Applied Science & Technology Annals Vol.1, No.1 (2020); 155-164 ISSN: 2717-5014 (Print). Available online at www.recast.tu.edu.np DOI: https://doi.org/10.3126/asta.v1i1.30295



Review Article

Nanomaterials for diagnostic, treatment and prevention of COVID-19

Subash Adhikari^{1*}, Usha Adhikari², Akash Mishra³ Bhim Sagar Guragain^{4,5}

¹ Unnati: Data Mapping and Mining Nepal, Kathmandu, Nepal; ORCID ID: 0000-0002-5838-0179

² Central Department of Biotechnology, Tribhuvwan University, Kathmandu, Nepal, ORCID ID: 0000-0002-1349-4287

³ Opioid Substitution Therapy, Narayani Hospital, Birgunj, Nepal, ORCID ID 0000-0003-2023-3269

⁴ Asean Institute for Health Development (AIHD), Mahidol University, Salaya, Thailand

E-mail: bhimsagarguragain@gmail.com, ORCID ID: 0000-0002-1510-1360

⁵ Public Health Office, Government of Nepal, Makawanpur, Nepal

Received: May 26, 2020; Accepted: June 14, 2020; Published: June 25, 2020

Abstract: The global outbreak of coronavirus disease (COVID-19) has set an alarming message for the research and discovery of new and advance technology. This is possible by either combining the convectional technology with modern discoveries or initiating new avenues of research using nanotechnology. The vast library of nanomaterials and its integration into modern technology can offer various possibilities for discovery of nanomedicines, nano-biosensors, nanocompounds for controlling the sever acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and other similar virus outbreaks. Here we review the ongoing approaches utilized in detection, treatment and prevention of SARS-CoV-2 and describe their advantages and drawbacks. Additionally, we provide the new and innovative technology that are currently being researched or commercialized with the aid of nanomaterials and nanotechnology for disease identification, treatment and control. We further suggest new research area based on natural product research that can provide new opportunities for jobs and economic movements during the post-COVID-19 pandemic.

Keywords: COVID-19; SARS-CoV-2; nanomaterials; nanotechnology

सारांश: विश्वमा फैलिरहेको कोभिड-१९ माहामारिले नौलो प्रविधिको खोज र अनुसन्धानलाई अगाडी बढाउनु पर्छ भन्ने सन्देस दिएको छ । यसलाई सफल बनाउन पुरानो प्रविधिलाई नयाँ प्रविधी सङ्ग गाँस्ने वा सुक्ष्म बिज्ञानमा आधारित नौलो प्रविधिलाई प्रोत्साहान दिन जरुरी छ । सुक्ष्म बिज्ञानको खोजबाट अहिले सम्म धेरै बस्तु र प्रविधिहरु पत्ता लागेका छन । यिनै बस्तु र प्रविधिको आधारमा सुक्ष्म औषधी सुक्ष्म बस्तुको मिश्रणबाट बनेको रोग पत्ता लगाउने साधन सुक्ष्म पदार्थहरु बनाउन सकिन्छ जुन अहिलेको कोरोना भाईरस र अरु यस्तै रोग नियन्त्रण गर्नकोलागी उपायोगी हुन सक्छ । यस लेखमा हामिले कोरोना जाँच उपचार र नियन्त्रणको लागी अहिलेसम्म चालिएका कदमको फाईदा र बेफाईदाका साथै अहिले सुक्ष्म बिज्ञान र प्रविधिको अधारमा कोरोना रोग सङ्ग लड्न भईरहेका अध्ययन अनुसन्धान र प्रयोग भईरहेका प्रविधिको बिबरण पेस गरेका छौं । हामिले प्राकृतिक जडिबुटिको प्रयोग र उपयोगिताको माध्यमबाट कोरोना रोग नियन्त्रणमा पुग्न सक्ने फाईदा र यसको अनुसन्धानबाट हुने आर्थीक फाईदाको बारेमा पनि आफ्नो अबधारणा प्रस्तुत गरेका छौं ।

^{*} Corresponding author, E-mail: subashadhikari@hotmail.com; Tel.: + 977-9866121207 © RECAST/TU

1. Introduction

Due to the continuous increase in number of coronavirus disease (COVID-19) cases ever since its origin in Wuhan, China on December 2019 World Health Organization (WHO), has characterized COVID-19 as pandemic on March 2020 (World Health Organization [WHO], 2020; Li, 2020). The primary reason that induced the global rise in the COVID-19 cases were the sudden origin of sever acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and the lack of preparedness and technology to mitigate the spread of the virus. These technological limitations were observed on the virus identification, testing and the prevention. Similarly, the early test for the COVID-19 was mostly based on clinical characteristics, chest imaging and ruling out of common bacterial and viral pathogens that caused pneumonia (Huang, 2020; Yang, 2020). Only at the later stage, the virus was confirmed as SARS-CoV-2 using real-time reverse transcription polymerase chain reaction (RT-PCR) (Huang, 2020; Wenjie, 2020). However, the RT-PCR based detection can take around 3-8 hours (Bustin, 2009, Jewerth, 2020) and more importantly, the common availability of RT-PCR reagent kits in pandemic, infrastructure for installing and measuring large quantity of samples by RT-PCR and the false positive result in asymptomatic patient after recovery by RT-PCR (Udugama, 2020) needs to be considered seriously as the reproductive number of SARS-CoV-2 is estimated to be around 3.28 in average (Liu, 2020). This has thus induced for the development of rapid (~ 30 min.) and easy to use testing kits outside of laboratory settings that are based on detection of human antibodies, blood serum, stool or nasal swabs generated in response to COVID-19 infection (Udugama, 2020; Advice. WHO, 2020). However, many of these test kits works on specific test patterns and infection stages of the COVID-19 patient. Hence, WHO has recommended for the development of nucleic acid and protein based testing and detection kits that can be used at the point of care for COVID-19 diagnostics (Report. WHO, 2020). Similarly, for the treatment of COVID-19 patients, 29 different therapeutic drugs have been tested worldwide until April, 2020 (Koch, 2020). Out of these. few of the drugs like Remdersivir, Hydroxychloroquine, Chloroquine and Favipiravir which have already been tested for antiviral and antimalarial cases have shown promising results (Koch, 2020; Milken, 2020; CDC, 2019; Zhang, 2020; Jiaxing, 2020, Wang, 2020). However, the use of drugs also depends on the country of use and upon the pre-existing medical conditions of COVID-19 patients (Y. Wang, 2020; Thomas, 2020). Together with detection and treatment, preventive measure against COVID-19 infection has been initiated by

pharmaceuticals companies, academic institutions and organizations worldwide (Editorial, 2020; Public. WHO, 2020). Some of the vaccine developers like CanSino Biologics, National Institute of Health and Moderna have already started second stage clinical trial against COVID-19 (Editorial, 2020; NIH, 2020; Thanh, 2020; N. NIH, 2020, TNYT, 2020).

More important, the material available and engineered for COVID-19 pandemic at present has been tested with conventional materials and technology. While the outcomes with conventional technology have not been satisfactory, the use of widely researched modern materials like quantum dots. low dimensional semiconductors and compounds can be possible alternatives at this peak stage of pandemic. The role of nanomaterials is also important in SARS-CoV-2 due to the fact that the viruses itself are core-shell nanostructure confined within the size of 60-140 nm (Huang, 2020; Hu, 2020; Chan, 2020; Sivasankarapillai, 2020). This thus allows the nanomaterials to bind, encapsulate and passivate the virus (Lauster, 2020; Curk, 2017; Martinez, 2011), allowing to study, engineer and design measures for detection, treatment and prevention of COVID-19 (Chan. 2020). Furthermore, the large surface to volume ratio, variable bandgap, highly luminescent and easy to integrate nano-dimensional materials offer additional benefits as compared to bulk (Khan, 2019; Nanotechnology, 2006) in fabricating detection kits, nano-medicines for coronavirus and virus specific vaccine for SARS-CoV-2 and other emerging viruses. This review will thus mainly focus on nanomaterials based technology that are currently used or being researched to passivate the pandemic as well as to prevent the COVID-19 and other possible virus outbreaks.

2. Nanomaterials application in COVID-19 pandemic

SARS-CoV-2 are spherical shaped and nanodimensional positive-stranded ribonucleic acid (RNA) viruses which are encapsulated inside a helical Nucleocapsid protein shell and enveloped by lipid membrane and three structural protein (membrane glycoprotein, nucleocapside protein and envelop protein) with spike protein on the outer layer (Li, 2016). This core-shell nano-structure and the crown-like spike protein outside of the virus surface in SARS-CoV-2 thus provides opportunities in engineering drugs, protective coatings and vaccines against COVID-19. This is because the lipid membrane can be easily destroyed by even soap molecules (Jabri, 2020) while the envelop and capsid can be compromised by physical treatments like UV

exposure, heating and desiccation as well as by chemical sanitization using acids, oxidants, alcohols or surfactants (Huang, 2020, Wigginton, 2020; Kampf, 2020). Similarly, neutralizing the spike protein outside the virus surface by antibodies and vaccines (Nanogrifi, 2020) and the idea of multivalent incorporating binders with the pathogens, enveloping the host cell and using the ligand scaffolds to prevent the pathogens adhesion (Chan, 2020; Lauster, 2020) are additional nano/bioengineering research fields that can be considered

for prevention of COVID-19 and other potential virus outbreaks as illustrated schematically in **Figure 1**. Additionally, the recent development of nanomaterials from Chinese scientists that can absorb and deactivate the virus with 96.5-99.9% efficiency can be another important discovery for the treatment and prevention of SARS-CoV-2 (Global, 2020). These nano-technological developments and their successful implication in virus identification, COVID-19 cure and preventive measures will be discussed in brief in the following sections

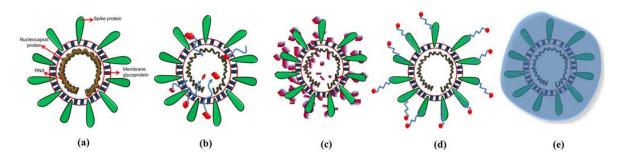


Figure 1. Nanomaterial for controlling SARS-CoV-2. (a) Schematic showing the SARS-CoV-2 and its constituents. (b) Insertion of nanoparticles into the SARS-CoV-2 for neutralizing the virus. (c) Nanomaterials based passivation of SARS-CoV-2 to control the growth and multiplication of virus. (d) Nanochemical functionalization of spike protein in SARS-CoV-2. The spike protein are known to be the main component of virus which allows to virus to interact with the human cells. (e) Encapsulation of SARS-CoV-2 with nanomaterial or nanocompounds which passivates the virus for growth as well as preventing the spike protein to functionalize with human cells.

2.1. Nanomaterials for diagnostic of COVID-19

During the early period of COVID-19 pandemic, lack of information about the virus led to many primary and secondary viral infectants (Udugama, 2020; Nanogrifi, 2020). At this primary infection stage, a combination of computed tomography imaging, whole genome sequencing and electron microscopy were used to screen and identify SARS-CoV-2 (Udugama, 2020; Report, WHO, 2020). However at the later stage, a number of RT-PCR based testing were used to detect SARS-CoV-2 genetically (Report, WHO, 2020). The limitation of mass and rapid testing with RT-PCR as well as the increasing number of COVID-19 cases globally led to the research and production of various diagnostic techniques based on nucleic acid, protein detected from clinical samples like serum, throat, nasal and nasopharyngeal swabs, blood and stool (Udugama, 2020). More importantly, many of these diagnostic modules are based on nanotechnology and nano-bio engineering techniques.

The major requirement of the testing kit in this global pandemic is minimum time required for measurement, availability of point of care testing and the easily accessible patients sample for testing purpose. This can be achieved with rapid diagnostic test (RDT) that gives result within 30 minutes using either the blood, stool or nasal swab at the place of patient convenience. The currently used RDTs works on a principal where the target antigen from

respiratory tract will bind to specific antibodies generating a visual signal (Advice, WHO, 2020) or through direct measurement of the antibiodies in the blood sample of the COVID-19 infectant (Liu, 2020; Pan, 2020). However these test can only be used to identify at some specific stage of infection as well as these antigen based test can detect various other respiratory disease giving false positive results thus limiting the test sensitivity to vary from 38 to 80% (Advice, WHO, 2020; Zhao, 2020). Hence a more accurate test based on the direct detection of RNA or protein in SARS-CoV-2 is required.

One of such rapid diagnostic kits works on the principal of direct isolation of RNA from patient sample. Gold and iron oxide nanoparticles are promising materials which have been extensively investigated so far (R&M, 2020; HMP, 2020; Candanosa, 2020). The World Nano Foundation (WNF) has identified a rapid diagnostic kits based on colloidal gold nanoparticles. As the second generation testing kits that has been introduced to improve the testing accuracy, reliability and rapid diagnostic of SARS-CoV-2, the antibody assay kit by WNF uses colloidal gold nanoparticles to detect the presence of immunoglobulin G and M (IgG and IgM) antibodies present in test serum (TWNF, 2020). Since metal nanoparticle surfaces can produce surface plasmon resonance (Jain, 2007) and various previous studies have gold used

nanoparticles based plasmons to detect the biological interaction of deoxyribonucleic acid (DNA) and RNA (TWNF, 2020; Nguyen, 2015), it is believed that the colloidal gold based detection kits can increase the sensitivity of SARS-CoV-2 detection by more than 1000 fold. Similarly, other development in the RDT using gold nanoparticles is based on plasmonic photothermal effect and localized surface plasmon resonance sensing (Qiu, 2020). As an alternative to PCR, the team of Jing Wang at Massachusetts Institute of Technology (MIT) using thermoplasmonic heat to produce localized surface plasmon resonance were able to make a DNA probe that can recognize specific RNA sequence of COVID-19 and attach them to gold nanoparticles for detection. Their device can also discriminate between two similar gene sequences thus providing accurate diagnostic of SARS-CoV-2 among many other similar virus sequences.

Besides plasmonic nanomaterials, researchers have also developed magnetic nanoparticles based rapid detection kits using iron oxide nanoparticles. The magnetic nanoparticles can bind with the biomolecules like RNA and DNA upon application of magnetic field (Chen, 2020) thus allowing rapid and reliable molecular diagnostic of SARS-CoV-2. One of such developments is Agappe Chitra Magna produced by Sree Chitra Tirungal Institute for Medical Sciences and Technology (SCTIMST), India which captures the RNA from CODID-19 patient using magnetic nanoparticles of iron oxide (HMP, 2020). These magnetic nanoparticle beads bind to the viral RNA and upon exposure of the magnetic field, it gives a highly purified and concentrated RNA. Also the advantage of large surface area in nanoparticles allows adequate quantity of RNA sample needed for analysis, enhanching the chances of identifying positive cases accurately. Similarly, Norwegian University of Science and Technology (NTNU) have developed tiny iron oxide nanoparticles coated with silica that can extract RNA from a solution containing the clinical sample. The solution cracks the virus releasing biological molecules including RNA. The silica covered magnetic nanoparticles attaches the RNA more strongly than isolated nanoparticles which are later pulled out of solution using magnetic excitation. This technique can measure 150,000 cases per week which is a major achievement for convenient and mass testing.

In addition to nanoparticle based detection kits, there are emerging research based on 2-dimensional (2D) materials like graphene, a high conductivity carbon based materials (Rodgers, 2020; Adhikari, 2016). A Korea research team at Basic Science Institute, have developed graphene based field-effect transistor that can detect SARS-CoV-2 in less than one

minute. The antibodies against SARS-CoV-2 attached on the graphene based biosensor device can detect the change in electrical current once the purified or cultured SARS-CoV-2 virus are added to bind with the antibody. This technique could enable health workers to rapidly diagnose without complicated and risky sample preparation steps. However the environmental stability of 2D materials, the large signal to noise ratio in electrical devices and the cost of the biosensor are still some critical issues that have to be reviewed extensively before its commercialization.

Besides these, there are also some developments in self-diagnostic test using isothermal amplification that usages inorganic quantum dots (Udugama, 2020; Kim, 2016; Everywell). These amplification techniques which enable battery-operated excitation and smartphone camera for capturing the emission can be next generation of SARS-CoV-2 detection research to control the pandemic. Similarly there are other developments like isothermal amplification serological tests, lateral flow tests. assay, electrochemical sensors, paper based systems and surface enhanced Raman scattering techniques developed to bring convenient and reliable diagnostic to control the global pandemic (Udugama, 2020).

2.2. Nanomaterials for treatment of COVID-19

Until the end of May, 2020, none of the countries around the globe have been successful in establishing a fixed medicinal treatment for COVID-19 pandemic. Additionally, the patient's physical health condition is one of the prime factors that determine the treatment procedure (Off, WHO, 2020; Newton, 2020). According to the WHO's "Solidarity" clinical trial for COVID-19 treatments plan, the treatment options under study are Remdesivir, Lopinavir / Ritonavir, Lopinavir / Ritonavir with Interferon beta-1 and Chloroquine or Hydroxychloroquine which were previously tested for Ebola, human immunio virus (HIV), sclerosis and malaria treatment (Solidarity, WHO, 2020). Among these therapeutics, multicenter clinical trials based cell culture study suggest that chloroquine displays potential therapeutic efficacy against COVID-19 (Gao, 2020) with minor side effects as reported by Chinese health officials (Jiaxing, 2020). Moreover, Chloroquine has been used in the field of nanomedicine for investigating the nanoparticle uptake in cells thus providing information about the nanoparticle interactions with the cells in presence of Chloroquine (Hu, 2020). This nanomedicines study can also provide valuable information about the viral replication mechanism at early stage of infection. More SARS-CoV-2 falls importantly, within the nanomaterial size regime of 60-140 nm (Huang, 2020), showing various possibilities for treatment and modification using various synthetic nanomaterials.

Theranostics is one of such newly emerged research area which involves detecting and neutralizing viruses using nanodrugs and nanomedicines with focus on diagnostics and therapy (Jeelani. 2014). This combination of diagnostic and therapy has great potential in controlling the COVID-19 pandemic as synthetic nanomaterials can be used to block the virus replication in the host, bind the pathogens and host cell, envelop the entire virus thus preventing all possible interactions and using ligand scaffolds for surface modification and functionalization to prevent the pathogen interception (Figure 1) (Chan, 2020, Lauster, 2020; Martinex, 2011). Additional advantage of nanomedicine is its ability to move through the human body in bloodstream without affecting other functions and more importantly, these nanoparticle in the nanomedicines can remain in the body to prevent further viral infection (Nanografi, 2020).

Researchers in Protein Production UK and The Rosalind Franklin Institute, United Kingdom, have isolated nanobodies which can bind with the spike protein of SARS-CoV-2. These high stability nanobodies are the nanostructured antibodies extracted in Camelids which can be used to create highly specific blocker against the virus. Stabilizing the spikes can also help in better imaging at the atomic level providing detail knowledge about the virus for future diagnostic, treatment and prevention research (Owens, 2020). Similarly, Elastrin Therapeutics have developed world's first humanized antibody against Inflammatory Storm, a condition that specifically damages exposed elastin fiber in the lungs (Collins, 2020). Since the critical stage of COVID-19 can damage the lung or generate lung disease, the treatment process using drug loaded nanoparticle can repair the elastic fiber in the lungs providing easy access for air sacs and blood vessels to deliver oxygen and blood. Similarly, the company have also developed metal complexes agent to prevent the reverse hardening of the arteries. These developments can be highly important to save a critical patient. Another important experimental therapies recommended by WHO is using conventional antibodies and nanobodies to neutralize the pathogens. For this a Canadian biotech company, Novobind, are developing next generation antidotes known as nanobodies. These nanobodies targeted to SARS-CoV-2 virus are predicted to identify and stick to the pathogens and neutralize its functions by enveloping the virus. Hence they can be used for creating a diagnostic tool or therapeutics against the SARS-CoV-2 virus. This lack of effective medicine has also provoked researchers to design drugs using computer simulations.

Among many potential drugs and therapeutics that are expected to work but have not been experimentally tested, can be modeled using

supercomputers. This can narrow down the potential drug list and narrow down the process of experimentally testing each drug on patients. One of such pioneering work is being carried out in University of Illinois, USA, where peptide inhibitors that prevents the virus infection in the human cell by blocking the spike protein of the SARS-CoV-2 has been simulated (Han, 2020). The research team has identified 15 amino acids that can directly interact with the viral spike protein. Among the various peptides developed, one had showed high stability and great potential for COVID-19 treatment, which is now being tested for clinical trials. Similarly, other development in COVID-19 treatments that are extensively researched in experimental laboratories are designing of nanoparticles that are similar in size to SARS-CoV-2 and can potentially disrupt the structure of virus thus halting the ability of the virus to survive and reproduce in human body. However, reducing the risk of nanoparticles in human body is also equally important for the long term human health. Hence considering the benefit of nanoparticles against the virus as well as its long term side effect, Thomas Webster in Northeastern University, Chemical Engineering Department have proposed Iron oxide nanoparticles, which are magnetic materials and are also important in human body especially for the synthesis of haemoglobin in red blood cells (Candanosa, 2020). More importantly, this magnetic material can be guided for targeted drug delivery in human organs using external magnetic field and the left over iron oxide nanoparticles can be used as an nutrient supplement for anemic cases during viral infection. Additionally, the idea of using photoactive nanomaterials to encapsulate the nanomedicine against SARS-CoV-2 and using electromagnetic radiation to rupture them at a targeted sites can be another nondestructive treatment procedure that can kill the target virus as well as destroy the nanomaterials (Nanografi, 2020; Shrestha, 2009).

2.3. Nanomaterials for prevention of COVID-19

The long term existence of the SARS-CoV-2 in the global human community and its consequences in human health are one of the most challenging issue faced by the world leaders and health professionals at present. Since viruses are part of the ecology and environment, they cannot be eradicated completely for few centuries. Hence the only solution at present is to live with them by developing the human immunity or by developing vaccines to prevent (suppress) the virus infection (transmission). WHO have activated an research and development (R&D) blueprint and a public statement for collaboration against COVID-19 that aims to using accelerate diagnostic and therapeutic along with vaccine research in order to fight against COVID-19 and similar other potential virus outbreaks (Public, WHO, 2020; R&D, WHO, 2020). WHO have also taken major responsibility in coordinating group of experts with diverse backgrounds working towards the development of vaccine for COVID-19 and supporting information channels between countries. As of 22 May, 2020, 10 candidates vaccine are in clinical evaluation while 114 candidate vaccines are in preclinical evaluation (Draft, WHO, 2020). CanSino **Biological** Among these Incorporation/Beijing Institute of Biotechnology, Moderna/National Institute of Allergy and Infectious Diseases (NIAID) have moved into phase 2 of the clinical evaluation. More importantly, Modera's Coronavirus vaccine containing a genetic material from the virus called messanger RNA (mRNA) has shown a safe and strong immune response in 8 healthy volunteers (TNYT, 2020). The vaccine test among larger group of population will determine the possibility for the final vaccine approval for global use and this might take at least 10-15 months. Hence until the commercial vaccine are available, we need to rely on the social preventive measures, treatment procedures and more importantly the past research and knowledge gained in similar virus outbreaks like middle east respiratory syndrome coronavirus (MERS-CoV) and SARS-CoV (Harapan, 2020).

Moreover, the Moderna/NIAID based lipid nanoparticle encapsulated mRNA vaccine that is previously studied for SARS-CoV and MERS has thus been used to stabilize the spike protein in (Safety, SARS-CoV-2 NIH). Another nanotechnology based vaccine is being developed by Novavax, an Indian biotechnology company which is currently moving into phase 1 of the clinical trial (Evaluation, NIH). The use of glycoprotein nanoparticles vaccine with or without Matrix-M immunological agent to improve the long term vaccine response are being studied currently as a SARS-CoV-2 vaccine candidate (Matrix-M, 2020). Similarly, preclinical trial of nanoparticle based on spike protein and other epitope developed by Saint Petersburg Research Institute of Vaccine and Serums in Russia (Draft, WHO, 2020; Russkiv, 2020) and self-assembling recently initiated protein nanoparticle research against protein spikes in SARS-CoV-2 developed by Ufovax, USA are other nano-technological vaccine candidates that are expected to have long term and stable results against COVID-19. Moreover, the successful implication of nanomaterial and nano-biotechnology based vaccines can motivate researcher to explore the vast library of widely studied nanoparticles into disease research.

2.4. Additional preventive measures for COVID-19 based on nanomaterials

Apart from the mandatory and permanent measure of using vaccine for disease prevention, there are many physical and social preventive measures that can be considered against any ongoing global pandemic. Considering the case of COVID-19, which are airborne and can be transmitted through respiratory droplets, faeces and fomites, strict precaution have to be taken in controlling the virus transmission (Modes, WHO, 2020). In this section, we review some of the technology developed to prevent the virus transmission and the measures taken with the aid of technology to control the widespread transmission of the virus in different part of the world.

During the early infection stage in China, SARS-CoV-2 were found in air ducts implying the virus can be transmitted through air conditioning system (Lu, 2020) and even through the stool of the patient who have tested negative for COVID-19 (Yong, 2020). Hence precautions should be taken in household to community level until there is no clear research based evidence about COVID-19. Hence it is advised that high efficiency particulate air (HEPA) filters should be used especially in the isolation area and hospitals where COVID-19 cases are treated. This is because HEPA filters are known to be efficient air filter with filtration efficiency increasing for particle diameter both less than and greater than 300 nm (NIOSH, 2014). This filter size is well below the mean diameter of the SARS-COV-2 virus size (Huang, 2020), hence preventing the airborne transmission.

Similarly, treatment of water is equally important together with the air to keep the virus from community transmission sources. Moreover, the trap and zap technology developed by a team of researcher from Rice University have demonstrated the feasibility of multimedia treatment process of air filtration and wastewater disinfection using a nanotechnology approach (NEWT, #EEC-1449500). Using a few layer graphitic carbon nitride activated by light, they could selectively absorb virus and degrade their antibiotic resistance gene, thereby disabling bacteria and viruses including SARS-CoV-2. The stainless steel and plastic materials are also an active host of SARS-CoV-2, surviving for upto 72 hours after application while copper metal and cations have broad spectrum antiviral effect allowing the virus to survive only for ~ 4 hours (van, 2020). Moreover, replacing many of the widely used stainless steel with cost-effective copper transportation, industries and household purpose is not feasible at present. Instead, developing of technology that is cost effective and less vulnerable is rather preferred. Nano-dimensional titanium

dioxide (TiO_2) is one of such materials which are extensively used in photocatalysis, solar cell, targeted drug delivery and elecrochromic research as they are highly stable, non-toxic and cost effective (Niraula, 2014; Fujishima, 2000; S. Adhikari, 2015). The C-Bond Systems together with MACOMA, USA have thus developed a photocatalytic TiO₂ nanoparticle coating that can be used in public utilities and mass gathering areas (Macoma, 2020). This coating can be one of the most effective multidimensional approaches in reducing the spread of airborne toxins and microscopic allergens including COVID-19. However, this technology works on the principal of UV illumination of TiO₂ to induce the photocatalytic properties limiting its use in indoor region. For this, NanoSeptic, USA has created mineral nano-crystal that can produce a powerful oxidation reaction. More importantly, this nanocrystal can be activated by visible light, fluorescent, light emitting diodes or sunlight, the oxidation reaction allowing to occur continuously. This thus provides a convenient and cost effect solution in disinfecting any organic contaminants in remote locations.

Another important preventive measure in controlling the COVID-19 transmission is using efficient personal protective equipment (PPE) for general public and frontline health workers. Facial masks are one of the largely consumed product besides testing kits and reagents. The important consideration that should be taken into account when choosing the facial mask is protection from the airborne particles of size similar to SARS-CoV-2. The commonly available surgical masks made of nonwoven fabrics while N95 masks using a particle filter capable of blocking at least 95% of airborne particles larger than 2.5 microns (Smith, 2016) are needed in large quantities daily. To meet this growing demand at present, nanotechnology can play an important role. The less material consumption using nanomaterials and nanotechnology can also help provide cost effective and efficient protective measure during this global pandemic. One of such example of facial mask research using nanotechnology is led by Iranian government by initiating west Asia's largest N95 mask industry (Statnano, 2020). With the aid of electrospun nanofiber technology which provides large surface area for filtering and can also be functionalized with different chemically active groups to capture and neutralize the nanosized particles and infectants (Jalili, 2006), the Iranian government aims to produce 4 million masks per day for domestic use and foreign export. Similarly, consideration should be taken in preparing hazma suits and other PPE like protective suits, facial shields, gowns, gloves, boots and goggles. The fabrics used in the suits and gowns should provide effective barrier to air and water

contaminants especially at the junction areas. Similarly, for the long term use of the PPE for health care workers, considerations should be taken in the ventilations, head flexibility. dissipation and equipment for communications (Huang, 2020). All these can be possible with the aid of efficient and multifunctional low dimensional materials like quantum dots and 2D materials. The low material consumption, flexibility, availability of materials from metallic, magnetic, semiconducting to insulating and wide knowledge achieved the from the characterization to device integration research offered by nanomaterials allows wide prospective for industrialization and commercialization of protective materials against airborne, waterborne, inorganic environmental objects and other surfaces contamination.

3. Discussion

Various past pandemics and alarming infections against bacteria and viruses have taught the government, industries, and individuals around the globe to focus and invest on research and study of various natural and artificial phenomenon continuously. This will help us develop new priorities for research areas and development which eventually will help us prepare for many of these global pandemic yet to arise in the future. Similarly, the area of materials science research which offers wide possibilities beyond the limitation of conventional materials should be prioritized. Understanding the need of detection, treatment and prevention in any natural and environmental pandemic can be dealt with the global community of scientist and researchers coming together into a common platform of discussion and sharing of ideas and results. While developing research priorities for treatment and prevention, it is also necessary to consider a universal medicine and vaccine that not only works for the current infection but also for past and future outbreaks of similar genomes. Apart from medication and vaccination, the physical and social research to develop various preventive measures should also be equally considered. This combined research plan will help prepare every individual socially and psychologically in fighting for bacterial and viral pandemic and also ease the social human movements.

4. Conclusions

The global demand of smart and efficient technology has motivated the research and knowledge capacities of academic and industries. This has thus provoked the conventional science to shift towards technological with the aid of nano dimensional materials. More importantly, disease research and medicine are most important research areas that constantly needs innovative science and technology not only for the present but for the possible disease outbreaks in future. In such, nanomedicine, nanoparticles for targeted drug delivery, smart biosensor based on nanomaterial and technology and nanochemical, nanocompound and nanodevices for passivation and neutralization of infectants can provide next generation of diagnostic, treatment and prevention for disease outbreak. Moreover, the toxicity and long term side effects of many nanometerials are still not fully explored in human health. In such, natural product based medicines and technology having a vast library of products and long term knowledge about its use and side effect can be an alternative research area. The green chemistry synthesis approach in developing natural product based nano-biomaterials can thus substitute many of the toxic and hazardous synthetic nanomaterials, opening new, green and cost effective research area and industry.

Acknowledgments: We thank Yadav Prasad Joshi, Manmohan Memorial Institute of Health Sciences for his valuable suggestion and feedbacks in the manuscript.

Author Contributions: SA conceived and planned the review; SA reviewed the nanomaterial and nanotechnological developments in COVID-19; UA reviewed the biotechnological and virus related works; AM reviewed the treatment measures taken in COVID-19; BSG reviewed the health and preventive measures taken during COVID-19 pandemic. S.A. compiled the paper.

Conflicts of Interest: The authors declare no conflict of interest.

Ethical approval: Not required given the nature of the article.

Funder information: No funding.

References

- Adhikari S, Perello DJ, Biswas C, Ghosh A, Luan NV, Park J, et al. Determining the fermi level by absorption quenching of monolayer graphene by charge transfer doping. Nanoscale. 2016 8(44):18710-7. DOI: 10.1039/C6NR05635K
- Adhikari S, Song Y-Y, Wang Y-M, Niraula M, Cho K, Dhungel SK, et al. Electrochemical protonation/de-protonation of titania nanotubes decorated with silver phosphate crystals: An enhanced electrochromic color contrast. Optical Materials. 2015 40:112-7. DOI: 10.1016/j.optmat.2014.12.004
- Bustin SA, Benes V, Garson JA, Hellemans J, Huggett J, Kubista M, et al. The MIQE guidelines: minimum information for publication of quantitative real-time PCR experiments. Clinical Chemistry. 2009 55(4):611-22. DOI: 10.1373/clinchem.2008.112797
- Candanosa M. R. Here's how nanoparticles could help us get closer to a treatment for COVID-19. 2020. Available from:

https://news.northeastern.edu/2020/03/04/heres-hownanoparticles-could-help-us-get-closer-to-a-treatment-forcovid-19/

- Candanosa M. R.. Here's how nanoparticles could help us get closer to a treatment for COVID-19. 2020. Available from: https://news.northeastern.edu/2020/03/04/heres-hownanoparticles-could-help-us-get-closer-to-a-treatment-forcovid-19/
- Center for disease control and prevention (CDC). Coronavirus disease 2019. 2019. Available from: https://www.cdc.gov/coronavirus/2019ncov/hcp/therapeutic-options.html
- Chan WCW. Nano research for COVID-19. ACS Nano. 2020;14(4):3719-20. DOI: 10.1021/acsnano.0c02540
- Chen X, Miller A, Cao S, Gan Y, Zhang J, He Q, et al. Rapid escherichia coli trapping and retrieval from bodily fluids via a three-dimensional bead-stacked nanodevice. ACS Applied Materials & Interfaces. 2020 12(7):7888-96. DOI: 10.1021/acsami.9b19311
- Collins F. Restoring the elastic of life. 2020. Available from: https://www.elastrin-therapeutics.com/
- Curk T, Dobnikar J, Frenkel D. Optimal multivalent targeting of membranes with many distinct receptors. Proceedings of the National Academy of Sciences. 2017 114(28):7210-5. DOI: 10.1073/pnas.1704226114
- Editorial. The race against COVID-19. Nature Nanotechnology. 2020;15(4):239-40. DOI: 10.1038/s41565-020-0680-y
- Everywell. At home lab testing made easy. Available from: https://www.everlywell.com/
- Fujishima A, Rao TN, Tryk DA. Titanium dioxide photocatalysis. Journal of Photochemistry and Photobiology C: Photochemistry Reviews. 2000 1(1):1-21. DOI: 10.1016/S1389-5567(00)00002-2
- Gao J, Tian Z, Yang X. Breakthrough: chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies. BioScience Trends. 2020 14(1):72-3. DOI: 10.5582/bst.2020.01047
- Global Times, Twitter. 2020. Available from: https://twitter.com/globaltimesnews/status/12442447933932 17536
- Han Y, Král P. Computational design of ACE2-based peptide inhibitors of SARS-CoV-2. ACS Nano. 2020 14(4):5143-7. DOI: 10.1021/acsnano.0c02857
- Harapan H, Itoh N, Yufika A, Winardi W, Keam S, Te H, et al. Coronavirus disease 2019 (COVID-19): A literature review. Journal of Infection and Public Health. 2020 13(5):667-73. DOI: 10.1016/j.jiph.2020.03.019
- Health Medical Pharma (HMP). Cost-effective kit used for coronavirus tests launched. 2020. Available from: https://www.business-standard.com/article/pti-stories/costeffective-kit-used-for-coronavirus-tests-launched-120052101552_1.html https://twitter.com/globaltimesnews/status/12442447933932 17536
- Hu TY, Frieman M, Wolfram J. Insights from nanomedicine into chloroquine efficacy against COVID-19. Nature Nanotechnology. 2020 15(4):247-9. DOI: 10.1038/s41565-020-0674-9
- Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The Lancet. 2020 395(10223):497-506. DOI: 10.1016/S0140-6736(20)30183-5
- Huang H, Fan C, Li M, Nie H-L, Wang F-B, Wang H, et al. COVID-19: a call for physical scientists and engineers. ACS Nano. 2020;14(4):3747-54. DOI: 10.1021/acsnano.0c02618
- Jabri F. How washing hands with soap destroys the coronavirus. 2020. Available from: https://globalhandwashing.org/how-washing-hands-with-soap-destroys-the-coronavirus/
- Jain PK, Huang X, El-Sayed IH, El-Sayed MA. Review of some interesting surface plasmon resonance-enhanced properties

of noble metal nanoparticles and their applications to biosystems. Plasmonics. 2007 2(3):107-18. DOI: 10.1007/s11468-007-9031-1

- Jalili R, Morshed M, Ravandi SAH. Fundamental parameters affecting electrospinning of PAN nanofibers as uniaxially aligned fibers. Journal of Applied Polymer Science. 2006 101(6):4350-7. DOI: 10.1002/app.24290
- Jawerth N. How is the COVID-19 virus detected using real time RT-PCR?. 2020. Available from: https://www.iaea.org/newscenter/news/how-is-the-covid-19virus-detected-using-real-time-rt-pcr
- Jeelani S, Reddy RC, Maheswaran T, Asokan GS, Dany A, Anand B. Theranostics: A treasured tailor for tomorrow. Journal of Pharmacy & Bioallied Sciences. 2014 6(Suppl 1):S6-8. DOI: 10.4103/0975-7406.137249
- Jiaxing Z. Zhong N. Academician led the expert group that the treatment of new coronary pneumonia was therapeutic. 2020. Available from: http://news.sciencenet.cn/htmlnews/2020/2/435861.shtm
- Kampf G, Todt D, Pfaender S, Steinmann E. Persistence of coronaviruses on inanimate surfaces and their inactivation with biocidal agents. Journal of Hospital Infection. 2020 104(3):246-51. DOI: 10.1016/j.jhin.2020.01.022
- Khan I, Saeed K, Khan I. Nanoparticles: properties, applications and toxicities. Arabian Journal of Chemistry. 2019 12(7):908-31. DOI: 10.1016/j.arabjc.2017.05.011
- Kim J, Biondi MJ, Feld JJ, Chan WCW. Clinical validation of quantum dot barcode diagnostic technology. ACS Nano. 2016 10(4):4742-53. DOI: 10.1021/acsnano.6b01254
- Koch S. First up for COVID-19: nearly 30 clinical readouts before end of April. 2020. Available from: https://www.biocentury.com/article/304658
- Lauster D, Klenk S, Ludwig K, Nojoumi S, Behren S, Adam L, et al. Phage capsid nanoparticles with defined ligand arrangement block influenza virus entry. Nature Nanotechnology. 2020 15(5):373-9. DOI: 10.1038/s41565-020-0660-2
- Li F. Structure, function, and evolution of coronavirus spike proteins. Annual Review of Virology. 2016 3(1):237-61. DOI: 10.1146/annurev-virology-110615-042301
- Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus–infected pneumonia. New England Journal of Medicine. 2020 382(13):1199-207. DOI: 10.1056/NEJMoa2001316
- Liu Y, Gayle AA, Wilder-Smith A, Rocklöv J. The reproductive number of COVID-19 is higher compared to SARS coronavirus. Journal of Travel Medicine. 2020;27(2). DOI: 10.1093/jtm/taaa021
- Liu Y, Liu Y, Diao B, Ren F, Wang Y, Ding J, et al. Diagnostic Indexes of a rapid IgG/IgM combined antibody test for SARS-CoV-2. medRxiv. 2020:2020.03.26: 20044883. DOI: 10.1101/2020.03.26.20044883
- Lu J, Gu J, Li K, Xu C, Su W, Lai Z, et al. COVID-19 outbreak associated with air conditioning in restaurant, Guangzhou, China, 2020. Emerg Infect Dis. 2020. DOI: 10.3201/eid2607.200764.
- Macoma Environmental Technology. Intelligent multi-functional nano coating technology. 2020. Available from: https://www.macoma.us/
- Martinez-Veracoechea FJ, Frenkel D. Designing super selectivity in multivalent nano-particle binding. Proceedings of the National Academy of Sciences. 2011 108(27):10963-8. DOI: 10.1073/pnas.1105351108
- MATRIX-M TECHNOLOGY. 2020. Available from: https://novavax.com/page/10/matrix-m-adjuvant-technology
- Milken Institute. COVID-19 Treatment and vaccine tracker. 2020. Available from: https://docs.google.com/spreadsheets/d/16DbPhF9OD0MH HtCR12of6yUcfiRzP_-XGkynEbnipds/htmlview

- Nanografi. COVID-19 and nanotechnology. 2020. Available from: https://nanografi.com/blog/covid19-andnanotechnology/
- Nanotechnology and nanomaterials. In Studies in Interface Science. 2006-23 (pp 1-69). Elsevier. DOI: 10.1016/S1383-7303(06)80002-5
- Nanotechnology-Enabled Water Treatment (NEWT). Nanosystems engineering research center for NEWT. #EEC-1449500. Available from: http://www.newtcenter.org/
- National Institute of Health (NIH). 2020. Available from: https://clinicaltrials.gov/ct2/results?cond=COVID-19
- Newton PN, Bond KC. COVID-19 and risks to the supply and quality of tests, drugs, and vaccines. The Lancet Global health. 2020 8(6):e754-e5. DOI: 10.1016/S2214-109X(20)30136-4
- Nguyen HH, Park J, Kang S, Kim M. Surface plasmon resonance: A versatile technique for biosensor applications. Sensors. 2015 15(5):10481-10510. DOI: 10.3390/s150510481
- NIH. Evaluation of the safety and immunogenicity of a SARS-CoV-2 rS (COVID-19) nanoparticle vaccine with/without matrix-M adjuvant. Identifier: NCT04368988. 2020. Available from: https://clinicaltrials.gov/ct2/show/NCT04368988?term=vacc ine&recrs=a&cond=covid-19&draw=2&rank=10
- NIH. NIH clinical trial of investigational vaccine for COVID-19 begins. 2020. Available from: https://www.nih.gov/news-events/news-releases/nih-clinical-trial-investigational-vaccine-covid-19-begins
- NIH. Safety and immunogenicity study of 2019-nCoV vaccine (mRNA-1273) for prophylaxis of SARS-CoV-2 infection (COVID-19). Identifier: NCT04283461. 2020. Available from: https://clinicaltrials.gov/ct2/show/NCT04283461
- Niraula M, Adhikari S, Lee DY, Kim E-K, Yoon SJ, Dhungel SK, et al. Titania nanotube-silver phosphate hybrid heterostructure for improved visible light induced photocatalysis. Chemical Physics Letters. 2014 593:193-7. DOI: 10.1016/j.cplett.2014.01.010
- Owens R. Protein Production UK. 2020. Available from: https://www.rfi.ac.uk/projects/protein-production-uk/
- Pan Y, Li X, Yang G, Fan J, Tang Y, Zhao J, et al. Serological immunochromatographic approach in diagnosis with SARS-CoV-2 infected COVID-19 patients. medRxiv. 2020:2020.03.13:20035428. DOI: 10.1101/2020.03.13.20035428
- Qiu G, Gai Z, Tao Y, Schmitt J, Kullak-Ublick GA, Wang J. Dual-functional plasmonic photothermal biosensors for highly accurate severe acute respiratory syndrome coronavirus 2 detection. ACS Nano. 2020. DOI: 10.1021/acsnano.0c02439
- Research and Markets (R&M). Nanotechnology and nanomaterials solutions for covid-19: diagnostic testing, antiviral and antimicrobial coatings and surfaces, air-borne filtration, facemasks, ppe, drug delivery and therapeutics. ID: 5023699. 2020. Available from: https://www.researchandmarkets.com/reports/5023699/nanotec hnology-and-nanomaterials-solutions-

for?utm_source=dynamic&utm_medium=GNOM&utm_code= mv5gfn&utm_campaign=1387098+-

+Nanotechnology+and+Nanomaterials+Solutions+for+COVID

19%3a+Diagnostic+Testing%2c+Antiviral+and+Antimicrob ial+Coatings+and+Surfaces%2c+Air-

Borne+Filtration%2c+Facemasks%2c+PPE%2c+Drug+Deli very+and+Therapeutics&utm_exec=jamu273gnomd

- Rodgers P. Nanoscience and technology. Nature Publishing Group. 2020:368. DOI: 10.1142/7439
- Russkiy MIR Foundation. Russian scientists to help develop Covid-19 antigen standard. 2020. Available from: https://russkiymir.ru/en/news/271406/

Shrestha NK, Macak JM, Schmidt-Stein F, Hahn R, Mierke CT,

Fabry B, et al. Magnetically guided titania nanotubes for site-selective photocatalysis and drug release. Angewandte Chemie International Edition. 2009 48(5):969-72. DOI: 10.1002/anie.200804429

- Sivasankarapillai VS, Pillai AM, Rahdar A, Sobha AP, Das SS, Mitropoulos AC, Mokarrar MH, Kyzas GZ. On facing the SARS-CoV-2 (COVID-19) with combination of nanomaterials and medicine: possible strategies and first challenges. Nanomaterials. 2020 10(5):852. DOI: 10.3390/nano10050852
- Smith JD, MacDougall CC, Johnstone J, Copes RA, Schwartz B, Garber GE. Effectiveness of N95 respirators versus surgical masks in protecting health care workers from acute respiratory infection: a systematic review and meta-analysis. Canadian Medical Association Journal. 2016 188(8):567-74. DOI: 10.1503/cmaj.150835
- Statnano. Iran leverages nanotechnology to launch west asia's largest face mask production plant. 2020. Available from: https://statnano.com/news/67581/Iran-Leverages-Nanotechnology-to-Launch-West-Asia%E2%80%99s-Largest-Face-Mask-Production-Plant
- Thanh LT, Andreadakis Z, Kumar A, Gómez Román R, Tollefsen S, Saville M, et al. The COVID-19 vaccine development landscape. Nature Reviews Drug discovery. 2020 19(5):305-6. DOI: 10.1038/d41573-020-00073-5
- The National Institute for Occupational Safety and Health (NIOSH), Guidance for filtration and air-cleaning systems to protect building environments from airborne chemical, biological, or radiological attacks. 2014. Available from: https://www.cdc.gov/niosh/docs/2003-136/
- The New York Times (TNYT). Moderna coronavirus vaccine trial shows promising early results. 2020. Available from: https://www.nytimes.com/2020/05/18/health/coronavirus-vaccine-moderna.html
- The World Nano Foundation (TWNF). Use of gold nanoparticles is the key advantage of 2nd generation Covid-19 rapid antibody Tests. 2020. Available from: https://static1.squarespace.com/static/5ad8857175f9ee9687e 844b6/t/5ea6a8f1c522de16ff69b5ad/1587980529949/White +Paper+Gen+2+Nano+particles+explanation+v4.4.pdf
- Thomas K, Sheikh K. Small chloroquine study halted over risk of fatal heart complications. 2020. Available from: https://www.nytimes.com/2020/04/12/health/chloroquinecoronavirus-trump.html
- Udugama B, Kadhiresan P, Kozlowski HN, Malekjahani A, Osborne M, Li VY, Chen H, Mubareka S, Gubbay JB, Chan WC. Diagnosing COVID-19: the disease and tools for detection. ACS nano. 2020 Mar 30;14(4):3822-35.DOI: 10.1021/acsnano.0c02624
- van DN, Bushmaker T, Morris D, Holbrook M, Gamble A, Williamson B, et al. Aerosol and surface stability of HCoV-19 (SARS-CoV-2) compared to SARS-CoV-1. medRxiv. 2020:2020.03.09:20033217. DOI: 10.1101/2020.03.09.20033217
- Wang M, Cao R, Zhang L, Yang X, Liu J, Xu M, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Cell Research. 2020 30(3):269-71. DOI: 10.1038/s41422-020-0282-0
- Wang Y, Zhang D, Du G, Du R, Zhao J, Jin Y, et al. Remdesivir in adults with severe COVID-19: a randomised, doubleblind, placebo-controlled, multicentre trial. The Lancet. 2020 395(10236):1569-78. DOI: 10.1016/S0140-6736(20)31022-9
- Wenjie T, Xiang Z, Xuejun M, Wenling W, Peihua N, Wenbo X, et al. A novel coronavirus genome identified in a clusterof pneumonia cases-Wuhan, China 2019–2020. China CDC Weekly, 2020 2(4): 61-62. DOI: 10.46234/ccdcw2020.017

- WHO. "Solidarity" clinical trial for COVID-19 treatments. 2020. Available from: https://www.who.int/emergencies/diseases/novelcoronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments
- WHO. Advice on the use of point-of-care immunodiagnostic tests for COVID-19. 2020. Available from: https://www.who.int/newsroom/commentaries/detail/advice-on-the-use-of-point-ofcare-immunodiagnostic-tests-for-covid-19
- WHO. Advice on the use of point-of-care immunodiagnostic tests for COVID-19. 2020. Available from: https://www.who.int/news-room/commentaries/detail/advice-on-the-use-of-point-of-care-immunodiagnostic-tests-for-covid-19
- WHO. Draft landscape of COVID-19 candidate vaccines. 2020. Available from: https://www.who.int/who-documentsdetail/draft-landscape-of-covid-19-candidate-vaccines
- WHO. Modes of transmission of virus causing COVID-19: implications for IPC precaution recommendations. 2020. Available from: https://www.who.int/newsroom/commentaries/detail/modes-of-transmission-of-viruscausing-covid-19-implications-for-ipc-precautionrecommendations
- WHO. Off-label use of medicines for COVID-19. 2020. Available from: https://www.who.int/newsroom/commentaries/detail/off-label-use-of-medicines-forcovid-19
- WHO. Public statement for collaboration on COVID-19 vaccine development. 2020. Available from: https://www.who.int/news-room/detail/13-04-2020-publicstatement-for-collaboration-on-covid-19-vaccinedevelopment
- WHO. R&D Blueprint and COVID-19. 2020. Available from: https://www.who.int/teams/blueprint/covid-19
- WHO. Report of the WHO-China joint mission on coronavirus disease 2019 (COVID-19). 2020. Available from: https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf
- Wigginton KR, Pecson BM, Sigstam T, Bosshard F, Kohn T. Virus inactivation mechanisms: impact of disinfectants on virus function and structural integrity. Environmental Science & Technology. 2012 46(21):12069-78. DOI: 10.1021/es3029473
- World Health Organization (WHO). Director-General's opening remarks at the media briefing on COVID-19. 2020. Available from: https://www.who.int/dg/speeches/detail/who-directorgeneral-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020
- Yang W, Yan F. Patients with RT-PCR-confirmed COVID-19 and normal chest CT. radiology. 2020 295(2):E3-E. DOI: 10.1148/radiol.2020200702
- Yong Z, Cao C, Shuangli Z, Chang S, Dongyan W, Jingdong S, et al. Notes from the field: isolation of 2019-nCoV from a stool specimen of a laboratory-confirmed case of the coronavirus disease 2019 (COVID-19). 2020 2(8):123-4. DOI: 10.46234/ccdcw2020.033
- Zhang L, Liu Y. Potential interventions for novel coronavirus in China: A systematic review. Journal of Medical Virology. 2020 92(5):479-90. DOI: 10.1002/jmv.25707

Zhao J, Yuan Q, Wang H, Liu W, Liao X, Su Y, et al. Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019. medRxiv. 2020:2020.03.02:20030189. DOI: 10.1101/2020.03.02.20030189