# Herbal Medicine, Traditional Practice, and Nutraceutical as Prospective Alternative Therapy for Post COVID-19 Syndrome

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**Abstract**

Following COVID-19 infection, a post COVID-19 patient may experience Post COVID-19 Syndrome (PCS). This disorder is significantly important for therapies because it can lower an individual's quality of life following COVID-19 infection. Several treatment approaches, including non-conventional therapies such as herbal medicine, traditional therapy, and nutraceuticals, have been suggested for PCS. This narrative review will thoroughly deliberate the pathogenesis of PCS and several alternative, non-conventional therapy modalities, along with their efficacy and side effects. A literature search using PubMed and ScienceDirect databases, using the keywords “Post COVID-19” AND “Herbal Medicine” OR “nutraceutical” OR “traditional therapy” AND “efficacy” OR “safety” to find relevant studies. Clinical trials examining the effectiveness, safety, and indications of these new treatments are covered in our study. According to our research, these approaches show a lot of promise for being both safe and effective for treating post-COVID-19 syndrome. Therefore, more in-depth research is needed on some different therapy modalities that were not addressed in this study but may present interesting avenues for future post-COVID-19 syndrome treatment.

Keywords: herbal medicine; nutraceutical; post COVID-19 syndrome; infectious disease; traditional therapy

## 1. Introduction

In December 2019, a new coronavirus called SARS-CoV-2 (severe acute respiratory syndrome coronavirus) was discovered. Before recent discoveries, it was thought that the COVID-19 pandemic was mostly driven by human-to-human transmission and that it had first spread zoonotically through a seafood market in Wuhan, China (Zhang et al., 2020). By November 2021, it is expected that almost three billion people, or 44% of the world's population, will have at least one case of SARS-CoV-2 (Li et al., 2020). The symptoms of COVID-19 including fever, dyspnea, sore throat, chest discomfort, and neurological, cardiomyopathy, thromboembolism, and gastrointestinal disorders, are comparable to those of viral pneumonia (Hope and Evering, 2022). While some patients exhibit no symptoms at all, the majority of patients report mild to severe symptoms (Chen et al., 2022). While most treatments have been effective in assisting patients in making a full recovery from this infection, some of them continue to induce symptoms even after a COVID-19 test comes back negative. This condition called Post COVID-19 syndrome.

Post COVID-19 Syndrome (PCS) is a group of persistent symptoms that occur in who have had a history of suspected or proven SARS-CoV-2 infection. The symptoms usually start to show up three months after the COVID-19 infection started, last for at least two months and have no other known cause. Estimates from the WHO suggest that 200 million individuals are either experiencing or have previously had long-term health effects from COVID-19 (Chen et al., 2022). Ten percent to 35% of those recovering from acute illnesses are thought to be impacted by Post COVID-19 Syndrome; hospitalized patients are more likely to be afflicted (Hope and Evering, 2022). Several organs may be affected by PCS, which also has a remission-relapse propensity and a markedly reduced quality of life Osmanov et al., 2022). Mast cell activation syndrome (MCAS) is linked to post-COVID-19 syndrome (PCS) and is typified by hyperactive mast cells releasing chemical mediators in excess and inappropriately. PCS can be caused by significant consequences from inflammatory reactions, host-microbiome alterations, reactivation of pathogens, and autoimmune mimicry (Jones et al., 2021).

To treat PCS, practitioners have tried their best. There are still large clinical and practical gaps in PCS treatment, even with the advent of several therapies. This does not provide suggestions for a specific therapy plan. Empirical data continues to be the cornerstone of therapy. Researchers are looking into how well histamine antagonist drugs like cimetidine, ranitidine, and famotidine, as well as antibiotics and antivirals like azithromycin, remdesivir, and favipiravir, work to suppress PCS. In the same way, monoclonal antibodies such as siltuximab, anakinra, and leronlimab work. Antidepressants may also enhance immune function and reduce peripheral inflammatory markers, according to some research (Koc et al., 2022). However the exact mechanism of action of these medications is unknown, and there are worries about long-term negative effects. Antivirals are one medication that can weaken the immune system. Patients become more vulnerable to opportunistic infections as a result.

Other treatment modalities, however, are also being researched since they are believed to be more effective and safe than conventional pharmacological therapy. A few instances of this are herbal medicine, and physical rehabilitation. This includes conventional methods such as tai chi, yoga, and acupuncture.

Herbal medication, such as Chinese Herbal medication (CHM), has been used in conjunction with conventional treatment to help prevent COVID-19 infection because of its various benefits (Chien et al., 2022). It has been demonstrated that Ayurveda and other commercial plant extracts can successfully alleviate fatigue and enhance overall health (Naureen et al., 2021). During the healing phase following an acute COVID-19 infection, non-pharmacological treatment management such as acupuncture, yoga, and Chinese martial arts (Tai Chi) is advised (Kim et al., 2022). The Acupuncture Association of China has even suggested guidelines for the use of moxibustion and acupuncture in treating COVID-19 and PCS (Zhang et al., 2020). Acupuncture, when paired with normal regimens, has been proven to be beneficial in relieving symptoms of anxiety, exhaustion, shortness of breath, loss of appetite, and insomnia with no negative side effects or consequences, according to several recent clinical trials (Jia et al., 2020).

Nutraceuticals, multivitamins, and mineral supplements, on the other hand, may be useful as PCS therapy possibilities because of their potential anti-inflammatory and anti-oxidative qualities (Singh et al., 2021). A study found that taking multivitamin supplements helped PCS patients' clinical symptoms (Koc et al., 2022; Rossato et al., 2021). Nicotinamide ribose, a kind of vitamin B3, is now showing promise in the treatment of chronic fatigue and cognitive impairment in two clinical trials. Probiotics, such as Lactobacillus plantarum, have been demonstrated in multiple studies to have beneficial effects on SARS-CoV-2-infected intestinal epithelial cells by functioning as an antiviral and by modifying the axis between the gut and the brain and the gut and lung (Liu et al., 2020).

The use of stem cells in treatment is gaining popularity among clinicians as well. In COVID-19 therapy, stem cells are commonly used as immunomodulatory agents to reduce the inflammatory process and prevent cytokine storms. Stem cells have been used in the past to treat a variety of diseases, such as autoimmune and viral disorders. Among the functions of stem cells include immunomodulation, regeneration potential, alveolar fluid clearance, and thrombotic prophylaxis (Jamshidi et al., 2021). The pathogenesis of PCS and potential alternative treatments, including herbal remedies, conventional therapy,and neutraceuticals, will be elaborated in detail in this paper.

## 2. Materials and Method

This review was conducted by searching for the efficacy, safety indication, and recommendation of using recent herbal medicine, traditional therapy, and nutraceutical for Post COVID-19 in two databases, PubMed (https://pubmed.ncbi.nlm.nih.gov and ScienceDirect(https://www.sciencedirect.com/). The Keyword is "Post COVID-19" AND "Herbal Medicine" OR "traditional therapy" OR "nutraceutical", AND "Efficacy" OR "safety".

The inclusion criteria are full-text literature and studies conducted within the last five years, and the research subjects were post COVID-19 patients who received herbal medicine, traditional therapy, or nutraceutical. The types of studies included in this review are in-silico studies, experimental (in vitro and in vivo), and clinical trials. The exclusion criteria were review articles without an English version.

## 3. Pathophysiology of Post COVID-19 Syndrome

The World Health Organization (WHO) states that the symptoms of post-COVID-19 syndrome (PCS) often appear three months after COVID-19 infection, persist for at least two months, and do not related with any other likely diagnosis. The two stages of PCS sequelae are (1) subacute or persistent COVID-19 symptoms, which include anomalies and manifestations and are identified by a negative Polymerase Chain Reaction (PCR) but the virus being found in the nasopharynx, that appear 4–12 weeks following the acute infection; and (2) Disorders and symptoms that manifest 12 weeks following the onset of the acute COVID-19 infection and are unrelated to any other condition are referred to as chronic or post-COVID-19 syndrome. A meta-analysis revealed that at least 45% of survivor of COVID-19 continued to have at least one residual symptom for an average of 126 days. The most common symptom recorded (28.4%–34.8%) was fatigue, which was followed by aberrant CT/X-ray patterns (45.3%), ground glass opacification (41.1%), and reduced carbon monoxide diffusion capacity (31.7%) (O'Mahoney et al., 2023).

Post COVID-19 syndrome patients may experience organ and tissue dysfunction as a result of systemic inflammatory response syndrome (SIRS). It is believed that PCS and Mast Cell Activation Syndrome are connected (MCAS). Stressor-induced interactions can lead to aberrant control of the activation of mast cell in PCS by inducing activation of mast cell genes via SARS-CoV-2 infection (Maxwell et al., 2021). Autoantibodies are produced during SARS-CoV-2 infection as a result of TLR activation on immune cells. Autoantibodies can also activate mast cells by interacting with mast cells' immunoglobulin receptors (Mukherjee et al., 2021). Following ACE2 expression, mast cells can release vasoconstrictor leukotrienes (LTs), which influence the pulmonary Renin-Angiotensin system (RAS). Several inflammatory mediators, such as histamine, prostaglandins (PGs), heparin, tryptase, Leukotrienes, and chemokines like Interleukin (IL)-1β and IL-6, are released when mast cells are stimulated. Adrenocorticotropic hormone (ACTH), cortisol, and corticotropic releasing factor (CRF) are all released in greater amounts under stressful circumstances when infected with SARS-CoV-2. Moreover, intestinal stress alters the gut microbiota, which has an impact on tryptophan metabolism, neurotransmitter release, and short-chain free fatty acids (SCFAs) release. All of these changes lead to a stronger activation of mast cells, which in turn produces more inflammatory cytokines. Thus, mast cells provide neurological, immunological, and endocrine pathways that link the gut and the brain (Fuchs et al., 2012).

To preserve immunological homeostasis, a balanced anti-inflammatory response would typically be triggered by COVID-19's strong pro-inflammatory and overactive immune responses (Range and Moser, 2013; Sugimoto et al., 2016). This would result in an immunosuppressive condition. Nonetheless, chronic immunosuppression may result in PCS (Cañas, 2020). Transformation-promoting factor β (TGF-β) is an immunosuppressive, profibrotic, and anti-inflammatory cytokine that is raised during and after SARS-CoV-2 infection to reduce excessive pro-inflammatory responses. However, in PCS this regulation does not work

properly. Thus, there is ongoing inflammation. According to a number of research (Goërtz et al., 2020), infection persistence also causes long-term immunological activation. Multisystem Inflammatory Syndrome (MIS) is a result of persistent infection activating autoreactive T lymphocytes via antigen presentation by antigen-presenting cells. While pro-inflammatory cytokine levels and MIS may be correlated, the severity of the first SARS-CoV-2 infection is not. One possible explanation for the delayed start of MIS following SARS-CoV-2 infection is adaptive immune response dysregulation. Similarly, in 52% of PCS patients, B cell activation and antiphospholipid autoantibody synthesis were noted (Koné-Paut and Cimaz, 2020). When combined, immunological dysregulation, autoimmune mimicry, pathogen reactivation, persistence of inflammatory responses, and modifications to the host microbiome may lead to PCS. **Table 1** describes the pathophysiology of PCS in various organ systems.

## 4. Clinical Manifestation of Post COVID-19 Syndrome

Acute infection intensity and duration influence the clinical presentation of PCS, which can take many different forms. Fatigue is the most common PCS symptom, affecting 17–72% of critically COVID-19 patients. Respiratory symptoms such as dyspnea (10–40%), exercise intolerance (10–40%), and chest pain (22%), are more common in patients with PCS. Cardiovascular symptoms, including hypertension, arrhythmias, and postural hypotension, are brought on by endothelial dysfunction and heart injury (Mitrani, Dabas, and Goldberger, 2020). Thirty percent of COVID-19 patients may experience gastrointestinal symptoms for more than two months following hospital discharge, including nausea, vomiting, diarrhea, bowel movements, and appetite abnormalities (Carvalho-schneider et al., 2020). Neuropsychiatric problems, including smell/gustatory impairment, affect 9–11% of individuals and can last for six to eight months with mild COVID-19 (Sugiyama et al., 2022). Anxiety and depression account for 26% and 40%, respectively, of psychiatric consequences in PCS patients that manifest six months after infection (Alemanno et al., 2021). Aggression, cognitive impairments, decreased social engagement, obsessive-compulsive disorders, and stress disorders account for 43% of these difficulties. Guillain-Barre syndrome, stroke ischemic, seizures, transverse myelitis, and, cerebral vasculitis, are among the neurological conditions that have been seen in PCS patients (Scoppettuolo et al., 2020). **Table 1** and **Figure 1** describe the clinical manifestation of PCS in various organ systems.

In severe conditions, patients with PCS can develop some complications. Pulmonary complications, including lung fibrosis and radiological abnormalities that may persist for up to six months, are the most common complications among individuals with PCS. Furthermore, pulmonary dysfunction in PCS patients results in reduced gas exchange even with normal lung computed tomography (CT) scans. Due to lung fibrosis or scarring, patients with PCS may have dyspnea and a chronic cough (Batiha et al., 2022). Neurological problems encompassing musculoskeletal disorders and peripheral and central neurological disorders, accounted for around 36.4% of the patient. Concerning COVID-19, headache (13.1%), fatigue (14.0%), and dizziness (16.8%) were the most common neurological symptoms. Moreover, COVID-19 has been connected to ataxia, disorientation, seizures, stroke, and other central nervous system symptoms and consequences. Due to the extreme burden of a significant inflammatory response, PCS patients may also experience anxiety, depression, and psychosis.

Acute SARS-CoV-2 infection-related brain stem injury also causes cardio-respiratory dysfunction because it damages the respiratory and vasomotor areas Sinus tachycardia, postural orthostatic tachycardia syndrome (POTS), endothelial dysfunction, autonomic dysfunction, and dysautonomia can all occur in PCS patients. In addition, 5% of hospitalized COVID-19 patients get Acute Kidney Injury (AKI), and up to 31% of patients experience renal issues as a result of endothelial injury, inflammation, and coagulopathy. Gastrointestinal issues that patients may experience as a result of persistent GIT inflammation include reduced appetite, nausea, vomiting, diarrhea, and abdominal pain. Changes in the gut microbiota after infection may increase the risk of

lung dysfunction and systemic inflammation (Al-Buhadily et al., 2021)

Endocrine complications include thyrotoxicosis, thyroiditis, and Gravis' disease also can happen. In male COVID-19 patients, disturbance of the pituitary-testicular axis may result in decreased sperm production, quality, and testicular function. A case-control study found that 9.3% of participants had a low cortisol response and 46.5% had an insufficient growth hormone response. Thyroid stimulating hormone and prolactin levels also rose noticeably, by 9.3% and 4.6%, respectively. Some individuals also have increased peripheral insulin resistance in addition to decreased pancreatic cell insulin production. One of the hematological consequences that increases the risk of heart thrombus and ischemic stroke is thromboembolism (Moreno-Perez et al., 2022) .

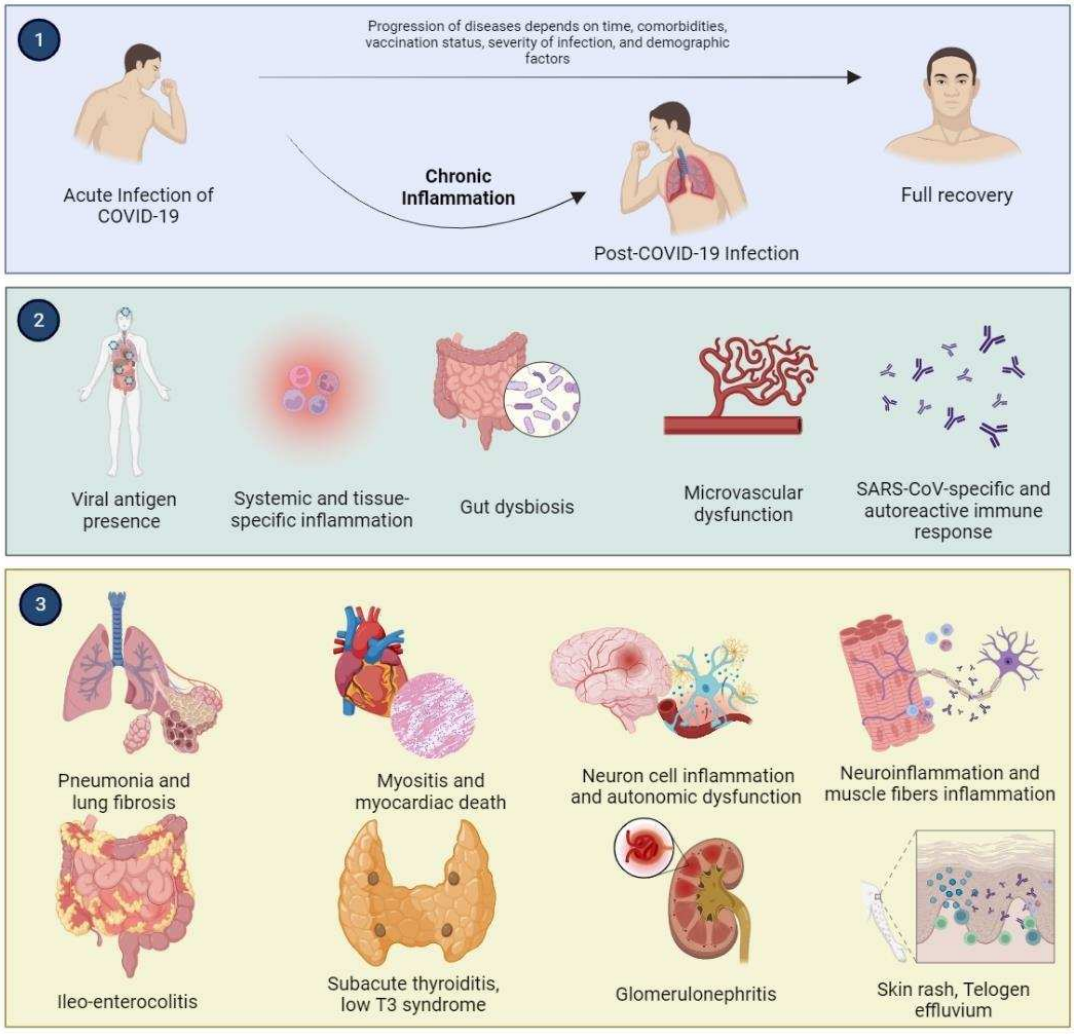


Fig. 1. Pathophysiology of Post-COVID-19 Syndrome. This syndrome occurs in some patients who experience acute COVID-19 infection (1). The chronic inflammation that occurs in PCS is caused by the persistence of viral antigens and an autoreactive immune response as well as intestinal dysbiosis and microvascular dysfunction due to acute infection (2). As a result, multi-organ failure occurs (3).

Table 1. Pathophysiology of Post COVID-19 Syndrome and Its Complication in Organ Systems

| Organ System | Pathophysiology(s) | Clinical Manifestation(s) |
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| Neurosensory | • Neuroinflammation is a chronic inflammatory process that activates brain microglia as a result of viral invasion or after the acute stage of the illness.<br>• Coagulation activation: Microthrombosis hinders neuronal transmission and tissue vascularization.<br>• Autoimmunity: atypical immune reaction during the acute stage of disease or molecular emulation of SARS-CoV-2 and host antigens.<br>• Abnormalities in brain metabolism.<br>• Remaining virus particles: support the low-level inflammatory reaction.<br>• Nerve root and peripheral trigeminal nerve activity. | • Chronic headaches<br>• Sleep disorders<br>• Olfactory and gustatory impairments<br>• Brain fog, memory and concentration problems<br>• Depression, anxiety, post-traumatic stress disorder<br>• Vertigo, imbalance, psychosis, and hallucinations<br>• Small fiber neuropathy<br>• Tremor in the posture<br>• Pain syndromes<br>• Neurodegenerative disorders<br>• Poor concentration<br>• Hearing loss<br>• Tinnitus<br>• Red eyes<br>• Sore throat |
| Musculoskeletal | • External variables, such as musculoskeletal conditions.<br>• Environmental factors: humidity, temperature, and social isolation.<br>• concomitant conditions.<br>• Congestion in the lymphatic-lymphatic system.<br>• Muscle bioenergetic diseases resulting from dysfunctional mitochondria.<br>• Myocytes distruption and activation of fibroblast.<br>• Alterations in the bone's microcirculation, including leukocyte aggregation, hypercoagulability, and vascular inflammation.<br>• Tension in joints and activated immunity. | • Fatigue<br>• Myalgia<br>• Joint pain<br>• Small joint arthritis |
| Immune system | • Chronic disorganized immune system activation: low-grade inflammation leading to multiple organ dysfunction. | • Altered immune system<br>• Increased risk of infection |

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| | • Mast cell activation syndrome<br>• Persistent infection<br>• Multisystem inflammatory syndrome in children (MIS-C). | |
| Gastrointestinal and hepato-biliary system | • Intestinal dysfunction following an infection<br>• Alterations in the microbiota; and harm to the liver and biliary system.<br>• Autonomic nervous system abnormalities (intestinal motility disorders). | • Appetite loss<br>• Pain in the abdomen<br>• Nausea<br>• Loss of weight<br>• Changes in bowel motility<br>• Irritable bowel syndrome<br>• Dysphagia |
| Renal system | • Invasion of renal cell virus<br>• The severity of prior severe illness<br>• Microangiopathy<br>• The renin-angiotensin-aldosterone pathway is disrupted<br>• The Glomerularopathy. | • Microhematuria |
| Endocrine system | • Pancreatic β cell invasion by a virus<br>• Direct injury to the thyroid gland, subacute thyroiditis, low T3 syndrome. | • Subacute thyrotoxicosis<br>• Persistent glycemic abnormalities<br>• Grave's diseases<br>• Hashimoto's thyroiditis<br>• Lipid abnormalities |
| Cardiovascular | • Myocardial injury can occur directly from viral infection, which is thought to be less prevalent, or indirectly through systemic inflammatory response.<br>• Desmosomal protein fibro-fatty displacement and cardiomyocyte death.<br>• Corticosteroids and renin-angiotensin-aldosterone system (RAAS) imbalance. | • Chronic headaches<br>• Sleep disorders<br>• Olfactory and gustatory impairments<br>• Brain fog, memory and concentration problems<br>• Depression, anxiety, post-traumatic stress disorder<br>• Vertigo, imbalance, psychosis, and hallucinations<br>• Small fiber neuropathy<br>• Tremor in the posture<br>• Pain syndromes<br>• T2 signal and positive LGE<br>• Myocardial oedema<br>• Pericardial effusion |

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| | | • Hemosiderin deposits<br>• Diastolic dysfunction<br>• Capillary abnormalities<br>• Arrhythmias<br>• Pulmonary hypertension |
| Respiration system | • An abnormal and persistent inflammatory reaction<br>• An excessive fibroblastic growth<br>• Leukocyte telomere length and lactate dehydrogenase levels as separate risk factors for the emergence of fibrotic-like abnormalities | • Dyspnea<br>• Persistent cough<br>• Asthma exacerbation<br>• Reduced carbon monoxide (DLCO) diffusin capacity<br>• Dyspnea, tachypnea, pleurisy; cough<br>• Disturbances in lung function (↓ FEV1, ↓ FEV1/FVC)<br>• Pulmonary fibrosis<br>• Crazy paving in the interstitial space<br>• Ground-glass opacity residual<br>• Abnormal diffusion<br>• Pulmonary embolism<br>• Pneumonia |
| Dermatological | • Immune responses<br>• Epitope spreading.<br>• Cryptic antigens are presented to functional T cells.<br>• The phenomenon of antibody-dependent enhancement (ADE) is observed when human hair follicle dermal papilla cells are directly attacked by viruses.<br>• The production of microthrombi in the coagulation cascade might block the blood supply to hair follicles.<br>• Underlying pro-inflammatory cytokines that are released as a result of chronic inflammation.<br>• Stress in the acute stage (stress related to emotions, fever). | • Skin rash<br>• Telogen effluvium<br>• Nail alterations |

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| Systemic manifestation | • The organs' modified homeostatic environment (stromal damage, less tissue-resident macrophages).<br>• Proinflammatory cells that persist.<br>• Modified generation of cytokines.<br>• Modified immunometabolic routes (heme-related metabolic pathways, ROS).<br>• The altered gut bacteria, epitope dissemination, and immunological antibodies. | • Chronic malaise<br>• Restriction of daily activities<br>• Asthenia |
| Laboratory abnormality | • Long-lasting proinflammatory cells that infiltrate neutrophils, plasma cells, effector T cells, monocytes, and PDCs<br>• Modified production of cytokines (IFN-α Type I , IFN-γ, and III, IL-6, TGF-B, and IL-1B)<br>• Modified immunometabolic routes (heme-related metabolic pathways, ROS)<br>• autoimmune Antibodies<br>• The spreading epitope<br>• Changes in intestinal microbiota | • Increased neutrophils, hepatocyte growth factor (HGF), matrix metalloprotease 7 (MMP-7), and lipocalin 2 (LCN-2)<br>• Increased D-dimer levels and anemia<br>• Anomali of lipids<br>• Abnormal liver function tests<br>• Thrombocytosis<br>• Elevated hemoglobin A1C (HbA1C)<br>• Reduced serum albumin<br>• Coagulation abnormalities<br>• Electrolyte abnormalities |

## 5. Recent Alternatif Therapy for Post COVID-19 Syndrome

### 5.1. Herbal Medicine

One of the most popular uses of herbal medicines is in Traditional Chinese Medicine (TCM). Traditional Chinese medicine (TCM) has long been used to treat a wide range of ailments in both home and foreign countries. For instance, it has been shown that Lianhuaqingwen (LH), a Chinese medicine made up of thirteen herbs, efficiently cures a variety of influenza viruses by regulating the immune system, preventing the spread of the virus, and reducing the length of time an H1N1 infection lasts. As a therapy, it is just as effective as oseltamivir (Xiong et al., 2020). Moreover, a retrospective analysis of from patients who acquired SARS-CoV-2 at Wuhan Ninth Hospital and General Hospital has shown that Lianhuaqingwen is helpful in the treatment of the virus. Combining LH can greatly lessen the severity of COVID-19 illness and ameliorate cardinal symptoms (Runfeng et al., 2020).

India is among the nations with the most advanced systems of herbal medicine, aside from China. For many years, Ayurveda has been the main medicine utilized to control many ailments. The antiviral and immunosuppressive properties of Ayurveda on T and B lymphocytes are known to lessen the inflammatory effects of COVID-19 infection (Dhane and Shinde, 2022). The M protein of SARS CoV-2 and other target proteins are susceptible to the antiviral effects of certain Ayurvedic ingredients, such as Tinospora cordifolia, Withania somnifera, and Ocimum sanctum, according to molecular docking research. Ayurvedic phytoconstituents (Maurya and Sharma, 2022) may block the SARS Corona Virus's papain-like protease and primary protease, as well as cause disruptions to the relationship between the host receptor ACE 2 and the viral S-protein RBD (Receptor Binding Domain) (Balkrishna et al., 2020; Shree et al., 2022).

In addition to providing relief during the acute stage of COVID-19 infection, a number of herbal remedies have demonstrated beneficial effects in PCS, particularly in easing lingering symptoms following negative COVID-19 test results. A number of active ingredients in herbal remedies, including green tea, kadha, and tulsinol from Ocimum sanctum (tulsi), actively work to minimize the onset of symptoms by inhibiting the NF-kB pathway and pro-inflammatory cytokine production (Kumar et al., 2020). The constituents, mechanisms of action, and therapeutic effects of various herbal medicines in treating PCS symptoms are presented in **Table 2**.

Compared to chemical treatments, herbal remedies seen more "natural" and "safer". However, as the body of research on herbal remedies grows, a growing number of side effects have been documented. These include reactions to the biologically active components of herbs, side effects brought on by contaminants, and chemical interactions between herbs and drugs. Gastrointestinal disturbances, including aberrant liver function, renal dysfunction, headache, nausea, vomiting, diarrhea, and appetite loss, are the most frequent side effects of herbal therapy (Wang et al., 2022). One of the conditions that is frequently linked to the usage of some Chinese herbs, such as Aristolochia fangchi, is nephropathy. The presence of pyrrolizidine alkaloids, which are unintentionally or intentionally added to herbal remedies, is another frequent cause of toxicity for these remedies. This alkaloid induces hepatotoxicity and eventually results in deadly veno-occlusion.

Table 2. Herbs Component and Mechanism of Action of Several Patent Herbal Medicine

| Herbal Medicine (s) | Origin | Theraupetic Effect(s) | Herb(s) component | Mechanism of Action(s) |
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| Jinhua Qinggan (JHQG) granules | Traditional Chinese Medicine (TCM) | • JHQG proved highly successful in combating the avian influenza A (H1N1) virus, for which it was advised.<br>• JHQG may also help influenza patients' immune systems work better.<br>• Empirical research indicates a positive impact on symptoms related to exhaustion, persistent cough, diarrhea, heightened appetite, chest discomfort, and muscle soreness. | Gypsum Fibrosum, Lonicera japonica, Prunus sibirica L., Ephedra sinica, Scutellaria baicalensis, Fritillaria thunbergii, Forsythia suspensa, Anemarrhena asphodeloides, Artemisia annua L., Arctium lappa L., Mentha haplocalyx Briq., and Glycyrrhiza glabra L. | **Anti-Inflamations**<br>• Prevents the release of cyto promote inflammation (IL-6, T IL-1β, , IL-4, IL-2 and IL-13).<br>• Prevents the release of chemokine protein-1, IL-6, T promotes protein-10.<br>• Inflammatory signaling path PI3K/Akt signaling pathwa kinase/signal transducer and a transcription (JAK/STAT) signal MAPK pathway, and nuclear fac (NF-κB), are blocked. |
| Lianhua Qingwen (LHQW) capsules | TCM | • LHQW is advised in addition to Western medication for the treatment of influenza, particularly avian influenza A (H1N1).<br>• RCT studies demonstrate an improvement in the symptoms of muscle soreness, increased hunger, persistent cough, and diarrhoea. | Ephedrae Herba, Armeniacae Semen Amarum, Lonicerae Japonicae Flos, Glycyrrhizae, Forsythiae Fructus , and Menthae Haplocaltcis Herba, Atractylodis Rhizoma, Pogostemonis Herba, and Gypsum Fibrosum | • Inhibits the TLR4 – Myd88 pathway.<br>• Decreases the generation of neutrophils, lymphocytes, and v cells.<br>• Reduces prostaglandin E2 (PGE in the vicinity of the hypothalam<br>• Restricts cyclooxygenase-2 expression. |
| Huashibaidu (HSBD) granules | TCM | • The treatment of epidemic toxin blocking in the lung, a pattern observed in severe COVID-19 cases, has been suggested to use HSBDF.<br>• Greatly reduces weariness, cough, and chest discomfort. eases dry mouth and headaches. | Glycyrrhizae Radix et Rhizoma, Gypsum Fibrosum, Ephedrae Herba, Ageratum rugose, Atractylodis Rhizoma and Descurainiae Semen Lepidii Semen, Poria, Pogostemonis Herba, Armeniacae Semen Amarum, Tsaoko Fructus, Pinelliae Rhizoma Praeparatum, Astragali radix, and Paeoniae Radix Rubra | • Represses the expression produced by LPS and re inflammatory cellular pathwa mediated by TLR.<br>• Prevents the synthesis of NO, iN 2, IL-6, and TNF-α.<br>• By preventing the synthesis of LTB4 metabolites, it lowers the COX, 5-LO, and 5-HETE.<br>• Blocks the Wnt/β-catenin a pathways. |
| Xuanfeibaidu (XFBD) granules | TCM | • The primary goal of treating COVID-19 individuals who are moderately to severely ill.<br>• Reduction of fever, shortness of breath, cough, and exhaustion. | Ephedrae Herba, Glycyrrhizae Radix et Rhizoma, Armeniacae Semen Amarum, Atractylodis Rhizoma, Descurainiae Semen Lepidii Semen, Atractylodis Rhizoma, Pogostemonis Herba, and Gypsum Fibrosum. | |

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| Lung Cleansing and Detoxifying Decoction (LCDD) (consists of Ma Xing Shi Gan (MXSG); She Gan Ma Huang decoction (SGMH), Xiao Chai Hu (XCH), and Wu Ling San (WLS)) | TCM | • The management of H1N1 influenza.<br>• The management of tonsillitis, asthma, and flu-like symptoms.Treatment of COVID-19 individuals, both severe and non-severe, is advised.<br>• Relieving early-stage extrapulmonary symptoms of diarrhea or problems related to the renal, hepatic, or cardiac systems. decreased sore throat, cough, and weariness. | Asari Radix Et Rhizoma, Belamcandae Rhizoma, Dioscoreae Rhizoma, Farfarae Flos, Aurantii Fructus Immaturus, Asteris Radix et Rhizoma, Armeniacae Semen Amarum, Citri Reticulatae Pericarpium, Zingiberis Rhizoma Recens, Scutellariae Radix, Cinnamomi Ramulus, Ephedrae Herba, Pinelliae Rhizoma, Tuckahoe, Herba Agastachis, and Glycyrrhizae Praeparata cum Melle Radix et Rhizoma | **Antioxidants**<br>• Boosts the activity of superoxide Ca2plus-ATPase, and Na ATPase, therefore lowering free Decreases oxidative stress indica and NO).<br>• Effectively combats hydroxyl free radicals<br>• Anti-lipoxygenase and ant properties.<br>• Reverse NADPH oxidase overex The ERK/Nrf2/HO-1 signaling upregulated.<br>• Preventing intracellular ROS fro up. strong DPPH-lowering action<br>• Higher glutathione and lower malondialdehyde in the lungs.<br>**Immunomodulators**<br>• TNF, IFN-γ, C-reactive prot peroxisome proliferator-activate gamma, and tumor protein P53 a of pro-inflammatory cytokine modulated.<br>• Modulates T helper cell differen 1, Th 2, and Th 17 and T receptor pathways.<br>• Enhances thymus and spleen fun<br>• Promotes the growth of CD4+ a cells.<br>• Increases the expression of IgM a<br>• Glycyrrhizin stimulates macrop natural killer (NK) cells via th pathways of Toll-like receptors Mitogen-Activated Protein Kinas |
| Banlangen granule (BLG) | TCM | • Detoxifying and therapeutic agent for exogenous fever, carbuncle sores, erysipelas, mumps, and epidemic heat syndrome.<br>• Treatment, management, and prevention of respiratory viral infections (viral hepatitis, influenza A subtype H1N1, and viral skin disorders).<br>• The method most frequently employed to stop COVID-19 infections. | Radix Isatidis | |
| Qu Du Qiang Fei I Hao Fang (QDQF1) | TCM | • Treat and prevent infections in the upper respiratory tract caused by influenza H1N1.<br>• Address bleeding, chronic weariness, anemia, appetite loss, phlegmatic problems, and weakness. | Radix Glycyrrhizae, Atractylodis Macrocephalae, Lonicerae Japonicae, Fructus forsythi, Astragali Radix, Saposhnikoviae Radix, Lonicerae Japonicae, and Forsythiae Fructus) | |
| Shufeng Jiedu | TCM | • Treatment for acute lung injury | Bupleurum chinense, Fallopia japonica, Forsythia | |

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| capsule (SFJD) | | (ALI) and respiratory infections.<br>• Treatment influenza A (H1N1)-related upper respiratory tract<br>• Treatment for Common cold, Acute Rhinitis, Herpangina, Acute pharyngitis, and Acute tonsilitis. | suspensa, Glycyrrhiza uralensis, Isatis indigotica, Patrinia scabiosaefolia, Phragmites australis, and Verbena officinalis |
| Jing Fang Bai Du pill (JFBD) | TCM | • Management of common cold, exogenous febrile illness, widespread epidemic infections, headache, lightheadedness, restlessness, body aches, cough from lung cold, and other symptoms.<br>• Epidemic infections, common cold, diarrhea, sores, and influenza are among the indications for cold dampness. | Bupleurum chinense DC, Ligusticum chuanxiong Hort., Angelica pubescens, Saposhnikovia divaricata, Poria cocos, Glycyrrhiza uralensis, Schizonepeta tenuifolia, Platycodon grandiflorum (Jacq.), Peucedanum praeruptorum, Notopterygium inchum, and Citrus aurantium L. |
| Qingfei Paidu decoction (QFPD) | TCM | • Suggested for the management of mild to severe COVID-19<br>• Hasten the resolution of cough symptoms; reduce exhaustion; and stimulate appetite. | Ephedra sinica, Glycyrrhiza uralensis, Semen Armeniacae, Gypsum Fibrosum, Cinnamomum cassia, Alisma *plantago-aquatica.,* Polyporus umbellaru, Atractylodes Macrocephala, Poria cocos, Bupleurum chinensis DC., Scutellaria Baicalensis Georgi., Pinellia ternata Zingiber officinale, and Aster tataricus |
| Ayush-64 | India Alternative and Complementary Therapies (IACT) | • Reduced cough, dyspnea, pyrexia, headache, and sore throat.<br>• Commonly used for the common cold, sore throat, cough, runny nose, fever, and other illnesses. | Alstonia scholaris R. Br., Picrorhiza kurroa Royle ex. Benth, Swertia chirata Pexbex. Karst, and Caesalpinia crista L., Ocimum sanctum, Cinnamomum verum, Zingiber oficinalae, Piper nigrum. |
| Ashwagandha | IACT | Well known as a rejuvenator drug indicated in dyspnea and cough. | Withania somnifera (L.) Dunal |
| Guduchi | IACT | Hepatoprotective, antimicrobial, | Tinospora cordifolia Willd. |

- Macrophages' phagocytic towards andrographolide
- Boost host cells' cellular response.
- Thoothuvalainei increases ant levels and inhibits lipid peroxida enzymes in the blood and liver.
- In host cells, flavonoids pr production of interferons that fig
- Inhibition of B-lymphocyte p elevation of hemagglutination reduction of serum IgA, IgM, and
- Focus on controlling the PD-1/IL control the invasion of macro neutrophils.
- Inhibition of the potentiation of c hypersensitivity (DTH) reaction by cyclophosphamide.
- Enhanced PMN cells, including and macrophages, as well as eosinophils, mast cells, and baso

**Organ Protections**

- Decreased apoptosis caused b reducing ALI incidence.
- It reduces pulmonary oedem inflammatory cell infiltration a expression of inflammatory cy
- Inhibit fibroblast collagen intestinal flora.
- Decrease cough sensitivity, iro agent, scavenges hydroxy superoxide radicals, and DPPH
- Relieve ox-LDL-induced oxid via the ERK/Nrf2/HO-1 signa

| | | | | |
|---|---|---|---|---|
| Ghanavati | | antioxidant, antitoxic, antidiabetic, hypolipidemic, anti-malarial, and anti-neoplastic. | | pathway, NOS, NO, and MDA<br>• Promote the growth and regu normal flora in the gut, such a Bifidobacteria, Lactobaci Lactococcus.<br>• Suppress alveolar epithelial initiated via NF-κB and p pathway.<br>• Decreases total neutrophil c helps clear the lungs, preve impairment—inhibition of A Converting Enzyme II (ACE2)<br>• Activating a transcription fac causes evading apoptosis in dependent manner in cardiomyocytes.<br>• Reversed the effects of reperfusion on the activitie peroxidation (LPO), catala glutathione peroxidase (G superoxide dismutase (SOD). |
| Chyawanpras ha | IACT | It is used to treat conditions like asthma, TB, allergic bronchitis, the common cold, and cough. | Phyllanthus emblica | |
| Nilavembu Kudineer (NVK) decotion | IACT | Antiviral for Chikungunya and Dengue virus. | Andrographis paniculata, Vetiveria zizanioides L., Santalum album L., Piper nigrum L., Cyperus rotundus L., Hedyotis corymbosa L.Lam., Plectranthus vettiveroides (K.C.Jacob), Zingiber officinale Roscoe., and Trichochanthes cucumerina L. | |
| Kaba Sura Kudineer (KSK) decotion | IACT | • It is commonly used for fever and respiratory diseases. It's used to treat pox viral infections and herpes infections.<br>• Accelerate the disappearance of cough, shortness of breath, breathlessness, and fever. | Piper longum L., Anacyclus pyrethrum L., Zingiber officinale Roscoe., Tragia involucrate L., Solanumanguivi Lam., Anisochilus carnosus, Costus speciosus, Tinospora cordifolia, Syzygium aromaticum, Clerodendrum serratum (L.), Andrographis paniculata (Burm.f.), Cyperus rotundus L., Terminalia chebula, Justicia adathoda L., and Sida acuta. | |

5.2. Traditional Practices

- Acupuncture

For many years, several problems have been addressed using acupuncture. The medical philosophy and treatment technique of acupuncture is predicated on the idea of applying pressure or tiny needles to particular body locations. Acupuncture aims to balance surplus energy that is flowing through specific body channels (Song et al., 2019). Acupuncture is often recommended for the treatment of pain, both acute and chronic, including fibromyalgia, rheumatoid arthritis, chronic daily idiopathic pain, migraine, tension headaches, myofascial pain syndrome, and nausea and vomiting (Schweiger et al., 2020). It is believed that acupuncture reduces inflammation (Kwon et al., 2018). Nonetheless, two particular contraindications deserve special attention: those who are expected to have psychosis or delusions, as well as patients who have an automatic implanted cardioverter-defibrillator (AICD) (Zhang J et al., 2022).

Additionally, acupuncture can lessen the intensity of anxiety and sadness, enhance sleep, treat insomnia, and improve cognitive damage following a stroke. Acupuncture also addresses physiology, neuropsychiatric problems, and olfactory impairment (anosmia, ageusia, and sleeplessness) (Liu et al., 2020). Acupuncture has the potential to be beneficial in treating some contemporary acute infectious diseases, acute bacterial dysentery, epidemic dengue fever, and severe acute respiratory syndrome (SARS) (Xu et al., 2021; Wang et al., 2020). Its benefits include fever reduction, phlegm and cough relief, gastrointestinal symptom relief, respiratory function improvement, and prevention of disease progression (Helianthi et al., 2022).

In mild-to-moderate COVID-19 patients, the combination of acupuncture and pharmaceutical medications has already shown promise, as evidenced by a noteworthy reduction in the length of cough symptoms compared to solo pharmaceutical therapy (Boehmer et al., 2020). Acetylcholine is released more when vagus cholinergic anti-inflammatory pathway is activated by acupoint stimulation. After binding to the α7nAChR receptor on macrophages, acetylcholine prevents the release of cytokines that promote inflammation. The anti-inflammatory adrenal-dopamine vagus-medullary pathway is triggered by stimulation of other sites, resulting in the production of dopamine. This neurotransmitter can bind to type I dopamine receptors and suppress pro-inflammatory cytokines such as IL-6, INF-γ, and TNFα. When acupoints are stimulated simultaneously, TLR-4 and NF-κB activation is inhibited, which lowers the release of pro-inflammatory cytokines (Boehmer et al., 2020; Wang and Pariante, 2021). In addition, it has been demonstrated that stimulation at sites LI4 and ST36 raises blood levels of cortisol and ACTH and directly suppresses the production of IL-6, which lowers ferritin and CRP. Additionally, acupuncture can enhance host-disease interactions and lessen the generation of ROS and NO (Morita et al., 2022).

According to clinical studies, patients were treated by two TCM-licensed acupuncturists (LAcs) who inserted auricular needles with insertion depths ranging from 0.1 to 1.0 cun before receiving body needles. Thirty minutes retention of needle in conjunction with De Qi, twisting, and lifting techniques has been shown to improve various PCS symptoms, including pain, ageusia, fatigue, anxiety, anosmia, brain fog, dyspnea during exercise, dry cough, chest pressure, and palpitations (Trager et al., 2022; Hampton and Bartz, 2021). No adverse effects have been reported.

- Yoga

Yoga is a comprehensive kind of physical and mental well-being that has its roots in ancient India. Numerous yoga practices, including asana (postures), dhyana (meditation), and pranayama (breathing exercises), seem to provide a variety of therapeutic benefits. Yoga has been shown to improve mental health, including lowering anxiety and sadness, as well as metabolic problems and low back pain (Saeed et al., 2019). Energy balance is achieved by yoga practice, and immune system performance depends on it. The hypothalamus's posterior or sympathetic region may be inhibited by yoga. This inhibition

optimizes the body's sympathetic response to stressful stimuli and restores the autonomic regulating reflex processes associated with stress. While blocking the regions in charge of anger, violence, and fear, yoga practice activates the positive pleasure centers in the middle forebrain and other areas that contribute to moods of contentment and pleasure. Reduced anxiety, heart rate, breathing rate, blood pressure, and cardiac output are the results of this inhibition. Regular yoga practice lowers levels of monoamine oxidase, an enzyme that degrades cortisol and neurotransmitters, and dramatically raises serotonin levels. This helps people get over their worry, tension, and despair (Bushell et al., 2020). Another advantage of yoga is increased mobility, which is achieved by increasing relaxation of the muscles and connective tissue around the bones and joints with continued practice. This is thought to be one of the reasons yoga is associated with reduced aches and pains. As a result, yoga has been suggested as a kind of rehabilitation for individuals who have had COVID-19 or who have symptoms of PCS. Through its anti-inflammatory, anti-oxidant, and immunomodulatory qualities as well as its ability to increase serotonin activity, yoga exerts organ-protective benefits on the cardiovascular and respiratory systems (Basu-Ray et al., 2022; Srinivasan et al., 2021).

In a clinical trial, quality of life, pulmonary ventilation, and muscle strength—particularly biceps and quadriceps—can all be enhanced by pursed lip breathing combined with bhastrika pranayama exercise three times a day for five minutes each session for six weeks. No negative effects have been documented (Macedo et al., 2023). An additional workout routine consists of 60 minutes of yoga practice twice a week for eight weeks. The breathing exercises consist of three parts: ten minutes of standing breathing, ten minutes of sitting breathing with an asana, and ten minutes of stretching breathing. These exercises have been shown to enhance sleep quality, lessen anxiety, depression, and stress episodes, relieve dyspnea, improve lung function and capacity, increase vital capacity, lower heart rate, lower systolic blood pressure, and raise tidal volume.

- Tai Chi

Chinese martial art tai chi is a form of light to moderate cardiovascular exercise that integrates mental and physical training. Tai Chi is one among the suggested physical exercises during the COVID-19 pandemic to enhance fitness, including boosting heart rate, blood pressure, body mass index, weariness, mental health, sleep difficulties, balance and motor control, and strength and aerobic capacity (Easwaran et al., 2021; Polero et al., 2021; Shu et al., 2021).

Tai Chi is an indirect anti-inflammatory and immunomodulatory agent since it can alter the immune system and pro-inflammatory cytokine responses. Both the innate and adaptive immune systems' cell counts can be raised by practicing tai chi. Engaging in regular Tai Chi exercise raises T cells and the percentage of natural killer (NK) cells, which raises the Th1 immune response and may improve antiviral function. Furthermore, Tai Chi can decrease CRP as well as proinflammatory cytokines like IL-1b, TNF-α, and IL-6 (Zouwt al., 2018). Tai chi also promotes the synthesis of other enzymes, including MnSOD, iNOS, and glutamylcysteine synthetase, which has an indirect antioxidant impact. By controlling elevated levels of cortisol, adrenaline, and insulin-like growth factor and boosting the synthesis of brain-derived neurotrophic factor and insulin-like growth factor—two neurobiological markers linked to emotional regulation—tai chi practice also lessens negative emotions like depression, anxiety, and melancholy (Zhang et al., 2019; Wu et al., 2022).

Five Tai Chi moves that were applied by the classic Cheng Man-Ch'ing Yang-style short form were used in several therapeutic investigations. For a duration of 12 weeks, patients participated in twice-weekly tai-chi courses, lasting roughly 60 minutes each. The outcomes of these studies demonstrate that PCS patients improve lung function, including FEV1/pred and FEV1/FVC, by strengthening their respiratory muscles and expanding their lung capacity. Diminish unfavorable feelings including despair, worry, and depression. improved bodily health statement, quality of sleep, and symptoms of exhaustion.

5.3 Nutraceutical and Supplementations

Anti-inflammatory, immunomodulatory, antiviral, and antioxidant compounds are known as nutraceuticals. Nutraceuticals frequently contain zinc, vitamins, curcumin, probiotics, selenium, and quercetin, among other ingredients, according to Barrea et al., 2022. These ingredients might provide alternative therapeutic and prophylactic effects for PCS and COVID-19 (Fratta et al., 2021; Pastor et al., 2021). Nutraceuticals are made up of active phytochemical components that are isolated from plants, food supplements, and functional foods. They are known to have medicinal properties (Catalano et al., 2022).

- Vitamins

  One of the supplements that is advised for PCS prevention, treatment, and recovery is vitamin C. It is well-recognized that some vitamins, including A, C, D, and E, can treat PCS and COVID-19 disorders. It has been demonstrated that ascorbic acid, sometimes referred to as vitamin C, has antithrombotic, anticancer, and antioxidant qualities. In general, fruits like oranges and kiwis as well as vegetables like spinach contain vitamin C (Zhao et al., 2021). Vitamin C can prevent thrombotic effects, minimize oxidative stress, lower inflammation, manage cytokine storms, and lessen vascular and alveolar damage, according to several clinical investigations on COVID-19 infection. Additionally, individuals with severe and serious COVID-19 showed a significant rise in CD4, lymphocyte count, and C- C-reactive protein (CRP) after administering vitamin C (Zhang J et al., 2021). A placebo-controlled pilot experiment by Zhang et al. (2021) demonstrated a substantial reduction in mortality with high-dose intravenous vitamin C (HDIVC) treatment, using a daily dose of 24 g of ascorbate. HIDIVC does not influence the length of ventilation discharge days in patients, although it may enhance lung function as indicated by an increase in the PaO2/FiO2 ratio (Tosaco et al., 2022). Giving 500 mg of liposomal vitamin C and l-arginine for 28 days improved endothelial function, muscle strength, gait performance, and fatigue in patients with PCS who had persistent fatigue, according to another RCT study. The patients also reported feeling less tired than before. Therefore, one may consider using this supplement to enhance athletic performance and lessen persistent COVID-19 symptoms.

  Furthermore, vitamin A has a clinical effect on weakness, tiredness, fever, and bodily aches. Along with improvements in symptoms like chills, coughing, shortness of breath, hyposmia, anorexia, and diarrhea, ten days after the intervention there was also a drop in the amount of C-reactive protein as well as white blood cell as compared to normal treatment alone (Rohani et al., 2022; Masnadi et al., 20218). Furthermore, vitamin A plays a crucial role in the formation of helper T cells, T cells, and B cells, all of which are essential for the maintenance of the immune system (Albergamo et al., 2023).

  Clinical investigations and recent meta-analyses have shown that vitamin D functions by altering the expression of ACE 2 and the renin-angiotensin system (RAS). This will induce the ACE2/Ang axis, 1-7, and press the ACE/Ang II/AT1R axes, hence reducing acute lung injury caused by lipoprotein (LPS). Furthermore, vitamin D stimulates defense systems like macrophages and lowers proinflammatory cytokines while raising anti-inflammatory cytokine levels, which can eradicate SARS-CoV-2. It also stimulates the creation of natural antimicrobial peptides. A clinical trial (Fernandes et al., 2018) found improvements in ferritin, lactase dehydrogenase, IL-6, CRP, and the ratio of neutrophils to lymphocytes in patients who received 60,000 IU of vitamin D supplements daily for eight days. Although vitamin D3 had a positive effect on COVID-19 infection, the findings of Fernandes et al. 2018 and Popescu et al., 2022 did not justify the use of a single dosage of 200,000 IU for the repair of cytokines, chemokines, and growth factors. Nevertheless, given that a number of other studies have indicated that a vitamin D deficit is a predictor of a bad prognosis for COVID-19 patients, supplementing with adequate levels of vitamin D can still provide the therapeutic benefits of immunomodulators (Fratta et al., 2021). Furthermore, a comprehensive approach to treating Telogen effluvium, also known as post-infection hair loss, is necessary to address one of the side effects of PCS. This approach involves the use of zinc, biotin, vitamins A, C, E, and D, as well as organic compounds like Omega-3 (Magdalena et al., 2022).

  There are high concentrations of vitamin E in green leafy vegetables, almonds, and sunflower and

olive oils. It's common knowledge that vitamin E is a strong antioxidant. As an antioxidant that protects cell membranes from oxidative stress, the component α-tocopherol has a defensive role. Because α-tocopherol may absorb reactive oxygen species (ROS), it can stop the oxidative burst that is linked to SARS-CoV-2. In addition, vitamin E promotes T-cell differentiation and proliferation, reduces the generation of inflammatory cytokines, and alters the inflammatory response in a number of organs, including the lungs. Studies with both human and animal models have shown that vitamin E enhances the immune response through nitric oxide production reduction, prostaglandin E2 reduction, cyclooxygenase-2 inhibition, T-lymphocyte communication, and modification of the Th1/Th2 ratio. Additionally, it controls protein kinase C to function as an immunoregulator.

- Mineral

  Zinc (Zn) is the second most prevalent metal in the human body. Moreover, zinc has antiviral, anti-inflammatory, immune-stimulating, and membrane-stabilizing properties. In the bone marrow, zinc stimulates the development of B lymphocyte cells. In COVID-19, zinc inhibits RNA polymerase activity. Zinc responds well to low dosages of hydroxychloroquine, which also reduces the number of patients who need to be admitted to the hospital (Rohani et al., 2022). The effects of type-I interferon (IFN) can be amplified by zinc. Supplementing with zinc gluconate reduces the influx of neutrophils into the airways, releases TNF-α, and prevents the transcription of inflammatory genes that are dependent on NFkB. By reducing inflammatory cytokines (IL-6 and IL-1β), zinc supplementation may help improve a protective type-I IFN response in COVID-19 (Pal et al., 2021).

- Fatty acids

  Omega-3 polyunsaturated fatty acids with a long chain, also known as n-3 PUFA, have been shown to have anti-inflammatory, antioxidant, and psycho-neuro-immunological properties. Omega-3 polyunsaturated fatty acids have been demonstrated to treat mood disorders by decreasing proinflammatory cytokines, reestablishing the HPA axis, changing the gut-brain axis, modulating nerve transmission via lipid rafts, and maybe improving immunity to both physical and mental effects. Treatment with UFA omega-3 is advised for neuropsychiatric issues brought on by PCS, such as brain fog, weariness, anxiety, and depression. Strong anti-inflammatory properties are shown by the D-series resolvins, maresins, and protectins from DHA as well as the E-series resolvins from the Omega 3 group EPA. These properties inhibit the migration of neutrophils and monocytes across epithelial cells, as well as the production of cytokines (TNF-α and IL-1β) and chemokines in wounded tissue. Furthermore, they facilitate the removal of leukocytes, apoptotic cells, polymorphonuclear neutrophils (PMN), and cell remains from inflammatory areas. Omega-3 polyunsaturated fatty acids (PUFAs) can directly reduce free radical levels because they can control pro-oxidant enzymes like nitric oxide synthase and antioxidant enzymes like superoxide dismutase (Darwesh et al., 2021).

  According to Lordan et al., 2020, PUFAs also promote the synthesis of endothelial nitric oxide synthase (eNOS), inhibit the expression of TGF-beta, enhance the production of advantageous prostaglandins, block the activity of angiotensin-converting enzymes, decrease the production of angiotensin II, and strengthen the parasympathetic nervous system. Because of their capacity to act on the platelet membrane via COX-1 and 12-LOX to reduce platelet aggregation and TX release and metabolize fatty acids in platelets to the advantageous oxylipine group, the PUFA omega-3, EPA, and DHA groups play a major role in the regulation of platelet function in hemostasis and thrombosis.

- Fermented foods

  Morinda citrifolia and Carica papaya are sources of fermented dietary supplements that have been shown to have anti-inflammatory, redox balancing, immunological modulation, faster regeneration, and memory-improving properties (Kharaeva et al., 2022). An RCT has demonstrated that this combination of vitamins can alleviate the clinical symptoms of Parkinson's disease (PCS), which include weakness, diminished mental and physical functioning, headaches, dizziness, insomnia, and insomniac episodes.

Treatment for psychological and mental health conditions also includes addressing apathy, anxiety, melancholy, and emotional instability (anger, irritability, sadness). Additionally, by lowering tachycardia, arrhythmia, and heart discomfort, this vitamin shields the heart. It also affects the bones, joints, and muscles, which helps prevent discomfort in those areas. In fact, it lessens hair loss and dry skin (Zhang K et al., 2022).

## 6. Conclusion

Studies on complementary and alternative therapies, including herbal remedies, conventional medicine, nutraceuticals and supplements, have demonstrated promising outcomes in treating problems that affect PCS patients. This is demonstrated by the patients' improved clinical conditions with no appreciable side effects. Because of this, these modalities represent a potentially effective alternative therapy for PCS patients. Although there are positive prospects for the combination of these alternative therapeutic approaches, there is still uncertainty regarding the safety and efficacy of the combined therapy due to potential side effects. In selecting alternative therapies for PCS patients, several factors should be considered, such as the patients' psychosocial, the alternative therapies' cost-effectiveness, and the clinical symptoms in the patients. It must be considered in order for medical professionals to identify and offer appropriate alternative therapies in order to treat PCS patients' symptoms as effectively as possible.

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