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REVIEW ARTICLE

NANOTECHNOLOGY IN BATTLE AGAINST CORONAVIRUS: AN OVERVIEW

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ABSTRACT:

The COVID-19 is an infectious disease and SARS-CoV-2 virus is the causative agent. The nanoparticles rages from 0.2nm to the 1000nm. The particle having less than 200nm shows greater effective application as drug delivery system. As the particle size decreases the surface area will increase hence the nano size material/ drug and formulation has advantage over the conventional dosage forms in the treatment of COVID-19. Along with this the nano medicines easily cross the different cellular membranes, cross the epithelial wall, permeate through the lung tissues and helps to target the lungs. The nanotechnology based diagnostic kits and therapeutics might lead us to stop this COVID-19. The nanotechnology-based formulation has ability to give promising vaccines because they are small in size and it will be act against viruses. So in future the nanotechnology has important role in fight against of COVID 19.

Keywords: COVID 19, nanoparticles, diagnosis, DNA based vaccine

1. Introduction to COVID-19 Outbreak

The COVID-19 is an infectious disease, which occurred in late December 2019 and was first reported in Wuhan, China. The SARS-CoV-2 virus were found to be as causative agent. COVID-19 has already infected Millions of people throughout world [1]. Those infected patients showed pneumonia like symptoms and it contains cough, fever and common cold. Mainly the SARS-CoV-2 virus attack on the lower and upper respiratory tracts in patients which are causing illnesses like common cold but it may become more serious, fatal forms abnormal lung computed tomography (CT) images of patients while declared that it mainly

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attacks respiratory system [2]. The Polymerase chain reaction (PCR) analysis is used as a diagnostic tool for study the infected patients. The strange pathogen was recognized using extremely useful next generation sequencing as an RNA virus On January 10, 2020 [3]. It was found similar to the genome sequence of severe acute respiratory-syndrome coronavirus (SARS-CoV) and the Middle East respiratory-syndrome coronavirus (MERS-CoV). Compared to SARS-CoV and MERS-CoV, SARS-CoV-2 virus is less fatal but more transmissible. Based on genomic sequence scientists have developed PCR kits for diagnosis of COVID-19.Various research is ongoing for the development of therapeutics and vaccine identification. Many antiviral, anti-malarial drug candidates are been undergoing clinical trials. Hydroxychloroquine is efficiently being used by physicians to treat the corona patients. Recently, Remdesivir got approval for time being as medication of COVID-19 [4]. Many prototype of vaccines are under evaluation in its efficacy to treat the new disease with many of them under investigation in phase I to phase III of clinical trials. It has been predicted that an effective vaccine will take at least 12"18 months for coming to market.

In twentieth century “nanotechnology” has arisen as game changer in drug discovery and their application due to its unique properties and ability to address the predicaments pertaining the current COVID-19 crisis that needs novel interventions to prevent, diagnose and treat the disease [5].

The nanoparticles rages from 0.2nm to the 1000nm. The particle having less than 200nm shows greeter effective application as drug delivery system. As the particle size decrease the surface are will increase hence the nano size material/ drug and formulation were advantage over the conventional dosage forms. Increasing the surface area automatically enhances the reactivity of drugs, for example improvement of solubility and dissolution rate of poorly soluble drugs. Along with this the nano medicines easily cross the different cellular membranes such as blood brain barrier (BBB), cross the epithelial wall, permeate through the corneal tissue and helps to target the posterior segment ophthalmic diseases [6]. Specifically the nanoparticles made up of the biodegradable polymers having biocompatibility and there is no need to removal of formulation after the drug therapy [6].

Till date, there are seven coronaviruses with ability to infect people, which four are 229E, NL63, OC43, and HKU1, it causes mild symptoms, however remaining coronaviruses may prove to be even dangerous and fatal. The first viruses among these was the SARS-CoV, which was observed in 2002 and faded by 2004; second is the MERS-CoV, prevalent in camels; and the recent is SARS-CoV-2 also known as COVID-19 – reported for the first time in China around late December 2019 – which as per many

scientists, has transformed itself in way steering the world into fate of pandemic. SARS-CoV-2 virions are spherical in shape having a diameter of 125 nm, with an outer coating of lipid envelope and the interior with a positive-sense single-stranded RNA genomes [7]. There are 4 varied types of proteins on the structures with the spike (S) protein playing a magnanimous part in attaching the virus to normal healthy cells and making a proper path in assisting it to enter the cells. The manifestations in form of symptoms of this new virus resembles that of flu, and further manifests itself first in the form of fever, mostly followed by a dry cough and fatigue. Lesser reported symptoms accounting for only 5% of the cases include a runny nose, sneezing, or sore [8]. It has also been observed that after infection within a week or so, patients suffered from breathlessness, with around 20% of the patients requiring critical treatment in hospitals. Certain elderly individuals, those with comorbidities and chronic health conditions, in them the early symptoms have been found to develop and mature into pneumonia, resulting chest tightness, chest pain, and difficulties in breath. In some cases, it was observed in certain individuals' symptoms observed were little to no, taking upto 14days, after being first exposed to the virus. Such patients were termed asymptomatic who shed virus and infecting others.

The rampant rise in the death tolls of COVID-19 is proving a threat to global health. Global efforts to curb the spread of this deadly virus is being implemented with researchers coming with novel techniques to identify the virus in patients as early as possible [9]. With more than 6 months passed there are still no established antivirals for COVID-19, but medical experts have been using numerous combinations of pharmaceutical agents to alleviate the symptoms. With situation worsening each day nanomedicine can prove to be critical factor in achieving control over this rapidly spreading disease [10]. At the preventive stage, there have been speculations on use of nanotech-enabled versatile and effective antimicrobial as well as antiviral compounds, which can be a personal protective means that can hinder and contain the virus spread to healthy individuals. Now, researchers have developed several nanomaterial based prototype vaccine candidates for COVID-19 [11]. In diagnostics, nanotechnology has been explored to develop sensors that can act as quick response COVID-19 tests. Also, nanomaterial based medicines have been center of attention for many researchers with many of them in clinical trials [12], [13]. Table 1 summarized the ongoing clinical trials of different therapeutics against COVID 19 [14].

Table 1 ongoing clinical trials of different therapeutics against COVID 19 as of accessed on 16 Sep 2020 from ref. https://clinicaltrials.gov/ct2/home

Clinical Trial Number	Study Title	Drug	Status	Phase	Allocation	Masking	Start Date	Estimated Completion Date	Summery
NCT04291729	Evaluation of Ganovo （Danoprevir ） Combined With Ritonavir in the Treatment of Novel Coronavirus Infection	Ganovo+ritonavir+/- Interferon nebulization	Completed	Phase 4	-	None (Open Label)	February 17, 2020	March 19, 2020	Study of the efficacy and safety of Ganovo combined with ritonavir for COVID-19.
NCT04261517	Efficacy and Safety of Hydroxychloroquine for Treatment of Pneumonia Caused by 2019-nCoV (HC-nCoV)	Hydroxychloroquine	Completed	Phase 3	Randomized	None (Open Label)	February 6, 2020	February 25, 2020	Study the efficacy and safety of hydroxychloroquine in the treatment of pneumonia caused by the COVID 19.
NCT04330638	Treatment of COVID-19 Patients With Anti-interleukin Drugs (COV-AID)	Anakinra, Siltuximab, Tocilizumab	Recruiting	Phase 3	Randomized	None (Open Label)	April 2020	December 2020	Study the safety and efficacy of Anakinra, Siltuximab, Tocilizumab in COVID 19.
NCT04304313	A Pilot Study of Sildenafil in COVID-19	Sildenafil	Recruiting	Phase 3	-	None (Open Label)	February 9, 2020	March 1, 2020	Study of efficacy and safety of G1(Sildenafil) in COVID-19 patients
NCT04315298	Evaluation of the Efficacy and Safety of Sarilumab in Hospitalized Patients With COVID-19	Sarilumab	Recruiting	Phase 2 Phase 3	Randomized	Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)	March 18, 2020	April 1, 2021	Study of efficacy of sarilumab in COVID-19 patient (severe and critical).
NCT04326920	Sargramostim in Patients With Acute Hypoxic Respiratory Failure Due to COVID-19	Sargramostim	Recruiting	Phase 4	Randomized	None (Open Label)	March 24, 2020	December 31, 2020	Study of efficacy of Sargramostim in COVID 19 and acute hypoxic respiratory failure.

NCT04331795	Tocilizumab to Prevent Clinical Decompensation in Hospitalized, Non-critically Ill Patients With COVID-19 Pneumonitis	Tocilizumab	Recruiting	Phase 2	Non-Randomized	None (Open Label)	April 2020	December 2020	Study the tocilizumab effect in decreasing signs, symptoms, and laboratory evidence of COVID-19 non-critical patients.
NCT04320615	A Study to Evaluate the Safety and Efficacy of Tocilizumab in Patients With Severe COVID-19 Pneumonia	Tocilizumab	Recruiting	Phase 3	Randomized	Double (Participant, Investigator)	April 3, 2020	September 30, 2021	Study the pharmacodynamics, pharmacokinetics efficacy and safety of tocilizumab in COVID-19 pneumonia.
NCT04280588	Fingolimod in COVID-19	Fingolimod	Recruiting	Phase 2	Non-Randomized	None (Open Label)	February 22, 2020	July 1, 2020	To determine efficacy of fingolimod against COVID-19.
NCT04325061	Efficacy of Dexamethasone Treatment for Patients With ARDS Caused by COVID-19	Dexamethasone	Recruiting	Phase 4	Randomized	None (Open Label)	April 3, 2020	October 30, 2020	To study the efficacy of dexamethasone in acute respiratory distress syndrome caused by COVID-19.
NCT04273321	Efficacy and Safety of Corticosteroids in COVID-19	Methylprednisolone	Recruiting	Not Applicable	Randomized	None (Open Label)	February 14, 2020	May 30, 2020	To explore glucocorticoids for COVID 19 tratment.
NCT04328441	Reducing Health Care Workers Absenteeism in Covid-19 Pandemic Through BCG Vaccine	BCG Vaccine	Recruiting	Phase 3	Randomized	Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)	March 25, 2020	December 25, 2020	Bacillus Calmette-Guérin Vaccination, a Randomized Controlled Trial.
NCT04315298	Evaluation of the Efficacy and Safety of Sarilumab in Hospitalized Patients With COVID-19	Sarilumab	Recruiting	Phase 2 Phase 3	Randomized	Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)	March 18, 2020	March 9, 2021	To evaluate the clinical efficacy of sarilumab in COVID-19 patients. (Critical and severe)

1 The nanotechnology the fight against COVID-19:

The nanoparticles rages from 0.2nm to the 1000nm. The particle having less than 200nm shows greeter effective application as drug delivery system. As the particle size decrease the surface are will increase hence the nano size material/ drug and formulation were advantage over the conventional dosage forms. Increasing the surface area automatically enhances the reactivity of drugs, for example improvement of solubility and dissolution rate of poorly soluble drugs. Along with this the nano medicines easily cross the different cellular membranes such as blood brain barrier (BBB), cross the epithelial wall, permeate through the corneal tissue and helps to target the affected organ. [6]. It is mandatory to reform the research and healthcare system if COVID-19 continues for more than a year such that research addresses the defaults in the healthcare segment. [15].

Nanomaterials are well known for their ability to be modified to target the disease. Due to its interesting properties of small size and large surface area it can act as carrier for bioactives like antibodies, RNA, etc. Recently Zhang *et al* entrapped the mRNA that encoded for receptor binding domain of SARS-COV-2 in lipid nanoparticle [16]. Abduljuawad *et al,* proposed through in-vitro studies how nano-clays could act as high affinity materials that can attract the COVID-19 virus to preferably attach to it than the human $hACE_2$ receptor. The S-spike of corona-virus interacts with nano-clays via van-der Waals interaction [17]. Previously PEGylated liposomal dexamethasone formulation have been developed for multiple myeloma and with its recent demand to treat COVID-19, it is speculated that the nanoparticle based dexamethasone formulation shall have the ability to be taken by macrophages thus having better uptake and efficacy [18]. Apart from this recent formulation by Paul *et al,* highlighted the use of lipid nanoparticle to encapsulate self-amplifying RNA vaccine that encoded for SARS-CoV-2 spike protein. The nanoformulation had high ability to produce specific IgG antibodies that could neutralize the virus[19].

DNA based vaccine are more stable as compared to the mRNA based vaccine, while the mRNA always be a no integrating hence it will be without any risk of mutagenesis. Additionally along with the stability, half-life of mRNA can be modified. Nanotechnology gives high quality options for development of vaccines for COVID-19. The nanotechnology includes liposomes, niosomes, nanocomposites are generally used for development of formulation which carry the vaccines through the cell membrane. The developed formulation will be improve the translocation of the plasmid DNA. The mRNA based vaccine are generally solid lipid nanocarriers, but now a day the development focusing on multifunctional nanocarriers. [20].

1.1 Rapid point-of-care diagnostics.

Both symptomatic patients having symptoms ranging from, fever, cough, and difficulties in breath or asymptomatic and such stealth carriers pose a threat to communal spread causing major concern to curtail its spread. The vital aspects lies in making available economic, rapid diagnosis are offered to medical professionals in critical conditions, hospitals and private isolation centers. This can prove to be a critical factor in saving frontline workers, the patients as well as spreading the virus to others [21].

1.2 Surveillance and monitoring

Diagnostics serve as major instruments that can control the spread of infection as it assists in mass surveillance. The rapid diagnostic kit is a vital aid to public health officials to check the spread of virus such that proactive steps can be taken in those areas. This can help predict escalation in needs, and direct the logistics needed in infected areas. A system is effective and successful when there is transparency in collaboration assisted with consistent communication and work between different government agencies, private and public health departments, private sectors and communities [22]. Mass testing is the need of hour as pointed by the World Health Organization and other agencies to cease the spread of virus. Current treatment strategies employed have ability to hinder the multiplication of the viral entity inside our body. Research on the nanobiotherapeutics can help to know the capability of SARS-CoV-2 in the way it infects the cells. Findings show that the SARS-CoV-2 having size around 60-140nm attaches to ACE-2[23–26].

1.3 Vaccine development

Vaccines prevent the patient from getting serious infection by assisting and improving the immunity in fighting virus. A potential vaccine candidate being identified is mRNA”lipid nanoparticle vaccine developed basis of primitive studies of COVID-19. In combating COVID-19, innovations in R&D and their tactful use can be most optimum approach. Nanotechnology based tools can identify, cure and avoid the disease spread. [27]. Opportunity still exits to develop the best medical need that can prove as frontline tools in fighting against this infectious virus. [27,28].

2 Conclusion:

COVID 19 is deadly pandemic disease spread very fast. It need to fast development of vaccines, diagnostic and treatment. However nanotechnology based diagnostic kits and therapeutics may be lead to stop this COVID 19. The nanotechnology based formulation will give promising vaccines because of they are small in size and it will be act against viruses. So in feature the nanotechnology having important role in fight against of COVID 19.

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4 Conflict of Interest Declaration:

Authors report no conflict of interest.

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