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Nanotechnology and Therapeutic Interventions in COVID–19: A Review

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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Review Article

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ABSTRACT

The topic and title concern the modern technology study and review with the aid and aiming the therapeutic interpretation and overall emphases on a novel corona virus disease called COVID-19, a respiratory disorder; to overcome the disease and its prevention, the article is determined here. As the modern technique to demonstrate the overview of the virus and its cause, prevention, treatment and how the so-called modern technique, namely "nanotechnology" and its various components and factors are valuable and helpful with their pharmacological effects, implications, and other therapeutic interventions in treating the viral infection is discussed and reviewed. Several essential factors with nanoparticles, nanomaterials, and technology-based applications by reduction of spreadability of infections with nanoformulation antibiotics and pharmaceuticals are demonstrated in the article. For increased patient and healthcare worker safety, nano-based antimicrobial technologies are included too. Again binding, entrance, replication, and budding of COVID-19 can be targeted by the antiviral properties of nanoparticles which is actual need of the study. One factor that restricts its use and should be further researched and altered is the toxicity-related inorganic nanoparticles observed and need to investigate further for vigilance, one must

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say. The article describes several facts about nanotechnology in treating and preventing infection and its therapeutic interventions.

Keywords: Nanotechnology; therapeutic interventions; Covid-19; nanoparticles; nanomaterials.

1. INTRODUCTION

Covid-19 which was severe, contagious and even the former disaster with a viral infection-causing virus; came into existence in the last two to three years across the world. It was not only spreadable and normal viral infection causing one but more infective and even lethal to human life too [1,2]. Covid is also defined and identified with the special name called SARSCoV-2Severe acute respiratory syndrome corona virus. It was first identified in China and then globally, it was then seen and suffered too. Then it was studied, and its different components were analysed with several tests and concluded with different variants as per experimental findings worldwide. Fig. 1 can demonstrate the life-cycle for SARS-CoV-2 [3].

Findings came across the result as it was causing severe to lungs and URT system rapidly along with multiple aches. Although the signs and symptoms of COVID-19 might vary, they commonly include fever, coughing, headaches, exhaustion, difficulty breathing, and loss of taste and smell. A virus exposure can cause symptoms one to fourteen days later. At least one-third of those who contract the infection don't have any symptoms at all [4,5]. Among those who experience symptoms conspicuous enough to be categorised as patients, the majority (81%) do so in a mild to moderate way, up to mild pneumonia. By contrast, 14% experience severe symptoms, such as dyspnea (Breathing difficulties) or hypoxia, or more than 50% lung involvement on imaging, and 5% experience severe signs, like shock, breathing failure, or multiple organ malfunction [6,7]. The chances of experiencing severe symptoms are higher in older adults. Some patients still suffer from a variety of side effects (long COVID) months after they have recovered, and harm. It was identified by some methods like the use of tests for antibodies to antigens and RT-PCR (Reverse transcription-polymerase chain reaction test), which works as a biosensor and leads to the detection of viral RNA in patients [8,7]. Also similar to that, RT-LAMP (Reverse transcription loop-mediated isothermal amplification) from a swab of nasal, mouth and throat helped in detection. Not only the AAT but in case of a higher score of infection detection, HRCT was another source to identify the risk and consequent treatment processes. Masks, sanitation, quarantine routines, incubation periods, and protective kits like PPE (Personal protective equipment)were used and followed with regulations and even to fight against the viruses. Vaccinationcamps were then provided, and hand washing and sneezing-coughing

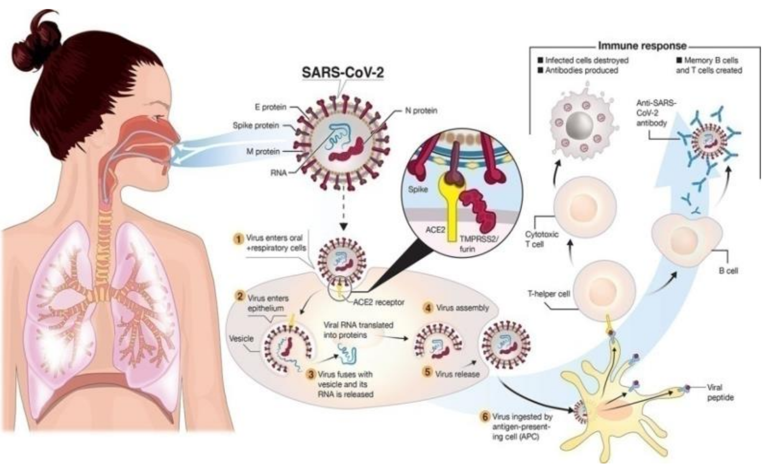

Fig. 1. Nanoparticle-based strategies to fight viral infections with a focus on COVID-19 (Edouard Mathieu, Hannah Ritchie, Lucas Rodés-Guirao, Cameron Appel, Charlie Giattino, Joe Hasell, Bobbie Macdonald, Saloni Dattani, Diana Beltekian, Esteban Ortiz-Ospina and Max Roser (2020) - "Coronavirus Pandemic (COVID-19)". Published online at OurWorldInData.org. Retrieved from: 'https://ourworldindata.org/coronavirus' [Online Resource]

activities were also prioritised; management involved the treatment of symptoms through supportive care, isolation, and experimental measures in past years as well. So this was a quick overview of the disease now, next to it, we are concerned about nanotechnology, which was the area of our interest for intervention and sources of treatment regime over the problem/disease.Nanotechnology is a defining technique used to concern with nano, that is, too small particle study and application in terms of time scale for the desired requirement in laboratories. It is the process of creating new structures, materials, and technologies by modifying matter at a scale close to the atomic level. The technique promises to advance science in many industries, such as healthcare, consumer products, energy, materials, and manufacturing.In pharmaceuticals, nanotechnology is used as a tool for procedural implications. As in NDDS; nanoparticulate drug delivery systems exist, including radiation, AIDS treatment, cancer treatment, and gene therapy. The technology enables the delivery of poorly water-soluble drugs and can bypass the liver, thereby preventing the metabolism on the first pass. Specifically designed absorption processes used by nanotechnology, including absorptiveendocytosis, boost the oral bioavailability of medicines that persist on the surface for a certain period. Examples of nanoparticles used as contrast agents in the biomedical field are – perfluorocarbon, which is used in imaging angiogenesis, cancer metastasesand blood clots. So, in the same way, it is a practical l and widely emerging field today in every sector wishing fornano substances, we can say. Fig. 2 has several applications for nanotechnology in healthcare systems [9].

Our concern in the literature is how it is helpful for COVID-19 to minimize the risk associated with it and in less quantity with significant experience in early detection, analysis and treatment approaching manner with nanotechnology. Hence, nanopharmaceuticals are being developed and used for research, manufacturing, and commercialization with medical development techniques. In the case of drugs and dosages, the smaller the particle size, the introduction to effectiveness can be modified and changed accordingly. Smaller particles mean improved solubility and bioavailability; nanoparticles boost superior efficacy because of their size and large surface area. Nanoparticles can follow a patient's health in real-time and detect disorders, such as alterations in the body's chemistry. In addition, they can be configured to collect data on specific body areas and toxin levels and report it to medical professionals. That is why the survey complies with the therapeutic interventions for COVID. Let's start with the discussion with several aspects behind it in brief [3,1].

2. COMPREHENSIVE REVIEW OF METHODS

2.1 Nanomaterials against Covid-19

As we have gone through the precautionary bases and measures from the pandemic, we can overlook the nanomaterials we used in that period. Also, it will be easy to discuss the pre-determined specifications and the use and how it helped us take precautions from getting infected with a virus attack.

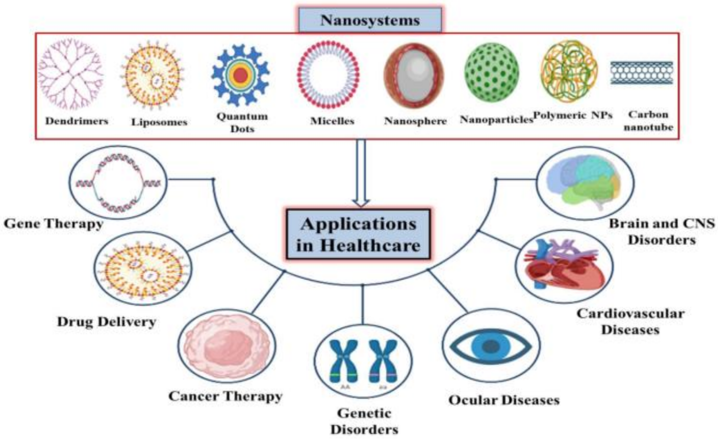

Fig. 2. Emerging applications of Nanotechnology in healthcare systems [10]

Some nanomaterials include inorganic nanoparticles (NPs), self-assembly proteins, polymeric NPs, and peptide-based NPs for precaution to mouth or surfaces of different face parts.

Three kinds of major NPs that have been reported to work against respiratory viruses are listed below

Polymeric NPs: As we have gone through the precautionary bases and measures from the pandemic, we can overlook the nanomaterials we used in that period. Also, it will be easy to discuss the pre-determined specifications and the use and how it helped us take precautions from getting infected with a virus attack.Some nanomaterials include inorganic nanoparticles (np), self-assembly proteins, polymeric NPs, and peptide-based NPs for precaution to mouth or surfaces of different face partsthat are made of polymers .They have intriguing qualities that make them appealing candidates for biological applications, including adjustable characteristics, practical synthesis techniques, and good biocompatibility. One well-known member of this group that has been given FDA approval for use in human body applications is poly (lactic-co-glycolic acid, or PLGA). The remarkable biocompatibility and biodegradability of the human body are to blame for this. Chitosan and N-(2-hydroxypropyl) methacrylamide/N-isopropyl acrylamide (HPMA/NIPAM), are two other examples that have shown promise as intranasal vaccinations against respiratory viruses.

Auto-assembly proteins NPs: These are produced by oligomerizing monomeric proteins and have been proven to be appropriate for biomedical applications.

Inorganic NPs: There is an extensive body of literature on the biological effects of inorganic NPs, such as metal oxide NPs, which performed well in antibacterial and antifungal tests. They are appropriate for biological applications due to characteristics like simplicity in synthesis, biocompatibility, and optical qualities. However, there aren't many inorganic NPs that work well against respiratory viruses, therefore they must be properly studied right away.

Peptide-based NPs: Previous research has suggested that peptide inhibitors (short-sequenced) and amino acid alterations may be able to treat illnesses brought on by the SARS-CoV virus. According to reports, a peptide-based vaccination expressing HRC's trimeric coil conformation stage could be the best therapeutic strategy for treating SARS-CoV-related infections. This strategy is made possible by peptide-based NPs. In another study, the P6HRC1 vaccine moiety was created by coupling a peptide ligand with a B-cell epitope from the SARS-B HRC1 spike protein and self-accumulating through dialysis in a refolding buffer. Results demonstrated that the scientists could produce the necessary conformation-specific antibodies that may have prevented SARS-CoV infections using NP-based methods. Recently, scientists have been developing novel peptide-based techniques based on early molecular dynamics simulation studies. A recent investigation found a peptide inhibitor derived from ACE2 to have considerable potential for inhibiting SARS-CoV-2. Additionally, repeated binding of peptides linked to nanocarriers was observed to boost binding efficacy.

Instead all these, there are some different types of nanomaterials as well as carriers and particles developed to fight against the infection; they are known as magnetic nanoparticles, quantum dots, metal nanoparticles, graphane nanosheets, carbon nanotubes, carbon dots, etc., for fighting against COVID 19.

Hence, we can find these many types of nanomaterials against COVID[2].

2.2 Therapeutic interventions in covid-19 with Nanotechnology

To accept COVID-19 as an approved therapeutic, several cell-based therapy approaches are currently undergoing clinical trials. These approaches include mesenchymal stem cells (MSCs), natural killer (NK) extracellular vesicles, cells, dendritic cells (DCs), modified lymphocytes, and novel cell-based vaccination platforms. The SARS-CoV-2 entrance and life cycle can be targeted during treatment using NPs. The S protein is crucial in blocking the first membrane fusion process, which allows SARS-CoV-2 entrance. Therefore, by preventing the S protein from attaching to host cells, therapeutic NPs can be created to pre-block SARS-CoV-2 entrance. Due to their ability to enhance detection, sensitivity, and signal amplification specificity in polymerase chain reaction analysis, nanostructured systems can potentially impact diagnosis. They can also be used for prophylaxis as vaccine adjuvants and for therapeutics for COVID-19 by directing antiviral drugs to specific viral targets. Fig. 3 can be easily understood for nanoparticle and strategies to defeat the infection [11].

Nucleic acid amplification tests (NAATs) like the polymerase chain reaction (PCR) are usually used to identify viral genomic RNA that encodes S and N proteins. The N protein is mainly found in antigen testing like LFTs. According to, NAATs are the gold standard for diagnosing SARS-CoV-2 infection. SARS-CoV-2 has generated several mutations that may allow immune evasion [12].

One or more base changes in the intended nucleotide sequence can be enough to deter the reaction since NAATs use nucleic acid primers to recognise and amplify their targets. The POC can employ LFTs since they are low-cost, simple, and quick to diagnose. The N protein is more stable across variations than the S protein, which should produce a less susceptible test for diagnostic evasion. As a result, a test that detects N protein rather than S protein should be more resistant to diagnostic evasion of SARS-CoV-2 N protein can be found in clinical samples and thanking enhanced mAbs and diagnostic procedures designed specifically for the virus too.

The N protein is relatively conserved between variants compared to the S protein. Therefore, a test that detects N rather than S protein should be more resistant to diagnostic evasion. In fact, since 2020, every rapid detection test that the FDA has approved under an EUA has still been advised for use in SARS-CoV-2 detection. Companies have created quick tests employing mAbs that were previously obtained from immunisations against the SARS-CoV N protein to retain high diagnostic efficacy for enhanced mAbs and diagnostic tests specifically for SARS-CoV. However, the N protein may be employed due to the ongoing accumulation of mutations in the protein may be utilised to keep diagnostic tests for SARS-CoV-2 that are specific and improved mAbs at high diagnostic efficiencies. SARS-CoV-2 N protein can be found in clinical samples using prototype LFTs. Fig. 4 can easily demonstrate the same explained above [12].

2.3 Nanocarriers:- Vaccine based approach

The most economical method of preventing infectious diseases is currently vaccination. Conventional immunisations may have low immunogenicity and, in most cases, only offer a minimal level of protection. The advent of immunisations based on nanoparticles has demonstrated great potential in resolving most of the drawbacks associated with traditional and subunit vaccinations. Nanoparticles' size, shape, functionality, and surface characteristics can now be precisely controlled because of recent developments in chemical and biological engineering. Immunogenicity is notably raised and antigen presentation is enhanced as a result. Nanovaccines can be precisely characterised by a combination of tests that are physicochemical, immunological, and toxicological. This narrative review will provide an overview of the present nano vaccines landscape.

Fig. 5 shows the different aspects for nanoparticle based delivery system [1,3].

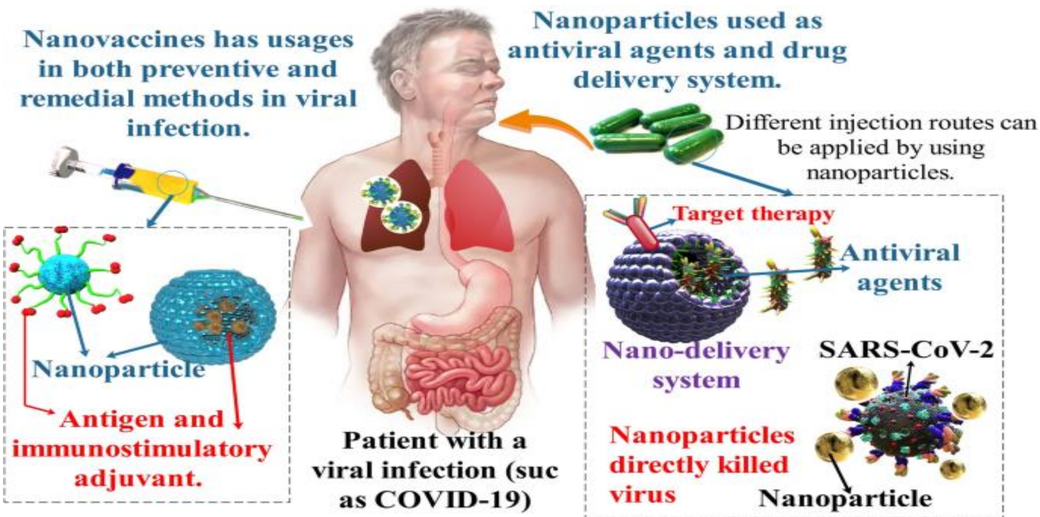

Fig. 3. Nanoparticle-based strategies to fight viral infections with a focus on Covid-19[14]

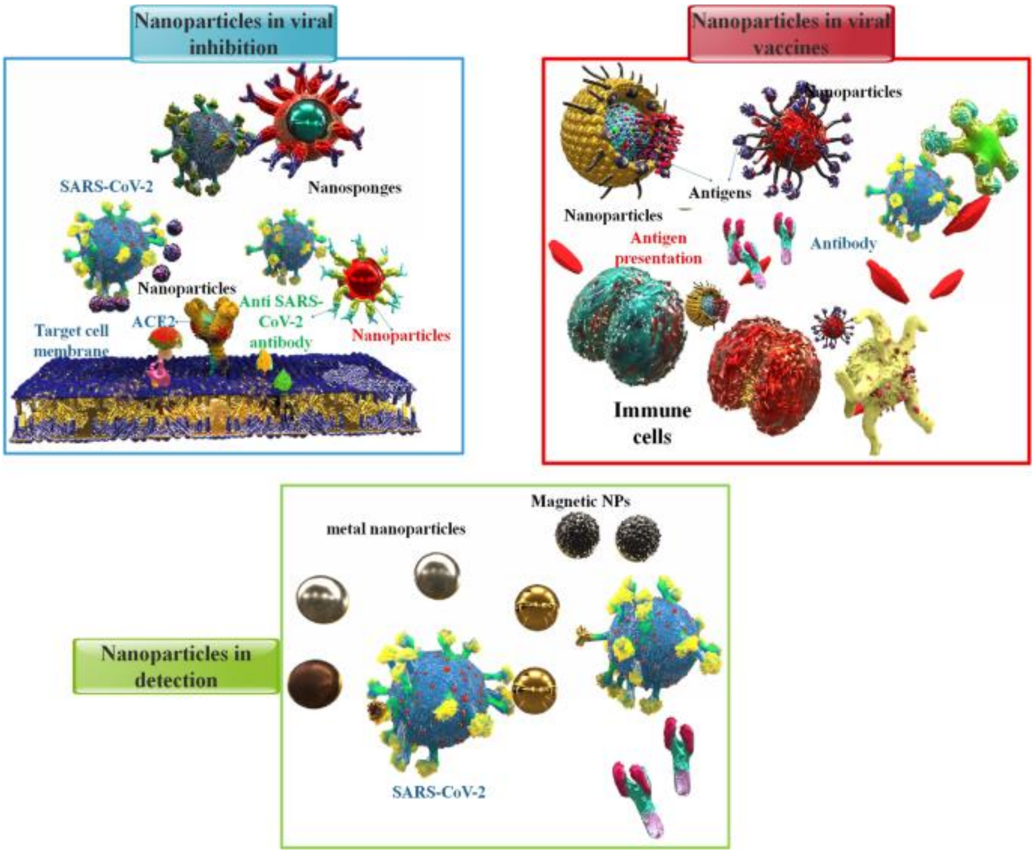

Fig. 4.Therapeutic interventions In Covid-19 With Nanotechnology [1,5]

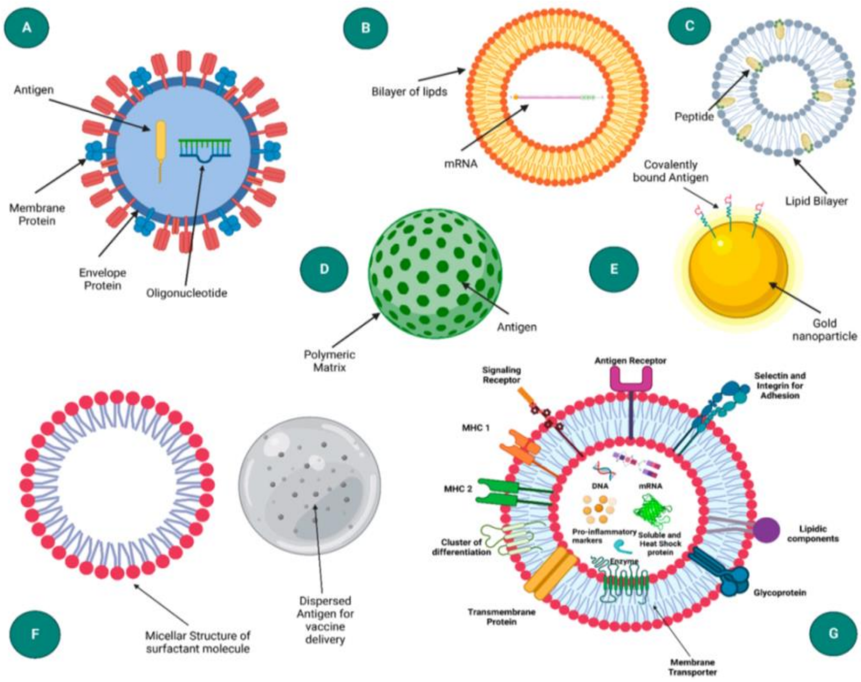

Fig. 5.Schematic representation of different nanoparticle based delivery system: (a) Virus-like particle, (b) liposome, (c) iscom (immune stimulating complexes),(d)polymeric nanoparticle, (e)onorganic nanoparticle,(f) emulsion, and(g) exosome. (created with biorender.com (accessed on 28 september 2022)[1,6]

Recently, new dangerous microbes have been introduced, making it harder to treat and immunise against infectious diseases. Notable achievements in the field of vaccine development have included the invention of novel immunisations as well as improving the efficacy of vaccinations that are currently on the market against certain diseases. Currently, live, attenuated organisms used in some immunisations carry the risk of regaining pathogenicity in immunocompromised patients, whereas protein fragments or dead pathogens are used in others. To avoid this, it is thought that creating risk-free, efficient vaccines in conjunction with suitable delivery technologies is a crucial requirement for achieving the desired humoral and cell-mediated protection against infectious illnesses. In recent years, there has been a lot of focus on nanoparticle-based vaccines to enhance vaccination effectiveness, immunisation methods, and targeted administration to elicit desired immune responses at the cellular level. These nanocarriers must be safe for human usage, shield the antigens from accelerated proteolytic degradation, aid in antigen absorption and processing by antigen-presenting cells, and regulate release to increase vaccine efficacy. These characteristics have already been achieved using nanocarriers made of lipids, proteins, metals, or polymers. When determining the effectiveness of vaccination, a number of physicochemical characteristics of nanoparticles are crucial. This review article focuses on using nanocarriers-based vaccine formulations and the methods for functionalizing nanoparticles to provide effective vaccine delivery and generate desired host protection against infectious illnesses [1,3] Fig.6 explainsthe nanoparticle carrier system [1]

Prevention, Diagnosis and treatment:- Fig. 7 for prevention, diagnosis and treatment [1,8].

The rate of global COVID-19 pandemic propagation is frightening. More people have been infected and killed by it than by SARS or MERS. The different clinical and public health issues caused by the CoViD-19pandemic can be greatly addressed by nanotechnology and nanomaterials. The products based on nanotechnology that are currently being created and used for the detection, avoidance, and treatment of CoViD-19 are analysed and examined in this review. This global pandemic and continuous combat plan have enough room for advancement in nanotechnology and nanomaterials. Hence we need to take proper precaution, measures over it and if caused by then should take proper treatment for fighting against the infection, vaccination is essential step and one should take the same too for fulfilment of so called statement “precautions are better than cure [9].

Fig. 8 may describes the battle against the disease [1,6].

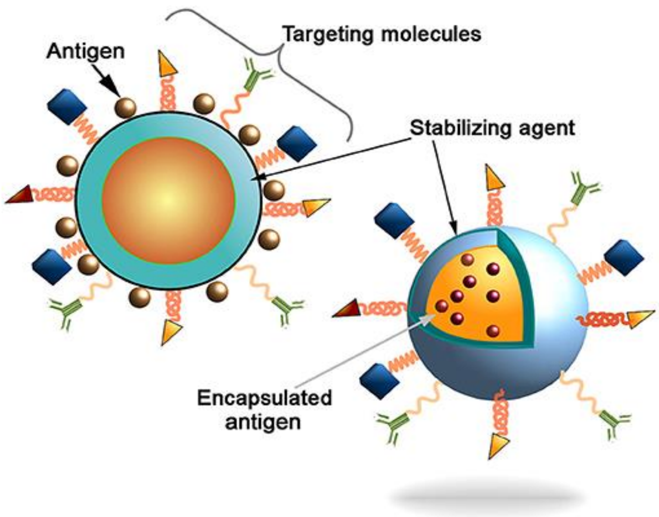

Fig. 6. Schematic representation of the nanocarriers. Antigen can be conjugated to the nanoparticles surface or incapsulated into core of the particles. Decoration of the nanoparticles surface with targeting molecules (e.g., Antibodies, Fab-fragments, peptides, etc) could further increase the delivery of particles into the antigen presenting cells (apcs) to induce innate and adaptive immune responses[1,5]

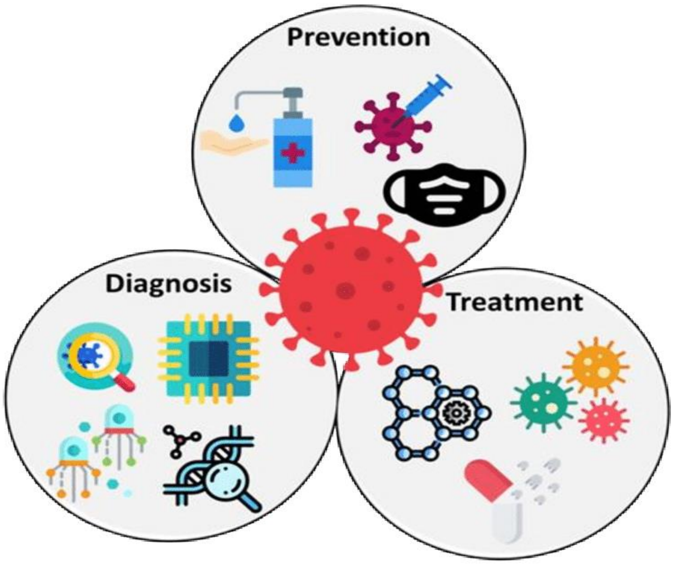

Fig. 7. Illustration of Nanotechnology-Based Prevention, Diagnosis, and Treatment for Covid-19 [1,8]

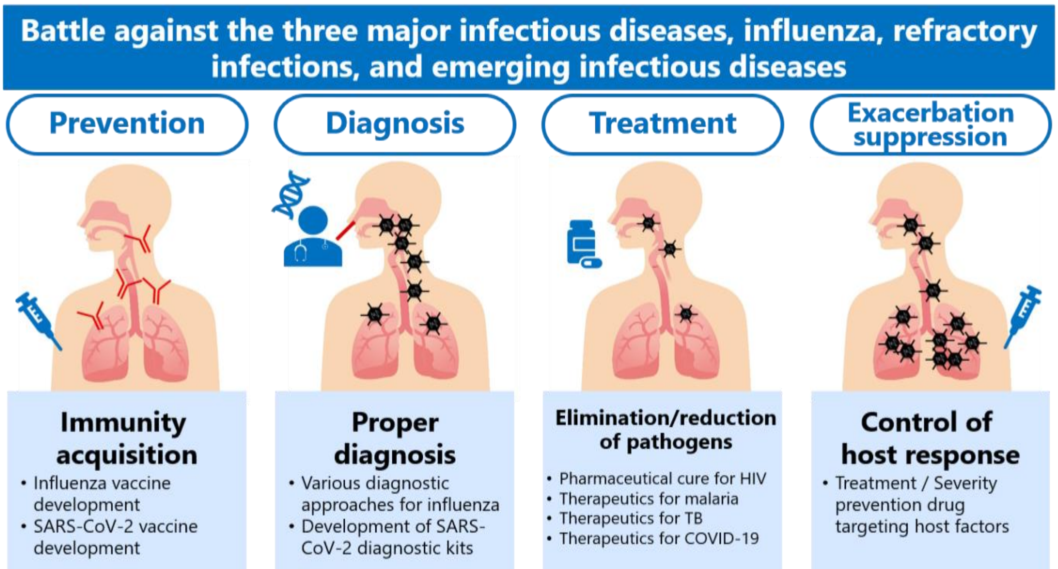

Fig. 8.Prevention, diagnosis and treatment of infectious disease [6] https://www.shionogi.com/global/en/innovation/randd/drug-discovery/what-we-are-focusing-on.html

3. LITERATURE REVIEWS

3.1 Nanotechnology Interventions in the Management of COVID-19: Prevention, Diagnosis and Virus-Like Particle Vaccines [1]

Through this research, several nanomaterials, including gold and magnetic nanoparticles coated with carboxyl group-containing polymeric, graphene, and poly amino ester materials, have been investigated to detect SARS-CoV-2 quickly. A crucial part in stopping the spread of COVID-19 was performed by personal protective equipment made with nanoparticles, including gloves, masks, clothing, surfactants, and Ag- and TiO_2-based disinfectants. As the virus-like particles provoke an immunological response, nanoparticles are used not only in vaccine administration but also in the case of lipid nanoparticles that enable the transport of mRNAbased Pfizer and Moderna vaccines. There are now 18 virus-like particle vaccines in pre-clinical development, with phase 3 trials for one of them, created by Novavax, disclosed. Additionally, a critical issue that needs to be solved rightnow to prevent a pandemic is psychosocial factors connected to vaccine resistance.

3.2 COVID-19 mitigation: Nano-technological Intervention, Perspective, and Future Scope [19]

COVID-19, which has been linked to 19 illnesses, has resulted in a catastrophic economic downturn globally and an unparalleled global health disaster with many fatalities. Implementing safe and efficient diagnostic and treatment methods to address this acute pathogenic coronavirus strain is crucial and demanding. Nanotechnology provides innovative therapeutic application alternatives to conventional diagnostic instruments that can prevent the disease from spreading further and eliminate the risk of this virus creating future pandemics. Physicochemically adjusted nanomaterials can improve the detection of viral antigens, nano vaccines, and cytokine storm inhibitors, all essential in the fight against COVID-19. Unique spike proteins on the viral surface can be successfully mimicked and interacted with by synthetic nanoparticles made at the nanoscale. Given this, we imagine the precise and simultaneous fusion of nanoscience and nanotechnology leading to new paths that can obstruct the formation of viruses and restrict the viral lifespan. Current and emerging nanotechnology techniques enable the creation of therapeutic and preventative pathways to control this illness and highlight essential nanoscience techniques for creating impending antiviral systems. In this review paper, we also summarise the most recent research on the effectiveness of nanoparticles (NPs) as antiviral or diagnostic tools for most viruses. In addition to significantly reducing inflammatory reactions, engineered NPs that can control the patient's immune response can also be used to create powerful nano-vaccines and medications to combat viral pandemics like COVID-19. In conclusion, cutting-edge strategies based on nanotechnology can be crucially used to combat upcoming pandemics, such as COVID-19, and function at the forefront of combating several new harmful viral threats.

3.3 Respiratory delivery of Favipiravir-tocilizumab Combination through Mucoadhesive Protein-lipidic Nanovesicles: Prospective Therapeutics against COVID-19[20]

In this paper, we theoretically suggested a duo-combination utilising protein-lipid nanovesicles containing the immunomodulator tocilizumab and the approved antiviral medication favipiravir as an effective anti-COVID-19 treatment. In COVID-19 patients, immunomodulation and antiviral activity were combined. When administered via respiratory mode, the suggested nanomedicine may increase the antiviral's efficiency and aid in limiting the virus and its consequences. This told nanomedicine may be helpful as a treatment option for patients with severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2).

3.4 Nanotechnology Advances in Pathogen- and Host-targeted Antiviral Delivery: Multipronged Therapeutic Intervention for Pandemiccontrol[2,1]

The author presents a review summarising and elaborating on the research and development of therapeutic nanoformulations against several pathogenic viral infections, such as the coronavirus, influenza, and HIV. Due to numerous advancements in nanotechnology during the past 20 years, the field of medication delivery has made considerable strides. The promise of obtaining effective viral eradication, broad-spectrum antiviral action, and resistance to viral alterations is examined, and in particular, nanotechnology breakthroughs towards better pathogen- and host-targeted antiviral drug delivery are reviewed. As several COVID-19 antiviral clinical trials show only modest improvement in disease treatment efficacy, nanocarrier approaches aimed at enhancing drug pharmacokinetics, biodistributions, and synergism are anticipated to not only support current disease treatment efforts but also broaden the antiviral toolbox against other emerging viral diseases.

3.5 Nanotechnology for COVID-19: Therapeutics and Vaccine Research [10]

To counteract this epidemic, we cover new and existing nanotechnology-based therapeutic and preventive strategies, emphasising the crucial areas in which nanoscientists should become involved.

3.6 Immunobiology and Nanotherapeutics of Severe Acute Respiratory Syndrome 2 (SARS-CoV-2): A current update [2,2]

An increase in the immunological dysfunction that is driving the infection getting spread may further exacerbate the inflammatory state. One of the most important therapeutic intervention strategies is to minimise inflammatory response and limit ACE2-mediated viral entry. Nanomaterials and their conjugates are interesting options in this regard. The entry and reproduction of viruses can be prevented by nanoparticles. A vaccination against SARS-CoV-2 is being developed using nanomaterials, which have also found use in targeted drug delivery. The history, spread, and clinical characteristics of SARS-CoV-2 are briefly outlined here. Later, we talked about how SARS-CoV-2 triggers the immune system. The possibility of nanotechnology as a technique for combating SARS-CoV-2 infection was finally covered in more detail. Developing treatment plans for SARS-CoV-2 will require a grasp of all of these concepts.

3.7 Nanotechnology Advances in Pathogen- and Host-Targeted Antiviral Delivery: Multipronged Therapeutic Intervention for pandemic control Repurposed Drugs, Molecular Vaccines, Immune-Modulators, and Nanotherapeutics to Treat and Prevent COVID-19 Associated with SARS-CoV-2, a Deadly Nanovector [2,1]

Recent developments in nanotechnology aiming at improving pathogen- and host-targeted antiviral drug delivery are reviewed, along with the promise for effective viral eradication, broad-spectrum antiviral action, and resistance to viral modifications. Given the unsatisfactory outcomes of multiple COVID-19 antiviral clinical trials, nanocarrier approaches targeted at improving drug pharmacokinetics, biodistributions, and synergism are expected to support ongoing disease management initiatives while expanding the antiviral arsenal against other newly emerging viral infections.

4. SUMMARY OF THE OUTCOMES

As addressed and outlined in the aforementioned literary work, nanotechnology is a potential weapon in the fight against covid. It can function in a way that allows for the targeted distribution of broad-spectrum antivirals to the affected area. Its various components, such as a drug delivery system aimed at innovative vaccines and medications based on nanomaterials, can be employed to treat and cure the patient. The pharmaceutical effects can be delivered via nanocarriers in a quick and emergency manner. Again, using nanotechnology will satisfy the therapeutic interactive and effective criterion for virus-like particle vaccines, diagnosis, and prevention. Future perspectives of pathogen- and host-targeted antiviral delivery, repurposed medications, molecular vaccines, immune-modulators, and to treat and prevent COVID-19 related with nanovector as well. Those are the outcomes from the review and hopefully will work further too.

5. EXISTING RESEARCH GAPS

According to recent research findings, the primary fact that I discovered with this review is that developing and applying nanomaterials, nanoformulations, or nano-based medication is not only the solution, but for example, we should create formulations that are truly available and reliable with financial, social, and pharmacological effect based nanotechnology leading not only to cure or treat but to completely eliminate it. In the future, researchers must focus on the next step in nanotechnology and its applications, as well as new findings addressing the usage and value for research as well as community advantages. According to these several papers and their findings, the gap in technology concerns drug availability, utility, reliability, and cost effectiveness.

6. CONCLUSION

For the purpose of the basic cellular mechanism has been extensively studied using bacteriophage genomes and elements of the equipment for making proteins. These studies involving nanosystems have led to the usage of several viruses as expression systems in biotechnology. antiviral features of nanoparticles/materials can also be used to target the binding, entry, replication, and budding of COVID-19. One of the factors that restricts its use and should be further researched and altered are the toxicity-related inorganic nanoparticles. But the review gives overview and brief information about nanotechnology with its therapeutic interventions and implications with regards to covid infection and prevention too. Engineered particles are drawn to damaged cells, allowing for direct therapy of particular cells. By using this method, sickness can be detected earlier and less harm is done to the body's healthy cells as well.

FUTURE SCOPE

Nanotechnology-based therapies should be fully implemented to combat COVID-19 and subsequent outbreaks in the following ways:

- Creation of contact tracing techniques
- Creation of novel surfaces and surface coatings that aid in virus resistance, adhesion, and inactivation.
- The future of nanomedicine requires the integration of some main characteristics like intelligence, multifunctionality, precision, and personalization.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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