TRENDS IN SCIENCES 2025; 22(12): 11481
https://doi.org/10.48048/tis.2026.11481
REVIEW ARTICLE

Nanomaterials and Vitamins to Combat Future Pandemics: Lessons from COVID-19: A Review

Ehsan Kianfar[1,*], Amar Yasser Jassim[2] and Ameer Abbas Mohammed[2]

[1]*Young Researchers and Elite Club, Gachsaran Branch, Islamic Azad University, Gachsaran, Iran*
[2]*Department of Marine Vertebrate, Marine Science Center, University of Basrah, Basrah, Iraq*

([*]Corresponding author: ehsankianfar775@gmail.com)

Received: 3 August 2025, Revised: 5 September 2025, Accepted: 12 September 2025, Published: 1 October 2025

Abstract

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has infected over 100 million people globally due to its high infectivity. After decades of efforts on the studies of nanomaterials, researchers have applied nanomaterials-based strategies to combat the pandemic of the coronavirus disease 2019 (COVID-19). First, nanomaterials facilitate the development of easy, fast, and low-cost diagnostic assays to detect SARS-CoV-2 and related biomarkers. Second, nanomaterials enable the efficient delivery of viral antigens to antigen-presenting cells or serve as adjuvants in the host, leading to vaccine development at an unprecedented pace. Lastly, nanomaterials-based treatments may inhibit SARS-CoV-2 replication and reduce inflammation. Overall, nanomaterials have played important roles in controlling this COVID-19 pandemic. Here, we provide a brief overview of the representative examples of nanomaterials-based diagnostics, vaccines, and therapeutics in the fight against COVID-19. The use and effectiveness of state responses is constantly evolving, particularly in relation to physical distancing policies during the COVID-19 pandemic. Testing is a measure of response performance and will be a central point during the infectious disease pandemic as all countries face similar situations. COVID-19 is a unique opportunity to assess and measure the success of a country, control its spread, and combat the social and economic impacts of interventions. By fighting the factors associated with testing and reporting, understanding the limits on COVID-19 case numbers will strengthen the country's response to these and future pandemics, and improve the reliability of the knowledge gained by cross-country comparisons. With amazing and amazing COVID-19, a lack of testing may not trust the efforts of the entire community, rather than the entire population. The emergence of novel strains of SARS-CoV-2 highlights the pressing need to investigate various strategies for enhancing pandemic resilience. Even though tried-and-true methods like social separation, masks, and vaccinations have proven effective, issues with immunizations make finding a global answer more complex. This paper underscores the pivotal connection between immunological resilience and vitamins, shedding light on the compromised immune response resulting from undernourishment. Vitamins become essential for protecting the body from viral invasion, particularly from SARS-CoV-2. Crucial roles in cellular activities are played by vitamin A, which is necessary for vision, and the B-vitamin complex, which supports energy synthesis and nerve function. In the context of viral infections, the significance of vitamin D, crucial for both immune system function and bone health, along with vitamin C and its ability to combat free radicals, becomes paramount.This research aims to to elucidate the specific effects and mechanisms by which essential vitamins (A, B, C, D, and E) contribute to the mitigation of COVID-19. By investigating the distinct roles of vitamins within the framework of the pandemic, this research seeks to clarify the potential benefits that these micronutrients may offer in mitigating the severity of COVID-19 and bolstering immune responses to combat viral infectons.

Keywords: Nanoparticles, COVID-19, SARS- CoV, MERS-COV, Vaccines, Drugs, Vitamins

Introduction

Coronaviruses constitute a diverse group of viruses, causing respiratory illnesses ranging from mild colds to severe conditions such as severe acute respiratory syndrome (SARS), Middle East Respiratory Syndrome (MERS), and the more recent COVID-19 [1-7]. Originating in animals, these zoonotic viruses were first identified in 1937, leading to 15% - 30% of common cold cases [8-12]. COVID-19, a global health concern, manifests as a severe pulmonary infection with symptoms including dry cough, shortness of breath and chills [13-15]. In severe cases, individuals may experience difficulty breathing, chest pain, confusion, and bluish lips or face, with potential complications including renal failure and pneumonia [16-18]. The pandemic's impact on different age groups, particularly those over 60, underscores the importance of early detection and medical attention [19-22]. Despite ongoing efforts, the lack of a 100% effective vaccine or treatment for COVID-19 remains a critical concern [23-27]. The situation is further complicated by emerging variants, particularly the delta and omicron variants, which have sparked concerns due to their varying infection rates [28-31]. COVID-19 is distinct from other coronaviruses due to its causative agent, varying symptoms, human-to-human transmission, and global impact. Past coronaviruses like SARS-CoV caused severe respiratory symptoms and limited outbreaks, while MERS-CoV led to severe symptoms and higher mortality rates [32-36]. Understanding these differences is crucial for treating COVID-19. Medical interventions, including vaccines, antiviral drugs, and steroids, aim to manage the virus's impact, yet challenges persist [37-41]. Shifting from virological treatments to preventive strategies, the significance of micronutrients in bolstering immune function and promoting respiratory health becomes evident. The World Health Organization (WHO) has approved the use of vitamins in COVID-19 treatment protocols. Vitamins, essential nutrients, are required in minimal amounts (less than 100 mg.day-1) and play crucial roles in body functioning, particularly in metabolic processes. Essential micronutrients like vitamins C, D, E, and A, play crucial roles in supporting the immune system [42-47]. Vitamin A has been proven to significantly reduce morbidity and mortality rates associated with various infectious diseases, including measles, diarrheal diseases, pneumonia, HIV infection, and malaria [48-53]. Vitamin B2, when combined with Ultraviolet (UV) light exposure, has been found to effectively reduce the titer of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) in human plasma products [54-58]. Vitamin C enhances chick embryo tracheal organ resistance to avian coronavirus infection [59-61], while vitamin D plays a role in coronavirus infections, with decreased levels in calves linked to Bovine coronavirus infection [62-65]. Vitamin E deficiency has been linked to an increase in myocardial injury in mice infected with coxsackievirus B3, an RNA virus [66-69]. Recognizing the accessibility and cost-effectiveness of vitamins, this review aims to explore their prophylactic and therapeutic roles in preventing and treating COVID-19 infections. Examining the anti-inflammatory, antioxidant, and immunomodulatory properties, this review aims to offer a comprehensive understanding of the potential benefits associated with them [70-73]. Protecting and supporting the body against illnesses with anti-aging qualities requires the appropriate nutrients in the optimum dose and mix. Micronutrients such as minerals, vitamins, essential fatty acids, trace elements, phytochemicals, and amino acids are essential for healthy cellular function and must be obtained through the diet. Orthomolecular medicine emphasizes the need for vitamins in the right proportions [74-79]. According to various reports (e.g., from the University of Bristol in England), vitamins are essential for preventing the spread of COVID-19, which have an effect similar to that of several newly developed drugs for the treatment of COVID (dexamethasone, lopinavir) [80-85]. Vitamins A, D, and K may help reduce viral infections [86-89]. The literature indicates that statins, utilized for lowering cholesterol levels, heighten the susceptibility to COVID [90-93], whereas Vitamin D tends to accumulate in adipose tissue but decreases in individuals with obesity [94-98]. COVID-19 negatively impacts populations deficient in essential vitamins, thereby constraining their capacity for recovery. For instance, among obese individuals, unlike other contentious vitamins associated with obesity, vitamin D deficiency is prevalent. Vitamin D plays a regulatory role in the renin-angiotensin system (RAS) and maintains a balance between pro- and anti-inflammatory cytokines, thereby contributing to the management of respiratory tract infections [99-102].

In a shared commitment to lessen the rapid transmission of SARS-CoV-2, noteworthy measures are underway to speed up the evolution of diagnostic practices, vaccines, and healing methods. Insights derived from previous studies on nanomaterials are currently being utilized to confront the COVID-19 pandemic [103-106]. Nanomaterials possess strategies that are recognized for their high sensitivity, rapid execution, and convenience for users. Colloidal gold nanoparticles have been authorized for emergency use by the Food and Drug Administration (FDA) for serological evaluations conducted at the point of care [107-112]. This approval enables the rapid detection of individuals who may have asymptomatic or previous SARS-CoV-2 infections. Additionally, nanomaterials are designed to guard antigen constituents until they contact antigen-presenting cells, thereby facilitating the vaccine production process [113-117]. Notably, Messenger RNA (mRNA) vaccines delivered through lipid nanoparticles have achieved regulatory approval at an unprecedented rate. Ongoing clinical assessments have indicated that the mRNA-1273 and Pfizer BioNTech (BNT162b2) vaccine candidates elicited robust cellar immune responses, characterized by $CD8^+$ cytotoxic T lymphocytes and $CD4^+$ T helper cells, coupled with elevated antibody levels aimed at SARS-CoV-2 [118-121]. In conclusion, nanomaterials can boost the pharmacokinetic and pharmacodynamic features of pharmaceutical drugs, which may help decrease the harmful impacts associated with drug treatments [122-128].

The 1st verified case of the coronavirus COVID-19 occurred in a 55-year-old Chinese man on November 17, 2019, as reported by the South China Morning Post [2]. An epidemic affecting over 213 nations and more than 704,753,890 infections occurred as a result of this case's global dissemination of the virus. More than 7,010,681 people have died from COVID-19 by April 13, 2024, according to Worldometer [2] and this number was still increasing. The World Health Organization (WHO) has released the therapeutic guideline for handling COVID-19, including respiratory support, antibiotics for secondary bacterial infection, and acute respiratory distress syndrome management [3]. Still, Scientists around the world are working furiously to better understand COVID-19, discover its secrets and unlock a cure. Nevertheless, coronaviruses include a wide range of illnesses, from the ordinary cold to more severe and even deadly ones, and they are the biggest family of viruses that target human breathing features. Coronaviruses cause serious illness in people [129-133]. This current coronavirus epidemic is the 3rd one to cause a worldwide health disaster this century. So far, over a hundred coronaviruses have been documented, with the majority being able to be transmitted between pigs, camels, bats, and cats.On the other hand, several viruses can only infect people via genetic alterations, which may cause whole new illnesses [134-139]. There are 7 coronaviruses known to date; 3 of them may cause fatalities, while 4 - OC43, 229E(HCoV-229E, Alphacoronavirus chicagoense), NL63(HCoV-NL63, Alphacoronavirus amsterdamense), and HKU1(HCoV-HKU1, Betacoronavirus hongkonense) - have showed very minor symptoms [4]. Initially, there was SARS-CoV, which emerged in late 2002 and went away in 2004 [31-35]. Then, in 2012, there was MERS-CoV, which emerged and was still circulating in camels. Lastly, in December 2019, SARS-CoV-2 (COVID-19) was discovered in China [5]. Following the previously recognized coronaviruses SARS-CoV and MERS-CoV in terms of threat, COVID-19 ranks high on the list. Stopping the transmission of the COVID-19 virus between individuals has, nevertheless, been the primary focus of numerous researchers from several professions. The progression of COVID-19 from animals to humans is seen in **Figure 1**.

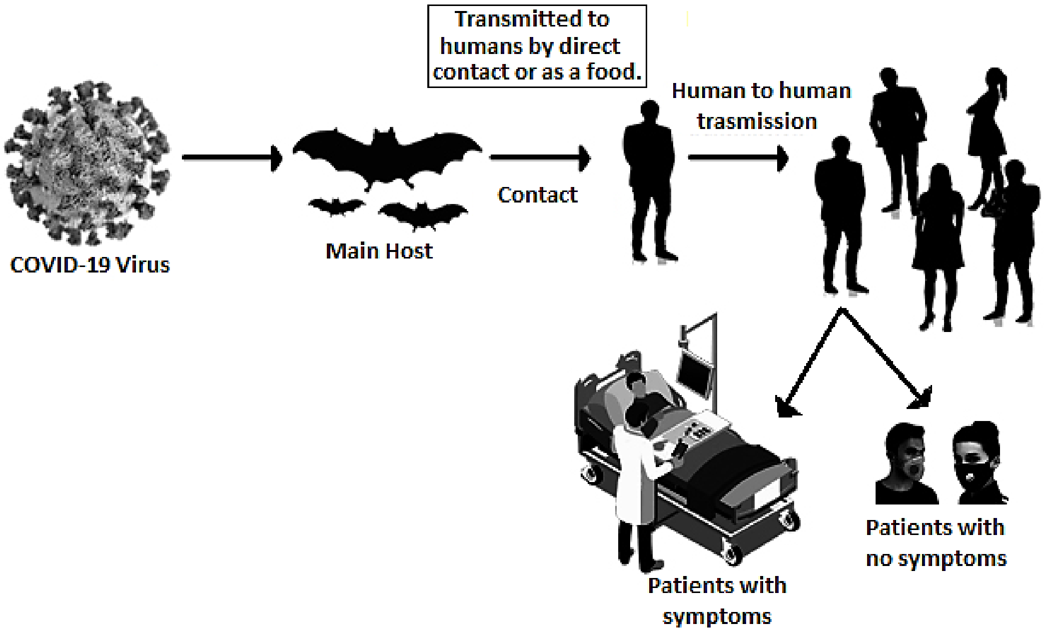

Figure 1 Spreading and transmission of the COVID-19 to humans [5].

Nanotechnology refers to a relatively recent technique that is being used in medical treatment. In the last ten years, this technology has played a pivotal role, offering innovative solutions to several issues concerning the detection, treatment, and prevention of coronavirus infections. Therefore, the purpose of this research is to identify and characterize nanotechnology materials with anti-COVID-19 and anti-infection properties. To better understand which nanomaterials may be more successful for prevention and treatment, it may be helpful to review the effects of nanomaterials in various situations for the coronaviruses SARS- CoV and MERS-COV [140-144].

Background

Most cases of COVID-19 infection are known to occur when people inhalate a drop of the virus. These droplets are produced when a COVID-19 infected patient coughs or sneezes, and then the droplets can swim around the surrounding surfaces, such as doorknobs, desktops and even protective devices for medical workers. According to guidelines for treating COVID-19 granted by the National Institutes of Health (NIH), healthy people can contract COVID-19 by touching contaminated surfaces from the virus. In a study on the survival of COVID-19, researchers discovered a live virus on the surface of a surgical mask 7 days later to the virus [12]. Therefore, it is important to examine potential facial masks based on nanomaterials with excellent properties for self-development to improve the efficiency of masks to block COVID-19. When it comes to disinfecting surface contaminants, many hospitals and medical institutions use traditional disinfecting methods such as UV disinfection and hydrogen peroxide turn. However, these types of disinfection methods are often unique. As soon as the UV lamp is turned off or hydrogen peroxide is decomposed, the virus can adsorb severely on the surface of the disinfected material, just as before disinfection. With the development of nanoscience and technology, self-development of nanomaterial surfaces can provide possible solutions to solve this problem.

Because of their interesting and distinct properties compared to their bulk substance, new possibilities have arisen in the field of drug development efforts because to advancements in nanomaterials [36-40]. Having at least 1 dimension of 100 nm or less, nanomaterials - also known as important nanotechnology items - have piqued a lot of people’s curiosity. Their qualities make them very suitable for a range of biological applications, such as the acquisition of pharmaceuticals, medical diagnostics, and therapies [8]. Nanomaterials may have targeted biological and antibacterial effects when their surfaces are altered [9]. A broad range of microorganisms, including viruses, fungi, and bacteria, have been shown to be susceptible to nanoparticles like gold, silver, copper, zinc, etc [41-45]. Coronaviruses have an average spheroidal size of 125 nm [11], RNA genome that is stable and a viral envelope made of single strands. The spike (S), envelope (E), membrane (M), and nucleocapsid (N) proteins make up the 4 structural subunits of coronaviruses. When it comes to binding the virus and getting it into the host cell's cells, the S protein is crucial. Thus, it is possible that medications and chemicals that target the S protein's mode of action might be an effective strategy to combat this virus [4]. For viral communication and entrance inhibition, nanomaterials with a large surface area and compatibility with various functional groups, such carbon quantum dots (CQDs) and gold nanoparticles (AuNPs), are great choices [46-49]. Researchers in Germany and France's Lille and Ruhr-University Bochum have shown that modifying CQDs with boronic acid ligands interferes with the function of the coronavirus S protein, making it far more difficult for the virus to enter host cells [4]. Nanomaterials added to cell culture media considerably reduced cell infection before and during coronavirus infection, according to the scientists. Interestingly, during the viral life cycle - which takes 5.5 h for coronavirus - a notable trend of reduced viral replication was seen. By entering the cell by endocytosis and binding to the protein in the virus, these medium-diameter 10 nm CQD might provide great answers to the coronavirus, halting the genome's reproduction [50-55].

Zhao *et al.* [124] also developed a COVID-19-biosensor system based on nanomaterials. This biosensor is combined with isothermal amplification via a 1-step reverse transcription loop based on nanomaterials, and the developed COVID-19-biosensor was successfully used in the diagnosis of COVID-19 patients. Furthermore, the required time was approximately 1 h, which was higher than the previous test time.

Bohn *et al.* [188] Most of our knowledge regarding the pathophysiological progression of COVID-19 was observed by laboratory lenses that rejected potential causal mechanisms from observed biomarker trends among patients. Based on current evidence, it is clear that direct SARS-COV-2 infection of several organs, as well as hypoxia and stress-related damage, may contribute to the pathophysiological progression of COVID-19. With this in mind, it remains to be seen which factors affect the transition from normal physiological to pathogenic inflammatory responses. The nuances of age-related immune responses appear to play a role, and disease severity in older populations is increasingly observed. Furthermore, limited data available in the pediatric population shows a spectrum of different and diverse diseases that are completely different from adults, further increasing the importance of age-related immune responses. In addition to age, new clinical and epidemiological data suggest gender-specific differences in the relationship between clinical features and cases and lethal COVID-19, which is poorly predicted in men. This disproportionate clinical epidemiology can be explained by gender-specific regulation of ACE2, the incidence of pre-existing comorbidities in men (i.e. hypertension, diabetes, cardiovascular disease), and sexual differences in viral immune responses described elsewhere. Genetic predispositions have also been proposed, such as polymorphisms in ACE2 and genetic variability in the histocompatibility complex (MHC). Finally, some comorbidities were associated with poor outcomes, perhaps due to the fact that organs and immune functions are already affected and are in an asymptomatic inflammatory state. In a series of trends in 5,700 patients in New York City, the most frequently observed comorbidities were hypertension, obesity and diabetes. These factors need to be observed more thoroughly to complete a clinical understanding of COVID-19. In addition to understanding related risk factors, there is growing suspicion of delayed but severe COVID-19 presentations, even after virus clearance, especially in children. This not only shows how important it is to define the time for antibody responses by serological testing in several age groups, but also indicates an increase in the complexity of COVID-19. This overview includes various potential pathophysiological mechanisms behind SARS-COV-2 infection. The evidence for these proposals is based on previous experiences with similar coronaviruses and on clinical features, clinical testing and pathological analysis of COVID-19 patients around the world. The exact contribution of risk factors to disease progression has not yet been partially defined. Furthermore, further testing is needed to examine the molecular mechanisms of action in both major drivers of COVID-19 and in both pediatric and adult population groups. This should affect the appropriate risk and treatment strategies. From our preliminary understanding, immunomodulatory therapy is probably more effective than it is intended to invade viral host cells. Furthermore, treatment approaches can continue to match the patient’s disease course by increasing early as the disease progresses to improve efficient antiviral responses and blocking inflammation after serious illness. To conclude, current evidence highlights that appropriate immune response is fundamental to COVID-19 pathogenesis, but much remains unknown regarding the key drivers of progression. As new therapeutic paradigms emerge, our understanding of disease pathophysiology will undoubtedly advance and not only inform current clinical practice for COVID-19 but fundamentally shape our understanding of immune involvement in systemic disease.

COVID-19

Hundreds of medicine towards COVID-19 are presently being studied in laboratories throughout the world. Although COVID-19 stocks similarities with different viruses and our know-how of its antiviral mechanisms retain to grow, the efficacy and aspect results of medicine presently used to deal with COVID-19 aren’t sufficient. Nanomaterials, which includes liposomes and PLGA(poly(lactic-co-glycolic) nanoparticles, may be used to encapsulate antiviral drugs; realise long-time period circulation, sustained release, and co-management of a couple of drugs; and enhance the general healing effect. Therefore, with the aid of using editing antibodies concentrated on the COVID-19 protein, nanomaterials can enhance drug availability even as decreasing aspect results, thereby making sure higher healing outcomes. Nanomaterials might also additionally quickly be used to supply angiogenic elements in aggregate with antiviral drugs, ensuing in stronger remedy of COVID-19 [125].

The outbreak of coronavirus disorder 2019 (COVID-19) due to a unique coronavirus has grow to be a public fitness emergency of global concern (PHEIC). The virus can reason extreme breathing disorder and might unfold from character to character. The virus has been named extreme acute breathing syndrome coronavirus 2 (SARS-CoV-2) primarily based totally on its look beneathneath electron microscopy [1]. COVID-19 has been particular a Public Health Emergency of International Concern (PHIEC) [2]. The Chinese Center for Disease Control and Prevention (China CDC) decided that SARS-CoV-2 contamination is the reason of the outbreak that commenced in in Wuhan City (CDC, 2020) [3]. The virus can reason extreme breathing illness, and human to human transmission has been showed [3]. Isolated viruses have been determined beneathneath electron microscopy and named SARS-CoV-2 [5]. As of March 23, 2020, 187 international locations and areas mentioned 38667 COVID-19 showed instances worldwide. Although the COVID-19 state of affairs has been suppressed these days in China, we nevertheless want to bolster the prevention and manipulate of the epidemic, enhance people`s recognition of shielding measures, and reduce the loss due to the virus to save you it from turning into a extreme international pandemic. This is the 0.33 time in human history, following SARS and MERS, that a coronavirus has triggered a tremendous epidemic. Given that the epidemic remains spreading and the proof that there are similarities the various 3 coronaviruses in phrases in their biological, scientific and epidemiological features, a evaluation the various 3 may be very useful to manual the development of remedy and prevention measures, and the similarities and variations the various 3 are in all likelihood to offer the important thing to addressing the COVID-19 epidemic. Coronaviruses are large, enveloped, positive-strand RNA viruses that may be divided into genera: α, β, γ and δ. There are 6 coronaviruses that reason disorder in humans, which includes 229E and NL63 of the α genus and OC3, HKU1, SARS-CoV and MERS-CoV of the β genus [1,6-8]. Human coronavirus (hCoV) contamination is particularly associated with the breathing, intestinal and anxious systems. In 2002 - 2003, SARS-CoV triggered a deadly disease of extreme acute breathing sicknesses in China; MERS-CoV turned into observed withinside the Middle East in 2012 [9,10]. Both of those coronaviruses are zoonotic pathogens that may reason extreme breathing disorder in humans, that could development to extreme acute breathing misery syndrome.

Zhou *et al.* [127], COVID-19 makes use of ACE2 as a mobile access receptor; ACE2 is sent at the epithelial cells of the alveoli, trachea, bronchi, serous bronchial glands, alveolar monocytes and macrophages withinside the breathing tract. ACE2 is likewise extensively expressed at the mucosa, inclusive of the eyelid, nasal cavity, lip, and oral cavity. The pathogenic mechanism of COVID-19 is clear, as proven in **Figure 2**. The virus enters the goal cells through ACE2 after which releases single-strand RNA (ssRNA), which mixes with the ribosome withinside the goal mobile and is translated to RNA replicase. The RNA replicas replica the ssRNA to supply negative-strand RNA, positive-strand RNA and RNA fragments, which integrate with the ribosome to supply a protein shell. The protein shell and the positive-strand RNA shape the brand new SARS-CoV-2 virions, which can be launched to contaminate greater goal cells (**Figure 2**).

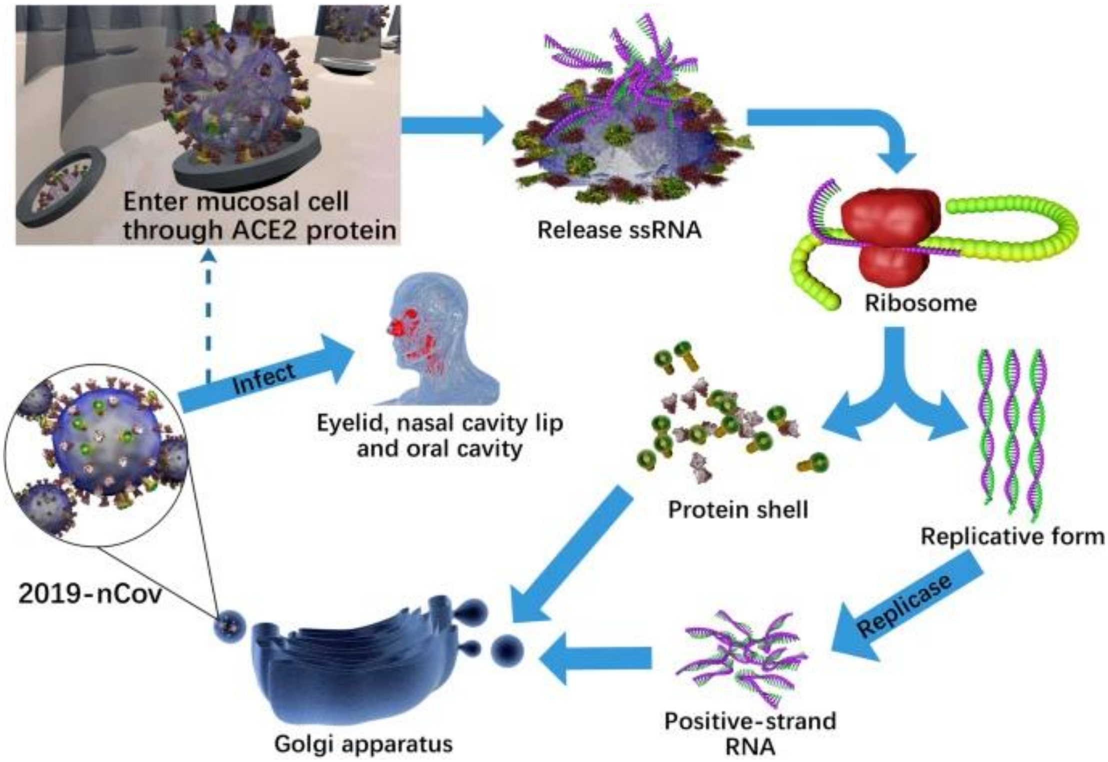

Figure2 SARS-CoV-2 infects the human body and its replication mechanism. SsRNA: Single string RNA, ACE2: Angiotensin converting enzyme 2 [127].

A novel coronavirus, COVID-19 or SARS-CoV-2, was discovered in Wuhan, central China, in late December 2019. It quickly spread to all provinces in China and a number of countries across the world. Coronaviruses (CoVs) are positive-stranded RNA viruses that are members of the subfamily coronavirinae. At an estimated length and thickness of 26 - 32 kilobases (65 - 125 nm), the genome of coronaviruses is the longest viral RNA known to science [56-61]. Middle East Respiratory Syndrome (MERS) and other fatal pneumonias may be caused by highly pathogenic coronaviruses (SARS), which mostly impact the lower airways [62-65]. Patients infected with COVID-19 have developed pneumonia, which is characterized by a high temperature, coughing, and shortness of breath [12], COVID-19 viruses, including SARS-CoV and MERS-CoV, are the most prevalent causes of these symptoms. Although the 2 viruses have certain similarities, one research found a stronger correlation between SARS-CoV and COVID-19. The 2 viruses vary in many ways, as seen in **Table 1** [13].

Table 1 Comparative analysis of biological features of SARS-CoV and COVID-19.

Characteristics	SARS-CoV	COVID-19
Emergence date	November 2002	December 2019
Area of emergence	Guangdong, China	Wuhan, China
Date of fully controlled	July 2003	Not controlled yet
Key hosts	Bat, palm civets and Raccoon dogs	Bat
Number of countries infected	26	213
Entry receptor in humans	ACE2 receptor	ACE2 receptor
Sign and symptoms	fever, malaise, myalgia, headache, diarrhea, shivering, cough and shortness of breath	Cough, fever and shortness of breath
Disease caused	SARS, ARDS	SARS-2, COVID-19
Total infected patients	8098	10,977,050
Total recovered patients	7322	6,125,404
Total died patients	776 (9.6% mortality rate)	522,764 (4.76% mortality rate)

Concerning the virus itself, the SARS-CoV-2 acute respiratory syndrome has temporarily replaced COVID-19 according to the worldwide viral taxonomy committee. Although 1st research linked SARS-CoV-2 infections to a particular local fish market and hypothesized animal-to-human transmission, more recent research has shown that the virus is mostly spread from person to person via retail outlets or interpersonal contact [14-16,66-70]. A recent research indicated that 41% of patients contracted SARS-CoV-2 while in the hospital [14]. Reports of an ever-increasing infection rate and instances of transmission from asymptomatic carriers lead most to believe that SARS-CoV-2 is effectively transferred to humans [71-75]. A member of the β-COV subgenus of sarbecoviruses, COVID-19 has an envelope-lined positive sense RNA. About 29,891 nucleotides make up the RNA genome, which encodes about 9,860 amino acids [Gen Bank No. MN908947]. The structural protein is encoded by S, E, M, and N in the following sequence: 5'UTR-replicase (orf1a / b), spike (S), envelope (E), membrane (M), nucleocapsid (N), and 3'UTR (see **Figure 3**) [19].

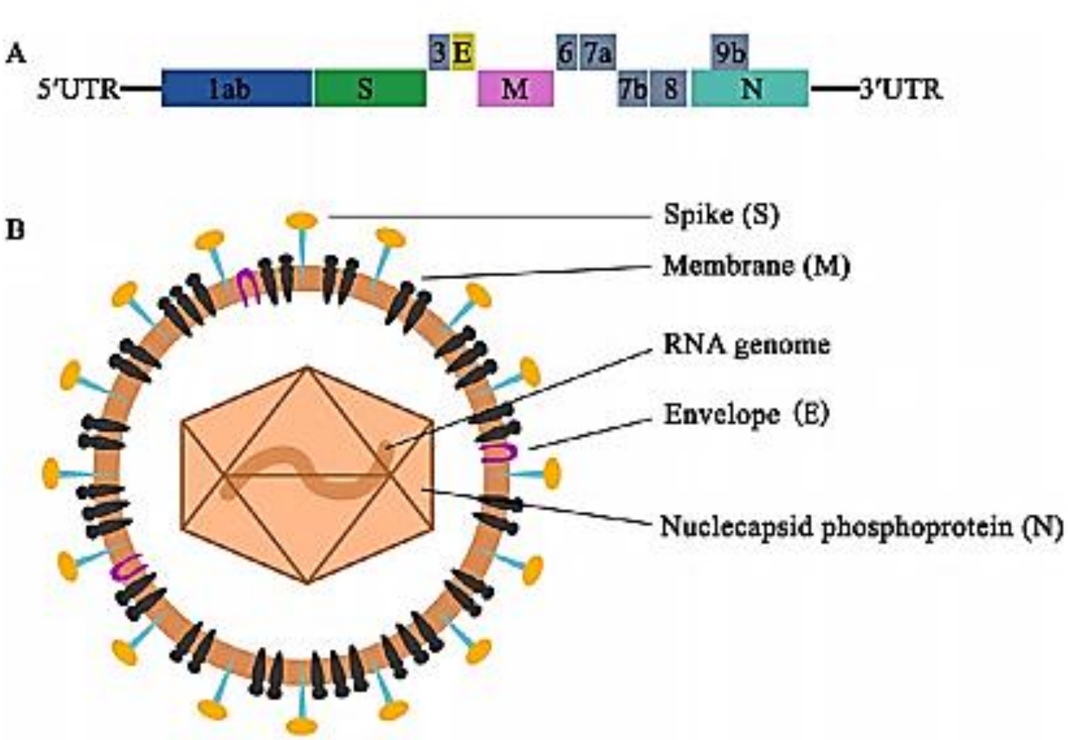

Figure 3 Virus structure and organization of COVID-19 genes. (A) The COVID-19 genome has 5 untranslated areas, 5 of which are primary genes; one is an open read frame (ORF) enclosure; the others are spike, membrane, and nuclear proteins; and the 6th is an ORF; ORFs 3, 6, 7A, 7b, 8b, and 9b are examples of progressively untranslated accessory proteins. (B) COVID-19 has 1 wolf, 4 proteins in its envelope, and positively sensing RNA in its genetic form. Nuclear proteins, including spike, protein envelope, and membrane proteins, encase the DNA at its core [15].

A phylogenetic analysis of COVID-19 found a 96.2% similarity with Bat-CoV RaTG13, a virus that originated in Yunnan, China in 2013. It is possible that both SARS viruses first appeared in bats before making their way to people. The degree of similarity between bat-SL-CoVZC45 and bat-SL-CoVZXC21 and COVID-19 is about 88% [76-80]. While around 50% of the similarities are with MERS-CoV, approximately 79% are with SARS-CoV [20-22]. There are a total of 6 primary open reading frames (ORFs) in the COVID-19 genome: ORF1a/b, S, E, M, N, ORF3b, and ORF8. Sixteen NSPs, which are involved in viral transcription and replication, are formed by proteolytic conversion of ORF1a/b pp1a and pp1ab polyproteins during replication. There is a novel small protein that ORF3b encodes, but its function is unknown [81-84]. A hidden protein alpha-helix, followed by 6 strands without related functional domains or motivations, is potentially encoded by the novel ORF8 [19].

A genomic sequence that is at least 70% identical to SARS-CoV is found in COVID-19. Glycoprotein genes for the COVID-19 spike are larger than those for the SARS-CoV spike. Spike protein encoding S1 and S2 domains is critical for receptor binding and membrane fusion, as well as for transferring potential during host tropical interaction. The SARS-CoV protein is 99% similar to the highly conserved COVID-19 S2 component. If you want to go right to the human receptor, you normally put the recipient-binding domain in the C-terminal domain of S1 [85-90].

Zhou *et al.* [23], COVID-19, similar to SARS-CoV, often utilizes angiotensin-converting enzyme 2 (ACE2) as its cell entry receptor in the human lung. The majority of these ACE2s are found on alveolar cells Type II (AT2). Therefore, to determine the efficacy of ACE2-targeting medications in COVID-19 treatment, more trials are necessary. It has been shown that patient nCoV genomic sequences are very similar to one another, with a similarity of over 99.9%, since 2019 [19-23]. As the virus continues to spread, it is crucial to closely monitor mutations.

Pizzorno *et al.* [189] In response to the current pandemic caused by the novel SARS-CoV-2, identifying and validating effective therapeutic strategies is more than ever necessary. We evaluated the in vitro antiviral activities of a shortlist of compounds, known for their cellular broad-spectrum activities, together with drugs that are currently under evaluation in clinical trials for COVID-19 patients. We report the antiviral effect of remdesivir, lopinavir, chloroquine, umifenovir, berberine and cyclosporine A in Vero E6 cells model of SARS-CoV-2 infection, with estimated 50% inhibitory concentrations of 0.99, 5.2, 1.38, 3.5, 10.6 and 3 μM, respectively. Virus-directed plus host-directed drug combinations were also investigated. We report a strong antagonism between remdesivir and berberine, in contrast with remdesivir/diltiazem, for which we describe high levels of synergy, with mean Loewe synergy scores of 12 and peak values above 50. Combination of host-directed drugs with direct acting antivirals underscore further validation in more physiological models, yet they open up interesting avenues for the treatment of COVID-19.

Simonis *et al.* [190], In this comparative review, we awareness on repurposed drugs with antiviral results towards SARS-CoV-2 in cell-primarily based totally assays as the ones materials provide extraordinary possibilities for a remedy early withinside the route of COVID-19 via way of means of inhibition of viral replication and is probably even appropriate for preventive techniques as proven for neuraminidase inhibitors in case of influenza. In contrast, immunomodulatory drugs can be extra useful in a later section of contamination, whilst the height of viral replication has been reached, and inflammatory methods dominate the pathophysiological process. This speculation is supported via way of means of the reality that repurposed immunomodulatory drugs like glucocorticoids appears to be useful in extreme or important COVID-19 whilst utilized in a later section after numerous days of symptomatic ailment however possibly now no longer withinside the 1st week after symptom onset. Many materials had been examined in vitro for his or her direct antiviral results on SARS-CoV-2 replication or their capacity to lessen cytopathologic results in Vero E6 cells. Of repurposed access and viral protease inhibitors, so far none has proven convincing proof that guide a medical improvement as unmarried agent towards COVID-19. Besides remdesivir which inhibits viral replication with an EC50 of 0.77 - 26.9 μM (relying on assay type, virus strain, and manner of calculating), different nucleoside/nucleotide analogs that focus on the viralRdRp like favipiravir, penciclovir, or ribavirin had been assessed however confirmed no or simplest susceptible pastime towards SARS-CoV-2. Inhibitors of viral protease had been additionally investigated however simplest lopinavir had mentionable antiviral pastime (EC50 5.25 - 26.62 μM). Unfortunately, the aggregate of lopinavir and ritonavir did now no longer display any medical results in a randomized managed trial. The anti-parasite drug CQ/HCQ became one of the maximum promising applicants towards COVID-19 primarily based totally on preclinical research however a medical advantage couldn’t be verified and a these days posted *in vivo* take a look at established no useful results in a non-human primate version of SARS-CoV-2 contamination. Recent research in vitro confirmed sturdy anti-SARS CoV-2 houses of compounds with one-of-a-kind and in part unknown modes of antiviral movement like nitazoxanide, cyclosporine A, emetine, and Hom harringtonine. Therefore, remdesivir is the simplest antiviral drug that established efficacy withinside the preclinical and medical setting. In the latter situation, it reduces time to restoration and might lessen mortality. A meta-evaluation that is to be had as preprint diagnosed a statistically massive discount in mortality (relative danger 0.69; (95% CI 09 0.99)) whilst pooling facts of the 2 to be had RCTs. Final consequences of the ACTT-1 trial will offer extra facts to assess results of RDV on mortality and virologic outcomes. In addition, a section 1b/2a trial comparing results of RDV on viral load whilst administered via way of means of inhalation of an aerosolized answer is being planned (NCT0 539262). The particularly modest impact of the drug can be explainable via way of means of itsvirostatic mechanism of movement and the reality that results had been studied after median 9 days of symptomatic ailment at the same time as viral replication is dominating withinside the 1st week of contamination. Early remedy with RDV became proven to be very powerful in a rhesus macaque version of SARS-CoV-2 contamination in which it decreased medical signs of infection, lung damage, and virus replication in lower respiratory tract specimen.

Harne *et al.* [191], The latest pandemic caused by the SARS-COV-2 virus remains a major global challenge for the health sector. The availability of new vaccines and drugs aimed at SARS-COV-2 and the outcome of COVID-19 have given the world hope for the end of the pandemic. However, the occurrence of mutations in the SARS-COV-2 virus genome in different months in different parts of the world is a permanent risk for public health. Currently, there is no single treatment to eradicate the risk of COVID-19. The broad communication of SARS-COV-2 based on the Omicron variant continues to work towards developing and implementing effective vaccines. Furthermore, there are indications that mutations in the receptor region of SARS-COV-2-Spike-glycoprotein have resulted in a reduced efficacy of the current vaccine by escaping antibody detection. Therefore, it is important to avoid the mechanisms of actively identifying izakayas, pubs, actively identify the long-term effects of COVID-19, and develop therapeutics aimed at SARS-COV-2 infection in human and preclinical models. This overview describes the pathogenic mechanisms of SARS-COV-2 infection and the host's natural and adaptive immune responses to infection. Addresses the ongoing need for the development of effective vaccines that provide protection against SARS-COV-2 and validated endpoint assays to assess vaccine vaccination in pipelines, drug therapy, antiviral medical therapies, and public health measures that have been continuously completed the COVID-199 pandemic.

Coronavirus binding with the ACE2 receptor

In order for SARS-CoV2 to infect a host cell, its spike protein must first connect directly to the ACE2 receptor on the surface of the cell [24]. The 2 SARS-CoV strains are quite similar, and this includes the spike proteins. Research into crystal structures and biochemical interactions has shown that the spike (S) protein of SARS-CoV has a strong binding affinity for human ACE2 [25].

Zhang *et al.* [25] mice were shown to have worsened lung damage after being injected with SARS-CoV spike (S). A specific injury that relied on ACE2 expression to block the renin-angiotensin pathway helped with this. Soiza *et al.* [26]. put liposomes, also known as Nanotrap particles, to use as a receptor decoy to bind to influenza. These liposomes were discovered to be very efficient in preventing influenza infections by competitively binding and capturing viruses. Prabakaran *et al.* [27], consensus that the region between amino acid residues 303 and 537 on the SARS-CoV Spike glycoprotein contains the ACE2 receptor binding site. A strong ACE2 homology model has been developed thanks to the sequence similarity. The negatively charged S-glycoprotein offers a possible binding site for the positively charged receptor-binding domain. To better understand ACE2's structure and function, Prabakaran *et al.* [27]. pointed to a potential binding site for the SARS-CoV S-glycoprotein on the ACE2 model. **Figure 4** shows the structure of an angiotensin-converting enzyme receptor

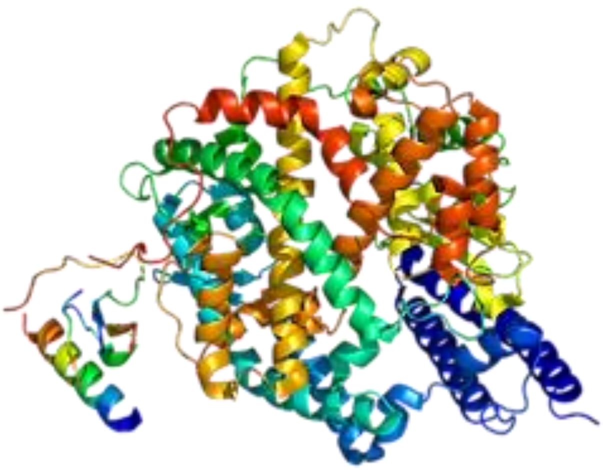

Figure 4 Structure of ACE2 receptor [27].

Li *et al.* [197] The pathogenic mechanism of COVID-19 as a new, severe, respiratory infection has not yet been fully determined. This is primarily due to the novelty of the disease. While many important questions have not been answered at the moment, it is only clear that we will begin to understand the pathogenic mechanisms of COVID-19. The current overview discussed the pathogenesis of COVID-19. The SARS-COV-2 Dysmun inflammatory response is thought to respond in a similar manner to SARS-COV and MERS-COV infection. Deep COVID-19 is characterized by organ dysfunction, hyperlipidemia, and lymphopenia. Immune dysfunction in patients with COVID-19, including lymphopenia, reduced $CD4^{+}$T-cell counts, and abnormal cytokine levels, are common features and can be critical factors associated with disease severity and lower outcomes. Direct damage and lysis of host cells by viruses is the most important pathogenic mechanism based on the host's inappropriate congenital and acquired immune responses. The molecular determinants that can constitute important differences in pathogenesis between highly pathogenic human coronaviruses (SARS-COV, MERS-COV, and SARS-COV-2) are currently unknown. Further incoming research into the pathogenesis of COVID-19 is important for developing new therapeutic strategies and developing effective vaccines for this strongly and fatal infection. As knowledge about etiology improves, smarter approaches to therapeutic treatments and vaccine development can be developed to combat this new, deadly disease.

Shirbhate *et al.* [198] Many international locations round the sector are experiencing severe social and monetary instability due to this COVID-19 pandemic when you consider that December 2019. Whilst many remedy alternatives are below trials in laboratories, however currently, not one of the accredited capsules had been launched to be used in opposition to COVID-19. Thinking of COVID-19 and its dating with ACE2, an in-intensity information of pathogenesis would possibly resource withinside the development of focused interventions to be able to modify this pandemic. The especially complicated dating persists among the RAAS and SARS-CoV pathogenicity, and with the aid of using analogy, SARS-CoV-2 pathogenicity withinside the occasions of COVID-19. A extensive information of viral pathophysiology indicates many healing techniques i.e., inhibition of SARS-CoV2 spike protein activation, inhibition of virus endocytosis, use of a soluble shape of ACE2, peptide or non-peptide analogs of ACE2, and maintaining ACE2/Angiotensin-(1 - 7)/Mas receptor pathway activation. Still, simple studies recommends that ACEIs and ARBs particularly have a protective position. Hence, greater researches are essential earlier than organizing the cutting-edge remedies of COVID-19 with already advertised AEIs/ARBs or switching to any new medications. Properly-planed potential and retrospective observational investigations, further to randomized managed scientific trials, are essential for growing the guidelines for the software of RAAS modulators in SARS-CoV-2 infection. The end result from randomized scientific trials will in addition outline the wider position and effectiveness of anti-RAAS sellers in opposition to COVID-19 pandemic. ACE2-focused healing method in opposition to SARS-CoV-2 might also additionally cause novel anti-COVID-19 number 1 or adjunctive sellers. The gift records on ACE2 receptors with relation to COVID-19 disorder could be useful in locating it's a hit remedy.

MERS-CoV

Saudi Arabia was the site of the 2012 outbreak of Middle East respiratory disease, more commonly known as MERS. **Figure 5** shows the MERS-CoV schematic.

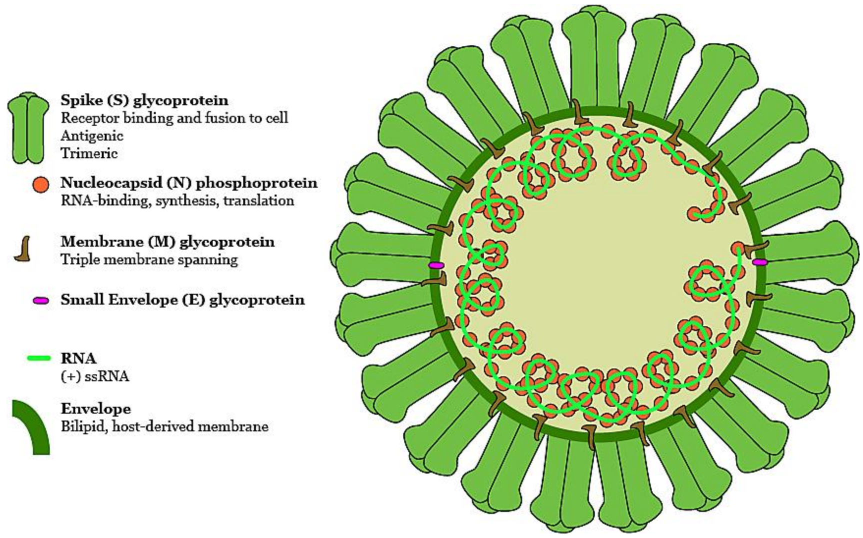

Figure 5 MERS-CoV Schematic [28].

Efficacy of nanomaterials on MERS coronavirus has been the subject of few recent research; nevertheless, 1 study using ferritin nanoparticles was undertaken. It has also been shown that the infection of MERS-CoV is mediated by the RBD's interaction with the host receptor hDPP4.

In 2014 [29], American scientists created coronavirus neutralizing antibodies in mice by administering nanoparticles containing a concentrated coronavirus spike protein. According to the research, the homologous virus was successfully prevented by the high rates of neutralizing antibody formation in response to coronavirus vaccination of nanoparticles. These results showed that coronavirus nanoparticles may elicit distinct anti-MERS-CoV antibody responses in mice, but that no universal anti-coronavirus response is used for the treatment of various coronaviruses. In order to optimize the generation of neutralizing coronavirus antibodies, they also investigated adjuvants. They found that utilizing Matrix-M1 or Alum produced far better neutralizing antibody products than using S nanoparticles alone. At long last, scientists figured out how to make full-length MERS-CoV spike nanoparticles that, when combined with adjuvants, may produce highly verified antibodies in mice [97-101].

The use of MERS-COV-injected mice in a 2015 patent study is based on animal experiments. [30] A specific kind of virus-like particle (VLP) nanoparticle was used to treat infected mice a few days after injection. Since the nanoparticles only carried viral proteins and not viral DNA, they posed no threat to human health. Recombinantly generated viral proteins self-assembled to create the nanoparticles, which elicited beneficial immune responses. Theoretically, we are not tied down, but we do believe that the particles' size, repeating structure, and particle nature had a role in the strong immune responses. Interestingly, the strong immune response could still be achieved without the use of an adjuvant. As a vaccine candidate, this offers a way to generate high-affinity antibodies by immunizing animals with an immunogenic mixture that includes a MERS-CoV nanoparticle [31].

The 2017 publication "Short time exposed of mice to MERS-CoV nanoparticles protect them from MERS-CoV infection" was the brainchild of American scientists.[32] Vaccination against MERS-CoV should aim squarely at the spike (S) protein, which is a receptor-binding, cell-induced immune domain that causes the body to produce antibodies that neutralize it *in vivo*. Using a recombinant MERS-CoV S vaccination with matrix-M1 adjuvant, the researchers demonstrated that mice developed protection to the virus. Vaccination of mice also demonstrated the safety of the adjuvant matrix-M1 formulation and recombinant MERS-CoV S nanoparticle vaccine. In vivo studies demonstrated that the MERS-S vaccine, which was an anti-body with a high titer, protected mice against MERS infection.

As a measure of protection, scientists in 2018 looked at the possibility that NPs made of antimicrobials could impede binding to hDPP4. After incubating the RBD-Protein with the mouse sera (1:10), it was shown that RBD-[SSG]-FR, RBD_FR, and RBD_immunized sera significantly decreased the binding of serum-mixed samples with the hDPP4 protein (93.3, 82.2 and 75.67% correspondingly). It is worth noting that the interference's relative performance is correlated with the NP-assembly's intervention. On the other hand, sera from FR-immunized mice did not suppress the interaction (negative control). Taken as a whole, the results show that NPs may produce an antibody response to MERS-CoV, which can effectively block the virus's attachment to the cell receptor, suggesting that they might be used as a vaccine [33].

In 2018 [34], in order to back safe and effective preventative measures, a group of researchers who have created new vaccination technologies banded together. The production of virus-like components and agonists for the stimulator of interferon genes (STING) is the basis of a novel nanoparticle vaccination. The STING agonists are the first to be expressed in capsid-hollow polymers of nanoparticles. These agonists have a pH-release profile that is beneficial, local immune activation that is conspicuous, and decreased reactogenicity, among other desired properties. Following antigen conjugation, nanoparticles show morphological similarities to natural viruses, enable code recovery from antigens, and kill lymph nodes and immune cells via the action of STING agonists. Extensive neutralizing antibodies and antigen-specific T-cell responses in mice that were vaccinated with the nano articular vaccine against MERS-CoV nanoparticles demonstrated the vaccine's effectiveness. Without using the MERS-CoV transgenic mouse model to decrease undesirable eosinophilic immunopathology, the researchers demonstrated that the nanoparticular MERS-CoV vaccination had an excellent safety profile in mice against a fatal MERS-CoV challenge. Incorporating candidates and unique adjuvants into the vaccine subunit using biocompatible hollow nanoparticles is a great way to speed up the development of effective and safe vaccination against emerging viral diseases.

An additional research group, which was also active in 2018 [35], created 2 vaccines against MERS-CoV: One using an aluminum adjuvant and the other using a recombinant serotype 5 adenovirus that encodes spike MERS-CoV (Ad5/MERS). Boost immunization of heterogeneous antibodies and homological immunization by spike protein nanoparticles were both enhanced by MERS-CoV neutralization, but both vaccines might induce specific MERS-CoV immunoglobulin G. Both spike protein nanoparticles and vaccination schemes like Ad5/MERS were shown to activate Th1 cells. By chance, we were able to gather Th1 and Th2 responses from Ad5/MERS and other heterologous primary-improvement immunization regimens. Additionally, a prolonged immune response to MERs-CoV may be achieved with the use of heterologous prime boost in an optimal mix of Th1/Th2 responses. In contrast, MERS-CoV can be protected against in mice by both homologous nanoparticle spike (S) proteins and heterologous premium increase vaccines. It seems that heterologous vaccination using Ad5/MERS and spike (S) protein nanoparticles would be the best way to prevent MMS-CoV infection, according to the results.

In January 2019 [36], a patent pertaining to the treatment of MERS-CoV was published in the USA. This development pertained to siRNA therapeutic formulations and methods used for the treatment and prevention of coronavirus (MERS-CoV) infections in the Emirates. The formulations include Liposome Conjugates (SLiC) and Histidine-Lysine Co Polymer (HKP) and SiRNA Co-Polymer (SLIC) SiRNA Co-Particulate Nanoparticles, as well as Spermine-Liposome Conjugates (siRNA cocks) that target viral genes. The patent outperforms ribavirin in terms of the preventative efficacy of HKP/siRNA, which consists of 2 siRNAs that target certain fluorine genes. The preventative impact of HKP/siRNA, which consists of 2 influenza-specific siRNAs, is also higher than that of Tamiflu®. Since the human respiratory system is involved in both influenza and MERS, the patent suggests a similar therapeutic strategy for treating MERS, using HKP/siRNA therapy, once the positive therapeutic impact is found.

In 2019 [37], as part of their work on MERS-CoV applications and diagnostic techniques, a group of Japanese researchers produced structural proteins in silkworm larvae and Bm5 cells. Through the use of bombycine signal peptides in affinity chromatography, the MERS-CoV spike (S) protein is released into the hem lymph of silkworm larvae. This protein does not include the membrane or cytoplasmic domain (SΔTM). The SΔTM-purified S-protein nanoparticles, which had a maximum length, were attached to a human dipeptidyl peptidase 4 (DPP4) receptor, which is involved in the replication of the coronavirus (MERS). A bioactive SΔTM in silkworm larvae was suggested by the authors. The production of MERS-CoV-like particles (MERS-CoV-LPs) was achieved by co-expressing spike proteins into the extracellular domains (ECD) and membrane (M) of proteins that are normally located outside of cells. This process included the establishment of MERS CoV LPs. Supernatant cultures have shown the presence of E and M proteins, but S proteins have not been identified as VLPs. We devised and validated a surfactant treatment and mechanical extrusion method using immuno-TEMs for protein-showing Nano vesicles with diameters of 100 to 200 nm. The cells used in this process could express either S protein or 3 structural proteins. To extract nanovesicles from recombinant protein displays in grown cells, mechanical extrusion proved to be an effective technique. The creation and identification of MERS-CoV vaccines using S protein-displaying Bm5 cell nanovesicles and purified SΔTM from silkworm larvae was a collaborative effort.

Researchers have also discovered other nanoparticles that have an antiviral impact. A Chinese research group, for instance, created a novel class of peptide inhibitors (PIH-AuNRs) based on gold nanorods in 2019. Coronavirus proteins are the specific targets of these inhibitors, which cause them to malfunction. Both *in vitro* and *in vivo* studies showed that PIH-AuNRs effectively blocked MERS-CoV-associated membrane fusion by virtue of their improved metabolic stability and biocompatibility. There is hope that the novel family of antiviral medicines known as PIH-AuNRs may be useful in the treatment of MERS in clinical trials [38].

Nanomaterials-based diagnostics for tracking sars-Cov-2

Assessment tools are key in the observation of SARS-CoV-2 dissemination, supporting the immediate recognition of infected persons and the initiation of appropriate responses. Currently, 2 conventional approaches, reverse transcription polymerase chain reaction (RT-PCR) and CT imaging, are typically applied in healthcare scenarios. RT-PCR is the predominant method for identifying various viral pathogens [102-107]. Chest CT scan images can reveal viral pneumonia and potential pathogenic mechanisms. Furthermore, an array of alternative technologies has significantly contributed to the diagnostic landscape of CRC. The reverse transcription-loop-mediated isothermal amplification (RT-LAMP) assay has obtained Emergency Use Authorization (EUA) for the expedited detection of viral RNA [108-113]. The use of next-generation sequencing (NGS) began with the aim of confirming the identity of the new coronavirus and has now been incorporated with other strategies, such as LAMP, to expand testing potential [114-116]. The latest innovations in microarrays have introduced a wide variety of antigens and DNA probes aimed at reliably detecting SARS-CoV-2 alongside other coronaviruses, clearly separating it from more ordinary viral infections such as the common cold. These advanced techniques facilitate robust testing with elevated diagnostic sensitivity and specificity. Nevertheless, there is an urgent need for novel methodologies capable of enabling the rapid testing of a substantial volume of samples. Nanomaterials offer promising avenues for the development of swift and convenient detection methods for diverse pathogens. To explore SARS-CoV-2, researchers have developed a set of bioassays involving gold nanoparticles (AuNPs). In summary, a notable number of bioassays that employ gold nanoparticles (AuNPs) have been initiated to confirm the presence of SARS-CoV-2. Upon examining this particular test strip, it was found that the sensitivity percentage stood at 88.66%, while the specificity percentage reached 90.63%, derived from assessments performed on a total of 397 and 128 blood specimens from individuals who were confirmed positive and negative for RT-PCR, respectively [20]. In a comparable setup of lateral flow tests, another study presented a rapid method utilizing gold nanoparticle to detect serum anti-nucleocapsid IgM [21]. Currently, a variety of rapid serological diagnostic assays leveraging gold nanoparticle have received Emergency Use Authorization (EUA) from the FDA. [13] In addition to detecting serum antibodies, gold nanoparticle have been used to recognize SARS-CoV-2 antigens or viral RNA sequences. For example, researchers synthesized gold nanoparticle -hACE2 conjugates and applied them to a microplate or cartridge surface that had been immobilized with anti-spike antibodies [22]. In the realm of identifying SARS-CoV-2, it has been noted that the spike proteins linked to this virus can be detected in an impressively brief period of just 15 min, employing either an advanced microplate reader or a handy handheld gadget that can be effortlessly paired with a mobile application created specifically for this task. Two varied academic works have elaborated on the creative technique of uniting gold nanoparticles (AuNPs) with antisense oligonucleotides (ASOs), developed to be complementary to the RNA sequence associated with the nucleocapsid gene of SARS-CoV-2. One of these studies employed thio-modified ASOs, which facilitated a colorimetric swab test conducted within tubes, thereby enhancing the ease of visual identification of viral presence [117-120]. Conversely, another study utilized unlabeled ASOs to achieve electrochemical detection on a specialized biosensor chip, illustrating a different methodological approach to the same problem of viral detection. The process of extracting viral RNAs from a swab sample resulted in the hybridization of nucleic acids, which subsequently led to the agglomeration of gold nanoparticle, an occurrence that became visually apparent to the naked eye, thereby providing a straightforward and effective means of assessment. This specific test is known to have the astonishing ability to identify SARS-CoV-2 RNAs at levels as low as 0.18 ng/μL, highlighting its exceptional sensitivity and promising role in clinical diagnostics. Such advancements in detection technologies underscore the critical importance of the rapid and accurate identification of viral pathogens in the ongoing efforts to manage and mitigate the impact of outbreaks. The integration of innovative nanotechnology with molecular biology techniques represents a significant leap in virology and public health diagnostics. Ultimately, the results shed light on the larger picture of successful approaches to the swift recognition of infectious agents, crucial for carrying out fitting public health actions [22]. In a separate and distinct investigation, gold Nano islands conjugated with DNA probes specifically designed to be complementary to the RNAs of the SARS-CoV-2 virus were meticulously positioned on the surface of a sensor chip, thus facilitating advanced detection methodologies. The intricate interplay of nucleic acid hybridization unfolds as DNA strands are fixed in place, engaging with viral RNA sequences, and is observed with great care using a combination of optical methods, particularly surface plasmon resonance, alongside thermal approaches, especially the plasmonic photothermal effect. Together, these features foster a highly advanced dual-function detection system that significantly boosts both the sensitivity and specificity of the assay. This innovative approach not only underscores the potential of nanotechnology in the realm of viral detection but also demonstrates the intricate interplay between biochemical interactions and physical monitoring techniques, thereby paving the way for future advancements in diagnostic capabilities [25]. In order to effectively identify the presence of COVID-19 in exhaled breath, gold nanoparticles (AuNPs) were meticulously conjugated with a diverse range of organic compounds that exhibited interactive properties with a multitude of volatile organic compounds found in respiratory exhalations, resulting in observable alterations in electric resistance. Through the utilization of both confirmed positive and negative control samples, the unique electric signature corresponding to COVID-19 infection was systematically discerned and classified using advanced machine learning algorithms, which were then employed to facilitate the accurate detection of infections. This innovative approach underscores the potential of nanotechnology and machine learning in biomedical diagnostics, particularly in the context of rapidly identifying infectious diseases based on breath analysis [26].

A comprehensive array of studies has been conducted on magnetic nanoparticles (NPs) in the context of immunoassays, underscoring a crucial approach for identifying and diagnosing SARS-CoV-2, the pathogen behind the COVID-19 outbreak. In a particular study documented in the literature, a sophisticated filtration column was employed, which was meticulously coated with spike proteins that effectively captured and retained specific antibodies present in serum samples, which were subsequently identified through the use of secondary antibodies conjugated with magnetic NPs to enhance the detection sensitivity [35]. Moreover, another scholarly investigation has disclosed the advancement in the fabrication of nanoparticles that possess a magnetic core, which is intricately enveloped by a gold plasmonic shell, thereby combining the advantageous properties of both materials. This revolutionary progress in nanoparticle technology not only suggests exciting possibilities for diverse applications in biomedicine and diagnostics but also underscores the continuous research directed at refining the capabilities and effectiveness of these nanostructures. Consequently, the integration of magnetic cores with plasmonic shells presents a novel avenue for enhancing the sensitivity and specificity of detection methods employed in complex biological samples. Ultimately, this innovative approach underscores the significant potential of engineered nanoparticles in revolutionizing diagnostic methodologies and improving analytical outcomes across diverse scientific disciplines [36]. The visualization of the signal produced by the accumulation of magnetic nanoparticles (NPs) within the confines of the column was achieved using a portable magnetic reader, a device that allows for the convenient detection of these particles in various settings. This cutting-edge methodology exposed a detection criterion that was similar to that of the enzyme-linked immunosorbent assay (ELISA), while considerably decreasing the time needed to administer the assay in contrast to established methods. Furthermore, another study documented the successful development of nanoparticles with a magnetic core encased within a gold plasmonic shell, thereby enhancing their functional capabilities. By harnessing cutting-edge magneto-plasmonic nanoparticles, experts were able to create a portable instrument specifically aimed at executing quick reverse transcription polymerase chain reaction (RT-PCR) amplification along with fluorescence detection of viral RNA from numerous samples, achieving this extraordinary achievement in a brief 17 min. Surprisingly, the detection limit devised by this portable tool was found to align closely with that of the conventional RT-PCR methodologies widely practiced in laboratory settings today. This development indicates a meaningful leap in the domain of rapid diagnostic technologies, as it supports swifter and more effective analysis of viral pathogens, which is critical in the scope of rising infectious diseases. Ultimately, the application of sophisticated nanoparticle technology in handheld diagnostic devices offers substantial potential for altering the realm of molecular biology and enhancing our readiness to address public health emergencies efficiently [36]. Furthermore, a DNA nanodevice identified SARS-CoV-2 RNA through a gel mobility shift resulting from hybridization with fragmented viral RNA [39]. In addition to standalone evaluations, nanomaterials have enhanced the sensitivity and specificity of SARS-CoV-2 diagnostic technologies, as evidenced by the reduction of false results and expedited testing time when combining crimsoned red encapsulated polymer nanoparticles with RT-LAMP compared to its use alone. [Immunization has emerged as a pivotal intervention for managing and ultimately eliminating the dissemination of numerous infectious agents [37,76]. Currently, specialists have embraced various methodologies to develop vaccines for COVID-19. For instance, live-attenuated vaccines employ genetically modified viral strains with diminished virulence or optimized codon configurations. Inactivated vaccines comprise complete virions cultured *in vitro* and are subsequently subjected to sterilization methodologies employing agents such as β-propiolactone. Vaccines developed using protein technology encompass either the recombinant full-length spike protein or the receptor-binding domain (RBD) component, produced via synthetic techniques or biological constructs. Nucleic acid-based vaccines utilize either DNA or mRNA to express antigens. Certain approaches have achieved regulatory endorsement for human use, whereas others are still navigating various phases of clinical review. Nanomaterials can operate as significant delivery systems for antigens and adjuvants. Secured authorization has been granted by regulatory authorities across numerous nations and regions, particularly the United States Food and Drug Administration and the European Medicines Agency. Both types of vaccines utilize messenger RNA platforms. The 0.5 mL unit of mRNA-1273 consists of 100 μg of mRNA that is enclosed in a formulation made of ionizable lipid nanoparticles, which contains SM-102, PEG-2000-DMG, DSPC, cholesterol, and sucrose [93]. Three additional mRNA-based vaccines utilizing various formulations of ionizable lipid nanoparticles are currently undergoing evaluation in clinical trials. Notably, MRT5500 encompasses additional mutations at the furin cleavage site to further stabilize the prefusion conformation. Simultaneously, lipid nanoparticles containing self-amplifying mRNA (SA-mRNA) coding for a prefusion-stabilized spike protein have emerged as viable vaccination options. In the field of vaccine delivery, a squalene-derived cationic Nano emulsion significantly enhances the transport of SA-mRNA encoding the spike protein. In a Phase I/II clinical trial (NCT04368988), a prime and boost vaccination method that combined the recombinant spike protein with Matrix M1 promoted the synthesis of anti-spike-specific antibodies, yielding neutralizing titers that matched those detected in symptomatic patients. In a comparable framework, MF59, a nano emulsion adjuvant that incorporates squalene, was employed in conjunction with a recombinant spike protein vaccine specifically formulated to target SARS-CoV-2. The Phase I clinical trial evaluating this vaccine (V451) was completed in December 2020 in Australia [54,42]. Therapeutic applications have seen the integration of nanomaterials for many years now [105-106]. Nanomaterials can safeguard encapsulated pharmaceuticals, enhance intracellular transport, optimize biodistribution, and serve as autonomous therapeutic agents [88,107]. In a noteworthy study, researchers encapsulated catalase inside a fragile polymeric shell, thus boosting the enzyme's stability and extending its half-life, which is vital for breaking down reactive oxygen species (ROS). Delivering the nano capsulated catalase via nebulization and intravenous infusion notably lowered cytokine levels and hindered SARS-CoV-2 replication in both mouse and primate studies [61,63]. The secreted ACE2 prevented hACE2- expressing 293T cells from being transduced by viral particles pseudotyped with the spike protein in vitro. Additionally, lipid or lipid-sourced nanoparticles (LNPs) were explored for the delivery of DNA or mRNA encoding neutralizing antibodies to treat COVID-19 [108,121-122].

Figure 6 shows that the coronavirus family includes the severe acute respiratory syndrome coronavirus (SARS-CoV). It is thought that SARS-CoV is a related virus that is transmitted to other animals by an unknown species, maybe bats. In 2002, this virus affected people in the southern Chinese province of Guangdong. More than 8,000 cases of SARS were reported in 2003, affecting 26 nations. Accidents in the lab or potential transfer from animals to humans have been the only known causes of instances since then (Guangdong, China).

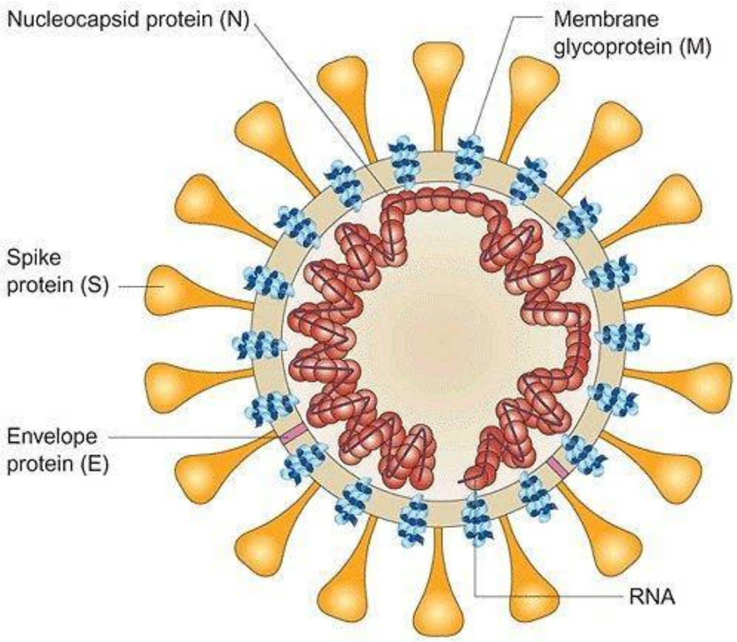

Figure 6 A Schematic Diagram of the SARS Coronavirus [128].

Researchers have looked on SARS-CoV vaccines employing nanocompounds, namely injectable mice infected with the virus and polyethyleneimine nanoparticles (PEI). In 2010, researchers in Korea and China (which researchers, should I cite them?) studied the immunological response of mice that were intranasally (i.n.) inoculated with SRAS DNA (pci-S) in the PEI/pci-S complex type of SARS.39 Injecting SRAS into the serum and IgA causes the animals to develop an immunity ($p < 0.05$). In addition, compared to animals injected with pci-S alone, those injected with PEI/pci-S showed significantly greater levels of S-specific IgG1 in lung washing. Mice vaccinated with both PEI and pci-S had a greater concentration of B220+ cells than mice inoculated with pci-S alone. These results demonstrated that intranasal vaccination with PEI/pci-S nanoparticles enhances antigen specific humor and cell immune responses. Finally, PEI is likely to have a major impact on B cell and T cell immunity by acting as a vector to disperse DNA vaccine in mucus.

In the USA, in 2014, 1 research group referred to in reference [29], as well as the MERS virus, using the same novel nanomaterial therapies. An innovative method for producing fully functional SARS-CoV nanoparticles that, when combined with adjuvants, may generate highly verified mice antibodies was also detailed by the researchers.

In 2019, another study group in Japan [40], administered vaccine nanoparticles made of gold and examined mice for signs of SARS-CoV infection. The spike (S) coronavirus protein, which promotes membrane fusion for cell entrance and binds to cell receptors, is a possible target for coronavirus blocking vaccines. However, studies in the lab have shown that after a diagnosis of SARS-CoV, lung eosinophilic immunopathology might occur due to inadequate vaccination. A SARS-CoV vaccine with ultraviolet inactivation previously used toll-like receptor agonists (TLRs) as an effective adjuvant, and gold nanoparticles (AuNPs) as a vaccinating antigen carrier were the 2 types of recombinant S protein adjuvants studied in this study. The majority of the mice that were vaccinated with more than half a milligram of SARS-CoV protein without an adjuvant showed eosinophilic penetration in their lungs, even though these animals had been acclimated to SARS-CoV infections. Neither the vaccine's efficacy nor the reduction of eosinophilia were improved by the AuNP-adjuvant protein, which triggered a rapid IgG reaction due to very severe inflammatory reactions. Test animals and animals with a S protein immunological status showed identical viral titers regardless of whether the animals were treated with or not given gold nanoparticle. The results of this study have been useful in developing a vaccine to protect people against dangerous coronaviruses that cause pneumonia. In order to combat the SARS and MERS coronaviruses, **Table 2** details the suggested usage of nanomaterials.

Despite the rapid increase in publications and commercial products on gold nanoparticle -based diagnostics in recent years, not many of them have carefully optimized the size and shape of gold nanoparticle in their assays. To develop highly sensitive testings for SARS-CoV-2, the selection of gold nanoparticle with proper size and shape is as important as the assay development itself. One beauty of using gold nanoparticle is that a wide range of sizes (a few to several hundred nanometers) and shapes (e.g., sphere, rod, core–shell, cube, star, cage, pyramid, Janus, etc.) of gold nanoparticle and even hybrids with other nanoparticles can be synthesized in a controlled manner through well-defined approaches. The size and shape of gold nanoparticle are closely associated with their physical and optical properties, which can greatly influence the performance of gold nanoparticle -based diagnostics. For spherical gold nanoparticle, 10–20 nm size is commonly chosen because of the ease of synthesis and good control of monodispersity as both smaller and larger gold nanoparticle tend to have a higher polydispersity index. When developing an assay, depending on the property of gold nanoparticle employed, that size range might not be ideal. Generally speaking, larger gold nanospheres have a larger absorption cross-section and magnitude of extinction. So for assays that reply on the absorption property, such as LSPR-based as well as many colorimetric assays like LFAs, larger gold nanoparticle have a better chance of obtaining a higher sensitivity relative to smaller gold nanoparticle. Similarly, gold nanoshells tend to have a higher sensitivity than gold nanospheres. However, this assumption always needs to be tested in each assay development as many other factors could influence the ultimate LOD as well [40].

Chowdhury *et al.* [194] To combat the rapid spread of fatal diseases, the immune system needs to be strengthened. This can only be achieved by consuming bioactive substances extracted from plants. Nanoencapsulation technology is unique and new. The effects of both foods and drugs affect new commercialization options. Nanoencapsulation using a strap of bioactive compounds is an approach that can improve its bioavailability, stability, and use in the pharmaceutical industry. Nanotechnology for encapsulating microbial compounds with biological activity properties offers many distinct advantages, from packaging to food processing. This includes improved bioavailability and stability. Controlled release and bioactive defense also offer safety benefits. To promote the safe marketing of health nanotechnology products for health nanotechnology, global legislation is needed to recognize the security and toxicology of these nanomaterials. In other words, new extraction and capsule technologies need to be developed and implemented for people with highly effective microbial bioactive activity that can be used in a variety of industries such as the food, pharmaceutical and beauty industries. Additionally, to ensure safe marketing and use, we need to understand the security and toxicology of nanocaps and implement global laws.

Mahapatra *et al.* [195] Scalable strategies for surface treatment, combining antiviral effects with liquid properties, are one of many possible approaches to improving the function of PPE, which could meet the high demand in the health industry and other aspects where the COVID-19 pandemic will be combated. Because photocatalytic therapy is available, we propose a cost-effective coating approach to produce water-fed coatings with additional disinfecting properties.

Shivanika *et al.* [196] To date, there has been no permanent cure for SARS-COV-2 disease in the onset of brime solutions and precursors that could act as potential antiviral agents against the disease. The motivation for this study was to discover a natural link that could be a potential antiviral means of inhibiting the virus SARS-COV-2-MPRO (PDB ID: 6LU7). We examined 200 previously reported natural antiviral connections from the literature and databases. The active location of the protease was determined on a Meta Pocket 2.0 online server. To clarify the interaction between liganden and MPRO, molecular docking was performed using Auto Dock .2.6 along with support software and Discovery Studio 3.5. Ten top connections with high binding energy were registered from 200 connections. Theaflavin-3'-Digallat (–12,1 kcal/mol), rutin (–11.33 kcal/mol), hypolicin (–11.17 kcal/mol), robustaflavon (–10.92 kcal/mol) - and (-) - solenolid a (–10.81 kcal/mol). This study was compared by docking with FDA approved viral protease inhibitors and MPRO. It was found that drugs such as atazanavir (–13.2kcal/mol), saquinavir (–12.7 kcal/mol), and darunavir (–12.50 kcal/mol) inhibit proteases very effectively and compare interactions with natural connections. This study also analyzed the efficiency of medicinal products currently running COVID-19 with the help of docking research. The natural connection to COVID-19 and the pharmacothermology and toxicity properties of the drug were reported and tested. Although FDA approved drugs had high binding energies, we found that the number of hydrogen bonds formed in MPRO was lower compared to the hydrogen bonds formed in the natural connections used in the study. Natural connections such as flavonoids, terpenoids, alkaloids, phenols, tannins, and saponins are plant metabolites and do not have mutant or carcinogenic properties. There are few or no side effects caused by natural connections. (-) - Solenorid A, Ginkedzin, Rainacantin E, Solvaline, and Bethulic acid met Lipinski's rules for the probability of oral medication. Rainacantin E filled all filters used to assess drug probability. For 50 ns, molecular dynamics were performed to assess stability and flexibility using stable protein and ligand complexes across Desmond packets, Schrödinger, and simulations. Overall, the plant compounds, which are part of our daily diet, have been found to be a very strong antiviral candidate against COVID-19, which can prevent infection. This study could serve as a street map for the discovery of natural antiviral connections. Therefore, the -ILICO study provided rapid and comprehensive insight into the results when checking connection libraries. Future studies will focus on other toxic proteins of SARS-COV-2, but in-silico studies. In vitro and in vivo clinical studies with upper links shown in studies that demonstrated the potential to inhibit proteases. Advances in bio nanotechnology have led to the development of targeted drug delivery systems using nonsynthetic metals, metal oxides and polymer nanoparticles. Nanomaterials improved electrical, electrical, optical, physical, chemical properties, high surface and permeability. Future studies will also focus on natural compounds as capping and reducing agents onto metal nanoparticles which will surely provide positive insights towards the cure of infection.

Table 2 Applications of nanomaterials to inhibit coronaviruses.

Virus	Nanomaterials	Size	Organism	Recommended application	References
MERS-CoV and SARS-CoV	Spike protein nanoparticles	25 nm	mice	Vaccine	[29]
MERS-CoV	Polymeric nanoparticles	26 nm	mice	Vaccine	[31]
MERS-CoV	Spike protein nanoparticles	---	mice	Vaccine	[32]
MERS-CoV	ferritin nanoparticles	multi (52 to 24 nm)	mice	Vaccine	[33]
MERS-CoV	hollow polymeric nanoparticles	10 nm	mice	Vaccine	[34]
MERS-CoV	Spike protein nanoparticles	80 nm	mice	Vaccine	[35]
MERS-CoV	Histidine-Lysine co-polymer (HKP) and Spermine-Liposome conjugates (SLiC) siRNA nanoparticle	150 nm	mice	Therapeutic	[36]
MERS-CoV	Spike protein nanoparticles	100-200 nm	silkworm larvae	Vaccine	[37]
MERS-CoV	Gold nanorods	18.0 ± 0.7 nm	mice	Antiviral	[38]
SARS-CoV	Polyethylenimine nanoparticles	194.7 ± 99.3 nm	mice	Vaccine	[39]
SARS-CoV	Gold nanoparticles	40-100 nm	mice	Vaccine	[40]

Biosensors

Biosensors with excellent selectivity, high sensitivity, and fast response have great potential in clinical testing of biological indicators and in the treatment of various diseases. Smart materials are a class of materials that can respond to external stimuli, such as pH, temperature, humidity, electric or magnetic fields, light, chemical compounds, and bio stimuli. Smart materials, such as hydrogels and nanomaterials (e.g., gold nanoparticles (AuNPs), quantum dots (QDs), carbon nanotubes (CNTs), and graphene), have been widely used in biosensing [199-208]. In addition, photonic crystals (PCs), which are periodic micro- or nanostructures that can control the reflection of light, provide an excellent biosensing platform to visually report target analytes. In addition, molecularly imprinted polymers (MIPs), a type of material with special recognition sites for binding to imprinted molecules, have been developed to recognize various biomolecules, such as proteins and enzymes, based on the changes in the refractive index and volume of MIPs. In general, integrating intelligent materials into biosensor platforms can enable fast, sensitive, reliable, and user-friendly diagnostics [214-217]. In particular, sensitive materials, such as electrochemical sensors, optical sensors, thermal sensors, piezoelectric sensors, impedance sensors, and interferometric biosensors, are often used as diagnostic platforms [123].

The role of vitamins in COVID-19

This review paper examines the role of vitamins in the COVID-19 pandemic, focusing on their impact on immune function, respiratory health, and overall well-being. It discusses the role of vitamins like vitamin C, vitamin D, and vitamin E in the virus's course and outcomes which synthesizes existing research and clinical observations to provide a nuanced overview of the potential benefits and limitations of vitamin supplementation, highlighting the intricate relationship between nutritional status and the body's response to viral infections. The potential role of Vitamin D in supporting immune responses has been a subject of extensive research since the pandemic began [140-150]. Adequate levels of vitamin D are linked to a well-functioning immune system, making it a crucial component in preventing COVID-19, a disease that requires a balanced diet for overall health and immunity. Its potential impact on COVID-19 prevention has garnered significant research and public interest, particularly in its role in immune function, with Vitamin D being a key player in discussions on its potential impact [243,253,263]. Vitamin D levels are linked to a robust immune system, and studies have found a link between vitamin D deficiency and increased susceptibility to respiratory infections, including those caused by viruses [151-160]. However, it is essential to note that while vitamin D is crucial for overall health, its direct and specific role in preventing COVID-19 is still an area of ongoing investigation. Vitamin C, known for its antioxidant properties, has been studied for its potential in preventing and mitigating respiratory infections, including COVID-19 [161-168]. It helps combat oxidative stress and supports the immune system. Studies suggest vitamin C supplements may reduce symptoms in COVID-19 patients [169-173]. However, the impact of vitamin C on preventing COVID-19 remains complex, and its efficacy is continually evaluated. Vitamins C and D are essential for strengthening the immune system and defending against viral infections. Vitamin C neutralizes free radicals and reduces inflammation, while Vitamin D is crucial for bone health and immune system modulation. Adequate vitamin intake may help combat infections, including viral ones. However, a balanced approach is needed, considering individual needs and potential interactions. Maintaining adequate levels of Vitamin C and Vitamin D can promote milder symptoms and expedite recovery in COVID-19 patients. Vitamin supplementation alone is not a cure, and public health measures, vaccination, and a comprehensive approach are crucial in managing the virus's impact. Excessive intake of fat-soluble vitamins like Vitamin A and D can cause toxicity and adverse health effects. These vitamins are stored in the body's fatty tissues and liver, and when their levels exceed the body's capacity, they can cause nausea, dizziness, liver damage, and hypercalcemia. Maintaining a balanced diet and adhering to recommended daily allowances is crucial to prevent potential risks associated with excessive vitamin intake. Vitamins play a crucial role in COVID-19 prevention, but they should not replace established public health measures like vaccination, mask-wearing, and hygiene practices, as they contribute to immune function. The immune response's complexity and the intricate interactions between vitamins and viral infections require a comprehensive understanding. As research progresses, evidence-based recommendations and a holistic approach are crucial for COVID-19 prevention and management. Essential vitamins like vitamin A, vitamin E, and B vitamins are crucial for maintaining a healthy immune system, immune cell function, antibody production, and defense against infections. Their impact on preventing COVID-19 is still under investigation, despite their importance for overall health. The effectiveness of vitamin supplementation in preventing or treating COVID-19 remains inconclusive due to the complexity of the immune response, individual variability, and the virus's multifaceted nature. The relationship between vitamins and COVID-19 requires a cautious, evidence-based approach, including vaccination, adherence to public health guidelines, and maintaining a balanced diet [174-175].

Limitations of the study on the role of vitamins in COVID-19

The study on vitamins' role in COVID-19 prevention has limitations, including potential publication bias and incomplete literature due to factors like research availability, language bias, and exclusion criteria. Positive outcomes may be more likely to be published, resulting in an incomplete representation of the evidence. The diversity of study, populations, and methodologies in research articles can hinder consistent conclusions and generalization of findings. The quality of included studies, such as lack of high-quality randomized controlled trials or methodological flaws, can also affect the reliability of the review's conclusions. The COVID-19 pandemic has limited long-term data on vitamin interventions' effects, necessitating long-term studies to understand sustained benefits, potential side effects, and overall effectiveness of vitamin supplementation in COVID-19 prevention. Vitamins are essential for overall health and immune function, but their potential drawbacks need to be understood. The review on the role of vitamins' role in COVID-19 has limitations, necessitating rigorous research, cautious supplementation, and a holistic approach to health to navigate the complexities of vitamin-COVID-19 prevention [179-182]. The review on the role of vitamins in COVID-19 prevention acknowledges limitations in the findings, including publication bias and incomplete literature. Factors such as limited research availability, language bias, and stringent exclusion criteria could contribute to an incomplete assessment of the overall evidence. The COVID-19 pandemic has increased the number of studies on vitamin interventions, complicating the synthesis of results and the reliability of the review's conclusions. The quality of the included studies, particularly high-quality randomized controlled trials, is crucial for the reliability of the review's conclusions. However, the scarcity of long-term data on vitamin interventions' effects is a significant limitation. The presence of publication bias and gaps in the literature may skew the review's findings, potentially presenting an overly optimistic view of vitamins' role in preventing COVID-19 [183-187]. It is crucial to explore the role of vitamins in COVID-19, discussing their benefits and drawbacks, and addressing the limitations of existing studies on the connection between vitamins and the virus. Vitamins are essential for maintaining health and supporting physiological functions, particularly in supporting a robust immune system. Vitamin C, for example, is known for its antioxidant properties, which neutralize free radicals and reduce inflammation. Vitamin D is vital for bone health and immune system regulation, while vitamins A, E, and B-complex are essential for bodily system function and metabolic processes, supporting energy production and cellular function. At the same time, excessive intake of vitamins can lead to adverse effects, as fat-soluble vitamins can accumulate and reach toxic levels, while water-soluble vitamins are typically excreted in urine, despite their potential health benefits. Excessive vitamin C intake can cause digestive issues, while relying solely on supplements without a balanced diet can lead to nutrient imbalances. It is crucial to consider individual needs, potential interactions, and seek professional advice when considering vitamin supplementation [179-184].

Numerous clinical studies have examined the delicate interrelationship between vitamin B levels and COVID-19 outcomes, providing valuable insights into the potential impact of this vital nutrient on the disease's progression. Observational studies have consistently revealed a link between low vitamin B levels and greater susceptibility to COVID-19 and worsening symptoms among those infected. Vitamin B supplementation as an auxiliary therapy method in COVID-19 patients has emerged as a viable route, with excellent results in symptom relief and overall clinical parameter improvement. The importance of vitamin B in immune function cannot be stressed, as it plays a critical role in the development and maturation of essential immune cells such as T cells, B cells, and natural killer cells. Furthermore, vitamin B is essential for creating cytokines and antibodies, which regulate the immune system's response to viral infections. Furthermore, vitamin B deficits have been identified as potential initiators in reducing the immune system's efficacy, making people more susceptible to infections. Recognizing the complex interactions between vitamin B and various therapy modalities is critical for effective COVID-19 management. Research has shown that combining vitamin B with other nutrients can have synergistic benefits, providing a holistic approach to strengthening the body's defense mechanisms. In addition, studies have looked into potential interactions between vitamin B and specific medicinal drugs, shedding light on the complexities of COVID-19 therapy options. Vitamin B is an essential component of immune function, which is involved in the generation and maturation of immune cells, such as T cells, B cells, and natural killer cells. It is also necessary to produce cytokines and antibodies that help regulate the immune system's reaction to viral pathogens. Vitamin B deficiencies can harm the immune system and make people more susceptible to infection. Understanding the possible interactions between vitamin B and other treatments and interventions is essential to effective management of COVID-19. Studies have suggested potential synergistic effects of vitamin B combining other nutrients and possible interactions with certain drugs. Vitamin C has been shown to have a synergistic effect with certain antiviral drugs, enhancing their efficacy. Studies have shown that it can potentiate the antiviral activity of medications used in the treatment of COVID-19, such as remdesivir. This synergistic effect may be due to vitamin C's ability to modulate the host immune response, enhance intracellular antiviral defenses, and improve the delivery of antiviral drugs to target cells. For example, vitamin C may enhance the effectiveness of certain antiviral medications used in the treatment of COVID-19. Besides, combining vitamin C with other antioxidants may have synergistic effects in reducing oxidative stress and enhancing immune function [192-193].

Pathogenetic mechanisms about the severity of the disease COVID-19

The global epidemiology of Coronavirus Disease 2019 (COVID-19) shows a wide range of clinical severity ranging from asymptomatic to fatal. Although clinical and laboratory characteristics of COVID-19 patients are well characterized, the pathophysiological mechanisms based on the severity and progression of the disease remain unclear. The 1st step in COVID-19 pathogen formation is viral invasion of target host receptors [209]. Virus SARS-COV-2 entries are described in detail elsewhere. In short, SARS-COV-2 is made up of 4 major structural glycoproteins; spikes (S), membrane (M), envelope (E), and nucleocap side (N). The M, E, and N proteins are critical of the assembly and release of viral particles, while the S-proteins are involved in viral binding and entry into host cells [210,211]. Similar to SARS-COV, several researchers have identified conversion of human angiotensin conversion to enzyme 2 (ACE2) as a receptor for SARS-COV-2 entry levels. SARS-COV-2 is primarily transmitted by cells that directly infect cells in the high amount of respiratory and upper respiratory tract cells, particularly through the nose of cilia and alveolar epithelial cells. In addition to the lungs, ACE2 is also expressed in a variety of other human tissues, including: Interestingly, SARS-COV-2 and SARS-COV S proteins have 72% homology to the amino acid sequence and have a higher affinity for the ACE2 receptor. After binding the host cells, the virus and the cell membrane fuse to allow the virus to enter the cell. For many coronaviruses, including SARS-COV, host cell binding alone is not sufficient to promote membrane fusion. This requires S protein priming or separation by host cell proteases or transmembrane serine proteases. In fact, Hoffman and colleagues showed that transmembrane serine protase 2 (TMPRSS2) is required for transmembrane serine protase 2 (TMPRSS2) to promote the entry of SARS-COV-2 into host cells [212]. Furthermore, in contrast to other coronaviruses, SARS-COV-2, the S-protein domain between the S1 and S2 subunits, was reported to have a furin-like split position. Although further modes of proteases are ubiquitous, we show that S protein priming at this gap may contribute to increased tropism and SARS-COV-2 mobility to expanded cells. However, it is necessary to determine whether input to the SARS-COV-2 host requires protease-mediated splitting, such as thumb. Blocking or inhibition of this processing enzyme serves as a potential antiviral target. Interestingly, SARS-COV-2 has developed a unique S1/S2 column point for its S protein. It is characterized by insertions in tetraacids that are missing in all other coronaviruses [213]. This molecular mimicry was identified as an efficient evolutionary adaptation that acquired several viruses for use in cellular host machines. As soon as the nucleocap side is deposited in the host cell's cytoplasm, the RNA genome is replicated and converted into structural and accessory proteins. It transports vesicles containing newly formed viral particles, integrates into the plasma membrane, and infects them in the same way as other host cells. Although many advances have been made in understanding the mechanisms in which SARS-COV-2 infiltration is occurring, additional research is needed to accurately accelerate the way in which the separation of S proteins by TMPRSS2 contributes to viral penetration by viral particle input and membrane printing contributes to viral penetration. Like other cytotoxic viruses, SARS-COV-2 infection via various processes such as pyrutosis induces respiratory multicellular cell death and damage. Virus-mediated cell death causes the release of various damage-associated molecular patterns (humidity) and pathogen-associated molecular patterns (PAMPs) that are thought to be recognized by sample recognition receptors in alveolar macrophages and endothelial cells. For example, great modal receptors (TLRs) primarily recognize PAMPs in the extracellular space, allowing the induction of proinflammatory cytokine transcription factors such as NF-κ, and activate interferon regulators that transmit type I interferon-dependent antiviral responses. In contrast, nucleotide binding recognizes that nucleotide-binding household leucine-rucin rich repeat protein (NLR) is recognized intracellularly by activation of inflammation and inflammatory and ProIL-1β to active IL-1&Bgr. It will be triggered. Circulating IL-1β levels in COVID-19 patients indicate local inflammatory activation without systemic symptoms. Overall, these processes promote increased secretion of proinflammatory cytokines and chemokines such as IL-6, type II interferon (IFN & GGR;), monoditene-chemoinduced protein 1 (MCP1), and interferon gamma-induced protein 10 (IP-10) and subsequent pulmonary ravisit, Imunger and Dendl herds. Direct viral infection of macrophages and/or dendritic cells is presumed to expand the release of additional cytokines and chemokines, which activates the recruitment of late immune cells of antigen-specific T cells and destroys virally infected alveolar cells. In addition to cytokine release and immune cell recruitment, another potential mechanism that could contribute to successful viral clearance is anti-board neutralization. The current literature shows that seroconversion occurs in COVID-19 patients 7-14 days after symptoms. However, the antibody kinetics of various immunoglobulins are less characterized, and the reported results are contradictory. Although currently available serological assays for trade do not include information on whether SARS-COV-2 antibodies confer immune protection, recent reports involving specialized laboratory neutralization assays have a significant correlation between mirrors of the SARS-COV spike spike/receptor binding domain (RBD) and neutralization capacity during the patient era [213].

Conclusion and outlook

Countless years of collective endeavors in nanomedicine have armed investigators with priceless insights and expertise, which have been essential in the innovation and improvement of diagnostics, vaccines, and therapeutic approaches for COVID-19. In the context of COVID-19 diagnosis, there is an urgent requirement for rapid testing methodologies that either match or surpass the sensitivity of RTPCR. Various testing modalities can be engineered to align with specific situational demands. For instance, diagnostic evaluations, surveillance testing, and entry screening may necessitate distinct levels of scalability and specificity tailored to specific objectives. Concerning vaccine development, both mRNA-1273 and BNT162b2, which are 2 lipid nanoparticle (LNP)-mRNA-based vaccines, have progressed to widespread vaccination in numerous nations. Ongoing assessment and enhancement of current vaccines by researchers is crucial as new SARS-CoV-2 variants emerge. Recent research has indicated that certain variants, including B.1.1.7 and B.1.351, exhibit different levels of resistance to antibodies produced by the BNT162b2 and mRNA-1273 vaccines. Such resistance may be attributed to substantial mutations, such as E484K, which is located within the spike protein. Currently, the FDA has not authorized or issued Emergency Use Authorization (EUA) for COVID-19 therapies that utilize nanomaterials. Nanomaterials may pave the way for the reapplication of established pharmacological drugs in the near future. Currently, dexamethasone is used to help patients with serious COVID-19 conditions. Prior to the pandemic, nano formulated dexamethasone demonstrated enhanced efficacy compared to its unformulated counterpart against various inflammatory conditions, primarily due to improved accumulation within macrophages. Recognizing the fundamental function of macrophages in critical COVID-19 instances, dexamethasone nanomedicine may provide an avenue to better target these cells with drugs, thereby increasing the success rate of treatment against the illness. Progress in nanomaterials provides potent tools for the rapid resolution of the ongoing global public health emergency. This thorough investigation into nanomaterial-centric strategies outlines a plan for the creation of novel and potent diagnostics, vaccines, and therapeutic approaches for COVID-19. These strategies can be swiftly implemented for future emerging pathogens. Progress in nanomaterials provides potent tools for the rapid resolution of the ongoing global public health emergency. This extensive report on nanomaterial-driven techniques provides a blueprint for the advancement of groundbreaking and efficient diagnostic tools, vaccines, and treatment options for COVID-19. These methods are capable of being swiftly implemented for future emergent pathogens.

In order to inhibit the action of the virus, it is feasible to construct a protein nano receptor that is similar to the original ACE2 receptor by applying what is known about the sequence of certain amino acids in the receptors and the SARS-CoV spike protein, as well as the link between them via active groups of amino acids, to the process of disease onset.

Another approach involves using the fact that nanoparticles attach so readily to thiol groups to connect to certain membrane glycoproteins that are abundant in cysteine residues. By blocking the viral particle’s ability to connect to cellular receptors, this contact may impede internalization. To copy RNA from an RNA template in the genome, RNA viruses use an enzyme known as RNA dependent RNA polymerase (RdRp). Inhibitors of viral RNA polymerase may attach to the structures of the enzyme’s active site or to other parts of the viral RNA genome, blocking the incorporation of nucleotides necessary for replication and transcription of viral RNA. The aforementioned methods should be sufficient, considering just a single coronavirus has been identified so far. Whether or whether nanoparticles should be linked together is an open question that requires further investigation in the future.

In this review, the analysed and analyzed papers primarily show silver, copper and polymer-based nanomaterials with efficient anti-SARS-COV-2 properties. The potential for strong viruses of copper and silver antimaterials with different forms and forms of manufacturing was to reduce the spread of COVID-19, reusable and homemade surfaces (e.g. respiratory masks and coating surfaces) in healthcare work environments. Biopolymers and biodegradable polymers in nanoform simulations quickly suggest that the collection of drugs for SARS-COV-2 and nanodecoy and manganese nanoparticles increases immune responses via immune-type immune responses as a simple, safe, safe and robust technique for vaccine adjuvants or antiviral active ingredients. Viral surfaces and adsorbents for capturing/inactivating SARS-COV-2 and other beta-COVs have also been proposed as adsorbents for inactivating coronaviruses. In the most modern nanobiosensor technology, nanostructured carriers for the submission of pulmonary drugs, SVLPs and polymer hydrogels have been noted as potential active ingredients for antiviral drugs, therapeutic vaccines, and immune-based therapy. A study using real clinic samples of COVID-19 patients showed that graphs were used for immunodiagnostic assays with specificity and geme potentially useful for serological testing and detection of infection.Molecular docking and dynamic simulations are powerful tools for investigating the relationship between receptor binding affinity for drug discovery using nanomaterials. Therefore, all nanotechnology examined by arithmetic tools was predicted to affect SARS-COV-2 adhesion to human host cell receptors and viral replication inhibiting viral infection.Plants and microorganisms, primary and secondary metabolites (e.g., phenols, terpenes, glycosides, polysaccharides, polyps), well-known antibacterial compounds delivered by spherical nanoparticles, have generated potential strategies to generate potential strategies to promote bio-soft strategies. Bioavailability and antiviral activity. Phenolic phytochemical methods had multisite inhibitors at several stages of viral input that affect the expression of viral antigens or inhibit genomic replication. Biologically degradable polymer nanoparticles are non-toxic and biocompatible options for pharmaceutical collection. Due to its high surface energy, its immeasurable potential for functionalization and its strongly bonding amino acids, silver and carbon-based nanomaterials have shown that they are likely to be used in various segments to control the diffusion of COVID-19. Therefore, the booth exhibited basic roles and secondary effects (as carrier and antiviral). Understanding the interface between checked nanomaterials and coronaviruses is fundamentally important for the design of targeted antivirals for COVID-19 infections. The potential for different types of connections on surfaces with different morphology, chemical diversity, excellent physical properties, and targeting capabilities, and synergistic effects between customers (e.g., nanocapsules and nanocomposites) have been justified as a potential nanomaterial "potential nanomedicine and prophylactic tool for covidisi and propofactory tools for covidisi and prophylactic tools for covidisi-199." Nanocarbones can act with coronavirus multivalent interactions (e.g., electrostatic interactions, hydrogen bonds, hydrophobic interactions) and spike proteins and lipid tails, membrane disruption, blocking cell invasion, and viral replication. The major mechanism of blocking cell viral infection inhibited cellular invasion of SARS-COV-2 cells by blocking the binding of RBD to human ACE2 receptors from spike proteins. However, sulfonate ligands on the surface of gold nanoparticles may inhibit fixation of SARS-Cov-2 cells by inhibiting the binding between the spike protein and the HS receptor.Many strategies inhibit ROS production, inhibit host cell apoptosis, inhibit endosomal acidification, and act as multi-tank inhibitors for viral hospitalization and replication. Photo-activated copper, silver, and TNP showed the highest possible potential for vircidal averages. No studies on environmentally friendly nanocellulose were determined. Nanocellulose was surprising to consider that due to the non-skin morphology of the nanofiber type, nanocellulose is sustainable, non-toxic, antibacterial, more biocompatible, relatively inexpensive, suitable carrier, and attractive to the pharmaceutical/biomedical industry. Additionally, nanocellulose has hydroxyl groups that can form hydrogen bridges with spike glycoproteins and stabilize ligand receptor complexes. For future possibilities, we believe in new attempts with more effort in non-toxic nanomaterials and nanomaterials. Nanomaterials have already been reported as non-cytotoxic as antiviral active ingredients. Therefore, toxicological assessment of strategies and trends in reviewed strategies for security close the major gaps in the literature and help overcome the main challenges of nanomaterials for health monitoring. Capless Nanosystems with V-Pase inhibition may be privileged targeted therapies to overcome the challenges of antiviral drug resistance. Future instructions can examine the pharmacokinetics of plant chemical conditions assessed by nanomaterials and identify their ability to assess targeting, circulation period, and ability to overcome biological barriers for drug reuse using healthy options. Furthermore, the lack of experimentation could promote new future efforts with unfired nanoparticles (eg, filamentous forms). We hope that research notes dealing with the role of nanotechnology can help researchers address the role of nanotechnology with coronavirus properties to address challenges related to SARS-COV-2-virus control, prevent instructions on developing new antiviral therapies, and prevent future pandemics.

The SARS-CoV-2 has a positive diploma of homology with SARS-CoV and MERS-CoV. Compared to the preceding SARS and MERS outbreaks, we located that COVID-19 has some similarities with reference to the contamination supply and scientific signs, however it additionally a few differences. For example, COVID-19 stocks a few routes of transmission in not unusualplace with SARS and MERS, which include respiration droplets, however COVID-19 also can be transmitted with the aid of using the fecal-oral path . It is vital to take into account all transmission routes while looking for to manipulate the epidemic and defend scientific workforce and the overall public. The epidemiological studies at the supply of contamination and the path of transmission may want to assist save you the similarly unfold of the epidemic. Different scientific signs might be used for the differential analysis of sufferers inflamed with the aid of using coronaviruses. The drug treatments or healing regimens that proved to be powerful for SARS or MERS provide new tactics to the scientific remedy of COVID-19, that is important withinside the prevention and manipulate of the COVID-19 epidemic. The Chinese government`s manipulate techniques in Wuhan and the lively cooperation of the humans have significantly contributed to China`s efforts to manipulate the outbreak, that is vital to the worldwide efforts to fight the epidemic. Testing medicines which have been proven to have antiviral consequences towards SARS-CoV or MERS-CoV might also additionally boost up the tempo of drug improvement on this emergency situation.

The COVID-19 pandemic has highlighted the importance of proactive and coordinated international efforts in addressing emerging viral threats, making a dedicated segment crucial for future perspectives on viral pandemics. The pandemic's impact requires robust healthcare systems, agile research infrastructure, and effective communication strategies. The rapid vaccine development and challenges of equitable distribution and global access necessitate collaborative initiatives and systemic inequalities. The pandemic has highlighted the importance of preparedness, rapid response capabilities, and data-sharing mechanisms for global resilience against future viral threats. Incorporating these lessons into future preparedness plans, fostering international cooperation, and fostering innovation in healthcare and public health systems will strengthen defenses against viral uncertainties. The relationship between vitamin levels and COVID-19 outcomes is complex due to confounding factors like pre-existing health conditions, socio-economic status, lifestyle choices, and genetic predispositions. To fully understand the dynamics between these variables, rigorous research methodologies, controlled trials, and comprehensive consideration of confounding variables are needed. The wide range of methodologies, sample sizes, and participant characteristics used in research makes it difficult to draw definitive conclusions. The lack of consistency in these aspects complicates results and limits generalizability. Standardizing methodologies, incorporating diverse sample sizes, and accounting for participant characteristics are essential steps to improve understanding of the complex relationship between vitamins and COVID-19. The COVID-19 pandemic's dynamic nature and evolving public health measures necessitate comprehensive, longitudinal studies to assess the relationship between vitamin status and COVID-19 outcomes accurately. Short-term studies may overlook key patterns and long-term effects, while longitudinal studies provide insights into the temporal dynamics of vitamin levels and their impact on the disease's course. Understanding the complex interplay between vitamins and COVID-19 outcomes requires acknowledging their potential benefits in supporting the immune system and reducing symptom severity, while also recognizing overdose risks and limitations in current research methodologies.

Most of our information on COVID-19 pathophysiological development has been located thru a laboratory lens, inferring ability causative mechanisms from located biomarker traits throughout sufferers. Based at the contemporary evidence, it's miles clean that, even though direct SARS-CoV-2 contamination of more than 1 organ in addition to hypoxia and stress-associated damage may also make a contribution to COVID-19 pathophysiological development, systemic infection and aberrant cytokine law is an indicator of sickness severity. Considering this, it’s miles nonetheless uncertain what elements impact the transition from regular physiological to pathogenic hyperinflammatory reaction. The nuances of age-associated immune reaction seem to play a role, with growing sickness severity located in older populations. Furthermore, restrained to be had information withinside the pediatric populace indicates a awesome and various spectrum of sickness absolutely unique from adults, in addition reinforcing the significance of age-associated immune responses. In addition to age, rising medical and epidemiological information advise sex-particular variations withinside the medical traits and case-to-fatality ratio of COVID-19, with worse diagnosis located in males. This disproportionate medical epidemiology can be defined via way of means of sex-particular law of ACE2, expanded prevalence of preexisting comorbidities in males (i.e., hypertension, diabetes, cardiovascular sickness), in addition to sex-particular variations in viral immune reaction, as defined elsewhere. Genetic predispositions have additionally been proposed, along with polymorphisms in ACE2 and genetic variability in histocompatibility complex (MHC) magnificence I genes. Finally, numerous comorbidities had been related to bad outcomes, in all likelihood because of the reality that organ and immune characteristic may also already be compromised and in a kingdom of subclinical infection. Notably, in a case take a look at collection of 5, 7 hundred sufferers from New York City, the maximum typically located comorbidities had been hypertension, obesity, and diabetes. These elements want to be located greater very well to finish our medical know-how of COVID-19. In addition to know-how applicable danger elements, there may be growing suspicion of behind schedule however extreme COVID-19 presentation, specially in children, even after viral clearance. This now no longer best indicates the significance of defining the timing of antibody reaction thru serological trying out in more than 1 age businesses however additionally factors towards the growing complexity of COVID-19.

Acknowledgments

Thanks to guidance and advice from Young Researchers and Elite Club, Gachsaran Branch, Islamic Azad University, Gachsaran, Iran.

Declaration of Generative AI in Scientific Writing

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

CRediT Author Statement

We know of no conflict of interest associated with this publication, and there has been no financial support for this work that could have influenced its outcome as corresponding author, I confirm that the manuscript has been read and approved for submission by all the named authors.

References

[1] J Ma. China’ s first confirmed Covid-19 case traced back to November 17, Available at: https://www.scmp.com/news/china/society/article/3074991/coronavirus-chinas-first-confirmed-covid-19-case-traced-back, accessed November 2019.

[2] S Zhao, J Ran, SS Musa, G Yang, Y Lou, D Gao, L Yang, D He and MH Wang. Preliminary estimation of the basic reproduction number of novel coronavirus (2019-nCoV) in China, from 2019 to 2020: A data-driven analysis in the early

phase of the outbreak. *International Journal of Infectious Diseases* 2020; **92**, 214-217.

[3] World Health Organization. *Laboratory testing for 2019 novel coronavirus (2019-nCoV) in suspected human cases: Interim guidance*. World Health Organization, Geneva, Switzerland, 2020.

[4] A Łoczechin, K Séron, A Barras, E Giovanelli, S Belouzard, YT Chen, N Metzler-Nolte, R Boukherroub, J Dubuisson and S Szunerits. Functional carbon quantum dots as medical countermeasures to human coronavirus. *ACS Applied Materials & Interfaces* 2019; **11(46)**, 42964-42974.

[5] YWang, H Kang, X Liu and Z Tong. Combination of RT-qPCR testing and clinical features for diagnosis of COVID-19 facilitates management of SARS-CoV-2 outbreak. *Journal of Medical Virology* 2020; **92(6)**, 538-539.

[6] A Tavakoli and MS Hashemzadeh. Inhibition of herpes simplex virus type 1 by copper oxide nanoparticles. *Journal of Virological Methods* 2020; **275**, 113688.

[7] A Mackie, S Gourcy, N Rigby, J Moffat, I Caprone and B Bajka. The fate of cellulose nanocrystal stabilised emulsions after simulated gastrointestinal digestion and exposure to intestinal mucosa. *Nanoscale* 2019; **11(6)**, 2991-2998.

[8] V Kumari, S Vishwas, R Kumar, V Kakoty, R Khursheed, MR Babu, V Harish, N Mittal, PK Singh, NS Alharthi, MA Hakami, FFA Alkhayl, G Gupta, GD Rubis, KR Paudel, M Singh, M Zandi, BG Oliver, K Dua and SK Singh. An overview of biomedical applications for gold nanoparticles against lung cancer. *Journal of Drug Delivery Science and Technology* 2023; **86**, 104729.

[9] J Liu, J Liu, S Attarilar, C Wang, M Tamaddon, C Yang, K Xie, J Yao, L Wang, C Liu and Y Tang. Nano-modified titanium implant materials: A way toward improved antibacterial properties. *Frontiers in Bioengineering and Biotechnology* 2020; **8**, 576969.

[10] JM Rajwade, RG Chikte and KM Paknikar. Nanomaterials: New weapons in a crusade against phytopathogens. *Applied Microbiology and Biotechnology* 2020; **104(4)**, 1437-1461.

[11] YA Malik. Properties of coronavirus and SARS-CoV-2. *The Malaysian Journal of Pathology* 2020; **42(1)**, 3-11.

[12] A Repici, R Maselli, M Colombo, R Gabbiadini, M Spadaccini, A Anderloni, S Carrara, A Fugazza, MD Leo, PA Galtieri, G Pellegatta, EC Ferrara, E Azzolini and M Lagioia. Coronavirus (COVID-19) outbreak: What the department of endoscopy should know. *Gastrointestinal Endoscopy* 2020; **92(1)**, 192-197.

[13] MA Shereen, S Khan, A Kazmi, N Bashir and R Siddique. COVID-19 infection: Emergence, transmission, and characteristics of human coronaviruses. *Journal of Advanced Research* 2020; **24**, 91-98.

[14] World Health Organization. *Middle East respiratory syndrome coronavirus (MERS-CoV)*. World Health Organization, Geneva, Switzerland, 2025.

[15] JFW Chan, KH Kok, Z Zhu, H Chu, KKW To, S Yuan and KY Yuen. Genomic characterization of the 2019 novel human-pathogenic coronavirus isolated from a patient with atypical pneumonia after visiting Wuhan. *Emerging Microbes & Infections* 2020; **9(1)**, 221-236.

[16] C Huang, Y Wang, X Li, L Ren, J Zhao, Y Hu, L Zhang, G Fan, J Xu, X Gu, Z Cheng, T Yu, J Xia, Y Wei, W Wu, X Xie, W Yin, H Li, M Liu, Y Xiao, …, B Cao. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet* 2020; **395(10223)**, 497-506.

[17] R Lu, X Zhao, J Li, P Niu, B Yang, H Wu, W Wang, H Song, B Huang, N Zhu, Y Bi, X Ma, F Zhan, L Wang, T Hu, H Zhou, Z Hu, W Zhou, L Zhao, J Chen, ..., W Shi. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *The Lancet* 2020; **395(10224)**, 565-574.

[18] R Wang, X Zhang, DM Irwin and Y Shen. Emergence of SARS-like coronavirus poses new challenge in China. *Journal of Infection* 2020; **80(3)**, 350-371.

[19] D Paraskevis, EG Kostaki, G Magiorkinis, G Panayiotakopoulos, G Sourvinos and S Tsiodras. Full-genome evolutionary analysis of the novel corona virus (2019-nCoV) rejects the hypothesis of emergence as a result of a recent recombination

event. *Infection, Genetics and Evolution* 2020; **79**, 104212.

[20] Y Zhao, Z Zhao, Y Wang, Y Zhou, Y Ma and W Zuo. Single-cell RNA expression profiling of ACE2, the putative receptor of Wuhan 2019-nCov. *bioRxiv* 2020. https://doi.org/10.1101/2020.01.26.919985

[21] P Zhou, XL Yang, XG Wang, B Hu, L Zhang, W Zhang, HR Si, Y Zhu, B Li, CL Huang, HD Chen, J Chen, Y Luo, H Guo, RD Jiang, MQ Liu, Y Chen, XR Shen, X Wang, XS Zheng, …, ZL Shi. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature* 2020; **579(7798)**, 270-273.

[22] Q Li, X Guan, P Wu, X Wang, L Zhou, Y Tong, R Ren, KSM Leung, EHY Lau, JY Wong, X Xing, N Xiang, Y Wu, C Li, Q Chen, D Li, T Liu, J Zhao, M Liu, W Tu, …, Z Feng. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *New England Journal of Medicine* 2020; **382(13)**, 1199-1207.

[23] P Zhou, XL Yang, XG Wang, B Hu, L Zhang, W Zhang, HR Si, Y Zhu, B Li, CL Huang, H Chen, J Chen, Y Luo, H Guo, RD Jiang, MQ Liu, Y Chen, XR Shen, X Wang, XS Zheng, …, ZL Shi. Discovery of a novel coronavirus associated with the recent pneumonia outbreak in humans and its potential bat origin. *bioRxiv* 2020. https://doi.org/10.1101/2020.01.22.914952

[24] H Xu, L Zhong, J Deng, J Peng, H Dan, X Zeng, T Li and Q Chen. High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. *International Journal of Oral Science* 2020; **12(1)**, 8.

[25] H Zhang, JM Penninger, Y Li, N Zhong and AS Slutsky. Angiotensin-converting enzyme 2 (ACE2) as a SARS-CoV-2 receptor: Molecular mechanisms and potential therapeutic target. *Intensive Care Medicine* 2020; **46(4)**, 586-590.

[26] RL Soiza, AIC Donaldson and PK Myint. The role of nanotechnology in the treatment of viral infections Lavanya. *Advances in Vaccines* 2018; **9(6)**, 259-261.

[27] P Prabakaran, X Xiao and DS Dimitrov. A model of the ACE2 structure and function as a SARS-CoV receptor. *Biochemical and Biophysical Research Communications* 2004; **314(1)**, 235-241.

[28] IM Mackay and KE Arden. An opportunistic pathogen afforded ample opportunities: Middle east respiratory syndrome coronavirus. *Viruses* 2017; **9(12)**, 369.

[29] CM Coleman, YV Liu, H Mu, JK Taylor, M Massare, DC Flyer, GM Glenn, GE Smith and MB Frieman. Purified coronavirus spike protein nanoparticles induce coronavirus neutralizing antibodies in mice. *Vaccine* 2014; **32(26)**, 3169-3174.

[30] G Bashiri, MS Padilla, KL Swingle, SJ Shepherd, MJ Mitchell and K Wang. Nanoparticle protein corona: From structure and function to therapeutic targeting. *Lab on a Chip* 2023; **23**, 1432-1466.

[31] G Smith, Y Liu and M Massare. *Immunogenic middle east respiratory syndrome coronaviruses (Mers-Cov) compositions and methods*. World Intellectual Property Organization, Geneva, Switzerland, 2015.

[32] CM Coleman, T Venkataraman, YV Liu, GM Glenn, GE Smith, DC Flyer and MB Frieman. MERS-CoV spike nanoparticles protect mice from MERS-CoV infection. *Vaccine* 2017; **35(12)**, 1586-1589.

[33] YS Kim, A Son, J Kim, SB Kwon, MH Kim, P Kim, J Kim, YH Byun, J Sung, J Lee, JE Yu, C Park, YS Kim, NH Cho, J Chang and BL Seong. Chaperna-mediated assembly of ferritin-based Middle East respiratory syndrome-coronavirus nanoparticles. *Frontiers in Immunology* 2018; **9**, 1093.

[34] LCW Lin, CY Huang, BY Yao, JC Lin, A Agrawal, A Algaissi, BH Peng, YH Liu, PH Huang, RH Juang, YC Chang, CT Tseng, HW Chen and CMJ Hu. Viromimetic STING agonist-loaded hollow polymeric nanoparticles for safe and effective vaccination against Middle East respiratory syndrome coronavirus. *Advanced Functional Materials* 2019; **29(28)**, 1807616.

[35] SY Jung, KW Kang, EY Lee, DW Seo, HL Kim, H Kim, TW Kwon, HL Park, H Kim, SM Lee and JH Nam. Heterologous prime-boost vaccination with adenoviral vector and protein nanoparticles induces both Th1 and Th2 responses against Middle East respiratory syndrome coronavirus. *Vaccine* 2018; **36(24)**, 3468-3476.

[36] PY Lu, V Simonenko, Y CAI, J Xu and D Evans. *Sirna/nanoparticle formulations for treatment of middle-east respiratory syndrome coronaviral infection.* The Patent Cooperation Treaty, Washington DC, 2017.

[37] T Kato, Y Takami, VK Deo and EY Park. Preparation of virus-like particle mimetic nanovesicles displaying the S protein of Middle East respiratory syndrome coronavirus using insect cells. *Journal of Biotechnology* 2019; **306**, 177-184.

[38] X Huang, M Li, Y Xu, J Zhang, X Meng, X An, L Sun, L Guo, X Shan, J Ge, J Chen, Y Luo, H Wu, Y Zhang, Q Jiang and X Ning. Novel gold nanorod-based HR1 peptide inhibitor for Middle East respiratory syndrome coronavirus. *ACS Applied Materials & Interfaces* 2019; **11(22)**, 19799-19807.

[39] BS Shim, SM Park, JS Quan, D Jere, H Chu, MK Song, DW Kim, YS Jang, MS Yang, SH Han, YH Park, CS Cho and CH Yun. Intranasal immunization with plasmid DNA encoding spike protein of SARS-coronavirus/polyethylenimine nanoparticles elicits antigen-specific humoral and cellular immune responses. *BMC Immunology* 2010; **11(1)**, 65.

[40] H Sekimukai, N Iwata-Yoshikawa, S Fukushi, H Tani, M Kataoka, T Suzuki, H Hasegawa, K Niikura, K Arai and N Nagata. Gold nanoparticle-adjuvanted S protein induces a strong antigen-specific IgG response against severe acute respiratory syndrome-related coronavirus infection, but fails to induce protective antibodies and limit eosinophilic infiltration in lungs. *Microbiology and Immunology* 2020; **64(1)**, 33-51.

[41] MF Alif, R Zainul, A Mulyani, S Syakirah, A Zikri, A Iqbal, M Abdullah and AA Adeyi. Comprehensive review of functionalized multi-walled carbon nanotubes: Emerging trends and applications in simultaneous detection of uric acid, dopamine and ascorbic acid. *Advanced Journal of Chemistry-Section A* 2024; **7(3)**, 319-337.

[42] FH Saboor and A Ataei. Decoration of metal nanoparticles and metal oxide nanoparticles on carbon nanotubes. *Advanced Journal of Chemistry, Section A* 2024; **7(2)**, 122-145.

[43] Z Soltani, M Hoseinzadeh and FH Saboor. Biomass gasification process enhancing using metal-organic frameworks. *Advanced Journal of Chemistry, Section A* 2024; **7(1)**, 89-109.

[44] EI Aduloju, N Yahaya, NM Zain, MA Kamaruddin and MAA Hamid. Green, sustainable, and unified approaches towards organic and inorganic analytes extraction from complex environmental matrices. *Advanced Journal of Chemistry, Section A* 2023; **6(3)**, 198-224.

[45] N Musheer, M Yusuf, A Choudhary and M Shahid. Recent advances in heavy metal remediation using biomass-derived carbon materials. *Advanced Journal of Chemistry, Section B: Natural Products and Medical Chemistry* 2024; **6(3)**, 284-345.

[46] M Molaeian, A Davood and M Mirzaei. Non-covalent interactions of N-(4-carboxyphenyl) phthalimide with CNTs. *Advanced Journal of Chemistry Section B* 2020; **2(1)**, 39-45.

[47] T Hadadi, M Shahraki and P Karimi. Methane, chlorofluorocmethane and chlorodifluoromethane adsorption onto graphene and functionalized graphene sheets: Computational methods. *Asian Journal of Green Chemistry* 2024; **8(6)**, 652-671.

[48] AA Omran, HFA Saedi, OH Salah, AH Kareem, MN Hawas and ZH Alzahraa. Boosted removal of sulfadiazine drug using multiwall carbon nanotubes and comparative with other adsorbents. *Asian Journal of Green Chemistry* 2024; **8(2)**, 150-160.

[49] S Ghasemi, F Badri and HR Kafshboran. Pd catalyst supported thermo-responsive modified poly (N-isopropylacrylamide) grafted Fe_3O_4@ CQD@ Si in heck coupling reaction. *Asian Journal of Green Chemistry* 2024; **8(1)**, 39-56.

[50] F Ali, S Zahid, S Khan, SU Rehman and F Ahmad. A comprehensive review on adsorption of dyes from aqueous solution by mxenes. *Asian Journal of Green Chemistry* 2024; **8(1)**, 81-107.

[51] F Banifatemeh. Polymerization of graphite and carbon compounds by aldol condensation as anti-corrosion coating. *Asian Journal of Green Chemistry* 2023; **7(1)**, 25-38.

[52] S Farajzadeh, PN Moghadam and J Khalafy. Removal of colored pollutants from aqueous solutions with a poly Schiff–base based on

melamine-modified MWCNT. *Asian Journal of Green Chemistry* 2020; **4(4)**, 397-415.

[53] RM Mhaibes, Z Arzehgar, MM Heydari and L Fatolahi. ZnO nanoparticles: A highly efficient and recyclable catalyst for tandem Knoevenagel-Michael-cyclocondensation reaction. *Asian Journal of Green Chemistry* 2023; **7(1)**, 1-8.

[54] M Nazifi, H Saeidian and S Taheri. Efficient synthesis of 3,4-dihydropyrimidin-2(1H)-ones catalyzed by a Cd-based covalent organic framework under solvent-free conditions. *Chemical Methodologies* 2024; **8(7)**, 504-520.

[55] Z Dourandish, FG Nejad, R Zaimbashi, S Tajik, MB Askari, P Salarizadeh, SZ Mohammadi, H Oloumi, F Mousazadeh, M Baghayeri and H Beitollai. Recent advances in electrochemical sensing of anticancer drug doxorubicin: A mini-review. *Chemical Methodologies* 2024; **8(4)**, 293-315.

[56] A Bahmani, A Taghvaei, F Firozian and G Chehardoli. Folic acid as an exploiter of natural endocytosis pathways in drug delivery. *Chemical Methodologies* 2024; **8(2)**, 96-122.

[57] ND Resen, EA Gomaa, SE Salem, AM El-Defrawy and MNA El-Hady. Cyclic voltammetry for interaction between mercuric chloride and diamond fuchsin (Rosaniline) in 0.05 M $NaClO_4$ aqueous solutions at 303 K. *Chemical Methodologies* 2023; **7(10)**, 736-747.

[58] ND Rasen, EA Gomaa, SE Salem, MN Abd El-Hady and AM El-Defrawy. Voltammetric analysis of lead nitrate with various ligands in aqueous solutions at 302.15 K. *Chemical Methodologies* 2023; **7(10)**, 761-775.

[59] LJ Juturi, R Palavalasa, SH Dhoria, S Jampani and V Miditana. Efficient removal of fluoride using sol-gel processed nano magnesium oxide. *Chemical Methodologies* 2023; **7(7)**, 569-580.

[60] MA Al-Azzawi and WR Saleh. Fabrication of environmental monitoring amperometric biosensor based on alkaloids compound derived from catharanthus roseus extract nanoparticles for detection of cadmium pollution of water. *Chemical Methodologies* 2023; **7(5)**, 358-371.

[61] F Hosseini, JF Kakhki, Z Salari and M Ebrahimi. Determination of tramadol in aqueous samples using solid phase microextraction fiber based on sol-gel coating reinforced with multiwall carbon nanotube followed by gas chromatography. *Chemical Methodologies* 2023; **7(5)**, 383-391.

[62] S Javame and M Ghods. Analysis of K-Banhatti Polynomials and calculation of some degree based indices using (a, b)-Nirmala index in molecular graph and line graph of TUC_4C_8 (S) nanotube. *Chemical Methodologies* 2023; **7(3)**, 237-247.

[63] S Sajjadifar, F Abakhsh and Z Arzehgar. Design and characterization of Fe_3O_4@ n-pr-NH_2@ Zn_3 (BTC) $_2$ magnetic MOF: A Catalyst for Dihydropyrimidine and 2-Amino-4H-Chromene synthesis. *Chemical Methodologies* 2024; **8(8)**, 550-568.

[64] ES Osipova and EA Gladkov. *Heracleum Sosnowskyi Manden*. as a source of valuable chemicals (elimination with utility). *Chemical Methodologies* 2024; **8(12)**, 944-956.

[65] T Hadadi, M Shahraki and P Karimi. Adsorption of some nitrophenols onto graphene and functionalized graphene sheets: Quantum mechanics calculations, monte carlo, and molecular dynamics simulations. *Chemical Methodologies* 2024; **8(10)**, 753-775.

[66] N Fatima, H Waheed, A Raza, A Mukhtar and F Ahmad. A critical review on membrane technology and its application in CO_2 capturing. *Chemical Methodologies* 2024; **8(9)**, 662-698.

[67] HM Hassan. Prevention of corrosion in the stainless steel metallic using the extract of some aquatic plants. *Chemical Methodologies* 2024; **8(6)**, 462-477.

[68] S Tajik, FG Nejad, R Zaimbashi and H Beitollai. Voltammetric sensor for acyclovir determination based on MoSe2/rGO nanocomposite modified electrode. *Chemical Methodologies* 2024; **8(5)**, 316-328.

[69] AM Abassa and FM Abdoonb. Synthesis, characterization, and applications of metal oxides of ZnO, CuO, and CeO_2 nanoparticles: A review. *Journal of Applied Organometallic Chemistry* 2024; **4(4)**, 349-366.

[70] MB Swami, GR Nagargoje, SR Mathapati, AS Bondge, AH Jadhav, SP Panchgalle and V More. A magnetically recoverable and highly effectual Fe_3O_4 encapsulated MWCNTs nano-composite for synthesis of 1,8-dioxo-octahydroxanthene

derivatives. *Journal of Applied Organometallic Chemistry* 2023; **3(3)**, 184-198.

[71] R Eftekhari, M Hojjati, S Khandan and SKH Sfandani. Green synthesis and cytotoxic activity evaluation of novel pyrimidoazepines. *Journal of Applied Organometallic Chemistry* 2025; **5(1)**, 28-52.

[72] M Khan, S Khan, M Omar, M Sohail and I Ullah. Nickel and cobalt magnetic nanoparticles (MNPs): Synthesis, characterization, and applications. *Journal of Chemical Reviews* 2024; **6(1)**, 94-114.

[73] MNS Awan, H Razzaq, OUR Abid and S Qaisar. Recent advances in electroanalysis of hydrazine by conducting polymers nanocomposites: A review. *Journal of Chemical Reviews* 2023; **5(3)**, 311-340.

[74] A Johnson. Investigating the effects of environmental applications on decomposition of zein nanoparticles in adsorbents in industry. *Journal of Engineering in Industrial Research* 2023; **4(2)**, 92-108.

[75] N Javadi and H Fakhraian. Investigation of enantiomeric separation of tiletamine drug using computational chemistry methods. *Journal of Medicinal and Pharmaceutical Chemistry Research* 2023; **5(7)**, 661-674.

[76] E Mahal and S Al-Mutlaq. Bio-based carbon nanomaterials synthesis from waste tea. *Journal of Medicinal and Pharmaceutical Chemistry Research* 2023; **5(3)**, 264-270.

[77] F Ali, S Fazal, N Iqbal, A Zia and F Ahmad. PANI-based Nanocomposites for the removal of dye from Wastewater. *Journal of Medicinal and Nanomaterials Chemistry* 2023; **5(2)**, 106-124.

[78] O Gideon, HS Samuel, EO Bulus, M Fatima, MI Matilda and UD Akpanke. Recent advances in biocompatible and biodegradable graphene materials for cutting-edge medical applications. *Journal of Medicinal and Nanomaterials Chemistry* 2024; **6**, 174-195.

[79] B Einollahi, M Javanbakht, M Ebrahimi, M Ahmadi, M Izadi, S Ghasemi, Z Einollahi, B Beyram, A Mirani and E Kianfar. Surveying haemoperfusion impact on COVID-19 from machine learning using Shapley values. *Inflammopharmacology* 2024; **32(4)**, 2285-2294.

[80] E Kianfar. Magnetic nanoparticles in targeted drug delivery: A review. *Journal of Superconductivity and Novel Magnetism* 2021; **34(7)**, 1709-1735.

[81] S Chupradit, M Kavitha, W Suksatan, MJ Ansari, ZIA Mashhadani, MM Kadhim, YF Mustafa, SS Shafik and E Kianfar. Morphological control: Properties and applications of metal nanostructures. *Advances in Materials Science and Engineering* 2022; **2022(1)**, 1971891.

[82] K Hachem, MJ Ansari, RO Saleh, HH Kzar, ME Al-Gazally, US Altimari, SA Hussein, HT Mohammed, AT Hammid and E Kianfar. Methods of chemical synthesis in the synthesis of nanomaterial and nanoparticles by the chemical deposition method: A review. *BioNanoScience* 2022; **12(3)**, 1032-1057.

[83] E Kianfar. Protein nanoparticles in drug delivery: Animal protein, plant proteins and protein cages, albumin nanoparticles. *Journal of Nanobiotechnology* 2021; **19(1)**, 159.

[84] AK Alkhawaldeh, AM Rheima, MM Kadhim, ZS Abbas, ADJ Al-bayati, ZT Abed, FMD Al-Jaafari, AS Jaber, SK Hachim, FK Ali, ZH Mahmoud, GB Pour and E Kianfar. Nanomaterials as transmitters of non-viral gene vectors: A review. *Case Studies in Chemical and Environmental Engineering* 2023; **8**, 100372.

[85] TM Joseph, S Azat, E Kianfar, KS Joshy, OM Jazani, A Esmaeili, Z Ahmadi, J Haponiuk and S Thomas. Identifying gaps in practical use of epoxy foam/aerogels: Review-solutions and prospects. *Reviews in Chemical Engineering* 2025; **41(3)**, 269-308.

[86] ZH Mahmoud, UAR Hussein, N Aljbory, MJ Alnajar, L Maleknia, A Mirani and E kianfar. Development of Vitex-derived polymer nanofibers using electrochemical sensors for the treatment of polycystic ovarian syndrome in rats as an animal model. *Biosensors and Bioelectronics: X* 2025; **22**, 100570.

[87] TM Joseph, MG Thomas, DK Mahapatra, AB Unni, E Kianfar, JT Haponiuk and S Thomas. Adaptive and intelligent polyurethane shape-memory polymers enabling next-generation biomedical platforms. *Case Studies in Chemical and Environmental Engineering* 2025; **11**, 101165.

[88] ZH Mahmoud, HNK AL-Salman, UAR Hussein, SM Hameed, AA Hussein, JM Abbas, SK Thajeel, WDKA Ghezy, and E Kianfar. Recent advances in the applications of smart nanomaterials in Biomedicine: A review. *World* 2025; **16(3)**, 2530005.

[89] AN Al-Jamal, AF Al-Hussainy, BA Mohammed, HH Abbas, IM Kadhim, ZH Ward, DK Mahapatra, TM Joseph, E Kianfar and S Thomas. Photodynamic therapy (PDT) in drug delivery: Nano-innovations enhancing treatment outcomes. *Health Sciences Review* 2025: **14**, 100218.

[90] AN Al-Jamal, UAR Hussein, N Aljbory, ZH Mahmoud, A Mirani, E Kianfar and L Maleknia. Electrospun ZnO and GSH co-loaded PU/CS nanofibrous films as potential antibacterial wound dressings. *Nano LIFE* 2024; **16(1)**, 2450028.

[91] ZH Mahmoud, UA Hussein, AM Dhiaa, AF Al-Hussainy, N Aljbory, MH Shuhata, MJ Alnajar, AS Aljaberi, DK Mahapatra, E Kianfar and TM Joseph. Nano-based drug delivery in cancer: Tumor tissue characteristics and targeting. *Trends in Sciences* 2025; **22(2)**, 9078.

[92] AA Adul-Rasool, DM Athair, HK Zaidan, AM Rheima, ZT Al-Sharify, SH Mohammed and E Kianfar. 0, 1, 2, 3D nanostructures, types of bulk nanostructured materials, and drug nanocrystals: An overview. *Cancer Treatment and Research Communications* 2024; **40**, 100834.

[93] AM Rheima, AA Abdul-Rasool, ZT Al-Sharify, HK Zaidan, DM Athair, SH Mohammed and E kianfar. Nano bioceramics: Properties, applications, hydroxyapatite, nanohydroxyapatite and drug delivery. *Case Studies in Chemical and Environmental Engineering* 2024; **10**, 100869.

[94] C Zeng, X Hou, M Bohmer and Y Dong. Advances of nanomaterials-based strategies for fighting against COVID-19. *View* 2021; **2(4)**, 20200180.

[95] B Udugama, P Kadhiresan, HN Kozlowski, A Malekjahani, M Osborne, VYC Li, H Chen, S Mubareka, JB Gubbay and WCW Chan. Diagnosing COVID-19: The disease and tools for detection. *ACS Nano* 2020; **14(4)**, 3822-3835.

[96] M Chung, A Bernheim, X Mei, N Zhang, M Huang, X Zeng, J Cui, W Xu, Y Yang, ZA Fayad and A Jacobi. CT imaging features of 2019 novel coronavirus (2019-nCoV). *Radiology* 2020; **295(1)**, 202-207.

[97] LE Lamb, SN Bartolone, E Ward and MB Chancellor. Rapid detection of novel coronavirus/severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by reverse transcription-loop-mediated isothermal amplification. *Plos One.* 2020; **15(6)**, e0234682.

[98] PN Hedde, TJ Abram, A Jain, R Nakajima, RRD Assis, T Pearce, A Jasinskas, MN Toosky, S Khan, PL Felgner and E Gratton. A modular microarray imaging system for highly specific COVID-19 antibody testing. *Lab on a Chip* 2020; **20(18)**, 3302-3309.

[99] HW Jiang, Y Li, HN Zhang, W Wang, X Yang, H Qi, H Li, D Men, J Zhou and SC Tao. SARS-CoV-2 proteome microarray for global profiling of COVID-19 specific IgG and IgM responses. *Nature Communications* 2020; **11(1)**, 3581.

[100] R Kumar, S Nagpal, S Kaushik and S Mendiratta. COVID-19 diagnostic approaches: Different roads to the same destination. *Virusdisease* 2020; **3(2)**, 97-105.

[101] N Rabiee, M Bagherzadeh, A Ghasemi, H Zare, S Ahmadi, Y Fatahi, R Dinarvand, M Rabiee, S Ramakrishna, M Shokouhimehr and RS Varma. Point-of-use rapid detection of SARS-CoV-2: Nanotechnology-enabled solutions for the COVID-19 pandemic. *International Journal of Molecular Sciences* 2020; **21(14)**, 5126.

[102] R Rappuoli, CW Mandl, S Black and ED Gregorio. Vaccines for the twenty-first century society. *Nature Reviews Immunology* 2011; **11(12)**, 865-872.

[103] M Jeyanathan, S Afkhami, F Smaill, MS Miller, BD Lichty and Z Xing. Immunological considerations for COVID-19 vaccine strategies. *Nature Reviews Immunology* 2020; **20(10)**, 615-632.

[104] H Wang, Y Zhang, B Huang, W Deng, Y Quan, W Wang, W Xu, Y Zhao, N Li, J Zhang, H Liang, L Bao, Y Xu, L Ding, W Zhou, H Gao, J Liu, P Niu, L Zhao, W Zhen, …, X Yang. Development of an inactivated vaccine candidate, BBIBP-CorV, with potent protection against SARS-CoV-2. *Cell* 2020; **182(3)**, 713-721.

[105] Q Gao, L Bao, H Mao, L Wang, K Xu, M Yang, Y Li, L Zhu, N Wang, Z Lv, H Gao, X Ge, B Kan, Y Hu, J Liu, F Cai, D Jiang, Y Yin, C Qin, J Li, …, Y Zhang. Development of an inactivated vaccine candidate for SARS-CoV-2. *Science* 2020; **369(6499)**, 77-81.

[106] PM Folegatti, KJ Ewer, PK Aley, B Angus, S Becker, S Belij-Rammerstorfer, D Bellamy, S Bibi, M Bittaye, EA Clutterbuck, C Dold, SN Faust, A Finn, AL Flaxman, B Hallis, P Heath, D Jenkin, R Lazarus, R Makinson, AM Minassian, …, AJ Pollard. Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: A preliminary report of a phase 1/2, single-blind, randomised controlled trial. *The Lancet* 2020; **396(10249)**, 467-478.

[107] B Sun and T Xia. Nanomaterial-based vaccine adjuvants. *Journal of Materials Chemistry B* 2016; **4(33)**, 5496-509.

[108] OS Fenton, KN Olafson, PS Pillai, MJ Mitchell and R Langer. Advances in biomaterials for drug delivery. *Advanced Materials* 2018; **30(29)**, 1705328.

[109] C Zeng, C Zhang, PG Walker and Y Dong. Formulation and delivery technologies for mRNA vaccines. C*urrent Topics in Microbiology and Immunology* 2022; **440**, 71-110.

[110] MD Shin, S Shukla, YH Chung, V Beiss, SK Chan, OA Ortega-Rivera, DM Wirth, A Chen, M Sack, JK Pokorski and NF Steinmetz. COVID-19 vaccine development and a potential nanomaterial path forward. *Nature Nanotechnology* 2020; **15(8)**, 646-655.

[111] J Kim, Y Eygeris, M Gupta and G Sahay. Self-assembled mRNA vaccines. *Advanced Drug Delivery Reviews* 2021; **170**, 83-112.

[112] L Quan, Y Zhang, BJ Crielaard, A Dusad, SM Lele, CJ Rijcken, JM Metselaar, H Kostková, T Etrych, K Ulbrich and F Kiessling. Nanomedicines for inflammatory arthritis: Head-to-head comparison of glucocorticoid-containing polymers, micelles, and liposomes. *ACS Nano* 2014; **8(1)**, 458-466.

[113] A Gauthier, A Fisch, K Seuwen, B Baumgarten, H Ruffner, A Aebi, M Rausch, F Kiessling, M Bartneck, R Weiskirchen, F Tacke, G Storm, T Lammers and MG Ludwig. Glucocorticoid-loaded liposomes induce a pro-resolution phenotype in human primary macrophages to support chronic wound healing. *Biomaterials* 2018; **178**, 481-495.

[114] M Merad and JC Martin. Pathological inflammation in patients with COVID-19: A key role for monocytes and macrophages. *Nature Reviews Immunology* 2020; **20(6)**, 355-62.

[115] C Wang, J Xie, L Zhao, X Fei, H Zhang, Y Tan, X Nie, L Zhou, Z Liu, Y Ren, L Yuan, Y Zhang, J Zhang, L Liang, X Chen, X Liu, P Wang, X Han, X Weng, Y Chen, …, XW Bian. Alveolar macrophage dysfunction and cytokine storm in the pathogenesis of two severe COVID-19 patients. *EBioMedicine* 2020; **57**, 102833.

[116] N Sohrabi, A Alihosseini, V Pirouzfar and MZ Pedram. Analysis of dynamics targeting CNT-based drug delivery through lung cancer cells: Design, simulation, and computational approach. *Membranes* 2020; **10(10)**, 283.

[117] V Fakhri, CH Su, MT Dare, M Bazmi, A Jafari and V Pirouzfar. Harnessing the power of polyol-based polyesters for biomedical innovations: Synthesis, properties, and biodegradation. *Journal of Materials Chemistry B* 2023; **11(40)**, 9597-9629.

[118] MA Turkia and TA Salman. A review on the synthesis of nanomaterials: Comparing traditional and biological green methods. *Journal of Chemical Reviews* 2024; **6(4)**, 458-481.

[119] PA Kalvanagh and YA Kalvanagh. Investigating the relationship between A/T 251 polymorphism of IL-8 gene and cancer recurrence after lumpectomy. *Eurasian Journal of Science and Technology* 2023; **3(4)**, 172-184.

[120] SE Baakili, A Semlali, KE Mabrouk and M Bricha. Synthesis method effect on acellular bioactivity of bioglasses: Structural analysis and solid-state NMR. *Journal of Applied Organometallic Chemistry* 2023; **3(4)**, 268-283.

[121] M Almajidi, TA Hamza and DY Alhameedi. An overview of the potential of mass spectrometry in the study of peptide drug conjugates. *Chemical Reviews* 2024; **6(4)**, 433-457.

[122] S Kianpour, H Hassani and GR Bardajee. Synthesis of porous polymer with biocompatible sodium alginate and 2-hydroxyethyl methacrylate monomers in high internal emulsion as drug

delivery substrate in releasing of doxorubicin. *Chemical Methodologies* 2024; **8(3)**, 200-216.

[123] Z Guo, H Liu, W Dai and Y Lei. Responsive principles and applications of smart materials in biosensing. *Smart Materials in Medicine* 2020; **1**, 54-65.

[124] Z Zhao, H Cui, W Song, X Ru, W Zhou and X Yu. A simple magnetic nanoparticles-based viral RNA extraction method for efficient detection of SARS-CoV-2. *bioRxiv* 2020. https://doi.org/10.1101/2020.02.22.961268

[125] RA Petros and JM DeSimone. Strategies in the design of nanoparticles for therapeutic applications. *Nature reviews Drug Discovery* 2010; **9(8)**, 615-627.

[126] MF Hossain, S Hasana, AA Mamun, MS Uddin, MII Wahed, S Sarker, T Behl, I Ullah, Y Begum, IJ Bulbul, MS Amran, MH Rahman, MN Bin-Jumah, S Alkahtani, SA Mousa, L Aleya and MM Abdel-Daim. COVID-19 outbreak: Pathogenesis, current therapies, and potentials for future management. *Frontiers in Pharmacology* 2020; **11**, 563478.

[127] ZH Mahmoud, HNK Al-Salman and E Kianfar. Nanoindentation: Introduction and applications of a non-destructive analysis. *Nano TransMed* 2024; **3**, 100057.

[128] MH Shoaib, FR Ahmed, M Sikandar, RI Yousuf and MT Saleem. A journey from SARS-CoV-2 to COVID-19 and beyond: A comprehensive insight of epidemiology, diagnosis, pathogenesis, and overview of the progress into its therapeutic management. *Frontiers in Pharmacology* 2021; **12**, 576448.

[129] AHJ Magham and SMN Baygi. Inclusion complexes of pachypodol with unmodified and modified cyclodextrin nanocarriers: Theoretical studies. *Chemical Methodologies* 2024; **8(8)**, 603-625.

[130] R Amirkhani, A Zarei, M Gholampour, H Tavakoli and A Ramazani. Computational study on inhibitory potential of natural compounds against SARS-CoV-2 main protease. *Chemical Methodologies* 2024; **8(2)**, 85-95.

[131] E Erdag. A molecular docking study: Benzoxazolone derivatives against SARS-CoV-2 omicron subvariant EG. 5.1. 2023; **7(11)**, 825-836.

[132] N Tadayon and A Ramazani. Molecular docking and dynamics analysis of COVID-19 main protease interactions with alkaloids from hyoscyamus niger and datura stramonium. *Chemical Methodologies* 2023; **7(11)**, 883-903.

[133] ZH Mahmoud, SA Hussein, EA Hassan, D Abduvalieva, RM Mhaibes, AAH Kadhum, SJ Nasier, E Kianfar and S Faghih. Characterization and catalytic performance of rGO-enhanced MnFe2O4 nanocomposites in CO oxidation. *Inorganic Chemistry Communications* 2024; 169, 113037.

[134] NA Londhe and K Krishnan. In depth computational screening of novel indane-1, 3-dione derivatives as potential anti-tubercular agents. *Advanced Journal of Chemistry Section A* 2024; **7(5)**, 576-606.

[135] M Vijayarathinam, A Kannan, P Akilan, V Chandrasekaran and T Gunasekaran. A novel approach in the synthesis of Indoloquinoline alkaloid analogues: Spectroscopic and DFT exploration, molecular docking of COVID-19 and ADMET properties. *Advanced Journal of Chemistry, Section A* 2024; **7(4)**, 417-437.

[136] DA Abdulkader, MM Jwaid, YF Muhsin, FW Tarkan, DA Shihab and HA Al-hussaniy. Computational screening of roxithromycin against the SARS-CoV-2 (COVID-19) coronavirus receptors by molecular docking. *Advanced Journal of Chemistry, Section A* 2024; **7(4)**, 477-488.

[137] R Yousefi and S Mokaramiyan. Investigation of Infections, deaths, and vaccination indicators associated with covid-19 in the six world health organization regions. *Eurasian Journal of Science and Technology* 2025; **5(2)**, 131-135.

[138] R Yousefi and S Mokaramian. An overview of the infection, mortality, and vaccination statistics of covid-19 from the beginning until July 19. *Eurasian Journal of Science and Technology* 2024; **4(3)**, 283-287.

[139] R Yousefi. The relationship between the average annual temperature of different countries and the rate of infection and mortality due to covid-19 infection. *Eurasian Journal of Science and Technology* 2024; **4(3)**, 264-270.

[140] G Trovas and S Tournis. Vitamin d and covid-19. *Hormones* 2021; **20(1)**, 207-208.

[141] KS Vimaleswaran, NG Forouhi and K Khunti. Vitamin D and covid-19. *BMJ* 2021; **372**, n544.

[142] M Bae and H Kim. The role of vitamin C, vitamin D, and selenium in immune system against COVID-19. *Molecules* 2020; **25(22)**, 5346.

[143] S Firouzi, N Pahlavani, JG Navashenaq, ZS Clayton, MT Beigmohammadi and M Malekahmadi. The effect of Vitamin C and Zn supplementation on the immune system and clinical outcomes in COVID-19 patients. *Clinical Nutrition Open Science* 2022, **44(4)**, 144-154.

[144] M Cámara, MC Sánchez-Mata, V Fernández-Ruiz, RM Cámara, E Cebadera and L Domínguez. A review of the role of micronutrients and bioactive compounds on immune system supporting to fight against the COVID-19 disease. *Foods* 2021, **10(5)**, 1088.

[145] PM Coates, JM Betz, MR Blackman, GM Cragg, M Levine, J Moss and JD White. *Encyclopedia of dietary supplements*. CRC Press, Florida, 2004.

[146] NR Hudson. *Present Knowledge in Nutrition 9th ed, Vol 1 (526 pages) and Vol 2 (967 pages), edited by Barbara A Bowman and Robert M Russell, 2006, hardcover, $110. International Life Sciences Institute, Washington, DC*. The American Journal of Clinical Nutrition, Washington DC, 2007.

[147] World Health Organization. *Global prevalence of vitamin A deficiency in populations at risk 1995-2005: WHO global database on vitamin A deficiency*. World Health Organization, Geneva, Switzerland, 2009.

[148] CB Stephensen and G Lietz. Vitamin A in resistance to and recovery from infection: Relevance to SARS-CoV2. *British Journal of Nutrition* 2021; **126(11)**, 1663-1672.

[149] Q Ye, B Wang and J Mao. The pathogenesis and treatment of the `Cytokine Storm' in COVID-19. *Journal of Infection* 2020; **80**, 607-613.

[150] M Al-Sumiadai, H Ghazzay and W Zabin. Therapeutic effect of vitamin A on severe COVID-19 patients. *Eurasian Journal of Biosciences* 2020; **14**, 7347-7350.

[151] World Health Organization. *IMAI district clinician manual: Hospital care adolescents and adults: Guidelines for the management of illnessess with limited-resources*. World Health Organization, Geneva, Switzerland, 2012.

[152] N Samad, S Dutta, TE Sodunke, A Fairuz, A Sapkota, ZF Miftah, I Jahan, P Sharma, AR Abubakar, AB Rowaiye, AN Oli, J Charan, S Islam and M Haque. Fat-soluble vitamins and the current global pandemic of COVID-19: Evidence-based efficacy from literature review. *Journal of Inflammation Research* 2021; **14**, 2091-2110.

[153] H Hemilä and E Chalker. Vitamin C can shorten the length of stay in the ICU: A meta-analysis. *Nutrients* 2019, **11(4)**, 708.

[154] MD Kornberg, P Bhargava, PM Kim, V Putluri, AM Snowman, N Putluri, PA Calabresi and SH Snyder. Snyder SH: Dimethyl fumarate targets GAPDH and aerobic glycolysis to modulate immunity. *Science* 2018; **360(6387)**, 449-453.

[155] S Thomas, D Patel, B Bittel, K Wolski, Q Wang, A Kumar, ZJ Il'Giovine, R Mehra, C McWilliams, SE Nissen and MY Desai. Effect of high-dose zinc and ascorbic acid supplementation vs usual care on symptom length and reduction among ambulatory patients with SARS-CoV-2 infection: The COVID A to Z randomized clinical trial. *JAMA Network Open* 2021; **4(2)**, e210369.

[156] GP Milani, M Macchi and A Guz-Mark. Vitamin C in the treatment of COVID-19. *Nutrients* 2021; **13(4)**, 1172.

[157] G Cerullo, M Negro, M Parimbelli, M Pecoraro, S Perna, G Liguori, M Rondanelli, H Cena and G D'Antona. The long history of vitamin C: From prevention of the common cold to potential aid in the treatment of COVID-19. *Frontiers in Immunology* 2020; **11**, 574029.

[158] MCM Vissers and RP Wilkie. Ascorbate deficiency results in impaired neutrophil apoptosis and clearance and is associated with up-regulation of hypoxia-inducible factor 1α. *Journal of Leukocyte Biology* 2007; **81(5)**, 1236-1244.

[159] AC Carr and S Maggini. Vitamin C and immune function. *Nutrients* 2017; **9**, 1211.

[160] B Leibovitz and BV Siegel. *Ascorbic acid and the immune response*. *In*: M Phillips and A Baetz (Eds.). Diet and resistance to disease. Springer, New York, 1981.

[161] Z Maghbooli, MA Sahraian, M Ebrahimi, M Pazoki, S Kafan, HM Tabriz, A Hadadi, M Montazeri, M Nasiri, A Shirvani and MF Holick. Vitamin D sufficiency, a serum 25-

hydroxyvitamin D at least 30 ng/mL reduced risk for adverse clinical outcomes in patients with COVID-19 infection. *PloS One* 2020; **15(9)**, e0239799.

[162] A Bassatne, M Basbous, M Chakhtoura, OE Zein, M Rahme and GEH Fuleihan. The link between COVID-19 and VItamin D (VIVID): A systematic review and meta-analysis. *Metabolism* 2021; **119**, 154753.

[163] JP Bilezikian, D Bikle, M Hewison, M Lazaretti-Castro, AM Formenti, A Gupta, MV Madhavan, N Nair, V Babalyan, N Hutchings, N Napoli, D Accili, N Binkley, DW Landry and A Giustina. Mechanisms in endocrinology: Vitamin D and COVID-19. *European Journal of Endocrinology* 2020; **183(5)**, R133-R147.

[164] JM Quesada-Gomez, M Entrenas-Castillo and R Bouillon. Vitamin D receptor stimulation to reduce acute respiratory distress syndrome (ARDS) in patients with coronavirus SARS-CoV-2 infections: Revised Ms SBMB 2020_166. *The Journal of Steroid Biochemistry and Molecular Biology* 2020; **202**, 105719.

[165] J Kaler, A Hussain, D Azim, S Ali and S Nasim. Optimising vitamin D levels in patients with COVID-19. *Journal of the Hong Kong Medical Association* 2021; **27(2)**, 154-156.

[166] J Xu, J Yang, J Chen, Q Luo, Q Zhang and H Zhang. Vitamin D alleviates lipopolysaccharide induced acute lung injury via regulation of the renin angiotensin system. *Molecular Medicine Reports* 2017; **16(5)**, 7432-7438.

[167] K Paria, D Paul, T Chowdhury, S Pyne, R Chakraborty and SM Mandal. Synergy of melanin and vitamin-D may play a fundamental role in preventing SARS-CoV-2 infections and halt COVID-19 by inactivating furin protease. *Translational Medicine Communications* 2020; **5**, 21.

[168] JE Han, JL Jones, V Tangpricha, MA Brown, LAS Brown, L Hao, G Hebbar, MJ Lee, S Liu, TR Ziegler and GS Martin. High dose vitamin D administration in ventilated intensive care unit patients: A pilot double blind randomized controlled trial. *Journal of Clinical & Translational Endocrinology* 2016; **4(C)**, 59-65.

[169] GE Carpagnano, VD Lecce, VN Quaranta, A Zito, E Buonamico, E Capozza, A Palumbo, GD Gioia, VN Valerio and O Resta. Vitamin D deficiency as a predictor of poor prognosis in patients with acute respiratory failure due to COVID-19. *Journal of Endocrinological Investigation* 2021; **44(4)**, 765-771.

[170] A Mendy, S Apewokin, AA Wells and AL Morrow. Factors associated with hospitalization and disease severity in a racially and ethnically diverse population of COVID-19 patients. *medRxiv* 2020. https://doi.org/10.1101/2020.06.25.20137323

[171] MG Traber and J Atkinson. Vitamin E, antioxidant and nothing more. *Free Radical Biology and Medicine* 2007; **43(1)**, 4-15.

[172] E Niki. Evidence for beneficial effects of vitamin E. *The Korean Journal of Internal Medicine* 2015; **30(5)**, 571-579.

[173] R Cecchini and AL Cecchini. SARS-CoV-2 infection pathogenesis is related to oxidative stress as a response to aggression. *Medical Hypotheses* 2020; **143**, 110102.

[174] S Devaraj and I Jialal. α-Tocopherol decreases interleukin-1β release from activated human monocytes by inhibition of 5-lipoxygenase. *Arteriosclerosis, Thrombosis, and Vascular Biology* 1999; **19(4)**, 1125-1133.

[175] GY Lee and SN Han. The role of vitamin E in immunity. *Nutrients* 2018; **10(11)**, 1614.

[176] R Chakraverty, S Davidson, K Peggs, P Stross, C Garrard and TJ Littlewood. The incidence and cause of coagulopathies in an intensive care population. *British Journal of Haematology* 1996; **93(2)**, 460-463.

[177] MA Crowther, E McDonald, M Johnston and D Cook. Vitamin K deficiency and D-dimer levels in the intensive care unit: A prospective cohort study. *Blood Coagulation & Fibrinolysis* 2002; **13(1)**, 49.

[178] FA Klok, MJHA Kruip, NJMVD Meer, MS Arbous, DAMPJ Gommers, KM Kant, FHJ Kaptein, JV Paassen, MAM Stals, MV Huisman and H Endeman. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. *Thrombosis Research* 2020; **191**, 145-147.

[179] F Zhou, T Yu, R Du, G Fan, Y Liu, Z Liu, J Xiang, Y Wang, B Song, X Gu and L Guan. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. *The Lancet* 2020; **395(10229)**, 1054-1062.

[180] CY Hsu, ZH Mahmoud, U Abdul-Reda Hussein, D Abduvalieva, FH Alsultany and E Kianfar. Biosurfactants: Properties, applications and emerging trends. *South African Journal of Chemical Engineering* 2025; **53**, 21-39.

[181] IJ Riphagen, CA Keyzer, NEA Drummen, MHD Borst, JWJ Beulens, RT Gansevoort, JM Geleijnse, FAJ Muskiet, G Navis, ST Visser, C Vermeer, IP Kema and SJL Bakker. Prevalence and effects of functional vitamin K insufficiency: The PREVEND study. *Nutrients* 2017; **9(12)**, 1334.

[182] Y Ajaj, HNK Al-Salman, AM Hussein, MK Jamee, S Abdullaev, AA Omran, MM Karim, AS Abdulwahid and ZH Mahmoud. Effect and investigating of graphene nanoparticles on mechanical, physical properties of polylactic acid polymer. *Case Studies in Chemical and Environmental Engineering* 2024; **9**, 100612.

[183] IEP Kenneth, AV Ifeoma and OP Ngozi. Pervasiveness of human immuno-deficiency virus (HIV), among individuals in Wukari, Taraba State, North-East Nigeria. *International Journal of Advanced Biological and Biomedical Research* 2024; **12(3)**, 237-247.

[184] EF Amin and M Haddadi. SERS technique for detection of COVID-19: A review. *International Journal of Advanced Biological and Biomedical Research* 2024; **12(2)**, 182-191.

[185] N Askari, S Shafieipour, F Noormand, EK Raviz and SK Falahatipour. TNF-alpha 308G/A polymorphism and serum level of TNF-α associated with covid-19 severity. *International Journal of Advanced Biological and Biomedical Research* 2023; **11(4)**, 221-231.

[186] MAH Roni, MG Mortuza, RRK Shaha, S Hoque and A Kumer. Identification of SARS-CoV-2 inhibitors from alkaloids using molecular modeling and *in silico* approaches. *Journal and Medicinals and Nanomaterials Chemistry* 2023; **5(4)**, 252-266.

[187] ElI Edache, A Uzairu, PA Mamza, GA Shallangwa and MT Ibrahim. Computer-aided drug design and molecular dynamic simulations of inhibitors of some autoimmune disorder therapeutic targets. *Progress in Chemical and Biochemical Research* 2024; **7(4)**, 345-377.

[188] MK Bohn, A Hall, L Sepiashvili, B Jung, S Steele and K Adeli. Pathophysiology of COVID-19: Mechanisms underlying disease severity and progression. *Physiology* 2020; **35(5)**, 288-301.

[189] A Pizzorno, B Padey, J Dubois, T Julien, A Traversier, V Dulière, P Brun, B Lina, M Rosa-Calatrava and O Terrier. *In vitro* evaluation of antiviral activity of single and combined repurposable drugs against SARS-CoV-2. *Antiviral Research* 2020; **181**, 104878.

[190] A Simonis, SJ Theobald, G Fätkenheuer, J Rybniker and JJ Malin. A comparative analysis of remdesivir and other repurposed antivirals against SARS-CoV-2. EMBO molecular medicine. *EMBO Molecular Medicine* 2021; **13(1)**, e13105.

[191] R Harne, B Williams, HF Abdelaal, SL Baldwin and RN Coler. SARS-CoV-2 infection and immune responses. *AIMS Microbiology* 2023; **9(2)**, 245.

[192] ML James, AC Ross, A Bulger, JB Philips and N Ambalavanan. Vitamin A and retinoic acid act synergistically to increase lung retinyl esters during normoxia and reduce hyperoxic lung injury in newborn mice. *Pediatric Research* 2010; **67(6)**, 591-597.

[193] RMLC Biancatelli, M Berrill, JD Catravas and PE Marik. Quercetin and Vitamin C: An experimental, synergistic therapy for the prevention and treatment of SARS-CoV-2 related disease (COVID-19). *Frontiers in Immunology* 2020; **11**, 1451.

[194] S Chowdhury, K Kar and R Mazumder. Exploration of different strategies of nanoencapsulation of bioactive compounds and their ensuing approaches. *Future Journal of Pharmaceutical Sciences* 2024; **10(1)**, 72.

[195] PS Mahapatra, S Chatterjee, MK Tiwari, R Ganguly and CM Megaridis. Surface treatments to enhance the functionality of PPEs. *Transactions of the Indian National Academy of Engineering* 2020; **5(2)**, 333-336.

[196] C Shivanika, SD Kumar, V Ragunathan, P Tiwari, A Sumitha and PB Devi. Molecular docking, validation, dynamics simulations, and pharmacokinetic prediction of natural compounds against the SARS-CoV-2 main-protease. *Journal of Biomolecular Structure & Dynamics* 2020; **40(2)**, 585-611.

[197] C Li, Q He, H Qian and J Liu. Overview of the pathogenesis of COVID-19. *Experimental and Therapeutic Medicine* 2021; **22(3)**, 1011.

[198] E Shirbhate, J Pandey, VK Patel, M Kamal, T Jawaid, B Gorain, P Kesharwani and H Rajak. Understanding the role of ACE-2 receptor in pathogenesis of COVID-19 disease: A potential approach for therapeutic intervention. *Pharmacological Reports* 2021; **73(6)**, 1539-1550.

[199] E Kianfar. Biocompatibility study of silica-based magnesium composites: A review. *Trends in Sciences* 2025; **22(9)**, 9868-9868.

[200] E Kianfar. Dendrimers in medicine: Properties, drug encapsulation mechanisms and applications. *Trends in Sciences* 2025; **22(8)**, 10085-10085.

[201] EKianfar. Advances in nanoelectronics: Carbon nanotubes, graphene, and smart polymers: A review. *Trends in Sciences* 2025; **22(7)**, 9843-9843.

[202] EKianfar and TM Joseph. Nanostructures for virus detection and tracking: An overview. *Trends in Sciences* 2025; **22(6)**, 9452-9452.

[203] WR Kadhum, M Budai, L Budai and E Kianfar. Adsorption and release profile analysis of oxytetracycline drug on functionalized graphene oxide nanoparticles. *Results in Materials* 2025; 100711.

[204] E Kianfar. Gold nanoparticles in photothermal cancer therapy: Current trends and outlook. *Trends in Sciences* 2025; **22(5)**, 9433-9433.

[205] CY Hsu, AM Rheima, ZS Abbas, MU Faryad, MM Kadhim, US Altimari, AH Dawood, ADJ Al-bayati, ZT Abed, RS Radhi, AS Jaber, SK Hachim, FK Ali, ZH Mahmoud, GB Pour and E Kianfar. Nanowires properties and applications: A review study. *South African Journal of Chemical Engineering* 2023; **46**, 286-311.

[206] QA Bader, NN Ahmed, AA Mohaimeed, AM Rheima, ZT Al-Sharify, DM Athair and E Kianfar. Recent advances in the applications of continuous and non-continuous nanofibrous yarns in biomedicine. *Fibers and Polymers* 2024; **25(10)**, 3623-3647.

[207] ZH Mahmoud, HNK AL-Salman, UAR Hussein, SM Hameed, AA Hussein, JM Abbas, SK Thajeel, WDKA Ghezy and E Kianfar. Recent advances in the applications of smart nanomaterials in Biomedicine: A review. *Nano LIFE* 2025; **16(3)**, 2530005.

[208] GL Ismaeel, SA Hussein, G Daminova, JMA Sulaiman, MM Hani, EH Kadhum, SA Khuder, SM Hameed, AR Al-Tameemi, ZH Mahmoud and E Kianfar. Fabrication and investigating of a nano-structured electrochemical sensor to measure the amount of atrazine pollution poison in water and wastewater. *Chemical Data Collections* 2024; **51**, 101135.

[209] FA Klok, MJHA Kruip, NJMVD Meer, MS Arbous, D Gommers, KM Kant, FHJ Kaptein, JV Paassen, MAM Stals, MV Huisman and H Endeman. Confirmation of the high cumulative incidence of thrombotic complications in critically ill ICU patients with COVID-19: An updated analysis. *Thrombosis Research* 2020; **191**, 148-150.

[210] HA Waggiallah, MM Eltayeb, AM Hjazi and YM Elmosaad. High expression of angiotensin-converting enzyme 2 receptor (ACE-2), transmembrane protease serine (TMPRSS), and P-selectin in platelets lead to thrombosis formation in COVID-19 patients. *European Review for Medical & Pharmacological Sciences* 2024; **28(5)**, 1847-1856.

[211] M Silingardi, F Zappulo, A Dormi, AM Pizzini, C Donadei, M Cappuccilli, C Fantoni, S Zaccaroni, V Pizzuti, N Cilloni, S Tantillo, A Guidi, R Mancini, GL Manna and G Comai. Is COVID-19 coagulopathy a thrombotic microangiopathy? A prospective, observational study. *International Journal of Molecular Sciences* 2025; **26(11)**, 5395.

[212] RA Campbell, E Boilard and MT Rondina. Is there a role for the ACE2 receptor in SARS-CoV-2 interactions with platelets? *Journal of Thrombosis and Haemostasis* 2021; **19(1)**, 46-50.

[213] S He, M Blombäck and H Wallén. COVID-19: Not a thrombotic disease but a thromboinflammatory

disease. *Upsala Journal of Medical Sciences* 2024; **129**, 10.48101.

[214] X Huang, Y Zhu and E Kianfar. Nano biosensors: Properties, applications and electrochemical techniques. *Journal of Materials Research and Technology* 2021; **12**, 1649-1672.

[215] MJ Ansari, MM Kadhim, BA Hussein, HA Lafta and E Kianfar. Synthesis and stability of magnetic nanoparticles. *BioNanoScience* 2022; **12(2)**, 627-638.

[216] MM Kadhim, AM Rheima, ZS Abbas, HH Jlood, SK Hachim and WR Kadhum. Evaluation of a biosensor-based graphene oxide-DNA nanohybrid for lung cancer. *RSC Advances* 2023; **13(4)**, 2487-2500.

[217] E Kianfar. Recent advances in synthesis, properties, and applications of vanadium oxide nanotube. *Microchemical Journal* 2019; **145**, 966-978.