Graphene Based Materials: Opportunities and Challenges in Nanomedicine

Abbreviations: GO: Graphene Oxide; rGO: Reduced Graphene Oxide; RNA: Ribonucleic Acid; siRNA: Small interfering RNA; DNA: Deoxyribonucleic acid; NIR: Near Infrared; NSC: Neural Stem Cell

Editorial

Volume 2 Issue 4 - 2015

Valentinas Snitka*

Kaunas University of Technology, Lithuania

***Corresponding author:** Valentinas Snitka, Research Center for Microsystems and Nanotechnology, Kaunas University of Technology, Studentu str. 65, Kaunas, Lithuania, Tel: +37037451588; Email: vsnitka@ktu.lt

Received: October 19, 2015 | **Published:** October 29, 2015

Editorial

Advances in nanoscience and nanotechnology, enabling the synthesis of new nanomaterials, development of the new nanoanalytical methods and devices, opened a number of new directions in a future medicine. New carbon materials are on the top of the list today. Carbon materials are known to be more environmentally and biologically friendly than inorganic materials and it is one of the most common elements in our ecosystem. In particular, graphite is a naturally occurring material, thus, it can be expected that graphene, a single layer of graphite, will be safe and useful for biological purposes. Graphene, a two-dimensional (2D) sheet of sp2-hybridized carbon atoms packed into a honeycomb lattice, has led to an explosion of interest in the field of materials science, physics, chemistry and biotechnology since the Andre Geim and Konstantin Novoselov, the researchers behind the discovery from the University of Manchester, were awarded the Nobel Prize in Physics in 2010 and as of 2014, the global market of graphene is reported to have reached $9 billion with the market predicted to expand further to roughly $100 billion. Aside from electronics [1], energy applications graphene due to its unique properties has attracted much attention in the scientific community for numerous potential applications in biotechnology, including biosensing, disease diagnostics, antibacterial and antiviral materials, cancer targeting and photothermal therapy, drug delivery, electrical stimulation of cells and tissue engineering [2-4].

Drug delivery

The capabilities to produce and manipulate object sizes in nanometer ranges were available only since last decade, there has been tremendous interest in the use of nano objects for more efficient methods of drug delivery. It has been reported that nanostructures have the ability to protect drugs from degradation, allow their target delivery, increase bioavailability, etc. [5-6]. The key to understanding the potential of nano objects as drug delivery carriers is that their minute size, smaller than cells and cellular organelles, allow them to penetrate basic biological structures, disrupting their abnormal functions. In the midst of a wide diversity of nanostructured drug delivery systems, graphene based architectures initially were envisaged as abnormal case keeping in mind their different nature in respect to biomolecules or cellular substructures.

However, it was found that graphene and especially its oxidized modification, graphene oxide, can be highly optimized for their specific functions in vivo and possess features that are often desired in drug delivery carriers. In biomedical applications and nanomedicine, GO have been utilized over existing drug delivery vectors due to their ability to cross cell membranes easily and their high surface area, which provides multiple attachment sites for drug targeting. Graphene oxide (GO) is a flexible two-dimensional carbon layer with oxygen-containing functional groups (epoxy, hydroxyl and carboxyl) – on the basal plane and at the edges. For drug delivery system GO branched by appropriate side substitutes represent a set of features like good solubility and stability in physiological solutions, also a unique ability of graphene structure to attach and deliver aromatic, water insoluble drugs. The first step to use graphene oxide as a drug delivery carrier is a functionalization of GO with functional molecule, particle, etc. [7]. GO can be successfully functionalized through its functional groupsusing both covalent bonding or via weak, non-covalent π–π stacking. In particular, GO was effectively functionalized with anticancer drugs like doxorubicin and porphyrins, as well, were successfully linked with graphene or GO via both π–π stacking and covalent bonding between amino and carboxyl groups [8].

Gene delivery

Non-viral gene therapy is a new way to treat various diseases caused by genetic disorders. However, the lack of efficient and nonmutagenic vectors or gene vehicles, make this technique unpredictable [9] and many researchers are looking for the synthetic vectors [10]. It has been shown that GO derivatives can improve the penetration of siRNA or plasmid DNA into cells protecting DNA from enzyme cleavage.Moreover, the cytotoxicity of cationic polyethylenimine is significantly reduced after complexation or conjugation with GO [11]. Additionally, graphene is absorbing near infrared (NIR) light with high efficiency and localized heating increase the uptake against cancer cells.

Photodynamic therapies

The strong optical absorbance of graphene-based nanoma¬terials in the NIR region makes them generally applicable as prognostic, diagnostic and therapeutic agents in the treatment of cancer and other disease states. The easy conjugation of graphene and GO with porphyrins makes

the graphene based materials as an attractive platform for photodynamic therapy of cancer [12].

Graphene for biosensing

rGO can be successfully used in order to develop highly efficient electrochemical and biological sensors thanks to their different functionalities which can be designed to be very sensitive to small changes in the chemical or biological environment. The responses have been obtained essentially by changes in conductivities, capacities or spectral changes. It was demonstrated the possibility to detect the glucose, nicotinamide adenine dinucleotide, haemoglobin, cholesterol, ascorbic and uric acid, dopamine, heavy metal ions and DNA [13]. In all these cases, the biosensors performed well with low working potentials, high sensitivities, low detection limits and long-term stabilities.

Tissue engineering

The development of highly organized and functional 3D complex scaffolds in vitro is of great importance in tissue engineering since native tissues and organs exhibit highly organized and multifunctional architectures composed of extracellular matrix, different cell types and chemical and physical signalling clues.It was demonstrated that fibrin-graphene hydroxyapatite was an excellent platform for osteoblast cell growth and maturation, showing very high viability rates compared with GO and functionalized graphene oxide [14]. In [15] have been reported that graphene sheets can support the required growth and differentiation of neural stem cell (NSC). The novel technique uses three-dimensional (3D) porous graphene foam. Provided that graphene foam can not only house the NSCs, but also control them electrically, itstands in competition with existing substrates for neural cell based therapy like glass or polymerpolydimethylsiloxane.

Toxicity

However, with the expanding use of GO in biomedical applications, a broader understanding of its toxicology is of high importance. Recently, several in vitro and in vivo studies examined the toxicity of GO. Both in vitro and in vivo studies have demonstrated the toxic effects of graphene oxide (GO). It is known that the cytotoxicity of GO appears because of physical damage to the cell plasma membrane [16] or the interaction of GO with toll-like receptor that may be the predominant molecular mechanism for GO induced macrophagic necrosis. However, the molecular basis for translocation and toxicity of GO is still largely unclear. Research results presented by different authors suggest that intracellular localization and impact of GO on viability of different cell types can vary with experimental conditions [17]. So, for the successful application of GO in nano-medicine the knowledge of the influence of GO on the viability of various cells and the search for the ways to reduce the toxicity of GO still remains an unsolved problem. One of the ways, which is also under investigation, is coating of nanoparticles with proteins. If the nanoparticles are pre-coated with proteins (protein corona is formed) the cytotoxicity is reduced. Albumin is one of the plasma proteins that bind to nanoparticles [18].

Conclusion

To date, the exploitation of graphene materials for nanomedicine applications remains at its infancy. Could graphene bring solutions to the challenges faced by the current nanomedicines and offer an efficient platform for theranostics and synthetic biology? Without major breakthrough, the answer to this question is quite challenging [7]. To solve the graphene solubility and aggregation problems which are the main challenge for the conjugation of graphene with therapeutically active molecules or active biological components, chemical functionalisation of graphene sheets or application of rGO may be the way to address these concerns

References

1. Novoselov KS, Geim AK, Morozov SV, Jiang D, Katsnelson MI, et al. (2005) Two-dimensional gas of massless Dirac fermions in graphene. Nature 438(7065): 197-200.
2. Chung C, Kim YK, Shin D, Ryoo SR, Hong BH, et al. (2013) Biomedical Applications of Graphene and Graphene Oxide. Accounts Chem Res 46(10): 2211-2224.
3. Hakimi M, Alimard P (2012) Graphene: Synthesis and Applications in Biotechnology-A Review. World Applied Programming 2(6): 377-388.
4. Dreyer DR, Todd AD, Bielawski CW (2014) Harnessing the chemistry of graphene oxide. Chem Soc Rev 43(15): 5288-5301.
5. Aggarwal P, Hall JB, McLeland CB, Dobrovolskaia MA, McNeil SE (2009) Nanoparticle interaction with plasma proteins as it relates to particle biodistribution, biocompatibility and therapeutic efficacy. Adv drug deliver Rev 61(6): 428-437.
6. Gao H, Yang Z, Zhang S, Cao S, Shen S, et al. (2013) Ligand modified nanoparticles increases cell uptake, alters endocytosis and elevates glioma distribution and internalization. Sci Rep 3: 2534.
7. Servant A, Bianco A, Prato M, Kostarelos K (2014) Graphene for multi-functional synthetic biology: The last 'zeitgeist' in nanomedicine. Bioorg Med Chem Lett 24(7): 1638-1649.
8. Grinceviciute N, Snopok B, Snitka V (2014) Functional two-dimensional nanoarchitectures based on chemically converted graphene oxide and hematoporphyrin under the sulfuric acid treatment. Chem Eng J 255: 577-584.
9. Whitehead KA, Langer R, Anderson DG (2009) Knocking down barriers: advances in siRNA delivery. Nat Rev Drug Discov 8(2):129-138.
10. Feng L, Zhang S, Liu Z (2011) Graphene based gene transfection. Nanoscale 3(3): 1252-1257.
11. Zhang LM, Lu ZX, Zhao QH, Huang J, Shen H, et al. (2011) Enhanced chemotherapy efficacy by sequential delivery of siRNA and anticancer drugs using PEI-grafted graphene oxide. Small 7(4): 460-464.
12. Rong P, Yang K, Srivastan A, Kiesewetter DO, Yue X, et al. (2014) Photosensitizer loaded nano-graphene for multimodal imaging guided tumor photodynamic therapy. Theranostics 4(3): 229-239.
13. Kuila T, Bose S, Khanra P, Mishra AK, Kim NH, et al. (2011) Recent advances in graphene-based biosensors. Biosens Bioelectron 26(12): 4637-4648.
14. Deepachitra R, Nigam R, Prohit SD, Thiagarajan H, Thotapalli PS (2014) In vitro study of hydroxyapatite coatings on fibrin

functionalized/pristine graphene oxide for bone grafting. Materials and Manufacturing Processes 30(6): 804-811.

15. Park SY, Park J, Sim SH, Sung MG, Kim KS, et al. (2011) Enhanced Differentiation of Human Neural Stem Cells into Neurons on Graphene. Adv Mater 23(36): H263-H267.

16. Hu W, Peng C, Lv M, Li X, Zhang Y, et al. (2011) Protein Corona mediated mitigation of cytotoxicity of Graphene Oxide. ACS Nano 5(5): 3693-3700.

17. Batiuskaite D, Grinceviciute N, Snitka V (2015) Impact of graphene oxide on viability of Chinese hamster ovary and mouse hepatoma MH-22A cells. Toxicol In Vitro 29(5): 1195-1200.

18. Zukiene R, Snitka V (2015) Zinc oxide nanoparticle and bovine serum albumin interaction and nanoparticles influence on cytotoxicity in vitro. Colloids Surf B Biointerfaces 135: 316-323.

Citation: Snitka V (2015) Graphene Based Materials: Opportunities and Challenges In Nanomedicine. J Nanomed Res 2(4): 00035. DOI: 10.15406/jnmr.2015.02.00035