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ROLE OF NANOMEDICINE FOR COVID - 19 - A REVIEW

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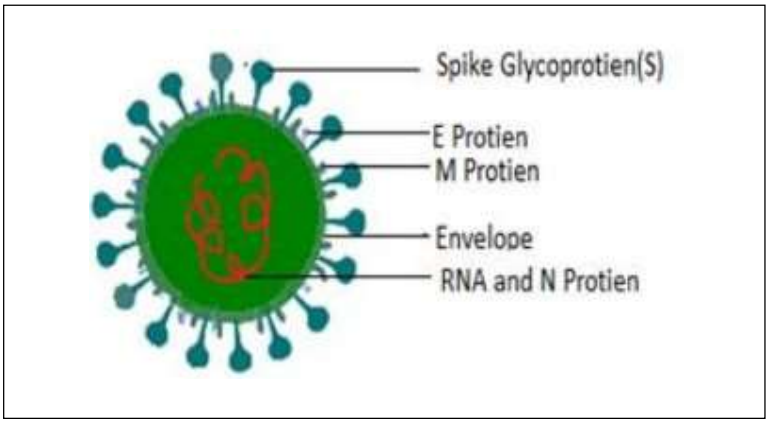
ABSTRACT:

COVID – 19 has been proved to spread a pandemic over the world within a few years.WHO declared COVID -19, which was caused by a new coronavirus, a global pandemic.Humans have been infected with seven distinct coronaviruses, three of which have caused significant outbreaks, namely MERS-CoV, SARS-CoV, and SARS-CoV-2.According to phylogenetic study of the genomes, recombination between SARS-like CoVs from pangolin and bat could have resulted in the creation of SARS-CoV-2 and COVID-19 epidemics. There are sixteen putative non- structural proteins including proteases, RNA- dependent RNA polymerase, helicase, other proteins involve in the transcription and replication of SARS-CoV-2 and four structural proteins, including spike protein(S), envelope (E), membrane (M), and nucleocapsid (N). With a high viral load in the body, SARS-CoV-2 infection causes a cytokine storm that damages the human lungs, especially in the elderly and those with immunosuppressive illnesses.Several medications have been repurposed and put to use.COVID-19 has been treated with a variety of techniques, including antiviral, antibacterial, and antimalarial drugs.Clinical trials are underway to develop effective vaccines, and some vaccines that have been approved for treatment, such as COVISHIELD, COVAXIN, ASTRA ZENACA, and SPUTNIK V vaccines, are being used to develop antibodies against COVID-19. However, due to the spread of virus variants, these vaccines are not expected to be 100 percent protective against the virus. With the help of nanotechnology's. The therapy of SARS-CoV-2 can be rendered more effective by targeting the viral cell directly and altering the genetic material's function.We summarized the function of nanomedicine in the treatment of SARS-CoV-2 in this review.

KEYWORDS: Nanomedicine, Nanoparticles, COVID- 19, SARS-CoV-2.

INTRODUCTION:

During the last century, different subtypes of influenza virus and this virus caused five different pandemic respiratory diseases and major reservoir of such viruses is pigs. The greatest pandemic history occurred between the 1918 and 1919. 21 million deaths were recorded worldwide. In 1918 H1N1 (Spanish flu), 1957 H2N2 (Asian flu), 1968 H3N2 pandemic, and the 2009 influenza A H1N1 (Swine flu). In the 2001 and 2012 the family of the coronavirus, the pandemics Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS) was originated[1, 2].In December 2019, an outbreak of coronavirus illness 2019 (COVID-19) was reported in Wuhan, Hubei Province, China, caused by a novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[3]The World Health Organization (WHO) designated the rapid increase in confirmed cases a global epidemic.[4] Many countries have seen a second wave of coronavirus disease-19 during the 2020 pandemic. India is currently facing this second wave nowadays, and this second wave is affecting young people more. Peak of the second wave approximately the 30th of May 2021 in India, and a third wave can be originated in India in october2021. This can be more fatal to children's[5].Coronaviruses are single- stranded RNA Viruses and are minute in size (65-125nm in diameter) and belonging to the family Coronaviridae and subfamily is Orthocoronavirinae, and belonging to the order Nidovirales, The subfamily Orthocoronavirinae is further classified into Alpha-, Beta-, Gamma- and Delta coronaviruses. Alpha- and Beta- coronaviruses are pathogenic to mammals including bats, pigs, human being, mice and cats. Gamma- and Delta- coronaviruses are pathogenic to bird but rarely infection to the mammals Respiratory Syndrome (SARS-CoV) and Middle East Respiratory Syndrome (MERS- CoV)[4, 6].The RNA genome of SARS-CoV-2 consists of four proteins and 30,000nucleotides. MERS-CoV has largest genomic size i.e. 30.11kb[6]. Coronaviruses contains spike- like projection of glycoproteins and present on their surface. And which look like a crown under the electron microscope. The structural proteins are made up of the envelope (E), membrane (M), and spike proteins (S). The S proteins, on the other hand, are in charge of connecting with the cellular membrane.These viruses are zoonotic, meaning they can pass between animals and humans[7]. There are three sorts of segments in a coronavirus spike: a big ectodomain, a brief intracellular tail, and a single-pass. Tran's membrane anchor is a protein that is found on the surface of the cell membrane[8]



CoronaVirus Replication:

Spike (S), Membrane (M), Envelope (E), and Nucleoside (N) proteins are the four primary types of structural proteins found in Corona virus particles. And they're all encoded in the viral genome's 3' end.And, with the help of structural proteins, coronavirus quickly replicates itself.The viral envelope is structured by M and E proteins. M proteins exist as a dimer in the virion. And adopt two various confirmations and promote membrane curvature and bind to the nucleocapsid. E Protein is found in small quantities within virion coronavirus E Protein are highly divergent E protein is Tran's membrane protein[9].Coronavirus spike proteins are the most important factors in virus attachment and entrance into the target cell.Angiotensin-converting enzyme 2 (ACE 2), which is produced by type two alveolar epithelial cells, is the receptor for SARS-CoV-2. The S proteins are cleaved to S1 and S2 subunits. The S1 subunit mediates ACE2 attachment through the Receptor – Binding Domain (RBD). The S2 subunit, containing the fusion peptide and trans membrane domains. And fusion of viral host cell membranes[10].

To allow fusion, coronavirus S protein must be proteolytically cleaved by host cell-derived proteases.SARS-CoV uses the cell surface serine protease TMPRSS2 for priming and entrance, with the support of endosomal cysteine proteases cathepsin B (Cat B) and Cat L. TMPRSS2 is expressed in the human respiratory tract. TMPRSS2 is to prevent SARS-CoV-2 entry in the lung cell lines and primary lung cell[11.] The 2 furin cleavage sites cause the replication and invasion of virus. S proteins caused after leaving the epithelial cell and furin is found in respiratory tract. It can cause the infection to spread through other cell. The interaction of TMPRSS2 and furine determine the degree of protein priming[1].

Challenges In COVID – 19 Treatments:

COVID-19 is caused by the virus SARS-CoV-2. Viruses can change their appearance due to replication, which is referred to as "mutation." A virus is dubbed a "variant" of the original virus if it has one or more mutations.If a virus spreads widely in a community, it can cause a variety of illnesses, including virus mutation. The majority of viral mutations have no effect on the virus's capacity to infect and cause disease.Changes in the genetics of viral material exist, and these changes have an impact on virus attributes such as severity and transmission[1].The vaccines developed for COVID-19, is the result of great triumphs that vaccines have had are having in the control of infectious diseases. As a result, mutations in the virus should not render vaccinations ineffective against one or more variants; instead, vaccine composition can be altered to defend against these variants[12].Antiviral drug used is interferon, which is effective against COVID-19. Antiviral drug interferon is used. This is effective against COVID-19.The HIV-1 protease inhibitors ritonavir and lopinavir, as well as the hepatitis C virus protease inhibitors danoprevir and favipiravir, are among the antiviral medicines available[13].Remdesivir, a nucleotide analog and it is developed for Ebola Virus, and it is reported as potential treatment of COVID-19. Remdesivir is a phosphoramidate prodrug with broad – spectrum activity against viruses such as SARS-CoV and MERS-CoV. The FDA has given Remdesivir, a viral RNA polymerase inhibitor, approval for the treatment of coronavirus.Remdesivir combined with chloroquine or interferon, as well as alone it demonstrated the blocking of SARS-CoV-2. Chloroquine and Hydroxychloroquine are antimalarial drugs. It was recently reported as potential broad spectrum antiviral drugs. Chloroquine increases endosomal PH, which prevent virus/cell fusion. Interferes with the glycosylation of cellular receptors of SARS-CoV Hydroxychloroquine is proposed to control the cytokine storm occurs in SARS-CoV-2 infected patients. Hydroxychloroquine is significantly more potent than chloroquine in vitro and lower potential for drug- drug interaction than chloroquine. The Taiwan CDC declared Hydroxychloroquine as an important anti SARS-CoV-2 agent on 26 March 2020[13, 14].

Nanomedicine For COVID-19:

Nanomedicine is branch of medicine and it is application of nanotechnology to medicine. The term nanomedicine was first established in late 1990[15]. Nanomedicine's further development will give various benefits, including bioavailability, dose-response, effectiveness, personalisation, and targeting ability[16]. In nanomedicine use knowledge and techniques of Nano science for disease prevention and medical biology. Nanomaterial used in the drug delivery and selection of the physicochemical features of drugs. Andnanoscale materials include,nanorobots, biocompatible nanoparticles. Nanoparticles are organic or inorganic[17].Structures and sizes in 1- 100 nm and it is similar to the DNA plasmid and antibodies[18].Nanomaterial are used

in the Health-care application such as imaging tools, wound dressing, sanitizers, diagnosis, anticancer therapies, pharmaceutical, vaccines, diagnosis techniques[19].Nanomaterials are obtained from the polymers and it is called as polymeric nanoparticles, surfactant, lipid and proteins are used in nanomedicine. Polymeric nanoparticles show a lot of promise for targeted drug delivery in a variety of diseases[20].Nanotechnology and Nanoscience open up new possibilities for treating diseases like pulmonary and haematological disease, as well as cardiovascular disease[21].Nanomaterials have been successfully used to capture, detect, or inhibit coronavirus cell replication/ cell entry in human host cells, preventing infection, and their potential for immunoengineering, diagnosis, nanovaccines, repurposing medication, and disinfectant surfaces targeting the novel coronavirus has been demonstrated (SARS-CoV-2).Nanocarbon, biopolymeric, copper, and silver nanoparticles could be used as virucidal and antiviral agents for reusable filter media and surfaces, as well as for self-cleaning.These nanoantivirals, copper, zinc, and silver, are utilised in COVID-19 management and nanomaterials to control other viral human infections such as HIV-1, influenza, hepatitis, herpes simplex, and zica virus[22].

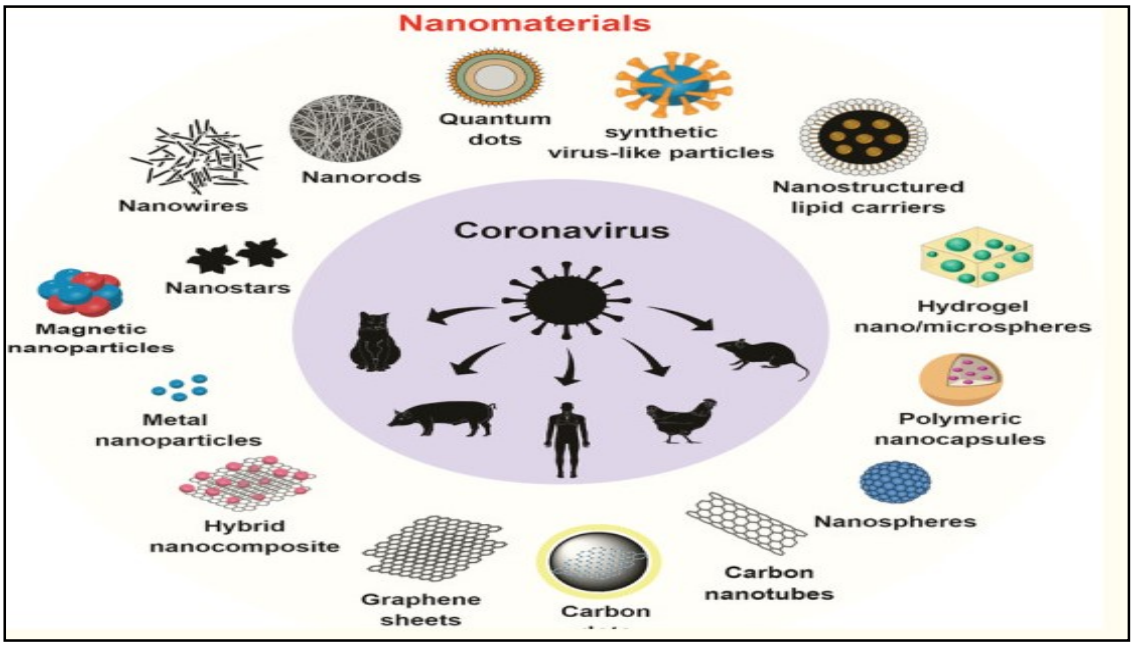


Figure 2. TYPES OF NANOMATERIALS22

Silver nanoparticles (Ag NPs) are metal nanoparticles with unique catalytic, chemical, electrical, and optical capabilities that can be adjusted by size, shape, surface nature, and other factors. Silver is suitable for all pathogen such as fungi, bacteria and viruses. Silver nanoparticles apply their antiviral effect on SARS-CoV-2 by disrupting disulfide bonds on the angiotensin converting enzyme-2 (ACE 2) receptor and spike proteins[23].Coppers have natural ability to help in the functioning of critical immune cell, including natural killer cells, B cells, T helper cells, macrophages and neutrophils and potential therapeutic agents against SARS-CoV-2 Internally and externally to the host. Copper has antiviral properties and is employed in nanomedicine, as well as being vital in the battle against inflammation. Copper nanoparticles may also increase the efficacy of antiviral drugs include, ritonavir, remdesivir and arbidol[24]. Lipid based nanoparticles are made up of lipid vesicles that transport lipophilic and hydrophilic drug to their target. Lipid based nanoparticles (e.g. Liposomes, Bilayers, Micelles)these nanoparticles serve a significant role in drug transport to the lungs for COVID-19, tuberculosis, and asthma treatment.Vaccines that are used to prevent and eradicate infectious disease infection.Nano vaccines' actions are influenced by their size, hydrophobicity, charge, and interactions with biomolecules in the biological system.Nano vaccines improve stability, half-life, and antibody-mediated and cell-mediated immunity stimulation, among other things. Nanoparticles operate through different mechanisms from inhibition of attachment, entry restriction to blocking of viral replication for COVID-19.Many nanoparticles for antiviral activity acting as a through inhibitors of viral entry, inactivating viruses, competing for receptor binding sites with virus and blocking of viral replication. Nanoparticles plays most important role in targeted and non-targeted drug delivery in patient suffering from COVID-19[25].

CONCLUSION:

COVID-19 is the most dangerous disease in worldwide. The number of peoples is affecting by a coronavirus in all countries. Many researchers are attempting to eradicate or minimize the coronavirus. Nanomaterials were used in the creation of vaccines as well as in the preparation of PEP items like as masks, sanitizers, and gowns. In this review, we have been focused on the nanomedicine to combat COVID-19 in that the replication in coronavirus, challenges in COVID-19 treatment. Inhibition of viral comprehension of nanoparticles and SARS-CoV-2 interactions using nanotechnology in a traditional medication delivery method. More studies are required so that a coherent fabrication of targeted therapeutics can meet. Nano technology could represent a convenient strategy along with other approaches to achieve the treatment of COVID-19.

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