"Application of nanotechnological based drugs in management of COVID 19"

A dissertation

submitted in partial fulfilment of the requirements for the degree of

Master of Technology

BIOMEDICAL ENGINEERING

BY
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(2K19/BME/03)

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CERTIFICATE

This is to certify that the M. Tech thesis entitled "**Application on nanotechnological based drugs in management of COVID 19**" submitted by **Miss Vaibhav Sharma (2K19/BME/03)** in the partial fulfilment of the requirements for the reward of the degree of Master of Technology, Delhi Technological University (Formerly Delhi College of Engineering, University of Delhi), is an authentic record of the candidate's own work carried out by her under my guidance. The information and data enclosed in this thesis is original and has not been submitted elsewhere for honouring of any other degree.

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DECLARATION

I, **Vaibhav Sharma** 2K19/BME/03 student of M. Tech. Biomedical Engineering, hereby declare that the Dissertation Project entitled "**Application of nanotechnological based drugs in management of COVID 19**" is submitted by me to the Department of Biotechnology, Delhi Technological University, Delhi in partial fulfilment of the requirement for the award of the degree of Master of Technology. This work is original and not copied from any source without paper citation. I have honoured the principles of academic integrity and have upheld the normal student code of academic conduct in the completion of this work.

DATE: **31st July2021**

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Abstract

The corona virus outbreak is wreaking havoc on healthcare and socioeconomic growth around the world. Furthermore, the rapid mutation of the corona virus, as well as adverse effects in a long use, is a significant public health issue. Therefore, innovative treatment methods are needed. In view of corona virus outbreak, this article is about the nanotechnology, that holds tremendous promise for understanding the virus's structure, development, and lifespan. Nanotechnology has the potential to open up new avenues for the advancement of cost-effective and scalable detection methods, personal protective equipment that is both secure and efficient, as well as modern medical solutions. We go through the basic contributions that nanotechnology can make in the fight against COVID-19 and other pandemics in greater detail. Since coronaviruses are nanoscale in size, nanobiotechnology holds the command in treating and controlling the surge of corona virus. The microbes and nanostructures interaction is rapidly revolutionising the biomedical sector, with benefits in therapeutic and diagnostic applications.

CHAPTER 1

NANOTECHNOLOGY

Nanotechnology may be used to supply a extensive variety of merchandise relevant to an similarly extensive plethora of clinical areas. “Creation,” “exploitation,” & “synthesis” are phrases related to the term "nanotechnology" is used to describe a technique that involves the use of very small substances that degree much smaller than 1 mm. “Nano” is a term that comes from the greek language “nanos”, which means " teeny-tiny, dwarf or very small". Nanotechnologies are usually labeled as dry, wet & computational. Wet nanotechnology is related to dwelling organisms inclusive of tissues, enzymes, membranes, and different mobile components. Dry nanotechnology is related to bodily chemistry and the manufacturing of inorganic items, inclusive of carbon & silicon. Computational nanotechnology is related to simulations of nanometer-sized structures. These three dimensions are (wet, dry & computational) rely upon every different for most beneficial functionality In latest years, noble steel nanoparticles had been the concern of centered studies because of their specific optical, electronic, mechanical, magnetic, and chemical residences which might be extensively one of a kind from the ones of the bulk materials (Mazur, 2004). These unique & specific residences may be due to their diminutive sizes & massive floor areas. For those reasons, steel nanoparticles have discovered makes use of in lots of programs in one of a kind fields, inclusive of catalysis, electronics & photonics. The creation of silver nanoparticles has received a lot of attention mainly big interest because of their numerous residences and makes use of, like optical & magnetic polarizability (Shiraishi and Toshima, 2000), electric conductivity (Chang and Yen, 1995), catalysis (Shiraishi and Toshima, 2000), antimicrobial & antibacterial activities (Baker et al., 2005; Shahverdi et al., 2007).

Lately, major importance has been given to research in nanotechnology field counting to its applications in versatile fields. This led to union of engineering sciences, chemical, physical, and biological which develop novel techniques in operating and controlling the study at the atomic level. The major reason of getting an utmost attention at the Nano-levels is its profound properties being exhibited by these materials at small size. Some changes are expressed in a noteworthy manner at Nano scale which is not much pronounced at micro-scale. One such example is surface area to volume ratio increases, which amends the catalytic, thermal and mechanical properties of the material. This change leads to increasing superiority of atoms present on the surface of the particle over those in the interior

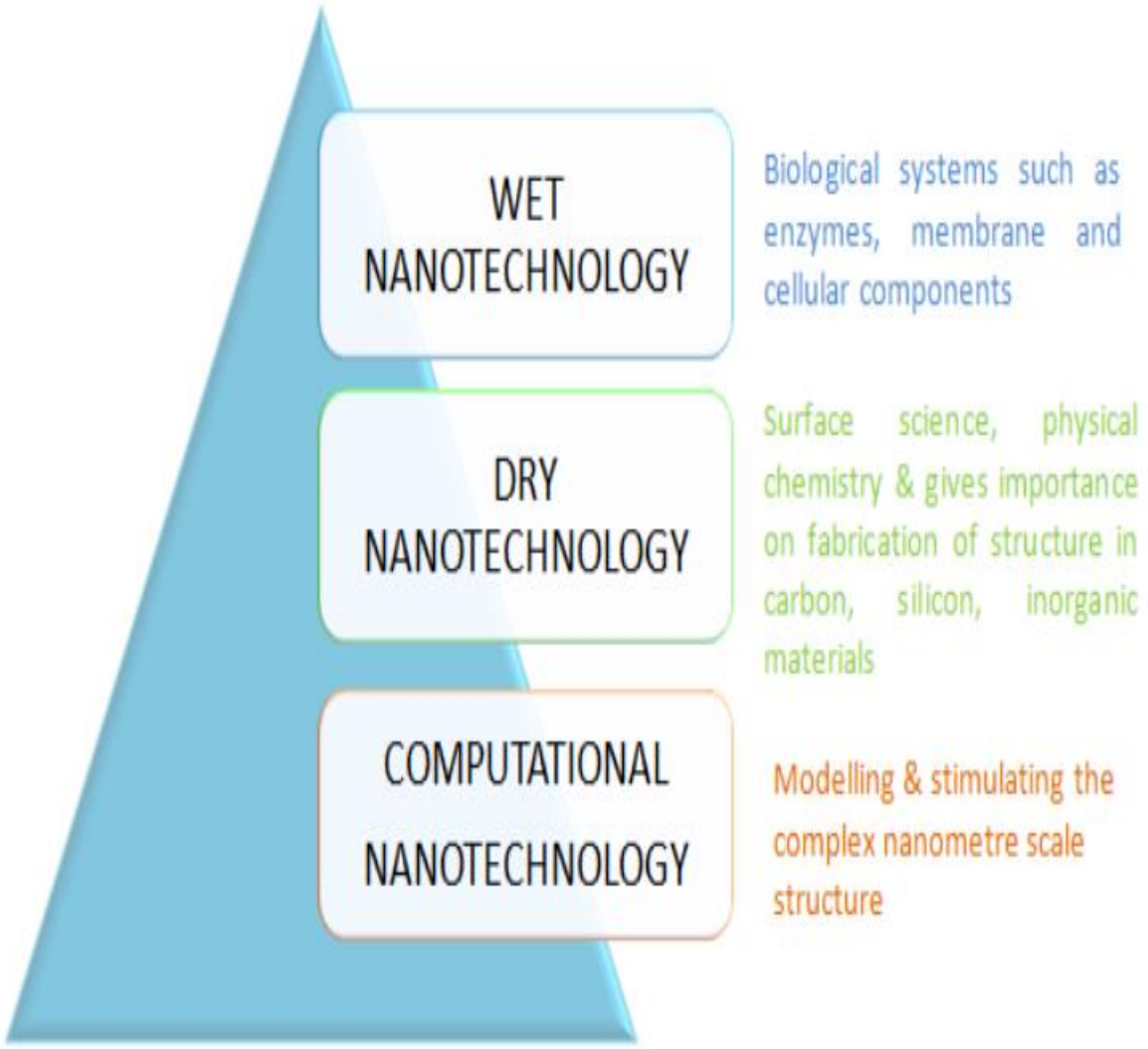

Fig 1.Different types of nanotechnology

In the treatment of many illnesses, getting medicinal compounds to the desired location is a critical issue. Poor biodistribution, unfavourable side effects, limited efficacy and a lack of selectivity define traditional medication use of drugs. Controlling drug delivery, for example, has the potential to circumvent these constraints by delivering drugs to the point of action. Furthermore, the drug delivery method protects the medication against fast breakdown or removal. It

also improves medication concentration in target tissues, allowing for lower therapeutic dosages.

When there is a mismatch between a drug's dosage or concentration & its healing or harmful effects, this sort of therapy is necessary. A more dependable technique in medication delivery is to target cells or particular tissues using specifically tailored carriers that are linked to medicines. Cell or tissue specific targeting is a term for this method. The foundation of nanotechnology is a more fundamental and effective technique that is reducing the size of a specific formulation and developing its routes for an appropriate drug delivery system. Nanoparticles have shown to have a lot of potential as medication carriers thanks to recent advances in nanotechnology. These approaches make nanostructures a desirable material for biological purposes, gaining prominence in pharmaceutical sciences as a result. Furthermore, these approaches aid in the reduction of toxicity, the enhancement of release, the improvement of solubility and bioavailability, and the provision of improved drug formulation options. Drugs in the nanoscale size range are available thanks to nanotechnology, which improves performance in a variety of dosage forms. The following are some of the advantages of nanosizing:

- Improved solubility
- enhanced oral bioavailability
- enhanced dissolution rate
- More surface area
- Less dosage amount required
- Faster start of therapeutic effect

Nanotechnology has transformed the field of medicine by allowing nanoparticles to be created & applied for diagnostics, treatments, & as biomedical research instruments. Nanotechnology now allows for molecular-level therapy, which might aid in disease treatment and aetiology. The created nanomaterials system, which can be readily utilised in the treatment & detection of different infection, notably cancer, is urgently required due to severe limitations of traditional medicines (such as non-specificity of drug action) (have significant drawbacks, such as low specificity or sensitivity & medication toxicity). Nanoparticles have recently been used to produce a number of innovative and advanced cancer detection techniques. Molecular research tools, fluorescent materials, medications including targeted antibodies, & contrast agents are all examples of nanostructures that have been developed. Nanoparticulate systems including paramagnetic nanoparticles, quantum dots, nanoshells, and nanosomes have

recently been utilised for diagnostic reasons. Nanotechnology has a superior safety profile when it comes to medicines with a high toxicity capability, & these nanoforms may be guided to operate exactly on target tissue using both active and passive methods. Other treatment techniques are also being explored, as an example, heat-induced ablation of cancer cells using nanoshells & gene therapy. The early-stage identification of cancer cells &/or particular tumour biomarkers, as well as the improvement of treatment efficiency, are all goals of nanoparticle-based drug delivery methods.

Drug targeting and delivery using nanoparticles

Specific medication targeting and delivery platforms based on nanoparticles minimise toxicity & other adversities while also improving the therapeutic index of the targeted medicine. Development of appropriate targeted delivery systems, which has been taking the lead in what nanotechnology has to offer, notably in cancer therapy, is a key goal of nanotechnology. is concerned with resolving the MDR issue. These types of tailored delivery systems based on medication ‘Nanosizing'

- Improved solubility
- enhanced oral bioavailability
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As a result of these benefits, the most effective targeted therapeutic nanoparticle has been developed, with capability to transform the drug development process & reshape pharmaceutical industry's landscape. Nanoparticles have showed promise in transporting variety of compounds to targeted locations in the body due to their unique physicochemical characteristics. These tailored nanomedicines may increase a drug's therapeutic index by boosting its effectiveness and/or tolerance in the body.

Nanomaterials

Nanoparticles are substances having normal length of much less than one hundred nanometers. These substances have emerged as primary actors in contemporary-day remedy in current years, with makes use of starting from assessment sellers in clinical imaging to gene vendors for particular mobileular distribution. Chemical reactivity, electricity absorption, and organic mobility are only a few of the features that distinguish nanoparticles from bulk substances simply due to their length.

Nanoparticles have a plethora of benefits in contemporary medicine. In certain cases, nanoparticles make it possible to undertake tests and treatments that would otherwise be impossible. Nanoparticles, on the other hand, provide distinct environmental and societal issues, notably in terms of toxicity. This study will focus on nanoparticles' important contributions to contemporary medicine, as well as the environmental and societal implications of their use.

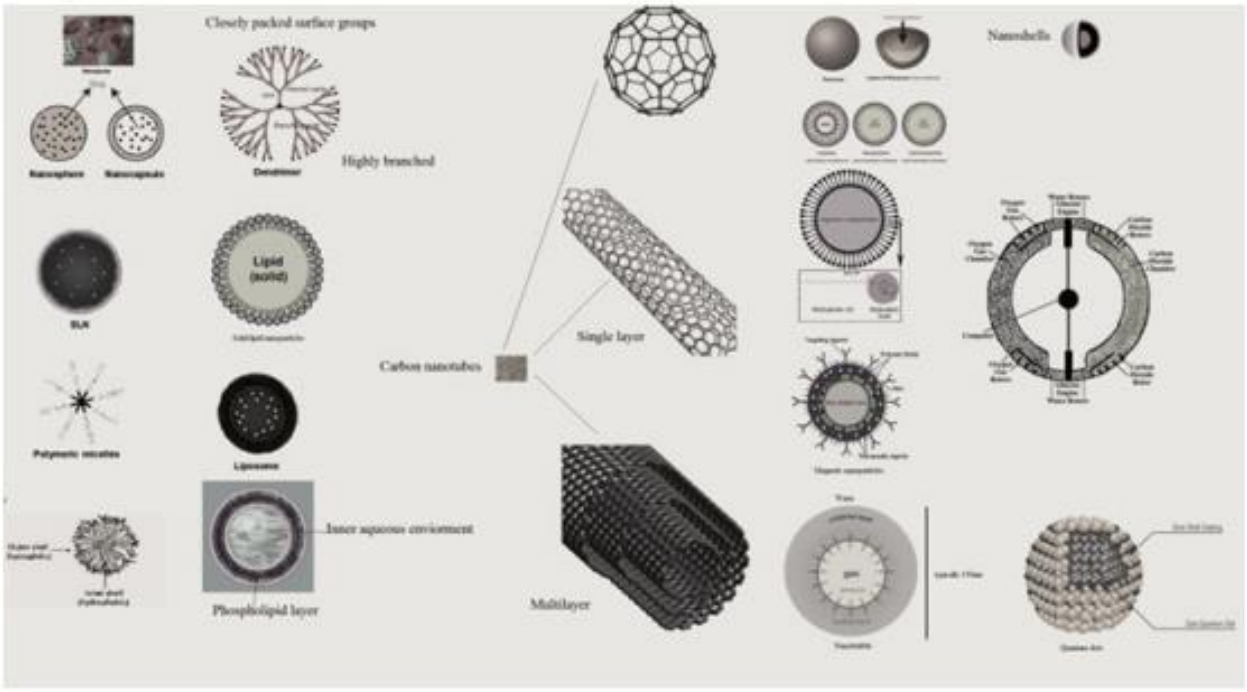

Fig. 2.1 Various nanoforms and their morphological features

Nanomaterials have a high biomedicinal efficiency on a variety of pathogens, as well as chemical stability because of its large surface to volume ratio. Biologically inspired nanoparticle preparation methods have emerged as a

critical topic of nanoscience in the twenty-first century. In all disciplines, the green mode produced phytomediated production of nanoparticles must acquire traction. Anticancer, nanomedicine, antibacterial agents, antioxidants, and diagnostics all benefit greatly from nanomaterials. Metal-related nanoparticles have a vital role in a different sectors, including electronics, medicine, biology, physics, and chemistry. Nanomaterials exhibit novel features in optics, biology, catalysis, and magnetic applications because of its large surface to volume ratio. The goal of this research is to give a broad overview of the function of nanoparticles in COVID 19 management.

CHAPTER 2

Types of nanomaterials

Nanoparticles are substances having normal length of much less than one hundred nanometers. These substances have emerged as primary actors in contemporary-day remedy in current years, with makes use of starting from assessment sellers in clinical imaging to gene vendors for particular mobileular distribution. Chemical reactivity, electricity absorption, and organic mobility are only a few of the features that distinguish nanoparticles from bulk substances simply due to their length.

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The various types nanomaterials and their uses in medicinal technology are described in the table on the next page.

Nanoparticles of various forms and their uses:

Types of nanoparticles	Applications
Solid lipid nanoparticles (SLNs)	Antiviral medications such maraviroc, efavirenz, darunavir, zidovudine, ritonavir, and lopinavir have been delivered using SLNs. As a result of this application, first-pass metabolism is reduced, and tissue distribution is improved.
Nano emulsions (NEs),	increases water solubility, bioavailability, and lymphatic absorption and this can be achieved by combining medicines like saquinavir or indinavir.
Polymer-based nanoformulations	Preventing early drug degradation, Improves pharmacokinetic characteristics and reduces negative effects by reducing nonspecific interactions in the serum. They also worked against HIV, HSV, and hepatitis B. have the ability to target monocytes and macrophages in the brain and lymphatic system, as well as combat viral infections such as HIV. The therapeutic agent molecules can shrink or enlarge when a polymer and a therapeutic agent are combined.
Dendrimers	have a high cell absorption rate, a prolonged circulation period, and a focused delivery system. Glycodendropeptide has recently been mentioned as a potential viral therapy. Also blocks viral entrance fusion which is effective in the treatment of HIV and HSV2. Organic nanoparticulated dendrimers can affect antibody-mediated responses and CD8+ T cell activation, as well as gene expression by inactivating small RNA.
Nanocapsules	Can be utilised for increased drug loading and targeted drug delivery. Nanocapsule was used to delivere azidothymidine triphosphate (AZT-TP) drug directly to the cytoplasm which was made up of a poly core. And polyethyleneimine to prevents “leakage” of AZT-TP.
Nanospheres	have a faster drug clearance rate. Acyclovir-loaded chitosan nanospheres are more effective than acyclovir alone in treating herpes.
Peptides	Antiviral effects can be found in peptides derived from natural and microbiological sources. It come from bacteria, plants, mammals, marine sources, frog skin and among other things. HIV, DENV, H1N1and HCV were all treated with it.
Carbon nano formulations (like Carbon nanotubes (CNTs), fullerenes and graphene oxide nanoparticles)	Used in delivery of chemotherapeutic drugs having high pulmonary toxicity.

	The vaccine for the foot-and-mouth virus can be made with functionalized carbon nanotubes that transport virus peptides. Graphene oxide (GO) is antibacterial and antiviral, and it inactivates viruses before they enter the cell. After 1 hour of incubation with GO, glycoprotein spikes in the virion membrane can be eliminated. Graphene's exceptional mechanical strength and surface loading capabilities make it ideal for carrying antiviral medicines. Fullerenes, that are completely made up of carbon atoms. They can impede HIV replication by filling the hole left by HIV proteases.
Quantum dots	QDs contain both optical and electrical features that are desirable. The QDs are used in viral illness sensing, imaging, and therapy. The conjugated quantum dot has been shown to be effective with anti-AIDS medications and can transport saquinavir over the BBB.
Gold nanoparticles (AuNPs)	AuNPs (gold nanoparticles) are used in biological imaging. AuNP can infiltrate lymphocytes and macrophages, which are HIV-replicating cells. It also stops HIV from replicating in mononuclear cells in the blood. By imitating a virus's target binding receptor, AuNP can cause viral deformation.
Silver nanoparticles (AgNPs)	These are antimicrobial and effective in therapeutic peptide delivery. Many viruses are resistant to silver nanoparticles (AgNPs), which can interfere with respiratory and electron transport chain enzymes. These trigger the ROS-mediated signalling pathway as well as the blocked agglutination of RBCs in fighting against H1N1
Zinc oxide nanoparticles	T cell and Ab-mediated responses to HSV-2 are improved by it which further can help to combat viral infection.
Iron nanoparticles (γ-Fe2O3/ Fe2O3/Fe3O4),	In viruses like, H5N2, HCV, and Zika can impede viral growth even at the post-entry cellular level.
Ttitanium nanoparticles (TiNPs)	For bacteriophages and H3N2 viruses, TiNPs with features like high solubility and photocatalytic activity can have broad antiviral capabilities.

CHAPTER 3

COVID 19

3 coronaviruses have been found in bats and have been transmitted to human populations & produced an ever-increasing breakout of a pandemic on a huge scale during the previous two decades (Perlman, 2020; Wang et al., 2020a). MERS (Middle East respiratory syndrome coronavirus) & SARS-CoV (severe acute respiratory syndrome coronavirus) (De Wit et al., 2016; Cui et al., 2019) are two previously known viral zoonotic viruses that may cause severe respiratory illness in humans (De Wit et al., 2016; Cui et al., 2019). (Luk et al., 2019; Phan, 2020). Since its emergence in Wuhan, China, in December 2019, SARS-CoV-2, new coronavirus (that causes COVID-19), has spread like a pandemic (Chan et al., 2020a). With a 2% fatality rate, it creates an acute and devastating illness. In humans, however, this new coronavirus is generally linked to a varying degrees of severity respiratory illness (Zhu et al., 2019; Perlman, 2020; Huang et al., 2020). As a weird and sophisticated pathogen, this virus has the potential to travel between species & cause a various level of illnesses (Fung and Liu, 2019). A virus is a prominent cause of zoonotic illness due to the frequent contact between people and animals. COVID-19 has become a worldwide health emergency owing to its human-to-human transmission (Chan et al., 2020a; Organization, 2020).

The World Health Organization (WHO) turned into notified in December 2019 of a pneumonia case with an unknown starting place found in a seafood marketplace in Wuhan, Hubei Province, China. Based on laboratory findings on the subject of extreme acute respiration syndrome (SARS) & Middle East respiration syndrome coronavirus, the aetiology turned into recognized as novel coronavirus (n-CoV) (MERS). Since a unmarried example of pneumonia in Wuhan, it has grown right into a worldwide phenomenon in a brief length of time. On January 30, 2020, WHO proclaimed the 2019-nCoV a Public Health Emergency of Global Concern, emphasising the want for worldwide action, global cooperation, solidarity, and teamwork to include the outbreak. On February 11, 2020, WHO named the unconventional coronavirus sickness COVID-19, and on March 11, 2020, WHO decided that COVID-19 can be categorised as a pandemic [1].

In humans, six coronaviruses had been diagnosed so far. HCoVs-NL63 (alphaCoVs);, HCoVs-229E HCoVs-OC43 & HCoVs-HKU1 (beta-CoVs); SARS-CoV (excessive acute breathing syndrome-CoV); & MERS-CoV (excessive acute breathing syndrome-CoV) (Middle East breathing syndrome-CoV). New coronaviruses had been found to rise up in human beings on a

ordinary basis. The great distribution and excessive incidence of coronaviruses, the excessive genetic variety of CoVs paired with common genome recombinations, & sports involving humans & animals are all elements contributing to this. The SARS-CoV-2 virus become diagnosed as a singular coronavirus in bronchoalveolar lavage fluid samples taken from a seafood marketplace in Wuhan, China, the usage of metagenomic sequencing techniques [2].

Virology of COVID-19

Coronaviruses are participants of the Coronavirinae subfamily of the Coronaviridae family, order nidovirales [3] & there are 4 genera withinside the subfamily: Alphacoronavirus, Gammacoronavirus, Betacoronavirus, & Deltacoronavirus Studies say, SARS-CoV-2 is an encapsulated, non-segmented, single-stranded positive-experience RNA virus with spikes at its outer surface. The virus debris are crown-fashioned and feature a diameter of 60–one hundred forty nm, as visible below an electron microscope (14-23). Spike (S) glycoprotein, envelope (E) glycoprotein, membrane (M) glycoprotein, & nucleocapsid (N) protein are 4 key structural proteins. The CoV Spike (S) glycoprotein binds to the host cell's cellular receptors, allowing viral entrance & pathogenesis (Zhu et al., 2018; Li, 2016). A virion is made up of 2 fundamental components: genomic RNA and a nucleocapsid, which is a protein capsid packed in a nucleocapsid. The spike glycoprotein trimmer (S) and the hemagglutininesterase form a phospholipid bilayer that surrounds the nucleocapsid (HE). Envelope (E), Spike (S), Nucleocapsid (N), & Membrane (M) structural proteins are found in all viruses. Aside from structural proteins, they have a number of non-structural and auxiliary proteins. In the viral capsid, the membrane (M) & envelope (E) proteins are grouped together with S proteins (Li, 2016; Luk et al., 2019; Fahimi et al., 2018). The RNA genome of the novel coronavirus-2019 (nCoV-2019) is 29891 nucleotides long, with 9860 amino acids encoded (Luk et al., 2019). The genome of the nCoV-2019 strain contains the following elements: 2 flanking untranslated regions (UTRs), a non-structural polyprotein (7096 aa), a single long open reading frame (ORF1ab) (7096 aa), four structural proteins – Spike (S) (1273 aa), Membrane (M) (222 aa), Envelope (E) (75 aa), Nucleocapsid (N) (419 aa), & 5 accessory proteins (ORF3a (Phan, 2020; Chan et al., 2020b). SARS-genome CoV-2's is equal to that of different coronaviruses. Genome length of SARS-CoV-2, which became currently

sequenced as a member of the coronavirus family, is about 29 nine kb (Lu R. et al., 2020).

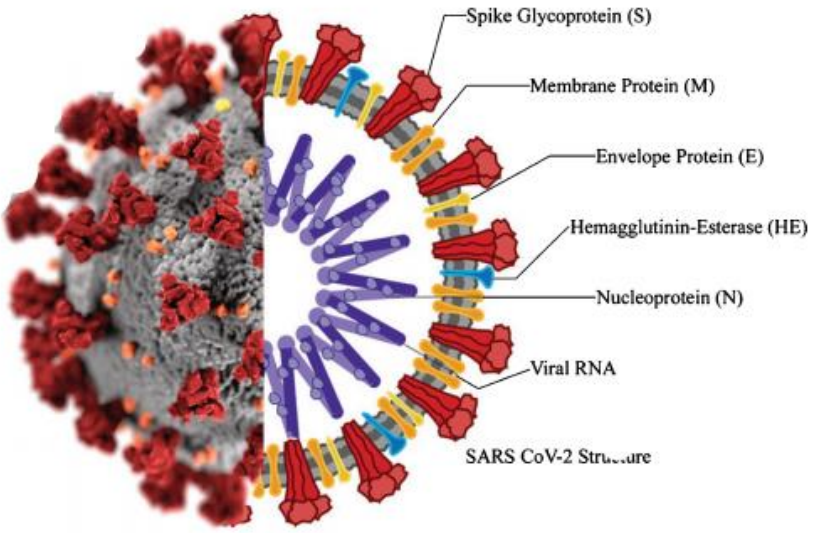

Fig. 2. Illustration of COVID-19 Structure

Spike glycoprotein is answerable for coronavirus access into host cells (S protein) (Li et al., 2005; Li et al., 2003; Li, 2016). Angiotensin-changing enzyme II (ACE2) receptors at floor of host cells are virus's essential focus (21-23). SARSCoV-2's C-terminal domain, is made from envelop-embedded spike (S) protein, binds to angiotensinogen (ACE2) receptor of host cell's (23). The molecular information of this interplay may be illustrated via way of means of fixing the crystal shape of the complicated formed. [4]

The above fig 2. illustrates the structure of covid 19. ACE2 receptors on host cells are the target interest of the corona virus which the widely present in the in human beings withinside the epithelia of the lung and small intestine, which would possibly offer viable routes of access for the SARS-CoV. Because coronavirus access depends on the spike glycoprotein, it's miles a promising antiviral goal. The S1 & S2 subunits are purposeful subunits that make up the S protein. The receptor binding domain (RBD) & N-terminal domain (NTD) make up the S1 subunit (RBD). The S1 subunit's activity is to bind to receptor at host cell (Mei-Yue Wang et al). The complete system of internalisation is confirmed via way of means of the diagram given below.

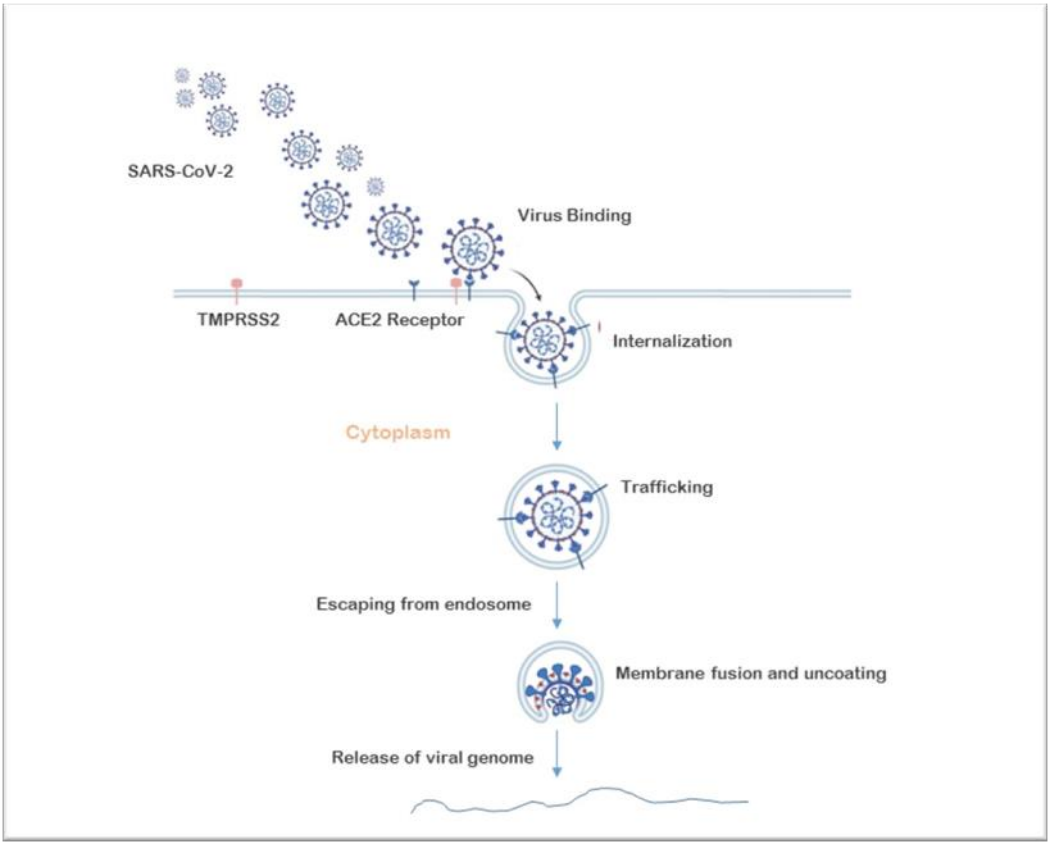

Fig.3 Interaction of corona virus to the host cell.

In the given figure 3, the interaction of corona virus to the host cell is described. At the molecular level, the earliest events of infection (i.e., the virus's contacts with ACE2-expressing target cells) are being unravelled. However, because patients with severe symptoms that appear after a few days or a week usually have a high viral load in their lungs, strategies that not only protect host cells from infection, but also target pre-existing persistent viruses and avoid life-threatening conditions including multiple organ failure& lung hyperinflammation are urgently needed. Through its protease action, the transmembrane serine protease 2 (TMPRSS2) aids cellular entrance. Virus particles are then absorbed and transported to endosomes. The viral DNA is released for protein synthesis because of the low pH of endosomes. New infectious particles are formed & discharged after viral RNA and protein synthesis.

CHAPTER 4

Nanomaterials based drugs in COVID 19

Nanoparticle synthesis has sparked a plenty of interest in latest years due to its numerous beneficial properties and applications in a variety of fields. Nanotechnology is a department of science and technology and generation involved with studies and improvement on scales smaller than one hundred nanometers. Nanomaterials are substances with a length variety of 1–one hundred nm (Bhushan B (2007)). Nanomaterials have dimensions at the nanoscale starting from 65–one hundred twenty five nm in diameter (Shereen MA et al, (2020)) and as a result, they've a excessive biomedicinal overall performance on a number of pathogens, in addition to chemical balance because of their massive floor to quantity ratio (K.Velsankar et al.,2020) Nanoparticles are deployed to have antiviral homes via a number of mechanisms. Nanoparticle's particular homes, consisting of (a) High floor location to quantity ratios that permits the massive drug payloads to be carried. (b) Tiny particle length can facilitate the drug transport into anatomically privileged locations. (c) Tunable floor fee can facilitate cell access via the negatively charged cell membrane. These all makes a nanoparticle a mighty remedy device virus (Lavanya Singh et al.,2017). Many nanotechnology-primarily based totally systems have previously been powerful in before-clinical research against warfare numerous human-viral-pathogens consisting of HIV virus, humans papillomavirus, and breathing viruses, herpes simplex and nano-technology gives a number techniques to fight viruses each out of doors and withinside the host (Carsten Weiss et al.,2020). Nanotechnology-primarily based totally strategies may be used to resource withinside the warfare towards COVID-19 and any viable pandemics in diverse methods like (a) to discover contamination or immunity, noticeably precise, rapid, and responsive exams have to be used (serological exams) (b) surfaces coatings which might be immune to viral adhesion and may inactivate viruses (c) improvement of gear of contact tracing (d) nanotechnology primarily based totally face masks (e) nanomaterials may be used for straight transport of broadspectrum anti-virals and-to assist centered treatment plans to the lungs in new vaccines and medicines

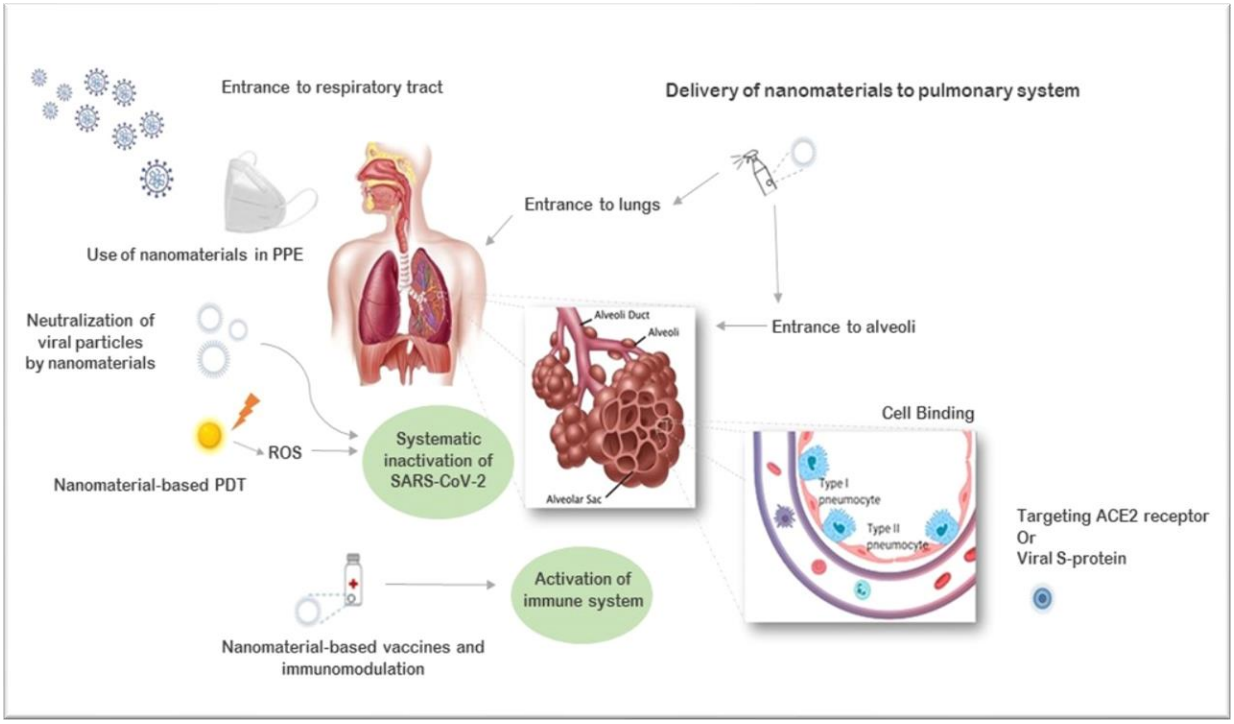

Fig1. Nanomaterials for COVID-19 prevention and treatment. SARS-CoV-2 can be prevented from entering the respiratory system by incorporating nanomaterials into personal protective equipment (PPE). Nanomaterials may also be used in inhalators to administer medicines to the lungs. Targeted nanoparticles (NPs) directed against angiotensin-converting enzyme 2 (ACE2) receptors or viral S protein can prevent viral particles from binding to cells in the alveoli. Various methods, such as neutralising NPs or photocatalytic nanomaterials, may be used to inactivate viral particles systemically.

Novel treatment; An engineered nanoparticle against corona virus- The nanotrap

Keeping this promising antiviral goal that spike glycoprotein is required for the entry of corona virus, scientists at Pritzker School of Molecular Engineering (PME) at the Chicago University harnessed and integrated the power of nanotechnology and immunology to create Nano traps, a new form of potent, powerful nanomedicine for containing and clearing SARS-CoV2. The SARS-CoV2 infections in humans cells and lung organs was totally stopped by the Nano traps. Nano traps are reliable, secure, stable, and mass-producible. The nano trap is about 500 nm in diameter is made by Pritzker School of Molecular Engineering (PME) at Chicago University to trap SARS-COV2 virus. The nano trap consisting of dense amount of ACE2 protein which could act like the real target cell

receptors for SARS-COV2 virus. As the virus binds to the nano traps, the traps aside the virus from other cells and direct it to the immune system for destruction. The designed nano trap is made up of FDA approved PLA (Poly Lactic Acid) polymeric core ACE2 receptors at surface and a liposomal shell. In principle, these nano traps may be used on other virus types too, potentially opening up a new way to combat the virus in the future. Despite the fact that the therapy is still in its early stages of development, the researchers believe it may be used to treat COVID-19 as a nasal spray (Min Chen et al). The below figure shows the mechanism of action of the designed nano trap.

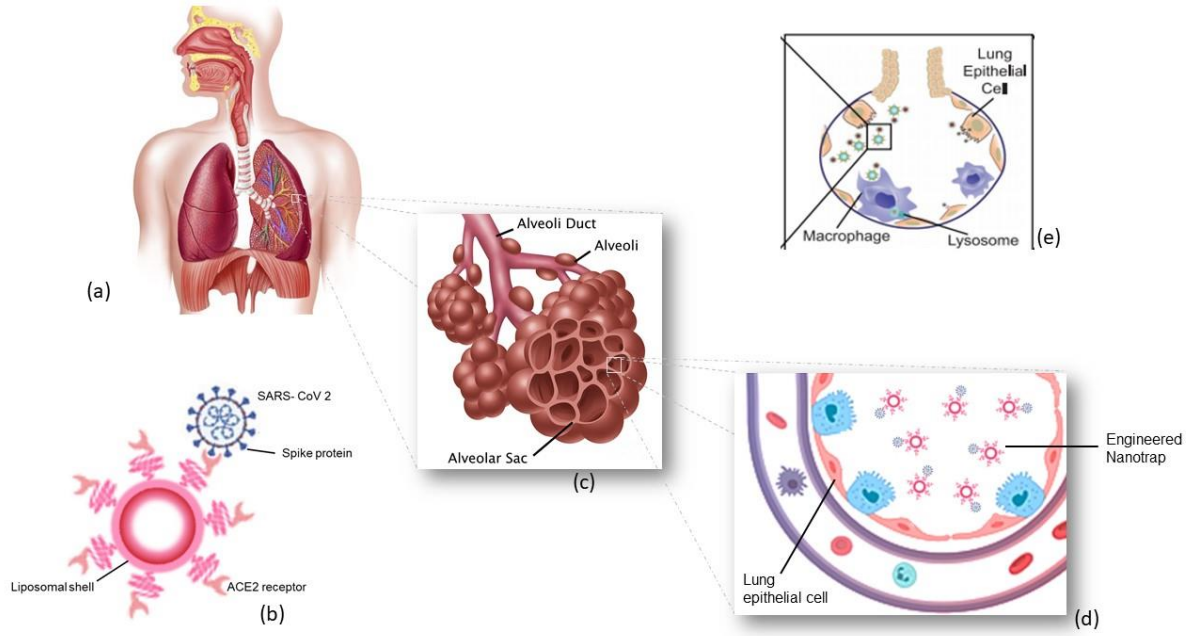

Fig.3. The above figures show the engineered nanotrap interacting with corona virus. (a) showing the inhaled nanotraps in lungs. (b) showing the interaction of corona virus and the nanotrap. (c) nanotraps reached the site of action ie. alveoli. (d) nanotrapes interation at the site of action and later engulfed by the macrophages.

SARS-CoV-2 Photodynamic Inactivation

Photodynamic therapy (PDT) was first used clinically against viruses in the 1970s, relying on the formation of reactive oxygen species (ROS) to destroy nucleic acids, virus proteins and lipids if present. Primarily photodynamic therapy is largely utilised to treat various oncological illnesses. Photodynamic treatment (PDT) is a novel way of inactivating SARSCoV-2, in sum to pharmacological and vaccine based anti-viral treatments. P.D.T uses a light-based viewpoint to attack target cells by exciting photosensitive compounds, known as

photosensitizers, with radiation with wave-length similar to absorption-spectrum to shape ROS (reactive-oxygen-species) withinside the oxygen presence, ensuing in mobileular . But Due to the hydro-phobicity of photo-sensitizers (PS), terrible target selectivity, and low tissue penetration capabilities, clinical usage of PDT is limited.selectivity, and low tissues penetrations capabilities, clinical usage of PDT is limited.

PDT using graphene and fullerene are also viable possibilities for virus inactivations. P.D.T was shown to be effectively against vesicular stomatitis viruses (VSV), influenza A virus (IAV), H.S.V-1, H.I.V-1, mosquito irido virus (MIV), Semliki Forestvirus (SFV), and phage MS2. Various 2D nanomaterials like graphene-based materials, graphitic-carbon-nitride, MXenes, tungsten-disulfide, black phosphorus & molybdenum-disulfide have also been found to significantly enhance the efficacy of photodynamic therapy for cancer treatment. As a result, it's important to check if nano-material-based P.D.T techniques can be used to in-activate SARS-CoV2.

Mesenchymal Stem Cells (MSC) transplantation has the potential to improve COVID-19 outcomes.

The study, which was published in March 2020, looked into the possibility of Mesenchymal Stem Cells (MSCs) transplantation improving the outcomes of COVID-19 pneumonia patients. There was a considerable improvement in the functional conditions of the individuals after a single dose of MSCs intervention, with no side effects. The pulmonary function of those individuals improved dramatically within two days of MSC implantation. As a result, MSC transplantation was proven to be effective. Other clinical trials assessing the efficacy and safety of MSCs extracted from a variety of allogenic sources such as adipose tissue, Wharton's jelly, bone marrow, and placenta for COVID-19 have also been registered and over 20 clinical trials have been registered.

MSCs are well-known for their high levels of regeneration and immunomodulatory activity. To mitigate acute respiratory distress syndrome (ARDS), regenerate and repair lung injury, and resist fibrosis, MSCs can release IL-10, VEGF, hepatocyte growth factor, and keratinocyte growth factor. MSCs have the ability to prevent T lymphocytes and macrophages from being abnormally activated and to drive their differentiation into regulatory T

cell subsets and anti-inflammatory macrophages. MSCs are an ideal contender among other current cellular treatments for the treatment of COVID-19 because of their functional characteristics. Because they lack the HLA Class II antigen, they are an excellent candidate for allogeneic transplantation. MSCs' regeneration and repair mechanisms are often based on their ability to replace injured cells, generate anti-inflammatory cytokines, and induce angiogenesis, among other things. Among the several current cell-based therapies for various disorders, MSCs are the most prevalent and widely explored cell type.

When MSCs come into contact with a hostile environment at the target location, they go through autophagy and apoptosis, releasing growth factors and cytokine-rich exosomes, which helps to mitigate disease pathophysiology. As a result, novel procedures and approaches involving stem cell-derived exosomes as an emerging modality have been brought to light, overcoming the constraints and problems of parent cells.

MSC-derived exosomes in covid 19 treatment

Exosomes have been studied extensively since their identification as a method of MSC paracrine impact in decoding the regenerative and molecular elements of treating various diseases. When compared to their biological counterparts, MSC-derived exosomes have various benefits, including high stability, low immunogenicity, simple storage, and the capacity to traverse the blood-brain barrier. The bilipid membrane composition, possibility for off-the-shelf availability, and biocompatibility of these exosomes make them an excellent choice for drug administration. As a result of these intriguing characteristics of exosomes, researchers are investigating their possible usefulness as a therapeutic and pharmacological intervention in the current COVID-19 pandemic. Exosome therapy, as established in the mechanistic approach, can likely avoid the immune system's cytokine storm and enhance endogenous healing through the reparative capabilities of exosomes.

Lee et al. reported in 2012 that exosomes from MSCs had a cytoprotective impact in a hypoxia-induced pulmonary hypertension mouse model. Exosome cargo and mechanistic function in asthma, acute respiration misery syndrome (ARDS), continual idiopathic-pulmonary-fibrosis (IPF), obstructive pulmonary disease (COPD), and pulmonary-arterial-hypertension (PAH), have all been investigated.

Exosomes produced from MSCs may play a role in preventing COVID-19 infection, as shown in a schematic diagram. The drug's synergistic action and exosomes could be used as an effective strategy once more. Exosome therapy, as shown in the mechanistic approach in Fig4., can prevent the immune system's cytokine storm and enhance endogenous healing through the exosomes' reparative capabilities and can act as a carrier for drug delivery.

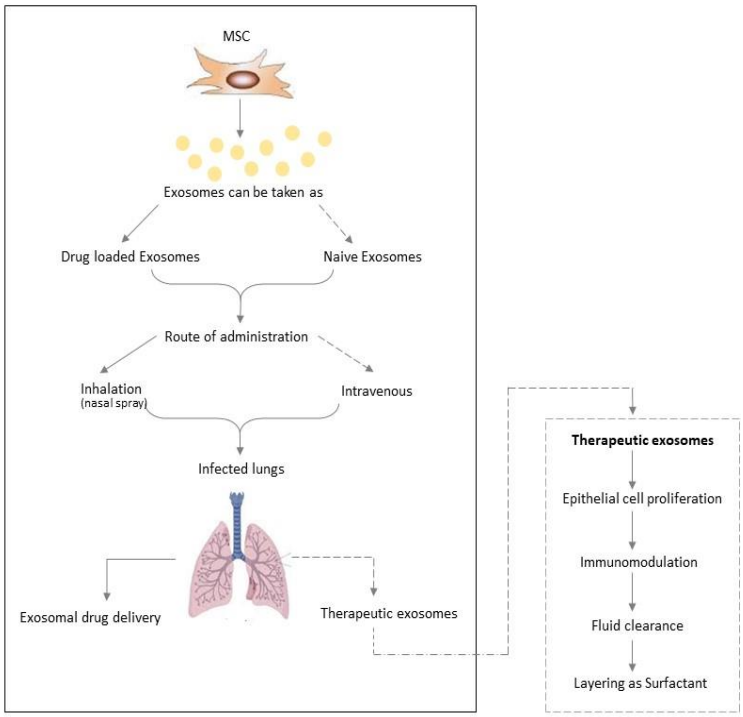

Fig4. The potential role of MSC-derived Exosomes in fighting COVID-19 infection is depicted in this diagram. The drug's synergistic action and exosomes could be used as an effective strategy once more. Here, the exosomes are taken in two ways (a) lungs treated with the drug loaded exosomes (b) lunges treated as naïve exosomes.

According to these findings, MSC-derived exosomes may have the following role in lung pathogenesis: (1) Lung epithelial cell protection and proliferation. (2) Lung Inflammation Reversal. (3) Lung macrophage polarization. (4) in controlling pulmonary edoema and protein permeability in the lungs.

As a result of these intriguing characteristics of exosomes, researchers are assessing their potential relevance as a therapeutic and pharmacological intervention in combating the current COVID-19 pandemic. The administration of MSC-exosomes has a great potential to recover the patient's damaged lungs through numerous pathways, and hence could be a therapeutic nanomedicine intervention for critically ill patients.

Corona virus inactivation using nanotechnology techniques in patients

The respiratory tract (upper airways, lungs) appears to be the main focus of SARS-CoV-2, though other organs (e.g., stomach, kidney) and the vasculature tend to be important targets as well. The uptake of ACE2 by various tissues is most likely determined by its expression.

We will attention our dialogue at the numerous alternatives for inactivating the virus withinside the deep lung and focused on the essential host cells for drug delivery, further to addressing immune-primarily based totally approaches, because the lung is the maximum seriously affected organ.

Because of The quite excessive The virus reaches the alveoli and enters alveolar epithelial kind II cells thanks to an excess of ACE2 and a favourable cell environment (AECII). For the virus, these cells form a clump., which then spreads throughout the lungs, ensuing withinside the loss of lung characteristic visible in intense cases. Airborne nanoparticles are fine acceptable to penetrate into the deep lung because to the physicochemical properties of such aerosols, which arise at the same length scale debris that penetrate maximal without difficulty to the deep airways. As a result, nanomedicine is now working on ways to use nanodevices to deliver medications, therapeutic proteins, and mRNAs to the lungs.

Several nanomaterials were formed, starting from polymers to dendrimers, oligomers, NPs, liposomes, and small molecules. However, powerful scientific translations has been hampered through the reality that after those compounds are diluted, their effectiveness is misplaced because the virus-compound complicated dissociates, permitting to re-start the replication cycle of viruses. Recently, it changed into proven that this dilemma may be triumph over through synthesizing nanoparticles that, as soon as bound, can irreversibly inhibit viral infectivity through completely destroying the virion, reigniting desire for a real, broad-spectrum antiviral drug. Since a drug precise to SARS-CoV-2 is to be developed, an awesome access inhibitor can be targeted on blocking off the interplay of the S spike protein with the cell ACE2 receptor.

Nanomaterials have emerged as potential immunomodulation techniques, capable of stimulating or suppressing immune responses.

Below are the examples in the table given, evidencing the tendency of nanomaterials to modulate the immune system depending on the

functionalization. Nanomaterials have evolved as intriguing immune modulation techniques, with the ability to either stimulate or decrease the immune response.

nanomaterials	**functionalization**	**impact**
graphene oxide (GO)	Amino acid (NH_2) group	With minimal toxicity, GO-NH_2 activates STAT1/IRF1 interferon signalling in monocytes and T cells, resulting in the development of T cell chemoattractants and polarisation of the immune response between macrophage 1 (M1) and T-helper 1 (Th1).
Pristine (a nanodiamond (ND's))	Amino acid (COOH) group ND-COOH	The non-toxicity of amino functionalized NDs (NDs-NH_2), even at high concentrations, suggests that this functionalization could be useful for improving immune-biocompatibility.
	ND-NH_2	Immune responses were more apparent with NDs-COOH (a reduction in monocyte viability was only seen at the highest concentration of NDs-COOH).
Carbon nanotubes		Enhancement of IL-6 release and overexpression of CD25 in human primary monocytes to promote immunological response.
Polystyrene (PS)	PS-NH_2	▪ Non- cytotoxic ▪ Reduces macrophage phagocytosis, which could be due to a drop in ATP.
	PS-COOH	▪ Non- cytotoxic ▪ On macrophages, the cell surface markers CD200R and CD163 were decreased. ▪ Inhibition of IL-10 secretion ▪ TGF-β1 is stimulated in macrophages. ▪ ▪ Induces mTOR kinase activation, a critical regulator of protein production, which could explain the increase in protein and ATP levels in macrophages.

Surprisingly, Authorized adjuvants like AS01 and AS03's capacity to boost adaptive immunity is connected to promote the STAT1/IRF1 interferon signalling which further results in the development of T cell chemoattractants and polarisation of the immune response between macrophage 1 (M1) and T-helper 1 (Th1) as mention in the table above. Recent studies on SARS-CoV and MERS-CoV indicate that developing a The Th1 response is important for infection management, and this may be true for SARS-CoV-2 as well.

Nanomaterials for immunomodulation have been examined and characterised by a number of firms and consortiums residences & cytotoxicity. The introduction of an adjuvant for medical use is a prolonged manner that normally takes a few years and entails complete Phase III randomised trials in massive and various cohorts of subjects. While novel adjuvants are not going for use withinside the contemporary pandemic, the SARS-CoV-2 outbreak presents an possibility to remember nanotechnology's ability for the growth of vaccine adjuvant It is critical to circulate cohesive pipelines spanning in vitro and in vivo research in this scenario on the way to discover candidate substances for medical trying out as vaccine adjuvants.

There has been evidence of immunomodulatory effects on innate immune signalling in particular. Nanomaterials like graphene oxide (GO), for example, can cause macrophages to express IL-1 in response to the inflammasome sensor (NLRP3). And By the same NRLP-induced method, alum, the most extensively used adjuvant in human vaccinations, induces the cytokine to be produced in macrophages. These data suggest that nanoparticles such as GO and alum could be beneficial in biomedical sector.

Remdesivir, an antiviral medication accepted with the aid of using The FDA has approved a COVID-19 treatment for adults in the United States, and it appears to be a potential treatment option. Nanotechnology has already been employed to improve the efficacy of Remdesivir in the context of other developing viral illnesses (Nipah virus), hinting that nanotechnology could be useful in the treatment of COVID-19 and other potential pandemics in the future.

Vaccination

The genetic collection of SARS-CoV-2, the coronavirus that causes COVID-19, was revealed on January 11, 2020, starting a global race to develop a vaccine to combat the disease. The scale of the COVID-19 pandemic's humanitarian and financial impact is driving evaluation of next-generation vaccine generation systems through novel paradigms to speed development, and on March 16, 2020, the COVID-19 pandemic, the primary The COVID-19 vaccine candidate moved quickly through human medical testing.

To facilitate the improvement of COVID-19 vaccines, COVID-19 vaccines, COVID-19 vaccines, COVID-19 vaccines, COVID-19 vaccines, COVID-19 vaccines, CO (CEPI) is taking part with international fitness government and vaccine makers. Vaccine improvement programmes posted via the WHO's respectable and continuously up to date list, in addition to different tasks discovered from publicly to be had and proprietary sources, are protected in our panorama database (5).

Vaccine designing

Vaccine design includes the selection of antigens, vaccine platforms, and vaccination routes and regimens. The immunogenicity of vaccine-derived viral antigens, whether or not an immunological adjuvant is required, and the type of protective immunity that is produced are all determined by the vaccine platform chosen. These characteristics also determine whether a vaccine is appropriate for a particular mode of immunisation and whether a prime–boost vaccination schedule is required to establish vaccine-mediated protective immunity and its long-term durability. Additionally, using live attenuated virus vaccines or inoculation through the respiratory mucosa will demand more extensive safety testing.

SARS-CoV-2 antigens selection.

SARS-CoV-2 viral antigens were chosen. Infectious virion structural proteins include S protein, N protein, matrix (M) protein, and envelope (E) protein. The N protein encircles the positive-stranded RNA genome, which is encased in a lipid

envelope made up of the host mobileular membrane and into which the other three proteins (S, M, and E) are inserted. Only antibodies directed in opposition to the S protein can wreck the virus and save you contamination withinside the case of SARS-CoV. As a result, at the least a chunk of the S protein is covered in all SARS-CoV-2 vaccines in development. Only the S1 area or the RBD may be affected (6).

Antibodies against the S protein as well as Non-neutralizing proteins (E and M) are created as a result of the other exposed proteins (E and M). Other structural (N) and/or non-structural proteins as vaccine antigens may help to promote a more balanced response involving both humoral and T cell-mediated immunity, as non-neutralizing and weakly neutralising antibodies are suspected to have a role in disease ADE. These could be highly expressed proteins, such as the N protein, or functional proteins with a high degree of conservation play an important part in the viral life cycle (7), (8).

Various platforms of vaccines: -

Live attenuated virus, recombinant viral-vectored vaccines that can be bioengineered to explicit goal pathogen antigens in vivo, inactivated or useless virus, protein subunit vaccines, virus-like particles (VLPs), and nucleic acid-based (DNA or mRNA) vaccines are all examples of vaccines that can be bioengineered to explicit goal pathogen antigens in vivo are the six sorts of vaccine structures. Antigens from the goal pathogen have to be added to or generated through the vaccination recipient, in addition to an contamination signal (including a pathogen-related molecular sample or damage-related molecular sample) that indicators and turns on the host immune system. Live attenuated vaccines might also additionally obviously deliver each of those components, while non-viral vaccine structures can supply antigens however regularly require the addition of adjuvants, that are synthetic alerts that alert the immune system (9).

Vaccine name	Vaccine platform	Developer	Clinical trial phase	Clinical trial registrations
BNT162b1/BNT162b2	RNA-based vaccine	Pfizer-BioNTech, Fosun Pharma	Phases I–III in USA, Germany, and China	NCT04368728, NCT04380701, NCT04523571
mRNA-1273	RNA-based vaccine	Moderna, NIAID	Phases I–III in USA	NCT04470427, NCT04405076, NCT04283461
INO-4800	DNA plasmid vaccine	Inovio Pharmaceuticals, International Vaccine Institute	Phases I–III in USA	NCT04447781, NCT04336410
GX-19	DNA plasmid vaccine	Genexine Consortium	Phases I and II in South Korea	NCT04445389
ChAdOx1 nCov-19 (AZD1222)	Adenovirus vector, non-replicating	University of Oxford, AstraZeneca	Phases I–III in UK, South Africa, USA and Brazil	NCT04324606, ISRCTN89951424, EudraCT2020-001228-32, PACTR202006922165132, EudraCT2020-001072-15
Ad26.CoV2-S	Adenovirus vector, non-replicating	Johnson & Johnson	Phases I–III in USA and Belgium	NCT04436276 NCT04505722 NCT04535453 NCT04509947
Ad5-nCoV	Adenovirus vector, non-replicating	CanSino Biologics Inc., Beijing Institute of Biotechnology	Phases I and II; phase II studies in China and Canada	ChiCTR2000031781, ChiCTR2000030906, NCT04341389 NCT04313127
Gam-COVID-Vac	Adenovirus vector, non-replicating	Health Ministry of the Russian Federation	Phases I–III in Russia	NCT04530396 NCT04436471 NCT04437875
PiCoVacc	Inactivated SARS-CoV-2	Sinovac Biotech	Phases I–III; phase III in China and Brazil	NCT04456595, NCT04383574, NCT04352608
COVID-19 vaccine	Inactivated SARS-CoV-2	Sinopharm, Wuhan Institute of Biological Products Co. Ltd	Phases I–III in China	ChiCTR2000034780, ChiCTR2000031809
BBIBP-CorV	Inactivated SARS-CoV-2	Sinopharm, Beijing Institute of Biological Products Co. Ltd	Phases I–III in China and United Arab Emirates	ChiCTR2000034780, ChiCTR2000032459
SCB-2019	Protein subunit	Clover Pharmaceuticals,GlaxoSmithKline, Dynavax	Phase I in Australia	NCT04405908
NVX-CoV2373	Protein subunit	Novavax	Phases I–III in Australia, USA and UK	NCT04368988 NCT04583995 NCT04533399

Above table is showing major CoVID-19 candidate vaccine platforms in clinical evaluation till early 2021 (10).

Drugs in COVID 19

The discovery of safe and effective biomedical/pharmaceutical products sparked an unprecedented response among the world's biomedical/pharmaceutical companies, powerful COVID-19 remedy strategies in reaction to this catastrophic international pandemic. The United States FDA and different regulatory businesses permitted Remdesivir, an antiviral medication, and monoclonal antibodies in opposition to SARS-CoV-2, consisting of bamlanivimab, in addition to the mixed utilization of casirivimab and imdevimab, for the remedy of COVID-19 inside a year. From a pathogenetic standpoint, due to the fact the viral contamination unfold fast to the lungs, COVID-19 pneumonia lung damage is thought to be caused by the host's immune system attacking inflammatory lung cells, a few researchers in comparison the intense immune reaction to the lung tissue to the cytokine typhoon syndrome visible in both the transplant or non-transplant settings. As a end result, cutting-edge efforts withinside the improvement of latest treatments are targeted on both controlling viral contamination with recognized antivirals or tablets Antiviral cytokines discovered in mobile subculture experiments, or cytokines with known antiviral

action, in combination with interferons or controlling immunopathogenesis with immunomodulators to permit the lungs to recover (10).

The first focus was on finding current medicines that could also have antiviral properties against SARS-CoV-2 replication.

A variety of well-known medicines, such as chloroquine, ribavirin, interferons, lopinavir/ritonavir, and others, Antiviral efficacy against SARS-CoV-2 has been reported.

Chloroquine

A long-acting antimalarial medication with a high lipid solubility, is well-known for its antiviral action that is pH-dependent, especially against the corona virus. Initial interest in hydroxychloroquine in conjunction with azithromycin was sparked by a tiny single-arm pilot trial in France that showed a decrease in viral load after treatment (11). Another research A study in China (n = 62 patients with mild/moderate pneumonia) demonstrated a positive impact when comparing hydroxychloroquine alone vs. standard treatment. A number of reports have come in from Spain, the United Kingdom, and the United States, on the other hand, showed that hydroxychloroquine and azithromycin had little therapeutic benefit in COVID-19 individuals (12).

QT prolongation and ventricular arrhythmia are additional recognised side effects of this class of medications. Although there is no solid evidence that azithromycin causes QT prolongation, it has been linked to an increase in cardiovascular mortality (47 cardiovascular events per million completed treatment courses), emphasising the possible danger. In fact, on March 29, 2020, the American College of Cardiologists published an opinion stating that physicians should be aware of this potential risk. Then, FDA withdrew the EUA on June 15, 2020, after analysing new scientific evidence and determining that the legal conditions for obtaining an EUA were no longer satisfied (13).

Ribavirin

In some of the early clinical trials, ribavirin was administered in conjunction with interferon. In the cell-based test, ribavirin acts as a viral-static agent. It's an RNA-dependent RNA polymerase inhibitor as well as a viral mutagen (ribavirin's sugar moiety is a pentose with hydroxyl groups in both the 2′ and 3′ positions, permitting integration into the RNA) that could stop the virus from replicating to fail despite replication. As a result, its efficacy as a monotherapy may only be

evident in terms of clinical outcome rather than viremia decrease, as seen in chronic hepatitis C trials. In the late 1990s, ribavirin was used with interferon to Hepatitis C is a single-stranded RNA virus that needs to be treated. Ribavirin and recombinant interferon have also been used together. demonstrated to be effective in suppressing the reproduction of MERS-CoV, a coronavirus (14).

Lopinavir–ritonavir

In vitro studies revealed that lopinavir–ritonavir had micromolecular IC-50 efficacy against SARS-CoV-2, indicating that this anti-HIV protease medication combination might have therapeutic action based on medicinal repurposing. According to According to a recent research based on a 199 COVID-19 patients randomised controlled trial, the combination of lopinavir and ritonavir provided no therapeutic advantage in adult COVID-19 patients. In another A triple combination treatment of interferon-beta-1b, ribavirin, and lopinovir–ritonovir was compared to lopinovir–ritonovir alone (control arm) in a phase II study and showed superior safety and efficacy in alleviating symptoms and reducing the duration of viral shielding and hospital stay in patients with mild to moderate HIV infection. COVID-19 (ClinicalTrials.gov: NCT0427668) (15).

Remdesivir is an RNA-dependent RNA polymerase inhibitor that was originally created for the Ebola and Marburg viruses, but has now been discovered to have good inhibitory efficacy against respiratory syncytial virus, Junin virus, Lassa Fever virus, and coronaviruses like SARS and MERS. It was also recently discovered to have potent antiviral action against SARS-CoV-2. It's an adenosine analogue intravenous prodrug. Early clinical trials in the United States revealed that remdesivir is efficient in lowering SARSCoV-2 virus load without causing major side effects (16). The FDA granted this medication an EUA for the treatment of COVID-19 infection in adults and children who are hospitalised with serious diseases. Remdesivir was authorised in Japan via an unusual approval procedure 8 days later, based on the identical dataset (10).

Umifenovir, Antiviral activity against SARS-CoV-2 was revealed in a virus cell culture test using a broad-spectrum antiviral that inhibits virus membrane fusion and is licenced for use in Russia for influenza purposes. A multicenter randomised controlled experiment is comparing umifenovir in conjunction with lopinavir/ritonavir vs the three drugs together with interferon(ChiCTR2000029573) (10).

Plasma immunotherapy

Early on, A treatment method including passive immunotherapy with plasma from COVID-19 convalescent patients was proposed. After receiving passive immunotherapy plasma, the patient's viral load dropped quickly, and his clinical condition improved., according to a small pilot research (5 patients) in China, demonstrating the viral neutralising activities in the convalescent patients' plasma (17).

Monoclonal antibodies

A range of pharmaceutical and biotech corporations have produced monoclonal antibodies in opposition to SARS-spike CoV-2's protein, which incorporates the RBD that binds to the hACE2 mobile receptor in the host. The bamlanivimab antibody was chosen as the first to be tested (LY-CoV555). With the high-dose group, there became a discount in the nasopharyngeal SARS-CoV-2 degree, as well as a discount in the pre-specific endpoint of COVID-19-associated hospitalisation, emergency branch visit, and so on, or a segment's downfall 2 a study comparing three doses of the medication to placebo (465 patients in four arms) in patients with mild-to-mild COVID-19 who presented within 10 days of symptom start. (6.3percentage in placebo vs 1.6 percentage ordinary for the 3 doses group) (18).

Prevention

Considering the numerous routes of COVID19 transmission thru cough, sneeze, and different biofluids, the primary line of defence towards this virus is to save you it from spreading via infected air, skin, or surfaces. Despite the truth that quite a few preventive equipment are to be had at the market, enormous studies and improvement continues to be underway in mild of nanotechnology to improve their preventative abilities in terms of lower toxicity, no side effects, high sterilisation functionality with low dosage, longer lifespan, and environmental and user friendliness (19-21).

Disinfectant and sanitizers

Alcohol and its derivatives are used in the majority of disinfectants and sanitizers on the market. These disinfectants protect the user for a relatively brief time, anything from a few seconds to minutes. The rapid volatile alcohol molecules evaporating off the user's skin causes this disadvantage. The user then starts carrying the germs again when they come into touch with a contaminated surface. Furthermore, because these disinfectants are caustic, they are neither user-friendly nor environmentally friendly. Such disinfectants may have an adverse effect on human or animal health or safety, including irritation of the eyes and skin, as well as allergies and inflammation. Because of the alcohol and hydrogen peroxide combination, they are also combustible and pose a constant risk of catching fire (19- 21). The next section will go through many research studies that have employed nanotechnology to remedy these flaws.

Metal nanoparticle-based disinfecting agents

Because of their antibacterial and antiviral characteristics, Silver, copper, and other metal nanoparticles (MNPs), & titanium have a wide range of uses in fields such as medicine, cosmetics, and disinfectant manufacturing. Viral infection occurs when the virus's nucleic acid is introduced into the host cell, followed by viral replication. Metal nanoparticles are thought to work on the virus's surface, physically preventing it from interacting with host cells. In contrast to alcohol-based disinfectants (22), MNPs such as silver and copper nanoparticles are environmentally and user-friendly, non-flammable, and non-volatile (23). In a nutshell, MNP-based disinfectants and sanitizers have enhanced the fabrication, safety, and health of MNP-based disinfectants and sanitizers. & life-span in mission to fight against COVID-19.

Naturally derived nanomaterials as adsorbents in disinfectants

Nanomaterials can also be made by extracting natural resources such as leaves, fruits, flowers, insects, and animals. Natural nanoparticles are environmentally beneficial, non-toxic, non-corrosive, user-friendly, and cost-effective. These nanoparticles operate as adsorbents in sanitizers, releasing disinfection molecules in a regulated way due to their greater effective surface area. Furthermore, because disinfectants based on these nanoparticles interact more with viruses present at the surface, the protective properties of disinfectants based on these nanomaterials are enhanced (24).

Nanopolymer-based disinfectants

Nanopolymer-based disinfectants with antibacterial characteristics, including PolyHMG (polyhexamethylene guanidine), have an extended powerful lifestyles duration, are cost-powerful, non-combustible, user- and environmentally safe, non-corrosive, and biodegradable Wero Water Services developed a disinfectant that is entirely based on PolyHMG & it is currently being used to clean buses and vehicles by the Prague public transportation business in the Czech Republic (25). PRELYNX PORTAL is a device created by Design.123 for scanning and cleaning COVID-19. Most lipophilic and hydrophilic viruses on the surface are inhibited by the portal's disinfection vapours, which are made of nanopolymer(26).

Groundwater disinfection with nanoelectrodes

Using a grid of nanometer-shaped electrodes with better surface properties, researchers from Bar-Ilan University have developed an environmentally benign method for disinfecting viruses, bacteria, and fungus. In a unique aquatic environment, the interaction of water and electrodes creates a cleaning substance (27). Nanomaterials have therefore been widely investigated for disinfectants because to their large effective surface area and antiviral characteristics, and they offer enormous promise in the fight against COVID-19.

Viruses disinfecting by light activated nanocoating

Mineral nanocrystals in light-activated nanocoatings are charged by visible light such as Incandescent, fluorescent, light-emitting diodes (LED), and sunlight are all examples of lighting. When these nanocrystals contact, a powerful oxidation reaction occurs, completely degrading all organic pollutants on the surface. These

coatings are often made up of nanoclusters of chemically altered metals, such as gold, embedded in a polymer matrix with antibacterial properties, and antiviral dye (including crystal violet and methylene blue). When uncovered to seen light, those dyes produce reactive oxygen species, which harm and kill viruses by damaging their protective membranes and genetic material. The antiviral activity of dyes has been further improved by utilising polymer matrix to synthesise nanocomposites containing metals such as gold, zinc, and silver. In terms of safety, these low-intensity visible light-activated coatings outperform UV light or high-intensity visible light-activated coatings (28), (29). Hwang et al. used crystal violet dye and gold nanoclusters to kill microorganisms effectively using low-flux white light. Nano Touch Materials, LLC has additionally introduced the introduction of a inexperienced nanocoating primarily based totally after being charged by visible light, on mineral nanoparticles that kills viruses by creating a large oxidation reaction at the surface (26), (28), (29).

Nanolayers with antiviral and antibacterial properties

Various nanomaterial-based disinfectant coatings have been utilised as a key preventative strategy against a variety of viruses and bacteria. These coatings serve an important role in the prevention of certain infectious diseases concerns due to their increased antiviral, antibacterial, and antifungal capabilities, as well as their larger effective surface area (30). NANO4LIFE EUROPE L.P. has announced the development of a surface charge-based sanitizer that uses the physical charge effect to inhibit and destroy microorganisms. Over the user's skin, sanitizer molecules produce a positively charged coating known as "swords" (31).

Masks and personal protective equipment (PPE)

Covering the face with a mask is one of the most effective COVID-19 prevention methods. Face protection is required for both sick and non-infected people. By covering his face, an infected person can limit the Transmission of virus produced **even as** coughing or sneezing, and a non-inflamed man or woman can guard himself from virus gift withinside the air as droplets or aerosols, objects, or accidental mucus membrane contact. Airborne or touch-based transmission of the virus necessitates the use of masks. N95 masks are frequently used face masks that filter out up to 95 percent of fine particles with a diameter of at least **300 nm**. Even while any type of face mask can successfully protect an individual from becoming infected, the mask itself gets fomite because this virus has the capacity to adhere to the textile surface. Long-term usage of masks can lead to respiratory problems and a drop in oxygen levels in the body. The widespread usage of masks

raises issues about how to dispose of them. Personal protection equipment is another safeguard employed by healthcare frontline employees (PPE). PPE kits are not antiviral or antibacterial in general. Antiviral nanocoating and novel nano-based materials in PPE, on the other hand, can improve its protective properties (32). PPE kits are not antiviral or antibacterial in general. Antiviral nanocoating and novel nano-based materials in PPE, on the other hand, can improve its protective properties. As a result, different In a different area, reports on nanotechnology-based inventions have been given to increase the protective efficiency of masks and other PPE, as well as to address other related difficulties.

Different metals and metal oxides, such as silver, gold, and copper nanoparticles, have a lot of promise for making antiviral coatings for face masks and PPE because of their large surface area and microbicidal capabilities. Under the Nanomission of the DST, Government of India, **A. K. Aggarwal et al.** developed a N9 nanosilver-based coating (33). In collaboration with Resils Chemicals and Nanoclean Global Pvt. Ltd., This nanosilver-based antiviral coating is being used in the production of triple-layer surgical masks. IIT Guwahati in India has recently announced the development of an antiviral spray based on copper and silver nanoparticles, which will be utilised in face masks and PPE (34). Because of their antiviral and antibacterial characteristics, Promethean Particles Ltd has created nanocopper particles that may be used in face masks and personal protective equipment (PPE). They worked with textile businesses to produce antiviral and antimicrobial textiles for the healthcare industry based on the incorporation of new copper nanoparticles into a polymer matrix such as nylon Sonovia Ltd. has developed a washable and design-friendly anti-pathogen fabric with antiviral properties that can be reused, based on zinc oxide nanoparticles. This manufactured fabric has been utilised to create antiviral masks known as **sonomasks**, and it has the potential to be employed in personal protective equipment. G. Parks et al. developed a nanomaterial-based antiviral covering that traps the virus and kills it &subsequently kills it via a chemical reaction triggered by UV light (35).

Masks and PPE kits based on nanofibrous membranes

Nanofibrous membranes with a large effective surface area are formed by a thick weblike network of nanofibers. These nanofibrous membranes are used in respiratory masks, allowing for better breathing and filtration. T. Rainey et al. claim to have developed a biodegradable mask based on nanocellulose nanofibers that can guard against pollutants as small as 100 nanometers (36). Nanocellulose nanofibers were derived Sugar cane bagasse and other agricultural trash are examples of waste plant material. Kim and his colleagues.(37) claim to have

developed filter masks based on orthogonally aligned nanofiber (100–500 nm). Insulation block electrospinning was used to create these nanofibres. The structures are orthogonally oriented to reduce pressure on the air filter and increase filtering efficiency. This nanofiber architecture is waterproof, has a 94 percent filtering effectiveness, and is non-deformable (despite the 20 hand washes). YAMASHINFILTER CORP (38) claims to have created a nanoresin with synthetic polymers and nanofibrous mask inner sheets. Because of its unique properties, such as high polarity and a larger effective surface area, nanoresin has been used to create 3-D masks. self-extinguishing, as well as heat and sound insulation.

Masks and PPE kits based on graphene and its derivatives

Graphene is a two-dimensional hexagonal arrangement of single carbon atoms, whereas graphene oxide is a two-dimensional hexagonal arrangement of single carbon atoms (GO) is the oxidised version of graphene. By eliminating oxygen groups with the help of reducing agents, GO may be converted to reduced GO (rGO). Single-layer materials having a wide effective surface area and a high absorption capacity for incoming visible light (2.3 percent) have been effectively used for sterilisation and heat generation. These materials are single-layer materials with a large effective surface area and a high visible light absorption capacity (2.3%), which have been successfully used for sterilisation and heat generating. Because of its superhydrophobicity and increased light absorption characteristics, graphene and its derivatives can be utilised to make masks, PPE, and other medical equipment. Directa Plus PLC claims to have developed masks based on graphene and its derivatives' microbe-static, antiviral, and non-toxic characteristics. LIGC Applications has also created the “Guardian G-Volt” face mask, which is made of laser-induced microporous graphene.

Conclusion

The COVID-19 epidemic has resulted in catastrophic human and economic losses throughout the world. The virus's transmission continues unabated, and the number of cases and deaths caused by it continues to rise on a daily basis. The requirement for this circumstance is for scientists, clinicians, and engineers to work together to battle the worldwide COVID-19 threat and to establish a strong response to future pandemics. A worldwide response is urgently needed to invest resources and boost science and technology research and development through multidisciplinary cooperation. It offers a lot of promise for breaking new ground in terms of developing future tools, the tools will be developed to prevent, diagnose, and cure various developing and resurfacing diseases. Analysis highlights the vast amount of nanotechnology research and development being done to prevent the COVID-19 epidemic. The globe is rapidly evolving in order to effectively combat the new virus, but worldwide commitment to research and development in this sector is critical.

This review attempts to endorse nanomedicine generation as a capability COVID-19 therapy, because of current bioinformatics studies into capability pharmacological goal webweb SARS-CoV-2 protein-binding sites, as well as new healing therapies (e.g., vaccinations, antibodies, herbal medicines) to eliminate SARS-CoV-2, As a result, research into nano-enabled therapeutic cargos has shown to be highly beneficial in terms of delivering medicines to the appropriate target tissue locations and regulating medication release based on a patient's virus load and other symptoms. Pharmacological aspects and advanced surface-active functional nanosystems techniques can be used to develop such nanomedicine medicines.

This pharmacologically relevant nano cargo demonstrated customisable features when combined with specially developed stimuli-responsive devices. paving the way for individualised COVID-19 management treatments to be developed. Nanomedicine is a significant strategy for innovative diagnostics, medical imaging, nanotherapeutics, vaccines, and the manufacture of biomaterials for regenerative medicine, and it has an impact across the board. For decades, drug-based nanoparticles have been developed. & several clinical studies for cancer, neurological, autoimmune, cardiovascular, and infectious illnesses are now underway, but only a handful have been approved for human use.

Nanoparticles can play a key function in COVID-19 pathogenesis at more than one levels because of their ability to dam viral access and inflamed mobileular protein fusion at some stage in preliminary attachment and membrane fusion.

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