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Potentialities of graphene and its allied derivatives to combat against SARS-CoV-2 infection

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1. Introduction

Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2/COVID-19; an acute respiratory disease) presently has an overwhelming side effect on the global health system. The SARS-CoV-2/COVID-19 pandemic outbreak was first reported in December 2019 from Wuhan metropolis, China, which has currently taken all over the world with recorded 250,750,795 cases of coronavirus, 5,067,619 deaths, and 226,979,345 recovered cases reported till 10th November 2021 [1]. Furthermore, the World Health Organization (WHO) has declared the SARS-CoV-2/COVID-19 pandemic as an emergency because of its severity and global spread [2].

Moreover, following the genomic studies, SARS-CoV-2/COVID-19 is in the betacoronavirus (ßCoV) clade as SARS-CoV and MERS-CoV [3]. Further, the coronavirus has a very similar genetic arrangement to the SARS-CoV virus [4]. The principal host of this SARS-CoV-2/COVID-19 is a bat animal, and this virus displays 96% similarity to the whole genome of bat coronavirus. The preliminary scientific signs of SARS-CoV-2/COVID-19 infections are headaches, gastrointestinal pain, fever, problems in breathing, and pneumonia with an unpredictable degree of severity [5]. In humans, SARS-CoV-2 is based on spike-protein (S-protein) and binds with the human enzyme Angiotensin-Converting Enzyme 2 (ACE2), which controls blood pressure. The human cell receptor binds this spike protein on the cell surface that accelerates the viral entry inside the cell and further initiates its replication in human cells [6]. Numerous...
researches are being performed to treat this sickness, but no specific medicine can completely cure the SARS-CoV-2 infection; apart from this, many other studies are under the trial period to date.

Nowadays, nano-based antiviral negotiators have the advantage of greater recognition for the cure of SARS-CoV-2 disease. Researchers have given GO much consideration because of its unique mechanical, electrical, and piezoelectric capabilities. GO is a thin sheet of carbon atoms grouped in a hexagonal pattern with a wonderful six-sided symmetry. GO has a large precise floor vicinity, excessive electric mobility and excellent conductivity. GO exhibits several functional clusters on its boundaries and oxygen-containing functional groups that play a significant role in antimicrobial and antiviral efficiency [7–9]. The antibacterial efficacy of GO and its derivatives against gram-positive and gram-negative bacteria is remarkable [10,11]. For the antibacterial activity of GO, physical and chemical interactions of GO sheets with bacterial cell walls are responsible [12,13], as the sharp edges of GO penetrate the bacterial cell wall, which causes RNA leakage that directly affects the integrity of the bacterial cell wall. Further, oxidative properties of GO leads to lipid peroxidation, which tends to kill bacterial cell [14,15]. Many graphene and carbon-containing compounds, such as GO, reduced graphene oxide (r-GO), fullerene, graphene quantum dots (GQDs), and carbon nanotubes (CNTs), are important in the treatment of SARS-CoV-2 infection [7,8].

Several scientific works of literature are available for the promising contribution of GO and its by-products for combating the SARS-CoV-2 pandemic [16]. In one such article, Figueroz et al. [17] reported a next-generation smart, low-cost, and triboelectric rechargeable respiratory mask with excessive filtration (>95%) efficiency. They had modified the propylene (PPy) layer in the N95 mask with polyvinylene fluoride (PVDF) and GO containing ink using an easy solution casting method. This modification brought a huge change in triboelectric voltage and charge of the undecorated PPY layer. Further, Chowdhery et al. [18] had described the role of nanotechnology and nano-based materials like graphene and related substances applicability for biosensors, nano-polymer based disinfectants, nano-electrodes for purifying groundwater etc., and they had also helped to understand the structure and life cycle of coronavirus in terms of nanotechnology. Furthermore, Palmeri and Papi [8] described the interaction between graphene and graphene-derived materials with different virions to inhibit or destroy the viruses. They also described graphene materials’ potentialities for fabricating filters, environmental sensors, and graphene wafers to control SARS-CoV-2 effects.

Furthermore, Udagama et al. [16] primarily described early diagnosis technologies based on nucleic acid and protein biomarkers in their work. They explained the analysis techniques of SARS-CoV-2 diseases, including enzyme-linked immunosorbent assay (ELISA), nucleic acid sequence-based amplification (NASBA), reverse transcription recombinase polymerase amplification (RTRPA), magnetic biosensor, magnetic ELISA, and DNA-assisted immunoassay. Further, Cordero et al. [19] reviewed the potential of graphene-based material in liquid biopsy and identifying SARS-CoV-2 infection; they also explained the possible implication of graphene-derived materials utilization for personal protecting equipment (PPEs) to fight against SARS-CoV-2 infection. Srivastava et al. [20] had reviewed the functionalized graphene and graphene-based materials in designing the field-effect transistor-based biosensors, piezoelectric effect and surface plasmon resonance-based diagnostic system. They also explained the capability of GO and its by-products for developing antiviral surface coating; 3D printed medicinal constituents, and nanofoams design for face masks and PPEs.

This review provides up-to-date and comprehensive information on the GO nanoparticles and their derivatives to combat SARS-CoV-2 infection, as GO nanoparticles have attracted a superb response in biomedical applications in recent years and are still constantly increasing at a rapid pace. Apart from the biomedical applications of GO nanoparticles, this review also offers an overview of GO nanoparticles’ traits that make them a powerful tool for addressing illnesses. All of these graphene-based composites would possibly help combat the SARS-CoV-2 outbreak. The records furnished in this forthcoming outline a potential approach for preventing SARS-CoV-2 contamination with graphene-based products. The electroconductive and hydrophobic properties of graphene and graphene-derived nanomaterials, together with their compatibility with SARS-CoV-2, could be used to construct various products. Hence, this study provides a complete evaluation of the GO and its derivatives, focusing on biomedical applications, and reviews the current state of GO nanoparticles in the biomedical domain and its possibilities regarding SARS-CoV-2.

2. Graphene and graphene-based derivatives

Graphene has emerged as one of the interesting carbon nanomaterials, and it was first distinguished through the momentous investigations done by Andre Geim and Konstantin Novoselov in 2004 after stripping off graphite with a sticky tape [21,22]. Graphene is a regular mono-layer carbon atom hybridized of sp2 with a compactly organized honeycomb-like structure. GO is an oxidized form of graphite treated with strong oxidizing agents. Mechanical [23], electrical [24], physical and chemical properties [25], ability to have a molecular barrier [26], and superior mechanical strength are some significant properties that cause graphene to have uncountable exploration effort to integrate graphene in polymers to synthesize nanocomposites [27,28].

Moreover, the r-GO is a derivative of GO, and when compared with GO, the r-GO has a lesser number of carbons to oxygen (C:O) ratio. Several methods are present to synthesize r-GO, such as laser irradiation, thermal annealing, photoemission, microwave-assisted reduction [29], and chemical reducing methods [30,31]. Further, many reducing agents are involved in synthesizing GO like hydrohalic acids, ascorbic acid, aluminum hydride, hydrazine hydride, thiourea, and sodium borohydrate. Among them, hydrazine hydrate (N2H4) is a widely used reducing agent; after that, on dissociation, it forms water and nitrogen to scavenge oxygen molecules. CNTs are an allotrope of carbon that is long, thin, and cylindrical. They are a type of graphite material and can be observed as rolled-up graphene sheets [32]. Fig. 1 shows different kinds of graphene-based derivatives.

2.1. Mechanism of graphene-based materials for prevention of SARS-CoV-2

Graphene has an excessive viral dilemma limit, consistent with previous take a look at. When tiny layers of reduced graphene oxide-Tungsten oxide (r-GO/TiO2) have been altered for photo-inactivation of virus invading bacteria beneath evident mild illumination in 2012, the key confirmation of graphene antiviral effects was discovered [7]. The coronavirus spike S1 protein receptor-proscribing location can interact with heparin and exchange compliance, keeping with recent studies. It provides guidance for advancing first remedial efforts by way of adapting heparin and glycosaminoglycans-based antiviral agents [33], in addition to sulfurous acid or sulphate treatment of graphene oxide-based surfaces. Using near-infrared (NIR) light, sulphur reacted NPs functionalized with r-GO were effectively employed to collect and photothermally pulverise herpes simplex infection type 1 [34]. This information raises the possibility of mixing GO detention with lung NIR remedies as graphene and GO absorbers fall within the NIR
tissue transparency frame, which in turn enables the incoming light to penetrate the body deeply. SARS-CoV-2 can be inhibit by utilizing a mixture of carbon dots with effective antimicrobial polyphenol curcumin [35]. The mix of Cyclodextrins-functionalized sulfonated graphene and curcumin-stacked cyclodextrins functionalized sulfonated graphene (GSCC) is used to treat respiration syncytial infection. The GSCC’s sulfonate clusters can mimic the cellular outside and constrain RSV infection through a cost-effective inhibition approach, replicating the mobile receptors implicated in the contamination connection. The consequence of GSCC NPs is because of a two-fold aspect: curcumin-mediated viral inactivation and self-awareness of the infection’s association to the host cellular layers [36]. Moreover, many researches have demonstrated the potentials of graphene and its derivatives as an excellent drug-delivery agent that can be effectively utilized to treat SARS-CoV-2; however, clinical trials of this are still not concluded, and a proper outlook is still required [37,38].

3. Various applications of graphene and graphene-based derivatives to combat SARS-CoV-2

3.1. Biosensors

To determine the SARS-CoV-2 quickly, many rapid biosensors have been developed that can help in proper management of the SARS-CoV-2 infection. Currently, several diagnostic kits use polymerase chain reaction (PCR) techniques, including reverse transcriptase-polymerase chain reaction (RT-PCR) for the detection of SARS-CoV-2 [39,40]. These RT-PCR-based techniques are very sophisticated and time-consuming to yield the diagnostic report, but it is a highly sensitive technique to date for determining this infection. Rapid antigen tests are also employed to diagnose the diseases, but sometimes it shows error; apart from this, this technique is also very sensitive. Therefore, there is a crucial need to grow a quick, economically viable, less time-consuming diagnostic tool to detect SARS-CoV-2 infection in the present scenario. However, biosensors are a suitable candidate for the detection of the virus. The matrix of biosensors has an important influence on the analytical device’s performance [41]. Moreover, with the rapid development of artificial intelligence, the Internet of Things (IoT), the Internet of Medical Things (IoMT), lab-on-a-chip, etc., many portable and rapid SARS-CoV-2 detection kits have been developed with high sensitivity, accuracy, selectivity, rapidness, reproducibility and low detection limit. They have enhanced the development of wearable sensors that enable the disease’s rapid diagnosis by keeping track of the patient’s health record. Moreover, intense studies are required to keep track of viral diseases; however, researches are going on, and it is believed that soon SARS-CoV-2 can also be traced [42–47]. Many researchers developed cost-effective and portable techniques like colorimetric, electrochemical lateral flow, SERS-based biosensors, etc.; many others are developing rapid, selective, and sensitive electrochemical biosensors fabricated from carbon-based and gold materials to determine the SARS-CoV-2 infections [48].

Further, graphene and graphene-derived materials are highly appreciated for designing effective biosensors due to their unique features like stable optical and electrochemical behavior, excellent electrocatalytic activities, and great thermal, mechanical, and electrical properties [49]. Joshi et al. [50] described the GO-based biosensors to determine the influenza virus. The detection limit for the target virus of this fabricated biosensor in saliva samples and peripheral blood smears (PBS) were determined as 26 and 33 PFU/mL, respectively. Huang et al. [51] fabricated a highly sensitive and selective sandwich-type immunosensor for detecting the avian influenza virus H7 (AIV H7); this biosensor was fabricated by conjugating Graphen@chitosan@gold nanoparticles (G@CS@Au NPs) with H7-monoclonal antibodies (MAbs) on the gold substrate and further, the G@silver NPs@CS (G@Ag NPs@CS) attached with
3.2. Personal protective equipment's (PPEs) and their allied derivatives are highlighted in Table 1. Moreover, few of the other biosensors fabricated by utilizing graphene care (POC) test, etc. due to their highly conducting nature. More importantly, it was found that this biochip exhibited selectivity against blood-borne antigens and can stand by for almost ten days at 5°C. Therefore, this biosensor can be considered portable, rapid point-of-care (POC) for early diagnosis of SARS-CoV-2 using real samples [52].

Further, graphene-based electrochemical biosensors are generally used for recognizing biomolecules of interest, and various studies have proved that these sensors can also be efficiently used to detect the SARS-CoV-2 [20], but to develop a reliable diagnostic device, the scientist needs to research more for fabricating a very reliable approach of biosensing mechanism. Furthermore, from the available scientific researches, it can be stated that the available electrochemical biosensors based on graphene and its allied derivatives are very rapid, sensitive, and selective owing to the extraordinary properties exhibited by this material; the hypothetical mode of mechanism for the recognition of the SARS-CoV-2/COVID-19 virus is highlighted in Fig. 3. Apart from the fabrication of electrochemical biosensors for the recognition of SARS-CoV-2/COVID-19, graphene and its allied derivative are also widely used in electrochemical biosensing applications (like reliable point-of-care (POC) test, etc.) due to their highly conducting nature. Moreover, few of the other biosensors fabricated by utilizing graphene and their allied derivatives are highlighted in Table 1.

3.2. Personal protective equipment’s (PPEs)

Graphene is a hexagonal sp² hybridized carbon atom, GO is an oxidized derivative of graphene, and r-GO is synthesized by thermal and other methods by reducing the oxygen content of GO using various reducing agents. Graphene and graphene-based derivatives show excellent thermal, mechanical, and antibacterial properties. These one atom thick materials have a huge surface area and a high absorbing ability for the incident beam of light (2.3%). However, graphene and graphene-derived materials are utilized to fabricate personal protective equipment (PPEs) kits and other equipment [57]. Graphene has the capacity to intervene as a solid lubricant, owing to its self-lubricating properties, smooth molecular lamellar arrangement, and simple shear capacity that plays a significant role [58]. Further, for preparing protective cloths, if fabric materials are altered with graphene and graphene-based derivatives, then it can help to improve the antimicrobial activity, higher elasticity, tensile strength, lightweight, waterproof, windproof, fire retardancy, abrasion resistance, conductive, homogeneous warmness intemperance of protective cloths [59–62].

Fig. 4 shows an efficient illustration of the noteworthy properties of GO nanomaterials that make them potential candidates for fabricating PPEs kits.

Fabrication of graphene and graphene-based protective cloths are prepared in many steps. The first stage, “pre-treatment of selected fibres,” eliminates dirt or contaminant particles from the surface of the fibres to allow for better contact with graphene materials. These fibres are then immersed in acetone or similar organic solvent for many hours, then washed with double deionized water before being dried in the oven. The “synthesis of GO” is the second step that uses strong oxidizing agents like KMnO₄, HNO₃ etc., however, several methods are reported for GO syntheses like modified Hummer’s, Hoffman, Brodie, chemical vapor deposition (CVD), epitaxial growth, etc. [63,64]. The third step consists of the “preparation of GO solution in water.” GO is embellished with many oxygen-containing functional clusters such as hydroxyl, carboxyl and epoxy [65,66], which make it hydrophilic and enhance the interfacial bonding with different fibres [67,68]. In this process, an appropriate amount of GO is added to distilled water and mixed thoroughly using a magnetic stirrer. Afterward, GO is completely disseminated in water by sonication this mixture. The oxygen-enriched functional clusters in GO sheets keep them stable in water [69]. Thus, GO is formerly centrifuged for further purification. The fourth step is “coating of GO on fabrics,” for this mostly, immersion and drying techniques are used for the coating, like plasma treatment [70], coupling agents [71], GO decorated with different...
“Reduction of GO coated fabrics” is the fifth step [74,75] with “characterization of graphene-modified fabrics” as the final phase for testing the different properties of protective suits like antimicrobial activity, self-cleaning behavior, thermal/flame resistivity, photo activity, wash fastness, mechanical, and electrical properties by slandered characterization methods. By following these steps, a complete graphene-based PPE-kit is prepared that has a high antimicrobial and antiviral efficiency. Table 2 shows the graphene and graphene-based fabrics that exhibit efficient properties for smart and personal protective cloth fabrication utility.

3.2.1. Graphene and graphene-based masks
The excellent properties of nanoparticles have made it possible to combat SARS-CoV-2 by developing antimicrobial films, diagnosis kits, nanosprays, therapeutics, etc. The SARS-CoV-2 infection is an infectious disease that spread through air droplets from the infected person to the normal individual, but it can survive on various surfaces for hours and still infect healthy individuals. Considering the masks as the physical technology that can block the transmission, but as time passes, newer variants of the SARS-CoV-2 are discovered, and therefore, it requires redesigning of masks that can efficiently block their transmission of new variants [37]. For the
bacterial cell through oxidative stress. Amongst the various carbon-based components, graphene, GO [86], and r-GO [74] are employed to make antibacterial masks and fabrics [87]. Laser-induced graphene (LIG) is used to improve the quality of self-decontaminating features of face masks. Another study [88] reported the LIG-based techniques to deposit the graphene on a viable clinical face mask. This study proved that the fabrication of graphene-coated face masks based on LIG techniques provide a superhydrophobic surface; it prevents virus-carrying droplets from adhering immediately to the surface of face masks. Huang et al. studied the LIG deposited face masks, showing 81.57% inhibiting the E. coli bacteria from a primary load of 107–108 CFU/mL. This mask shows self-cleaning and self-sterilizing residences, which pledge the re-use of these face masks. This face mask showed 100% inhibitory properties compared to E. coli when irradiated at 0.75 kW m⁻² solar light for 10 min [89]. Currently, the Bonbouton company fabricates a graphene-based face mask, which is economical and reusable [90]. Another business enterprise, Zen Graphene Solutions Ltd., had recommended a nanocomposite of GO ink with silver nanoparticles that successfully eliminates the other strains of the SARS-CoV-2/COVID-19 virus [91]. Directa Plus PLC has been appealed to improve graphene-centered face masks to eradicate the risk of coronavirus [92]. “Guardian G-Volt” face masks based on LIG

same, nanotechnology has come forward as a brilliant opportunity to design masks that can efficiently prevent the spread of the SARS-CoV-2. One of the highly utilized nanoparticles that gained much spotlight during the pandemic is graphene [84].

Graphene shows excellent antibacterial activity. The first antibacterial activity of graphene was reported in 2010. According to these findings, GO revealed a 95.5% inhibition in the E. coli bacterial pathogen. The sharp boundaries of GO can penetrate the microbial cell wall and are accredited to the destruction of the bacterial cell wall. Kumar et al. [85] had described the great antibacterial activity of GO and explain that the production of reactive oxygen species (ROS) has destructed the protein and lipid molecules of the techniques can effectively kill the confined microbes in the filter out of mask effectually obstructive ~99% contaminants having a size of more than 0.3 μm [93]. Table 3 shows the commercially available graphene and graphene-based face mask and its remarkable properties.

Further, Fig. 5 shows the expressive representation of a graphene-based three-layered mask to protect against the SARS-CoV-2 virus and other bacterial agents. In this mask, the graphene layer is used as a filter. This graphene layer is highly effective in the prevention against different types of bacteria and viruses. According to previously reported works, graphene shows good antibacterial activity, and sharp edges of GO that can penetrate the
bacterial cell wall and kill the germs. The fabric is modified with a polypropylene layer in the second layer; this polypropylene-based fabric layer has amazing properties like fine filtration, low-pressure drop, and great barrier properties for liquid and particles. The inner layer of this mask is made up of 100% cotton because cotton fibers are highly hydrophilic and have highly virus-blocking efficiency compared to other fabrics like silk, chiffon, and polyester. This three-layered mask, along with the graphene layer, may offer excellent protection against bacteria and viruses. This invention can majorly benefit the healthcare and frontline workers as they are highly exposed to the virus. Moreover, these kinds of novel development can help in breaking the chain of spreading the SARS-CoV-2.

### 3.3. Graphene-based antiviral surface and coatings

A new disastrous SARS-CoV-2 virus started to evolve and spread all over the world [98]. The most common pathway for spreading the SARS-CoV-2 virus in humans is sub-micron-sized respiratory droplets [99]. In addition, after getting into contact with any contaminated gadgets or surfaces, a person can become infected by touching their eyes, nostrils, and mouth. According to a recent study, the SARS-CoV-2 virus is substantially more stable on particular surfaces [100]. Further, several studies clarify that the SARS-CoV-2 virus lifetime span on diverse surfaces like, on a plastic surface, this virus can continue to exist 72 h, on the copper surface, it survives 4 h, on cardboard, it lives 24 h, on tissue and printed paper it lives 3 h, on wood 2 h, and on cloths, the life span of this virus is 2 h, and unfortunately in an external cover of the clinical mask, it has a lifespan of even seven days [36]. Thus, in the present situation of the SARS-CoV-2 pandemic, protective surface/coating play a great function in controlling the viral unfold over excessive touch additives and products [59–61]. Graphene and its derivatives have shown a broad-spectrum inhibitory effect against various bacteria and fungi in previous researches [101,102]. The antibacterial activity of GO and r-GO/SO3 composite against Herpes Simplex Virus Type-1 (HSV-1) was investigated by Sametband et al. [103]. Comparative antibacterial activity of graphene and its derivatives such as GO, GO-polyvinylpyrrolidone (PVP) composite, r-GO, GO poly (diallyldimethylammonium chloride) (PDDA) composite with predecessors of graphite and GO were discussed by Ye and co-workers [104]. They had demonstrated the antibacterial action of GO against a variety of microorganisms, including Pseudorabies virus (PRV, a DNA virus) and procline epidemic diarrhea virus (PEDV, an RNA virus). Yang et al. [105] described antiviral activity against the respiratory syncytial virus (RSV), which would be similar to SARS-CoV-2 and infects both lobes of the respiratory tract in children and the elderly. In contrast to the RSV virus, they employed nanocomposites of curcumin-loaded-cyclodextrin functionalized sulfonated graphene composite (GSCC); the GSCC composite inhibited the host cells of this virus and reduced its effects. In another study, nanocomposites of GO-silver were used for inhibiting the consequence of porcine reproductive and respiratory syndrome virus (PRRSV) [106].

According to these studies, graphene and graphene-based derivatives are effective for different gram-positive and gram-negative bacteria, enveloped and non-enveloped viruses, and DNA and RNA-containing viruses. Therefore, graphene and graphene-based derivatives are used to develop antibacterial surfaces and coatings that can effectively prevent various bacteria and
viruses, including the SARS-CoV-2 virus. These graphene-based antiviral surfaces and coatings can be used in hospitals, laboratories, operation theatres, incubators, ventilators, public places, etc., to avoid the spread of harmful viruses. The GO/rGO-SO₃ composites with different metal ions enhance the antibacterial activity of this compound and are used in the construction of effective antiviral covering strategies; further, the GO/rGO-SO₃ coatings using copper metal/ions are also a good candidate for antiviral surfaces and coatings. Copper metal/ions are used in the construction of composites with different metal ions to enhance the antibacterial etc., to avoid the spread of harmful viruses. The GO/rGO-SO₃ composites with different metal ions enhance the antibacterial activity of this compound and are used in the construction of effective antiviral covering strategies; further, the GO/rGO-SO₃ coatings using copper metal/ions are also a good candidate for antiviral surfaces and coatings. The GO nanoparticles are a progressive method for combating the spread of harmful viruses.[119] Even though the utilization of water-dispersible GO as the immobilized framework had been proposed as another procedure to defeat the disadvantages of flawless graphene,[120] the protecting property of GO brought about by the aliphatic sp³ hybridized area[121] caused it to be mandatory to work on the conductivity by work concentrated decrease or different techniques.

### 3.4. Graphene-based multilayer nanofoam

Nanofoams are porous substances with nano-sized pores that have an extensive variety of intrinsic and tailorable features. Along with their extremely low density, excessive surface area, interconnected nanoporous structure, wonderful mechanical electricity, excessive electrical and thermal conductivities, high chemical and corrosion resistance, and antimicrobial efficiency, multilayer graphene nanofoams are particularly essential.[110,111] As an outcome, nanofoams display the design nicely and improve the spread of components required to fight infectious infections like SARS-CoV-2.

It has been accounted that low conductive mesoporous carbon or silica-based hybrid demonstrates high surface region, huge pore volume, and inborn stacking capacity, which can help in strong glucose oxidase (GOD) immobilization for the immediate electrochemistry and biosensing.[112,113] Nanofoams can be synthesized by various techniques, namely chemical vapor deposition (CVD), non-template approach, electrochemical reduction method, freeze-drying, sol-gel and template association of GO, 3D printing, and sugar blowing approach[114] by utilizing diverse carbon precursors like SAP, polymers, pitches, coal, graphite, GO, etc. In this manner, the transformed pristine graphene with huge mesopores [mesocellular graphene froth (MGF)] can earnestly procure both the inordinate conductivity and the strong immobilization of GOD. Overall, the graphene nanosheets in MGF are most likely isolated from one another with the guide of the pore spaces (no longer agglomeration), and these properties may be helpful for immediate electrochemistry and sensitive glucose detection.

The hydrophobicity and irreversible agglomerates of the flawless graphene are prepared by mechanical cleavage, oxidation—decrease, synthetic fume statement, epitaxial progress, and so forth, which can be achieved much of the time by low and temperamental stacking of protein.[115] Further, the redox concentration of chemical particles, GOD was profoundly covered in its sugar blowing approach[114] by utilizing diverse carbon precursors like SAP, polymers, pitches, coal, graphite, GO, etc. In this manner, the transformed pristine graphene with huge mesopores [mesocellular graphene froth (MGF)] can earnestly procure both the inordinate conductivity and the strong immobilization of GOD. Overall, the graphene nanosheets in MGF are most likely isolated from one another with the guide of the pore spaces (no longer agglomeration), and these properties may be helpful for immediate electrochemistry and sensitive glucose detection.

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explicitly comprise drops that are sub-5 μm in size. For the most part, drops that are bigger than 5 μm, do not travel significant distances and settle inside 1–2 m because of the gravitational power [124]. Notwithstanding, vaporizers are more modest and lighter and thus can stay coating noticeable all around for expanded periods which can seriously build the spread of the infection [125]. Hence, the utilization of facial cover gives an actual obstruction that restrains openness to respiratory drops [126]. Nevertheless, it is costly, in restricted inventory, and its filtration effectiveness for particles with sizes less than 300 nm is around 85% because of the bigger pore size in the channel layer (~300 nm) [127]. Also, the Coronavirus infection has been displayed to have a place with the beta-CoVs classification with an elliptic or round shape and size in the scope of 65–125 nm [128], which affirms the requirement for the advancement of more effective filtration covers.

To overwhelm the previously mentioned issues, Al-ETab et al. [129] improve the nanoporous layer (down to 5-nm pores) that can be appended on a reusable N95 mask and supplant after each utilization which possibly will be utilized in better N-95 face covers than proficiently block SARS-CoV-2, which has a bigger size than the size of nanometers made in polyimide film [130]. The permeable layer depends on a normally hydrophobic polymer to such an extent that the drops that come into contact with the veil will roll and slide over the cover because of the enormous tendency point of the film when worn on the face mask. The layer is created by first manufacturing a Si-based nanoporous layer through designing and potassium hydroxide (KOH) carving a silicon-on-encasing wafer. The delivered permeable format is then utilized as a hard cover to move the examples onto a super slight and hydrophobic wafer. The delivered permeable format is then utilized as a hard manufacturing a Si-based nanoporous layout through designing

biocompatible systems with a high graphene content (20 and 60 vol% of solid). According to the researchers, the graphene flakes and polyacrylate-co-glycolide (PLGA) ink were made by mixing a PLGA and dichloromethane solution with a graphene dispersion. This preserved an electrical conductivity of over 800 S/m. The author developed mechanically strong graphene scaffolds using this ink and extrusion-based 3D printing.

To strengthen chitosan-lactic acid conditions and make conductive hydrogels, Sayyar et al. [137] utilized varying amounts of r-GO. Extrusion printing made it simple to assemble these composites into 3D scaffolds. Systems with 30 layers of each graphene/chitosan dissipated were printed from a 200 m distance across ramble at a feed speed of 150 min⁻¹ and a strand isolating of 0.6 m, with a 0°/90° direction, a feed speed of 150 min⁻¹, and a strand isolating of 0.6 m. The thought of 3 wt% graphenes achieved a 200% development in flexibility. The fibroblast (L-929) cells that stuck and developed on numerous layers of the 3D platform were embedded into the subsequent designs. These scaffolds turned out to be good conducting substrates for electro-responsive cell growth [137].

The present outbreak demonstrates the need for dispersed manufacture of important things, and 3D printing could aid in the development of numerous components like personal protective equipment [PPEs (face masks, respirators, and face shields)], viral swabs, and ventilator parts [138]. Because graphene and GRM have appealing properties, composites of GRM-metal or GRM-polymer might be used as base materials for 3D printing instead of just metals or polymers to produce superior components or systems. Face masks and oxygen masks composed of GRM-polymer composites would also protect humans from the virus because GRMs have natural antiviral properties and help kill it.

Hence, graphene and its derivatives have created a big room for exploring its various benefits in the biomedical domain; moreover, with the onset of the SARS-CoV-2, ample opportunities in science and research have started to generate, that can benefit both humankind as well as nature. Further, the SARS-CoV-2 has taken away many lives, but the healthcare workers were the most affected by the pandemic. Therefore, this review aims to provide insight into the various potentialities of graphene and its derivatives for combating the SARS-CoV-2 that can be helpful for various researchers, textile industries, environmentalists, and healthcare workers to enhance their research and studies for the betterment of society. Further, many researches on different other materials like metals [139], two-dimensional materials like MXenes [140] and borophenes [141], etc., have been concluded, which show their utilities in combating this viral pandemic.

4. Graphene’s cytotoxicity

The evaluation of nanomaterial’s cytotoxicity is crucial for a complete knowledge of their biological function. The use of nanoparticles to mark therapeutic cells in-vitro is becoming more prevalent, and nanoparticles’ potential impacts on aesthetic cells are becoming more apparent. Carbon-based nanomaterials, in general, exhibit specialized antimicrobial effects and are low in cytotoxicity. It was reported that graphene-supported antiviral biomarkers had been verified in contrast to an unambiguous virus and that type of antiviral nanomedicines can also boost biocompatibility and reduce medication cytotoxicity. Graphene sheets’ two-dimensional design and adversely charged surfaces can be deprived of many stretches, communicate with microscopic organisms and infections, break their plasma membrane, and kill them. Graphene sheets, depending upon their concentration, can also interact with live cells [142]. Graphene sheets inactivate the infection before it infiltrates the cells, and the sharp edges of
Graphene and its compounds cause cytotoxicity in vitro and in vivo. The graphene sheet's antiviral mobility is based on its interaction with the structure by direct association, according to trial discoveries. The graphene sheet's antiviral mobility is based on direct association, according to trial discoveries. Antiviral activity and toxic impact of graphene were tested in this study, and it was determined that graphene has a non-toxic influence with good antiviral activity at low concentration levels but a low toxic influence at higher concentration levels. These findings indicate that graphene and its derivatives are less hazardous than other carbon materials, making them viable for next-generation antiviral materials. When proteins, such as serum proteins, surround these nanosheets, the cytotoxicity is dramatically reduced. As a result, while they are poisonous to bacteria, they are not as hazardous to humans or other mammals. Hence, they have the potential to be effective against SARS-CoV-2.

The toxicity of GOs/r-GOs is thought to be reduced by diffusing them in polymers to generate polymer nanocomposites as graphene nanoparticles are tightly linked to the polymer matrix of nanocomposites to which they are immobilized. Furthermore, the polymer matrix can encapsulate GO/r-sharp GOs edges, preventing them from penetrating the cytoplasm. Accordingly, huge surface-region graphene nanofilbers, especially for osteoblasts, give viable areas to cell bond and expansion (bone cells). Moreover, oxygenated GO groups can diminish the hydrophobicity of the polymeric matrix, approaches have been explored to connect and disseminate more easily on the polymer surface [144]. Table 5 shows graphene, and its compounds that causes cytotoxicity in vitro and in vivo. This method brings up new possibilities for using graphene nanoparticles in biomedical applications such as enhanced bone fixation devices, scaffolds, and implants in orthopedics. Prior to clinical use, more safety testing and research must confirm that such polymer nanocomposites are biocompatible with human tissues.

### 4.1. Market aspects of graphene-based products

The onset of SARS-CoV-2 has opened a vast gateway for research, and with the advancement in technology, new materials and techniques are being invented for combating the pandemic. Graphene is also one of the emerging materials that is being considered for its immense utility in combating the virus. However, specifically, graphene nanomaterials have gained much spotlight due to their unique small size, excellent properties, and high antimicrobial efficacy in exploring their utilities for prevention, detection, and treatment of SARS-CoV-2. Several studies have shown the commercialization of graphene, basically in electronics, aeronautics, semiconductors, etc., that encompasses more than 50% utilization of graphene. With the ever-increasing demand for graphene in the healthcare sector due to the outbreak of SARS-CoV-2, it has been anticipated that by 2027, the graphene market will experience a 39% annual growth rate and achieve a market size of USD 2864 million [156]. Many top-tier companies have developed a variety of face masks, prophylactic, SARS-CoV-2 diagnosing kits, biosensors, etc., by using graphene-based nanomaterials; however, a lot of research is still needed to be conducted for mature market handling.

Apart from the urgent demand for vaccines to combat SARS-CoV-2, the marketing monitoring of graphene-based materials should have carefully proceeded. Conventional limitations like instability of graphene or quick aggregation properties need to be properly addressed before their release in the market. Moreover, the impact of SARS-CoV-2 has made a hope that the graphene market will increase surely, but the corporates should always check and consider the risks and opportunities of graphene in the market. Further, consideration of the impact of SARS-CoV-2 on commodity, prices, supply chains, etc., can affect the market and hence the corporate needs to be prepared with alternative and backup strategies. However, a loss of market was observed in the fields of electronics as the SARS-CoV-2 affected the transportation and demand of graphene [157]. Moreover, incorporating the productivity of graphene-based materials will eventually increase its sales and demands worldwide, which will increase the import and

### Table 5

| Materials | In vitro | Different Cell tissue | Dosage variation | Cytotoxic/biological effect | References |
|-----------|---------|-----------------------|-----------------|---------------------------|------------|
| GO        | In vitro| The outermost cell of Skin (Keratinocyte) | 0.4, 1, 2, 3, 7, 11, 33, and 100 g/mL at 3−72 h | Reactive oxygen species generation is dose and time dependant. | [145] |
| GO-PEG    | In vitro| Mouse osteoblast progenitor cells (SAOS-2; MC3T3-E1; RAW-264.7) | For 24 h, 75 μg/mL | GO-PEG accumulates on F-actin, resulting in the construction of reactive oxygen species (ROS). | [146] |
| GO-NH₂    | In vivo | Mice | 250 μg/kg | There was no pulmonary embolism. | [147] |
| r-GO; r-GO-PEG | In vivo | Human lung cell (A549) | 1−200 μg/mL | Toxicity that is dose dependent. | [148] |
| r-GO-PEG  | In vivo | Albino mice | 10 mg/kg | Apoptosis at a concentration of >25 μg/mL. | [149] |
| GO        | In vivo | Human Erythrocyte | For 3 h at different concentration such as, 3.12, 6.25, 12.5, 25, 50, 100, and 200 μg/mL | Size and dose dependent | [150] |
| GO        | In vivo | Rabbits | 100–300 μg/eye | There was no alteration found in the appearance of the eyeball or the intraocular pressure. | [151] |
| hGO; GO   | In vivo | B6 mice | 2 mg/kg | In alveolar macrophages, hydrated GOs caused more significant lung irritation and lipid peroxidation than GOs individually. | [152] |
| Green r-GO | In vivo | Human Lymphoblastic cell | 50, 100 and 250 μg/mL | At >100 μg/mL, lysosomal integrity is lost. | [153] |
| TRG       | In vivo | Vero cell of monkey | 1, 5, 10, 300 μg/mL for 24 h | Apoptosis at >100 μg/mL. | [154] |
| GO        | In vivo | Swine Spermatozoa | 1−4 h at 0.5, 1, 5, 10, and 50 μg/mL | Toxicity that is dose dependant. At a concentration of >10 μg/mL, cells die. | [155] |
export of graphene and graphene-based materials. The increase in stocks can benefit the economy of a country in pandemic times.

5. Limitations and challenges

Even though graphene's antibacterial activities have been demonstrated, but its utilities for COVID-19 treatment instantly is still on its infant stage. In ducklings diseased with the Novel duck reovirus, the only relevant in-vivo investigation for virus treatments confirmed the effectiveness of GO-hypercin [158]. However, it is worth mentioning that graphene's in-vivo toxicity is still up for discussion. Compared to other nanostructured materials, graphene-based materials can overcome biological obstacles but are not as cytotoxic to macrophages and crucial cells in the immune system. The numerous dose concentration, surface chemistry, and contact path used for the evaluation make conclusions on graphene toxicity challenging [159]. Its instability and aggregation in solution are additional issues. Moreover, graphene exhibits difficulties in interfacial interactions between textile and graphene when used in manufacturing PPE kits, which can be overcome by modifying graphene with the fiber's surface to enhance interfacial interactions. However, some problems of graphene-based nanomaterials, like the production of large-scale, high-quality graphene-based nanomaterial, are not possible. Therefore, the experts need to look into enhancing the production and marketing of graphene-based nanomaterials for PPE kits [161].

Many studies and research papers have started to concentrate on the harmful effects of the SARS-CoV-2 in the environment [162]. At a certain level, it has been acknowledged that the SARS-CoV-2 occurrence has reduced global warming and pollution levels due to the worldwide lockdown and decrease in mobility of the people. But, on the other hand, the SARS-CoV-2 is believed to have increased biomedical waste, which has led to an increase in plastic, water, and soil pollution. The improper disposal of the safety kits and diagnosis kits has led to various side effects as choking of sewage pipelines, death of marine animals and death of multiple birds and stray animals. Moreover, the open-disposal system has increased the generation of new air-borne diseases, spreading at a high rate these days.

The safe and proper disposal of the safety equipment is one of the major factors which can limit their wide utilities, as in the case of graphene-based nanomaterials, various regulatory rules and laws for their proper disposal should be amended as the graphene-based nanomaterials can cause certain toxicity in both living tissues and the environment. Certain disposal techniques that can be adapted are like, graphene-based nanomaterials should not be dumped with the general waste in drains or sinks; if any acid or reductants have been used to disperse the graphene-based nanomaterials, then it should be first neutralized and then disposed of; with the help of different chemical waste disposal companies, these graphene-based nanomaterials can be decomposed; and appropriate disposal protocols should be set up and should be communicated to all users as well as to non-users, along with their combination with various scientific disciplines should be properly managed.

6. Conclusion and prospects

The SARS-CoV-2 pandemic has spread worldwide and is still not stopping, which has led to the loss of several lives, and the country's economy has also suffered. Nevertheless, the spread of the virus is not ended yet and presently, several mutants and variants are appearing, which are more dangerous and harmful than the previous one. There is an urgent need to develop the tremendous diagnostic device and treatment strategy of the evolving and re-emerging diseases to combat SARS-CoV-2 pandemic situations in the present situation. Graphene and graphene-based derivatives are suitable candidates to fight against coronavirus due to their excellent antibacterial activity, great electrical and thermal conductivity. In this evaluated literature, we have mentioned in detail about graphene and its derivatives, which can be used to prepare medical components, devices, PPEs, effective masks, biosensors, antiviral coating, 3D printed graphene and graphene-based nanofoams. The use of medical components and PPEs based on graphene-based materials are very appropriate because these medical kits and PPEs are very lightweight, easy to use, protect from UV-rays, and show great antibacterial activity, good thermal and electrical conductivity. Despite the excellent properties of graphene and its derivatives, many graphene fabricated fabrics like cotton, polyester, etc., are still not adaptable for large-scale manufacturing. Moreover, graphene is a monoatomic thick nano-material and can cause discomfort for the user, so graphene-based clothing should be modified with other materials to ensure sustainability and comfort. Graphene and graphene-based sensors are good alternatives to sense the SARS-CoV-2 virus and other virulence diseases.

Further, graphene-based coatings and surfaces assume a critical part in controlling the viral spread over high-contact segments and items because of their remarkable antibacterial activity. GO and its allied derivatives are the new expectation for the battle against these intense sicknesses differently; this demonstrates that the path of graphene and graphene-based materials for medical care applications is as yet distant into what is to come. Indeed, graphene and graphene-based materials hold a great potential compared with other unique materials owing to their unique and tremendous electrical, chemical, and mechanical properties. In the future, properties of graphene-based constituents can be modified through control functionalization for great commercial applications. Further, the increase in the utilities of graphene-based nanomaterials in the biomedical domain will also increase the market opportunities and increase the country's economy. However, major limitations possessed by graphene-based nanomaterials should be preferred and should be resolved for better results. However, the outbreak of SARS-CoV-2 has increased the biomedical pollution like open disposal of PPE kits, diagnosing kits, medical tools, masks, etc., which have led to the spread of contamination in nearby water bodies, soil and air. Similarly, better disposable protocols are needed to be set up for the proper and safe disposal of graphene-based medical wastes. So graphene and graphene-based materials are used to improve science and technology for medical and healthcare utilities to combat the recent critical scenario of the SARS-CoV-2 pandemic. It will also play a vital role in combating other future pandemics caused via viruses, bacteria, fungi, etc.

Author's contributions

Ayesha Hashmi contributed by conceptualization, investigation, resources, data curation, and writing—original draft preparation. Vanya Nayak and Kshitij RB Singh contributed by resources, writing—original draft preparation and writing—review and editing. Bhawana Jain, Mitisha Baid, and Frank Alexis contributed by formal analysis and writing—original draft preparation. Ajaya Kumar Singh contributed by validation, investigation, resources, writing—review and editing, supervision, project administration, and funding acquisition.
Declaration of competing interest

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

Acknowledgments

This work was supported by the Chhattisgarh Council of Science and Technology (CCOST), Raipur, Chhattisgarh, India (Reference no. 2094/CCOST/MRP/2017).

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