doi: http://dx.doi.org/10.11606/issn.1679-9836.v100i5p486-493 Rev Med (São Paulo). 2021 Sept-Oct;100(5):486-93.

Technological innovations in the post-pandemic period: an analysis of the graphene's antimicrobial property

Inovações tecnológicas no período pós-pandemia: uma análise da propriedade antimicrobiana do grafeno

Juliana Sabio Lira[1], Jorge Mauricio Bronze Batista Junior[1], Natália Moles dos Santos[1], Luiggi Cavalcanti Pessôa[2]

Lira JS, Batista Junior JMB, Santos NM, Pessôa LC. Inovações tecnológicas no período pós-pandemia: uma análise da propriedade antimicrobiana do grafeno / *Technological innovations in the post-pandemic period: an analysis of the graphene's antimicrobial property*. Rev Med (São Paulo). 2021 Sept-Oct;100(5):486-93.

ABSTRACT: Nanomaterials are emerging as possible solutions to contemporary public health challenges. Among these materials, graphene has received attention from the scientific community due to its properties and particularities, such as lightness, rigidity, thermal and electrical conductivity and, mainly, its antimicrobial potential. In the context of medicine, recent research addresses the application of this material in personal protective equipment, due to the containment in the transmission of potential viruses. During the coronavirus pandemic, graphene proved to be a material with considerable relevance for study; however, there is a lack of information in the literature that systematically uses the knowledge of this nanocomposite and its properties and applications specifically for the health area, in order to provide a thorough understanding of antimicrobial performance and attest to its biomedical employability. This study aims to contribute to a review of the literature of articles published in the last five years, using free access platforms as a database. The objective is to analyze and systematize the panorama of technological innovations of graphene in the scope of public health, identifying and investigating five main aspects: temporal evolution of publications, most relevant properties, forms of presentation of the graphene nanocomposite, possible effects of its application to human health, as well as the main obstacles. It was concluded that the number of articles published on the compound has increased significantly in recent years, especially in the year 2020, that the antimicrobial function stands out promisingly among the other functions addressed, in addition to the nanomaterial gaining notoriety due to its applicability in biosensors by enabling the recognition and elimination of pathogens, as well as therapeutic effects brought about by nanomedicines that use graphene as a carrier.

Keywords: Graphene; Nanocomposite; COVID-19; Anti-bacterial agents; Personal protective equipment; Biosensing techniques; Public health; Technological innovations.

RESUMO: Os nanomateriais estão emergindo como possíveis soluções para os desafios contemporâneos de saúde pública. Dentre esses materiais, o grafeno tem recebido atenção da comunidade científica devido às suas propriedades e particularidades, como a leveza, rigidez, condutibilidade térmica e elétrica e, principalmente, seu potencial antimicrobiano. No contexto da medicina, pesquisas recentes abordam a aplicação desse material em equipamentos de proteção individual, em função da contenção na transmissão de potenciais vírus. Em meio a pandemia do coronavírus, o grafeno revelou-se como um material com relevância considerável para estudo; no entanto, nota-se uma falta de informações na literatura que utilizem de forma sistematizada o conhecimento deste nanocomposto e suas propriedades e aplicações especificamente para a área da saúde, de modo que proporcione o entendimento aprofundado acerca do desempenho antimicrobiano e ateste a sua empregabilidade biomédica. O presente estudo visa contribuir com uma revisão da literatura de artigos publicados nos últimos cinco anos, utilizando como base de dados plataformas de livre acesso. O objetivo é analisar e sistematizar o panorama das inovações tecnológicas do grafeno no âmbito da saúde pública, identificando e investigando cinco principais aspectos: evolução temporal das publicações, propriedades mais relevantes, formas de apresentação do nanocomposto grafeno, possíveis efeitos de sua aplicação à saúde humana, assim como principais entraves. Dessa forma, uma revisão da literatura foi realizada nas bases de dados PubMed e SCOPUS entre agosto de 2020 e março de 2021 com os termos de busca "Graphene applications and medicine and antimicrobial". Os artigos incluídos são de livre acesso e foram publicados na língua inglesa, entre os anos de 2015 e 2021. Concluiu-se que o número de artigos publicados sobre o composto aumentou significativamente nos últimos anos, sobretudo no ano de 2020. A função antimicrobiana se destaca de forma promissora entre as demais funções abordadas, além do nanomaterial ganhar notoriedade em decorrência da sua aplicabilidade em biossensores ao possibilitar o reconhecimento e eliminação de patógenos, assim como efeitos terapêuticos trazidos pelos nanomedicamentos que utilizam o grafeno como carreador.

Palavras-Chave: Grafeno; Nanocomposto; COVID-19; Agentes antibacterianos; Equipamento de proteção individual; Técnicas biossensoriais; Saúde pública; Inovação tecnológica

1. Universidade Anhembi Morumbi. ORCID: Lira JS – https://orcid.org/0000-0002-5173-347X; Batista Junior JMB - https://orcid.org/0000-0002-0302-5487; Santos NM - https://orcid.org/0000-0002-0485-8392. E-mail: julianasabiolira@gmail.com, mauriciobronze@gmail.com, nataliamoless@gmail.com
2. Orientador, Universidade Federal da Bahia. https://orcid.org/0000-0001-5586-7187. Email: luiggi.pessoa@ufba.br
Endereço para correspondência: Juliana Sabio Lira. Rua Bela Cintra, 201 – apart. 71 A, Consolação. São Paulo,SP. CEP: 01415000. E-mail: julianasabiolira@gmail.com.

INTRODUCTION

In the last decade, graphene nanomaterial has gained a prominent position in the scientific community due to the particularities of the material and its favorable applications, involving the detection and destruction of infection-causing microorganisms, chemical and biomedical sensing, tissue engineering and bioimaging[1]. This graphite-derived compound is considered a two-dimensional material, as it has a thickness equivalent to one atom and a flat surface[2]. Furthermore, the hexagonal arrangement of the strong carbon bonds are also features that should be highlighted about the material. Its electronic structure results in properties that translate into greater mechanical resistance than steel[3], higher electronic mobility than silicon, higher thermal conductivity than copper[4], surface area greater than that observed for graphite and still a lighter material than many others[5]. The particularities and possible applications of the material have generated enthusiasm since its initial discovery in 2004[6] by researchers at the University of Manchester[7], this work earned them the Nobel Prize in Physics in 2010.

Graphene was the starting point for the synthesis of new 2D materials, materials that fit into the concept of industry 4.0. Conception that encompasses the current moment in a Fourth Industrial Revolution, where the evolution of information technology and its introduction in the production processes is transforming the traditional industry, taking it to a new level of organizational development. It is characterized by a set of technologies that allow the fusion of the physical, digital, and biological world. The benefits of these new technologies will be used in the development of equipment, systems and materials that can benefit society in general.

This nanocomposite, in addition to its resistance, conductivity and lightness properties, has a significant contact surface area, where 1.0 gram allows it to cover a surface of 2700 m^2[8]. Thus, there is the possibility that even when a single molecule enters contact with the surface of graphene, it can modulate its electrical properties, making nanomaterial a thorough biosensor[9]. These two-dimensional materials also stand out for their strong interaction with light: a single layer of graphene can absorb 2.3% of visible light incident[10]. This property becomes extremely relevant regarding the generation of heat and, consequently, the sterilization of materials, making the material potentially beneficial for applications in the medical-hospital environment.

Viruses are pathogens with the potential to destroy cells, tissues, and organs. The best way to prevent the population against viral diseases is through vaccination, a process that stimulates the body's own defense against specific infectious agents. However, the development and application of a vaccine is a complex process that requires time and study for a safe and effective result.

Coronaviruses belong to the Coronaviridae family, they are enveloped RNA viruses[11]. One of the main characteristics of coronaviruses concerns its ability to replicate in epithelial cells and pneumocytes in the lower respiratory tract in humans and, thus, cause pneumonia and, in severe cases, acute respiratory distress syndrome (ARDS)[12]. The available evidence to date shows that the transmission of the virus between humans occurs through close contact with respiratory droplets produced at the time of exhalation, during a sneeze or cough; by direct contact with infected people; or, more rarely, through contact with fomites[13-14]. Regarding the structure of this microorganism, it is possible to mention the presence of genomic material of simple positive sense RNA, directly assisting in protein synthesis, which occurs at a greater speed in the generation of new copies virus in the infected cell. The presence of envelope, membrane, nucleocapsid (which involves viral RNA) and the presence of Proteins Spike or Protein S, which is a glycoprotein spike.

The Spike protein is one of the most important components for the viral replication of SARS-CoV-2, given the relationship with the enzyme that facilitates the entry of the virus into the host cell, the angiotensin-converting enzyme 2 (ECA2)[15]. Efforts have been made in different parts of the world to create vaccines with the aim of neutralizing spike proteins and, consequently, preventing their interaction with ECA2. However, the appearance of new mutations in these proteins can hinder the advance of antibody production and lead to widespread ineffectiveness. In view of this, the procedure of breaking the envelope would be a valid measure in the fight against the virus.

Surfactant compounds, such as dodecyl sulfate, cause the rupture of the viral compartment[16] and have been widely explored for antiviral application, however, their toxicity and restricted use have made it necessary to investigate new materials. From the observation of new materials, graphene compounds are revealed as allies in the virus inactivation procedure, capturing pathogens through their electrostatic interaction, interaction with specific antibodies and ligands. The possibility of permanent virus inhibition by breaking the viral envelope by graphene-based platforms with a functionalized surface with polyglycerol sulphate and different sizes of aliphatic chains reinforces the role of graphene in combating viral infections[17]. The purpose of inhibition was studied at SARS-Cov-2, and it was found that the rupture of the viral envelope is the result of the presence of long alkyl chains[18].

The 2019 coronavirus pandemic (COVID-19) has turned into an alarming global public health problem mainly because, to date, there are no vaccines against all the mutations that COVID-19 can undergo [19], making it impossible to protect individuals through this medium. Due to the lack of an effective method of immunization and a high rate of transmissibility and mutability of the virus[20], the pandemic has brought urgency to the

development of alternative methods of individual and collective protection. With an exponential increase in cases of the disease and the lack of an effective pharmacological treatment, prophylactic measures were the main devices used to try to contain the progress of Sars-CoV-2[21]. It is possible to recognize that protective masks significantly reduce exposure to viruses and allow the reduction of its spread among the population[22]. However, in the context of the COVID-19 pandemic, contact with infected patients associated with the low availability of adequate personal protective equipment (PPE 's) collaborate for the highest incidence of disease among health professionals[23].

Data from the epidemiological bulletin made available by the Ministry of Health point to an increasing spread of the disease among health professionals, among the suspected cases, 21.4% were confirmed by COVID-19 in Brazil[24-25]. It is also estimated that approximately 21.07 % of the cases of SARS and 17.86% of MERS were in this category[26]. That said, it is of utmost importance that new studies be developed on materials with antimicrobial potential[27], so that in this way they can be applied to surfaces and equipment for the protection[28] of health professionals. health and population in general. Graphene, due to its antimicrobial properties and significant particularities, has been shown to be a promising material for wide use in Medicine, including the application in personal protective equipment.

OBJECTIVES

The aim of this work is to analyze and systematize the panorama of technological innovations of graphene in the scope of public health, identifying and investigating five main aspects: temporal evolution of publications, most relevant properties, forms of presentation of the graphene nanocompound, and possible effects of its application to human health.

METHODOLOGY

The present study is a literature review carried out from electronic databases, using PubMed and SCOPUS platforms for data collection. The search took place between August 2020 and March 2021, works in English, published between 2015 and 2021. The search terms consisted of "Graphene applications and medicine and antimicrobial". The inclusion criteria were works dated from 2015 to 2021, published in English, with free access in full in a database platform, original and review articles, clinical trials, multicenter and observational studies. Exclusion criteria were isolated chapters from books, theses and monographs, congress or conference proceedings, publications on non-institutional websites, works with animal studies and studies without applicability to the medical field or which did not address graphene's activity against microorganisms. 55 articles corresponding to the established criteria were reviewed.

RESULTS

Studies published between 2015 and 2021 revealed different presentations of graphene. As this nanocompound associates with another material, it will present a new property of interest. Only a minority of 5.7% of the works identified graphene in its pure form, while 34.3% of the works reported the use of graphene in its oxidized version (graphene oxide). On the other hand, the largest portion of 54.3% referred to the use of graphene associated with another nanocompound (eg silver, copper) and 5.7% reported the application of graphene quantum dots.

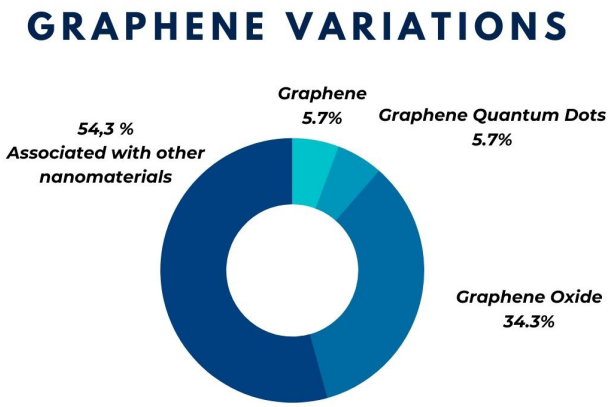

Figure 1 - The graph shows the proportions found in the reviewed articles of graphene variations

The properties addressed of the compound and its derivatives proved to be the most diverse, in 54.3% of the articles the main attribute of graphene was the antimicrobial property, 20% of the works brought the material as a potential instrument for the sensing and identification of microorganisms, 20% of the articles presented the therapeutic function as in nanomedicines and phototherapy and 5.7% brought other functions, such as the use of graphene in diagnostic methods.

Of the articles reviewed, 51.4% of graphene applications are aimed at use on surfaces and antimicrobial substances; 25.7% related graphene to the function of sensing microorganisms; 17.1% related the material to a drug-carrying substance and 5.7% linked graphene to other applications such as application in diagnostic methods and phototherapy.

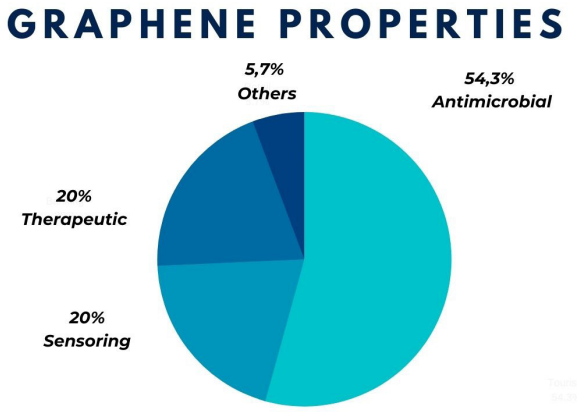

Figure 2 - The graph shows the proportions found in the articles reviewed for the properties of graphene, including the antimicrobial, sensing, therapeutic and other properties

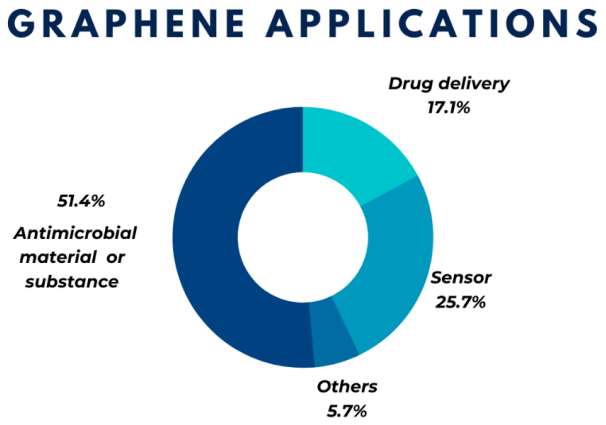

Figure 3 - The graph shows the proportions found in the revised articles of graphene applications

DISCUSSION

Temporal evolution of research

It is possible to notice a significant increase in the number of publications between 2015 and 2020, showing a progressive interest of the scientific community in developing and understanding the applications of the material in question. As it is a material with numerous relevant properties and a huge potential for application in new technologies for the healthcare area, its study has been increasingly recurrent and in-depth. This deepening aims not only to assimilate the particularities of graphene and identify possible negative effects, but also to reach the ideal applications so that the material's potential is explored in its magnitude.

An increase in the number of articles published each year was identified. In 2015, 2016 and 2017, 2, 6 and 15 articles were published, respectively. In the years 2018 and 2019, the number of articles was the same as in 2017; however, in 2020 there was a significant increase, with 37 articles published.

The conception of technological innovations about individual and collective protection materials against pathogens that still do not have a cure is necessary not only at the time of the pandemic, but in the long term, considering the medical-hospital environment as a priority.

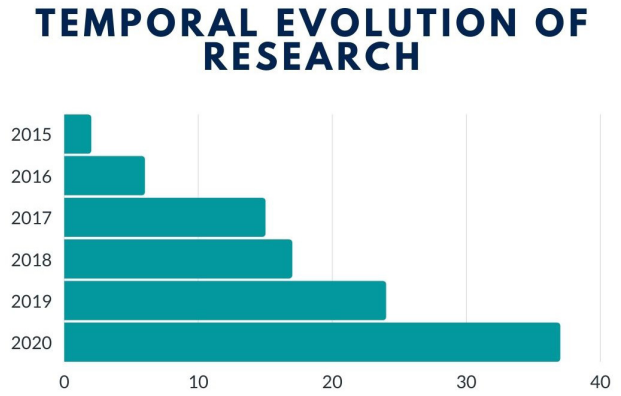

Figure 4 - The graph shows the temporal evolution of publications on the themes, in the platforms mentioned in methodology

Graphene Presentations

The different presentations of the nanocomposite are important to confer different properties depending on factors such as: association of graphene with other compounds such as zinc and silver oxide; compound size, among other conditions. From the conception of the material together with the scientific development, several methods for production and extraction have been developed and are continuously improved. Depending on the quality of the desired product and the application for which it is intended, one or more methods can be used. Some of the applied methods are thermal or chemical reduction, mechanical exfoliation, anodic bonding, ultrasonic cleavage, among others[29]. From these processes, different presentations of the material are obtained.

The presentation most frequently addressed in the available evidence concerns the association of graphene with other nanocomposites. This association proved to be favorable for combining the characteristics of graphene, important properties of other materials, enabling a more effective and multiple mechanism of action. The main associations found were graphene and / or graphene oxide, allied mainly to silver oxide and zinc oxide. Recent studies have shown that silver nanoparticles and zinc oxide associated with graphene oxide have a better

antimicrobial and antifungal action when compared to the use of graphene oxide alone. The bactericidal effect of graphene oxide with nano-silver is due to the destruction of the cell membrane and inhibition of cell division[30]. Zinc oxide nanoparticles, on the other hand, are a great resource for protein immobilization due to their high isoelectric point[31]. Graphene oxide compounds with various metal nanoparticles are attracting increasing interest due to their wide scope in biomedical applications.

The second most common presentation is graphene oxide. It is an oxidized carbon-based material that contains functional groups (such as carboxyl, hydroxyl, carbonyl, among others) so that this compound can be easily functionalized with organic compounds of interest, producing hybrid materials with important properties and uses. This compound has been studied for application in detection, sterilization, and barrier against microorganisms, allowing a new perspective on the antimicrobial efficacy of different nanomaterials, mainly graphene in its oxygenated version.

In addition, it was possible to identify other presentations less frequently, such as the quantum dots of graphene. They are extremely small semiconductor particles, whose dimensions do not exceed 100 nanometers in diameter. Under these conditions, their optical and electrical properties differ from the properties shown by macroscopic semiconductors. Quantum dots are one of the main materials in nanotechnology applications. From this presentation, promising applications were revealed due to the biocompatibility and bioluminescence of the material[32-33].

Graphene properties

In the case of antiviral activity, graphene oxide, when isolated, has the ability to inhibit infections caused by enveloped viruses, with low cytotoxicity. In the case of antiviral action against non-enveloped viruses, the oxidized version of graphene must be used in association with silver and silver oxide[36]. Regarding antimicrobial activity, it was found that, in contact with graphene oxide associated with silver or not, there is a loss of morphological integrity in both gram-negative and gram-positive bacteria. Process that often causes cell membrane disruption and leakage of intracellular content.

Graphene applications

From the observed properties, several applications of the material were proposed for use in the medical-hospital environment, being mostly explored its use on surfaces and antimicrobial substances. Because it has a wide variety of uses, graphene is being studied in association with biosensors. Graphene's large surface area and excellent electrical conductivity allow it to act as a strand of electrons between the redox centers of an enzyme or protein and the surface of an electrode. Fast electron transfer facilitates the precise and selective detection of biomolecules[37]. Thus, the material, incorporated into a highly complex system, would be used to identify microorganisms, and based on this identification, collaborate in the elimination of these infectious agents. In addition, the reviewed articles reveal that graphene sheets incorporated into biosensors provide ultra-sensitive detection such as antibodies.

Personal protective equipment can also be optimized with the incorporation of graphene. Due to its good dispersibility and hydrophilic nature, graphene interacts smoothly with polymeric fibers, giving protective clothing unique and relevant properties such as mechanical resistance, thermal and electrical conductivity, chemical activity, flame onset delay, antimicrobial properties, among others[38]. Graphene also gives the fabric lightness and breathability, providing better comfort to healthcare professionals who need to wear PPE. Thus, due to the high risk of contagion, the use of masks is essential by health professionals in their work routine, especially considering the hospital environment, with the production, use and quality of PPE being an obstacle to public health in the context of the pandemic. Surgical masks are made of polypropylene and are intended to be used in a unique way, in addition, they can cause environmental problems due to inadequate disposal. Thus, laser-induced graphene has good applicability in the production of photothermal surgical masks, with a self-cleaning mechanism due to the activated absorption coefficient that increases its temperature due to exposure to sunlight and, consequently, provides the reuse of safety equipment and enhances the individual's protection against the virus. However, it is still necessary to implement ways to enhance the commercialization and popularization of these masks[39].

Therefore, the use of the graphene compound in personal protective equipment can be an alternative to try to contain the spread of the coronavirus, while there is still no cure or other more effective method for its elimination. Furthermore, it can be used as a protective barrier against other diseases such as Ebola and respiratory syncytial virus (RSV)[40] infection, which, even after much study, was not successful in curing. It is also important to point out that, like COVID-19, other diseases caused by new microorganisms can arise, and graphene, as one of the numerous properties of antimicrobial action, can be a great way to contain new diseases so that they do not become a pandemic.

Main obstacles

Although graphene has promising applications mainly in the health area, it is necessary to identify and understand the main negative effects resulting from its production, use and disposal. From the understanding of

these obstacles, the scientific community becomes able to seek the modifications or ideal solutions so that the material is used and explored in its magnitude, without causing harm to users and the environment.

Among the main disadvantages of its use, there is the toxicity resulting from contact with the material. This achievement has been studied in more depth by nanotoxicology, which addresses the adverse effects on human and environmental health associated with nanoparticles[41]. The main source of nanotoxicity comes from exposure to graphene associated with nanoparticles derived from metals such as copper, silver, magnesium, sodium, potassium, calcium, and iron. The second most recent source of nanotoxicity derives from these nanoparticles, serving as new platforms for delivering drugs to the specific target site in therapeutic measures, such as nanomedicines[42-43]. Thus, it is necessary to counter the benefits of graphene in nanomedicines with the risks associated with toxicity for the individual.

The environmental impacts derived from contact with graphene must also be considered when making a decision on its use and, mainly, on its disposal. Since the material has antimicrobial properties, it is essential to consider how this property can affect the environment in which it is deposited. Upon contact with the soil, graphene generates an impact, mainly due to its small diameter and large surface area [44]. In contact with the surface, the material causes a drastic reduction in the local population of microorganisms, causing an imbalance of the ecosystem due to the breakdown of the microbiome, which has significant consequences for the existence and maintenance of life in the environment [45].

In addition, the low quality of graphene obtained through production processes[46-47] was recognized as having an unfavorable impact. The various existing methods are continuously improved so that they are optimized to obtain a better-quality product. Depending on the quality of the desired product and the application for which it is intended, one or more methods can be used.

FINAL CONSIDERATIONS

It is concluded that, from the proposed methodology, it was possible to analyze and systematize the panorama of technological innovations of graphene in the scope of public health, identifying and investigating five main aspects: temporal evolution of publications, most relevant properties, forms of presentation of the graphene nanocompound, and possible effects of its application to human health, opening up new possibilities for the development of technological innovations in different areas of activity.

From the literature review, it was possible to identify a significant increase in investigations and in the number of publications on the material in the last 5 years. The growing number of publications and exploration of graphene applications reveals the relevance and prominence of the material and its possible uses for the scientific community, especially in the health area.

The deepening in relation to the presentations and associations of graphene allowed us to conclude that there is a significant amplification in the antimicrobial potential resulting from the association of the oxygenated version of the compound, graphene oxide, with other materials, mainly silver and zinc oxide.

From the particularities of the material, promising applications for the health area derive with different purposes, mainly regarding its antimicrobial effect generated by the oxidative stress in microorganisms. The main technological innovations about the material were: personal protective equipment, surface protection in the medical-hospital environment, biosensors for identification and consequent elimination of pathogens, as well as for therapeutic purposes in nanomedicines, among others.

Finally, it is necessary to consider that although its potential has been explored and its characteristics have been studied recurrently in the last 5 years, more in-depth studies are needed so that all its properties are known and identified and can be applied in their magnitude. Although it is necessary to better understand the toxicological effects of the material to make its application safer, it is concluded in this review that graphene appears to be an excellent material for the field of medicine, especially because it is another artifice to protect the society in the face of a new epidemic.

Conflict of interest: The authors declare that they have no conflicts of interest.

REFERENCES

1. Zhao X, Yang M. Graphene nanocomposites. Molecules. 2019;24(13):2440. https://dx.doi.org/10.3390%2Fmolecules24132440
2. Wang P, Cao Q, Yan Y, Nie Y, Liu S, Peng Q. Graphene surface reinforcement of iron. Nanomaterials (Basel). 2019;9(1):59. doi: 10.3390/nano9010059.
3. Das Sarma S, Adam S, Hwang EH, Rossi E. Electronic transport in two-dimensional graphene. Rev Mod Phys. 2011;83:407. doi = 10.1103/RevModPhys.83.407
4. Wang J, Mu X, Sun M. The thermal, electrical and thermoelectric properties of graphene nanomaterials. Nanomaterials (Basel). 2019 feb;9(2):218. doi: 10.3390/nano9020218
5. Balandin AA, Ghost S, Bao W, et al. Superior thermal

conductivity of single-layer graphene. Nano Lett. 2008;8(3):902-907. doi: 10.1021/nl0731872.

6. Novoselov KS, Geim AK, Morozov SV, Jiang D, Zhang Y, Dubonos SV, Grigorieva IV, Firsov AA. Electric field effect in atomically thin carbon films. Science. 2004;306:666-9. doi: 10.1126/science.1102896.

7. Novoselov KS, Geim AK, Morozov SV, Jiang D, Zhang Y, Dubonos SV, Grigorieva IV, Firsov AA. Electric field effect in atomically thin carbon films. Science. 2004;306:666-9. doi: 10.1126/science.1102896.

8. Huang X, Qi X, Boey F, Zhang H. Graphene-based composites. Chem Soc Rev. 2012,41:666-86. doi: 10.1039/c1cs15078b

9. Peña-Bahamonde J, Nguyen HN, Fanourakis SK, et al. Recent advances in graphene-based biosensor technology with applications in life sciences. J Nanobiotechnol. 2018;16:75. https://doi.org/10.1186/s12951-018-0400-z

10. Chen L, Liang J. An overview of functional nanoparticles as novel emerging antiviral therapeutic agents. Mater Sci Eng C Mater Biol Appl. 2020;112:110924. doi: 10.1016/j.msec.2020.110924.

11. de Wit E, van Doremalen N, Falzarano D, Munster VJ. SARS and MERS: recent insights into emerging coronaviruses. Nat Rev Microbiol. 2016;14:523-34. https://doi.org/10.1038/nrmicro.2016.81.

12. Cui J, Li F, Shi Z-L. Origin and evolution of pathogenic coronaviruses. Nat Rev Microbiol 2019;17:181-92. https://doi.org/10.1038/s41579-018-0118-9.

13. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497-506. doi: 10.1016/S0140-6736(20)30183-5.

14. Li Q, Guan X, Wu P, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med. 2020 Mar 26;382(13):1199-207.

15. Sternberg A, Naujokat C. Structural features of coronavirus SARS-CoV-2 spike protein: Targets for vaccination. Life Sci 2020;257:118056. https://doi.org/10.1016/j.lfs.2020.118056.

16. Samrat SK, Tharappel AM, Li Z, Li H. Prospect of SARS-CoV-2 spike protein: potential role in vaccine and therapeutic development. Virus Res 2020;288:198141. https://doi.org/10.1016/j.virusres.2020.198141.

17. Chen Y-N, Hsueh Y-H, Hsieh C-T, Tzou D-Y, Chang P-L. Antiviral activity of graphene–silver nanocomposites against non-enveloped and enveloped viruses. Int J Environ Res Public Health. 2016;13:430. https://doi.org/10.3390/ijerph13040430.

18. Cheng C, Li S, Thomas A, Kotov NA, Haag R. Functional graphene nanomaterials based architectures: biointeractions, fabrications, and emerging biological applications. Chem Rev. 2017;117:1826-914. https://doi.org/10.1021/acs.chemrev.6b00520.

19. Sifuentes-Rodríguez E, Palacios-Reyes D. COVID-19: The outbreak caused by a new coronavirus. COVID-19: la epidemia causada por un nuevo coronavirus. Bol Med Hosp Infant Mex. 2020;77(2):47-53. doi: 10.24875/BMHIM.20000039.

20. Li H, Liu SM, Yu XH, et al. Coronavirus disease 2019 (COVID-19): current status and future perspectives. Int J Antimicrob Agents. 2020;55(5):105951. doi: 10.1016/j.ijantimicag.2020.105951.

21. Falavigna M, Colpani V, Stein C, Azevedo LCP, Bagattini AM, Brito GV, et al . Diretrizes para o tratamento farmacológico da COVID-19. Consenso da Associação de Medicina Intensiva Brasileira, da Sociedade Brasileira de Infectologia e da Sociedade Brasileira de Pneumologia e Tisiologia. Rev Bras Ter Intens. 2020;32(2):166-96. https://doi.org/10.5935/0103-507X.20200039.

22. Prather KA, Wang CC, Schooley RT. Reducing transmission of SARS-CoV-2. Science. 2020;368(6498):1422-4. doi: 10.1126/science.abc6197.

23. Mhango M, Dzobo M, Chitungo I, et al. COVID-19 risk factors among health workers: a rapid review. Saf Health Work. 2020; 11(3):262-265. doi: 10.1016/j.shaw.2020.06.001.

24. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Boletim Epidemiológico Especial. Doença pelo Coronavírus COVID-19. Brasília; 2020. In: Semana Epidemiológica; 25 jun. 2020 [citado 08 ago. 2020]. Disponível em: https://www.saude.gov.br/images/pdf/2020/August/06/Boletim-epidemiologico-COVID-25-final--1-.pdf.

25. Xiao J, Fang M, Chen Q, He B. SARS, MERS and COVID-19 among healthcare workers: a narrative review. J Infect Public Health. 2020;13(6):843-8. doi: 10.1016/j.jiph.2020.05.019

26. Tabah A, Ramanan M, Laupland KB, et al. Personal protective equipment and intensive care unit healthcare worker safety in the COVID-19 era (PPE-SAFE): an international survey. J Crit Care. 2020;59:70-5. doi: 10.1016/j.jcrc.2020.06.005

27. Lotfi M, Hamblin MR, Rezaei N. COVID-19: Transmission, prevention, and potential therapeutic opportunities. Clin Chim Acta. 2020;508:254-66. https://doi.org/10.1016/j.cca.2020.05.044

28. Singhal T. A review of coronavirus disease-2019 (COVID-19). Indian J Pediatr. 2020;87(4):281-6. doi: 10.1007/s12098-020-03263-6

29. Zou X, Zhang L, Wang Z, et al. Mechanisms of the antimicrobial activities of graphene materials. J Am Chem Soc. 2016;138(7):2064-77. doi: 10.1021/jacs.5b11411

30. Vieira Segundo J, Vilar E. Grafeno: Uma revisão sobre propriedades, mecanismos de produção e potenciais aplicações em sistemas energéticos. Rev Eletrônica Materiais Processos. 2016;11(2):54–57. Disponível em: http://www2.ufcg.edu.br/revista-remap/index.php/REMAP/article/view/493/387.

31. Hsueh YH, Hsieh CT, Chiu ST, et al. Antibacterial property of composites of reduced graphene oxide with nano-silver and zinc oxide nanoparticles synthesized using a microwave-assisted approach. Int J Mol Sci. 2019;20(21):5394. doi: 10.3390/ijms20215394

32. Kumar S, Ahlawat W, Kumar R, et al. Graphene, carbon nanotubes, zinc oxide and gold as elite nanomaterials for fabrication of biosensors for healthcare. Biosens Bioelectron. 2015;70:498-503. doi: 10.1016/j.bios.2015.03.062

33. Zheng XT, Ananthanarayanan A, Luo KQ, Chen P. Glowing graphene quantum dots and carbon dots: properties, syntheses, and biological applications. Small. 2015;11(14):1620-36. https://doi.org/10.1002/smll.201402648

34. Mcmahan RS, et al. In vitro approaches to assessing the toxicity of quantum dots. In: Quantum Dots: applications in biology. New York, NY: Humana Press; 2014. p.155-63.

35. Chen M, Sun Y, Liang J, et al. Understanding the influence of carbon nanomaterials on microbial communities. Environ Int. 2019;126:690-8. doi: 10.1016/j.envint.2019.02.005

36. Rutala WA.: Disinfection, sterilization, and waste disposal; in Wenzel RP, editor. Prevention and control of nosocomial infections. Baltimore: Williams & Wilkins; 1987. p.257-82.

37. Chen YN, Hsueh YH, Hsieh CT, Tzou DY, Chang PL. Antiviral activity of graphene-silver nanocomposites against non-enveloped and enveloped viruses. Int J Environ Res Public Health. 2016;13(4):430. doi: 10.3390/ijerph13040430

38. Kuila T, Bose S, Khanra P, Mishra AK, Kim NH, Lee JH. Recent advances in graphene-based biosensors. Biosens Bioelectron. 2011;26(12):4637-48. doi: 10.1016/j.bios.2011.05.039.

39. Pal K, Kyzas GZ, Kralj S, Gomes de Souza F. Sunlight sterilized, recyclable and super hydrophobic anti-COVID laser-induced graphene mask formulation for indelible usability. J Mol Struct. 2021;1233:130100. https://doi.org/10.1016/j.molstruc.2021.130100.

40. Tabah A, Ramanan M, Laupland KB, et al. Personal protective equipment and intensive care unit healthcare worker safety in the COVID-19 era (PPE-SAFE): an international survey. J Crit Care. 2020;59:70-5. doi: 10.1016/j.jcrc.2020.06.005.

41. Goel S, Hawi S, Goel G, Thakur VK, Agrawal A, Hoskins C, Pearce O, Hussain T, Upadhyaya HM, Cross G, Barber AH. Resilient and agile engineering solutions to address societal challenges such as coronavirus pandemic. Mater Today Chem. 2020;17:100300. doi: 10.1016/j.mtchem.2020.100300.

42. Gendelman HE, Anantharam V, Bronich T, Ghaisas S, Jin H, Kanthasamy AG, Liu X, McMillan J, Mosley RL, Narasimhan B, Mallapragada SK. Nanoneuromedicines for degenerative, inflammatory, and infectious nervous system diseases. Nanomedicine. 2015;11:751-67. http://dx.doi.org/10.1016/j.nano.2014.12.014

43. Yang K, Li Y, Tan X, Peng R, Liu Z. Behavior and toxicity of graphene and Its functionalized derivatives in biological systems. Small. 2013;9:1492-503. doi: 10.1002/smll.201201417

44. Seabra AB, Paula AJ, Lima R, Alves OL, Durán N. Nanotoxicty of graphene and graphene oxide. Chem Resn Toxicol. 2014;*2* (2):159-68. doi: 10.1021/tx400385x

45. Chen M, Sun Y, Liang J, Zeng G, Li Z, Tang L, Zhu Y, Jiang D, Song B. Understanding the influence of carbon nanomaterials on microbial communities. Environ Int. 2019;126:690-8. https://doi.org/10.1016/j.envint.2019.02.005

46. Keshavan S, Calligari P, Stella L, Fusco L, Delogu LG, Fadeel B. Nano-bio interactions: a neutrophil-centric view. Cell Death Dis. 2019;10(8):569. doi:10.1038/s41419-019-1806-8

47. Lee EJ, Balasubramanian K, Weitz RT, Burghard M, Kern K. Contact and edge effects in graphene devices. Nature Nanotech. 2008;3:486-90. https://doi.org/10.1038/nnano.2008.172

Submeted: 2021, April 01
Accepted: 2021, October 21