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Antiviral performance of graphene-based materials with emphasis on COVID-19: A review

Tahereh Seifi, Ali Reza Kamali

Energy and Environmental Materials Research Centre (E2MC), School of Metallurgy, Northeastern University, Shenyang 110819, China

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ABSTRACT

Coronavirus disease-2019 has been one of the most challenging global epidemics of modern times with a large number of casualties combined with economic hardships across the world. Considering that there is still no definitive cure for the recent viral crisis, this article provides a review of nanomaterials with antiviral activity, with an emphasis on graphene and its derivatives, including graphene oxide, reduced graphene oxide and graphene quantum dots. The possible interactions between surfaces of such nanostructured materials with coronaviruses are discussed. The antiviral mechanisms of graphene materials can be related to events such as the inactivation of virus and/or the host cell receptor, electrostatic trapping and physico-chemical destruction of viral species. These effects can be enhanced by functionalization and/or decoration of carbons with species that enhances graphene-virus interactions. The low-cost and large-scale preparation of graphene materials with enhanced antiviral performances is an interesting research direction to be explored.

1. Coronaviruses; structure, transmission and taxonomy

During the last two decades, coronaviruses (CoVs) have been the cause of local and global epidemics, including Severe Acute Respiratory Syndrome (SARS) [1–6], Middle East Respiratory Syndrome (MERS) [7–10], and Porcine epidemic diarrhea virus (PEDV) with the mortality rate around 10%, 35% and 95% respectively, threatening human health and economic well-being. For instance, the latter caused ten percent reduction of pig population in the USA in 2013 [11,12]. Currently, the pandemic outbreak of the febrile respiratory disease, so called COVID-19 [13,14] has created a global transmission network, leading to an international crisis related to the catastrophic losses of human lives and financial meltdowns. As such, the exploration of effective antiviral agents that can be effective on COVID-19 is of great importance. Given this, the current article concerns the potential capability of graphene-based materials for antiviral therapy applications.
To this end, first a brief review on the basic aspects associated with coronaviruses is made, based on which the influences of drugs are discussed.

Coronaviruses are categorized as pleomorphic enveloped viruses with single-strand positive sense RNA genome ranging 26–32 kb in size [15–18]. The genome of CoVs is packaged into a helical capsid surrounded by a virion envelope, containing at least three proteins including the spike, membrane and envelope-types proteins. The schematic representation of coronavirus virion structure, and spike proteins are illustrated in Fig. 1 [19,20].

Furthermore, other types of proteins such as hemagglutinin esterase may also exist on CoVs. It should be mentioned that the membrane and envelop proteins are considered as transmembrane proteins that are important in the virus assembly. In contrast, the spike proteins play an essential role to infect the host cells [19–21]. The structure of spike proteins available on the surface of virion is shown in Fig. 1b, in which the crown shaped protein is formed of two domains, namely an amino (N)-terminal domain (subunit S1), and a carboxy (C)-terminal domain (subunit S2). Subunit S1 is responsible for binding of the virus to the host cell receptors, while subunit S2 causes the membrane fusion that allows entering viral genomes into the host cell [19,22,23]. Therefore, COVID-19 can infect human cells through binding of its S proteins to human ACE2 (angiotensin converting enzyme 2) receptor, which is a transmembrane protein on the cell surface [24,25].

The explosive nature of COVID-19 transmission can be correlated to its biological features. In this regard, CoVs is of the order Nidovirales, Coronaviridae family, and the Coronavirinae subfamily. The latter can be classified into four genera of alphacoronavirus, betacoronavirus, deltacoronavirus, and gammacoronavirus [20,21,26–29]. The first two are the pathogenic agents for mammals, the third one would affect the avian and mammalian species, and the last one infects birds [20,30]. The gene source for alpha- and betacoronavirus are bats whereas birds are the gene source for gamma- and deltacoronavirus [30,31]. Ye et al. [32] reported that wild birds like sparrows can also be involved in transmission of porcine deltacoronavirus to pigs [32], highlighting the complexity of the transmission chain. Likewise, civets and camels have been reported to be able to serve as the intermediate hosts for SARS-CoVs and MERS-CoVs, respectively, further highlighting the potential for interspecies transmission [33–35]. Similarly, bats and snakes may act as intermediate hosts for case of COVID-19 [36,37].

2. Animal and human infectious coronaviruses

Coronaviruses can be the source of infection in animal and human populations. Here we briefly review these viruses. In terms of animal infectious coronaviruses, alphacoronaviruses include transmissible gastroenteritis virus [38], porcine-respiratory coronavirus [39] and porcine-epidemic diarrhea virus [40] infecting pigs; feline-CoV affecting cats [41]; bat coronaviruses such as Scotophilus bat CoV-S12, Rhinolophus bat CoV-HKU2, Miniopterus bat CoV 1A/B and CoV-HKU8 infecting various species of bats [42–45].

For the case of betacoronaviruses, there are four subgroups of A, B, C and D. The subgroup A includes bovine-coronavirus (BCoV) in cows [46], porcine hemagglutinating encephalomyelitis virus in pigs [47], equine CoV in horses [48,49], mouse hepatitis CoV in rodents [50] and rabbit CoV-HKU14 in domestic rabbits [51]. Moreover, SARS-related Rhinolophus bat CoV-HKU3 belongs to the subgroup B [52], while Tylonycteris bat CoV-HKU4 and Pipistrellus bat CoV-HKUS belong to the subgroup C [53–55]. The subgroup D of betacoronaviruses include Rousettus bat CoV-HKU9 [55,56]. On the other hand, infectious bronchitis virus, turkey coronavirus, beluga whale coronavirus SW1 and bottlenose dolphin CoV-HKU22 are members of genus gamma-coronavirus [57–60]. Also, avian infectious deltacoronaviruses include bulbul CoV-HKU11, thrush CoV-HKU12, munia CoV-HKU13, white-eye CoV-HKU16, sparrow CoV-HKU17, magpie robin CoV-HKU18, night heron CoV-HKU19, wigeon CoV-HKU20 and common moorhen CoV-HKU21 [30,61]. In addition, porcine deltacoronavirus infects pigs [62,63].

Human coronaviruses (HCoVs) can cause severe infections, as for the case for COVID-19. HCoVs include HCoV-229E, HCoV-NL63 (alphacoronavirus), HCoV-OCA43, HCoV-HKU1 (betacoronavirus-A), HCoV-SARS (betacoronavirus-B), as well as HCoV-MERS (betacoronavirus-C) [30,33,34,53,54,64,65]. It should also be mentioned that various bat species are reported to be the origin of different human coronaviruses [66,67]. Recently, the International Committee on Taxonomy of Viruses (ICTV) has divided the genus betacoronavirus into five subgenera, namely embecovirus, sarbecovirus, merbecovirus, nobecovirus and hibecovirus. Based on this, SARS-CoV and COVID-19 belong to the subgenera sarbecovirus and MERS is the member of subgenus merbecovirus [68,69].

It should be mentioned that coronaviruses generally cause respiratory, gastrointestinal, hepatic, and central nervous system diseases in humans and animals with various severity [13,57,63,70]. The clinical symptoms of HCoV often include one or more of fever, cough, sneeze, respiratory distress, wheeze, pharyngitis, nasal discharge, nasal congestion, sputum, rhinorrhea, chills, muscle aches, headache, and gastrointestinal tract symptoms [71–84]. COVID-19 can cause additional issues such as loss of taste/smell, nausea and vomiting, anorexia, liver dysfunction, hyperglycaemia, septic shock and ventilator-associated pneumonia [85–90] as well as conjunctivitis [91,92]. The emergence of new versions of coronaviruses, threatening Fig. 1. The schematic illustration of (a) the typical coronavirus virion structure, highlighting the presence of three types of proteins marked as “P.” generated based on information extracted from [19]. (b) Coronavirus spike protein; subunit S1: the receptor-binding, subunit S2: the membrane-fusion; TM: the transmembrane anchor; IC: the intracellular tail and the viral envelope generated based on information extracted from [20].
the human and animal health, has highlighted the importance of the discovery of effective antiviral agents, as will be discussed in the next section.

3. Antiviral strategies against coronaviruses

The effective fight against viruses requires the detailed knowledge of ways through which the virus can invade host cells. This involves three main steps of (a) the cellular attachment and entry, (b) the replication of viral genome and viral proteins expression, and (c) the assembly, maturation, and exocytosis. Therefore, viruses rely on their host cell proteins and processes based on the above mentioned mechanisms [93]. Fig. 2 illustrates the essential steps involved in the virus replication cycle [94]. This can also highlight possible ways to combat against viruses, based on which, an effective antiviral material should inhibit at least one of the virus replication cycles.

As presented in the right side of Fig. 2, an antiviral target may attack a virus at any stage of its replication cycle. Not to mention that targeting the early steps of the virus entry is considered as an appropriate strategy for therapeutic intervention. It is because the inhibitor can attack the virus extracellularly, providing a larger accessibility to the virus, and less damage to the host cell [94].

**Fig. 2.** The schematic illustration of possible steps involved in the virus replication cycle as well as possible ways by which viruses can be inactivated. Accordingly, the virus first binds to the cell. Subsequently, the virus or its genome enters in the cytoplasm of the cell, followed by the liberation of the genome from its the protective capsid. It is then transcribed, and the viral mRNA directs the host cell to synthesize viral enzymes and capsid proteins, and to assemble new virions, which are then released from the cell. The virus can be targeted by antiviral drugs at each step of the cycle mentioned above, as shown in the right side of the image [94].
For the case of COVID-19, like any other new infectious disease without definitive and/or effective treatments, two major strategies are considered to counteract the infection, based on drug repurposing and the discovery of novel drugs. Drug repurposing can be a feasible strategy for combating epidemic diseases, since it considerably shortens the time of drug development, supporting a swift response to the spread of the novel virus species. As an example of the drug repurposing for COVID-19, one can indicate metal-based drugs which have been suggested as promising candidates to control the coronavirus [95]. Metallodrugs such as the gold drug auronofin (2,3,4,6-tetra-α-cetyl-L-thio-β-D-glycol-pyranoses-S-(triethyl-phosphine)-gold(I)) has shown antiviral influences against COVID-19 in vitro [96]. However, the general problems associated with the use of metal compounds is valid here as well, including the systemic toxicity [97]. Based on molecular mechanics-assisted structure-based virtual screening method, Terai et al. [98] reported a list of drug repurposing candidates which can be used as inhibitors of COVID-19. These drugs include lidovidomycin, quisinostat, spirofylline, bexurixat, pemetrexed, edotecarin, diniprofylline and fluropofylline [98].

Furthermore, some medicines such as chloroquine, hydroxychloroquine, remdesivir, tocilizumab and lopinavir/ritonavir have shown controlling effects on COVID-19 patients [99-104]. In addition to these, zinc supplements exhibit inhibitory effects on the replication of COVID-19 in infected cells, when used with chloroquine [105]. While this strategy of treating COVID-19 is promising, further examinations should be conducted in order to evaluate the performances and side effects of such drugs which may appear in the presence of the new virus species.

Computational simulations can provide valuable information that is difficult or expensive to be obtained experimentally. Speciale et al. [106] conducted a fundamental study based on the computational analysis, and reported on the potential of silibinin to prevent COVID-19 entry into cells due to the formation of a stable complex between COVID-19 spike protein receptor binding domain (RBD) and silibinin. Moreover, silibinin was found to be effective for inhibiting COVID-19 replication due to interactions with aminoacidic residues on the active site of COVID-19 main protease [106]. Another study based on the molecular docking showed that doxepin could inhibit viral entry into the host cells due to binding to ACE2. In this case, doxepin exhibits hydrophobic interactions, and supports hydrogen bonding with COVID-19 spike protein RBD [107]. Another molecular simulation-based research demonstrated the inhibitory ability of glucocorticoids (betamethasone, dexamethasone, hydrocortisone, fludrocortisone, ciclesonide and triamcinolone) against COVID-19 via binding interactions between the selected glucocorticoids and COVID-19 main protease pocket amino acids [108]. A combination of such computational analyses using the available drugs with sufficient experimental trials is required for the successful delivery of efficient drugs for new viruses.

The second strategy in combating COVID-19, which is based on discovering novel drugs, is more complicated and time consuming. It is because the process of new drug discovery requires more fundamental theoretical studies, the production of new drugs and various evaluations to confirm the efficiency of the developed drugs in vitro, then in vivo. Furthermore, additional experiments are needed to ensure the biocompatibility as well as environmental safety of such compounds, leading to the requirement for additional funding and time. Despite these limitations, the second strategy of combating new viral infections has the higher potential of providing drugs with unique advantageous properties, than those currently available. In this regard, strengthening the immune system can be an important factor in reducing the mortality of viral diseases, which may be combined with herbal drugs. The latter can be produced from various parts of plants such as seeds, barks, flowers, roots, stems, and fruits for immunomodulating and strengthening the immune system [109,110]. Moreover, the alkaloids, flavonoids and polyphenol exist in some plants such as garlic, peppermint, oregano, ginger, licorice, tulsi, turmeric, echinacea, aegalus, and fennel can cause the release of antibodies and interferons toward viral infections [109]. For instance, Echinacea®, a herbal medicine derived from Echinacea purpurea, has been shown to be effective in inactivation of HCoV-229E, MERS-CoV, SARS and COVID-19 at least in vitro [111]. Also, based on the molecular docking technique, Thuy et al. [112] reported the inhibitory effect of garlic essential oil toward COVID-19 due to the strong interactions between the 17 organosulphur compounds of the garlic essential oil and the amino acids of the ACE2 protein as well as the main protease PD68L07 of COVID-19.

Furthermore, organometallic compounds such as sodium copper chlorophyllin synthesized from chlorophyll show antibacterial and antiviral activity [113,114]. An enhanced level of antiviral activities can be achieved using nanomaterials, as discussed in the next section.

4. Application of nanotechnology in virus therapy

Nanotechnology has been playing a vital role in the recent progress of biomedicine and bioengineering, including the synthesis and application of therapeutic nanomaterials for various applications such as cancer diagnosis and therapy, drug delivery and tissue engineering [115-117].

Likewise, nanotechnology and nanoscience may open new windows in combating various pathogens including COVID 19, in different ways such as detecting the virus, diagnosis of viral infection and nanovaccines, such as lipid nanoparticles, for the prevention and/or the therapy of COVID-19 infection [118-129].

In general, two approaches can be distinguished in the application of nanomaterials against viruses. One approach considers an external stimulus which can kill viruses [130]. The other approach is related to the interaction between the surfaces of the viruses and the nanomaterial employed as the antiviral agent.

The first approach may be implemented by the application of light or Near Infrared (NIR) irradiation. For example, Akhavan et al. [131] reported on the photoinactivation performance of thin films of graphene-tungsten oxide nanocomposites against bacteriophage MS2 viruses under visible light irradiation. In this case, the protein capsid photodegradation and efflux of the RNA are identified as the mechanisms of bacteriophage MS2 virus inactivation [131].

The second approach highlights the antiviral performances of nanostructured materials. It was reported that human coronaviruses can survive on non-living surfaces, including glass-, plastic- or metal-surfaces for nine days [132]. Therefore, using surfaces with the ability to kill pathogens would be highly beneficial to prevent the spread of infections. Perhaps one of the first reports on the impact of nanostructured topography toward COVID-19 was presented by Hasan et al. [133] who demonstrated the antiviral performance of the surfaces of nanostructured aluminium 6063 alloy against COVID-19. The alloy was synthesized by the wet etching technique. The use of such nanostructure surfaces can be an interesting approach toward the reduction of environmental contaminations and hospital infections, and consequently, the transmission of COVID-19. Copper alloy surfaces are also reported to possess anti-pathogenic performance, reducing the infectious disease transmission from fomites [132,134-137]. The surfaces of copper alloy, therefore, may limit the spread of COVID-19 [138]. As for comparison, COVID-19 could survive for three days on plastic and stainless steel surfaces, but no live COVID-19 could be detected on copper alloy surfaces only after four hours of exposure [139]. In fact, copper has been shown to have antiviral ability against both enveloped and nonenveloped various genomes (single or double strand DNA and RNA) such as human immunodeficiency virus type 1 (HIV-1), bronchitis virus and poliovirus [140,141].

As another example of metallic materials with antiviral performance, one can name silver nanoparticles. Immunofluorescence studies confirmed that the polyvinylpyrrolidone polymer coated with...
10 nm silver nanoparticles could inhibit COVID-19 infection towards VeroE6/TMPRSS2 cells. Here, the effect of nanostructuring was highlighted, since the application of silver particles with sizes around 100 nm could not provide an appropriate antiviral performance [142].

Apart from alloys and coatings, the antiviral performances of nanoparticles in powder forms have also been of interest. For instance, silver nanoparticles with the sizes of 2–15 nm exhibit antiviral activity against COVID-19 [142]. However, since metallic nanoparticles are highly reactive in powder forms, the application of metal oxide powders is of importance. As a good example in this field, one can indicate the antiviral performance of tin oxide (SnO₂) nanowires against HSV-1 infection. In this case, SnO₂ nanowires work as a carrier of negatively charged structures that compete with HSV-1 attachment to cell bound heparan sulfate, and therefore, inhibit the entry and the subsequent cell-to-cell spread [143]. SnO₂ has also been used for the destruction of antiviral drugs, such as abacavir after the treatment of HIV [144].

The strategy of using metal oxide nanostructures is attractive, since such materials can be produced at low-cost using environmentally friendly approaches [145–147]. As another example of using metal oxides, Abo-zeid et al. [148] reported on the potential application of iron oxide nanoparticles to inactivate COVID-19. Their results obtained using molecular docking studies show that both Fe₃O₄ and Fe₂O₃ are able to interact with the spike protein of COVID-19 (subunit S1 in Fig. 1b), but Fe₂O₃ binding was found to be more stable. According to this study, under the influence of iron oxide nanoparticles, COVID-19 can lose its ability to attach to the host cell receptors [148].

It follows from what is mentioned above that the characteristics of surfaces of nanostructured materials can provide a critical influence on their antiviral performances. In fact, the application of non-toxic substances that can effectively combat COVID-19 and future viral outbreaks should be very important towards the control of virus infections. One of those non-toxic nanomaterials is graphene, as discussed in next sections.

5. Graphene-based materials

As an interesting member of carbon nanostructures, graphene, the building block of graphite, can be defined as an atomically two-dimensional layer of hexagonally bonded carbon atoms. Such carbon structure can exhibit outstanding properties such as large specific surface area, high mechanical strength, high electron conductivity as well as strong thermal, optical and catalytic characteristics [149–160]. Graphene-based materials are referred to those materials that contain single or few-layer graphene or graphene oxide [161,162] in their structures. Furthermore, high quality graphene materials may be produced at large scales using low cost methods that employ highly available resources such as graphite [163,164], biomass [165] and waste plastics [166,167], making them attractive for commercial applications.

These unique properties of graphene and its derivatives have made these nanostructured materials suitable for various biological and medical applications [168] including anti-pathogenic applications [169–177], biosensors [178–184], bioimaging [185–192], tissue engineering [193–196], drug delivery [197–201]. Therefore, the interactions between graphene materials and viruses should be of great interest.

It should be mentioned that the antibacterial activity of graphene nanomaterials can be explained based on various effects including membrane-, oxidative-, and/or photothermal- stresses as well as charge transfer, and the entrapment effect of graphene materials on various bacterial species, as recently reviewed elsewhere [255]. In comparison with bacteria, relatively very little is known about the antiviral performances of graphene materials, mainly because of significant differences in the size of virus (2–300 nm) and bacteria (500–5000 nm), which makes the viral studies more difficult and/or expensive to be conducted [256,257]. This article reviews the antiviral activity of graphene nanomaterials, based on the available literature.

6. Interactions between graphene-based materials and viruses

As briefly discussed above, graphene-based materials can be used in various biomedical fields, including the rapid and accurate detection of virus species, personal protective equipment such as masks, gowns and gloves, as well as the antiviral applications [202–210]. One important and common aspect of these studies is related to the interactions between the virus and graphene-based materials.

Chowdhury et al. [211] reported on the electrochemical detection of Hepatitis E virus (HEV) by a graphene-based nanocomposite, defined as nitrogen- and sulfur-co-doped graphene quantum dots (QDs) and gold embedded polyaniline nanowire [211]. Here, gold nanoparticles loaded polyaniline nanowire enhances the electron transfer process and provides a large surface area on which the monoclonal antibody-conjugated graphene QDs can be loaded. The latter could provide active sites for the target HEV. Introducing an external electrical pulse during the virus accumulation step increases the sensitivity of the antiviral agent towards HEV compared to other conventional electrochemical sensors. It is because the external electrical pulse can cause the expansion of the surface of the virus as well as the length of the antibody-conjugated polyaniline chain [211]. This research may highlight the capability of graphene QDs (with sizes of around 500 nm) to be effectively attached to the virus species.

This example highlights that interactivity of graphene with surrounding environment plays a key role in the overall performance of the material. It should be mentioned that graphene edge can be of particular interest due to the presence of dangling bonds, representing at least two times greater reactivity in comparison with the basal plane [212,213].

In contrast with graphene, graphene oxide (GO) is the oxidized form of graphene with hydroxyls, epoxides, diols, ketones, or carboxyl functional groups located on its surface. The presence of oxygen on the edges and basal planes of GO increases its hydrophilicity, water dispersibility, and attachability in comparison with graphene [214,215]. Given this, Song et al. [216] further highlighted the capability of GO to capture EV71 (the agent of hand, foot and mouth disease) and H₄N₉ (the agent of avian influenza A virus) at 56 °C. GO was found efficient for the destruction of the coating proteins available on these viruses and extracting the viral RNA in an aqueous environment. This interaction leads to the superficial bioreduction of GO, leading to its conversion into graphene form, while killing the virus [216].

It should be mentioned that the graphene formed by the reduction of GO is often called reduced graphene oxide (rGO). The reduction of GO can also occur during thermal reduction treatments [217,218].

Ziem et al. [219,220] produced thermally rGO sheets functionalized by polysulfated dendritic polyglycerol. This functionalized rGO material showed antiviral performance against a range of viruses comprising orthopoxviruses, herpes simplex virus type 1 (HSV-1) and equine herpesvirus type 1 (EHV-1). These viruses cause the significant global health problems such as HSV-1 and orthopoxviruses that infect humans, and EHV-1 that infects horses. It was demonstrated that the binding of polar polymers to the carbon material leads to enhanced solubility in water. It also results in a bio inert multifunctional surface that is easily accessible for further post-modification and biological interactions. The subsequent sulfation of the material promotes the interaction of the material with viruses. Here, graphene scaffolds with the large surface area provide the opportunity to increase the valency of the dendritic polyglycerol sulfate groups [219,220].

As shown in Fig. 1, for the binding and entering of viruses into the host cell, the virus must first interact with the host cell surface receptors. In viral envelope glycoproteins, heparan sulfate proteoglycans and chondroitin sulfate proteoglycans function as the cell surface receptors [221,222]. Given this, functionalized graphene materials can prevent cellular viral infections based on the interaction between
negatively charged functional groups which mimic cell surface heparan sulphate [219,220]. In addition to this, the size of graphene flakes and the degree of sulfation could influence the antiviral activity of the functionalized graphene materials. Accordingly, the flake sizes of around 300 nm together with around 10% functionalization could provide the optimum performance [220].

Elechiguerra et al. [223] coated silver nanoparticles with carbon, bovine serum albumin and poly N-vinyl-2-pyrrolidione, and evaluated the antiviral performances of the resultant materials against HIV-1 virus. Out of these samples, carbon coated silver nanoparticles showed a higher level of antiviral performance [223], which could be related to their surface chemistry, providing a higher reactivity against the virus.

The feline coronavirus (FCoV), and the infectious bursal disease virus (IBDV) have been used to evaluate the antiviral performances of graphene materials. FCoV belongs to the genus alphacoronavirus with its positive-sense, single-stranded RNA and a lipid envelope (Fig. 3a). Cats show feline infectious peritonitis because of this virus, and the spread of the virus is possible through the direct contact with infected secretions [224]. IBDV is a member of the family Birnaviridae and the genus Avibirnavirus. It is a non-enveloped virus with double-stranded RNA (Fig. 3b) [225,226]. This virus is responsible for the infectious bursal disease, also called Gumboro disease in young chickens, inducing immunosuppression, leading to a significant economic losses [227,228].

Chen et al. [229] evaluated the antiviral activity of GO and GO-Ag nanocomposites against FCoV and IBDV. The schematic structures of these viruses as well as the graphene-based antiviral species are shown in Fig. 3. It was found that GO-Ag exhibits a higher level of antiviral activity than GO. Accordingly, the GO-Ag nanocomposite was capable of controlling FCoV and IBDV by 25% and 23%, respectively; whereas GO only showed 16% inhibition of FCoV and no inhibition against IBDV. Antiviral mechanism involved in the antiviral performance of GO and GO-Ag could be explained based on the structural features, highlighted in Fig. 3. The antiviral performances of graphene materials could be explained based on chemical/physical interactions with viruses. Based on this, the opposite surface charges of antiviral species (GO and GO-Ag) from one side, and both viruses from the other side, could cause binding between graphene materials and viruses. Under this condition, GO could interact with the lipid molecules of the enveloped virus. Additionally, the binding of Ag and –SH groups of viral proteins in both enveloped and non-enveloped viruses provides an additional interaction. This binding is critical in order to control the infection of IBDV. For the case of GO-Ag and non-enveloped viruses, GO nanosheets play a minimal direct role in the overall antiviral activity of the nanocomposite. Instead, GO contributes to the overall performance of the antiviral agent by providing a substrate for silver particles to be well dispersed without obvious aggregation [229]. Further investigations confirm the electrostatic interactions between GO/ rGO species and oppositely charged lipid membranes, leading to the adsorption of graphene materials followed by the rupture of the liposome [230,231].

Such an electrostatic force-driven interaction has also been described for the case of porcine epidemic diarrhea virus with positive-strand RNA genome from genus alphacoronavirus, and also the pseudorabies virus with double stranded DNA genome from genus alphaherpesvirus [232]. Here, the antiviral mechanism of GO against these viruses was discussed to be based on the interaction between negatively charged surfaces of GO with sharp edges, and positively charged viruses. It should also be noted that GO could only show an antiviral activity if used before the viral absorption, so that the application of GO simultaneously or after viral infection, had no effect on the infection [232].

As another example, Sametband et al. [233] reported that the charge density is the most important factor influencing the antiviral properties of GO and rGO–SO₃ against HSV-1. Both graphene materials mentioned above could prevent the attachment of the viruses to host cell surface receptors, mimicking heparan sulfate biological activities. It should be added that the heparan sulfate, GO and rGO–SO₃ all have a negative charge [233].

Fig. 3. The schematic illustration of (a) the enveloped feline coronavirus, (b) the non-enveloped infectious bursal disease virus, (c) the GO, and (d) the GO-Ag antiviral agent. Regenerated from [229].
As could be realized from the cases mentioned above, the surface physiochemical properties of GO, rGO and the structures based on these nanocarbons exhibit essential roles in their antiviral performance, influencing cells viability [234,235]. In this context, it was observed that the nano-topology of the graphene layers have a significant implication on the biological/mechanical properties of graphene augmented aluminia nanofiber scaffolds, which in turn plays an important role in their antiviral performance against human pathogenic viruses (HPeV1 and IAV) through binding with viruses. Since the performances of graphene materials rely on surface-dependent reactions, their concentration and the exposure time period should also be important factors influencing their overall antiviral activity. A good example here is the work of Yang et al. [236] who investigated the concentration–dependent antiviral performance of the curcumin-loaded β-cyclodextrin functionalized sulfonated graphene composite (GSCC) toward respiratory syncytial virus (RSV). The latter is an enveloped virus with negative-sense single-stranded RNA, belonging to the Paramyxoviridae family. This virus causes respiratory disease in infants and young children [237]. The incubation of RSV with different concentrations of GSCC (0–5 μg/mL) prior to the infection demonstrated the dose-dependent performance of the graphene material for the inactivation of the virus. A GSCC concentration of 1.25 μg/mL could significantly reduce the viral titers, while the viral titers could not be detected at all at the concentration of 2.50 μg/mL, indicating that the virus had lost the ability to infect cells. It was further shown that GSCC could block the receptors of Human laryngeal epithelial type 2 (Hep-2) cells, providing an inhibitory role against the infection [236].

Here, it is relevant to mention about the antiviral performance of carbon quantum dots (CQDs), which are categorized as mainly sp² graphene structures with sizes of typically less than 10 nm [238,239].

Due to their structural features, CQDs are capable of being functionalized with various functional groups to provide antiviral activities. For instance, CQDs functionalized with boric acid showed antiviral activity against HCoV-229E. Here, two mechanisms were found to be responsible for antiviral activities: 1) the prevention of the infectious interactions between host cells and viruses, achieved by the attachment of CQDs (with an average diameter of around 7 nm) to the S-protein of viruses; and 2) the ability of CQDs to inhibit the RNA genomic replication. The presence of boronic acid functions proved to be vital for revealing the antiviral activity [240]. Similar results were obtained by Barras et al. [241] who reported on the ability of 4-aminophenylboronic acid hydrochloride functionalized carbon nanodots to prevent HSV-1 infection. Fig. 4 highlights the antiviral activity of CQDs.

In examples highlighted above, the presence of surface functional groups on graphene materials exhibit an important role in binding of the antiviral agent to the virus species. However, molecular dynamics simulations have confirmed the binding capability of graphene as well [242,243]. For example, simulations conducted by Raval et al. [242] show a strong binding efficiency between pristine multilayer graphene produced by mechanical exfoliation, and spike receptor binding domain of SARS-CoV-2 virus. In this case, the binding energy between graphene flakes and the virus increased with increasing the number of graphene layers of the flakes. Accordingly, a value of around –28.01 Kcal/mol was calculated for the changes of Gibbs free energy involved in the binding process for graphene flakes containing seven layers. It was discussed that the number of edge sp²-type carbon atoms increases with increasing the layers, promoting the surface reactivity of the graphene material.

The other point that deserves attention is that graphene materials can be loaded with magnetic materials, and therefore, can provide with extra benefits associated with the magnetic properties obtained. For example, Deokar et al. [244] produced sulfonated magnetic nanoparticles (MNPs) loaded on rGO (SMRGO). Upon irradiation of the composite with near-infrared light, the nanocomposite material could effectively capture and photothermally destroy HSV-1 with an efficiency of around 99.99%, superior to that of magnetic nanoparticles alone, as can be realized from Fig. 5. The excellent performance of the graphene-based material was attributed to its virus capture efficiency, high surface area, and excellent photothermal properties of graphene, combined with the electrostatic interactions between of MNPs with viral particles [244].

In addition to the examples provided on the antiviral properties of graphene-based materials mentioned above, the use of graphene in the process of synthesizing 2D antiviral drugs has also been reported. For instance, Mohammadiar et al. [245] produced 2D hyperbranched polyglycerol via a bottom-up graphene-assisted approach. It was demonstrated that the sulfated 2D hyperbranched polyglycerol structure fabricated using this strategy provides a higher degree of interactions with viral proteins of enveloped viruses (HSV-1, EAV and COVID-19) in comparison with the 3D version. The higher activity of the 2D structure was attributed to its greater surfaces at the same mass. As the result, more sulfate groups would be accessible on the 2D drug, which leads to the stronger interaction of the drug with the heparan sulfate receptors on the virus surfaces.

The state-of-the-art knowledge about the antiviral performances of graphene based materials, summarized above indicates several mechanisms by which graphene materials can potentially combat coronaviruses, perhaps, including COVID-19. Despite the valuable knowledge available, there are still various ambiguities and controversies involved in the antiviral application of graphene materials, including the virus mutation, the interactions between graphene and various
human genetics, side effects, and the associated cytotoxicity [246–251]. These issues should be considered in future studies.

7. Remarks and conclusions

The virus outbreaks that threaten the health of people worldwide provide the motivation to search for efficient antiviral agents. Given this, the current article concerned the antiviral performances of selected nanomaterials, with an emphasised on the antiviral performances of graphene-based materials. In terms of drug development, there are two strategies for combating coronaviruses including COVID-19, comprising drug repurposing and the discovery of novel drugs. Following the second strategy, Table 1, provides a summary of the performances of some antiviral agents, to inactivate coronaviruses, comprising iron oxide and silver nanoparticles, as well as nanostructured aluminum 6063, and copper alloys. While appropriate antiviral performances can be achieved using these materials, other parameters such as the safety, toxicity, and cost of antiviral agents can play an important role in the possibility of their large scale application. Among the novel antiviral materials highlighted in Table 1, graphene-based materials may provide advantages of large availability, non-toxicity and low-cost.

Fig. 6 summarizes the main antiviral performances of graphene-based materials discussed in this article. Graphene materials show excellent inhibitory antiviral effects against enveloped and non-enveloped viruses, including RNA and DNA viruses. These performances which are attributed to the physicochemical properties exhibited on the surfaces of these materials, can be used to control the COVID-19 pandemic. Therefore, knowing the possible interactions between coronaviruses and graphene-based materials has been the

Table 1

| Material (concentration) | Type of virus | Genome | Antiviral activity |
|--------------------------|---------------|--------|--------------------|
| GO; GO-Ag (0.1 mg/ml against FCoV, and 1 mg/ml against IBDV) | FCoV (+); IBDV (-) | FCoV (RNA); IBDV (RNA) | 16.3% (GO against FCoV); −0.4% (GO against IBDV); 24.8% (GO-Ag against FCoV); 22.7% (GO-Ag against IBDV)* [229] |
| GO (6 μg/mL) | PRV (+); PEDV (+) | PRV (DNA); PEDV (RNA) | Reduction from 5 × 10^7 to 2.5 × 10^5 pfu/mL [232] |
| Cationic QDs (125 μg/mL) | PEDV (+) | RNA | Inhibition the virus entry over 50% [258] |
| Graphene quantum dots | HIV (+) | RNA | IC_{50} (37.6 ± 6.23 μg/mL); EC_{50} (>19.90 μg/mL)** [259] |
| Al 6063 surfaces | RV-16 (-) | RNA | 3–4 log_{10} reduction viable virus [260] |
| Sulfonated magnetic nanoparticles functionalized with rGO (SMRGO) (100 ppm); Spherical magnetic Fe nanoparticles (MNP) (100 ppm) | HSV-1 (+) | DNA | without NIR light: 34.38% (MNPs) and 34.97% (SMRGO); Under NIR light: 79.06% (MNP) and 99.99% (SMRGO) [244] |
| Spherical Ag nanoparticles (NPs < 20 nm); Ag nanowires (D = 60 nm, Ag NW60), and (D = 400 nm, Ag NW400) / 3.125–12.5 μg/mL | TGEV (+) | RNA | The percentage reduction at different concentrations. At 3.125 μg/mL: 7.05% (Ag NPs), 18.04% (Ag NW60) and 15.48% (Ag NW400); At 6.25 μg/mL: 32.12% (Ag NPs), 38.06% (Ag NW60) and 28.94% (Ag NW400); At 12.5 μg/mL: 67.35% (Ag NPs), 53.90% (Ag NW60) and 58.65% (Ag NW400) [261] |
| Gold nanorod-based heptad repeat 1 peptide inhibitor | MERS (+) | RNA | More than 90% [262] |
| Copper oxide-containing filter/ 5% (wt/wt) copper oxide particles | HIV-1 (+); RSV (+); Influenza A(+) | HIV-1 (RNA); RSV (RNA); Influenza A(RNA); Rhinovirus 2 (RNA); Adenovirus type 1 (DNA);Vaccinia virus (DNA) | Log_{10} reduction: 4.6 (HIV-1); 1.5 (RSV); 1.77 (Influenza A); 2 (Rhinovirus 2); 2.2 (Adenovirus type 1); 0.47 (Vaccinia virus) [263] |
| Copper-graphene nanocomposite (5 μM) | Influenza A | RNA | -50% reduction [264] |

* Antiviral activity % = \left( \log_{10} \left( \frac{\text{TCID}_{50} \text{ml of virus}}{\text{TCID}_{50} \text{ml of treatment}} \right) \right) \times 100%

** IC_{50} is the half maximal inhibitory concentration in vitro for inhibition the activity of RNA-dependent DNA polymerase. EC_{50} is the half maximal effective concentration for reduction 50% the HIV-1-induced cytopathic effect in MT-4 cells.
center of the research activities in the field. Graphene and its derivatives exhibit the ability to inactivate different viruses through various mechanisms, namely photothermal activity and inhibit cellular infection by binding the nanomaterials to the S-protein of viruses or host cell receptors. Two important characteristics of graphene materials are based on their capability to be functionalised, and also be used as the substrate to homogeneously load other antiviral agents. Given this, those characteristics of graphene materials influencing their antiviral performances include the surface area, charge density and the concentration of graphene materials, as well as the type and size of loaded particles, the type and degree of functional groups. On the other hand, the virus characteristics such as being enveloped or non-enveloped viruses, and the time of usage the nanomaterials (virus pre-treatment, virus co-treatment, cell pre- and post-treatment) also play essential roles in determining the antiviral activity of graphene-based materials. Finally, it should be emphasised that carbon materials can provide multi-functional performances which can be employed for the decomposition of organic pollutants [252,253], adsorption of heavy metals [254] and killing of infectious pathogens, increasing the efficiency of carbons towards environmental protections. The development of efficient carbon-based materials can support the global efforts towards combat bacterial [255] and viral infections.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Fig. 6. Summary of main mechanisms involved in the antiviral performances of graphene materials, comprising the inhibition of the virus/cell binding, electrostatic trapping and the photothermal destruction.

References

[1] Rota PA, Oberste MS, Monroe SS, Nix WA, Campagnoli R, Icenogle JP, et al. Characterization of a novel coronavirus associated with severe acute respiratory syndrome. Science 2003;300:1394–9.
[2] Kuiazeck TG, Erdman D, Goldsmith CS, Zaki SR, Peret T, Emery S, et al. A Novel Coronavirus Associated with Severe Acute Respiratory Syndrome. New England Journal of Medicine 2003;348(20):1953-66.
[3] Marra MA, Jones SJM, Astell CR, Holt RA, Brooks-Wilson A, et al. The Genome Sequence of the SARS-Associated Coronavirus. Science 2003;300:1399-404.
[4] Peiris JSM, Lai ST, Poon LLM, Guan Y, Yam LYC, Lim W, et al. Coronavirus as a possible cause of severe acute respiratory syndrome. Lancet 2003;361(9366):1319-25.
[5] Peiris JSM, Guan Y, Yuen KY. Severe acute respiratory syndrome. Nature Medicine 2004;10(312):588-97.
[6] D. Feng N.a. Jia L-Q, Fang J.H, Richardson X-N, Han W-C, Cao et al. Duration of symptom onset to hospital admission and admission to discharge or death in SARS in mainland China: A descriptive study 14 2009 28-35
[7] Ahmed AE. Estimating survival rates in MERS-CoV patients 14 and 45 days after experiencing symptoms and determining the differences in survival rates by demographic data, disease characteristics and regions: A worldwide study. Epidemiology and Infection 2018;146(4):489-95.
[8] de Groot RJ, Baker SC, Baric RS, Brown CS, Drosten C, Enjuanes L, et al. Middle East Respiratory Syndrome Coronavirus (MERS-CoV): Announcement of the Coronavirus Study Group. Journal of Virology 2013;87:7790
[9] Ashar El, Hui DSC, Memish ZA, Drosten C, Zumla A. The Middle East Respiratory Syndrome (MERS). Infect. Dis. Clin. N. Am. 2019;33(4):891–905.
[10] Zaki AM, van Boheemen S, Bestebroer TM, Osterhaus ADME, Fouchier RAM. Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. New England Journal of Medicine 2012;367(19):1814–20.
[11] Chen Q, Li G, Stasko J, Thomas JT, Stensland WR, Pillatzki AE, et al. disease outbreak among swine in the united states. Journal of Clinical Microbiology 2014;52(1):234–43.
[12] Stevenson GW, Hoang H, Schwartz KJ, Burrough ER, Sun D, Madson D, et al. Emergence of Porcine epidemic diarrhoea virus in the United States: Clinical signs, lesions, and viral genomic sequences. J. Vet. Diagn. Invest. 2013;25:649–54.
[13] Hui DS, I Azhar E, Memish ZA, Ntoumi F, Kock R, Dar O, et al. novel coronavirus outbreak in Wuhan, China. Int. J. Infect. Dis. 2020;91:264–6.
[14] Wang C, Horby PW, Hayden FG, Gao GF. A novel coronavirus outbreak of global health concern. Lancet 2020;395(10223):470–3.
[15] Chen Yu, Guo D. Molecular mechanisms of coronavirus RNA capping and methylation. Viral. Sin. 2016;31(1):3-11.
[73] Kaiser L, Regamey N, Roihla H, Defneerz C, Frey U. Human coronavirus NL63 associated with lower respiratory tract symptoms in early life. The Pediatric Infectious Disease Journal 2005;24(11):1015-7.

[74] Davis BM, Foxman B, Monto AS, Baric RS, Martin ET, Uzicanin A, et al. Human coronaviruses and other respiratory infections in young adults on a university campus: Prevalence, symptoms, and shedding. Influenza Other Respi. Viruses 2012;6(2):98-99.

[75] Esper F, WeiBel C, Ferguson D, Landry ML, Kahn JS. Coronavirus HKU1 infection in the United States. Emerging Infectious Diseases 2006;12(3):775-9.

[76] Esper F, Ou Z, Huang YT. Human coronaviruses are uncommon in patients with gastroenteritis. Journal of Clinical Virology 2010;48(2):131-3.

[77] Valverde A, Dina J, Gouarin S, Petitjane J, Corbet S, FremyH. Detection of the new human coronavirus HKU1: A report of 6 cases. Clinical Infectious Diseases 2006;42(5):634-9.

[78] Gerna G, Pericelli E, Saraini A, Campanini G, Piralla A, Rovida F, et al. Human respiratory coronavirus HKU1 versus other coronavirus infections in Italian hospitalised patients. Journal of Clinical Virology 2007;38(3):244-50.

[79] Zhang S-F, Tuo J-L, Huang X-B, Zhu X, Zhang D-M, Zhou K, et al. Epidemiology characteristics of human coronaviruses in patients with respiratory infection symptoms and phylogenetic analysis of HCoV-OC43 during 2010-2015 in Guangzhou. PLoS ONE 2018;13(1):e0191789.

[80] Friedman N, Alter H, Hindiyeh M, Mendelson E, Avni YS, Mandelboim M. Human coronavirus infections in Israel: Epidemiology, clinical symptoms and seasonal occurrence of HCoV-19. Viruses 2018;10:1515.

[81] Zeng ZQ, Chen DH, Tan WP, Qiu SY, Xu D, Liang HX, et al. Epidemiology and clinical characteristics of human coronaviruses OC43, 229E, NL63, and HKU1: a study of hospitalised children with acute respiratory infection in Guangzhou, China. European Journal of Clinical Microbiology & Infectious Diseases 2018;37:363-9.

[82] Lew TWK, Kwok TK, Tai D, Earnest A, Luo S, et al. Acute Respiratory Distress Syndrome in young children. Evid. Based. Med. 2003;9(3):118-20.

[83] Hui DSC, Zumla A. Severe Acute Respiratory Syndrome Historical, Epidemiologic, and Clinical Features. Infect. Dis. Clin. N. Am. 2019;33(4):869-88.

[84] Al Salayyim HJ, Khordm SH, Al Mummar SH. Demographic, clinical, and outcomes of confirmed cases of Middle East Respiratory Syndrome coronavirus (MERS-CoV) in Najran, Kingdom of Saudi Arabia (KSA): A retrospective record based study. J. Infect. Public Health 2020;13(9):1342-6.

[85] Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2019;395 (2020):507-13.

[86] Yang X, Yu Y, Xu J, Shi H, Xu J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Resp. Med. 2020;8:475-81.

[87] D’Souza G, Springer G, Gustafson D, Kassaye S, Alcaide ML, et al. COVID-19 symptoms and SARS-CoV-2 infection among people living with HIV in the US: the MACS/WHIS combined cohort study. HIV Res. Clin. Pract. 2020;1–10.

[88] Lin Lu, Jiang X, Zhang Z, Huang S, Zhang Z, Fang Z, et al. Gastrointestinal symptoms of 95 cases with SARS-CoV-2 infection. Gut 2020;69(5):997-1001.

[89] Glavina A, Biočina-Lukenda D, Mravk-Stipetić M, Markeljević JK. Oral Coronaviruses in children. Virological and Epidemiological Investigation into SARS-CoV-2 Resistance of Compounds in Garlic Essential Oil. ACS Omega 2020;5(14):8312-20.

[90] Soltysik K, Myiliwal-Kurdziel B. Chlorophylls and their Derivatives Used in Food Industry and Medicine. Mini - Reviews in Medicinal Chemistry 2017;11:1942-29.

[91] Kaptz K, Zhou QTHSM, LewisBrown S. Piezoelectric Nano-Biomaterials for Biomedicine. Nanotechnology for COVID-19: Therapeutics and Vaccine Research. ACS Nano 2020;14:776-82.

[92] Ruiz-Hitzky E, Darder M, Wicklein B, Ruiz-Garcia C, et al. Nanotechnology Responses to COVID-19. Adv. Healthe. Mater. 2020;9:2000094.

[93] Medhi R, Srini P, Ngo N, Tran H-V, Lee TR. Nanoparticle-Based Strategies to Combat COVID-19. Adv. Healthe. Mater. 2020;9:2000094.

[94] Cieplak P, Dandekar T, Greenblatt M, et al. Structure and Collinear, Retrospective, Observational Study. Lancet Resp. Med. 2020;8:475-81.

[95] Wunder A, Ano J, Krasiva M, Szelag-Szliczynska M. Nanotechnology and Clinical Features. Infect. Dis. Clin. N. Am. 2019;33(4):869-88.

[96] Akhavan O, Choobtashani M, Ghaedeh E. Protein degradation and RNA efflux of viral nucleic acids in the context of virucidal photodynamic effects of chlorophyll. Journal of Physical Chemistry C 2011;115:9653-9.
Warren SL, Little ZR, Kervil CW, Colwell R. Human coronavirus 229E remains infectious on common touch surface materials 2015;6(6).

Hansen J, Pyle A, Millar G, Spann K, et al. Antiviral Nanostructured Surfaces Reduce the Viability of SARS-CoV-2. ACS Biomaterials Science & Engineering 2020;6(9):4858–61.

Luo J, Hein C, Ghanbaja J, Pierson JF, Mücklich F. Bacteria accumulate copper ions and inhibit oxide formation on copper surface during antibacterial efficiency tes. Microb 2019;127:102759.

Michels HT, Michels CA. Copper alloys-The new old' weapon in the fight against infectious disease. Microbiology 2016;10:23–45.

Molteni C, Abicht HK, Solioz M. Killing of bacteria by copper surfaces involves dissolution copper. Applied and Environment Microbiology 2010;76 (12):4099–101.

Noyce JO, Michels H, Kervil CW. Inactivation of influenza A virus on copper versus stainless steel surfaces. Applied and Environmental Microbiology 2007;73 (8):2748–50.

Scully JR. The COVID-19 Pandemic, Part 1: Can Antimicrobial Copper-Based Alloys Help Suppress Infectious Transmission of Viruses Originating from Human Contact with High-Touch Surfaces?. Corrosion 2020;76:523–7.

van Doremalen N, Bushmaker T, Morris DH, Holbrook MG, Gamble A, Williamson BN, et al. Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1. New England Journal of Medicine 2020;382(16):1564–7.

Raha S, Mallick R, Basak S, Duttaprer AK. Is copper beneficial for COVID-19 patients?. Medical Hypotheses 2020;142:109814.

Ishida T. Antiviral Activities of Cu+ Ions in Viral Prevention, Replication, RNA Degradation, and for Antiviral Efficacies of Lyric Virus, ROS-Mediated Virus. Cogent Chemistry. Cogent Sci. New 2018;7:146436–68.

Jeremiah SS, Miyakawa K, Morita T, Yamaoka Y, Ryo A. Potent antiviral effect of silver nanoparticles on SARS-CoV-2. Biochemical and Biophysical Research Communications 2020;539(1):195–200.

Trigilia J, Anton E, Szudovich E, Mihira YK, Aledun R, Shukla D. T. Oxide nanowires suppress herpes simplex-1 virus entry and cell-to-cell membrane fusion. PLoS ONE 2012;7:48147.

Zhou C, Wang X, Li X, Liu H, Huang N. High-efficiency electrochemical degradation of antiviral drug abacavir using a penetration flux porous TiO2–SnO2–Sb anode. Chemosphere 2019;225:304–10.

Kamali AR, Divitini G, Ducati C, Fray DJ. Transformation of molten SnCl2 into copper oxide: a study of the reaction. Journal of Materials Chemistry A 2019;8(1):259–64.

Kamali AR, Fray DJ. Solid phase growth of tin oxide nanostructures. Materials Science and Engineering B 2012;177(1):819–25.

Kamali AR. Thermokinetic characterisation of tin (II) chloride. Journal of Thermal Analysis and Calorimetry 2014;118:403–7. USA.

Abo-zeid Y, Ismail NSM, McLean GR, Hamdy NM. A molecular docking study repurposes FDA approved iron oxide nanoparticles to treat and control COVID-19 infection. European Journal of Pharmacological Sciences 2020;153:105465.

Han Y, Qi K, Boey F, Zhang H. Graphene-based nanocomposite containing Indolicidin and Graphene oxide against disseminated Escherichia coli infection. Microb通告 2020;51:110527.

Cheong YK, Arpe MP, Benito A, Chen D, Cristofoletti NL, Kerai LV, et al. Synergistic antibacterial activity of PEGylated graphene oxides and copper nanoparticles against Candida albicans. Nanomaterials 2020;10:819.

Safari Narges, Golafshin Nashin, Kharazhi Mahshid, Reza Toroghinejad Mohammad, Uotome Lizette, Malda Jos, et al. Stable and Antibacterial Magnesium-Graphene Nanocomposite-Based Implants for Bone Repair. ACS Biomaterials Science & Engineering 2020;6(11):6253–62.

Nalini A, Vento F, Piferi V, Pinerio A, Mazzaglia A, et al. Polymer-based graphene derivatives and microwave-assisted silver nanoparticles decoration as a potential antibacterial agent. Nanomaterials 2020;10:2226.

Innocenzi P, Stagli L. Carbon-based antibacterial nanomaterials: Graphene, C-dots, and fullerenes. A perspective. Chemical Science 2021;11:6606–22.

Vermisoglou E, Pandékč D, Jaryalamulu K, Pykal M, Êbreit L, Kolari M, et al. Human virus detection with graphene-based materials. Biosensors & Bioelectronics 2020;166:112436.

Afshari Savannah, Lerner Mitchell B, Goldstein Jason M, Lee Joo, Sang Xiaoling, Bagarozzi Dennis A, et al. Novel graphene-based biosensor for early detection of Zika virus infection. Biosensors & Bioelectronics 2018;100:85–8.

Fani Mona, Rezayi Majid, Menskat Zahra, Rezaee Seyed Abdolrahim, Makvandi Mohammadreza, Ahmad Sandwich, et al. A Novel Printed Electrochemical Biosensor Based on a Gold Nanoparticles-Reduced Graphene Oxide-Polypropylene Nanocomposite to Detect Human T-Lymphotropic Virus-I. IEEE Sensors Journal 2020;20(16):6255–29.

Wan Jiaqi, Bao Xiaochen, Wei Wei, Zhang Xiuhua, Wang Shengfu. Ultrasmall Electrochemical Biosensor for HIV Gene Detection Based on Graphene Stabilized Gold Nanochips with Exonuclease Amplification. ACS Applied Materials & Interfaces 2015;7(33):18752–6.

Anik Ú, Tepeli V, Sayhi M, Niri J, Diousi M. Towards the Electrochemical Diagnostic of Influenza Virus: Development of Graphene-Au Hybrid Nanocomposite Modified Influenza Virus Biosensor Based on Neuraminidase Activity. Analyst 2017;142:1510–9.

Kinnamons D, Krishnan Siddharth, Brosler Samantha, Sun Evan, Prasad Shalini. Screen Printed Graphene Oxide Textile Biosensor for Applications in Inexpensive and Wearable Point-of-Exposure Detection of Infection for At-Risk Groups. ACS Synthetic Biology. 2019;8(3):487–96.

Li J, Jin X, Feng M, Huang S, Feng J. Ultrasonic and highly selective electrochemical biosensor for HIV gene detection based on amino-reduced graphene oxide and β-cyclodextrin modified glassy carbon electrode. International Journal of Electrochemical Science 2020;15:2727–38.

Lu H, Li W, Dong H, Wei M. Quantum Dots for Optical Bioimaging. Small (Weinheim an der Bergstrasse, Germany) 2019;15:1902136.

Kadian S, Manik G, Das N, Roy P. Targeted bioimaging and sensing of folate receptor positive cancer using folate-conjugated sulfonated-doped graphene quantum dots. Microchimica Acta. 2020;187:458–75.

Santos Carla IM, Rodriguez-Pérez Laura, Gañacholes Gil, Pinto Sandra N, Melle- Franco Manuel, Marques Paula AAP, et al. Novel hybrids based on graphene quantum dots covalently linked to glycol corroles for multiphoton bioimaging. Carbon 2020;166:164–74.

Kuo Wen-Shuo, Sheng Xing-Can, Chang Chia-Yuan, Kao Hui-Fang, Lin Sheng-Han, Wang Jiu-Yao, et al. Multiplexed Graphene Quantum Dots with Excitation-Wavelength-Dependent Luminescence for Cytotoxicity Assay, and in Ultraviolet-Near Infrared Bioimaging. ACS Nano 2020;14(9):15102–9.
putative interactions with SARS-CoV-2 virus investigated through computational studies 1 10 10.1080/07391102.2020.1817788

[243] Gupta SK, Soni HR, Jha PK. Electronic and phonon bandstructures of pristine few layer and metal doped graphene using first principles calculations. AIP Advances 2013;3:032117.

[244] Deokar Archana R, Nagvenkar Anjali P, Kati Inna, Shani Lior, Yeshurun Yosef, Gedanken Aharon, et al. Graphene-Based “Hot Plate” for the Capture and Destruction of the Herpes Simplex Virus Type 1. Bioconjugate Chemistry 2017;28(4):1115–22.

[245] Ehsan Mohammadifar Vahid Ahmadi Mohammad Fardin Gholami Alexander Oehrl Oleksandr Kolyvushko Chuanxiong Nie et al. Graphene-Assisted Synthesis of 2D Polyglycerols as Innovative Platforms for Multiviral Vaccine Interactions 2009003 10.1002/adfm.202009003

[246] Grubaugh ND, Hanage WP, Rasmussen AL. Making Sense of Mutation: What D614G Means for the COVID-19 Pandemic Remains Unclear. Cell 2020;182:794–5.

[247] Priyanka Saha Arup Kumar Banerjee Prem Prakash Tripathi Amit Kumar Srivastava Upanasa Ray 405 2020 10.1042/BSR20201312

[248] Dyer O. Covid-19: Denmark to kill 17 million minks over mutation that could undermine vaccine effort. BMJ 2020;371:m4338.

[249] Pachetti M, Marini B, Giudici F, Benedetti F, Angeletti S, et al. Impact of lockdown on Covid-19 case fatality rate and viral mutations spread in 7 countries in Europe and North America. J. Transl. Med. 2020;18:338.

[250] Maria ED, Latini A, Borgiani P, Novelli G. Genetic variants of the human host influencing the coronavirus-associated phenotypes (SARS, MERS and COVID-19): Rapid systematic review and field synopsis. Human Genomics 2020;14:230.

[251] Ahmed SF, Quadeer AA, McKay MB. Preliminary identification of potential vaccine targets for the COVID-19 Coronavirus (SARS-CoV-2) Based on SARS-CoV Immunological Studies. Viruses 2020;12:254.

[252] Lin Y, Tian Y, Sun H, Hagio T. Progress in modifications of 3D graphene-based adsorbents for environmental applications. Chemosphere 2021;270:129420.

[253] Wei S, Kamali AR. Dual-step air-thermal treatment for facile conversion of PET into porous carbon particles with enhanced dye adsorption performance. Diamond and Related Materials 2021;107:107914.

[254] ur Rehman Saeed, Ullah Najeeb, Kamali Ali Reza, Ali Khurshid, Yerlikaya Cemile, ur Rehman Hanif. Study of thallium(III) adsorption onto multiwall carbon nanotubes. New Carbon Materials 2012;27(6):409–15.

[255] Seifi Tabereh, Kamali Ali Reza. Anti-pathogenic activity of graphene nanomaterials: A review. Colloids Surf. B Biointerfaces 2021;199:111509. https://doi.org/10.1016/j.colsurfb.2020.111509.

[256] Arashia VH, Forbes S. Viral clearance strategies for biopharmaceutical safety. Pharmaceutical Technology 2001;25:26–31.

[257] Prussin Aaron J, Marr Linsey C, Bibby Kyle J. Challenges of studying viral aerosol metagenomics and communities in comparison with bacterial and fungal aerosols. FEMS Microbiology Letters 2014;357(1):1–9.

[258] Ting D, Dong N, Fang L, Lu J, Bi J, Xiao S, et al. Multisite inhibitors for enteric coronavirus: antiviral cationic carbon dots based on curcumin. ACS Appl. Nano Mater. 2018;1:5451–9.

[259] Prussin Aaron J, Marr Linsey C, Bibby Kyle J. Challenges of studying viral aerosol metagenomics and communities in comparison with bacterial and fungal aerosols. FEMS Microbiology Letters 2014;357(1):1–9.

[258] Ting D, Dong N, Fang L, Lu J, Bi J, Xiao S, et al. Multisite inhibitors for enteric coronavirus: antiviral cationic carbon dots based on curcumin. ACS Appl. Nano Mater. 2018;1:5451–9.

[259] Iannazzo Daniela, Pistone Alessandro, Ferro Stefania, De Luca Laura, Monforte Anna Maria, Romeo Roberto, et al. Graphene Quantum Dots Based Systems As HIV Inhibitors. Bioconjugate Chemistry 2018;29(9):3084–93.

[260] Hasan Jafar, Xu Yanan, Yarlagadda Tejani, Schwarz Michael, Spans Kirsten, Yarlagadda Prasad KDV. Antiviral and Antibacterial Nanostructured Surfaces with Excellent Mechanical Properties for Hospital Applications. ACS Biomaterials Science & Engineering 2020;6(6):3608–18.

[261] X. Lv, P. Wang, R. Bai, Y. Cong, et al., Inhibitory effect of silver nanomaterials on transmissible virus-induced host cell infections, Biomaterials 35 (2014) 4195-4203.

[262] Huang X, Li M, Xu Y, Zhang J, Meng X, An X, et al. ACS Applied Materials & Interfaces 2019;11:19799–807.

[263] Ting D, Dong N, Fang L, Lu J, Bi J, Xiao S, et al. Neutralizing viruses in suspensions by copper oxide-based filters. Antimicrobial Agents and Chemotherapy 2007;51(7):2605–7.

[264] Das Jana Indrani, Kumbhakar Partha, Banerjee Saptarshi, Gowda Chinmayee Chowde, Kedia Nandita, Kuila Saikat Kumar, et al. Copper Nanoparticle–Graphene Composite-Based Transparent Surface Coating with Antiviral Activity against Influenza Virus. ACS Appl. Nano Mater. 2021;4(1):352–62.