Lethal Interactions of SARS-CoV-2 with Graphene Oxide: Implications for COVID-19 Treatment

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ABSTRACT: The rapid transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-driven infection signifies an ultimate challenge to global health, and the development of effective strategies for preventing and/or mitigating its effects are of the utmost importance. In the current study, an in-depth investigation for the understanding of the SARS-CoV-2 inactivation route using graphene oxide (GO) is presented. We focus on the antiviral effect of GO nanosheets on three SARS-CoV-2 strains: Wuhan, B.1.1.7 (U.K. variant), and P.1 (Brazilian variant). Plaque assay and real-time reverse transcription-polymerase chain reaction (RT-PCR) showed that 50 and 98% of the virus in a supernatant could be cleared following incubation with GO (100 μg/mL) for 1 and 60 min, respectively. Transmission electron microscopy (TEM) analysis and protein (spike (S) and nucleocapsid (N) proteins) decomposition evaluation confirm a two-step virus inactivation mechanism that includes (i) adsorption of the positively charged spike of SARS-CoV-2 on the negatively charged GO surface and (ii) neutralization/inactivation of the SARS-CoV-2 on the surface of GO through decomposition of the viral protein. As the interaction of S protein with human angiotensin-converting enzyme 2 (ACE2) is required for SARS-CoV-2 to enter into human cells, the damage to the S protein using GO makes it a potential candidate for use in contributing to the inhibition of the worldwide spread of SARS-CoV-2. Specifically, our findings provide the potential for the construction of an effective anti-SARS-CoV-2 face mask using a GO nanosheet, which could contribute greatly to preventing the spread of the virus. In addition, as the effect of surface contamination can be severe in the spreading of SARS-CoV-2, the development of efficient anti-SARS-CoV-2 protective surfaces/coatings based on GO nanosheets could play a significant role in controlling the spread of the virus through the utilization of GO-based nonwoven cloths, filters, and so on.

KEYWORDS: graphene oxide, SARS-CoV-2, antiviral, surface functional groups, viral protein decomposition

1. INTRODUCTION

The novel coronavirus-driven disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), first broke out in Wuhan, China, and quickly spread around the world, threatening people’s lives and their economic activities.1 As of June 2021, more than 173 million people worldwide have been infected, with fatalities of over 3.7 million attributed to COVID-19, making it one of the most fatal pandemics in history.2 The explosive spread of infection remains a threat to humanity, and preventing the spread of this virus is an urgent issue confronting the world. Vaccination against SARS-CoV-2 has now been widely initiated; however, it is said that it will take several years for this measure to approach full effectiveness. Moreover, the appearance of vaccinated people who can still become infected and spread the virus is also a major concern.3 Thus, strategies for preventing or mitigating the rapid spread of SARS-CoV-2 infection, such as the development of anti-SARS-CoV-2 products, including face masks for use in everyday life, will continue to play a critical role in controlling the spread of the virus.

Nanomaterials continue to attract attention in a wide range of fields including material science, environmental science, mechanical engineering, energy, and biomedicine because of their unique physicochemical properties including high surface area (surface-to-volume ratio).4−6 In particular, the tunable physical and chemical properties of two-dimensional materials (2DMs) facilitate efficient interactions between the viruses and
2DMs, making them ideal candidates for many applications including biosensors with high sensitivity and selectivity. The nanoscale-enabled diagnostic tools are likely to be developed for the rapid detection of SARS-CoV-2 infections, which will enable us to keep SAR-CoV-2 under control. Graphene oxide (GO) is a widely studied 2DM with a thickness of about 1 nm and a width of several tens of micrometers or more. It is composed of a robust carbon backbone and abundant oxygen-containing functional groups including epoxy groups, hydroxyl groups, and carboxyl groups. GO can be manufactured easily and inexpensively by oxidizing graphite followed by exfoliation. The oxygen functional groups make GO hydrophilic and facilitate GO biotechnology applications. Also, due to their low toxicity to the human body, GO materials have become promising candidates for use in the next generation of biologically active materials. So far, GO and some of its derivatives have been reported to have clear inhibitory effects against particular bacteria, fungi, and viruses. Also, some recent studies have provided theoretical background and experimental evidence on their effectiveness against SARS-CoV-2. However, insights into how the anti-SARS-CoV-2 activity of GO might be implemented for widespread practical use for preventing the spread of the virus have been lacking. In this report, we demonstrate the virus inhibitory properties of GO and present the results of an in-depth investigation involving three SARS-CoV-2 strains (Wuhan, U.K., and Brazilian). GO suppresses SARS-CoV-2 infectivity by 95% or more when incubated with GO for 60 min (based on real-time reverse transcription-polymerase chain reaction (RT-PCR) or plaque assays). Further, we elucidate this antiviral mechanism as being due to the interaction of GO with SARS-CoV-2, causing the decomposition of viral proteins (Scheme 1). This highly reliable anti-SARS-CoV-2 activity clearly indicates that GO shows much promise for incorporation in GO-coated masks and protective clothing as well as for imparting antiviral properties to various objects in the form of a coating agent.

Scheme 1. Adsorption of SARS-CoV-2 via the Oxygen-Containing Functional Groups of GO Followed by Reduction of S and N Proteins of SARS-CoV-2 on the GO Surface Responsible for the Inactivation of the SARS-CoV-2 Virus

2. RESULTS AND DISCUSSION

2.1. Inactivation of SARS-CoV-2 Using GO Nanosheets. GO was purchased from Nippon Shokubai Co with an oxidation degree of 33%, with the oxygen functional groups mainly present as epoxy groups (Figure S1). In aqueous dispersion, GO exists as monolayer sheets of thickness 1 nm and length several micrometers (Figure S1). More details of the GO employed, including its Fourier transform infrared (FTIR), UV adsorption, and Raman spectra, are given in the Supporting Information and Figure S1. Wuhan, U.K. (QK002 and QHN001), and Brazilian (TY7-501 and TY7-503) strains of SARS-CoV-2 were used in the investigation of the antiviral activity of GO against SARS-CoV-2 by employing plaque assay and real-time RT-PCR.

Before proceeding to the antiviral study of GO, we validated the possible cytotoxic impact of GO exposure to Vero cells (Figure S2). For this purpose, the cells were treated with GO in different concentrations (50, 100, and 200 μg/mL) with and without fetal bovine serum (FBS n = 5) and incubated for 1 and 4 h. When the cells were treated with GO at a concentration of 100 μg/mL with FBS for 1 and 4 h, the cell viabilities were about 95 and 92%, respectively (Figure S2a). On the other hand, the removal of FBS from these conditions resulted in 93% (1 h) and 82% (4 h) cell viability (Figure S2b). These findings suggest that 100 μg/mL concentration of GO has little effect on cell proliferation, and this concentration was chosen for the subsequent antiviral experiments.

To test the effect of GO on SARS-CoV-2, we treated the virus stock with 100 μg/mL GO for 60 min and quantified viral RNA in the supernatant after centrifugation by real-time RT-PCR. As shown in Figure 1a, a significant reduction of viral RNA in the supernatant was observed (about 37.5-fold). Also, this antiviral effect was time-dependent, with a reduction of 50% after 1 min, 70% after 10 min, and 98% after 60 min (Figure 1b). Next, we measured SARS-CoV-2 infectivity under the same conditions by plaque assay. As shown in Figure 1c,d, typical cytopathic effects were observed in the absence of GO. However, the treatment of the virus stock with GO significantly decreased the plaque-forming unit (PFU) from $5 \times 10^4$ to 0.35 $\times 10^3$ PFU/mL (Figure 1c,d). This antiviral effect was also investigated for the other SARS-CoV-2 strains (Brazilian variants: TY7-501 and TY7-503; U.K. variants: QK002 and QHN001). In all cases, the addition of GO to virus stocks reduced about 98% of viral infectivity compared to without GO. These observations indicate that the antiviral activity of GO is not specific for one SARS-CoV-2 variant, and it can be anticipated that the anti-SARS-CoV-2 potency of GO will be broadly effective for other SARS-CoV-2 strains.

2.2. Insight into SARS-CoV-2 Inactivation Using GO Nanosheets. Fundamentally, SARS-CoV-2 particles contain four structural proteins: N, membrane (M), S, and envelope (E) proteins in addition to viral genomic RNA (Figure 2a). The surface of GO is negatively charged (Figure S3), while that of SARS-CoV-2 is positively charged. These opposite charges result in an electrostatic interaction between GO and SARS-CoV-2. As a consequence, the suppression of viral infection by GO can be attributed to this direct interaction between GO and SARS-CoV-2. To obtain more insight into the anti-SARS-CoV-2 properties of GO, SARS-CoV-2 was incubated with GO, and a TEM image analysis confirmed the presence of the above interaction between GO and SARS-CoV-2.
CoV-2. In Figure 2b, SARS-CoV-2, which was harvested from the culture medium using Vero cells but was not treated with GO, showed the typical ultrastructure of SARS-CoV-2 surrounded by a crownlike corona with an integrated envelope and spikes. Interestingly, after incubation with GO for 1 h, the SARS-CoV-2 particle was found to be adsorbed tightly onto the GO surface, and the crown and envelope disappeared (Figures 2c and S4). This observation indicates that GO interacts directly with the viral particles (through electrostatic attraction) and inhibits their function by disrupting their structural integrity. To further probe the damage to the virus surface in the presence of GO, we examined the existence of S and N proteins using Western blotting (Figure 2d) at 24, 48, and 72 h. Clearly, both the S and N proteins were stable over time in the absence of GO. However, interestingly, virus stock treated with GO showed a significant decrease of the S and N proteins, with the quantification of each band intensity supporting these results (Figure 2e,f). In addition, the enzyme-linked immunosorbent (ELISA) assay showed that a log scale decline in the quantity of N protein was also seen in the presence of GO (Figure 2f). Taken together, these observations clearly indicate that GO can directly interact with viral particles and destroy their S and N protein structures, thereby leading to the disruption of viral function. The spike glycoprotein is critical for the entry of the coronaviruses in the host cell, so it is an attractive antiviral target that can be successfully destroyed using GO nanosheets.

2.3. Roles of the Oxygen-Containing Functional Groups of GO in the SARS-CoV-2 Inactivation. To probe the role of the oxygen functional groups in GO on its anti-SARS-CoV-2 activity, the antiviral activities of two differently reduced GO (rGO) materials, chemically reduced...
GO (C-rGO) and thermally reduced GO (T-rGO), were investigated employing the same experimental conditions as for GO. The synthetic methods are described in the Materials and Methods. X-ray photoelectron spectroscopy (XPS) analysis was used to confirm the degree of oxidation in each case. The oxygen contents of C-rGO and T-rGO were decreased to 11 and 19%, respectively (Figure S5). The hydrophilicity of rGO disappeared due to the decomposition of most of the oxygen-containing functional groups. In view of this, dimethyl sulfoxide (DMSO) was used as a solvent to prevent aggregation during this experiment and was tested for its effect of SARS-CoV-2 infectivity by plaque assay. As shown in Figure 3a, it is clear that the addition of DMSO to viral stock has little effect. Under these conditions, the antiviral activity of GO and rGO against SARS-CoV-2 was evaluated. Compared to GO, C-rGO and T-rGO had very poor antiviral activity (Figure 3a,b). The relative anti-SARS-CoV-2 performance of GO and rGO follows the order GO ≫ T-rGO > C-rGO, which is in line with the degree of oxygen-containing functional groups present on the respective carbon backbones. So, the marked difference in antiviral properties between GO and rGO correlates well with the number of oxygen-containing functional groups present in these materials.
An overview of the SARS-CoV-2 inactivation using GO nanosheets is illustrated in Scheme 1, which shows the adsorption of SARS-CoV-2 on the surface of GO nanosheet followed by the inactivation of SARS-CoV-2 through decomposition of spike protein on the surface of GO. Using molecular docking modeling, the enhanced interaction of GO with the viral spike (ACE2 cell receptor) as well as with the spike-ACE2 complex have been previously reported.17 The advantages of SARS-CoV-2 inactivation using GO nanosheet can be utilized for protective surfaces/coatings to prevent the further spreading of SARS-CoV-2. Because GO is a carbon-based material, it can be readily fabricated into fibers, nonwoven cloths, and so on—a feature that can be potentially utilized for the development of anti-SARS-CoV-2 masks, filters, cloths, etc. Moreover, GO can be combined with a variety of fibers and surface materials to provide effective anti-SARS-CoV-2 coatings. In this view, we have extended our study toward the utilization of GO in the nonwoven fibers and a coated surface in a practical mask. A mask of nonwoven fibers type, incorporating 5% GO in a nonwoven thermoplastic polyurethane fiber (GO-TPU), is in its final development stage. The SEM images of bare TPU fiber and GO-TPU fiber are shown in Figure S6a,b, respectively. On the other hand, Figure S7a,b illustrates the SEM images of bare practical mask surface and the attachment of GO nanosheets on the mask's surface. Moreover, Figure S8 compares the anti-SARS-CoV-2 efficiency of a commercial filter (PTFE syringe filter, pore size: 0.22 μm) while passing the virus solution through the filter followed by employing plaque assay to the filtrate virus solution, GO-modified filter (first GO (1 mg/mL, 0.5 mL) passed through the filter followed by virus solution), activated carbon modified filter (first activated carbon (1 mg/mL, 0.5 mL) passed through the filter followed by virus solution), and a commercial antibody mask (CROSSEED Corporation; polypropylene nonwoven fabric containing antibodies derived from goose eggs) layer as a filter. Obviously, GO shows significantly higher anti-SARS-CoV-2 activity compared to others. Therefore, along with some existing studies on graphene and other 2D materials to combat COVID-19,24–29 the present results clearly have implications for (i) the design of nanoplatorms for face masks and other personal protective equipment and (ii) the development of antiviral surfaces/coatings for use in a number of roles for mitigating the spread of the current infections.

3. CONCLUSIONS

In the present study, after demonstrating the anti-SARS-CoV-2 ability of GO, a primary concern has been understanding the virus inactivation route involving the use of GO. To this end, we have utilized TEM analysis and particular protein survival concentrations using the western blot procedure to gain further understanding of the SARS-CoV-2 inactivation process. The adsorption and subsequent decomposition of S and N proteins are attributed to the anti-SARS-CoV-2 activity of GO. The functional groups of GO clearly play the prime role in this inactivation. The GO sheets are functionalized on both sides, which provide an efficient contact between the positively charged virus and the negatively charged GO. The current in-depth findings of the GO anti-SARS-CoV-2 activity are expected to play a key role in the implementation of GO-based infrastructure with/post COVID-19 society as well as to prevent any future virus spreading.

4. MATERIALS AND METHODS

4.1. rGO Preparation. rGO was synthesized from GO using two well-established chemical reductions and thermal reductions routes. In the chemical reduction method, 30 mL of hydrazine monohydride (98%, Wako Ltd.) was added to 300 mL of GO dispersion (1 g/L) and the mixture was heated at 110 °C for 24 h. After that, the solid rGO was separated by filtration and washed with pure H2O several times to remove unreacted hydrazine. In the thermal reduction case, the dried GO powder was sandwiched between heat-resistant glass sheets and heated at 200 °C for 1 day under air.

4.2. X-ray Photoelectron Spectroscopy (XPS). XPS was performed on a Theta Probe (Thermo Fisher Scientific) instrument. A monochromatized X-ray source (Al Kα, hv = 1486.6 eV) was used for the measurement, which was performed under vacuum at a pressure higher than 10−8 mbar.

4.3. Raman Spectroscopy. Raman spectra were recorded on a Raman spectrometer (NRS-3100, JASCO, JP) equipped with a DFPP laser excitation source operating at 532 nm. The laser beam diameter was 1 μm, and the measurement was carried out under atmospheric conditions.

4.4. Atomic Force Microscopy (AFM). A multimode microscope (Nano cute) operated by a scanning probe microscope controller was used for AFM measurement. The substrate was prepared by dropping the dispersion on a natural mica substrate.

4.5. Fourier Transform Infrared (FT-IR) Spectroscopy. FT-IR spectra were recorded on a Spectrum Two (PerkinElmer) instrument.

4.6. Ultraviolet–Visible (UV–Vis) Absorption. UV–vis absorption spectra were recorded on a ultraviolet–visible spectrometer (UV-3600, Shimadzu, JP) coupled with a 1.00 cm quartz cell.

4.7. Key Reagents. Vero cells (JCRB0111) were cultured in EMEM (Wako, Cat# 051-07615) supplemented with 10% heat-inactivated fetal bovine serum (FBS) (NICHIREI, cat# 175012) and 1% penicillin/streptomycin (P/S) (Wako cat# 168-23191). VeroE6/TMPRSS2 cells (JCRB1819) were maintained in 10% FBS/DMEM (Wako, cat# 041-29775) containing 1 mg/mL G418 (Wako, cat# 070-06803) and 1% P/S. SARS-CoV-2 Wuhan strain, SARS-CoV-2/Hu/DP/Kng/19-020 strain (Genbank accession no. LC528232), was provided by Drs. Tomohiko Takasaki and Jun-Ichi Sakuragi (Kanagawa Prefectural Institute of Public Health). SARS-CoV-2 lineage B.1.1.7 (U.K. variant) QK002 (GISAID ID: EPI-ISL_768526), and QHN001 (GISAID ID: EPI-ISL_804007) strains, and lineage P.2 (Brazilian variant) TT7-501 (GISAID ID: EPI-ISL_833366) and TT7-503 (GISAID ID: EPI-ISL_877769) strains were obtained from National Institute of Infectious Diseases. Viruses were propagated in Vero cells, and plaque-forming unit (PFU) was determined as described below.

4.8. Plaque Assay and Real-time RT-PCR. Plaque assay and real-time RT-PCR were performed as described previously.30 The detailed procedures are shown in the Supporting Information.

4.9. Quantification of S and N Proteins. The day before infection, 3 × 105 VeroE6/TMPRSS2 cells were plated in a six-well plate. The next day, 10 μL of the viruses (3 × 104 PFU) were inoculated into VeroE6/TMPRSS2 cells and incubated at 37 °C. At 2-day postinoculation, the viral supernatant was harvested and mixed with 1 mg/mL of GO (final concentration: 100 μg/mL). At the indicated time, the mixtures were frozen at -80 °C until sample preparation. All mixtures were centrifuged at 22 000g for 2 h at 4 °C, and the supernatants were removed and then resuspended in 50 μL of buffer [100 mM Tris-HCl (pH6.8), 12% β-mercaptoethanol, 4% sodium dodecyl sulfate (SDS), 20% glycerol, 0.05% bromophenol blue]. After boiling at 98 °C for 10 min, 5 μL of the samples was used for the quantification of N protein by ELISA (Proteintech, cat# KE39997). Western blotting was performed as described previously.31,32 The detailed procedure is described in the Supporting Information.

4.10. Transmission Electron Microscopy (TEM) Analysis. At 2 days after inoculation into Vero cells, viral supernatant was harvested and mixed with 1 mg/mL GO (final concentration: 100 μg/mL). The
mixtures were centrifuged at 15 000 rpm for 2 h at 4 °C, and the supernatants were removed and then resuspended in 50 μL of a fixative containing 2.5% glutaraldehyde and 2% paraformaldehyde in 0.1 M phosphate buffer (PB, pH 7.4) on ice. After centrifuging and rinsing, specimens were processed for conventional TEM analysis as follows: postfixation in cold 1% OsO4 for 2 h, en bloc staining in 1.5% uranyl acetate for 30 min, dehydration with a graded series of ethanol, infiltration with propylene oxide, and embedded in epoxy resin. Ultrathin sections (65 nm) were cut, stained with uranyl acetate and lead citrate, and examined in TEM (HT7700, Hitachi) at 80 kV. For observations with the negative-staining method, centrifuged specimens were fixed with 2.5% glutaraldehyde and 2% paraformaldehyde in 0.1 M PB, and 10 μL of the pellets was dropped onto a carbon-coated copper grid. After removing excessive solutions using a filter paper, 10 μL of 1.5% uranyl acetate was applied onto the grid, excessive solutions were removed again, and then the grid was dried and examined in TEM.

**ASSOCIATED CONTENT**

Supporting Information
The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsanm.1c02446.

Characterizations and fundamental properties of GO; procedures for plaque assay, real-time RT-PCR, and western blotting; cytotoxicity of GO on Vero cells; ζ potential distribution of GO; TEM image of SARS-CoV-2 on the surface of GO; XPS C 1s spectra of rGO prepared under different conditions; SEM images of 5% GO-modified TPU fiber layer; SEM images of a typical GO-coated practical mask; and comparison of the anti-SARS-CoV-2 efficiencies of different substrates used as a filter (PDF).

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**REFERENCES**

(1) Zhou, P.; Yang, X.; Lou Wang, X. G.; Hu, B.; Zhang, L.; Zhang, W.; Si, H. R.; Zhu, Y.; Li, B.; Huang, C. L.; Chen, H. D.; Chen, J.; Luo, Y.; Guo, H.; Jiang, R.; Di Liu, M. Q.; Chen, Y.; Shen, X. R.; Wang, X.; Zheng, X. S.; Zhao, K.; Chen, Q. J.; Deng, F.; Liu, L. L.; Yan, B.; Zhan, F. X.; Wang, Y. Y.; Xiao, G. F.; Shi, Z. L. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature 2020, 579, 270–273.

(2) COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE), Johns Hopkins University (JHU), https://coronavirus.jhu.edu/map.html (accessed June 9, 2021).

(3) Madhi, S. A.; Baillie, V.; Cutland, C. L.; Voysey, M.; Koen, A. L.; Fairlie, L.; Padayachee, S. D.; Dheda, K.; Barnabas, S. I.; Bhorat, Q.; E.; Briner, C.; Kwatra, G.; Ahmed, K.; Aley, P.; Bhikha, S.; Bhorat, Q.; Hwa, S.-H.; Jose, A.; Lambe, T.; Labuschere, M.; Malahleha, M.; Masenya, M.; Masilela, M.; McKenzie, S.; Molapo, K.; Moultrie, A.; Oelofse, S.; Patel, F.; Pillay, S.; Rheed, S.; Rodel, H.; Rossouw, L.; Taoushanis, C.; Tegally, H.; Themb太阳城, A.; van Eck, S.; Wibmer, C. K.; Durham, N. M.; Kelly, E. J.; Villafana, T. L.; Gilbert, S.; Pollard, A. J.; de Oliveira, T.; Moore, P. L.; Sigal, A.; Izu, A. Efficacy of the
ChAdOx1 nCoV-19 Vaccine against the B.1.351 Variant. N. Engl. J. Med. 2021, 384, 1885–1898.
(4) Ménard-Moyon, C.; Bianco, A.; Zadeh, K. K. Two-Dimensional Material-Based Biosensors for Virus Detection. ACS Sens. 2020, 5, 3739−3769.
(5) Khin, M. M.; Nair, A. S.; Babu, V. J.; Murugan, R.; Ramakrishna, S. A review on nanomaterials for environmental remediation. Energy Environ. Sci. 2012, 5, 8075−8109.
(6) Kalantar-Zadeh, K.; Ward, S. A.; Zadeh, K. K.; Omar, E. M. E. Considering the Effects of Microbiome and Diet on SARS-CoV-2 Infection: Nanotechnology Roles. ACS Nano 2020, 14, 5179−5182.
(7) Krishnamoorthy, K.; Veerapandian, M.; Yun, K.; Kim, S. J. The chemical and structural analysis of graphene oxide with different degrees of oxidation. Carbon 2013, 53, 38−49.
(8) He, J.; Zhu, X.; Qi, Z.; Wang, C.; Mao, X.; Zhu, C.; He, Z.; Li, M.; Tang, Z. Killing dental pathogens using antibacterial graphene oxide. ACS Appl. Mater. Interfaces 2015, 7, 5605−5611.
(9) Xie, J.; Ming, Z.; Li, H.; Yang, H.; Yu, B.; Wu, R.; Liu, X.; Bai, Y.; Yang, S. T. Toxicity of graphene oxide to white rot fungus Phanerochaete chrysosporium. Chemosphere 2016, 151, 324−331.
(10) Sametband, M.; Kalt, I.; Gedanken, A.; Sarid, R. Herpes simplex virus type-1 attachment inhibition by functionalized graphene oxide. ACS Appl. Mater. Interfaces 2014, 6, 1228–1235.
(11) Ye, S.; Shao, K.; Li, Z.; Guo, N.; Zhou, Y.; Li, Q.; Lu, Z.; Chen, L.; He, Q.; Han. H. Antiviral Activity of Graphene Oxide: How Sharp Edged Structure and Charge Matter. ACS Appl. Mater. Interfaces 2015, 7, 21571–21579.
(12) Du, T.; Lu, J.; Liu, L.; Dong, N.; Fang, L.; Xiao, S.; Han, H. Antiviral Activity of Graphene Oxide-Silver Nanocomposites by Preventing Viral Entry and Activation of the Antiviral Innate Immune Response. ACS Appl. Bio Mater. 2018, 1, 1286−1293.
(13) Deokar, A. R.; Nagvenkar, A. P.; Kalt, I.; Shani, L.; Yeshurun, Y.; Gedanken, A.; Sarid, R. Graphene-Based [hot Plate] for the Capture and Destruction of the Herpes Simplex Virus Type 1. Bioconjugate Chem. 2017, 28, 1115−1122.
(14) Reina, G.; Iglesias, D.; Samori, P.; Bianco, A. Graphene: A Disruptive Opportunity for COVID-19 and Future Pandemics? Adv. Mater. 2021, 33, No. 2007847.
(15) Palmieri, V.; Papi, M. Can graphene take part in the fight against COVID-19? Nano Today 2020, 33, No. 100883.
(16) Srivastava, A. K.; Dwivedi, N.; Dhand, C.; Khan, R.; Satishk, N. Can Graphene-based Materials Play a Role in the Fight against COVID-19? Science Reporter, NIRCAIR-CSIR: India, 2020; Vol. 57, pp 32−35.
(17) Mallakpour, S.; Azadit, E.; Hussain, C. M. Fight against COVID-19 pandemic with the help of carbon-based nanomaterials. New J. Chem. 2021, 45, 8832−8846.
(18) Song, Z.; Wang, X.; Zhu, G.; Nian, Q.; Zhou, H.; Yang, D.; Qin, C.; Tang, R. Virus Capture and Destruction by Label-Free Graphene Oxide for Detection and Disinfection Applications. Small 2015, 11, 1171−1176.
(19) Motozono, C.; Toyoda, M.; Zahradnik, J.; Saito, A.; Nasser, H.; Tan, T. S.; Ngare, I.; Kimura, I.; Uru, K.; Kosugi, Y.; Yue, Y.; et al. SARS-CoV-2 spike L452R variant evades cellular immunity and increases infectivity. Cell Host Microbe 2021, 29, 1124−1136.e1−e11.
(20) Anderson, B. D.; Ikeda, T.; Moghadasi, S. A.; Martin, A. S.; Brown, W. L.; Harris, R. S. Natural APOBEC3C variants can elicit differential HIV-1 restriction activity. Retrovirology 2018, 15, No. 78.
(21) Ikeda, T.; Molan, A. M.; Jarvis, M. C.; Carpenter, M. A.; Salamando, D. J.; Brown, W. L.; Harris, R. S. HIV-1 restriction by endogenous APOBEC3G in the myeloid cell line THP-1. J. Gen. Virol. 2019, 100, 1140−1152.