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REVIEW

Innovative Non-Pharmacological Therapies for SARS-CoV-2 Infections: Advances, Challenges and Future Directions

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The COVID-19 pandemic has necessitated diverse therapeutic approaches, including drug-free therapies to complement pharmaceutical interventions. This review examines the current landscape, challenges and future perspectives of non-drug therapies for COVID-19. Critical approaches include oxygen therapy, mechanical ventilation, prone positioning, physical therapy, nutritional support, psychological support, hydration management and alternative therapies such as acupuncture and phototherapy. Despite their potential, these therapies face significant challenges, including disease variability, resource limitations, patient-specific factors, infection control issues and the need for robust clinical evidence. Future perspectives highlight the technological advancements such as telehealth, wearable devices and artificial intelligence; improved respiratory support systems; integrated multidisciplinary care; extensive public health initiatives; stringent clinical trials; personalized medicine; global health equity; mental health integration; lifestyle modifications and preparedness for future pandemics. Addressing these challenges and leveraging advancements will enhance the effectiveness and accessibility of drug-free therapies, improving patient outcomes and bolstering healthcare resilience against future pandemics.

Keywords: COVID-19, Drug-free remedies, Nutritional support, Clinical trials, Integrated care.

INTRODUCTION

The deadly virus SARS-CoV-2 caused the COVID-19 pandemic, which impacted global health and economic sectors severely. In response to this issues, the pharmaceutical industry is actively engaged in the development of vaccinations and other medicines that can preserve life [1]. The significance of drug-free therapy has garnered considerable attention and such therapies are essential for multiple reasons (Fig. 1).

Non-pharmacological therapy can augment pharmaceutical interventions, improving overall patient outcomes. For instance, the oxygen therapy and mechanical ventilation are essential for managing severe respiratory symptoms, a common and life-threatening fatal sign of coronavirus disease. These interventions help in maintaining an adequate oxygenation and support vital functions while drug treatments work to combat the viral infection and reduce inflammation [2]. Similarly, the medications and other drugs utilized in the emergency situations may induce significant adverse drug responses and problems. Administration of drug-free therapy, barring extremely perilous circumstances, might yield substantial outcomes in reducing adverse actions. For instance, prone positioning improves oxygenation in needy people without drugs [3]. The following section will discuss several factors related to the innovative non-pharmacological therapies for SARS-CoV-2 infections.

Holistic patient care: Different stages of health, such as psychological, physical and social, have been impacted a lot by this pandemic. The histological approach, nutritional improve-

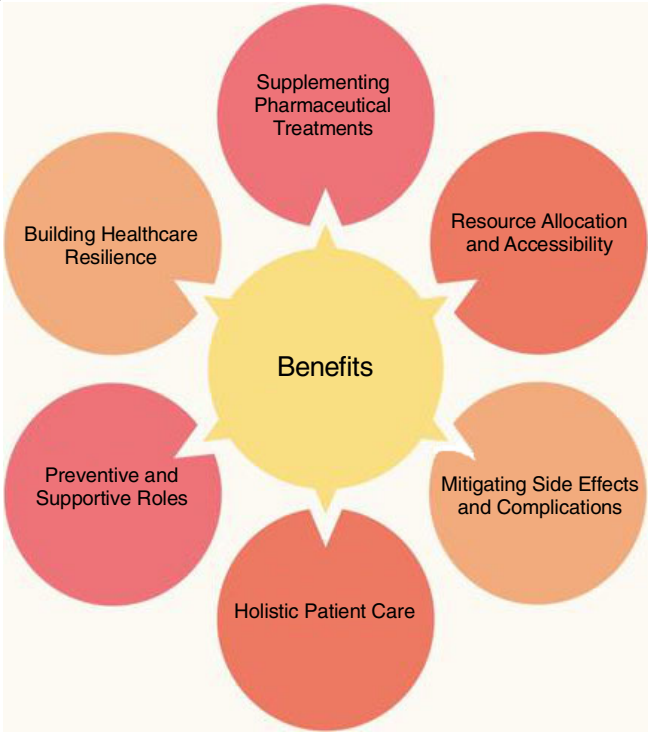

Fig. 1. Benefits of non-pharmaceutical interventions

ments, psychological support and physical therapy are major areas of drug-free therapy. These care models enhance faster recovery and better life quality [4].

Preventive and supportive roles: Non-drug therapy makes a significant contribution to the management of any viral infection, including COVID. Effectively managing mild to moderate symptoms at home, alleviating the psychological burden of the pandemic and reducing the transmission of the virus can be achieved through telehealth consultations, community health education and mental health support. These interventions also promote long-term health by encouraging preventive health practices and lifestyle modifications [5].

Resource allocation and accessibility: The availability of treatments and beds in the healthcare system has been substantially increased during the peak crisis. In response to a significant prevalence of ailments, drug-free therapy emerged, encompassing home care and outpatient facilities. It is crucial for the developing countries with inadequate healthcare facilities to adopt alternatives to enhance their healthcare systems [6].

Building healthcare resilience: Integrating non-pharmaceutical drugs improves the healthcare systems by diversifying treatment alternatives and reducing dependence on pharmaceutical resources, which can be disrupted during global health crises. These therapies enhance resilience by strengthening the capacity to manage future instances of COVID-19 or other infectious diseases using interventions which may be readily modified and expanded [7]. The significance of drug-free therapies in the context of COVID-19 lies in their ability to supplement pharmaceutical treatments, provide easily accessible and complete care, mitigate the adverse effects of medicines and strengthen healthcare systems under pressure. As the epidemic continues, it is crucial to include and refine these non-pharmaceutical methods to improve patient outcomes and bolster healthcare systems worldwide [8].

Current drug-free therapies for COVID-19: Existing non-pharmaceutical treatments for COVID-19 include a range of supportive and complementary methods designed to enhance patient results and general well-being. Essential interventions include administering oxygen therapy and placing the patient in a prone posture. These interventions are vital for effectively controlling respiratory distress and enhancing the body's oxygen level. Telemedicine is essential for delivering healthcare services from a distance and minimizing the spread of viruses. Ensuring adequate nutrition, hydration and electrolyte balance promotes patient well-being and facilitates healing [9].

Physical therapy and rehabilitation also help mitigate the effects of prolonged bed rest and enhance functional recovery, while psychological support addresses the mental health challenges posed by the pandemic. Additionally, acupuncture and herbal medicines are being explored for their potential to alleviate the symptoms and boost immune response, though more rigorous research is needed to validate their efficacy [10]. These drug-free therapies complement conventional medical treatments, emphasizing a holistic approach to patient care during the COVID-19 pandemic (Fig. 2).

Vaccination: Vaccinations are classified into several types, including viral carrier, protein-related vaccinations, live-lessened or inactivated virus vaccines, nucleic acid vaccines such as m-RNA and DNA and VLP vaccines (Table-1). Multiple patents were submitted to develop doses for the prevention of viral infections [11]. The vaccinations are administered to healthy human volunteers to expedite the clinical trial process, bypassing stages II and III. Previously deemed unethical, if executed with meticulous care, precise medical protocols and under medical oversight, it can expedite the availability of emerging vaccines to the general public. Most of the vaccines have a specific preventive efficacy against viruses and demonstrate a minimal infection rate following vaccination. However, the exploration of developing novel vaccines that have a longer duration of prevention against the virus and can reduce the time of clinical phases II and III is still pending. From a mechanical standpoint, the efficacy and safety of vaccinations could be compromized in the event [12].

Virus particles: The virus particle vaccine contains proteins that closely resemble the virus part, but they do not possess any active elements, which helps to reduce its ability to cause infection significantly. The host's immune system recognizes the virus particle just like it would identify a virus, resulting in the induced production of minimizing antibodies. This combination is highly effective in enhancing the body's immune response against the virus, specifically by promoting the production of IgG2b/IgG2a antibodies. The FDA has fast-tracked its approval for the commencement of phase III of a clinical trial. The biotech vaccine combines the receptor binding domain (RBD) of SARS-CoV with the hepatitis B surface antigen (HBsAg). This combination induces immunity to generate antibodies against the RBD. The vaccine utilizes enveloped virus particles that express a modified glycoprotein. The trial is currently in phase one or two and has been identified [13].

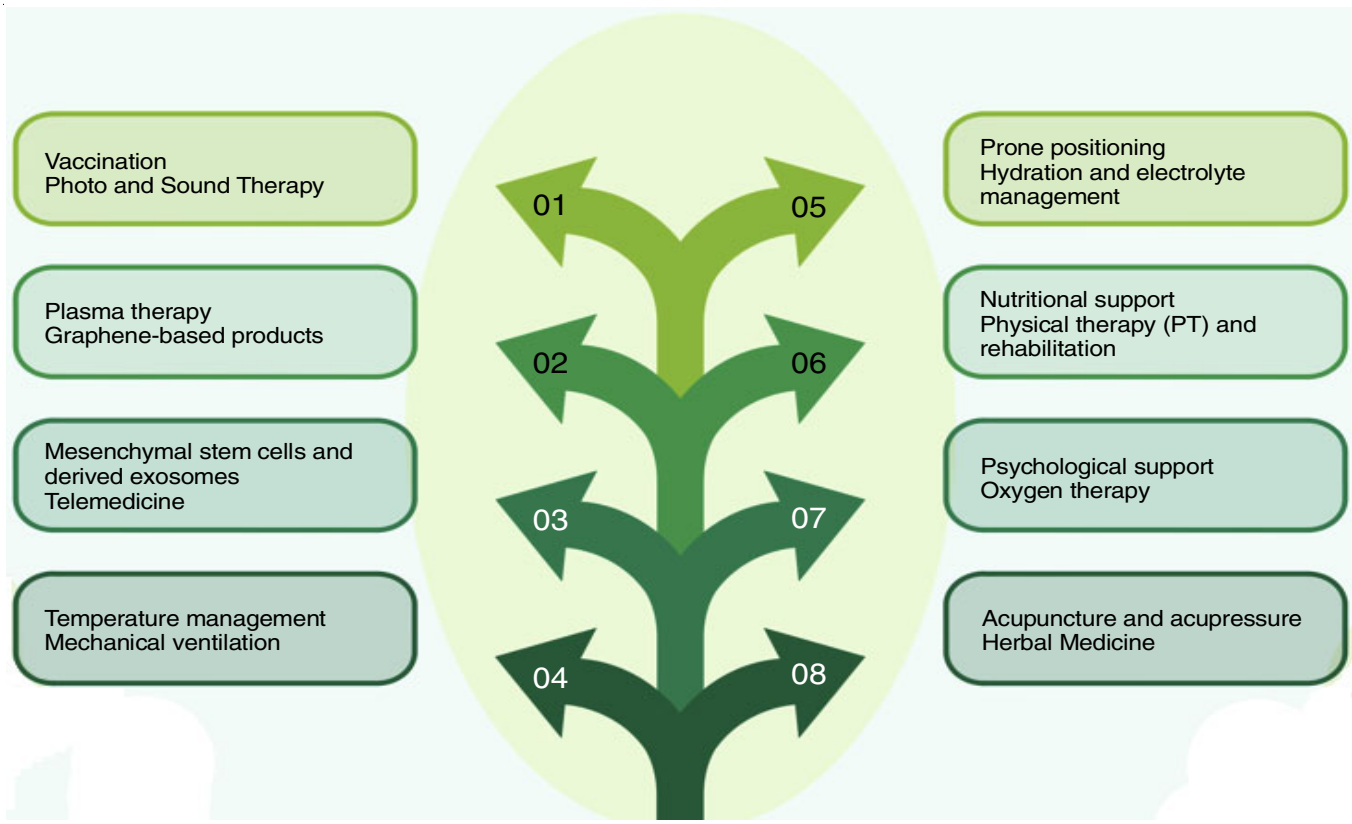

Fig. 2. Current drug-free therapies for COVID-19

TABLE-1
POTENTIAL VACCINES FOR COVID-19

Vaccine	Classification	Function	Clinical trial
CoVLP	VLP	Engineered S-protein adjuvated	Phase III
RBD SARS-CoV-2 HBsAg	VLP	Conjugated with hepatitis B surface antigen	Phase one or two
VBI-2902a	VLP	Expressing modified (S) glycoprotein	Phase one or two
Novavax	Protein vaccine	S-protein purified from Baculovirus	Phase three
INO-4800	DNA vaccine	Plasmid pGX9501 encoding S-protein	Phase two or three
ZyCoV-D	DNA vaccine	Non-integrating plasmid	Phase one or two
Ad26.COV	Adenovirus vector vaccine	Ad26 vector is replication incompetent	Phase three
Ad5-nCoV	Adenovirus vector vaccine	Adenovirus type 5 vector	Phase three
Covishield	Adenovirus vector vaccine	Adenovirus modified to be replication deficient	Phase three
BBIBP-CorV	Inactivated vaccine	β-Propiolactone-mediated inactivation	ChiCTR2000032459
CoronaVac	Inactivated vaccine	β-Propiolactone-activation	Phase three
Covaxin	Inactivated vaccine	Inactivation of β-propiolactone	Phase three
QazCovid-in®	Inactivated vaccine	Inactivated SARS-CoV-2	Phase three
Sputnik V	Inactivated vaccine	Combines two adenoviruses	Phase three
BNT162b2	mRNA vaccine	Lipid nanoparticle-based mRNA vaccine	Phase three

Recombinant protein-based vaccine: These vaccines do not contain any genetic material and come in different forms, such as full-length S protein and multi-epitope. Given that the preliminary content is not replicating, these vaccines are non-infectious and are distinct from the DNA or inactivated vaccines. The vaccine Novavax is developed using advanced technology that involves purifying the S-protein from Sf9 cells through overexpression of Baculovirus. It is combined with a patented adjuvant called Matrix M™, based on saponin. This innovative approach ensures the vaccine's effectiveness [14].

DNA vaccines: DNA vaccines are utilized to boost immunity and are widely regarded as non-toxic due to their neither replicating nor infectious quality. These sets can be single or multiple polypeptides, providing immunity to the host. They can trigger both cell-mediated and humoral immunity, resulting in comprehensive immunity. DNA vaccine (INO-4800), developed by Inovio company, was currently in phase two or three of trials and has shown promising results, with 100% immunogenicity. The plasmid pGX9501 contains the complete sequence of the S protein. ZyCoV-D vaccine was developed by Zydus Cadila, a plasmid that does not integrate with the gene of interest and is in the initial stages of a clinical trial [15].

Adenovirus vector-based vaccine: A modified adenovirus creates a vaccine containing the S protein gene. The virus poss-

esses faulty replication, which makes it well-suited for antigen formation. Janssen has completed phase three clinical trials, demonstrating a 66.3% reduction in symptoms. Another example is Ad5-nCoV, in phase three of a clinical trial. Covidshield vaccine was developed by changing the replication mechanism of deficient chimpanzee adenovirus to produce the S protein. These reports indicate that elevated levels of antiplatelet antibodies may be a contributing factor. Other side effects, although less frequent, include tiredness, headaches, itching at the injection site, swelling, muscle discomfort and fever. All of these vaccines showed no signs of genotoxic efficacy. The Sputnik V vaccine was prepared and utilized to generate a combination of two adenoviruses and S-protein. During the phase III clinical trials (NCT04530396, NCT04564716), it demonstrated an efficacy rate of 91.4% [16].

Inactivated vaccine: Inactivated vaccines consist of virus strains that have been fully attenuated, rendering them incapable of replication. However, these vaccines do necessitate the administration of booster shots. They can trigger both natural and acquired immune responses in the host. Another vaccine Bharat Biotech, India, developed is an inactivated virus created in Vero cells. This results in a more effective response to stimulating T-cells and mitigates the immunopathology caused by a virus. The treatment administration has demonstrated an impressive response rate of 80.6%. Currently, it is in phase three of a clinical trial. The vaccine developed by Sinovac Biotech China has shown 51% immunity for 84% of patients who require medical treatment [17].

mRNA vaccine: The mRNA vaccines consist of mRNA strands that encode the S protein. These strands are then enclosed in lipid nanoparticles, allowing efficient delivery to host cells. Given that the gene cipher for the complete S protein possesses a notable advantage compared to other vaccines that target specific domains of the S-protein. This advantage lies in its effectiveness even when the virus behaves to mutational changes. Additional benefits include their inefficiency in modifying the DNA as they specifically target the cytosol, the absence of infection risk and their superior efficiency compared to adenoviral vaccines [18]. Three mRNA vaccines were developed by famous pharmaceutical companies Pfizer, Biotech and Moderna. One of them revealed impressive effects of approximately 95% efficacy. Phase IV was also completed and came into utilization. Various adverse effects are observed, such as local irritations and swelling at the site of injections–additionally, various other side actions, such as headache, chills and myalgia. Increasingly, no genetic-related case was observed. The vaccine developed by Pfizer demonstrated 89% significance. This was an outstanding achievement compared to other antivirals [19].

Miscellaneous: The vaccine for BCG was also used in the trial for tuberculosis. Certain vaccines have several benefits in boosting immunity against viruses. Western Australia observed effectiveness in their vaccine against coronavirus. The vaccine called Lentiviral from China activates the T-cells and is adequate to the maximum extent [20].

Photo and sound therapy

Ultraviolet blood irradiation: Ultraviolet rays, especially in the 240-280 nm range, are employed for disinfection, whereas 300-320 nm rays treat the condition of psoriasis. Ultraviolet irradiation of blood revealed the potential benefits in immune responses. It also kills the viruses, however, more research is needed to validate its efficacy [21].

Sound therapy: Sound therapy, a non-invasive and drug-free intervention, leverages the therapeutic effects of music and sound to improve mental and physical well-being, making it a promising complementary approach to managing COVID-19. This therapy can alleviate anxiety, depression and stress, which are common among COVID-19 patients, by using techniques such as music therapy, binaural beats and guided meditation with sound baths. These interventions can enhance relaxation, improve sleep quality and potentially support immune function, contributing to overall recovery. While further research is needed to substantiate its efficacy specifically for COVID-19, the accessibility and safety of sound therapy make it a valuable adjunct to traditional medical treatments [22].

Plasma therapy: Recovered corona patients contain active antibodies that can boost the immunity in infected patients. Plasma therapy reduces elevated cytokine concentration linked to severe disease and improves symptoms such as breathing issues and fever [23].

Graphene-based products: Graphene, a material with unique properties, can be modified to create different forms, such as graphene oxide (GO), reduced graphene oxide (rGO) and graphene quantum dots (GQDs). These modified forms have various applications in the field of biomedicines [24]. Graphene and its derivatives exhibit antimicrobial characteristics attributed to electron mobility, resulting in cytoplasmic efflux and breakdown of the lipid membrane [25]. As a result, there is an increase in oxidative stress and eventual cell death. Feline coronavirus can bind to a surface with a negative charge, like GO or rGO, through hydrogen bonding and electrostatic interaction [26]. This surface has a lipid layer with a positive charge, which helps destroy the virus. Therefore, products coated with graphene and its derivatives will have a remarkable ability to eliminate viruses in biomedical applications. Single or multi-layered graphene derivatives can cover masks, personal protective equipment (PPEs) and benchtops [27,28]. It can also be offered in mist spray form, as a disinfectant, similar to air purifiers or as clean wipes coated with GO or rGO nanoparticles for sanitization purposes [29]. The nasal or oral spray can also be formulated to inhibit the S-protein of SARS-CoV-2. Although there have been numerous speculative applications, it is still necessary to conduct experimental studies to validate the concept [30].

Mesenchymal stem cells and derived exosomes: Stem cell modification plays a vital role in the treatment of coronavirus infections. Mesenchymal stem cells are examples of such events. It was done by modulating immune systems, preventing fibrosis and lung regeneration. It releases cytokines and regulates macrophages and T-cells for lung healing [31].

Telemedicine: Telemedicine was significantly impacted during the pandemic due to quarantine and lockdown circumstances. This has been the provision of frequent patient care and depreciation of the risk of virus transmission. This technique helped the health professionals treat, diagnose and continuously

counsel the patients without physical meetings. Telemedicine has kept immense value in managing chronic conditions, giving essential mental encouragement and effective symptom reductions. These methods revealed a reduced burden on health facilities and increased accessibility of services. The rapid integration and adoption of telemedicine into the health system could strengthen the healthcare system even for future pandemics [32].

Temperature management: Managing body temperature effectively is essential to the cautious treatment of viral infection. The aim is to regulate the body temperature and reduce symptoms and complications. Several therapies are available to minimize fever with antipyretic drugs. Hyperthermia is very common during infection; cooling measures like cold packs or tepid sponging may be beneficial. The optimum temperature management is essential to inhibit metabolic strain and reduce febrile convulsions and various temperature-related implications [33-35]. These techniques facilitate a rapid recovery and the stability of patent conditions. Immune-compromized patients such as children and oil-age patients should be taken into special precautions.

Mechanical ventilation: Air ventilation plays a vital role in treating viral infections, especially coronavirus. Mechanical ventilation is essential to support patients with respiratory distress and failure–the enrichment of oxygen to the lungs using different devices that help with ventilation [36,37]. The recovery of the lungs depends on eliminating carbon dioxide and providing a continuous supply of oxygen to breathe. However, precision is required to use mechanical ventilation because it may harm the patients in various circumstances. Health professionals need to monitor it while using it on corona-infected patients. The patients required intensive care to treat the ventilation strategies, including low tidal volume ventilation and prone positioning, improving the outcomes.

Prone positioning: Posture plays a significant role during breathing, especially when the patient is infected with the coronavirus. Prone posture involves placing the person on their abdomen and breathing can increase oxygenation in severe suffering. This method increases the function of the lungs through blood flow and ventilations, enhancing respiratory secretions. Consequently, it improves oxygenation and makes patients comfortable breathing for the seep recovery of the lungs. Observations reveal that the sustained prone situation and early positioning enhance the recovery. However, it may be crucial in critical conditions or for patients with severe complications [38].

Hydration and electrolyte management: Hydrating and managing electrolytes play a significant role in managing corona patients–these assists in resolving fluids and electrolyte imbalance, which may increase due to treatment. The infection symptoms such as fever, shortness of breath, chill, cold, body pain and loss of senses can be improved by hydration and electrolytes enticements in the body [39].

Mechanisms and significance

Fluid balance: To prevent side or adverse effects, dehydration and overhydration are essential to maintaining proper fluid balance. Dehydration contributes to reducing blood pressure and kidney-related complications [40].

Electrolyte homeostasis: Certain electrolytes such as calcium, magnesium, potassium and sodium are essential for acid-base equilibrium, nerve conduction and muscle contraction. The coronavirus disrupts the balance of electrolytes, which is important to monitor and appropriate management [41].

Nutritional support: Proper nutrition can minimize the risk, enhance the immune system and enhance recovery. A well-balanced diet such as proteins, vitamins and minerals, can improve immunity and promote overall health. A well-planned nutritional plan during the treatment of illness and hospitalization may enhance fast recovery. During the COVID-19 pandemic, the implementation of effective nutritional support strategies is essential for the improvement of patient resilience and the facilitation of recovery [42].

Multivitamins: Immunity plays a vital role in recovering from any illness. Specific reports prove the efficacy of vitamins in enhancing or boosting immune responses [43,44]. Zinc blocks the viral entry by targeting ACE2 and TMPRSS@ and regulates ACE2 expression [45]. Multivitamins such as A, B, D, E, *etc.*, revealed a potential reduction in inflammation and boosting immunity [46].

Physical therapy (PT) and rehabilitation: Physical therapy (PT) and rehabilitation play a crucial role in comprehensive COVID-19 management, addressing the challenges patients face during their recovery from severe illness [47]. PT interventions prioritize restoring respiratory function by incorporating breathing exercises, airway clearance techniques and respiratory muscle training. These interventions are vital in minimizing the likelihood of complications such as pneumonia and enhancing oxygenation. In addition, PT is crucial in addressing musculoskeletal deconditioning and weakness due to extended periods of bed rest and mechanical ventilation [48].

Rehabilitation strategies

Early mobilization: Active exercises and early mobilization can reduce the complications connected with the immobility of the recovery process. This technique is for managing and promoting pulmonary rehabilitation [49].

Individualized treatment plans: Treatment is designed by considering each individual's requirements and the disease status. This may lead to the exact treatment of the illness based on their clinical status and rehabilitation objectives [50].

Multidisciplinary collaboration: Collaboration helps in various ways to manage the patients in multidirectional. The MOU and the respiratory therapist, physicians, occupational therapists and nurses will provide comprehensive recovery [51].

Tele-rehabilitation: Tele-rehabilitation services also played a significant role during the pandemic. It provided continuous support to patients who were in the process of recovery. This method prioritizes individuals' health and well-being through reduced infection [52].

Psychological support: In most situations, mental support plays a vital role in disease recovery. Psychological support is essential for comprehensive care of the emotional consequences of illness. Several emotional challenges such as depression, distress and anxiety, can be caused during infections and treatment [53]. A variety of factors may cause these challenges

and may enhance the mindfulness-based approaches and counselling are essential [54].

Oxygen therapy: Oxygen therapy is essential for the treatment of COVID-19 patients who are experiencing respiratory difficulties, particularly those who are experiencing acute respiratory distress syndrome (ARDS) and have low oxygen levels in their blood [55]. This therapy emphasizes the improvement of oxygenation and tissue perfusion, the alleviation of respiratory distress and the provision of support for essential organ function. It encompasses a variety of delivery methods and strategies tailored to each patient's individual requirements and it also includes continuous surveillance of clinical response and oxygenation parameters [56-60].

Alternative therapies

Acupuncture and acupressure: Acupuncture and acupressure are alternative therapies have also been explored for their potential benefits in managing symptoms associated with COVID-19 [61,62]. Acupuncture involves inserting thin needles into specific points on the body to stimulate nerves, muscles and connective tissue to restore balance and promote healing. Acupressure, on the other hand, applies pressure to these same points using fingers, palms or devices without using needles. Both techniques are believed to modulate the immune response, reduce inflammation, alleviate pain and improve respiratory function, which can be particularly beneficial for COVID-19 patients experiencing respiratory distress and systemic symptoms. Despite the limited and inconclusive research on the direct efficacy of acupuncture and acupressure in treating COVID-19, these therapies are generally considered safe when performed by trained practitioners. They may provide adjunctive support in managing symptoms and promoting overall well-being during recovery [63]. Nevertheless, additional rigorous clinical trials are required to verify these findings [64].

Herbal medicines: Herbal medicines have attracted attention as a complementary approach to managing COVID-19, particularly in symptom alleviation and immune function support [65]. Numerous conventional herbal remedies, including ginger (*Zingiber officinale*), honeysuckle (*Lonicera japonica*) and licorice root (*Glycyrrhiza glabra*), are purported to have immunomodulatory, antiviral and anti-inflammatory properties that may help in the alleviation of respiratory symptoms, the reduction of inflammation and the promotion of overall recovery. For example, licorice root is recognized for its glycyrrhizin content, demonstrating antiviral activity against respiratory viruses [66]. Ginger and honeysuckle have traditionally alleviated respiratory symptoms and improved immune response. However, more comprehensive clinical studies are needed to evaluate the efficacy and safety of herbal medicines for COVID-19. It is crucial to exercise caution in light of the potential for drug-herb interactions and the inconsistent quality of botanical products. To guarantee the safe and effective use of herbal medication in COVID-19 care, consulting with qualified healthcare professionals is crucial [67]. The efficacy of Lianhua Qingwen capsules, a traditional Chinese herbal medicine, in patients diagnosed with COVID-19 was also investigated in a prospective, randomized, controlled trial conducted at multiple centers. The findings suggested that there may be benefits to reducing the duration and intensity of symptoms. Nevertheless, these discoveries necessitate further investigation [68].

Mind-body interventions: The mental well-being and immune systems of individuals affected by COVID-19, including patients and healthcare personnel, have been the subject of research on the effects of mindfulness-based interventions and yoga. These interventions are designed to mitigate stress, improve mechanisms and increase resilience during the pandemic [69].

Clinical trials: Numerous clinical trials have been conducted or are presently in progress to evaluate the efficacy and safety of therapies that do not involve medication for the treatment of COVID-19 [70].

Regulatory approvals: Depending on the regulatory framework in various countries or regions and the specific therapy, the approval process for drug-free therapies against COVID-19 can vary significantly. Drug-free therapies, including herbal remedies, acupuncture and nutritional supplements, are frequently perceived as complementary or alternative treatments. These therapies may not undergo the same rigorous approval process as pharmaceutical medications. In numerous countries, herbal remedies are regulated through specific frameworks, which are part of traditional or complementary medicine practices. Regulatory bodies frequently request evidence of safety, quality and efficacy through various methods, including conventional use, scientific studies and clinical trials. Safety assessments, efficacy data from clinical studies and compliance with good manufacturing practices (GMP) are typically required during approval. Rather than receiving specific sanctions for treatment indications, these therapies are generally subject to regulation under healthcare licensing or accreditation systems for practitioners. Regulatory oversight guarantees that practitioners are adequately qualified and comply with established safety protocols. In most jurisdictions, supplements, including vitamins and minerals, are subject to regulation as food products, with varying degrees of oversight. Regulatory agencies frequently require adherence to safety standards, precise labelling and high-quality manufacturing practices. Health claims concerning the prevention or treatment of COVID-19 are meticulously scrutinized and must be substantiated by scientific evidence. It is important to observe that regulatory approvals for these therapies, particularly for COVID-19, may be scarce or non-existent in numerous instances [71]. During public health emergencies like the COVID-19 pandemic, regulatory agencies may streamline review processes for specific therapies under emergency use provisions, ensuring they meet safety and quality standards. In general, drug-free therapies are considered necessary in providing supportive care. However, it is crucial to have reliable evidence of their safety and effectiveness to protect public health and make informed decisions regarding their use in managing COVID-19 [72].

Key challenges

Severity and variability of disease: Patients go through a variety of symptoms and disease severities, which makes it challenging to establish a uniform approach to non-drug inter-

ventions. COVID-19 has the potential to worsen rapidly, necessitating a swift transition from non-drug to drug-based and invasive interventions [73].

Resource limitations: There is often a shortage of oxygen therapy devices, ventilators and personal protective equipment (PPE) due to high demand, particularly during peak surges. Delivering top-notch care, particularly for complex procedures such as prone positioning and mechanical ventilation, necessitates well-trained healthcare professionals, who may be limited in number [74].

Patient-specific factors: Some individuals, particularly older patients and those with additional health conditions, may have difficulty tolerating specific therapies or may need more intensive interventions. Individuals who have pre-existing mental health conditions may encounter problems in following specific supportive therapies [75].

Infection control: Physical therapy, rehabilitation and other hands-on interventions carry a potential risk of virus transmission to healthcare workers and other patients due to close contact. Balancing the need for effective therapy with the importance of preventing nosocomial infections can present a significant challenge [76].

Implementation and compliance: Ensuring patients consistently follow through with therapies like respiratory exercises, nutritional support and psychological interventions can be difficult, especially without direct supervision. Limited access to technology or internet services can hinder the effectiveness of telemedicine, particularly in underserved areas [77].

Psychosocial and cultural barriers: Misconceptions about COVID-19 and its treatments can prevent patients from seeking or adhering to appropriate therapies. Cultural attitudes toward health and medical interventions can influence the acceptance and implementation of non-drug treatments [78].

Efficacy and evidence: Establishing the efficacy of numerous non-drug therapies is challenging due to the absence of extensive, well-controlled clinical trials. Subsequently, their utilization and acceptability may fluctuate. The perception of the efficacy of therapy can occasionally be influenced by the act of receiving it, making it more difficult to measure the actual clinical benefits accurately [79].

Healthcare infrastructure: In healthcare systems that are already overburdened, providing sufficient space and facilities for interventions such as physical therapy and prone positioning can be challenging. A collaborative approach that involves multiple disciplines is frequently required for successful implementation, but it can be challenging to coordinate, especially in environments with limited resources [80].

Training and education: Specialized training in non-drug therapies, including advanced mechanical ventilation techniques, prone positioning and respiratory physiotherapy, is necessary for healthcare workers. Although it can be challenging to achieve on a large scale, it is essential to raise awareness and advocate for the appropriate use and benefits of non-drug therapies [81].

Monitoring and follow-up: Non-drug therapies necessitate consistent monitoring to guarantee that treatment plans are adjusted as required. Nevertheless, this can present logistical difficulties, particularly for patients receiving treatment at home. It is necessary to maintain ongoing coordination and resources to guarantee long-term rehabilitation and recovery support, particularly in the aftermath of severe cases [82].

Critical views: Concerns regarding the efficacy, safety and potential impact on public health strategies of drug-free therapies for COVID-19 have been expressed by specific individuals. Even though these therapies, including acupuncture, sound therapy and herbal remedies, can alleviate symptoms and promote overall health, their efficacy in preventing or treating COVID-19 has yet to be definitively demonstrated through rigorous clinical trials. Relying exclusively on these therapies rather than evidence-based ones may lead to delayed access to proven interventions and jeopardize patient outcomes, particularly in severe cases requiring immediate medical attention. In addition, the potential for adverse interactions with conventional medications, the absence of standardized protocols and the varying quality control of herbal supplements all contribute to significant safety concerns. Critics contend that promoting therapies that have not been proven effective can result in false hope and misinformation, which could impede the implementation of scientifically validated preventive measures and vaccination campaigns. Consequently, it is crucial to exercise prudence when contemplating the integration of drug-free therapies into the administration of COVID-19. To ensure patient safety and efficacy, this strategy should emphasize regulatory oversight, comprehensive research and adherence to established public health guidelines [83].

Future perspectives: As we consider the future, the emphasis on drug-free therapies against COVID-19 necessitates implementing effective public health strategies, utilizing the most recent advancements in medical technology and adopting interdisciplinary approaches to enhance patient care and outcomes [84]. We should investigate several critical areas (Fig. 3).

Technological innovations: They are enhancing telemedicine platforms to provide remote monitoring, virtual consultations and ongoing patient support, particularly in regions with restricted healthcare access. Continuous care and adherence to non-drug therapies can be supported by improving the integration and accessibility of telehealth. Wearable technology enables health care practitioners and patients to benefit from real-time feedback, activity tracking and vital sign monitoring. These tools will encourage people to stay committed to their rehabilitation routines and help in the early detection of deteriorating conditions. In order to tailor non-drug therapies to each patient's specific profile, optimize treatment plans and forecast outcomes, AI systems are analyzing patient data [85].

Enhanced respiratory support: Developing innovative non-invasive ventilation techniques and portable devices that provide adequate respiratory support while minimizing the likelihood of complications. Improving oxygen delivery systems, such as portable oxygen concentrators and high-flow nasal cannula devices, guarantees that patients receive adequate oxygenation in less resource-intensive environments or at home [86].

Integrated multidisciplinary care: To holistically address patient well-being, promote comprehensive care models

Fig. 3. Future perspectives of drug-free therapies

that integrate psychological counseling, nutritional support, physical rehabilitation and medical monitoring. Creating inclusive platforms that enable healthcare professionals from various disciplines to exchange insights, coordinate care plans and monitor patient progress, thereby facilitating collaboration [87].

Community and public health initiatives: Conducting comprehensive public health campaigns to educate communities on the benefits of vaccination, the importance of non-drug interventions and the effectiveness of infection control measures. Establishing community programs and support networks to facilitate the recovery of individuals, provide mental health resources and facilitate the acquisition of essential services [88].

Research and evidence-based practice: To evaluate the efficacy and safety of various non-pharmacological treatments, we are carrying out comprehensive clinical trials. This involves investigating different approaches and combinations of therapies. Promoting data sharing and collaboration among researchers and healthcare institutions to expedite the advancing and widespread adoption of evidence-based practices [89].

Personalized medicine: Creating individualized, patient-specific, non-pharmaceutical treatment programs by analyzing genetic, metabolic, and phenotypic data. Emphasizing the importance of taking proactive steps and providing timely support based on an individual's unique risk factors and health profile [90].

Global health equity: Promoting for a fair allocation of resources, technology, and training to low- and middle-income nations to enable the effective implementation of non-pharmacological therapy. Investing in global healthcare infrastructure and staff development to improve the capacity for delivering great care and managing future health emergencies effectively [91].

Mental health integration: Integrating routine mental health assessments and treatments into the normal treatment for COVID-19 patients to mitigate the emotional impact of the illness. Developing initiatives aimed at enhancing resilience and coping strategies for patients, families and healthcare professionals to mitigate the enduring mental health effects of the epidemic [92].

Environmental and lifestyle modifications: Improved air quality and reduced exposure to hazardous substances are two examples of the environmental changes that will benefit people's respiratory health. Positive improvements in lifestyle, including more exercise, better nutrition and less stress, have a multiplicative effect on health and immunity [93].

Future pandemic preparedness: To develop comprehensive preparedness programs that incorporate effective non-pharmaceutical interventions for future pandemics, one might utilize the knowledge gained from the COVID-19 experience. The potential to alleviate the strain on healthcare systems is achieved by implementing efficient response systems to deploy the alternative therapies during the initial phases of outbreaks promptly [94]. Nanotechnology possesses considerable promise in combating viral infections, providing novel approaches for precise medication delivery, improved therapeutic effectiveness and reduced adverse effects in treatment [95]. Lesser known or unexplored the medicinal plants may offer antiviral properties through bioactive compounds, augmenting immune response and inhibiting viral replication [96].

Conclusion

In conclusion, the drug-free therapies offer diverse approaches that can complement conventional medical remedies in the treatment of COVID-19. These therapies like sound treatment, telemedicine, temperature management, mechanical ventilation, prone positioning, hydration and electrolyte management, nutritional support, physical and rehabilitation, oxygen therapy, psychological support, acupuncture, acupressure and herbal medicines, help to improve patient outcomes, ease symptoms and improve overall well-being. Although some specific

therapies, such as prone positioning and oxygen therapy, are widely acknowledged for treating respiratory distress, others, such as acupuncture and herbal medicines, require additional scientific validation. These therapies often provide additional support alongside conventional treatments rather than being used as replacements. Ensuring the safety, quality and efficacy of these interventions is of utmost importance and their integration into COVID-19 care should be guided by evidence-based practices, with regulatory oversight playing a crucial role. Highlighting a comprehensive approach that considers individuals' physical, mental, dietary and recovery requirements can enhance results and overall well-being. Ongoing research and stakeholder cooperation are crucial for developing comprehensive care strategies to integrate drug-free therapies into COVID-19 treatment successfully plans.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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