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REVIEW ARTICLE

Futuristic role of nanoparticles for treatment of COVID-19

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ABSTRACT

COVID-19 is a brand new contagious sickness caused by a brand new coronavirus referred to as intense acute breathing syndrome coronavirus 2 (SARS-CoV-2). COVID-19 is a disease that has reached each continent inside the global; it has overloaded the medical system international and it has been declared a plague by using the arena health agency. presently there are not any set up or tested treatments for COVID-19, that is permitted worldwide. Nanoparticles are described as stable colloidal particles ranging in size from 10 to 1000 nm. Nanoparticles provide many advantages to larger particles including multiplied surface-to-volume ratio and improved magnetic properties. Over the last few years, there was a regularly developing interest in the usage of nanoparticles in distinct biomedical packages inclusive of focused drug transport, hyperthermia, photoablation therapy, bioimaging and biosensors. in this review we've got hypothesize the class and synthesis of nanoparticles with diverse remedies along with photobiomodulation, drug shipping gadget, electrochemical nanotechnology biosensors, hydrothermotherapy and photocatalytic pastime which can be used for remedy and prevention of COVID-19 to lower the severity of moderate and slight instances of Coronavirus. We address current in addition to emerging therapies and prophylactic techniques that may allow us to efficaciously fight this pandemic and additionally can also assist to discover the key areas where nano-scientists can step in.

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1. Introduction

COVID-19 is a growing communicable virus which has affected significantly on nature, humanity along with global financial system. The appearance of COVID-19 has exaggerated plenty of people spherical the world and has come to be an extreme risk to human life (Lai *et al*., 2020). some of the nations has delivered vaccine to combat with this virus but no absolute treatment has been yet authorised for this pandemic ailment. This pandemic has turn out to be challenging to countries that has tough-pressed policy architects to recourse the social distancing and regular lockdowns (Block *et al*., 2020). leading-edge apparatuses in particular nanotechnology need to be sturdily considered to block this virus. Nanotechnology-primarily based gear has shown enormous function in preclinical studies towards the variety of pathogens along with respiratory

viruses, herpes virus, human papillomavirus and HIV (Mainardes *et al*., 2020). Nanoparticles, debris that have size in variety of nanometer may be drawn particular interest toward control of COVID-19 virus because of its exclusive homes inclusive of clean fabrication and alteration, low value, suitable small length, and so on (Patra *et al*., 2018). Polymeric, inorganic and peptide-based totally nanoparticles are favorable tools for the treatment of COVID-19 virus (Swierczewkska *et al*., 2018; Pelaz *et al*., 2017).

The nanotechnologies primarily based guidance are the encouraging rising interpretations which might be promoted from outstanding homes such as ratio of higher floor vicinity to quantity, calm surface alteration, greater physicochemical balance and precise optical properties which could cause lower toxicity and better efficiency which makes them extra effective for the effective prevention, treatment and analysis of viral contaminations particularly COVID-19 virus (Zhu *et al*., 2020; Thakur *et al*., 2020; Rupp *et al*., 2007). currently, various nanoparticle-based totally antiviral retailers along with gold, silver, titanium, iron, cadmium and polymeric nanoparticles have haggard the attention of researchers because of it particular optical and encapsulation properties for prevention, treatment and diagnosis of various viral infections like HIV, Ebola, HSV and influenza (Tsang *et al*., Sharma *et al*., 2021b). The extensive aptitudes of nanotechnology are credible that distinctiveness on this subject which could considerably affect against COVID-19 virus (Tyo *et al*., 2020).

Nanotechnology clenches a developing area of medical sciences which can be consumed essentially in different areas. Phytochemicals constituent are most valuable and promising nominees for fabricating green based nanoparticles that owns great potential toward viral infections and long-lasting diseases (Nadaroglu *et al*., 2017: Herlekat *et al*., 2014). Plant arbitrated nanoparticles are low cost-effective, eco-friendly and quickly synthesized at the same time that plays an important role such as a stabilizing or capping agents (Sharma *et al*., 2020a: Sharma *et al*., 2020b). Thus, green approach offers an enormous advantage over physical and chemical approaches because particles formed using this approach are more steady with the preferred size and shape (Anu *et al*., 2020).

2. COVID-19

Severe acute respiratory syndrome coronavirus 2 (SARSCoV-2) has induced the latest rash of coronavirus 2019 (COVID-19). In November, 2019 it turned into outbreak in Wuhan, China and now it has diseased hundreds of thousands of people global and change into a global threat (Khan *et al*., 2020). COVID-19 virus belongs to the subfamily of "Coronavirinae" which are a cluster of enclosed virus with the single-stranded RNA genome about 60-140 nm in size which have capability to contaminate no longer most effective humans however also animals (Dhama *et al*., 2014; Schoemam *et al*., 2019). Short mutation, one-of-a-kind tissue tropism, move-species conversation and variation to diverse epidemiological situations are the relevant functions of this organization of virus (Zhou *et al*., 2020; Li *et al*., 2020a; Chen *et al*., 2020; Liu *et al*., 2020). This group is composed exclusive sorts of virus which belongs to Nidovirales, Cornidovirineae and Coronavirinae circle of relatives. The Coronavirinae own family incorporates three subfamilies: Letovirinae (Alphaletovirus) and Orthocoronavirinae (Alphacoronavirus), Betacoronavirus, Gammacoronavirus and Deltacoronavirus (Decaro *et al*., 2010; Sturman *et al*., 1983; Helmy *et al*., 2020). In 1960, first human coronaviruses have been identified with six exclusive identities. Four of them includes OC43, 229E, NL63 and HKU1 that reasons communal bloodless and gastrointestinal infections while the last includes SARS-CoV and center East respiration Syndrome Coronavirus (MERS-CoV) with excessive morbidity and mortality which have engrossed a plenty of interest and feature brought about extremely good problem (Hassan *et al*., 2020). The causal agent of COVID-19 virus has a 95.3, 88 and 83 % nucleotide likeness to bat CoV RaTG13, SARS-like CoV ZXC21 and SARS-CoV respectively (Hua *et al*., 2020; Shimizu 2020). The common ways of transmission of respiration sicknesses are physical touch and fomites. The transmission of the virus via physical touch denotes to the direct transmission of virus from an infected person to next person and so forth whereas fomites talk to the oblique transmission through halfway objects (Wu *et al*., 2020). Fever, cough and tiredness are the primary signs and shortness of breath, headache, anorexia, sore throat, vomiting are a few conjoint indicators of COVID-19 virus (Chan *et al*., 2020a).

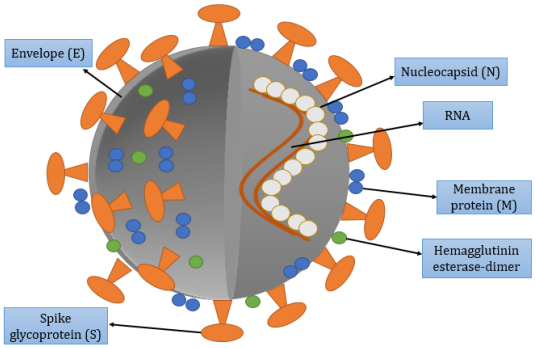

Figure 1. Structure of COVID-19 virus.

COVID-19 has numerous constituents that subsidize to its pathogenesis: spike (S) glycoprotein, small envelope (E) protein, matrix (M) protein and a nucleocapsid (N) protein of the spherical particles in this virus with size in between 60 and 110 nm (Huang *et al*., 2020; Lovato *et al*., 2020; Bai *et al*., 2020) as shown in Fig. 1. Localized in the endoplasmic Reticulum-Golgi region, the N proteins interact with the (+)ssRNA and forms a helical nucleocapsid to promote viral replication within the multitude cell (Astuti 2020). The M protein have large structure with three transmembrane domains and liable for virus shape, size and assembly (Kabir *et al*., 2020). The E protein is profusely uttered inside the vesicle trafficking organelles of the infected cell and elaborate at multiple stages for repetition processes of SARS-CoV-2 (Jiang *et al*., 2020). N and S proteins are expressly important because these are liable for viral infection and arbitrate the virus to enter in host cells (Li *et al*., 2020b; Shereen *et al*., 2020).

Even though daily large number of diseased sufferers are growing simultaneously as per the data is given in **Table 1** (Situation by WHO region) and no formally permitted capsules is approved against COVID-19 virus (Jin *et al*., 2020). The current managements are based totally on symptomatic remedy and increase the immunity of breathing device to fight against this virus (Zumla *et al*., 2020). Some of studies scientists are finding the transmission similarities among the SARS-CoV-2 and SARS-CoV to mature capsules centered to key proteins which might be involved in viral replication and proliferation (Chan *et al*., 2020b; Vellingiri *et al*., 2020). These days, the boom of antiviral capsules has jammed the researcher's attention closer to those capsules which may be used towards numerous forms of viruses consisting of new versions (Jackmam *et al*., 2016; Revuelta *et al*., 2018). To overawed the margins and progress of antiviral remedies, multidisciplinary studies hard work is required in the direction of the increase of alternative antiviral rehabilitations for unique stages in repetition cycle (Mohammadi *et al*., 2019). In this want, nanotechnology have attracted the increasing interest and already is getting used for treatment of viral infections because of its better capability (Singh *et al*., 2017a; Szunerits *et al*., 2015).

3. Nanotechnology against COVID-19

In today's technology, one of the promptly emerging conceptions in last few years is nanotechnology that have taken incredible growth. The nanoparticles contain typical physical and chemical properties that have potential to mature new electronic devices with impending proposals in broad diversity of disciplines (Mirzaei *et al*., 2017). Nanoparticles are the particles which are measured in nanoscale (10^{-9} m) size with value-added conductive in nature, catalytic reactivity, and chemically stable due to its larger surface with respect to volume ratio (Agarwal *et al*., 2017). Various predictable chemical approaches are used to fabricate bulk nanoparticles that's involve toxic

WHO Region	COVID cases confirmed
Europe	133 Million
Americas	128 Million
South-East Asia	51 Million
Eastern Mediterranean	19 Million
Western Pacific	15 Million
Africa	8 Million

Table 1. COVID cases confirmed by different WHO region (Source: World Health Organisation)

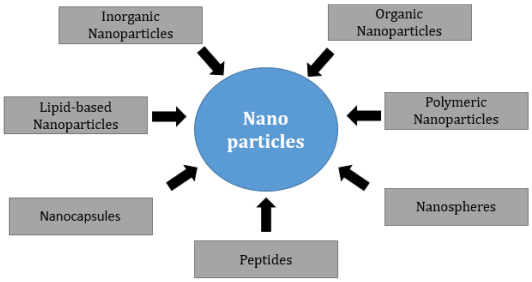

Figure 2. Schematic diagram of classification of nanosystems.

chemically agents to maintain its stability that toxic to environment. To overcome this, green approach is growing as nontoxic and eco-friendly by using plant extract known as biosynthesis of nanoparticles that acts as a capping agents (Salam *et al*., 2014).

To normalize the chemical toxicity from environment, green approach of metal oxide nanoparticles is being used that permits a uniform shape and size of nanoparticles (Anastas *et al*., 2010). The nanoparticles are classified into different nanosystems categories such as inorganic nanoparticles, organic nanoparticles, lipid-based nanoparticles, polymeric nanoparticles, nanocapsules, nanospheres and peptides as shown in **Fig. 2**. For bio-medical applications, enhancement in bio-degradable, functionalized and bio-compatible nanoparticles is being persisted as a fabulous energetic area for research (Cai *et al*., 2007; Thakur *et al*., 2021a; Zhang *et al*., 2011).

3.1 Synthesis

The preparation of green synthesized nanoparticles with uniform size and morphology can be achieved by recommended approaches "top-down" and "bottom-up" (Thirumalai *et al*., 2010). In the top-down approach, the bulk materials are broken into small units whereas in the bottom-up approach it deals with chemical reactions that deliver the metal atoms by controlling aggregation (Rajkumar *et al*., 2017; Zou *et al*., 2013). Various methods are being used for synthesizing green nanoparticles due to their enormous utilities in the medical applications (Parida *et al*., 2011). Many biological agents like microorganisms, fungi, plant extracts, etc. are used in green synthesis because of their biocompatibility (Dhandapani *et al*., 2012; Makarov *et al*., 2014). Green approach leads to unique chemical and physical properties of nanoparticles due to larger surface area with respect volume on compared to bulk material with the same composition and it also allow to use as catalysis, drug delivery, anticancer, antibacterial and many more applications (Nadaroglu *et al*., 2017; Herlekar *et al*., 2014). The natural bio-logical agents such as plants, bacteria, fungi, biodegradable polymers, sugar, etc., have numerous benefits over chemically reducing agents such as sodium citrate, sodium borohydrate, sodium dodecyl sulfate (Swierczewska *et al*., 2011). This approach considered as easy and eco-friendly, require low pressure and temperature, very low consumption of toxic materials and neglect the use of synthetic agents for the fabrication of green nanoparticles (Alexandridis *et al*., 2011). The green approach has capability to control the morphology (shape & size) of nanoparticles such as nanorods, nanospheres, nanoporous and nanowires., that substantial role in several trending applications (Das *et al*., 2017; Gahlawat *et al*., 2019).

3.2 Mechanism of formulation of nanoparticles

For the synthesis of nanoparticles, an aqueous or non-aqueous solution of metal precursor is dissolved with a reducing agent such as plant extract (Polte *et al*., 2010a). The whole process is conceded with existence of stabilizing or capping agent that effects the aggregation of nanoparticles (Polte *et al*., 2010b). The stabilizing agent get absorb on the surface of nanoparticle and provides a repulsive force like steric stabilization or electrostatic stabilization that can overturn the aggregation (Xia *et al*., 2009). Based on chemical mechanism nanoparticles it consists of three phase synthesis mode, namely, precipitation of metal atom, nucleation and crystal nuclei growth (Polte *et al*., 2010c; Polte *et al*., 2012).

In first phase (Precipitation), the reducing agent is mixed with precursor solution of metal atom where it gets condensed while the concentration of metal atom is continuously accumulative (Minati *et al*., 2014). In second phase (Nucleation), when the concentration of metal atom goes beyond the critical supersaturation, it begins to gather and form crystal nuclei. With the formulation and crystal nuclei of growth, the concentration of metal atom starts to decrease (Majeric *et al*., 2020). In third phase (Crystal nuclei growth), huge amount

of metal atom is consumed and the concentration of metal steadily drops down below the critical supersaturation and growth of nuclei governs the whole process (Bang *et al*., 2010). When the concentration goes below the saturation level, the growth of crystal nuclei gets discontinued and formulation of pure nanoparticles is finally prepared (Shang *et al*., 2013; Khan *et al*., 2014). The first and second phase of mechanism plays an important role whose mixing of precursor and reducing agent effect the amount and uniformity of size of nanoparticles (Jana *et al*., 2001; Ji *et al*., 2007). To attain the green nanoparticles with identical morphology and deviation of small size, the suitable regulation of ingredients, concentration and forth of two phase agents, it is vital to normalize the efficiency of mixed reaction (Van *et al*., 2009). So the control ability of microfluid reaction process is an imperative condition to accomplish the green nanoparticles with uniformly particle size and consistent morphology (Bin *et al*., 2009; Majeric *et al*., 2015).

4. Treatment of COVID-19 Virus

4.1 Photobiomodulation therapy

In latest years, photobiomodulation treatments have produced massive effects in decreasing lung inflammation. due to the potential impact of photobiomodulation remedy on immune responses it is able to be a powerful treatment for COVID-19 virus. Genetic checking out well-known shows that SARS Covid-19 is probably in the Betacoronavirus class with diffused and moderate symptoms that contribute to immune damage causing cytokine launch syndrome which sooner or later ends in acute respiration distress syndrome (Ortiz-Prado *et al*., 2020; Shi *et al*., 2020). To deal with this issue, alternative healing procedures for irritation are photobiomodulation therapy additionally known as low-level laser remedy. It's miles a one-of-a-kind approach of nearby area for developing irritation, which has been used since the ultimate 50 years (Mussttaf *et al*., 2019). It's far described as when a low-electricity laser or a mild emitting diode of 1-500 mW is used to regenerate tissue and decrease irritation and pain. an excellent spectral light in red or near infra-purple (600-900 nm) with a power of 1-5000 mW/cm^2 is used in photomodulation therapy (Carvalho *et al*., 2017). It is able to regulate cellular and cell metabolism, signaling, infection and chemical messengers that in addition the effect of decreasing extreme lung inflammation and the local balance of immune responses. Li *et al*. cautioned that the focus of remedy must be on prevention of infection and improved immunity in the first section of the medical reaction so that within the early ranges of the immune response the pressure of the lungs and prevention of acute respiratory disease be prioritized (Li *et al*., 2020c).

Acute lung infection is linked to an elevated wide variety of polymorphonuclear neutrophils within the interstitial area and the release of different pro-inflammatory cytokines, together with IL-1β, IL-6, IL-8, TNFα, MCP-1 and MIP-1. About 36-48 hours after these activities, cytokine secretion returns to everyday within the bronchoalveolar lavage fluid despite the fact that the number of polymorphonuclear neutrophils,

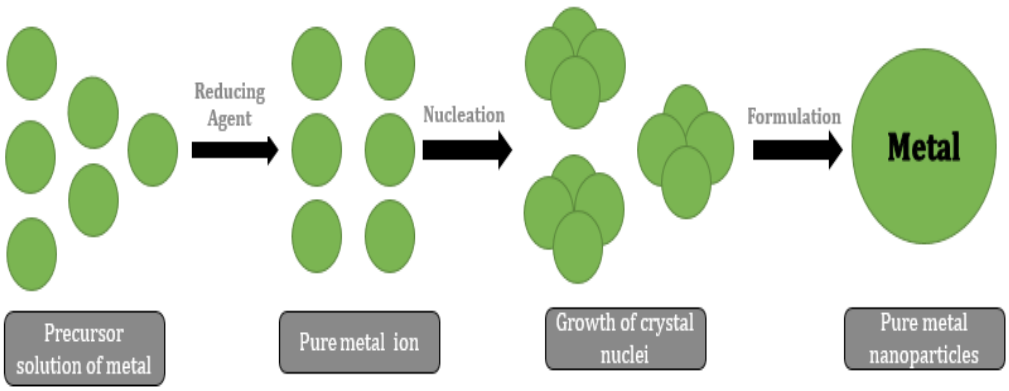

Figure 3. Formulation of nanoparticles.

monocytes, macrophages and lymphocytes increases and lung characteristic due to collagen formation. numerous research has shown that polymorphonuclear neutrophils can also play a primary role in regulating all the above-mentioned immune responses with growing numbers of polymorphonuclear neutrophils, monocytes and macrophages. further to the inhibitory impact on inflammatory cell chemotaxis, polymorphonuclear neutrophil may additionally reduce the range of leukocytes present in inflammatory regions (Curv *et al*., 2016). Increased stages of IL-1β are related to reduced analysis in sufferers with acute respiratory misery syndrome. IL-1β plays a key role in beginning inflammatory methods (Oliveira *et al*., 2014). This cytokine additionally will increase neutrophil survival rate and promotes irritation. Polymorphonuclear neutrophils can reduce the occurrence and severity of acute respiratory misery syndrome by means of decreasing the extent of IL-1β. IL-6 is a pleiotropic cytokine that plays a crucial position in acute respiratory misery syndrome pathophysiology and is related to decreased ailment analysis. patients with Acute respiratory misery Syndrome show an expanded level of IL-6 in the lungs and plasma. IL-eight contributes to acute breathing distress syndrome pathophysiology, neutrophil chemotaxis and lung survival. Polymorphonuclear neutrophils can significantly reduce the extent of IL-eight inside the lungs, lessen acute respiration misery syndrome and decrease its mortality price (Curv *et al*., 2016). TNFα is liable for adhesion and activation of neutrophils, coagulation and edema. it may also promote the release of IL-6. TNFα stages are typically high inside the serum and lungs of patients with acute respiration distress Syndrome. Polymorphonuclear neutrophils are useful in decreasing TNFα ranges in both web sites (Curv *et al*., 2016; Oliveira *et al*., 2014). MCP-1 plays a key function in monocyte activation, and its stage rises in lung infection. Monocyte migration may be decreased by means of polymorphonuclear neutrophils because of the discount of MCP-1 (Oliveira *et al*., 2014).

Every other manner to triumph over the response of severe irritation within the lungs is to treat photobiomodulation. Anti-inflammatory and rejuvenating homes of photobiomodulation were proven to deal with persistent lung infection, voice injury, periodontitis and oral ulcers (Lavaee *et al*., 2019; Costa *et al*., 2016; Gandhi *et al*., 2019; Lou *et al*., 2019). As compared with capsules such as immunosuppressive tablets consisting of corticosteroids photobiomodulation has greater trendy aspect results and its systemic outcomes are constrained. numerous studies have said continuous consequences of photobiomodulation on anti-inflammatory lung diseases. De Lima *et al*. examined the impact of photobiomodulation on acute respiration distress Syndrome in mice. They observed that TNFα had a large impact on neutrophil uptake and migration which performed a crucial position in acute respiration misery syndrome pathogenesis. Photobiomodulation successfully reduced neutrophilic penetration and TNFα levels in bronchoalveolar lavage fluid and extended cAMP and decreased TNFα m-RNA in alveolar macrophage. these activities decreased the prevalence of acute respiration misery syndrome (De Lima *et al*., 2011). Oliveira *et al*. examined the impact of photobiomodulation on acute respiratory misery syndrome in mouse fashions and found that photobiomodulation decreased the quantity of neutrophilic migrations in the lung tissue and in the end decreased the severity of the sickness (Oliveira *et al*., 2014). Mehani compared the immunomodulatory outcomes of photobiomodulation with respiration physical remedy in sufferers with persistent pulmonary disease. each of these techniques have been described as clinically beneficial due to the fact photobiomodulation changed into effective in decreasing IL-6 levels and increasing CD4 + / CD8 + levels (Mehani *et al*., 2017). Different experimental and healing studies additionally said fine results of photobiomodulation on acute and continual pulmonary inflammation and extreme lung irritation caused by ischemic-intestinal recurrence (Da Cunha *et al*., 2018; De Lima *et al*., 2013). Additionally, it has been counseled that photobiomodulation can be beneficial in reducing pulmonary fibrosis (De Brito *et al*., 2020). Therefore, in view of the pathophysiology of COVID-19 and the capacity wonderful outcomes of photobiomodulation therapy in modulating immune feature, this treatment can be effective in treating COVID-19 contamination with acute respiration depression.

4.2 Drug delivery system

The medical growth of COVID-19-centered tablets requires the identity of the appropriate shipping gadget that complements drug absorption and

ensures excessive intracellular shipping at the same time as preserving proper balance between the preferred organ (lung) and circulatory device (Singh *et al*., 2020). Get right of entry to a managed release structure that can keep a small lively concentration of a specific drug substance can substantially lessen the effects of conflict and might reduce liver burden as nicely (Van Dijk *et al*., 2018). Numerous nanosystems had been studied to test their motion against SARS COVID the usage of polysaccharides nanoparticles, mesoporous nanoparticles, graphene oxide silver nanocomposites, hybrid colloid silver nanoparticles and quantum dots (Zhao *et al*., 2013; Theobald 2020; Chen *et al*., 2016). Focused transport of a paid drug through the network corporation system ensures complete web page performance and minimal toxicity, while controlled release structures maintain powerful complete-fledged drug overload at the same time as reducing the stabilization of the drug-carrying environment, for this reason decreasing centered global drug overload. forthcoming facet results (Loczechin *et al*., 2019; Ari 2020).

Aerosol-based drug shipping structures exist as a basis for current lung problems. but, the evacuation of aerosols and droplets containing respiratory microorganism all through the management of aerosol remedy will increase the probabilities of involuntary transmission of viral particles. delivery of aerosolized injections to sufferers with COVID-19 consequently endangers the safety of medical examiners (Ari 2020). Novochizol, a superior drug delivery gadget, which mixes nanoparticle-based totally aerosol method threatens capacity leads and has high promise for the possible delivery of capacity COVID-19 pills and in addition maintains complete attention in infected lungs. this first-section polysaccharide nanosystem includes completely indestructible and biocompatible chitosan nanoparticles that adhere tightly to the pulmonary epithelia while, making sure continuous drug launch. in addition, the device additionally tolerates the undesirable machine distribution of the drug (Balkrishana *et al*., 2021).

Mesoporous silica nanoparticles with high biocompatibility and chemical balance have passed off as the very best attention of encapsulation and safety of nucleic acids. Nanoparticles can be especially synthesized to bind oligonucleotide mutations of a magnificent length which include DNA, RNA and siRNA (Tarn *et al*., 2013). To promote the development of mRNA and pDNA-based totally vaccines, N4 Pharma, a drug organisation excellent recognized for developing nano shipping structures. these silica-nanoparticles are a novel nucleic acid with uncommon residences of polyethyleneimine. This location holds nuclear acids such as mRNA / pDNA passing through the cell and protects them from nuclear enzymes. the primary advantage of silica-nanoparticles is they do no longer harm the cellular membrane when testing cells as compared to lipid shipping systems and do not produce any inflammatory reactions inside the injection web page or systemic facet consequences (Tarn *et al*., 2013).

The Theranostic nanoparticles system incorporates therapeutic drug particles which can be presented as an effective drug shipping machine to seize COVID-19 viral transmission. The theranostic-based nanoparticle drug transport system offers verified ways to control anti-bacterial and anti-intranasal shipping mechanisms. They can be divided into three wide categories: organic, inanimate and natural compounds similar to or compounds of protein nanoparticles. The network corporation system efficaciously paralyzes the transport of drug-linked mucosal pathways and keeps excessive concentration of the provider drug at the site of infection while transmitting destructive detrimental results on wholesome cells and tissues (Itani *et al*., 2020). As it's far widely recognized that this infectious virus includes the COVID-19 virus which specifically initiates their infection at the floor of the mucous membranes and mucosal treatment presents a powerful method to incorporate the COVID-19 contamination. The covalent conjugation of therapeutics and hydrophilic polymer backbone with self-immolating linker molecule presents a powerful drug shipping method to supply antimicrobial pills. The hydrophilicity of the polymer backbone provides physiological coherence even as compounding will increase the stream time of the carrier drug molecule by way of offering stability in opposition to enzymatic degradation (Singh *et al*., 2017b). Recognizing the peptidomimetic environment of most COVID-19 therapeutic tablets particularly concentrated on viral principal protease, polymer-drug conjugates offer lots wanted mechanisms as drug companies whilst ensuring protease safety and offering

appropriate hydrophilicity to molecules pills to communicate. for their mobile purposes (Dai *et al*., 2020).

Plants and their herbal products are very powerful in treating chronic breathing diseases by way of identifying complex mechanisms underlying the pathophysiology of this ailment (Prasher *et al*., 2020). however, the usage of antiretroviral drug approach is questionable because of the lack of suited clinical trials demonstrating its efficacy towards the underlying virus (Yang 2020). The development of herbal steel nanoparticles within the form of uncooked substances thru the use of plant life presents an exceptionally green mechanism related to its life-shape, low toxicity, value effectiveness and durability (Mitra *et al*., 2020). The steel nanoparticle provides diverse applications such as vector shipping of medicine and allows the inhibition of viral access into the host mobile thereby stopping its unfold to healthy cells (Yang *et al*., 2016). Similarly, the unique physical, chemical, magnetic and optical residences of the noble steel nanoparticles facilitate the detection of viruses and biosensing backward metabolites produced via viral infections. Inexperienced nanoparticles are synthesized with highest quality performance or biodegradable polymer additionally complements its tolerance to wholesome cells and tissues (Draz *et al*., 2018).

Research data on drug delivery systems because the closing 25 years has been investigated for a spread of medical purposes and may be used inside the COVID-19 epidemic because of international emergency. Nanotechnology-primarily based techniques may additionally play a crucial function in enhancing the identification and production of COVID-19 vaccines. In this age of superior nanoscience, the device can get right of entry to all of the important gear inclusive of theranostics, nucleic acid exams such as reverse transcription polymerase chain reaction (rt-PCR), computed tomography, and protein trying out necessary to combine such techniques into possible techniques and play a key function in fighting these outbreaks.

4.3 Electrochemical nanotechnology biosensors

Nanotechnology has countless packages in lots of regions which includes apparel, sensors, eye contact, agriculture, food, electrical structures, electronics and biomedical packages. Nanoparticles have better cloth and chemical properties such as melting, comparison, visibility, toxicity, thermodynamic, coloration and magnetic houses as compared to many materials relying on their size (Jeenandam *et al*., 2018). Iron oxides are normally used in microelectronic circuits, sensors, piezoelectric gadgets and as catalysts due to differences in electronic shape. Oxygen gaps inside the oxide nanoparticle form a special atomic association than the bulk that enhances the chemical and physical capabilities in area of iron oxides (Singh *et al*., 2017a). The sizes of nanoparticles range between 1-100 nm which provides a huge amount of extent measurement for the development of biosensors structures that can be used for the detection of viruses consisting of antibodies, enzymes, DNA, cells and proteins (Mokhtarzadeh *et al*., 2017). By using applying nanotechnology techniques to viral biosensors it could triumph over the negative aspects of contemporary viral detection methods by means of decreasing the cost and time of detection. Nanoparticles used in biomedical sensors have functional electrical and mechanical properties that contribute to the development of the electrochemical, optical and magnetic homes of biosensors (Li *et al*., 2017). Diverse forms of nanomaterials used for diagnostic and biosensing which include nanoparticles, nanocomposites, carbon nanotubes, quantum dots and graphene or graphene-based nanomaterials (Pena-Bahamonde *et al*., 2018).

Electrochemical biosensor is a sensor that has been used as a quantitative or semiquantitative evaluation of oxidation in addition to a discount in excessive specificity and sensitivity to electroactive species. it really works with the aid of potentiometric, amperometric, conductometric, polarographic, capacitive or piezoelectric methods (Kumar *et al*., 2018). Reworking the active body into an electrochemical transducer for electrode operation, the vital layer is the touch between the electrode and the analyzed location (Grabowska *et al*., 2014). The generated contemporary is without delay associated with the attention of electroactive species and the transducer present within the biosensors will become conductive and assists in the attachment of the bio-popularity issue to the surface (Krejcova *et al*., 2012). The suitable materials or electrodes used to design the

electrochemical biosensors are gold, silver, nickel, copper, platinum, mercury and diverse carbon electrodes containing carbon as an electrical detail (Grabowska *et al*., 2014). Electrode transducers are regularly used for detection of viruses because of local adjustments and the interaction of electrochemical transducer electrodes. Currently, several researchers are developing glycocalyx-based biosensors that form a dense layer at a concentration of 100 mM and are considered to be naturally occurring viral receptors with a selection of viral subtypes (Dziabowska *et al*., 2018). Modification occurs due to the inability of the biorecognition element represented by the receiver in place of the electrode. By applying an AC field to the electrode, positive dielectrophoresis will cause bacterial particles to attract nerves. The sensor will detect the signal of the virus particles and further amplification will be performed by the amplifier and then convert the amylometric, potentiometric or impedimetric frequency signal. Due to the easy localization and compatibility of the electrochemical transducer electrodes they used for viral detection (Krejcova *et al*., 2015).

According to the above, electrochemical biosensors can be used for direct, easy, inexpensive and rapid detection of patients with SARS-CoV-2 virus. Non-structural proteins ORF8 and E2 surface glycoprotein SARS-CoV-2 can bind to porphyrin 1-Beta Chain Hemoglobin and release heme. Biosensor receptors are made up of 1-Beta Chain of Hemoglobin so if the model allows, SARS-CoV-2 proteins will bind to hemoglobin molecules in a transducer that releases part of the heme that produces an electrical signal, taking into account the measurement. heme focus before and after. investigation.

4.4 Hydrothermotherapy

The term hydrothermotherapy comes from the Greek words for "Hudor" meaning water, "Thermo" for heat and "Therapeia" for healing, also known as hydrotherapy. It is the wise use of water of any kind that combines ice and steam indoors or outdoors to treat disease (Calthrop *et al*., 2013). Hydrothermotherapy is a unique form of synthetic fever for the human body because the simplest benefit of the fever within the contamination is the higher existence expectancy of the host and the shorter length of the disease (Zellner *et al*., 202). Self-produced warmness has an antiviral effect due to the fact when a human and rhinoceros' box is immersed in warm bathtub water at a temperature of 113 ^{o}F the temperature decreased the virus to 90 % replication, but it did not kill human cells (Conti *et al*., 199). Infectious retailers can prompt the flu as a protection mechanism (Cannon *et al*., 1998). Influenza frequently happens when monocytes come into touch with viruses and bring about an increase in IL-1 that's a flu-like reaction as IL-1 is pyrogen (Dinarello *et al*., 1986; Banet 1986). IL-1 additionally plays a position in cell and humoral immune function towards the pathogen (Shimizu 2020). Influenza promotes the migration of leukocyte and neutrophils into the place wherein the pathogen is gift and turns on T mobile characteristic (Hanson *et al*., 1983). The maximum crucial thing is nuclear issue kappa B that's responsible for activating IL-1, IL-6 and IL-eight and also influencing the other two pathways of p53 protein and warmth-surprise component protein 1 (Perkins 2007).

The most not unusual technique used in hydrothermotherapy remedy is sauna. for the duration of the sauna method, the frame temperature rises to 102 ^{o}F among 15-20 min. This reasons dilation of blood vessels in the pores and skin and produces about 1lb of weight reduction because of sweating which increases heart fee and decreases peripheral resistance (Sohar *et al*., 1976; Podstawski *et al*., 2020). The hematological effects of sauna elevated hemoglobin, range of white blood cells and platelets inside everyday limits (Laukkanen *et al*., 2018b). Sauna also lowers the level of Serum C-reactive protein (CRP) associated with low systemic irritation due to the fact excessive CRP levels may have a terrible impact on immunity (Laukkanen *et al*., 2018b; Tilg *et al*., 2006; Ernst *et al*., 1990). Studies have shown that white blood cells are multiplied after one Finnish sauna consultation and the response changed into extra in athletes and included a growth in neutrophils and monocytes (Pilch *et al*., 2013). An examine by means of a collection of Finnish sauna users has shown a lower in systemic inflammation and oxidative pressure (Kunutsor *et al*., 2018).

Another advantage of hydrothermotherapy is that the remedy of hyperthermia reasons a high level of IL-6 without the use of IL-1-beta or tumor necrosis element (TNF) which may additionally

prevent cytokine storms because of a growth in IL-6 itself appears to lessen irritation Kunutsor *et al*., 2018; Raison 2017; Raison *et al*., 2018). One growth in IL-6 is the way workout reduces irritation which is the same as fasting and vegetarian diets (Pedersen *et al*., 2008; Wueest *et al*., 2014; Montalcini *et al*., 2015). The impact of hyperthermia on coronavirus infection by means of interferon activation seems to be fine at excessive temperatures of 104.9°F (Robins *et al*., 1989). Hyperthermia reasons the synthesis of gamma interferon in mobile cultures (Downing *et al*., 1987a). In rhesus monkey hyperthermia increases alpha interferon and non-interferon antiviral properties (Neville *et al*., 1988). All of this can contradict the consequences of the virus as interferon has the capacity to lessen or forestall viral infections (Downing *et al*., 1987b). A possible alternative to hyperthermia is that it may paintings towards viruses that growth membrane fluid in each viruses and goal tissues that have an effect on the pathogenesis of a particular virus (Dynlacht *et al*., 1992; Owens *et al*., 1995). The blessings of hyperthermia aren't only advantages related to the immune gadget however also benefits from different systems consisting of cardiovascular, respiratory and integumentary systems (Zaccardi *et al*., 2017; Kunutsor *et al*., 2017; Hannuksela *et al*., 1988).

all of the above recommendations may be decreased to including decreasing body temperature weakening the immune system or enhancing the immune machine (Rabenau *et al*., 2005; Lamarre *et al*., 1989) and using warmness remedies which includes steam baths, saunas or warm showers appear to be associated with lower incidence of contamination and lower mortality rates. As a result of viruses along with COVID-19 (Del Rio *et al*., 2020). it is able to be hypothesized that more than one remedies followed by way of a cold are the first powerful method of preventing and treating moderate to excessive coronavirus 2 contamination and this technique is followed with the aid of a large wide variety of people in each community that effect of the COVID-19 virus.

4.6 Wastewater treatment via Photocatalytic activity

Photocatalytic activity provides an effective disinfectant in infected water with minimum manufacturing risk. a spread of contaminants is determined in contaminated water, especially those discharged from the health center consisting of drug residues, chemical materials, radioisotopes, bacterial pathogens and at some point of the remedy of COVID-19 patients (Achak *et al*., 2021). The first lines of the COVID-19 virus were found by researchers from the Netherlands in contaminated medical institution water (Medema *et al*., 2020). Later Wu *et al*. found COVID-19 viruses in clinic infected water believed to be transmitted from the faces of an infected character (Razzolini *et al*., 2021). As in many nations around the arena, many research has determined the presence of COVID-19 inside the human frame in COVID-19 patients without or with gastrointestinal signs and symptoms (Vickers 2017). Those harmful pollutants are the best germs that may represent the chemical, biological and bodily risks of public and environmental health.

Photocatalytic hobby or degradation includes photocatalyst semiconductor oxides appearing as heterogeneous catalysts inside the presence of electromagnetic radiation. They act as dwelling or non-dwelling organisms accumulated from any environment or suspended from beverages or gases that come in contact with solid depend. Photocatalysts use photocatalytic reactions to break down water and create hydrogen and this situation occurs due to a technique known as photocatalytic oxidation and discount (Kim *et al*., 2003). Photocatalytic pastime falls into three principal categories:

(1) formation of photoinduced rate service

(2) separation of price provider and distribution to the surface of the photocatalyst

(3) oxidation and discount reaction on the surface of the photocatalyst (Nasir *et al*., 2020).

Zhang *et al*., 2021, proposed the development of photocatalysis inside the combat towards contamination from the water system. They observed that MS2 bacteria were effectively killed via using TiO_2 nanoparticles as photocatalyst inside the presence of UV rays. major studies are targeted on growing a TiO_2-primarily based photocatalyst that can block viruses wherein there are seen mild rays (. Later, doubtlessly diverse metals other than TiO_2 which include

iron oxide, silver, alumina and copper oxide have been tested for bacterial extraction within the presence of visible light (Giannakis *et al*., 2017; Hu *et al*., 2010; Ditta *et al*., 2008). These photocatalyst are very effective as an answer for sanitation and waste disposal because of non-toxic, reasonably-priced and bulky. diverse metal photocatalysts have been efficiently used to inhibit viruses inclusive of phage MS2, bacteriophage Qβ, phage f2, murine norovirus and human adenovirus (Cho *et al*., 2005; Lee *et al*., 1998; Zuo *et al*., 2015; Cho *et al*., 2011; Lee *et al*., 2008; Yu *et al*., 2015; Li *et al*., 2008). Photocatalysis technology also utilized carbon-primarily based photocatalyst which attracted extra interest to the wastewater system and better potential for herbal light harvesting (Thakur *et al*., 2021b; Chi *et al*., 2019; Sharma *et al*., 2021a). These non-metal photocatalyst compounds consist of carbon-primarily based materials including fullerene, carbon nanotube, carbon dot and graphitic carbon nitride are designed to kill bacteria (Alias *et al*., 2020; Moor *et al*., 2014; Moor *et al*., 2015; Banerjee *et al*., 2012; Barras *et al*., 2016; Sengupta *et al*., 2021; Zhang *et al*, 2021; Sharma *et al*., 2021c).

The photocatalysis method of disinfection is by destroying the shell and the bacterial capsid. Genetics, minerals, and proteins are released within the virus and cause the virus to malfunction (Pan *et al*., 2020). The photocatalysis process of this virus occurs on the surface of the film and is explained by the depletion of photodegradation of the viral protein capsid and as a result the release of viral RNA is covered with a layer of protein (Pandey *et al*., 2009). When the virus reacts to the surface of the catalyst, active radicals such as O^{2-}, HOO^{-} and HO^{-} are synthesized that help stabilize CH bonds and reduce viruses (Habibi-Yangjeh *et al*., 2020). Photocatalytic activity based on semiconductor materials can be briefly described as shown in Fig. 4.

When a semiconductor is illuminated light electron-generated electron (e^{-}) and hole (h^{+}) are produced and shared with other substances to form ROS including H_2O_2, H^{+}, and O^{2-} and these ROSs contribute to the process of photocatalytic degradation bacterium that continues to form active forms of oxygen and attack the cell membrane (Regmi *et al*., 2018). Coenzyme A in the cell membrane is damaged and leads to respiratory obstruction which depends on the fixed cell membrane, decrease or loss of cellular respiratory function and ultimately lead to cell death (Byrne *et al*., 2015).

To study the electricity of photocatalysis as another antibody solution for COVID-19, information the way to efficaciously shut down and destroy germs, in particular coronaviruses at some stage in photocatalytic disinfection is critical. it may assist to broaden an extra efficient and powerful photocatalyst with

(1) layout morphology in step with virology

(2) assembling or working with transition metal ions

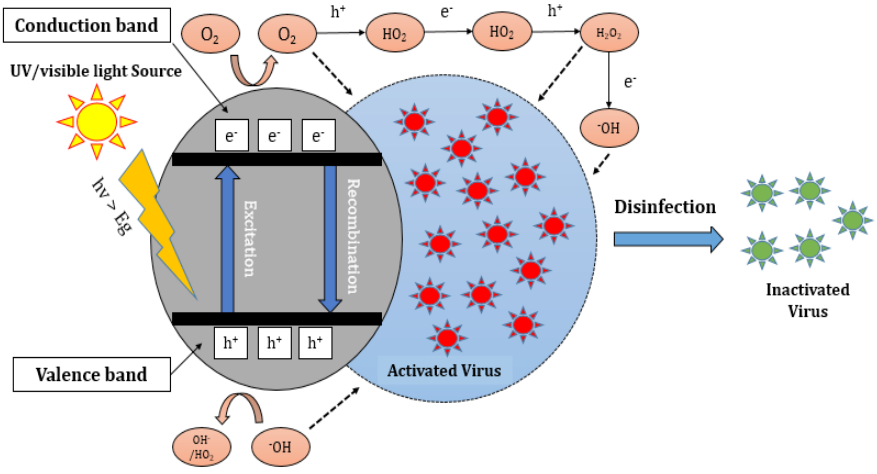

Figure 4. Photocatalytic mechanisms on virus inactivation.

(3) to make numerous compounds or photocatalyst for green use of power and recuperation.

Giant increase in proof suggesting the presence of the pathogenic novel SARS-CoV-2 in contaminated water. The disinfection through photocatalyst became substantially examined and found out that within the presence of electromagnetic radiation photocatalysts can lessen any microorganism unfold inside the vicinity or pollute the air which include the current lethal COVID-19 virus. Researchers are running to enhance the stability and effectiveness of photocatalyst inside the presence of visible spectrum radiation similar to the sun's rays so that protection have to be guaranteed before use in a public setting. Its miles were hoping that photocatalyst could be marketed and extensively well-known inside the near destiny which will clean up pollutants and kill deadly species together with the COVID-19 virus.

5. Conclusion

By then December 2019, the SARS-CoV-2 epidemic had claimed many lives and located nations round the world in a country of surprise. the character of this epidemic of COVID-19 has highlighted the emergence of latest technological proposals as a means of containing and stopping the unfold of sickness. Deficiency of accredited antimicrobials or vaccines and coffee efficacy and the prevalence of adverse reactions require unique treatment techniques towards the COVID-19 virus. presently, there are different authorized guidelines for the safety of COVID-19 but it's miles very crucial to prevent its spread and remedy with numerous techniques which include isolation of inflamed sufferers, use of contraceptives, antibiotics and instant screening programs. As new structures, nanotechnology assets result in the improvement and development of diverse nanoscale structures for the prevention, remedy and analysis of COVID-19 virus. Creatures based totally on nanotechnology can offer managed and continuous launch of antigens and healing agents as well as disrupt cellular penetration to improve the prevention and treatment of COVID-19 viruses. This evaluate discusses how chemical and artificial nanoparticles may be used to save you the spread of the virus, enhance the performance of defense structures and boom the accuracy of COVID-19 diagnostic treatment with photobiomodulation, drug shipping device, electrochemical biosensors, and hydrotherapy and wastewater remedy photocatalytic pastime. In addition, nanoparticles enhance conventional treatment options and help triumph over their barrier as these nanoparticles can be modified to carry antibodies to goal cells and simultaneously spark off the immune reaction in opposition to the virus. The effectiveness, stability and safety of nanoscale-based prevention and treatment structures and diagnoses need to be evaluated by means of appropriate medical conclusions. Ongoing research on the way to deal with these issues must preserve. subsequently, nanotechnology gives some thrilling packages to sell the COVID-19 virus prevention, remedy and prognosis.

6. Conflict of Interest

There is no conflict of interest between the authors as all played them specify role.

7. References

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