M. Microstructure and antibacterial efficacy of graphene oxide nanocomposite fibres. Journal of colloid and interface science, 2020, 571: 239-252.

[6] Liu, L. et al. Recent progress of graphene oxide-based multifunctional nanomaterials for cancer treatment. Cancer nanotechnology, 2021, 12(1): 1-31.

[7] Renu Saharan et al. Exploring graphene and its potential in delivery of drugs and biomolecules. Journal of Drug Delivery Science and Technology, 2023, 84(1): 104446.

[8] Lai WF, Wong WT. Use of graphene-based materials as carriers of bioactive agents. Asian J Pharm Sci, 2021, 16(5): 577-588.

[9] Zaiki Y, Iskandar A, Wong TW. Functionalized chitosan for cancer nano drug delivery. Biotechnol Advances, 2023, 67:108200.

[10] Mousavi, S.M., Babazadeh, M., Nemati, M. et al. Doxorubicin-loaded biodegradable chitosan-graphene nanosheets for drug delivery applications. Polymer Bulletin, 2022, 79: 6565–6580.

[11] Pei X, Zhu Z, Gan Z, Chen J, Zhang X, Cheng X, Wan Q, Wang J. PEGylated nano-graphene oxide as a nanocarrier for delivering mixed anticancer drugs to improve anticancer activity. Sci Rep, 2020, 10(1): 2717-2732.

[12] Li Q, Wen J, Liu C, et al. Graphene nanoparticle based self-healing hydrogel in preventing postoperative recurrence of breast cancer. ACS Biomater Sci Eng, 2019, 5(2): 768-779.

[13] Li, R., Wang, Y., Du, J. et al. Graphene oxide loaded with tumor-targeted peptide and anti-cancer drugs for cancer target therapy. Sci Rep, 2021, 11(1): 1725-1735.

[14] Sattari S, Adeli M, Beyranvand S, Nemati M. Functionalized Graphene Platforms for Anticancer Drug Delivery. International Journal of Nanomedicine, 2021, 16: 5955-5980.