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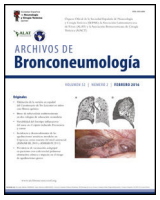

Editorial

[Translated article] Graphene and Lung

Grafeno y pulmón

Andrei Geim (1958) and Konstantin Novoselov (1974) are two Russian physicists based in Manchester, UK, whose discovery of graphene earned them the Nobel Prize in Physics in 2010. Graphene is an allotropic variant of carbon characterized by a single layer of carbon atoms in a hexagonal arrangement. It originates from graphite and was obtained in 2004 by simply separating the layers of graphite using ordinary sticky tape.[1] Since then, graphene has been hailed as the material of the present and the future. Its almost two-dimensional structure (the thickness of a carbon atom) makes it ultra-light and flexible, while its hardness is unmatched. It is also an excellent conductor of electricity, but does not retain heat. It has a myriad of applications in daily life, both in the world of communications and in construction.[2] Various medical applications have been proposed for graphene, mainly in the treatment of some types of cancer, as neuronal implants that facilitate auditory and visual nerve conduction, and bone or muscle substitutes, etc., but it is in the field of imaging and electromedicine where the greatest advances are envisaged. Recently, it has been used to line nasobucal masks, in the hope of adding antibacterial and antiviral activity to its qualities of resistance and tractability.[3]

Almost immediately after its discovery, numerous interactions with humans were described. In 2012, a review was published on the possible biological effects of graphene, highlighting its ability to interact with oxidation-reduction systems and the possibility of it generating granulomas and fibrosis.[4] After the publication of this review, greater attention was paid to the forms of presentation of graphene (few-layer graphene, ultrathin graphene, graphene oxide, micro- and nanographene, etc.), how it might penetrate the organism (by inhalation, implants, injections), and the analysis of its effects. The first experimental studies on the pulmonary consequences of graphene inhalation were published by Korean researchers,[5,6] who suggested that the potentially toxic effects in the lung correlate with the concentration and duration of contact. Rats that inhaled graphene oxide at low concentrations (<0.5 mg/m^3) over a few hours showed no evidence of pulmonary graphene uptake. Prolonged inhalation of graphene was traced in alveolar macrophages and lung lymph nodes, establishing a provisional toxicity index of over 1.88 mg/m^3. Final toxicity appears to be regulated by the ability of graphene oxide-reducing free radicals to bind to cell membranes. The mechanism of oxidative stress would be similar to that of other materials, precipitating the inflammatory response, aging and carcinogenesis. Other mechanisms, such as apoptosis, autophagy, necrosis or epigenetic changes, all capable of producing not only lung damage, but also liver and neuronal[7] damage, cannot be ruled out.

A review by Fadeel et al.[8] prompted the development of a database as part of a European project (www.graphene-flagship.eu) to study the beneficial and harmful effects of graphene on health. The potentially toxic mechanisms can be summed up as oxidative stress, inflammation, and carcinogenesis, always as a factor of concentration and the form of penetration. Lower doses do not induce toxicity, and higher doses may produce inflammation that resolves when exposure ceases. It has been emphasized that this mechanism depends not only on dose, but also on the reactivity and size of the inhaled particles. These graphene particles do not reach the pleural space and there are no signs of mesothelial tumor formation or granulomas, differentiating the mechanism clearly from asbestos or carbon nanotubes, which, in contrast, do appear in the pleural space and are responsible for mesothelioma.[9] The authors stress that the type of carbon derivatives used must be specified, that longitudinal toxicological studies must be conducted, and that modern transcriptomics, proteomics, and metabolomics tools must be applied to study the mechanisms that produce toxicity.

The potential toxicity of graphene and other nanoparticles on the respiratory system must be taken into consideration when these materials are used in different applications that involve their entry into the lung.[10] The effects will depend not only on the type of material inhaled, but also on the size of the molecules, their chemical state and whether the pulmonary defense mechanisms are exceeded. The level of susceptibility of each individual will be determined by the time period during which the autophagy mechanism is activated, depending on their personal situation (chronic or acute disease). According to the most recent toxicity studies, the key elements are the inhaled dose and whether autophagy mechanisms are exceeded, thus inducing cellular oxidative stress.[11]

Graphene, like other nanomaterials, has been used in numerous settings, many of which have been in the health sector. We will have to be vigilant about the use of these products and the routes by which particles can penetrate the respiratory system, but the information available to date appears to offset any pessimism. Indeed, the advantages seem to far outweigh the possible adverse effects.

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References

1. Novoselov KS, Geim AK, Morozov SV, Jiang D, Zhang Y, Dubonos SV, et al. Electric field effect in atomically thin carbon films. Science. 2004;306:666–9, http://dx.doi.org/10.1126/science.1102896.
2. Amor García M. Grafeno: biografía de un material [trabajo fin de grado en Filosofía]. Departamento de Historia de la Ciencia, UNED; 2017.
3. Palmieri V, Bugli F, Lauriola MC, Cacaci M, Torelli R, Ciasca G, et al. Bacteria meet graphene: modulation of graphene oxide nanosheet interaction with human pathogens for effective antimicrobial therapy. ACS Biomater Sci Eng. 2017;3:619–27, http://dx.doi.org/10.1021/acsbiomaterials.6b00812.
4. Sanchez VC, Jachak A, Hurt RH, Kane AB. Biological interactions of graphene-family nanomaterials: an interdisciplinary review. Chem Res Toxicol. 2012;25:15–34, http://dx.doi.org/10.1021/tx200339h.
5. Han SG, Kim JK, Shin JH, Hwang JH, Lee JS, Kim TG, et al. Pulmonary responses of Sprague-Dawley rats in single inhalation exposure to graphene oxide nanomaterials. Biomed Res Int. 2015;2015:376756, http://dx.doi.org/10.1155/2015/376756.
6. Kim JK, Shin JH, Lee JS, Hwang JH, Lee JH, Baek JE, et al. 28-Day inhalation toxicity of graphene nanoplatelets in Sprague-Dawley rats. Nanotoxicology. 2016;10:891–901, http://dx.doi.org/10.3109/17435390.2015.1133865.
7. Ou L, Song B, Liang H, Liu J, Feng X, Deng B, et al. Toxicity of graphene-family nanoparticles: a general review of the origins and mechanisms. Part Fibre Toxicol. 2016;13:57, http://dx.doi.org/10.1186/s12989-016-0168-y.
8. Fadeel B, Bussy C, Merino S, Vazquez E, Flahaut E, Mouchet F, et al. Safety assessment of graphene-based environment. ACS Nano. 2018;12:10582–620, http://dx.doi.org/10.1021/acsnano.8b04758.
9. Takagi A, Hirose A, Futakuchi M, Tsuda H, Kanno J. Dose-dependent mesothelioma induction by intraperitoneal administration of multi-wall carbonnanotubes in p53 heterozygous mice. Cancer Sci. 2012;103:1440–4, http://dx.doi.org/10.1111/j.1349-7006.2012.02318.x.
10. Di Cristo L, Grimaldi B, Catelani T, Vázquez E, Pompa PP, Sabella S. Repeated exposure to aerosolized graphene oxide mediates autophagy inhibition and inflammation in a three-dimensional human airway model. Mater Today Bio. 2020;6:100050, http://dx.doi.org/10.1016/j.mtbio.2020.100050.
11. Zhang L, Ouyang S, Zhang H, Qiu M, Dai Y, Wang S, et al. Graphene oxide induces dose-dependent lung injury in rats by regulating autophagy. Exp Ther Med. 2021;21:462, http://dx.doi.org/10.3892/etm.2021.

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