The latest strategies in the fight against the COVID-19 pandemic: the role of metal and metal oxide nanoparticles

Shadpour Mallakpour, Elham Azadi and Chaudhery Mustansar Hussain

The outbreak of the COVID-19 epidemic, which appeared at the end of 2019, has had a tremendous impact on the entire world, both in terms of health, economics and the environment. So far, extensive strategies have been implemented for the fast diagnosis, prevention, control and treatment of the SARS-CoV-2 virus. Advances in technologies based on metals and metal oxides nanoparticles such as Ag, Au, Cu2O, TiO2, Fe3O4, have opened up new perspectives in this regard. These materials have been extensively used for the management of COVID-19 due to their unique features. These materials have been applied for the preparation of antiviral face masks, coatings, different immuno sensors, etc. In this review, we summarize and highlight the latest technologies, implementations and achievements based on metal and metal oxide nanoparticles in order to fight the emerging coronavirus. We present the preventive and diagnostic strategies to control this epidemic with the help of metals and metal oxide nanoparticles.

1. Introduction

A year ago, a new and unknown viral disease appeared in China, extended rapidly in the world, and up to now has killed countless people. This pandemic is known as 2019-nCoV or COVID-19 and is produced via the SARS-CoV-2 virus. The COVID-19 epidemic has seriously affected everyone’s life and the economies of countries. Generally, viruses as infectious pathogens rely on host cells to continue their life cycle. Structurally, they are mainly composed of nucleic acids, structural proteins and lipid membranes. It has been reported that the SARS-CoV-2 virus is more contagious than SARS, and therefore, it spread to all continents in a short time. The routes of transmission of SARS-CoV-2 can be observed in Fig. 1, including touching infected surfaces or coughing and respiratory droplets.

On the other side, the SARS-CoV-2 virus has harmful effects on the environment and organisms due to the prevalence of this disease. Waste and sewage from hospitals and laboratories enters the environment, endangering the lives of organisms, and also, due to the increasing use of personal protective equipment such as disposable masks and gloves and the release of them into the environment, people are more exposed to infection. Therefore, reducing the health risks and controlling the SARS-CoV-2 virus is of great importance. Most of these problems can be solved through prevention, rapid diagnosis, disinfection and management of the COVID-19 epidemic. Rapid and timely diagnosis of SARS-CoV-2 infection through immuno sensors, disinfection by antiviral materials, and the provision of personal protective equipment with reusable and antiviral capabilities can prevent further spread of the virus and improve the environment, life and economies of nations.

The World Health Organization recommends the use of personal protective equipment in addition to social distancing. So far, solutions and protocols have been proposed in order to disinfect surfaces and quickly detect SARS-CoV-2, prevent its spread and control it. Nanotechnology plays a significant role in this regard. With the help of nanotechnology, diverse antiviral coatings, biosensors, and personal protective equipment have been prepared. So far, diverse materials have been designed and developed using various polymers and carbon nanomaterials for diagnosing infection with SARS-CoV-2 and controlling its spread. Diagnostic kits for timely identification, antimicrobial masks with a self-cleaning function, antimicrobial coatings and antiviral cloths to protect people, especially medical staff on the front line, have been developed.

Fortunately, metal and metal oxide nanoparticles have been useful in this regard. Metals and metal oxides have been widely...
studied due to their exceptional and novel features. Numerous applications of these materials have been reported in various industries, including medicine and pharmacy. Reports have indicated that metallic, metal oxide, or other nanoparticles such as Ag, Au, Cu, Cu₂O, CuO, SiO₂, Fe₃O₄ and TiO₂, can reduce risks related to the COVID-19 epidemic. In fact, valuable substances based on metals and metal oxides can be beneficial in reducing and controlling this disease and saving the world. Antiviral and antibacterial materials such as coatings or face masks are used to inactivate SARS-CoV-2 and reduce secondary microbial infections. Various portable bio-sensors with the help of metals and metal oxides can detect SARS-CoV-2 in a short time and reduce its spread.

So, due to the value of metal and metal oxide nanoparticles to control the epidemic of the virus worldwide, it is necessary to collect the latest strategies and new achievements in this regard and make them available to interested researchers. This review examines the use of metals and metal oxides such as Cu, Ag, Au, Fe₃O₄, CuO in the development of useful tools to combat the SARS-CoV-2 virus crisis.

2. The role of gold nanoparticles during the COVID-19 crisis

Au nanoparticles with unique properties, including optical properties, localized surface plasmon resonance, inherent photostability and a great extinction coefficient are widely used in the preparation of colorimetric bio-sensors. In a recent study, a colorimetric bioassay was developed employing nano-Au particles capped with thiol modified antisense oligonucleotides for the nucleocapsid phosphoprotein of SARS-CoV-2 and was used to diagnose COVID-19 in a short time (about 10 min) (Fig. 2). In the presence of the target RNA sequence of the virus, the surface plasmon resonance shows a change and so, selective ‘naked-eye’ diagnosing can be performed. Generally, the advantages of this study were that it does not require any sophisticated instrumental techniques, and a low detection limit (0.18 ng μL⁻¹) was obtained.

A low-cost and simple nanoplasmonic bio-sensor chip and point-of-care device was developed for the fast and one-step diagnosis of infection with SARS-CoV-2, which could help to control the severe pandemic, by employing Au nanoparticles.

Professor Shadpour Mallakpour, an organic polymer chemist, graduated from the chemistry department of the University of Florida (UF), Gainesville, Florida, USA in 1984. He spent two years as a post doc at UF. He joined the Department of Chemistry, Isfahan University of Technology (IUT), Iran, in 1986. He has held several positions such as the chairman of the Department of Chemistry and deputy of research, Department of Chemistry at IUT. From 1994–1995 he worked as a visiting professor at the University of Mainz, Germany, and from 2003–2004 as a visiting professor at Virginia Tech, Blacksburg, USA. He has published more than 850 journal papers and more than 400 conference papers and has received more than 30 awards. The most important award given to him was for the selection of the first laureate on fundamental research, at the 21st Khwarizmi International Award in 2008. He has been listed in the top 1% of scientists in Chemistry in the ISI Essential Science Indicators since 2003. He is also listed in the top 2% of scientists in polymers in 2020. He was selected as an academic guest of the 59th Meeting of Nobel Prize Winners in Chemistry, 2009, at Lindau, Germany. He has presented many lectures as an invited or keynote speaker at different national and international conferences or universities. He has been a member of the organizing and scientific committees for many national and international conferences. He has also been the chairperson of many national and international meetings. In recent years, he has focused on the preparation and characterization of polymer-based nanocomposites to be used as bioactive materials as well as adsorbents and photocatalysts for remediation technology.

Elham Azadi received her BSc in the field of chemistry in 2011. Also, she received an MSc in organic polymer chemistry in 2014 from the Isfahan University of Technology (IUT), Isfahan, Iran. Currently, she is a PhD student in organic polymer chemistry at IUT. Her research interests include bio-materials, high-performance polymer-inorganic nanocomposites and metal oxide NPs and the removal of hazardous pollutants.

Chaudhery Mustansar Hussain, PhD is an Adjunct Professor, Academic Advisor and Director of Chemistry & EVSc Labs in the Department of Chemistry and Environmental Science at the New Jersey Institute of Technology (NJIT), Newark, New Jersey, USA. His research is focused on the applications of nanotechnology & advanced materials, environmental management, analytical chemistry and various industries. Dr Hussain is the author of numerous papers in peer-reviewed journals as well as a prolific author and editor of several scientific monographs and handbooks in his research areas published with Elsevier, the Royal Society of Chemistry, John Wiley & sons, CRC, Springer etc.
To achieve this aim, using a replica molding procedure, a sensor chip was prepared on a poly(ethylene terephthalate) substrate with an Au layer with a specified length, depth, and thickness on it (Fig. 3a). The findings confirmed the ability of the sensor chip to diagnose infection with SARS-CoV-2 in <15 min with good sensitivity. In this work, an innovative and portable device controlled via a smartphone app was developed for the quick demonstration and measurement and sensitive detection, as well as investigating the dynamic binding curves of SARS-CoV-2 on the bio-sensor (Fig. 3b). For the handheld devices, the quantification limit of the virus was 4000 particles in 15 minutes. Thus, these low-cost devices with extraordinary time efficiency can be applied for a fast diagnosis of COVID-19.

In another study, using functionalized Au nanoparticles with antibodies, a colorimetric bio-sensor for the single-step colorimetric detection of SARS-CoV-2 using throat and nasal swabs was prepared. Due to the surface plasmon resonance feature and the color change from blue to red owing to the interaction in a colloidal suspension, colorimetric diagnosis was performed. Samples (45 positive and 49 negative) were
examined with the prepared bio-sensor and compared with PCR results. The outcomes confirmed the effectiveness of the prepared colorimetric bio-sensor. The features of the prepared colorimetric bio-sensor were sensitivity to the infecting virus, reliability and being a cheap and fast tool.

Plasmon resonance is one of the dramatic phenomena that results from the interaction between light and matter. Plasmonic immunoassays monitor the refractive index changes caused by antigen-antibody interactions. In a study, with the help of Au nanoparticles, a plasmonic immunosensor was reported to identify the spike protein of SARS-CoV-2.\textsuperscript{28} The sandwich-shaped structure of this immunoassay is shown in Fig. 4, in which the Au nano-sheet was functionalized with a SARS-CoV-2 spike protein antibody. In addition, Au nano-rods were conjugated with an antibody to enhance the sensitivity. Therefore, by the antigen (SARS-CoV-2 in serum)/antibody interaction, this research team described a sandwich-shaped immunoassay using Au nanorods to improve the output signal.

Since one of the most important priorities to quickly improve public health is the diagnosis of COVID-19 disease, in an investigation, by a combination of plasmonic photothermal and localized surface plasmon resonance features, a plasmonic bio-sensor to diagnosis infection with SARS-CoV-2 was developed.\textsuperscript{29} To achieve this aim, a DNA receptors-functionalized Au nano-islands chip could perform fast, highly sensitive, as well as reliable virus detection through hybridization of nucleic acids. To improve the action of the sensor, thermo-plasmonic heat was produced on the same Au nano-islands chip, when illuminated at their plasmonic frequency. The localized plasmonic photothermal effect was able...
to raise the hybridization temperature and facilitate the exact differentiation between the two gene sequences. The prepared bio-sensor was very sensitive to SARS-CoV-2 sequences, showed a low detection limit, and could detect a particular target in a multi-gene combination.

In a recent study, by using computational and theoretical approaches, the capability of functionalized nano-Au particles as antiviral agents was studied for blocking the RBD (receptor-binding domain) of SARS-CoV-2. Owing to their large size, they cover the entire binding surface of the RBD of the virus. The findings showed the remarkable effects of the modified Au nanoparticles on the RBD and the strong interaction with the SARS-CoV-2 glycoprotein. The new peptide-functionalized Au formed a stable complex with RBD and Au was a good choice for antiviral agents toward SARS-CoV-2. Also, in another study, via the indirect immune-chromatography technique, lateral flow tests based on colloidal Au nanoparticles were prepared to quickly detect the IgM antibody toward SARS-CoV-2. For the preparation of lateral flow strips, the analytical membrane was covered in the SARS-CoV-2 protein, and IgM and Au nanoparticles were conjugated for the formation of the detection reporter. By changing the IgM amount and pH, the Au-based assay was optimized. The performance of this system was estimated via the analysis of serum samples and compared with the PCR outcomes. This system showed outstanding selectivity from other viruses, 100% sensitivity, short duration (15 min), and a small amount of serum for the test (10–20 µL) were needed. Other advantages of lateral flow tests for the diagnosis of COVID-19 were the low cost, easy operation, and high stability.

3. The role of silver nanoparticles during the COVID-19 crisis

Silver has excellent performance against bacteria, viruses, and fungi, and today, it is widely used to prepare antibacterial materials in diverse applications such as biomedical materials, antibacterial sprays and fabrics, and so on. In fact, this nanoparticle with great performance toward microorganisms is used as a biocide for various surfaces such as medical equipment and wound dressings. Studies have shown that Ag nanoparticles have antiviral properties against hepatitis, influenza, and HIV. They can also be effective in controlling SARS-CoV-2. In this regard, Ryo and coworkers evaluated the effect of Ag nanoparticles on SARS-CoV-2 and studied them to find the best concentration and size for the most efficient inhibition of SARS-CoV-2. Different concentrations and sizes of Ag were considered, and it was observed that particles with a diameter of 10 nm at a concentration of 1–10 ppm are effective toward SARS-CoV-2. Toxicity was observed at concentrations of 20 ppm and above. Studies have shown that Ag effectively inhibits virus entry into cells. Therefore, this study confirmed the antimicrobial properties of Ag for SARS-CoV-2 but it should be used with caution due to its toxicity.

Twenty percent of the world’s mortality is due to infectious diseases, and about a third of that is caused by viruses. Therefore, nanomaterials with antimicrobial properties are very effective in this regard. In a study, Au/Ag core/shell nano-rods were fabricated through the coating of a Ag shell on Au nano-rods, and the antiviral performance of them toward the coronavirus was examined. The antiviral activity of Ag nanoparticles is attributed to the release of Ag+. The interaction between the coronavirus and the shell (Ag) prevents the virus from entering the host cell and also prevents virus replication. Mechanistic studies have shown that these Au/Ag core/shell nanostructures prevent coronavirus entry and the apoptosis induced by virus infection. Further experiments showed that by increasing the number of infected viruses cells, intracellular ROS is produced, which leads to the oxidation of Ag and the release of Ag+, which has excellent antiviral properties (Fig. 5). These prepared nanostructures have good potential to fight coronavirus diseases such as COVID-19, SARS, and MARS.

4. The role of copper and copper oxide nanoparticles during the COVID-19 crisis

Compared to noble metals, copper is less expensive and has been used for centuries. Copper-based coatings can be used to protect humans. Copper and copper oxide nanoparticles have excellent antibacterial and antiviral properties and are used in diverse applications. They have also been shown to be very effective against the coronavirus 229E. Indeed, the presence of these antimicrobial nanoparticles in the preparation of
antiviral coatings with good performance controls the spread of coronavirus. While the SARS-CoV-2 virus can survive on plastic and steel surfaces for several days, it can survive on copper surfaces for 4 to 8 hours. By releasing the copper ions from these materials, ROS are produced, which causes damage and the death of pathogens. So far, copper and copper oxides have been used to prepare antibacterial and antiviral agents to combat SARS-CoV-2. For example, a research team reported an effective and inexpensive method for preparing copper/ZIF-8 MOF (metal–organic framework) nanocomposites and showed that by covering the fibers in face masks with these materials, reusable masks with antibacterial and antiviral properties can be prepared.37 The prepared nanocomposite showed good chemical and thermal stability. When pathogens were placed on the mask filters, they were inactivated by ions released from the composite. The resulting ROS can interact with the bacterial membrane and disrupt its metabolism (Fig. 6). So, these materials showed enhanced antibacterial performance toward S. mutans and E. coli. Also, the antiviral activity of the product against SARS-CoV-2 was evaluated and the results showed a 55% reduction in virus replication after 48 hours. Compared to the Remdesivir drug, the prepared composite demonstrated good anti-SARS-CoV-2 performance even at extremely low, drug-like concentrations (<10 ppm by mass). The toxicity of

Fig. 6  (a) Schematic of the Cu@ZIF-8 functionalized filter medium and its filtration mechanism against microbe-containing aerosol droplets. (b) The probable antibacterial mechanism shown by core–shell Cu@ZIF-8 NWs. SEM images of (c) the bare filter medium containing E. coli. (d) the Cu@ZIF-8 NWs loaded filter medium showing deformation of the E. coli membrane suggesting cell death (NWs: nanowires). This figure has been reproduced from ref. 37 with permission from John Wiley & Sons, copyright 2020.
the resulting composites was also studied and their effect on the inflammatory response was investigated and the results showed their good biocompatibility. Interestingly, the antimicrobial activity and cytotoxicity of the fabricated Cu/ MOF was greater than that of Cu or the MOF alone. Likewise, due to the thermal and chemical stability, these masks were resistant to abrasion. Other advantages of this method include the simplicity, low cost and reduced environmental waste.

A team of researchers developed a personal protective coating with self-sterilizing properties with the help of active copper (a new configuration of copper) which was able to inactivate the virus and kill pathogens in 30 seconds. These materials have the ability to be used in face masks and other protective equipment. Cellulose/polyester fabric loaded with active copper showed good antiviral properties. Therefore, face masks can be treated with it.

Because SARS-CoV-2 is viable on solid objects for a week, exposure to these solids can cause human infection. So far, coatings have been developed to reduce the lifetime of the virus on objects. Behzadinasab et al. developed and tested an anti-SARS-CoV-2 porous coating with the help of a CuO/polyurethane film (10–16 μm). The reason for using polyurethane is that this polymer has the capability to cover diverse surfaces. The purpose of this research was to provide a coating for the rapid inactivation of SARS-CoV-2, with the ability to cover various solids, having the appropriate strength, as well as maintaining its antiviral effect during use. This antiviral coating can be used for various commercial, home and medical surfaces including cell phones, doorknobs, pens, keyboard buttons, and more (Fig. 7). In fact, with the help of these coatings, the fear of touching objects will be reduced, and SARS-CoV-2 transmission from the surfaces will be reduced. After one hour on the coated glass and steel, the amount of the virus was reduced by 99.9% compared with the uncoated samples. The prepared coating maintained its strength after water immersion (for 13 days) and also washing with 70% ethanol. In addition, it can retain its mechanical integrity and strength by scraping (though not heavy and intentional scratching) and cutting with a blade.

In another study, a powerful and highly transparent antiviral coating for influenza or coronaviruses was prepared using copper oxide-embedded graphene as an antiviral agent and poly(vinyl alcohol). This prepared coating can be used for a wide range of surfaces to reduce the transmission of respiratory viral infections. Structural investigation demonstrated the even dispersion of the CuO and Cu2O nanoparticles on 2D graphene sheets. These graphene structures interact with the peptide bilayer membrane to rupture and inactivate the virus. Also, copper oxides can inactivate the virus by inhibiting protein activity. With the help of the polymer, a completely transparent coating without any stains was prepared (Fig. 8b). By the immersion method, a transparent glass coating was prepared for the cell phone. The optical transmission spectra confirmed the transparency of the prepared coating. According to the findings, with the help of this antiviral coating, the spread of COVID-19 can be prevented (Fig. 8c). Another interesting point is that after mixing the CuO/graphene nanocomposite with the poly(vinyl alcohol), no change in the antiviral properties was observed. On the other hand, the presence of the polymer formed a film and a completely transparent coating to cover the mask, door handles, and medical equipment.

Touching face masks while using them increases the risk of transmitting COVID-19. Because copper and copper oxides have strong antiviral features, textiles can be impregnated with these materials to reduce infection. In one study, surgical face masks and N95 masks, in which the outer layer was impregnated with copper oxide, were developed to prevent SARS-CoV-2 transmission. These masks were able to reduce levels of the virus by about 99% after a few minutes of virus contact with the masks.

To reduce infection caused by the coronavirus through surfaces, as well as reducing the anxiety caused by touching surfaces, in one study, a robust hydrophilic anti-SARS-CoV-2 CuO coating was prepared by the dispersion of Cu2O on the glass surface and heat treatment at 700 °C for production of a CuO layer with ≈30 μm thickness from the oxidized Cu2O. In 30 minutes and 60 minutes, 99.8% and 99.9% of SARS-CoV-2 was inactivated. This coating maintained its hydrophilicity for at least 5 months. Also, no change
in the robustness of the coating was observed after exposure to ethanol (70%) and bleach (3 wt%). The produced coating showed potential for use on metal door handles (Fig. 9).41

5. The role of iron-based nanoparticles during the COVID-19 crisis

Magnetic Fe₃O₄ nanoparticles, with many advantages like high surface area, outstanding magnetism, easy modification, etc., are ideal carriers with respectable separation ability. In this regard, a new method with high sensitivity, accuracy and stability to detect COVID-19-specific IgG, as well as IgM, was developed.42 Indeed, a fluorescence immunoassay technique to determine human IgG in serum samples by using nanotechnology based on Fe₃O₄ and quantum dots was designed. To achieve this aim, mouse antihuman IgG was coupled on the surface of functionalized Fe₃O₄ nano-spheres and employed as an immune capture probe. Also, to achieve better sensitivity, quantum dot nano-beads were coupled with rabbit antihuman IgG as a fluorescence detection probe. In the presence of a human IgG antibody, a sandwich-shaped immune-complex is formed, and, after magnetic separation, the precipitate has a strong fluorescence signal. In the absence of a human antibody, no fluorescence signal is observed. This fluorescence-linked immunosorbent assay had many benefits, for example fast operation, low detection limit, wide linear range, great accuracy and sensitivity, as well as good performance compared to customary analytical approaches. In another study, a test strip was designed with the help of Fe₃O₄ to detect SARS-CoV-2 in 15 min. Magnetic Fe₃O₄ nano-beads were coupled with particular antibodies, and the spike protein of SARS-CoV-2 acted as a coating antigen to capture specific antibodies against coronavirus. Owing to their exceptional magnetic features, Fe₃O₄ nano-beads are
used for generating diverse kinds of detection signals like magnetic and color signals as well as simplifying the detection procedure.43

So far, antiviral studies have been performed on iron oxides. A research team used a molecular docking study to investigate the interactions of iron oxides (Fe$_2$O$_3$ and Fe$_3$O$_4$) with the

Fig. 10 NanoPCR assay schematics for COVID-19 diagnostics. (a) TEM images of MPNs with a core–shell \( \text{Zn}_{0.4}\text{Fe}_{2.6}\text{O}_4-\text{Au} \) structure. Left: a 16 nm magnetic core was encased by a 12 nm Au shell. Right: elemental mapping of Au and Fe showed an area-specific distribution of the core and Au shell structure. (b) Target RNA regions for nanoPCR tests. The \( N_1 \) and \( N_2 \) genes are for SARS-CoV-2 detection, whereas the \( RPP30 \) gene serves as a control for human sample confirmation. ORF, open reading frame; S, spike; E, envelope; M, membrane; N, nucleocapsid. (c) High-speed nanoPCR diagnostic flow for SARS-CoV-2 detection: (1) 3 min of RNA extraction using a disposable RNA preparation kit; (2) 11 min of RT–PCR by magneto-plasmonic thermocycling; and (3) 3 min of detection and diagnosis via MFS by application of an external magnetic field for MPN removal. (d) A disposable RNA extraction kit with preloaded buffers and a simple plunge system. (e) A compact nanoPCR instrument for POC application (MPNs: magneto-plasmonic nanoparticles). This figure has been reproduced from ref. 45 an open access article from Nature, copyright 2020.
SARS-CoV-2 protein required for binding to host cell receptors. Studies have shown that iron oxides interact effectively with the glycoproteins of SARS-CoV-2. These interactions are expected to alter the glycoprotein structure of the virus and inactivate them.

The diagnosis of COVID-19 is made by a reverse transcription PCR test in a laboratory and the test time is about 2 hours. So, a research team developed a fast-performing portable device named nano-PCR for COVID-19 detection in 17 minutes (using plasmonic heating through magneto-plasmonic nanoparticles). Microscopic images of the magneto-plasmonic nanoparticles with a core/shell construction and also, a schematic of the nano-PCR assay to detect COVID-19, are presented in Fig. 10. The prepared nano-PCR showed several advantages: (1) it is portable, reliable and accurate (> 99%), with a sensitivity of > 80% and a specificity of > 97%, (2) due to the reduction in the PCR reaction time, detection can take place on-site. Due to these advantages, ambulatory clinics can be established without the need to transport samples. Samples from 75 patients were examined and outstanding diagnostic accuracy was attained.

Because the SARS-CoV-2 virus significantly affects medical systems, the economy, and our daily life, one of the most important strategies right now is to control the spread of SARS-CoV-2. For the fast diagnosis of it, in a recent study, a biosensor was designed based on functionalized magnetic nanoparticles for the detection of mimic SARS-CoV-2 in an AC magnetic field. Mimic SARS-CoV-2 containing spike glycoproteins as well as polystyrene beads were applied. The experimental outcomes demonstrated that the proposed approach allowed for the fast diagnosis of mimic SARS-CoV-2. Another advantage of this study was the low detection limit (0.084 nM). The suggested method had excellent potential for the design of a low-cost and point-of-care device. Also, another major advantage of these biosensors based on magnetic nanoparticles compared to others, is the possibility of the acceleration of the antigen–antibody reaction kinetics through the manipulation of the functionalized particles via external magnetic field gradients.

6. The role of TiO₂ nanoparticles during the COVID-19 crisis

The photocatalytic activity of self-disinfecting surfaces is a useful tool in times of the COVID-19 crisis. Titanium dioxide, TiO₂, is another metal oxide with great features and uses that shows great antibacterial, antiviral and photocatalytic performance, and can be effective in fighting COVID-19. In this regard, in a study, the photocatalytic performance of nano-TiO₂ was explored for the deactivation of coronavirus through UV irradiation for application in grocery stores as well as hospitals. Nano-TiO₂ particles were deposited on glass coverslips and the results showed good virucidal efficacy. This study confirmed the effectiveness of TiO₂-coated surfaces for the disinfection of coronaviruses.

In another study, a sensitive and cheap electrochemical bio-sensor based on cobalt-functionalized nano-TiO₂ was developed for the fast diagnosis of SARS-CoV-2 infection in nasal/saliva secretions by sensing the spike protein (RBD) on the virus surface. To achieve this aim, TiO₂ nanotubes were fabricated by an electrochemical anodization method. Then, by the wetting process, functionalization of them was performed. The direct detection of SARS-CoV-2 in patient samples can be observed in Fig. 11. The prepared bio-sensor successfully detected SARS-CoV-2 protein in low amounts and showed a linear response for a short time of approximately 30 s.

Nano-TiO₂, with many advantages like a high surface area and photocatalytic activity, is a good metal oxide for the preparation of antiviral photocatalysts. Zhong and co-workers examined the influence of TiO₂ nanoparticles on pathogens such as coronavirus in 0.4 mW cm⁻² irradiation at a wavelength of 375 nm (low irradiation similar to the natural light source is an advantage). To achieve this aim, nano TiO₂ particles were prepared via a hydrothermal process. Then, an illumination device using a TiO₂ photocatalyst, LED chips, a current source and a cooling system was fabricated for treatment of the virus. The outcomes showed that the prepared photo-activated TiO₂ could proficiently inactivate human viral pathogens, such as SARS-CoV-2. ROS, especially hydroxyl radicals (·OH), were responsible for inactivating the pathogens. This prepared photocatalyst showed potential application in medical equipment and air filters, as well as surface coatings.

7. The role of other nanoparticles during the COVID-19 crisis

Since the outbreak of COVID-19, countless cases of alcohol poisoning have been reported in developing countries, in some cases causing death. After ingestion, methanol is absorbed through the gastrointestinal tract and metabolized in the liver to form toxic aldehydes and formic acid (Fig. 12a). So, a
Fig. 12  (a) After consumption of laced beverages, methanol is metabolized to toxic formaldehyde by alcohol dehydrogenase (ADH) and subsequently to formic acid in the liver. Methanol and ethanol diffuse from the blood to the breath in the alveoli. (b) Fully integrated and handheld methanol detector to analyze exhaled breath sampled in bags (e.g. Tedlar). Results are communicated by WiFi to a smartphone. (c) Experimental protocol: volunteers consumed a standardized meal 3 h before the onset of measurements (gray shaded) and an individually calculated amount of ethanol within 1 h afterward (gray shaded). Breath was sampled (red diamonds) every hour and ethanol concentration was measured by a commercial breathalyzer (Drager) and subsequently spiked with 10–1000 ppm methanol. Every methanol-spiked breath sample was then measured with the handheld detector and the proton-transfer-reaction time-of-flight mass spectrometer for characterization and validation. This figure has been reproduced from ref. 52 with permission from the American Chemical Society, copyright 2020.

Fig. 13  (a) Sequential process for fabricating dual-mode SiO$_2$@Au@QD fluorescent labels, (b) schematic of a dual-mode LFIA biosensor, (c) preparation of the S protein-conjugated SiO$_2$@Au@QD labels (QD: quantum dots). This figure has been reproduced from ref. 53 with permission from the American Chemical Society, copyright 2020.
research team built a low-cost, portable detector as a quick tool for detecting methanol poisoning. The system consists of a Pd-doped SnO$_2$-based gas sensor with a separation column that connects wirelessly to a smartphone (Fig. 12b). The performance of this system was evaluated. 20 people volunteered and the detection performance was confirmed by examining their breath after drinking alcohol. By agreeing with the mass spectrometry results, the detector was able to successfully predict the concentration of methanol.$^{55}$

A research team reported a sensitive, rapid and accurate technique to simultaneously detect SARS-CoV-2 antibodies (IgM/IgG) employing a lateral flow immunoassay bio-sensor based on a SiO$_2$@Au@quantum dot-conjugated spike protein.$^{53}$ This assay, which was 100 times better than the Au-based lateral flow immunoassay, was completed in 15 minutes and needed 1 $\mu$L of serum sample. As shown in Fig. 13a, this assay was formed on the basis of a layer-by-layer assembly method. First, SiO$_2$ nanospheres (200 nm) were prepared, and then, a positively charged polymer [poly(ethyleneimine)] was placed on its surface. Then, negatively charged nano-Au (4 nm) was formed on them for producing a strong colorimetric signal. After that, a second layer of the same polymer and finally, carboxylated quantum dots were created for providing a good fluorescence signal. The spike protein of SARS-CoV-2 was conjugated (by covalent coupling) to the SiO$_2$@Au@quantum dots and anti-human IgM/IgG were deposited on test lines of the strip to obtain a sensitive diagnosis of COVID-19 (Fig. 13b). The outcomes verified high sensitivity as well as specificity (100%) to detect infection.

In a similar study, an ultra-sensitive and fast bio-sensor based on a SiO$_2$@Au core/shell was proposed for the detection of anti-SARS-CoV-2 IgM/IgG. SiO$_2$@Ag was introduced as a stable signal reporter in the lateral flow immunoassay system. 68 clinical serum samples (49 negative and 19 positive) were evaluated and the outcomes were 100% accuracy and specificity.$^{54}$ In order to prepare a face mask during the COVID-19 epidemic, a research team used SiO$_2$ to develop a flexible nanoporous membrane to prepare a N95 mask with specific sizes, densities and thicknesses. It also helped with self-masking of more than 85 liters per minute was possible, which made the mask look like a real one.$^{55}$

8. Conclusions

Due to the devastating effects that the COVID-19 pandemic has on public health, the economy and the environment, many efforts are being made to control this crisis, and researchers around the world are seeking materials and methods in this regard. Metals and metal oxides nanoparticles like Ag, Au, Cu, Cu$_2$O, Fe$_2$O$_3$, TiO$_2$, and others have been reported to play an important role in the diagnosis and control of the coronavirus. Diagnostic sensors that can detect the virus in a matter of minutes and the preparation of antibacterial and antiviral masks, coatings, and other materials are among the many applications of metal and metal oxide nanoparticles in order to fight COVID-19 and preserve the world.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Acknowledgements

We are immensely grateful for the financial support from the Research Affairs Division of the Isfahan University of Technology (IUT), Isfahan. I. R. Iran, and the Iran Nanotechnology Initiative Council (INIC) Tehran. I. R. Iran. We would also like to show our gratitude to the National Elite Foundation (NEF), Tehran, I. R. Iran, and the Center of Excellence in Sensors and Green Chemistry, IUT.

References

6. Z. Shang, S. Y. Chan, W. J. Liu, P. Li and W. Huang, ACS Infect. Dis., 2020, 2, DOI: 10.1021/acsinfecdis.0c00646.