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Insight from nanomaterials and nanotechnology towards COVID-19

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ABSTRACT

The pandemic coronavirus disease 2019 (COVID-19) becomes one of the most dreadful disease in the history of mankind in the entire world. The covid-19 outbreak started from Wuhan city of China and then rapidly transmitted throughout the world causing mass destruction and seldom. This sporadical disease has taken many lives due to sudden outbreak and no particular vaccines were available at the early wave. All the vaccines developed are mostly targeted to spike protein of the virus which involves the encapsulation of mRNA and nanoparticles. Nanotechnology intervention in fighting against the covid-19 is one way to tackle the disease from different angles including nano coating mask, nano diagnostic kits, nano sanitizer, and nano medicine. This article highlights the intervention of nanotechnology and its possible treatment against the covid-19. It is high time to come together all the units of material science and biological science to fight against the dreadful COVID-19. As an alternative strategy, a multidisciplinary research effort, consisting of classical epidemiology and clinical methodologies, drugs and nanotechnology, engineering science and biological apprehension, can be adopted for developing improved drugs exhibiting antiviral activities. The employment of nanotechnology and its allied fields can be explored to detect, treat, and prevent the covid-19 disease.

1. Introduction

On last year of 2019 December 31, a novel strain of corona virus was reported by authorities of China which is responsible for severe illness. The covid-19 was not known to us until it was classified as a family of severe acute respiratory syndrome (SARS) and middle east respiratory syndrome (MERS) [76]. Covid-19 was declared as a pandemic on March 11, 2020, by World Health Organization (WHO). Now the entire globe is affected by the disease and cases rise in most of the countries by the second wave. More than 151,404,330 people were infected by this disease out of which total fatality stand at 3,183,177. India become one of the most affected country in the world next to United State of America by the second wave at the early period of 2021 (Worldometer, 2021; [10,62, 67].

The coronavirus which causes COVID-19 disease is belongs to Betacoronavirus group with having single stranded positive RNA [13]. This virus is belonging to family coronaviridae in order Nidovirales [61]. Family coronaviridae is a large family which causes different symptoms including common cold, fever to SARS and MERS. Coronaviridae have two sub-families such as Torovirinae and Coronavirinae. In mammals and birds, coronaviridae causes diseases [26]. Betacoronaviruse and alphacoronavirus can cause disease to mammals however, human respiratory illness is caused by Betacoronavirus only. Other coronavirus category such as Deltacoronavirus and Gammacoronavirus causes illness in birds and some mammals [82]. The disease transmission rate is very fast as compare to other diseases [59]. The structural outward produced from the cell surface of the virus called as spikes, plays an important role in

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case of transmission of viral genome (Fig. 1). By the help of spike virus attached on the host cell surface and transfer the viral genome into the host cell successfully. Spike is nothing but a protein which is responsible for a crown like structure. Spike protein attaches to the receptor protein Angiotensin-converting enzyme 2 gene (ACE2).

The world is fighting against corona virus pandemic and the disease is transmitting through droplets during coughing and sneezing [5]. Although, there are vaccines available for the general people to control the transmission of COVID-19, maintain hygiene, social distancing, self-isolation, wearing mask, using of hand sanitizers are still adopted [6]. In this worst condition, different molecules and materials science are trying to develop their own way of fighting and treating this deadly virus [32]. In this regard, use of nanoparticles and nanotechnology will be an another option to fight against the COVID-19. Nanoparticles are now used in wearing mask to reduce virus load, hand sanitizer, disinfectants, personal protective equipment and antiviral drug development which are under process to effectively kill the virus.

1.1. Potential drugs of corona virus

A sudden outbreak of viral pneumonia in Wuhan city of China on December 2019 causes loss of lives and it has spread rapidly in many other countries. On March 11th' 2020, WHO has announced the epidemic of this deadly disease as pandemic. Unfortunately, there is no specific antiviral drugs which can be used to prevent or treatment of COVID-19, even though the vaccines are available. The efficacy of the vaccines is also another doubt. According to experience of health workers and scientists, some of the drugs which are under clinical trials shows positive effect in treatment of ill patients. Chloroquine, an antiviral drug used for the treatment of malaria found to be effective in treatment of COVID-19 by preventing the entry of virus and inhibiting glycosylation of viral ACE-2 or quinine reductase 2 up to some extent [33,43]. According to Chinese experts, patients suffering from mild, moderate and severe of COVID-19 can medicates chloroquine with dose of 500 mg twice in a day for around 10 days [87]. An analogue of chloroquine, 'hydroxychloroquine' found to be more effective and useful in diagnosis and shows better result than chloroquine [37]. Combination administered of both hydroxy-chloroquine and azithromycin reported to have some beneficial in treatment against covid-19 [77]. Also reported that some of the drugs like ribavirin, penciclovir, nitazoxanide, nafamostat, chloroquine, remdesivir and favipiravir shows potential effect against covid-19. Remdesivir is a drug which is under clinical trials for Ebola and Marburg disease but observed to have good effects in treatment against this mystery disease by inhibiting the activity of virus [12,14]. Remdesivir is often given to those patients which shows severe symptoms and need intensive care and oxygen. Apart from this, anti-viral drug such as HIV-AIDS, ACS-09 is also used as protease inhibitor incorporating with ritonavir. Another protease inhibitor anti-viral drug, camostat mesilate also shows effective results against SARS-CoV-2 in *in vitro* analysis of lungs cell by blocking viral cellular activity and maturation. To control this outbreak in China, possible treatments with their Traditional Chinese Medicine (TMC) have also been tried by Chinese and a good impact was seen in patients at early stage. Traditional Chinese Medicine like capsules of Shu Feng Jie Du and Lian Hua Qing Wen give positive outcomes in treatment of this lethal disease. However, different vaccines are developed by the different companies and countries, but the question is on its efficacy. None of the vaccines shows absolute efficacy against the disease and moreover the virus turns its different shapes by producing mutant

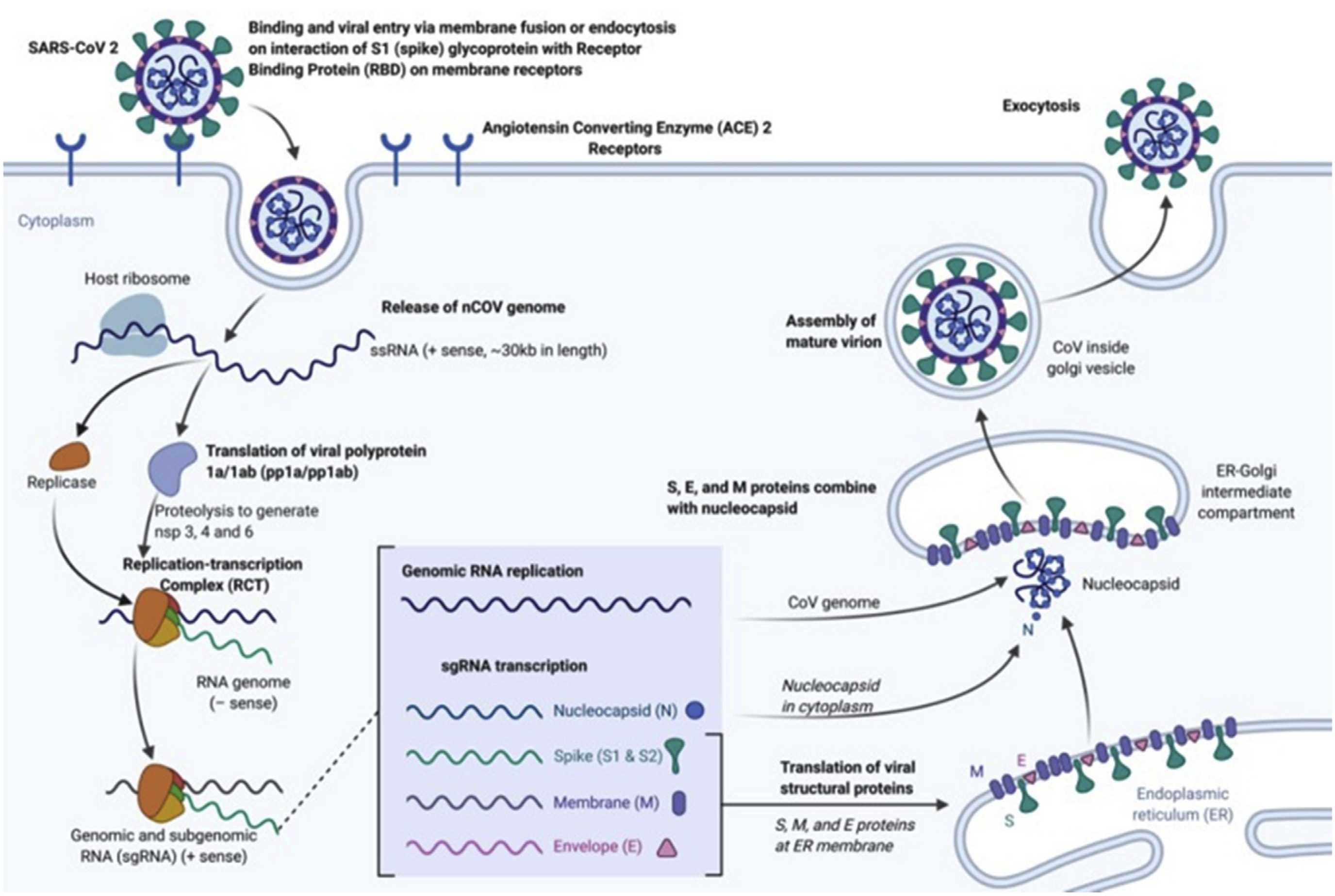

Fig. 1. Representing the steps of viral infection and mode of action of anti-bodies (adapted and reproduced from Cascella et al., 2020 under the terms of the Creative Commons Attribution 4.0 International License (http://creativecommons.org/licenses/by/4.0/). Potential effect of Chloroquine on SARS-CoV-2.

varieties which are seems to be more lethal and rapid transmission than the earlier variant. This makes the innocent people quite nuisance for opting the vaccine as the last option to treat against the covid-19. However, it is also reported that the existing vaccines (covishield and covaxine) can still be effective against the mutant variant available in India.

1.2. Favipiravir

It is drug approved for treatment against the influenza in China. This drugs usually inhibits the RNA-dependent RNA polymerase. Apart from the action against the influenza virus, this antiviral drug can also be administered against the different RNA virus including COVID-19 [16]. It may have potential to act against the SARS-CoV-2.

1.3. Ribavirin

It is a nucleotide derivative usually consist of guanosine analogue which can inhibits the replication of RNA and DNA genetic materials by inhibiting RNA capping. It is used as antiviral drugs against the respiratory syncytial virus, SARS-CoV and MERS-CoV. In the case of covid-19 this drug is playing some role in treating the virus [20].

1.4. Lopinavir-ritonavir

Anti-HIV drugs (ritonavir, lopinavir and darunavir) are also showing positive effect while treating with the coronavirus disease 2019. This therapeutic effect might be due to the inhibition of the CEP_C30 (corona virus endopeptidase). A combination of these two drugs are more effective against the SARS-CoV and MERS-CoV infections as reported in many studies [7,35].

1.5. Remdesivir

It is a drug consist of nucleotide sequence rich in adenosine having monophosphoramidate prodrug. It blocks the RNA-dependent RNA-polymerase in its nucleoside sequence. This drug is used as antiviral drugs against the hepatitis B virus, HIV, filoviruses, paramyxovirus, SARS-CoV and MERS-CoV [50]. This drug usually works only after the virus enters inside the host cells. It can obstruct the virus RNA for its replication inside the host cell. Subsequently, the viral RNA chain complex for further transcription will be inhibited and terminated the synthesis of new proteins or RNA [57].

Severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) is a positive sense single stranded RNA virus that leads to cause coronavirus disease. World health organization named it as coronavirus disease 2019 (covid-19) on February 11, 2020. The unexpected outburst of this disease causes chaos in public and there is no proper remedy of this disease. Numbers of drugs and vaccine have been developed and some are under trials with some positive and negative impacts. Treatment of ill patients by Traditional Chinese Medicine (TCM) and combination treatment with Western medicine has also shown some positive remedy against the covid-19. Among the drugs, Chloroquine and its analogue drug hydroxychloroquine and remdesivir emerge as one of the most promising drugs that can be effectively used in severe conditions against COVID-19. Chloroquine is substitute form of natural quinine which was synthesized 70 years back in Germany by Bayer in 1934 [49,80]. Quinine is a compound which is found naturally in bark of Cinchona trees. It is an old anti-viral drug usually prescribed and approved for the patients suffering from malaria. It also has some efficacy in the treatment of HIV-AIDS and autoimmune disease. The anti-viral properties of chloroquine were also tested against other different RNA viruses such as rabies virus [72], polio virus [31], hepatitis A virus [8,69], hepatitis C virus [41], influenza A and B virus [39], influenza A H5N1 virus [84] and dengue virus [55]. In treatment of dengue virus, it interferes the pH dependent endosome and divided the entry of enveloped virus [71]. Chloroquine helps in treatment of hepatitis A by inhibiting its virus surface and preventing the replication of entire viral cycle. It also helps in post-translational modification of proteases and glycosyltransferases which occur in endoplasmic reticulum or Trans Golgi network vesicles. There is some past evidence of Chloroquine treating in other disease of coronaviruses. It has shown beneficial effect in the treatment of SARS-CoV-1 and restrain *in vitro* analysis of the replication of HCoV-229E in epithelial lung cell culture [9,29,30]. Chloroquine is also playing an important role in treatment by acting as anti-viral and anti-inflammatory. Invitro analysis of Vero E6 cells with Chloroquine against the infection of SARS-Cov-2 shows positive effect with concentration of (EC_{50}) 0.77 μM [77]. *In-vivo* examination of Chloroquine against SARS-C0V-2 on Vero E6 cells was successful at effective concentration (EC_{90}) of 6.90 μM [36].

The mechanism of action of Chloroquine in host cell is to helps in blocking viral entry and early stages infection of Vero E6 cells. Its mode of action also includes the inhibition of quinine reductase 2 which is a structural neighbor of Uridine diphosphate -N-acetylglucosamine 2-epimerases [33,75]. For now, Chloroquine is considered as one of the most promising drugs to fight against covid-19. The treatment reports in China also revealed that patients treated with Chloroquine shows gradual decrease in fever and becomes better in lung tomography (LT) images. The recovery from the disease was also observed to be better and faster than other drugs. Although it has many positive effects in treatment of covid-19, there is some minor risk if it is used in high dose for long period. Some reports on cardiomyopathy were observed after use of Chloroquine for long period [56]. Therefore, use of Chloroquine with high dose for short period or low dose for long period is recommended for the treatment.

1.6. Nanomaterials

Nanomaterials refer to materials of single unit small size between 1 and 100 nm [1,2,46]. The technology that used this nano sized material is known as nanotechnology. The nanomaterial is one billionth of a meter i.e. 10^{-9}m in size. The size of nanomaterial can be compared with viruses and other pathogen scales. Therefore, they have the properties to identify and eliminate undesired pathogens [53,54]. The origin of nano based materials can be naturally occurred, unintentionally released and manufactured. Nanomaterials manufactured by human are according to their certain purposes. Naturally occurred nanomaterials includes different types of nanoparticle exist in our environment such as forest fires products, ash released from volcanic eruption, ocean spray and radioactive decay of radon gases. It can also be formed due to the process of weathering. The chemical composition of nanomaterial can be metals, metal oxides, polymers, carbon, semiconductors, bio molecules and compounds and their shape can be spheres, needles, platelets and tubes [3,4,60]. The nanomaterials are divided according to their number of dimensions. They are nanoparticles, nanofiber, nanoplate and nanoribbon. Nanoparticles have three external dimensions, nanofiber with two external dimensions, nanoplate with one and when two large dimensions are very different, they are referred as nanoribbon. Again, it can be categorized on the basis of materials they contain i.e. nanocomposite, nanofoam, nanoporous and nanocrystalline. Nanocomposite consist of solid particle at one specific region and have one dimension on nanoscale whereas nanofoam can be of liquid or solid matrix, one phase is filled with gaseous phase and another phase with dimension [89]. Nanoporous material is solid and has nanopores but nanocrystalline material consists of crystal grains in the nanoscale. Recently, nanomaterials are utilized in many fields and proved their advantages over other technology. They are being exploited in manufacturing industries of sports, cosmetics and clothing. They are also utilized in products of health care as paints, filters, insulation and as additives. Nano based artificial enzymes are used for bio sensing, anti-bio fouling, diagnosis of tumor and targeted drug delivery. Filtration of very minute harmful virus can be detected through high quality nanofilters. The application of nano objects widely in mobile phones and computers as sensors make advances in processing. Potential impacts of this technology also include cleaner energy, better storage energy and treatment of water to bring a safety and clean environment for human kind. In field of agriculture and horticulture, they are used in storage, processing, packaging and against deterioration of food. The nano sensors can be used for screening of crop growth, checking of soil condition and detection of pathogen in plants [42]. With the advent of this technology in few decades, it has shown its ability in modifying and development of different field. Therefore, a new generation has been introduced and revolutionized the entire scenario of sciences.

Nanotechnology is a multidisciplinary applied science field that stringently utilize the nanomaterials and its physio-chemical properties with some other molecules for developing a value-added product that may include nanoformulation, drug delivery, nanofertilizer, nanomedicine etc. [44–46]. Nanoparticles can be utilized in developing antivirals drugs that act by interfering with viral infection, particularly during attachment and entry. Usually, virus get attached and entered inside the host cell through their spikes starts multivalent interactions with viral surface components and cell membrane receptors [22]. The antiviral drugs are designed in such a way that it blocks the viral entry into the host cell and prevents topical microbicides [18,38,74]. Viruses are the entities that causes various disease and death of many animals, birds and even human beings worldwide. Several viral diseases that emerged in the last few decades including SARS, MERS, Ebola, Nipah Virus and recent pandemic covid-19 have entrenched human population worldwide.

Viruses are, indeed, very intelligent, in the sense they can develop an extraordinary genetic adaptability to resist against the antiviral inhibitions and sometimes mutated inside the host cell to creates new strain that will acquire resistance to most of the antiviral compounds. Perhaps, because of this new strain formation leads to huge obstacle in development of drugs. Therefore, multidisciplinary research efforts consisting of classical epidemiology, clinical trials, pharmacologist, nanotechnology, traditional medicines [64], bioactive [15] essential oils [47] compounds etc. are highly essential to combat against the COVID-19 [65]. Nanotechnology has emerged as smart material to specifically targeted at the site of infection and stopping the viral replication to contain further transmission inside the host cell (Fig. 2). Metal nanoparticles such as silver or gold possess virucidal activity against the broad spectrum of viruses. The interaction between metal nanoparticles and viral surface glycoproteins, may induce antiviral activity and stops viral genome replication (DNA or RNA). Metal nanoparticles used against different therapeutic or prophylactic treatment should be properly optimized in order to minimize the toxicity effect that may develop at long term exposure.

In combating with COVID-19, the potential areas of nanotechnology intervention can play a major role in rapid diagnostics, surveillance and monitoring, therapeutics and vaccine development [13]. Also, It can be explored to detect, treat, and prevent the COVID-19 disease. Nanomaterials with antiviral properties can be utilized as coating materials in personal equipment or in disinfection against the corona virus or in developing vaccines or immunomodulators [79]. In diagnosis, nanosensors are being developed for rapid, low-cost, and simple detection against the SARS-CoV-2. For the treatment, nanoparticles are allowed to form a composite with other drugs for controlled and targeted delivery of antiviral drugs to the pulmonary system to inhibit the viral replication [79]. It can reduce the virus load on the infected surface. The electrical and optical properties of nanomaterials are being adapted in development of point-of-care biosensor as diagnostic methods. Using of nanoparticles in biosensor increased the sensitivity and this enable us to detect the analytes at low concentration. This facilitated the rapid diagnosis and isolation of the infected patient due to the SARS-CoV-2. Thus, nanotechnology provides an ample opportunity to fight against the current pandemic in diagnosis, developing vaccines, drug delivery, treatment, protective coating in personal equipment, and reducing virus load in mask.

Gold nanoparticles (AuNPs) are one of the most attractive nanomaterials due to its biocompatibility with most of the molecules. It has certain properties like optoelectronic properties which are substantially explored in developing different biosensors [25]. AuNPs have been extensively used in lateral flow assays (LFAs) specially in providing color change in the test. These biosensors are employed in diagnosis of influenza, Zika, hepatitis B and interestingly LFAs was used in detecting the covid-19 [73]. Apart from this, magnetic nanoparticles and

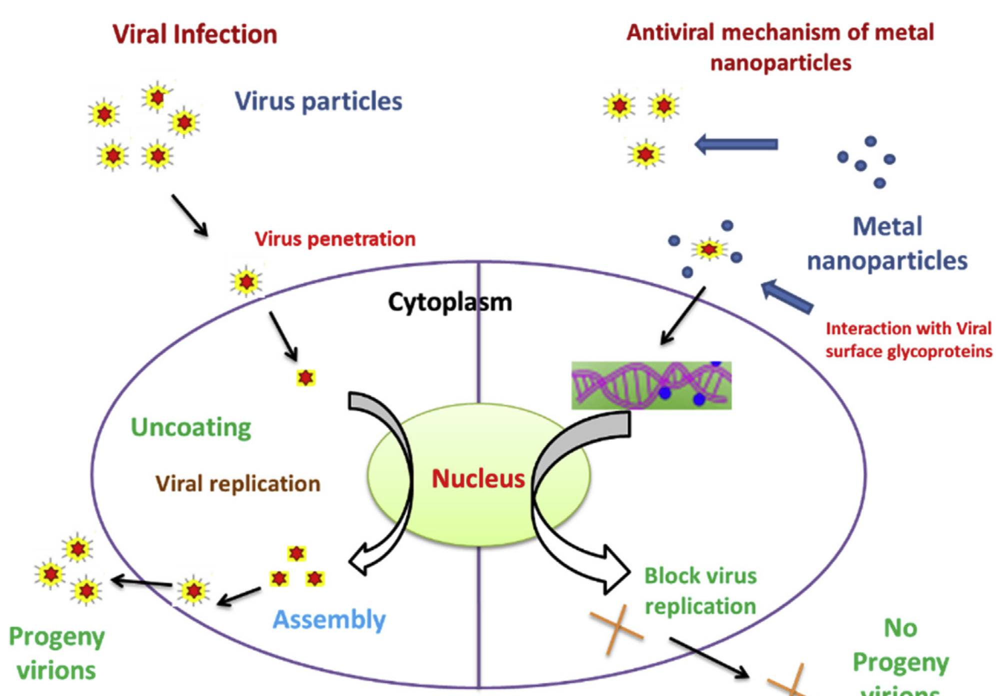

Fig. 2. Schematic representation of antiviral mechanisms of Nanoparticle.

graphene-based field-effect transistors (FET) biosensors are also attempted to detect the SARS-CoV-2.

1.7. Silver nanoparticles to fight against covid-19

Silver nanoparticles are nano size particles of silver between 1 - 100 nm and have distinct properties of optical, high electrical conductivity, stability, and low sintering temperatures. They are utilized by incorporating with other products ranging from photovoltaic to biological and chemical sensors. One of the important applications of silver nanoparticles is that they can be used as anti-microbial coatings. It has anti-bacterial properties and effective against the growth of bacteria. Its effectiveness was recorded both from gram positive and gram-negative bacteria [66,78]. It is applied in dental work, surgery applications, wounds and burns treatment and bio medical devices as silver based compounds are greatly harmful for microorganisms. Additional application includes use of it as a catalyst and in household goods. Silver nanoparticles have catalytic redox attribute quality for biological agents like dyes and chemical agents like benzene. Silver based nanoparticles can synthesize biologically and synthetically. Biologically they can be synthesized from organic matrix of bacteria and mostly found in lactic acid producing bacteria. It has also been demonstrated that use of silver at very small concentration is not harmful to human kind.

In this worst situation of world due to the spread of COVID-19, many researchers are studying potential uses of silver nanoparticles to bring an alternative way in treatment of this unfortunate disease. But, as of now, there is no definite analysis for the treatment. The viral infection of COVID-19 starts in the nasopharynx or bronchial tree portion of respiratory system. The infection increases after the pathogen moves down to lower portion of respiratory system. Later, when the infection is severe it spreads and weakens our immune system which may lead to loss of life. So, the treatment of ill patients at early stage when the infection is in upper portion in respiratory system is successful to some extent. It is reported that colloids nanoparticles can be used as antiviral with a size of 3–7 nm size [86]. Minimun Inhibitory Concentration (MIC) for anti-viral application is about 10μ/ml, deposition fraction of targeted tissue under oral breathing should be 5 μm of aerosol droplets and for breathing cycle losses use of continues aerosol source with increasing dose at 3 times of breath actuated nebulizer source. Use of silver particles for inhalation as suspension or solution can be differentiated into two types. They are ionic silver and colloidal silver. Ionic silver are atomic silver ions which can dissolve in water and have superior quality in terms of topical or external solution. Silver ions are formed when it is oxidized and kills germs, bacteria and yeasts. Whereas, Colloidal silver are made up of tiny nano particles of metallic silver or chunks which are more effective for internal use as they can stay unaffected by stomach acid. It is found in many products that are available in market at very low particle concentration and they come in form of injection or can directly apply to the skin. Colloidal silver nanoparticle has properties to cure, strengthens our immune system, fight against bacteria and viruses, use in treatment of cancer, hepatitis B and HIV-AIDS. Its mode of action are; i) it binds directly to the DNA of virus, damage the hydrogen that keeps cell together and kills the virus ii) it act as a foil by covering the cell membrane of virus thus, preventing from infection iii) it performs as catalyst by binding in to oxygen molecules and makes a barrier between the host cell and the virus (Fig. 1). A naturopathic doctor Sherrill Sellman stated that silver solution shows some effectiveness by deactivating and boosting the immune when experimented on some strains of coronavirus. Therefore, it can be concluded that there is scope for silver nanoparticles in treatment of COVID-19 but, more research, trial and positive information is required for its application.

Silver nanoparticles (AgNPs) exhibits antibacterial, antiviral and anti-influenza properties (Aderibigbe et al., 2017 and Haggag et al., 2019) besides its other therapeutic applications including wound care [89]. The toxicity level of such nanoparticles should be considered before its direct testing to the human being. However, silver nanoparticles are often used as inhaler through suspensions or solution in water. In both the cases, the molecules existence is different due to its particle size. Ionic silver particle may be suspended in the water due to its large size whereas colloidal silver solution has nanoparticle size of 1 nm–100 nm diameter. Both the molecules have antibacterial properties [70]. In antiviral properties, colloidal particles have ten times more potent than ionic silver [34]. This might be due to its nano range particles and concentration level in the solution.

The colloidal silver particles in the size of between 3 and 7 nm can be highly effective against the viral infection. However, its potential effect on the respiratory infections is not known properly. On treatment with the virus, the minimum inhibition concentration (MIC) of colloids is about 10 μg/ml, showing better effectiveness against the target tissue concentration of 25 μg/ml. These colloidal silver nanoparticle formulations may be effective for preventing the respiratory viral infections and may also be treated against the SARS-CoV-2 [86].

1.8. Nanoparticles coated kits against COVID-19

Nanotechnology plays an important role in diagnosis, prevention and treatment of COVID-19. It also provides social responsibilities. Nanotechnology is used in vaccine preparation by the help of nano carriers. A reusable mask called Guardian G-volt is developed based on laser techniques and electrical charge used to kill the pathogen. This mask is developed by Respilon group which is capable to inhibit viruses, bacteria, airborne particle and air pollution. In this mask, nanofiber technology is exploited with three multiple layers. A special type of nanosanitizer is being developed using silver ions and titanium oxide.

1.9. Chloroquine and nanoparticles interaction

Chloroquine has been shown to be a broad-spectrum regulator of nanoparticle and inhibits the aggregation of engineered nanoparticles of different sizes (14–2600 nm) with different forms (spherical and discoidal) when treated in cell lines as well as in the mononuclear phagocyte mice method [51,81]. Researchers have also revealed that chloroquine can control in reducing the expression of phosphatidylinositol binding clathrin assembly protein (PICALM), one of the 3 most plentiful proteins in clathrin-covered pits [81]. PICALM has potential to inhibit clathrin-mediated endocytosis (CME). This CME is a main pathway for artificial nanoparticles internalization [81]. The protein stages of clathrin and clathrin adaptor protein 2 (AP2) were unchanged in macrophages treated with chloroquine [81], indicating PICALM-unique outcomes, in preference to a popular discount in proteins related to clathrin-structured endocytosis.

While, comparison to chlorpromazine (a clathrin-structured endocytosis inhibitor), chloroquine became significant drugs helping in preventing nanoparticles uptake by macrophages [81]. In non-clathrin mediated nanoparticles uptakes, PICALM can play secondary position. Additionally, chloroquine can prevent from lysosome acidification, by hindering fusion with endocytic vesicles. Prevention of lysosome fusion is likely to intervene with upstream endocytic trafficking, causing a 'visitors jam' state of affairs that blocks effective delivery of cargo to and from the cell membrane [51].

Chloroquine is an authorised malarial drug having vast potential in treatment of different diseases. Chloroquine based nanomedicine is quite interesting due to its smooth uptake in cells, and this might have potential for the treatment of COVID-19. Nanomedicine can be extensively used in delivering the drugs to a specific area [58]. Recent multicentre scientific trials and cellular tradition studies advocated that the 70-year-old malaria drug, chloroquine, might also probably show therapeutic efficacy towards COVID-19 (corona virus disease 2019), an unexpectedly spreading viral contamination that can purpose pneumonia-induced dying in about 2.5% of infected individuals. There is a possibility of chloroquine and its derivative can treat COVID-19 up to some extent, however a concrete interpretation can only be developed after clinical trials.

In the line of producing an approved and effective vaccine for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), it is also important to investigate on the potential of prophylactic and/or therapeutic effects of the existing/newer drugs that can reduce the virus load in the cell by interfering its spike protein/cell membrane. Chloroquine and its spinoff, hydroxychloroquine, have a long records as secure and less expensive tablets to be used as prophylactic measures in malaria-endemic regions and as day-by-day remedies for autoimmune illnesses, but there is side effect like-eye damage after being used for long time. Although preceding research have discovered that chloroquine has therapeutic pastime towards viruses, such as human coronavirus OC43 in animal models and SARS-CoV in cell culture studies. However, exact mechanism of chloroquine against the COVID-19 as antiviral property is not known. Chloroquine and nanoparticles interaction in cells may prevent viral replication prior to entry to the host cell.

1.10. Nanotechnology intervention in detection and diagnosis of COVID-19

The genome sequences of SARS-CoV-2 have been fully developed. Efforts have been done on robust nucleic acids extraction from complex clinical samples for further subsequent molecular diagnosis. Although the RT-PCR based detection kits for COVID-19 are being developed, timely diagnosis of COVID-19, wear mask and making social distancing are the only few protocols one need to follow in order to break a chain of transmission until vaccine came into picture. A study on carboxyl polymer coated magnetic nanoparticles (pcMNPs) was used efficiently in viral RNA extraction and sensitive detection of SARS-CoV-2 via RT-PCR (Table 1). These pcMNPs have several advantages than the traditional column-based nucleic acids extraction methods. Firstly, in pcMNPs, the two different steps usually taken in traditional nucleic acid based where virus lysis and RNA binding are put together and these pcMNPs-RNA complex can be directly introduced into RT-PCR by giving remarkably RNA extraction protocol. Secondly, pcMNPs can easily binds with the viral RNA by giving out 10 copy higher sensitivity in SARS-CoV-2 in the RT-PCR. Moreover, this technology can easily be fully automated without expending much laborious and optimization difficulties. Overall, this technology has high simplicity, robustness, excellent performance and thus exhibits a great potential in order to diagnoses the SARS-CoV-2 [87].

In another testing kits developed through novel Loop-mediated Isothermal Amplification (LAMP)-based test seems to be more rapid, simple, reliable than other diagnosis kits. This new novel kits are named as COVID-19 RT-LAMP-NBS. The beauty of this techniques is that LAMP assay merged with the reverse transcription, multiplex analysis where nanoparticles-based biosensor is used. The entire assay is facilitated in one step single tube reaction. This assay is simple and easy to use platform avoiding all the complex process like electrophoresis, reagents preparations, using of expensive instrument which often come across in other techniques. This assay is quite interesting in the fact that it has high specificity, sensitivity, feasibility, low cost and ease of use in diagnosis of COVID-19 [88].

Table 1
A comparison of spin column- and pcMNPs-based extraction method in SARS-CoV-2 virus RNA extraction.

Parameter	Spin column[1]	pcMNPs[2]
Complexity	Multi-step and assistant with a high-speed centrifuge	One-step and assistant with a magnet
Option	Manual only	Manual and automated
Safety	Require toxic reagents (chloroform/phenol, chaotropic salts)	No toxic reagents
Quality and productivity	High purity but limited productivity	High purity and high productivity
Elution	Require large-scale elution buffer	Directly treatment of a wide range of tested samples (food; animal; blood; pharynx; sputum and so on)
For RT-PCR	RNA elution products	RNA elution products or MB adsorbed RNA products without elution
Extraction Time for Multiple Samples	>2 h	~30 min

1-Commerical RNA Purification: QIAGEN 52906 QI Aamp Viral RNA Mini Kit; Real-time RT-PCR instrument: Roche Light Cycler 480.2) This work: functional pcMNPs-based RNA extraction and real-time PCR amplification (Bio-Red) [86].

Cloth masks, and surfaces impregnated with ionic zinc oxide (Zno; Zn2+–O2−) nanoparticles (Krol et al., 2017) with wurtzite shape or perhaps PEGylated ZnO-nano-particles [21] (or oxozinc) in all like to have powerful antibacterial and antiviral efficacy [28,85]. The incorporation of ZnO- nanoparticles into materials can make them stable and capable of kill pathogens on contact [63]. Preliminary information suggests that 2019-nCoV enters pulmonary cells through angiotensin 2 (ACE-2) and blocks the enzyme that degrade angiotensin II [83]. Resultant extra local concentration of angiotensin II causes pulmonary hypertension and edema, acute respiration distress syndrome, and pneumonia-related death.

After completion of scientific trials, mRNA-1273 vaccine is already rolled out for public immunization. mRNA-1273 is a novel lipid nanoparticle (LNP)-encapsulated mRNA-based vaccine that encode the genetic materials of the stabilized spike (S) protein of SARS-CoV-2 [24]. It has been evolved with the aid of the biotech company Moderna Therapeutics who become already running on SARS-CoV and MERS-CoV vaccines which have been used to SARS-CoV-2. The RNA part of the vaccine instructs cells to express the S protein to elicit the immune response. After having shown ability in animal testing, the vaccine is rolled out for further public immunization. Numerous other mRNA-based vaccines (e.g. CureVac, BNT162 by BioNTech & Prifzer) are also developed for further public used. The BioNTech mRNA vaccine (Mainz, Germany) is also encapsulates the nucleic acid with glycol-lipid nanoparticles of size 80 nm [24].

A particular antiviral drug having efficient and high potential to treat against covid-19 is not known at this condition. However, it is being reported that some of the existing drugs by repurposing it's uses can be effective up to some extend to treat mild, and severe condition of the COVID-19 patient. These antiviral drugs may include anecdotal use of medicine like lopinavir, ritonavir, interferon-1b, RNA polymerase inhibition remdesivir, and chloroquine and its derivative [52,68]. Zinc nanoparticles have been shown to have inhibitory consequences on H1N1 viral load, though their effect in COVID-19 is unknown and untested [21]. Vitamin C supplementation has a few functions in prevention of pneumonia and its effect on COVID-19 desires evaluation [23]. Efforts to increase a vaccine are underway, with the intention to be a primary device to contain this epidemic (Geneva international fitness company, 2020).

1.11. Future challenges

Designing and development of effective vaccine by using nanomaterials and nanotechnology to counter the current pandemic disease needs to be proved safe and secure by looking to all the recent developed molecules and drugs. It is also required to undergo several clinical trials before launching to the markets. The challenge is also lying in the formulation of nanoparticle where engineered nanomaterials and therapeutic drugs that target to the virus capsid, nucleic acid and envelope are not well known. Although it has possessed various antiviral activities, a concrete determination is highly essential. It is also required to have a high through put analysis of nanoparticles and their formulation in diagnosing COVID-19.

2. Conclusion

Nanotechnology is being used from a period of time. Nanotechnology is a revolutionary science with scope in different fields. In case of covid-19 virus nanoparticles and nanotechnology will plays remedial solution for future drugs, vaccine, kits, diagnosis, prevention and monitoring etc. Till now no specific medication procedure against covid-19 is developed. By Minimum inhibitory concentration using nanotechnology, the virus can be disrupted itself on the surface of host cell without allowing to enter either stopping the genome replication inside the cell. SARS-CoV-2 and nanotechnology is the current topic of interest for the researcher to do more research and experiments to come to a concrete solution for the ongoing pandemic.

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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Abbreviations

SARS severe acute respiratory syndrome
MERS middle east respiratory syndrome
WHO World Health Organization
ACE2 Angiotensin-converting enzyme 2 gene
TMC Traditional Chinese Medicine
SARS-CoV-2 Severe acute respiratory syndrome corona virus 2
LT lung tomography
MIC Minimum inhibitory concentration
PICALM phosphatidylinositol binding clathrin assembly protein
CME clathrin-mediated endocytosis
AP2 adaptor protein 2
COVID-19 corona virus disease 2019

Author contribution and ethical statements

YDS, BJ, RN, MKP, equally contributed. YDS, have edited final draft manuscript. RN, BJ curated the data. MKP, YDS had conceptualized the idea. All authored have written, reviewed and edited the manuscript.

Ethics approval and consent to participate

It is a review article. No ethics approval is required.

Human and animal rights

It is a review article. No animals were used in the study.
Availability of data and materials-Not applicable.

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