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Protection, disinfection, and immunization for healthcare during the COVID-19 pandemic: Role of natural and synthetic macromolecules

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HIGHLIGHTS

- The effective role of synthetic and natural polymers during the COVID-19 pandemic
- Preparation of personal protective equipment using various polymers was reviewed.
- Fabrication of antiviral materials to prevent the spread of the SARS-CoV-2
- Polymers can be used to design immunosensors for detection of SARS-CoV-2.

GRAPHICAL ABSTRACT

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ABSTRACT

The world is trying to improve public health while the outbreak of the COVID-19 is at its worst. So far, countless people have died from the COVID-19 disease and it is still a serious threat to human health. Synthetic and natural polymers are unavoidable materials in the healthcare sector. During the COVID-19 outbreak, diverse medical equipment and devices were designed and developed by using these macromolecules for the protection, disinfection, and immunization applications. Synthetic polymers such as polypropylene, polystyrene, poly(lactic acid), poly(ethylene terephthalate), and so forth have been successfully applied for the design and fabrication of diverse face masks, shields, anti-viral coatings, as well as diagnostic kits. Natural polymers having great features such as biodegradability and environmentally friendly are made from algae, plants, and animals. These polymers including sodium alginate, chitosan, cellulose, and gums have been shown a critical role in the fabrication of personal protective equipment, immunosensors, and anti-viral spray for control and fight against COVID-19. Besides, the problem of plastic waste can be solved by replacing them with natural polymers. This mini-review aims to show the application of polymer-based materials during the COVID-19 epidemic.

Contents

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1. Introduction

COVID-19, as an emerging viral respiratory disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), brought panic around the world. SARS-CoV-2, as a positive-sense single-stranded RNA virus containing lipid envelope with club-shaped spike (S) glycoproteins on the virion surface, is the last discovered member of coronaviruses (Luan et al., 2020). SARS-CoV-2 is thought to be spread often through respiratory droplets, so, the World Health Organization has recommended the use of personal protective equipment in addition to social distance to control and prevent the spread of COVID-19 (Chen et al., 2021; Polman et al., 2021; Saadat et al., 2020; Wu et al., 2020).

This global emergency has created an unprecedented scientific movement around the world to control and combat COVID-19. This pandemic has also lead to an urgent need for medical equipment and devices. On the other side, these days, a lot of pressure is put on the medical staff and it is urgently necessary to provide medical devices and personal protective equipment including masks, antimicrobial clothes, and face shields, etc. In addition, the early detection and control of COVID-19 are the most essential cases in this regard. Besides, the stress that is created in the general public during this period lead to a weakness of immune system. Therefore, it is required to strengthen the immune system with the help of nutrients. Diverse polymeric materials (i.e. petroleum-derived polymers and bio-based polymers) such as polyethylene, polypropylene, poly(vinyl chloride) (PVC), poly(lactic acid) (PLA), have been used for the fabrication of medical equipment such as face shields, masks, gloves, and clothes. Furthermore, polymers have a special place in the preparation of drugs and vaccines (Alghounaim et al., 2020; El-Atab et al., 2020; Gadhave et al., 2020; Huang et al., 2021; Lee et al., 2021; Leung and Sun, 2020a; Ray et al., 2020; Ullah et al., 2020; Weaver et al., 2020; Wesemann et al., 2020; Zhao et al., 2020). However, in some cases, the high cost of biopolymer production avoids them from being utilized as alternatives for other polymers. Natural polymers such as chitosan, alginate, gums, and cotton are active ingredients, which have a long history in traditional medicine due to their anti-viral activities. These natural polymers are made from algae, plants, and animals, and can be used as an attractive alternative for the preparation of environmentally-friendly materials (Encalada, 2018; Gironès et al., 2012).

Biopolymers have been effectively used in different industries (Mallakpour et al., 2020, 2019; Mallakpour and Khadem, 2019; Mallakpour and Ramezanzade, 2020; Nasrollahzadeh et al., 2021; Polman et al., 2021), these natural macromolecules have been successfully applied for the formulation of anti-viral drugs, increase the immune system, and drug delivery systems (X. Chen et al., 2020; S. Yang et al., 2020). Polysaccharides show the anti-SARS-CoV-2 effect, and so far, they exhibited an effective influence on SARS-CoV-2 (X. Chen et al., 2020). Besides, there is no concern about plastic waste due to the biodegradability of these macromolecules.

Due to the widespread utilization of polymers (both synthetic and natural polymers) in controlling and fighting the COVID-19 crisis, there is an obligation for getting data and gathered information concerning polymers. In this study, the importance and role of synthetic and natural polymers in controlling and counteracting COVID-19 are expressed.

2. Application of polymeric materials during COVID-19 pandemic

2.1. The role of synthetic polymers during the COVID-19 pandemic

2.1.1. Polypropylene

The use of surgical masks for a long time causes discomfort to users and causes the production of bacteria. To overcome this significant problem, a new antibacterial fibrous membrane was prepared for the convenience of users by employing nanocomposites containing polypropylene nonwovens and conductive inorganic nanomaterial (boron nitride nanoparticles) (Xiong et al., 2020). For the preparation of nanocomposite, ultrafine fiber nonwovens were prepared by melt-blown processing and treated by oxygen plasma for the activation surface. In the next step, it soaked in a suspension containing quaternary ammonium salt, an antibacterial agent, and boron nitride. The structure of the prepared masks is shown in Fig. 1a. The achieved results showed that the prepared fiber membrane-based mask exhibited a thermal comfort and antibacterial performance. A quaternary ammonium salt-boron nitride nanoparticle possesses a positive charge, which can electrostatically interact with bacteria with a negative charge and bacteria are inactivated through the penetration of a long chain of quaternary ammonium salt into cell membranes as schematically shown in Fig. 1b.

2.1.2. Polystyrene

Recently, electret fibers based on polystyrene/poly(vinylidene fluoride) hybrid were prepared. For example, a membrane was designed and prepared for the development of an effective face mask by applying electrospinning technique (Li et al., 2020) (Fig. 2). The obtained hybrid structure exhibited an enhanced electret feature as well as porosity due to the electrical polarization behaviors of these polymers. Poly(vinylidene fluoride) and polystyrene belong to the strongly and weakly polar polymers owing to their high and very low dielectric constants and easily in electrospun. Scanning electron microscope (SEM) images of the prepared electret polystyrene/poly(vinylidene fluoride) are shown in Fig. 2c. The membrane was successfully prepared by using the produced fibers and efficiently utilized as a core layer of protective respiratory N95 masks, which have a number of advantages such as

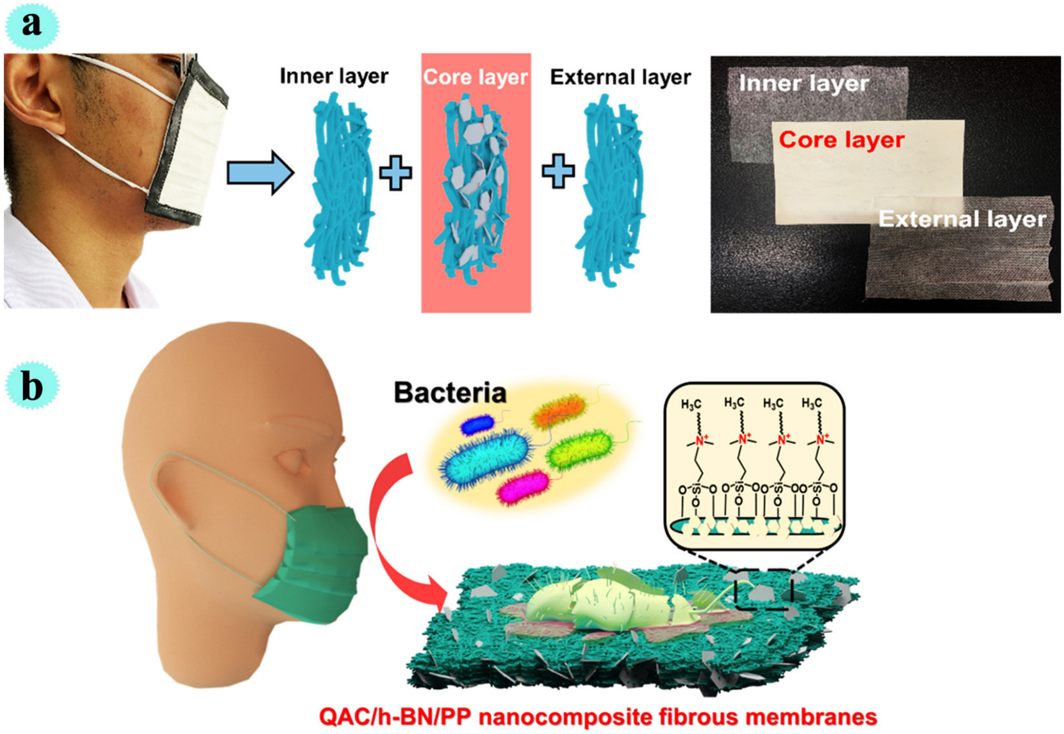

Fig. 1. (a) The schematic depiction of the prepared QAC/h-BN/PP nanocomposite fibrous masks (b) Antibacterial mechanism of QAC/h-BN/PP nanocomposite fibrous masks. (QAC/h-BN/PP: Quaternary ammonium salt/hexagonal boron nitride/polypropylene). Reprinted from Xiong et al. (2020) with permission from American Chemical Society. Copyright (2020) American Chemical Society).

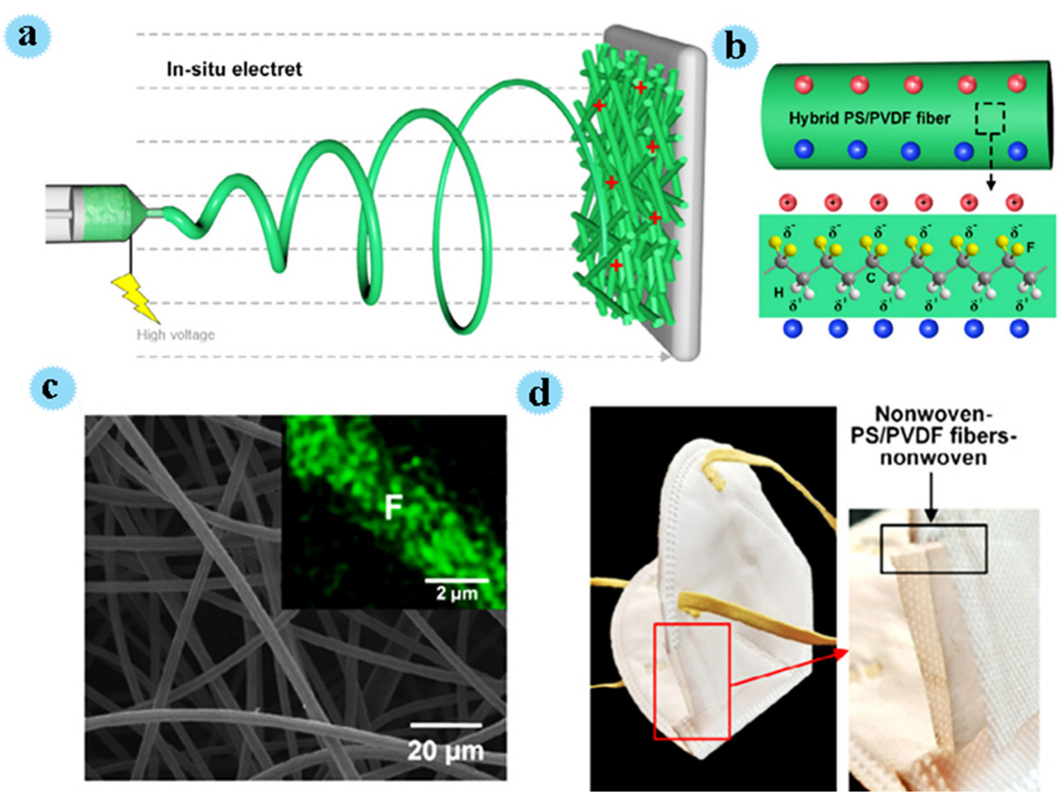

Fig. 2. (a) A schematic overview of electrospinning process, (b) Schematic illustrating the contribution of PVDF on electret effect, (c) SEM images of electret PS/PVDF fibers, (d) A N95 respirator using PS/PVDF-2 fibers as the core material (PS/PVDF: polystyrene/poly(vinylidene fluoride). Reprinted from Li et al. (2020), with permission from Elsevier . Copyright (2020) Elsevier.

long life, outstanding filtration proficiency (99.752%), and low resistance to air (72 Pa) etc.

In an interesting study reported by Chen and colleagues, a sensitive and rapid immunoassay based on Ln-doped nano-polystyrene particles was developed for the sensitive detection of anti-SARS-CoV-2 IgG antibodies (Z. Chen et al., 2020). For this purpose, Ln-doped polystyrene nanoparticles were synthesized by applying a mini-emulsion polymerization technique, and then, treated with rabbit and mouse IgG antibodies. To prevent the agglomeration of nanoparticles, the antibody molecules were cross-linked. In this study, SARS-CoV-2 phosphoprotein was immobilized on the nitro-cellulose membrane for the recognition of IgG, (Fig. 3). Positive and negative samples (7 and 12 samples) of human serum were evaluated using this system and compared with PCR results. Except for one case, the achieved results were consistent with the results obtained from PCR analyses. It can be concluded that this approach can be successfully used for the monitoring of the COVID-19.

2.1.3. Poly(vinyl alcohol) (PVA)

Nowadays, disposable medical clothes consist of polymer-coated layers that are widely used by healthcare workers, protect them against viruses and bacteria. However, impermeable structures and moisture absorption cause discomfort. To solve this problem, medical protective clothes with super-absorbent features were developed by using polymeric materials for the adsorption of moisture and improve comfort (L. Yang et al., 2020). For this purpose, poly(acrylic acid-*co*-acrylamide) (PAAAM)/PVA super-adsorbent fibers were produced via the wet-spinning process. Then, a composite layer including PAAAM/PVA, ethylene-propylene, and bamboo pulp fibers was prepared (Fig. 4). After gluing this layer to the inner surface of the nonwoven fabric, the prepared material showed outstanding absorption capacity towards sweat and moisture and controlled the amount of moisture inside the medical staff's clothes, and created comfortability for them. Besides, the thermal resistance of this coating was higher than conventional materials. The moisture absorption performance of the prepared polymeric adsorbent was carried out (Fig. 4c, d). The achieved results confirmed that the prepared coating exhibited a great absorption efficiency compared to the usual fabric.

Due to the current situation, the urgent need for antimicrobial materials such as protective face masks is growing due to the inactivating performance of SARS-CoV-2 (Maio et al., 2020; Mart et al., 2021). In a study conducted by Mart and co-workers, a face mask filter was developed by a bio-functional coating of benzalkonium chloride for the rapid inactivation of SARS-CoV-2. Anti-viral tests with SARS-CoV and Phage Phi 6 (bio-safe model of viral) were performed. The obtained data indicated that the prepared filter can successfully deactivate pathogens (Mart et al., 2021).

In recent years, researchers put so much effort into the development of antimicrobial agents using PVA to fight microorganisms. In a recent study, diverse concentrations (0.5%, 1.5%, 2.5%, and 3%) of *Aloe vera* gel were inserted into the PVA matrix for the production of antimicrobial electrospun nanofibers (Khanzada et al., 2020). For this purpose, PVA was dissolved in deionized water and then, *Aloe vera* gel was added to the polymer solution. After stirring of this solution at 60 °C, a clear solution with certain viscosity was obtained. In the next step, a syringe was filled with the final polymer solution and placed in an electrospinning instrument. Finally, nanofibers were produced and then cross-linked with glutaraldehyde. The antimicrobial performance of the produced nanofibers was investigated towards Gram-positive (*Staphylococcus aureus*) as well as Gram-negative (*Escherichia coli*) bacteria. The obtained results showed that the prepared electrospun nanofibers exhibited great antimicrobial performance. Thus, it can be concluded that these nanofibers are great nanomaterials for the design and production of the protection clothes against COVID-19.

2.1.4. PLA

For the design and development of effective face masks for the healthcare workers for long-term usage, nanofiber-based membranes, as protective equipment for the control COVID-19 pandemic, were prepared by using electrospinning technique through the incorporation of activated charcoal (1%, 5%, and 8%) into PLA (Buluş et al., 2020). The morphological, physical, tensile features and filtration efficiencies of the developed membranes were investigated. For the preparation of nanofibers, PLA granules were mixed with dimethylformamide to obtain a polymer solution. After that, 1%, 5%, and 8% of activated charcoal were added to the polymeric solution. Finally, nanofibers were produced by applying the electrospinning process. Thinner fibers were

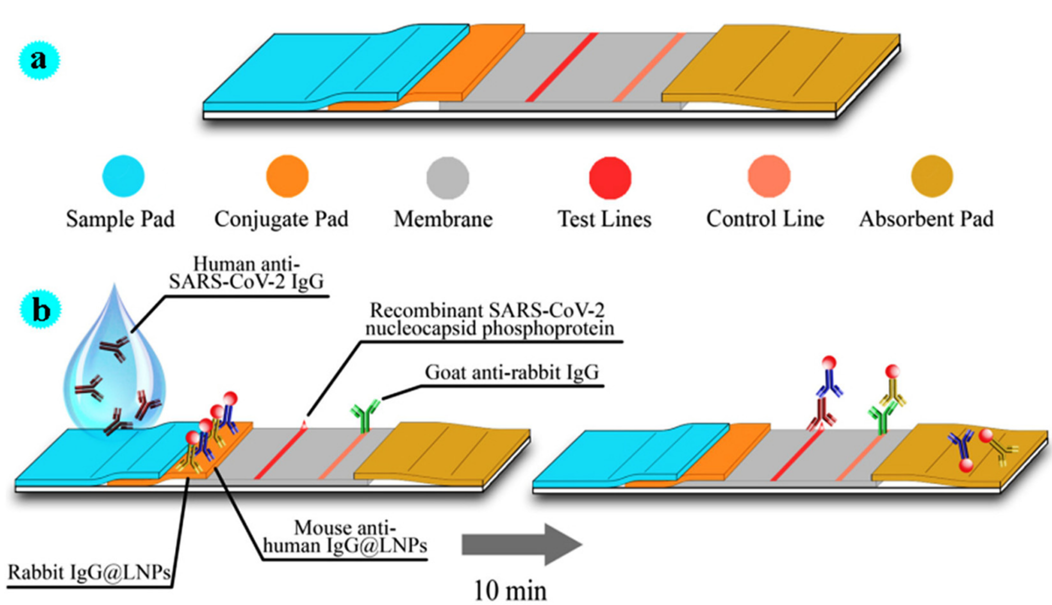

Fig. 3. The schematic representation of the design and fabrication of the developed assay, (a) Lateral flow test strip. (b) Assay. Reprinted from Chen et al. (2020) with permission from American Chemical Society. Copyright (2020) American Chemical Society.

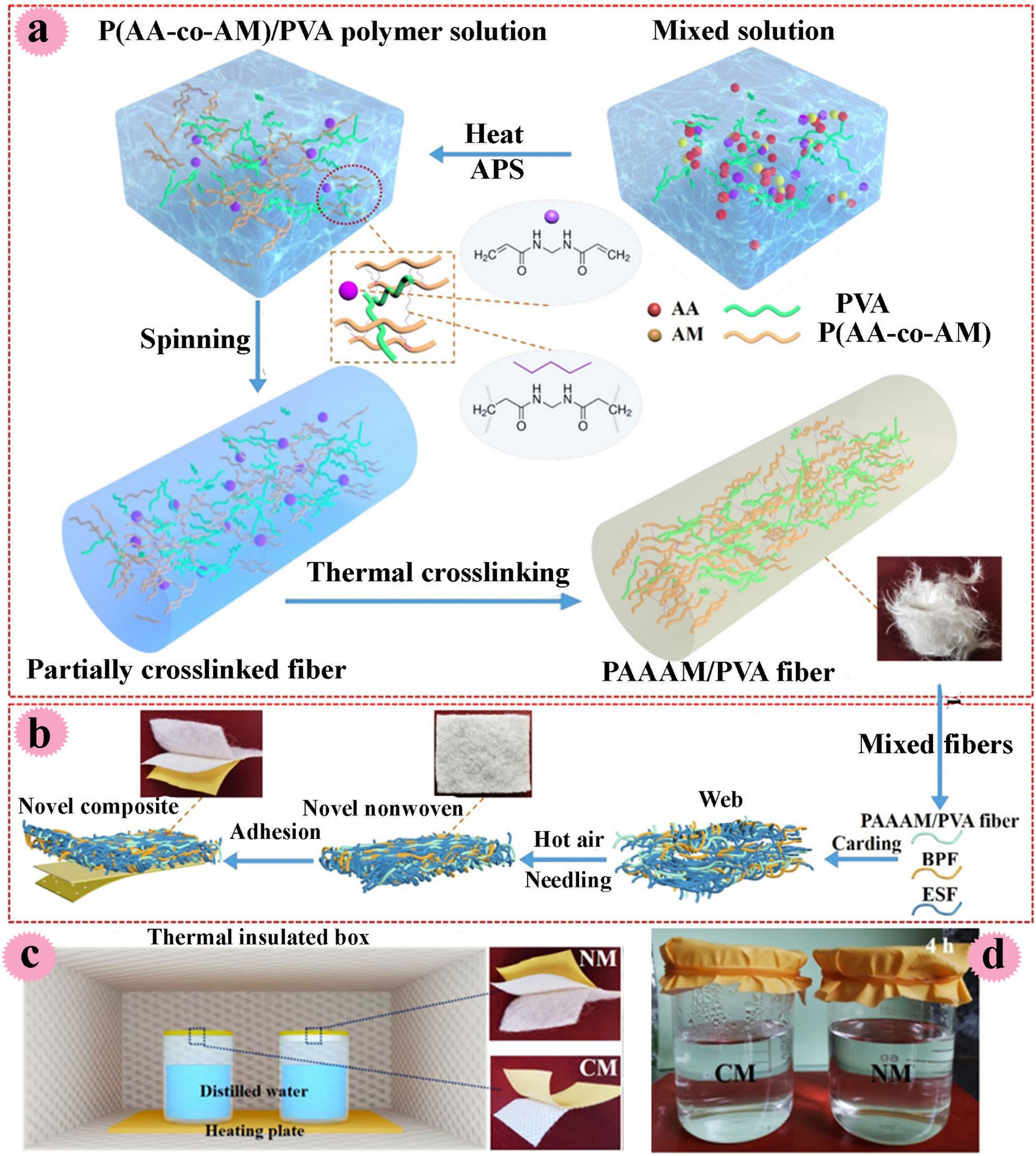

Fig. 4. Preparation processes of a: PAAAM/PVA fibers and b: highly hygroscopic and strong antistatic medical protective clothing material c, d: Simulated moisture absorption experiment. Reprinted from Yang et al. (2020) with permission from Springer Nature. Copyright (2020) Springer Nature.

produced with the increasing amounts of activated charcoal. The highest electrical resistance value was achieved for the composites containing 8% activated charcoal and filtering efficiency was obtained ≥98%. In another study, PLA-based face masks for frontline workers were designed and developed by applying 3D-printing technique [Fused Deposition Modelling (FDM)] (Vaňková et al., 2020). The achieved outcomes showed compact structures of the product so that the gap between the filaments is small and the pores in the PLA are closed. The decontaminating efficiency of the polymer surface was evaluated with the help of disinfectants such as ethanol 70%. This research team concluded that the protective masks made from PLA have a compact structure and effectively protects people against microorganisms. Complete disinfection of the surfaces of this polymer against bacteria and viruses was investigated and good results were obtained. Also, disinfectants did not change the surface properties, pore size, and did not cause mechanical damage. Therefore, these prepared masks can be successfully used in the COVID-19 pandemic.

These days, we are facing an increase in demand and the need for disposable N95 respirators due to the spread of the COVID-19. However, a reusable elastomeric respirator can be a good substitute. On the other hand, most of the reusable respirators are not able to out exhalation. In a feasibility study, an adapter was designed and manufactured using a 3D-printing process and employing PLA for filtering the out exhalation (Liu et al., 2020). In this feasibility study, the function of the modified respiratory systems was examined. Eight people (5 men and 3 women) volunteered for the test, and the respiratory rate examination, as well as end-tidal CO_2 monitoring, were performed during and after 60 min. The standard deviation for CO_2 monitoring and respiratory rate was (4.5 (0.5) kPa and 4.6 (0.4) kPa) and (17 (4) breaths.min^{-1} and 17 (3) breaths.min^{-1}). It was reported that 4 people felt uncomfortable, one reported dizziness, and pressure on the faces, and resistance to exhalation occurred for the rest.

Due to the widespread of the COVID-19 pandemic and the lack of medical equipment, Westphal and colleagues designed and developed flexible frames for the production of face shields by applying 3D printing technology (Westphal et al., 2020). In their study, the frames were printed by applying the FDM method using polylactide and polyethylene terephthalate glycol filaments (1.75 mm diameter), which are a usual FDM material and biocompatible polymer for biomedical uses. High-quality frames were successfully produced by applying a photopolymer and stereolithography manufacturing process and compared with FDM-based frames. The price and quality of the prepared frames were different due to the applied different techniques. FDM-based frames were cheaper and less expensive, while SLA-based frames created smoother and cleaner surfaces.

As mentioned above, during the COVID-19 pandemic, polymers are unavoidable materials in the healthcare sector such as preparation of personal protective equipment (face mask, shields, clothes, etc.), sensors, medications, delivery systems, dietary supplements to improve the immune system, and so on. For example, Schmitt et al. reported the design and development of a polymer-based face mask to protect medical staffs who are exposed to patients infected with COVID-19. For this purpose, they employed various polymers including [poly (methyl methacrylate), PLA, and PVA] for the preparation of a full-face mask to cover the entire face (eyes, nose, and mouth) (Schmitt et al., 2021). In this study, adapters were fabricated by a 3D-printing technique employing PLA, and PVA was applied as a supporter for supporting overhangs of >45° in adapters. This personal protective equipment, which is used for the whole face, is made of a modified snorkel mask, with a 3D-printed adapter and two filters (Fig. 5). Air pathways by adapter can be observed in Fig. 5f. SARS-CoV-2 dimension is between 60 and 140 nm and these virus particles in the air can be transported through droplets up to a few millimeters. The filtration proficiency of this full-face mask was investigated with the help of NaCl particles below 500 nm. Also, based on the required standards, this full-face mask, and a commercial type of respirator were compared. Pressure drops, quality factor, and resistance to disinfection (70% ethanol), as well as filtration proficiency of the prepared mask, were measured. The achieved results confirmed that the developed mask can be successfully used against the SARS-CoV-2 virus.

2.1.5. Poly(ethylene terephthalate) (PET)

Polypropylene and PET are the most widely used materials for the preparation of air filters and respirators. However, these polymeric materials are not easily degraded in the environment. Disposable breathing apparatus based on these materials generates indestructible plastic waste. In this regard, the nontoxic respirator was fabricated using non-toxic fiber-forming polymers such as poly(vinyl butyral and poly(vinylidene fluoride-*co*-hexafluoropropylene) and a facile technique by solution blow spinning, (Lee et al., 2020) (Fig. 6a). In this spinning process, the polymer solution enters the nozzle through the syringe, and using incoming airflow and the specified distances, the fibers are produced on a vacuum-based mesh. After performing the filtration test, the surface of the disposable respirator was examined using SEM (Scanning Electron Microscope) images. As shown in Fig. 6d, aerosol particles are collected on the surface of the fibers.

2.1.6. Other polymers

The particle size of the SARS-COV-2 is around 100 nm, which can be transmitted through respiratory drops. Preparing a filter with a size of 100 nm can be very effective to prevent the spread of the SARS-COV-2. Recently, a nanofiber filter having 100 nm size using poly(vinylidene fluoride) to catch COVID-19 in the air was developed (Leung and Sun, 2020b). The nanofibers with a suitable diameter (84, 191, 349, and 525 nm) and without defects in morphology were successfully prepared by applying the electrospinning technique. Subsequently, the prepared nanofibers were electrostatically charged. The fiber diameter had an important effect on the performance of the filter. The efficiency of the prepared filters in trapping the SARS-CoV-2 was reported to be 90 to 94%. So, these filters are useful for removing contaminants that cause chronic diseases.

To fight the SARS-CoV-2 virus, a research team organized two types of cellular nano-sponges from plasma membranes of human lung epithelial type II cells or human macrophages (Zhang et al., 2020). For the fabrication of nano-sponges, the membranes were prepared, purified, and then, coated on the surface of poly(lactic-*co*-glycolic acid) nanoparticles using ultrasound technique. Nano-sponges made from human cell membranes (cells that were targeted by the SARS-CoV-2) have protein receptors to entre SARS-CoV-2 to cells (Fig. 7). These are the prey for the virus, and the interactions between them, prevent the virus from entering and controlling the infection. Studies have shown that after nano-sponge's incubation, the SARS-CoV-2 virus is neutralized and cannot infect the cell.

On the other hand, the permitted emergency drug for COVID-19 has not resulted in significant improvement until now. Ivermectin drug is an anti-inflammatory and anti-viral agent. In a study reported by Surnar and colleagues, polymeric nanoparticles loaded with Ivermectin were developed for COVID-19 therapy (Surnar et al., 2020). In their study, they investigated the effect of the target drug on reducing expression of the spike protein of the virus and receptor angiotensin-converting enzyme 2. This new nanoformulation provided the drug to enter the bloodstream gradually and keeps the amount in the blood at a therapeutic dose. In the reported study, poly(lactide-*co*-glycolide)-b-poly-(ethylene glycol)-maleimide, polymeric nanoparticles were prepared and labeled with Fc immunoglobulin in order to across the gut epithelial barrier and enter the bloodstream. Besides, drug-loaded polymer nanoparticles could inhibit the nuclear transport activity mediated by proteins like importin $\alpha/\beta1$ heterodimer (Fig. 8).

In an interesting research, Sun and *co*-workers prepared polymeric nanofibrous membranes containing vitamin K components with antibacterial and anti-viral functions for the production of personal protective equipment with antimicrobial and anti-viral features during COVID-19,. The influence of polymer constructions was also investigated (Sun et al., 2020). Vitamins Ks are natural photoactive materials that produce ROS (reactive oxygen species) under photoirradiation. In this study, daylight active functional polymers including hydrophobic and hydrophilic polymers [(polyacrylonitrile and poly(vinyl al*co*hol-co-ethylene), respectively] were used as matrix and blended with vitamin K. Under daylight (D65, 300–800 nm) and UV-A (365 nm) radiation, the organized nanofibrous membranes showed strong photoactivity in producing ROS ($^1O_2$, H_2O_2, $HO\cdot$) and in <90 min, the proficiency of antibacterial as well as anti-viral reached to >99.9% (Fig. 9). Poly(vinyl al*co*hol-*co*-ethylene)-based membranes produced more ROS and showed better antibacterial and anti-viral

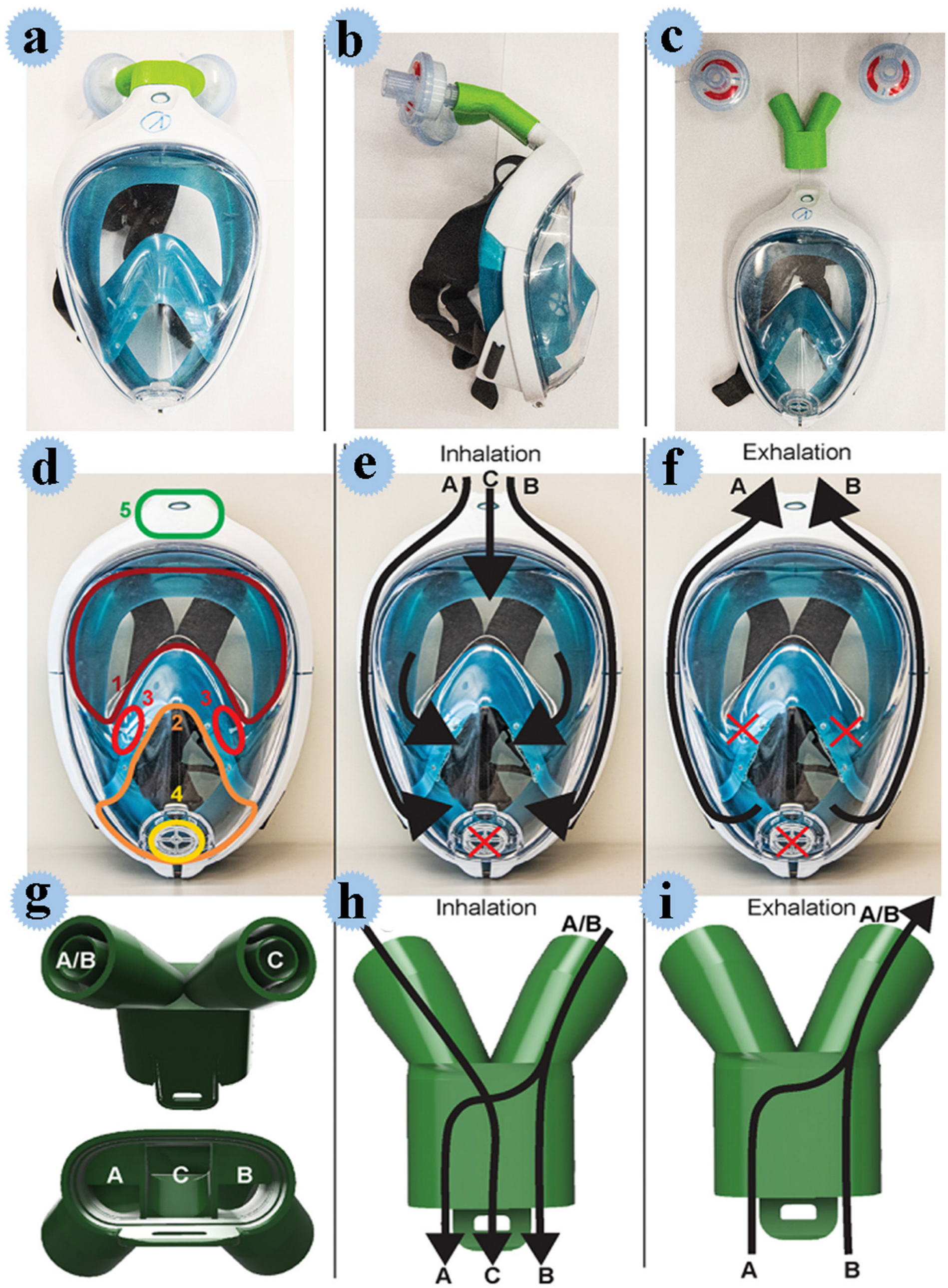

Fig. 5. Pictures of the assembled full-face mask: (a) front view, (b) side view, and (c) expanded view showing the different components. Snorkel mask and 3D-printed adapter, panel (d) shows the subdivisions of the mask: the upper chamber (marked "1") encloses the eyes and the lower chamber (marked "2") covers the mouth and nose. They are separated by a piece of silicone holding two unidirectional valves (marked "3"). The lower chamber contains the unidirectional chin valve (marked "4"). The port for the adapter is located on the top (marked "5"). Panel (e) shows the airways during inhalation, as the air enters from all three inlets on top, marked "A", "B", and "C". Panel (f) shows the airways during exhalation (with a sealed chin valve) only involving the side channels, marked "A" and "B". Panels (g) and show the 3D-printed adapter; the two medical filters are connected to the ports marked "A/B" and "C" in panel. The airflows through the adapter are shown in panel (h) for the inhalation and in panel (i) for the exhalation. The channels "A" and "B" merge into one channel (marked "A/B") inside the adapter. Reprinted from Schmitt et al. (2021) with permission from American Chemical Society. Copyright (2021) American Chemical Society.

properties compared to polyacrylonitrile-based nanofibers. Besides, the membranes prepared from the copolymer retained their properties after 5 times of contact with bacteria and viruses, which shows high durability and reusability. It should be noted that these non-toxic antimicrobials can be efficiently used for the preparation of personnel protective equipment such as anti-viral face masks.

2.2. The role of natural polymers during the COVID-19 pandemic

2.2.1. Cotton and cellulose

Cotton swabs can be successfully used for the design and fabrication of immunosensors for the sensitive detection of various pathogens including the COVID-19 virus. In an interesting research carried out by Eissa and Zourob, an immunosensor based on the combination of electrochemical assays and cotton fibers was developed for the sensitive detection of the COVID-19 virus in a facile, affordable, and fast way (Eissa and Zourob, 2021). The prepared immunosensor exhibited two functions: sample collection and detection. In the preparation of this immunosensor, carbon electrodes were utilized for immobilization of Nucleocapsid antigen after the functionalization of the surface. The schematic depiction of the preparation of the developed immunosensor towards the COVID-19 virus is shown in Fig. 10. After placing the N antigen on the surface of the electrode and blocking with the help of BSA, a cotton cover was used to improve the absorption of nasal samples. The

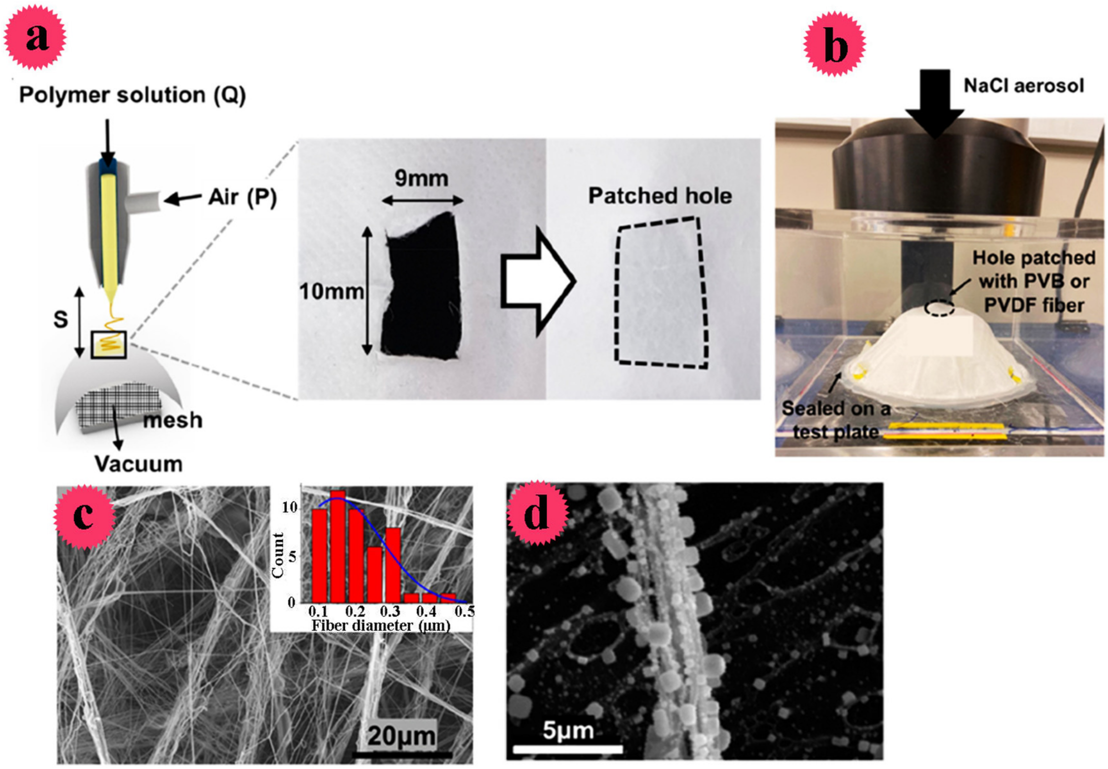

Fig. 6. (a) Schematic of solution blowing setup; (b) filtration test setup, (c) SEM images and size distribution histogram of as-spun fibers, (d) SEM image of the PVDF-HFP fiber after the filtration test. (PVDF-HFP: Poly-(vinylidene fluoride-co-hexafluoropropylene). Reprinted from Lee et al. (2020) with permission from American Chemical Society. Copyright (2020) American Chemical Society.

obtained results indicated that the developed immunosensor displayed excellent selectivity, selectivity towards the target COVID-19 virus with a low detection limit.

Due to the highly contagious nature of the COVID-19 virus and its destructive effects worldwide, the best way to prevent it is to use three-layer masks as well as social distance. On the other hand, doctors and front-line staff are at greater risk. Therefore, more protection and safety materials can be developed by using the antibacterial and anti-viral coatings and clothing. Considering this, Chauhan and Kumar reported the preparation of protective clothes with antibacterial and anti-washable (durable) properties for the health workers (Chauhan and Kumar, 2020). In their study, the achieved experimental data confirmed that the prepared protective clothes having anti-viral coatings showed good chemical and thermal stability (up to 160 °C) and could be used after repeated washing several times. Also, this coating showed excellent anti-stain and anti-pollution capability (non-

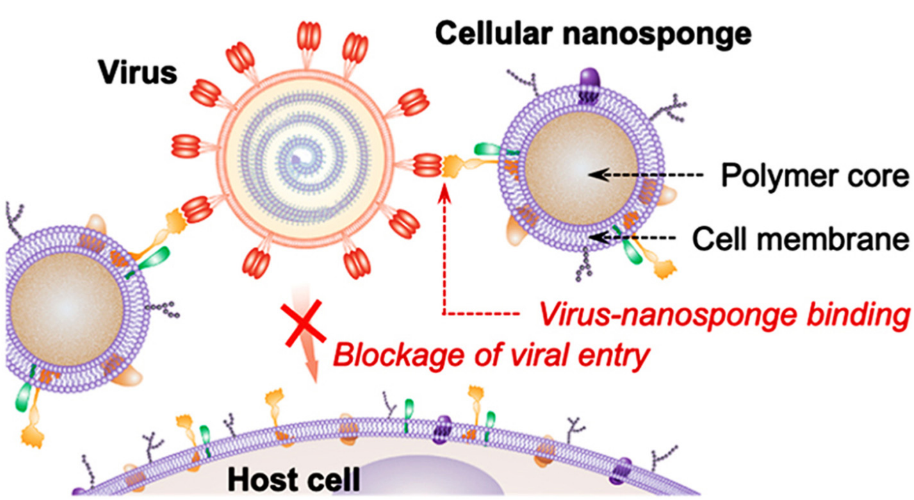

Fig. 7. Schematic mechanism of cellular nanosponges inhibiting SARS-CoV-2 infectivity. The nanosponges were constructed by wrapping polymeric nanoparticle (NP) cores with natural cell membranes from target cells such as lung epithelial cells and macrophages (MΦs). The resulting nanosponges (denoted "Epithelial-NS" and "MΦ-NS", respectively) inherit the surface antigen profiles of the source cells and serve as decoys to bind with SARS-CoV-2. Such binding interaction blocks viral entry and inhibits viral infectivity. Reprinted from Zhang et al. (2020) with permission from American Chemical Society. Copyright (2020) American Chemical Society.

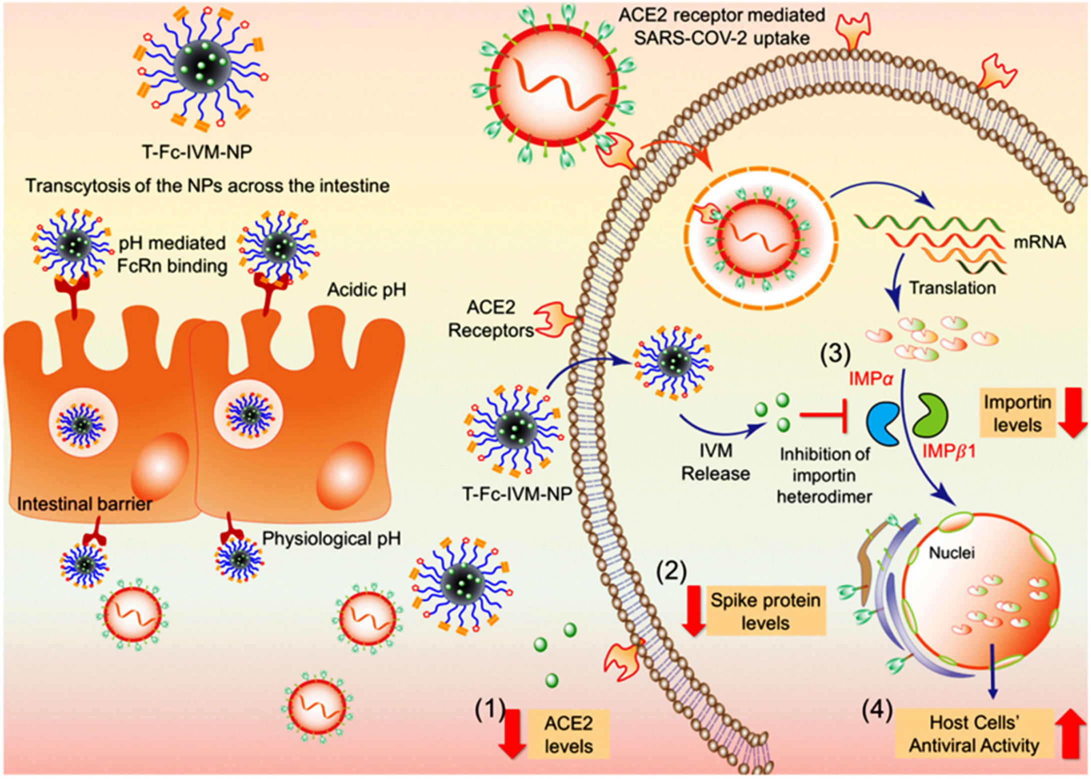

Fig. 8. Graphical representation showing that the targeted-Fc-IVM-NPs in the acidic gut lumen bind to FcRn receptors, allowing NPs to transcytose across the intestinal barrier and release at the physiological pH of the blood. IVM delivered via T-Fc-IVM-NPs shows the ability to (1) decrease ACE2 receptor levels, (2) decrease SARS-CoV-2 spike protein levels, and (3) decrease levels of the nuclear transport proteins importin α and β1, which leads to (4) an increase in the anti-viral activity of infected cells. (ACE2: Angiotensin-converting enzyme 2, IVM: Ivermectin). Reprinted from Surnar et al. (2020) with permission from American Chemical Society. Copyright (2020) American Chemical Society.

adhesion of contaminated soil and ink). The antifungal and antibacterial properties of this coating were tested using *E. coli* and *A. niger* and great features were reported. In this process for fabrication of coating, *Aloe vera* was used as an antimicrobial, anti-viral agent, and waterproof material. And hexadecyltrimethoxysilane reduced the contact of water and other liquids with the cotton fabric. Excellent water repellency was observed from the coated fabrics (164° water contact angle). The presence of polysaccharides and anthraquinones in *Aloe vera* causes anti-viral properties in linen fabric. Polysaccharides interact with viral particles and reduce the replication and absorption period of the virus. Also, polysaccharides containing high uronic acid and negative charge cause uptake of t-RNA, prevent aminoacyl-transfer-ribonucleic acid-ribosome interaction, and inhibit protein synthesis. This research group showed two anti-viral mechanisms: Elimination of viruses containing aerosol due to its superhydrophobicity, and inhibition of protein synthesis due to the presence of *Aloe vera* on the surface.

On the other hand, face shields are usually produced by using polymeric materials. Common plastic materials used to make face shields during the COVID-19 period are synthetic polymers such as PET and PVC that accumulate plastic waste. Cellulose acetate as a natural and environmentally friendly polymer can be successfully used as a substitute for face shields. However, this polymer is not very effective due to its low hydrophobicity. To overcome this drawback, cellulose acetate was modified with hexamethyldisilazane to increase hydrophobicity (Lee, 2020). After surface oxidation through oxygen plasma, an increase in the hydrophobicity of the films was achieved. In fact, hexamethyldisilazane was covered with oxygen plasma and caused polymer to become super-hydrophobic while maintaining the transparency of the films. Through this modification, effective face shields can be prepared from cellulose acetate.

2.2.2. Gum

Pathogens such as the COVID-19 virus can enter the body through respiratory droplets. For preventing the spread of the disease and protect individuals, a composite nasal spray containing polysaccharide (gellan gum and carrageenan) was formulated and its anti-viral properties were investigated by Moakes and colleagues (Moakes et al., 2020). This study aimed to provide a protective coating for the upper respiratory tract. In their study, the prepared nasal spray showed high anti-viral performance. By using this spray, it comes in direct contact with the nasal mucosa (Fig. 11). Careful selection of the polymer can improve the life-time of the spray and cause it to interact with the mucosa, which is called mucoadhesion. A wide range of polysaccharides such as pectin, alginate, dextran, gellan, and carrageenan are capable of adhering to the mucosa. These polymers were classified based on their ability to form a uniform coating. Gellan and carrageenan were more effective, therefore, they were mixed and added to the phosphate-buffered saline solution to be hydrated after a while. The schematic diagram of the inhibition of the COVID-19 virus is shown in Fig. 11b. Removal of the virus can be performed 1) by trapping in the spray layer and removal through negative pathways, 2) blocking the uptake of the virus into cells due to the formation of a polymer coating that is a barrier to the surface of the cells, 3) a steric barrier can form around the surface of the virus, blocking the absorption of the virus.

It has been reported that polysaccharides, including natural sulfated polysaccharides, have a strong inhibitory effect on viral infections. Indeed, sulfated polysaccharides can efficiently bind the viral protein to prevent the virus from entering the host cell. They can also attach to spike glycoprotein and stop it from entering the cell. In this regard, a research team investigated 4 types of sulfated polysaccharides (i.e. Sea cucumber sulfated polysaccharide, fucoidan from brown algae, iota-

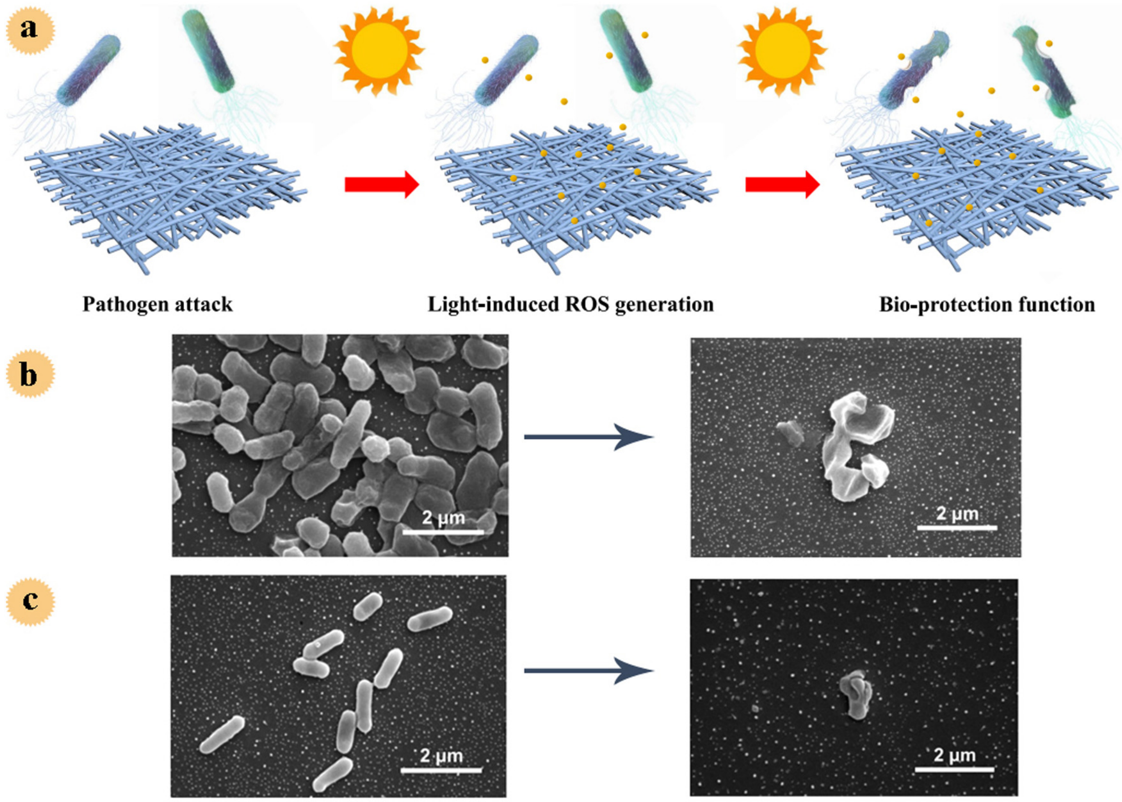

Fig. 9. (a) Schematic illustration of the photoactivated biocidal function of VNFMs, SEM morphology of (b) *E. coli* and (c) *L. innocua* without any treatment and SEM morphology of *E. coli* and *L. innocua* on PVA-co-PE/VK3 VNFM after D65 irradiation. (VNFMs: VK-containing nanofibrous membranes, VK: vitamin K). Reprinted from Zhang et al. (2020) with permission from American Chemical Society. Copyright (2020) American Chemical Society.

carrageenan from red algae, and chondroitin sulfate C from shark) for COVID-19 virus inhibitory activity (Song et al., 2020). Among them, sea cucumber sulfated polysaccharide, carrageenan, and fucoidan showed high anti-viral activity. The strongest inhibitory activity was related to sea cucumber sulfated polysaccharides. The achieved results also showed the binding of polymer to spike protein and preventing

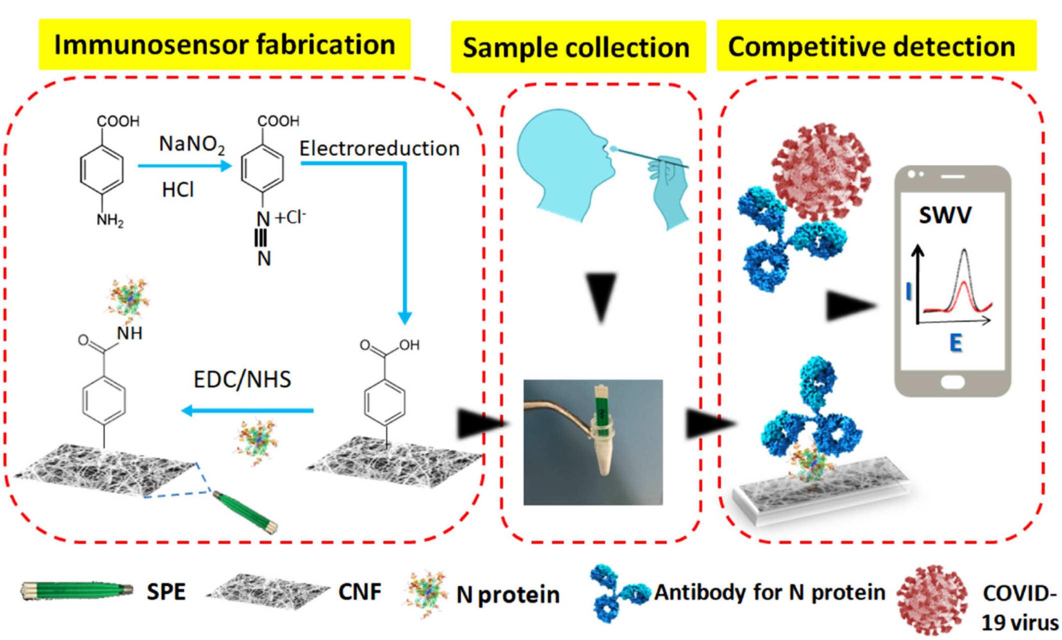

Fig. 10. The schematic depiction of the preparation of cotton-tipped electrochemical Immunosensor for COVID-19 virus; (A) Sample Collection Using the Cotton-Tipped Electrode, (B) Functionalization of the Carbon Nanofiber Electrode Using Electroreduction of Diazonium Salt and the Attachment of the Virus Antigen, (C) Detection Principle Using Competitive Assay and SWV Technique (SWV: Square wave voltammetry). Reprinted from Eissa and Zourob (2021) with permission from American Chemical Society. Copyright (2021) American Chemical Society.

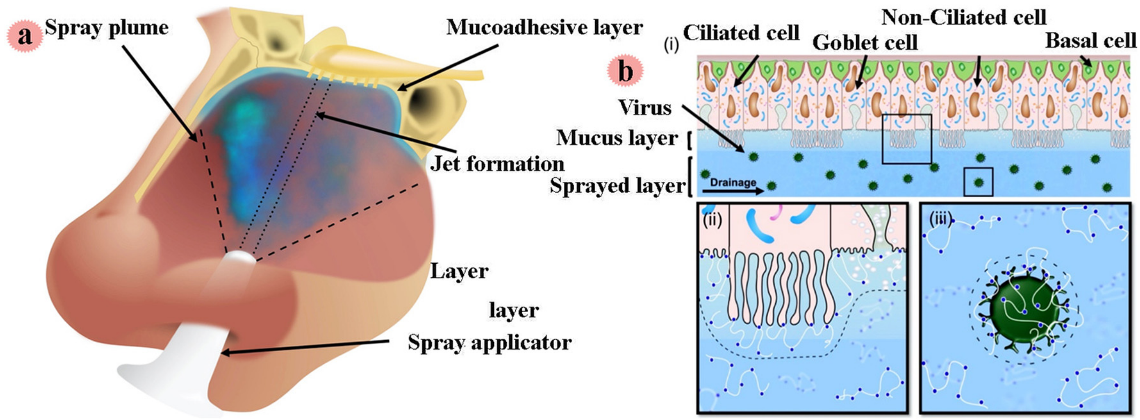

Fig. 11. (a) The schematic demonstration of the application of a nasal spray to the nasal cavity. (b) schematic diagram showing the nasal epithelium covered in the nasal spray: (i) demonstrates potential removal of the virus via trapping within the sprayed layer and elimination through native pathways, (ii) demonstrates potential blockage of virus uptake into the cells as the polymer creates a steric barrier across the cell interface, and (iii) demonstrates potential inhibition of virus uptake by creating a steric barrier around the interface of the virus. Reprinted from Moakes et al. (2020), a free access article.

the COVID-19 from entering cells. In general, these polysaccharides are very useful in treating, preventing, and fight against COVID-19.

Another research team investigated the anti-viral performance of λ-carrageenan towards influenza (A and B) and COVID-19. The obtained results from cell culture studies showed that this polysaccharide effectively inhibits influenza and COVID-19 viruses. Also, toxicity was not observed for the host cell in 300 μg/ml. This polysaccharide reduced the expression of virus cells and reduced the production of virus progeny by binding to virus receptors (Jang et al., 2020).

2.2.3. Hyaluronic acid

Hydroxychloroquine is used for the treatment of autoimmune diseases such as systemic lupus erythematosus, primary Sjögren's syndrome and rheumatoid arthritis. It is reported to be a potent broad-spectrum anti-viral agent (Kumar et al., 2021; Yao et al., 2020). However, it exhibits some systemic toxicity. By modifying and conjugating these drugs, toxicity can be significantly reduced. In this regard, a drug conjugate was proposed using hyaluronic acid and Hydroxychloroquine drug (Khan and Aroulmoji, 2020). Indeed, the conjugation between Hydroxychloroquine and polysaccharide can be achieved via OH groups of Hydroxychloroquine. It is expected that the intrinsic toxicity of the drug with this method will be less, increase the bioavailability, control release of the drug, and its effectiveness will be more to fight the COVID-19.

2.2.4. Chitosan

Recently, a research team showed the inhibition of COVID-19 by employing N-(2-hydroxypropyl)-3-trimethylammonium chitosan chloride (HTCC) as a kind of modified chitosan. Based on in-vitro as well as ex-vivo outcomes, viral infections can be blocked by this modified polymer (Milewska et al., 2020). HTCC prevents the virus from entering the host cell by interacting with the spike protein. The obtained outcomes exhibited that HTCC successfully inhibits the replication of the COVID-19 and could be a promising drug candidate for the COVID-19.

In another reported study, a strategy was reported to prevent and control the COVID-19 using β-chitosan (Alitongbieke et al., 2020). The binding of β-chitosan to the COVID-19 virus was investigated, and the inhibitory effect of this biopolymer on the virus-induced inflammation was studied. Indeed, COVID-19 can destroy the human respiratory epithelial cells through interaction with the human angiotensin-converting enzyme II (ACE2). The results showed a significant therapeutic effect of β-chitosan. β-chitosan prevented the virus from attaching and destroying ACE2. So, this study could be a useful resource for the fight against COVID-19.

2.2.5. Alginate

Alginate has been successfully used in anti-inflammatory, anti-oxidant, and anti-viral drugs due to its biocompatibility, non-toxicity, and mucoadhesive properties (Fabra et al., 2018; Zhu et al., 2020). Besides, alginate can effectively scavenge free radicals and cause the release of cytokine and its control. It is recommended alginate and its derivatives, as a therapeutic supplement for the COVID-19, can significantly reduce inflammation and strengthen the immune system. When the COVID-19 virus enters the body, the blood viremia increases and causes a storm of cytokine, so, inflammation and a decrease in T lymphocytes happened. This research team presented a hypothetical chart for treating the COVID-19 with alginate. Patients suffer from unregulated immune responses associated with cytokine storm and lymphopenia. The addition of this biopolymer to viral drugs can reduce inflammation and increase immunity. Alginate can also be used to activate the immune system by activating macrophages or it can be applied as a capsulation to the inactivated virus during vaccination routine for enhancement of the body response and production of specific antibody (El-Sekaily et al., 2020) (Fig. 12).

COVID-19 has also caused stress and anxiety in children and adults worldwide. Stress harms human health by creating free radicals. In this condition, a healthy diet is needed. Vegetable volatile oils contain active ingredients that show antioxidant and antibacterial properties, can kill free radicals. For this purpose, a dairy product (cow's milk yogurt) with high antioxidant properties was prepared by using sodium alginate and volatile oils from lavender, basil, mint, and fennel antioxidants were entered the sodium alginate, and this polymer acted as a drug carrier for releasing antioxidants to yogurt. The antioxidant activity of yogurts was tested using the DPPH (2,2-diphenyl-1-picryl-hydrazyl-hydrate) technique. The obtained results confirmed the high antioxidant properties (Ţiţa et al., 2020).

In another study, the anti-viral activity of alginate nanocomposite films containing carbon nanofibers was investigated (Sanmartín-Santos et al., 2020). Certain amounts of alginate and carbon nanofibers were weighed and dissolved in water. After the addition of $CaCl_2$ solution, the films were prepared in a petri dish, and then, dried. The outcomes showed anti-viral activity for these films coliphages T4r, which showed good potential for anti-viral protection materials.

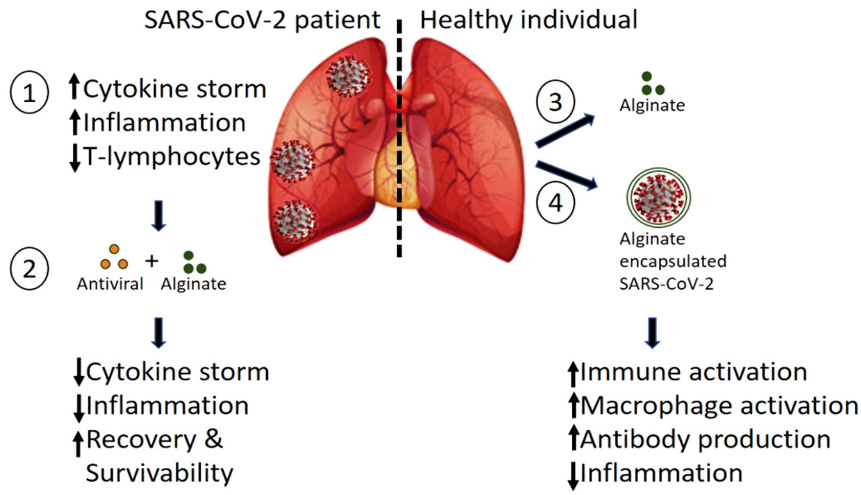

Fig. 12. Hypothetical diagram of alginate application to treat Covid-19 patients. 1- Covid-19 patients suffer from dysregulated immune response accompanied by cytokine storm and lymphopenia (decrease in T-lymphocytes). 2- Here we postulate that adding alginate supplement to the anti-viral medications can enhance patient immunity, reduce inflammation and increase recovery and survivability of patients. Alginate supplement can either be administrated to health individual to boost their immune system through macrophage activation (3) or can be used as encapsulation to inactivated SARS-CoV-2 during vaccination routine to enhance body response and specific antibody production (4). Reprinted from El-Sekaily et al. (2020), an open access article.

2.2.6. Pectin

Pectin, as another natural polymer, can also be effective in COVID-19 therapy. Indeed, citrus peels including lemons and oranges contain flavonoids that can attach to the COVID-19 virus receptors to prevent and treat the infection. Computational studies by Indonesian researchers have shown that hesperidin as an abundant flavonoid in citrus peels has the greatest affinity for binding to COVID-19 receptors and can prevent viral infections. Also, Chinese researchers have reached similar conclusions about hesperidin. Pectin is full of this flavonoid, which is an effective drug. Because of the effectiveness of pectin, a research team introduced a process for the industrial preparation of pectin containing this flavonoid through the rapid processing of fruit skin waste (Meneguzzo et al., 2020).

3. Conclusions

Due to the severe contagion and lack of public safety, COVID-19 has spread rapidly all over the World. This epidemic has created an urgent need for medical equipment and devices. Also, they could be very well needed after pandemic, which is so called post- pandemic. Researchers and scientists are seeking to provide effective personal protective equipment, diagnostic kits, anti-viral agents, and effective drugs to control and combat COVID-19. The demonstrated studies in this review indicated that the developed synthetic or natural macromolecules, therapeutic supplements, anti-viral sprays, protective coating, various masks, shields, immunosensors, drug carriers, can be helpful to reduce concerns globally during COVID-19 pandemic and post-pandemic. Indeed, natural, and synthetic polymers are unavoidable materials in the healthcare sector during this pandemic. Polypropylene, polystyrene, poly(lactic acid), poly(ethylene terephthalate), and natural macromolecules such as sodium alginate, chitosan, cellulose, and gums with biodegradability and environmentally friendly features can be successfully applied for the design and fabrication of several materials including face masks, shields, anti-viral coatings, as well as diagnostic kits.

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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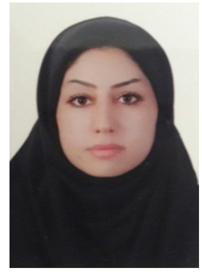

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