Biomedical applications of graphene: from functionalisation to biodistribution and biodegradation

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Abstract

Since its isolation in 2004, graphene has emerged as a fascinating nanomaterial with unique structural, thermal, mechanical, optical, and electrical properties. Intensive research is ongoing to investigate applications of graphene and graphene oxide (GO) in many fields, including the development of nanoelectronic devices, nanocomposite materials, as well as in biotechnology and nanomedicine. Nevertheless, despite its high potential in various fields, major challenges still remain, in particular related to its low dispersibility in organic solvents and in water, which hampers full exploitation of some of its properties. To counteract this issue, rational functionalisation chemistry is needed to improve processability and impart graphene with novel properties. In this context, GO is an interesting platform for the design of graphene-based hybrid materials. The polar oxygen-containing functional groups of GO render it highly hydrophilic, resulting in a good dispersibility in water and many other solvents. In addition, the derivatisation of these oxygenated functions is a versatile and effective method to prepare chemically functionalised graphene for a wide range of applications. Due to the high reactivity of the oxygenated moieties, mainly epoxy, hydroxyl, and carboxyl groups, several derivatisation reactions may occur concomitantly. The reactivity of GO with amine derivatives has been exploited in the literature to design graphene-based conjugates, mainly through amidation. In this talk, I will report our investigations on the reactivity between GO and amine functions, which leads to ring opening of the epoxides, and not to amidation.[2] We also prove using magic angle spinning (MAS) NMR that there is a negligible amount of carboxylic acid groups in GO samples from different sources, hence eliminating the possibility of amidation reactions with amine derivatives.

The outstanding properties of GO and its large surface area offer a variety of opportunities for applications in the biomedical field, such as therapy, imaging, diagnosis, and regenerative medicine. Health impact, biopersistence, and environmental accumulation are key issues for the development of graphene-family nanomaterials in nanomedicine and other related areas. It is thus essential to assess their systematic toxicological effects before their use in different domains. In this context, I will present whole body imaging and pharmacokinetic data following intravenous administration of GO functionalised with a radionuclide in mice.[3] The results show that the thickness of GO is one of the key parameters influencing its pharmacological profile. Understanding human health risk associated with the rapidly emerging graphene-family nanomaterials represents a great challenge because of the diversity of applications and the wide range of possible ways of exposure to this type of materials.

I will also report our study on the biodegradation of GO by the human myeloperoxidase (MPO) derived from neutrophils.[4] It is fundamental to elucidate the key aspects associated with the biodegradability of graphene-family nanomaterials for their real translation into possible clinical innovations as well as for their safe disposal in the environment. The degradation capability of the enzyme on three different GO samples displaying a variable dispersibility in aqueous media has been compared, revealing that MPO failed in degrading the most aggregated GO sample, but succeeded to completely metabolise highly dispersed GO. I will also present our work on the derivatisation of GO with specific molecules able to enhance the catalytic activity of horseradish peroxidase, leading to accelerated degradation of GO.[5] The results demonstrate that functionalisation can modulate the enzymatic biodegradability of GO. Our finding will certainly help to guide further development of future biomedical applications using GO, for instance by designing biodegradable carriers for drug delivery.

References

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