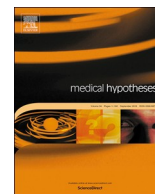




Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Are graphene and graphene-derived products capable of preventing COVID-19 infection?



Pawan Kumar Raghav, Sujata Mohanty*

Stem Cell Facility, DBT-Centre of Excellence for Stem Cell Research, All India Institute of Medical Sciences, New Delhi 110029, India

ARTICLE INFO

Keywords:

Graphene
Graphene oxide
Reduced graphene oxide
COVID-19
SARS-CoV-2
ACE2

ABSTRACT

The Severe Acute Respiratory Syndrome CoronaVirus 2 (SARS-CoV-2) causes the new coronavirus disease 2019 (COVID-19). This disease is a severe respiratory tract infection that spreading rapidly around the world. In this pandemic situation, the researchers' effort is to understand the targets of the virus, mechanism of their cause, and transmission from animal to human and vice-versa. Therefore, to support COVID-19 research and development, we have proposed approaches based on graphene and graphene-derived nanomaterials against COVID-19.

Introduction

The entry of SARS-CoV-2 in human relies on its Spike-protein (S-protein) interaction with human Angiotensin-Converting Enzyme 2 (ACE2), a human cell surface receptor that facilitates viral entry and replication, which is similar in pathogenesis to that of SARS-CoV [1]. The advancement of nano-based antiviral agents gained the popularity to be used for the treatment of COVID-19 [2]. Several studies have used immunomodulator proteins encapsulated nanoparticles against SARS-CoV, which can also be assessed to eradicate SARS-CoV-2 [3,4]. Graphene and graphene-derived (graphene oxide (GO), reduced graphene oxide (rGO), and graphene quantum dots (GQDs)) nanomaterials have wide biomedical applications. Graphene is a hydrophobic material, and its two-dimensional structure represents a sheet of sp²-hybridized carbon atoms [5]. In contrast, the GO is hydrophilic in nature and has electronic properties [6]. The reduction of GO through the thermal process produces rGO, which is a highly hydrophilic material with lesser oxygen content [7]. Besides, in stacked graphene, the layers stick together on top of each other through π - π -stacking interactions [8]. However, this spacing is significantly increased due to intercalated oxygen groups in the interlayers of GO and rGO [9]. Interestingly, these graphene and graphene-derived nanomaterials have both antimicrobial and antiviral efficiency [10–12]. The antibacterial properties of graphene [13], and graphene-derivatives [14,15], are mainly because of their electron movement towards bacteria. This migration causes cytoplasmic efflux, decreases metabolism, affects lipid membrane, induces oxidative stress, produces reactive oxygen species (ROS), loss of glutathione, and finally causes bacterial death [16]. It has been

reported that lipid bilayer of feline coronavirus is adsorbed on the surface of GO and rGO through hydrogen bonding and electrostatic interactions [17]. Among graphene-derived materials, GO has the highest negative charge, which can have a higher affinity for positively charged viruses. Subsequently, the binding of these graphene-derived materials destroyed the viral membrane [18,19], and confirmed the GO efficacy against viruses [20]. However, the graphene surface can also be modified by conjugating with the negatively charged antivirals such as heparin, drugs, and heparan sulfate [21,22]. This increases the modified graphene affinity with positively charged residues of the viruses, which has been used to develop a diagnostic or therapeutic product [23]. Similarly, rGO modified with sulfate derivatives effectively exterminate herpesvirus strains, swine fever, and orthopoxvirus [24]. Recently, a company, Bonbouton developed an economical and reusable graphene mask [25]. Another company, Zen Graphene Solutions Ltd. has proposed a composite ink of GO and silver nanoparticles that effectively eradicates other strains of coronavirus [26]. Moreover, a graphene-based air purification technology is under-development that could help to kill coronaviruses [27]. Thus, identification and development of possible treatments and approaches are required globally, either to block S-protein or to eradicate the SARS-CoV-2.

Central principle

To emphasize the molecular mechanism underlying the interaction between S-protein and nanoelectromechanical materials such as graphene and graphene-derivatives (GO, rGO, and GQDs) to block SARS-CoV-2 interaction with human ACE2.

* Corresponding author.

E-mail address: drmohantysujata@gmail.com (S. Mohanty).

<https://doi.org/10.1016/j.mehy.2020.110031>

Received 22 May 2020; Received in revised form 17 June 2020; Accepted 20 June 2020

Available online 24 June 2020

0306-9877/ © 2020 Elsevier Ltd. All rights reserved.

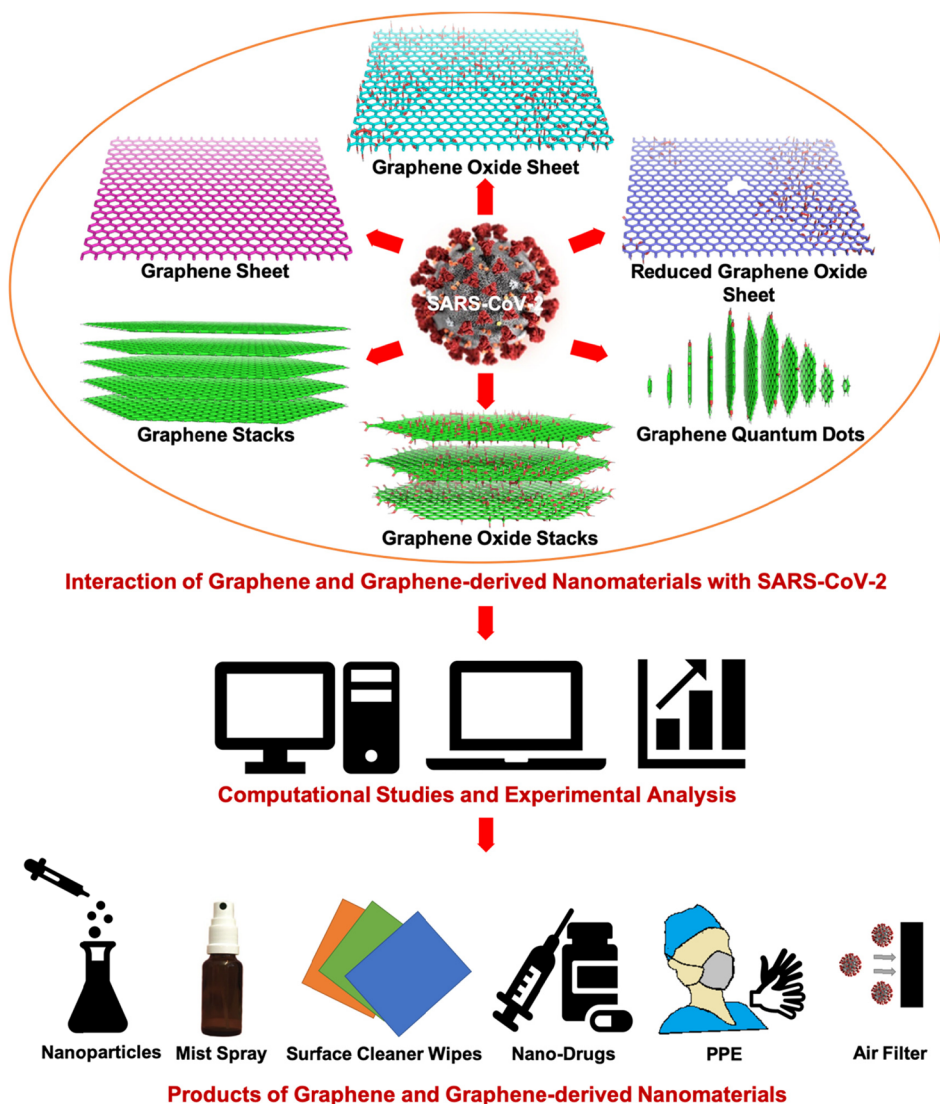


Fig. 1. Schematic representation of graphene, and graphene-derived nanomaterials interaction with SARS-CoV-2 and their applications. The identification of association (binding) or dissociation (repelling) capability of nanomaterials with SARS-CoV-2 can be verified primarily computationally and then experimentally. The interaction analysis helps to decide the development of the product such as nanoparticles, mist spray, surface cleaning wipes, nano-drugs, PPE (Personal Protection Equipment), or air filters. SARS-CoV-2 image source: <https://phil.cdc.gov/PHIL/Images/23311/23311.tif>.

Hypothesis and conclusion

Owing to electroconductive properties, graphene and its derivatives can interact with several biomolecules, translocate within the endosome or lysosome, cross the plasma membrane, and regulates mitochondrion, nucleus, and the cytoskeleton. Notably, the hydrophobicity of graphene increases with an increased number of graphene layers [28]. Therefore, considering all these features, we have suggested a potential graphene-based therapeutic approach, and to determine whether it can be virucidal, it would likely be proven as an economical and efficient treatment against COVID-19 (Fig. 1). Primarily, the affinity and stability of single and multilayer graphene and graphene-derived nanomaterials for SARS-CoV-2 can be computationally elucidated using docking and molecular dynamics (MD) simulations studies, respectively. Afterward, the findings can be verified using molecular and cell biology assays to determine the associations compared to SARS-CoV-2 and ACE2 complex (control). The mono or multi layered graphene and graphene-derivatives can be used as products in the form of mist spray to block the entry of coronaviruses or can be applied to fabrics for substantially enhanced protection. Therefore, personal protective equipment (PPE) should be coated with increased

layers of graphene or graphene-derived materials to keep PPE dry that will prevent or repel the aerosol transmission of SARS-CoV-2. All these graphene-based composites would likely be facilitated to combat against the COVID-19 pandemic. The information comprised in this perspective provides a hypothetical approach that would likely help in preventing COVID-19 infection using graphene-based products. Several products can be developed by considering the electroconductive and hydrophobic properties of graphene and graphene-derived nanomaterials, or their affinity with SARS-CoV-2. GO and silver nanoparticles composite conjugated with antivirals can potentially trap and kill SARS-CoV-2. The mist spray can be used to clean any object's surface and for human body sanitization. However, it can also be used as a nasal or mouth spray to block/mask the S-protein of SARS-CoV-2 substantially. Also, surface cleaner wipes coated with graphene or graphene-derived nanomaterials can be a better option to disinfect the infected area. The graphene-based nano-drugs conjugated with antivirals can be an effective and successful formulation. Reusable PPE coated with modified nanomaterials with enhanced capacity to repel the SARS-CoV-2 is necessarily required to prevent aerosol transmission in medical healthcare workers. The SARS-CoV-2 present in the environment can be filtered by introducing the multiple layer nanomaterials with modified positive

charge filters in the air purification and air-conditioning devices, capable of killing SARS-CoV-2.

Acknowledgements

We acknowledge the support from All India Institute of Medical Sciences (AIIMS), New Delhi & Department of Biotechnology (DBT), Ministry of Science & Technology, Government of India (grant no. BT/01/COE/07/03).

Conflict of interest

The authors declare no conflict of interest.

Author contributions

PKR and SM designed research; PKR analyzed data; PKR and SM performed research; PKR searched and read the articles; PKR prepared the figure; PKR and SM wrote the paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.mehy.2020.110031>.

References

- [1] Hanff TC, Harhay MO, Brown TS, Cohen JB, Mohareb AM. Is there an association between COVID-19 mortality and the renin-angiotensin system—a call for epidemiologic investigations. *Clin Infect Dis* 2020. <https://doi.org/10.1093/cid/ciaa329>.
- [2] Khan S, Siddique R, Shereen MA, Ali A, Liu J, Bai Q, et al. The emergence of a novel coronavirus (SARS-CoV-2), their biology and therapeutic options. *J Clin Microbiol* 2020. <https://doi.org/10.1128/JCM.00187-20>.
- [3] Wohlford-Lenane CL, Meyerholz DK, Perlman S, Zhou H, Tran D, Selsted ME, et al. Rhesus theta-defensin prevents death in a mouse model of severe acute respiratory syndrome coronavirus pulmonary disease. *J Virol* 2009. <https://doi.org/10.1128/jvi.01363-09>.
- [4] Wiley JA, Richert LE, Swain SD, Harmsen A, Barnard DL, Randall TD, et al. Inducible bronchus-associated lymphoid tissue elicited by a protein cage nanoparticle enhances protection in mice against diverse respiratory viruses. *PLoS One* 2009. <https://doi.org/10.1371/journal.pone.0007142>.
- [5] Banerjee AN. Graphene and its derivatives as biomedical materials: Future prospects and challenges. *Interface Focus* 2018. <https://doi.org/10.1098/rsfs.2017.0056>.
- [6] Hummers WS, Offeman RE. Preparation of graphitic oxide. *J Am Chem Soc* 1958. <https://doi.org/10.1021/ja01539a017>.
- [7] Pei S, Cheng HM. The reduction of graphene oxide. *Carbon N Y* 2012. <https://doi.org/10.1016/j.carbon.2011.11.010>.
- [8] Eigler S, Hirsch A. Chemistry with graphene and graphene oxide – Challenges for synthetic chemists. *Angew Chemie - Int Ed* 2014. <https://doi.org/10.1002/anie.201402780>.
- [9] Sheng Y, Tang X, Peng E, Xue J. Graphene oxide based fluorescent nanocomposites for cellular imaging. *J Mater Chem B* 2013. <https://doi.org/10.1039/c2tb00123c>.
- [10] Akhavan O, Choobtashani M, Ghaderi E. Protein degradation and RNA efflux of viruses photocatalyzed by graphene-tungsten oxide composite under visible light irradiation. *J Phys Chem C* 2012. <https://doi.org/10.1021/jp301707m>.
- [11] Palmieri V, Papi M. Can graphene take part in the fight against COVID-19? *Nano Today* 2020. <https://doi.org/10.1016/j.nantod.2020.100883>.
- [12] Bhattacharjee S, Joshi R, Chughtai AA, Macintyre CR. Graphene Modified Multifunctional Personal Protective Clothing. *Adv Mater Interfaces* 2019. <https://doi.org/10.1002/admi.201900622>.
- [13] Hu W, Peng C, Luo W, Lv M, Li X, Li D, et al. Graphene-based antibacterial paper. *ACS Nano* 2010. <https://doi.org/10.1021/nn101097v>.
- [14] Han W, Wu Z, Li Y, Wang Y. Graphene family nanomaterials (GFNs)—promising materials for antimicrobial coating and film: A review. *Chem Eng J* 2019. <https://doi.org/10.1016/j.cej.2018.10.106>.
- [15] Zhao J, Deng B, Lv M, Li J, Zhang Y, Jiang H, et al. Graphene oxide-based antibacterial cotton fabrics. *Adv Healthc Mater* 2013. <https://doi.org/10.1002/adhm.201200437>.
- [16] Ji H, Sun H, Qu X. Antibacterial applications of graphene-based nanomaterials: Recent achievements and challenges. *Adv Drug Deliv Rev* 2016. <https://doi.org/10.1016/j.addr.2016.04.009>.
- [17] Song Z, Wang X, Zhu G, Nian Q, Zhou H, Yang D, et al. Virus capture and destruction by label-free graphene oxide for detection and disinfection applications. *Small* 2015. <https://doi.org/10.1002/sml.201401706>.
- [18] Rui L, Liu J, Li J, Weng Y, Dou Y, Yuan B, et al. Reduced graphene oxide directed self-assembly of phospholipid monolayers in liquid and gel phases. *Biochim Biophys Acta – Biomembr* 2015. <https://doi.org/10.1016/j.bbmem.2015.02.018>.
- [19] Frost R, Jönsson GE, Chakarov D, Svedhem S, Kasemo B. Graphene oxide and lipid membranes: Interactions and nanocomposite structures. *Nano Lett* 2012. <https://doi.org/10.1021/nl203107k>.
- [20] Chen YN, Hsueh YH, Te HC, Tzou DY, Chang PL. Antiviral activity of graphene–silver nanocomposites against non-enveloped and enveloped viruses. *Int J Environ Res Public Health* 2016. <https://doi.org/10.3390/ijerph13040430>.
- [21] Naskalska A, Dabrowska A, Szczepanski A, Milewska A, Jasik KP, Pyrc K. Membrane protein of Human coronavirus NL63 Is responsible for interaction with the adhesion receptor. *J Virol* 2019. <https://doi.org/10.1128/jvi.00355-19>.
- [22] Jones ST, Cagno V, Janeček M, Ortiz D, Gasilova N, Piret J, et al. Modified cyclodextrins as broad-spectrum antivirals. *Sci Adv* 2020. <https://doi.org/10.1126/sciadv.aax9318>.
- [23] Ziem B, Azab W, Gholami MF, Rabe JP, Osterrieder N, Haag R. Size-dependent inhibition of herpesvirus cellular entry by polyvalent nanoarchitectures. *Nanoscale* 2017. <https://doi.org/10.1039/c7nr00611j>.
- [24] Ziem B, Thien H, Achazi K, Yue C, Stern D, Silberreis K, et al. Highly efficient multivalent 2D nanosystems for inhibition of orthopoxvirus particles. *Adv Healthc Mater* 2016. <https://doi.org/10.1002/adhm.201600812>.
- [25] <https://www.bonbouton.com/covid-mask>.
- [26] <https://www.mining.com/graphene-ink-may-be-used-to-fight-novel-coronavirus/>.
- [27] <https://www.graphene-info.com/>.
- [28] Munz M, Giusca CE, Myers-Ward RL, Gaskill DK, Kazakova O. Thickness-dependent hydrophobicity of epitaxial graphene. *ACS Nano* 2015. <https://doi.org/10.1021/acsnano.5b03220>.