SUNTEXT REVIEWS

SunText Review of Cardiovascular Sciences

Open Access
Review Article
Volume 1:1

Herbal Remedies for Management of COVID-19 Induced Myocarditis

Ghaffari M*

College of Science and Health, Benedictine University, USA

***Corresponding author:** Ghaffari M, College of Science and Health, Benedictine University, USA; Tel: +1 (630)829-2270; E-mail: mghaffari@ben.edu

Received date: 07 June 2021; **Accepted date:** 21 June 2021; **Published date:** 27 June 2021

Citation: Ghaffari M (2021). Herbal Remedies for Management of COVID-19 Induced Myocarditis. SunText Rev Cardiovasc Sci 1(1): 104.

Abstract

Novel Coronavirus (COVID-19), which first appeared in late 2019, is a pandemic that has spread over the world. This virus quickly spread over the world due to its great transmissibility, creating serious health problems. COVID-19 is easily transmitted from person to person. When an infected individual coughs or sneezes, it spreads through their respiratory secretions, such as fluid droplets. This virus not only harms the lungs, but it also harms the heart. The virus causes inflammatory cells to infiltrate the body, causing significant edema. All of these factors can have a negative impact on heart function, leading to the development of HF. Myocarditis can be caused by a virus-induced cell-mediated autoimmune response. Edema of the cardiac interstitium, as well as necrosis of the myocardium and interstitial connective tissue, are symptoms of this form of virus-induced myocarditis. There are currently no specific medications that can effectively block the virus. In-silico, in-vitro, and in-vivo techniques were used to explore several natural treatments and chemicals, including alkaloids, terpenes, flavonoids, and benzoquinones, but there was insufficient data. Natural antiviral compounds having a broad antiviral range could provide a safe, effective, and low-cost platform for discovering new SARS-CoV-2 treatments. This article summarizes the epidemiology and pathophysiology of COVID-19, as well as herbal therapies that can target inflammation, inflammatory cells, and the respiratory and cardiac consequences that come with them.

Keywords: COVID-19; Myocarditis; Herbal medicine; Inflammation

Introduction

The World Health Organization (WHO) declared the COVID-19 outbreak a pandemic on March 11, 2020, after it was first reported on December 8, 2019 in China's Hubei region. Dr. Zhang Jixian of Hubei Provincia Hospital of Integrated Chinese and Western Medicine identified this condition as an infection with a novel beta coronavirus [1]. Coronaviruses are single-stranded RNA viruses that belong to the Coronaviridae family of viruses. Within the coronavirus family, there are four different genera, Alphacoronavirus, Betacoronavirus, Gammacoronavirus, and Deltacoronavirus. Middle East respiratory sickness (MERS-CoV), SARS CoV, SARS-like bat CoV, and now SARS-CoV-2 are all members of the Betacoronavirus lineage within the Coronaviridae subfamily [2]. Despite the fact that it has a preference for the lungs, where it produces interstitial pneumonitis, in the most severe instances, multiorgan failure ensues. COVID-19 appears to have intricate interactions with the cardiovascular (CV) system. Understanding the underlying pathobiology of coronavirus infection is critical for better understanding the relationships between cardiovascular disease (CVD) and COVID-19 [1]. SARS-CoV-2 infects the host cell by triggering cell membrane receptors, notably the ACE2 receptor, to recognize the virus's spike proteins. Lung, kidney, heart, and gastrointestinal cells all have ACE2 receptors. The viral envelope merges with the host's cell membrane after this interaction and a conformational shift in the spike protein, releasing the viral RNA into the host cell. The viral RNA replicates its genetic material and synthesizes new proteins once inside the host cell [2]. Integrins may also be used by SARS-CoV-2 to enter the host cell. Integrins are a class of cell-surface receptors made up of non-covalently linked subunits that identify and bind to ECM proteins and regulate cell survival, proliferation, differentiation, and migration [2]. COVID-19 infection is linked to systemic inflammation, a pro-inflammatory cytokine storm, and sepsis, which can lead to multiorgan failure and death. There is a time lag between the onset of symptoms and the occurrence of cardiac injury. COVID-19 binds to the transmembrane ACE2 to gain access to host cells such as type 2

pneumocytes, macrophages, endothelial cells, pericytes, and cardiac myocytes, causing inflammation and multiorgan failure. Infection of endothelial cells or pericytes, in particular, could cause significant microvascular and macrovascular dysfunction. It can also destabilize atherosclerotic plaques and explain the development of acute coronary syndromes when combined with immunological over-reactivity [1]. Despite the fact that the virus's primary organ of harm is the lung, COVID-19 is now considered a systemic disease that affects a wide range of other critical organs, including the heart, liver, and kidney. However, it's still unclear whether organ and tissue damage in COVID-19 individuals is a direct or indirect result of the viral infection [3]. The virus could target organs and tissues that have ACE2 expression. ACE2, a major regulator of blood pressure and cardiac contractility, is known to be highly expressed in cardiovascular cells [4]. Patients with COVID-19 have been reported to have changes in cardiac-specific biomarkers in their peripheral blood. As previously indicated, hs-cTnI is a specific biomarker for myocardial damage. Other non- or less-specific cardiac biomarkers, such as creatine kinase (CK), creatine kinase MB isoenzyme (CK-MB), and lactate dehydrogenase, may also rise in COVID-19 cardiovascular problems (LDH). The biomarkers, on the other hand, may not always change in the same way [5]. Recent autopsy findings revealed significant levels of inflammatory infiltrates in the lung and heart tissues, demonstrating the inflammatory character of tissue damage caused by SARS-CoV-2 infection. SARS-CoV-2 has the potential to directly infect cardiomyocytes, resulting in viral myocarditis and damage. However, the precise cellular process by which SARS-CoV-2 infects and damages cardiomyocytes has yet to be identified. COVID-19 treatment has largely been limited to supportive measures because of the lack of a specific therapy for this condition to date. Pre-existing health problems raise the likelihood of cardiovascular comorbidity, which leads to a worse prognosis. COVID-19-induced myocardial damage is more common in patients over 60 and those with diabetes [6].

Coronavirus Related Cardiovascular Consequences

Myocarditis and/or pericarditis can be caused by the coronavirus, which may or may not be accompanied with pneumonia. Heart failure, arrhythmias, diffuse ST-segment abnormalities, and substantial production of myocardial enzymes such as natriuretic peptides and troponin are all symptoms of this myocarditis. COVID-19 patients have been documented to experience a variety of cardiovascular problems. Acute myocardial damage, myocarditis, arrhythmia, pericarditis, heart failure, and shock are all common consequences [7-10]. The etiologic agent of COVID-19, severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2), can infect the heart, vascular tissues, and circulating cells via ACE2, the host cell receptor for the viral spike protein. Acute cardiac damage is a common extra pulmonary symptom of COVID-19, and it can have long-term repercussions. Myocarditis is difficult to diagnose because of its diverse clinical presentation, which can range from asymptomatic left ventricular systolic dysfunction to mimicking the symptoms of acute myocardial infarction. Myocarditis is characterized by inflammation brought on by immune system cells' activity. Natural killer cells come first, within 5 days of viral infection, according to animal studies, followed by CD4 and CD8 T cells 5 to 7 days later. T cell invasion is accompanied by neutrophil and macrophage infiltration, which contributes significantly to the pathophysiology of myocarditis. When there is a long enough period of inflammation, Th17 T cells have been found to enter the myocardium [11].

COVID-19 cardiovascular epidemiology

COVID-19 is a disease that affects the cardiovascular system. Patients with acute myocardial infarction were older, with a higher prevalence of previous CVD, according to a new statistic. COVID-19 patients with acute heart damage accounted for 12% of the total. Furthermore, a rent review article found that cardiac Troponin, a biomarker of myocardial damage, was elevated in roughly 5–25 percent of hospitalized COVID-19 cases [12]. In 3470 COVID-19 patients, a systematic analysis of 72 papers from different countries found a pooled prevalence of cardiovascular disease and hypertension of 8.3% and 13.3%, respectively [13].

The pathophysiology of patients with COVID-19

COVID-19 can damage cardiomyocytes by recognizing ACE2 receptor infections and generating numerous inflammatory responses, according to the pathophysiology of COVID-19 patients. ARDS can generate an inflammatory storm and/or an oxygen supply imbalance by directly damaging infected cardiac cells via ACE2 receptors on these cells. Cardiovascular symptoms are common in COVID-19 individuals as a result of systemic inflammatory reactions and immune system dysfunction. COVID-19 infection has been linked to myocardial injury due to a cytokine storm triggered by an unbalanced response including Th1 and Th2 cells, which can result in respiratory failure, hypoxemia, shock, or hypotension. Myocardial damage occurs during an infection, especially in people with chronic CVD, since the burden on the heart is increased and there is an imbalance in the oxygen supply and demand. Angiotensinogen, renin, angiotensin II (Ang II), Ang II receptors, such as AT1 and AT2 receptors, and angiotensin converting enzyme (ACE) make up the renin-angiotensin system (RAS). ACE2 is found in venous and arterial smooth muscle cells, as well as endothelial cells, and is involved in the immunological response and cardiovascular mechanisms that lead to myocardial injury. COVID-19 infection is caused by the viral spike protein binding to ACE2, according to

several studies. One major proteinase is encoded by all coronaviruses. This major proteinase is known as a 3C-like proteinase. As a result, the coronavirus enzyme is known as one major proteinase is encoded by all coronaviruses. This major proteinase is known as a 3C-like proteinase. Coronavirus 3C-like proteinase, or 3CLpro, is the name given to the coronavirus enzyme. The 3CLpro is similar to the 3Cpro, which is the major picornaviral protease. Coronaviruses also contain one (group 3) or two (groups 1 and 2) papain-like proteases, known as PLP1pro and PLP2p, respectively. The coronavirus replication complex is controlled by the primary viral proteinase (3CLpro). It may be an appealing therapeutic target. PLpro might also be regarded an important target for antiviral medicines because to its significant role. For the SARS coronavirus (SARS-CoV) and SARS-CoV-2 to reach the host target cells, ACE2 is a functional receptor. As a result, ACE2 inhibition could be evaluated for antiviral research against SARS- CoV and SARS-CoV-2 [13]. As a result, these three proteins are promising targets for therapeutic development. Inflammatory reactions triggered by COVID-19 infection are classified as primary or secondary. Prior to the formation of neutralizing antibodies, the major inflammatory response usually occurs after viral infections. Adaptive immunity and antibody neutralization are the first steps in the secondary inflammatory response. Myocardial damage is observed to be worsened in patients with increased inflammatory activity, platelet activation, increased thromboxane production, and reduced fibrinolytic function after an acute infection. The early inflammatory and immunological response has caused a significant cytokine storm [IL-6, IL-7, IL-22, IL-17] during COVID-19's rapid proliferation. C-reactive protein (CRP) levels that are elevated in COVID-19 patients indicate the presence of inflammation. In addition, patients with CAD had higher levels of inflammatory cytokine expression in epicardial adipose tissue (EAT). COVID-19 infection can cause a variety of heart symptoms, including myocardial damage, arrhythmia, and even cardiac collapse. Increased high-sensitivity cardiac troponin I (cTnI) levels have been found to indicate myocardial damage due to COVID-19 infection in some patients. Heart failure has been proposed as one of the most common COVID-19 consequences, which could be caused by worsening preexisting cardiac dysfunctions as well as newly formed cardiomyopathy and myocarditis [14,15]. Patients with COVID-19 in the early stages may have a normal or low total white blood cell count, as well as a low lymphocyte count. As a result of the higher ratio of neutrophils to lymphocytes that occurs with lymphopenia, the higher ratio of neutrophils to lymphocytes is considered a negative prognostic factor. LDH, muscle enzymes, and C-reactive protein levels may be elevated in patients. In critically ill patients, the thrombogenic biomarker D-dimer may rise, blood lymphocyte counts fall steadily, and laboratory changes in multiorgan damage biomarkers become noticeable. The lung and heart tissues contain significant levels of inflammatory infiltrates, demonstrating the inflammatory character of tissue damage caused by SARS-CoV-2 infection [12].

COVID-19 Treatment and Management

COVID-19 is primarily treated with supportive care. Support is frequently necessary for myocarditis-related diseases such as arrhythmia and heart failure. There is currently no specific treatment for this condition. SARS-Cov-2 RNA transcription was reduced when broad-spectrum antiviral medicines like Remdesivir were used. These medications are still being studied in clinical trials. ACE inhibitors and angiotensin receptor blockers, neutralizing antiviral plasma, stem cell transplantation, anti-ischemic therapy, and traditional herbal medicines are among the other treatment options. Blocking the angiotensin-converting enzyme (ACE), which is required for SARS-CoV-2 cell adhesion, is one of the most intriguing mechanisms. As a result, two proteins, 3C-like protease (3CLpro) and angiotensin-converting enzyme 2 (ACE2), have been proposed as potential targets for screening medicines for their capacity to suppress SARS-CoV-2 replication and proliferation. The ability of herbal therapies developed from traditional medicines to cure myocarditis is now being researched. These medicines might be made up of extracts from a single plant species or extracts from numerous sources. The sections that follow provide an overview of complementary and herbal medicine.

Herbalism and complementary medicine

The term complementary medicine refers to a wide range of health-care techniques that aren't part of a country's traditional or conventional medicine and aren't fully incorporated into the dominant health-care system. In certain countries, they are used interchangeably with traditional medicine. The purpose of this review is to summarize the effects of a few herbal treatments on the cardiovascular and immune systems. Herbal medicines include herbs, herbal materials, herbal preparations, and completed herbal products that contain active substances, plant parts, other plant materials, or combinations thereof as a supplemental medical method. Herbal products, botanical goods, and phytomedicines are items manufactured from botanicals or plants that are used to treat ailments or maintain health. Taking herbal supplements has been around for thousands of years [7]. Herbal supplements are considered foods by the FDA, not medicines. As a result, they are exempt from the same testing, manufacturing, and labeling requirements as pharmaceuticals. Complementary and alternative medicine (CAM) has exploded in popularity in the United States in recent years. The Institute of Medicine claimed in their book, Complementary and Alternative Medicine in the United States, that more than one-third of

American adults use some type of CAM, and that annual visits to CAM providers outnumber visits to primary care physicians. Herbal drugs are regulated by the FDA as dietary supplements in the United States. The approval and marketing of herbal remedies in the European Union is governed by national legislation. If a product has been used in the European Union for at least 15 years (traditional use registration), no clinical testing or efficacy trials are required [11]. Herbal items have labels that explain how herbs might affect various bodily functions. Herbal supplement labeling, on the other hand, cannot relate to the treatment of specific medical diseases. This is due to the fact that herbal supplements are not subjected to the same clinical research or manufacturing regulations as prescription or over-the-counter pharmaceuticals [8]. Herbal drugs, unlike conventional drugs, do not require clinical trials or formal regulatory permission before being marketed, and as a result, their efficacy and safety are rarely demonstrated. Although herbs have been shown to have an influence on biological mechanisms associated to the cardiovascular system, there is a dearth of data on clinical effects. Physicians should always evaluate their patients' use of herbal drugs and discuss the potential advantages and adverse effects with them. Herbs have been utilized for medical purposes for thousands of years in the past. Herbal drugs have been more popular in cardiovascular medicine than in other medical professions. Digoxin and digitoxin, which are derived from Digitalis lanata and Digitalis purpurea, respectively; reserpine, which is derived from Rauwolfia serpentina and was originally used to treat psychosis; and acetylsalicylic acid (aspirin), which is obtained from willow bark. Efficacy of herbal treatments in treating myocarditis is being studied in a number of clinical trials. One of the problems with employing these medicines is that the contents of these mixtures are mostly unknown, as well as the heterogeneity of herbal medicines. Based on the pathophysiology of COVID-19 and its multisystem effects, herbal treatments with antiviral activity, immune system enhancement, and anti-inflammatory effects are some of the therapeutic methods that can be used. The following section will go over these topics.

Herbal Remedies

Medicinal herbs and extracts have been utilized for decades in ethnobotany, traditional Chinese medicine (TCM), and Ayurvedic medicine because they appear to have favorable effects on health. A recent study in Wuhan, China, found a link between the TCM notion of "invigorating spleen and removing moisture" and an improvement in new coronavirus pneumonia (NCP), highlighting the relevance of intestinal function and microenvironmental balance. The treatment comprised TCM ingredients such quercetin, luteolin, and kaempferol [16-18].

1,8-Cineole: (Eucalyptol)-is a natural chemical found in a variety of plants, including cardamom and bay leaf. It's a monoterpene oxide and cyclic ether. It possesses anti-inflammatory and bronchodilatory properties, and it has a high pharmacological effect against respiratory disorders. It's used to treat a wide range of respiratory and inflammatory conditions. Furthermore, it has been demonstrated that it inhibits the expression of NF-B in humans [19-23].

6-gingerol: Turmeric contains a bioactive compound called 6-gingerol. It contains anti-inflammatory, antiviral, antibacterial, anti-diabetic, anti-oxidant, and anti-cancer properties, according to studies. TNF-, IL-2, and IL-8 expression in infected cells were all regulated by 6-gingerol. It inhibits the cell's production of pro-inflammatory cytokines [23].

Anethole: It is a phenlypropanoid (natural aromatic chemical) generated from essential oils. It's found in fennel seed and star anise. Anethole decreased TNF-, IL-6, and IL-1 expression in infected mice, according to a study. Anti-inflammatory cytokine (IL-10) expression rose at the same time.

Apigenin: It is a flavonoid that can be found in large concentrations in parsley, celery, onions, oranges, and plants. Apigenin has been shown to have antioxidant, antihyperglycemic, anti-inflammatory, and antiapoptotic effects (in myocardial ischemia). Biological effects, such as cytostatic and cytotoxic activity against various cancer cells, antiatherogenic and protective actions in hypertension, cardiac hypertrophy, and autoimmune myocarditis, have been detailed in a recent review, indicating additional potential health advantages. The mechanism of action of apigenin is based on its modulatory actions on dendritic cells, which are responsible for immunological homeostasis [18].

Astragaloside IV (ASIV): It is a pharmacologically active component of Astragalus membranaceus, a traditional Chinese medicine with anti-inflammatory, antifibrotic, antioxidant, antiasthma, and immune-regulatory properties [14]. Several studies have showed that using ASIV can help in the treatment of cardiovascular disorders such hypertension, myocardial infarction, and cardiomyopathy. ASIV increased cardiac function and reduced cardiac hypertrophy in studies by upregulating Nrf2, which was largely done via boosting the Nrf2/HO-1 signaling pathway [21].

Capsaicin: A phytochemical found in chili peppers. In cells, capsaicin reduces the expression of NO, TNF-, and IL-1. Furthermore, it stimulates IB expression while preventing NF-B p65 from translocating from the cytoplasm to the nucleus. It also stopped NOS and COX-2 from working in cells. It stopped NF-B from activating. As a result, it inhibited pro-inflammatory signaling in infected cells [23].

Carvone: Peppermint oil contains carvone, a bioactive molecule (essential oil). Because of its pharmacological and biological qualities, it is widely used as an antiviral, antibacterial, anti-inflammatory, anti-cancer, and anti-oxidant. Carvone has the

potential to suppress neuraminidase (NA). Carvone linked to the influenza virus's neuraminidase active site successfully [23].

Cinnamaldehyde: A naturally occurring phenylpropanoid component of cinnamon essential oil. It has anti-inflammatory, anti-viral, anti-oxidant, anti-immunomodulatory, anti-bacterial, anti-cancer, and anti-cholesterol properties, among others. In lung-damaged tissues, it reduced viral generation and inflammation [23].

Coconut oil: Consumption has been linked to a variety of health advantages, including improved antibacterial, antifungal, antiviral, antiparasitic, antidermatophytic, antioxidant, and immunostimulant activity. The medium-chain fatty acids (MCFA), particularly lauric acid, which is the most abundant in coconut oil, are responsible for the wide range of antimicrobial properties. In the human body, lauric acid is transformed to monolaurin, which has the antibacterial and antiviral properties stated previously [18].

Curcumin (Curcuma longa): Turmeric is made from the dried rhizome of Curcuma longa, a widely used spice in meals and Ayurvedic medicine. It has a number of pharmacologic qualities, including antioxidant, anti-inflammatory, and antifibrotic effects. Curcumin, a polyphenol produced from turmeric, has been studied for its antiviral properties against SARS-CoV-2. The possible mechanism of action relies on the Ang II type 1 (AT1) receptor protein level being reduced and the Ang II type 2 (AT2) receptor being upregulated. Even at high oral quantities, curcumin is not hazardous, and it is already licensed and widely utilized in the food business. Curcumin inhibited the expression of pro-inflammatory cytokines such as IL-6, IL-10, IFNc, and MCP-1 via reducing NFB p65 phosphorylation [18].

Diallyl trisulfide: The organosulphur compound diallyl trisulfide was obtained from garlic. It has a number of medicinal qualities, including antiviral, anti-inflammation, antibacterial, anti-cholesterol, and anti-oxidant effects. Asthma, cancer, heart disease, osteoarthritis, and acute or chronic liver injury have all been treated with it [23]. **Diosgenin**-is a phytocompound derived from fenugreek seed extract that is a steroidal sapogenin. It has been found to have antiviral, antioxidant, anti-inflammatory, anti-diabetic, anti-viral, anti-oxidant, anti-inflammatory, anti-diabetic, and anti-diabetic properties, as well as in hypercholesterolemia and gastrointestinal ailments. Diosgenin inhibited viral mRNA expression and, as a result, viral replication via inhibiting STAT3 expression [23].

Eugenol: The phenolic component obtained from essential oil is eugenol (allyl chain-substituted guaiacol). Eugenol is found in clove, cinnamon, nutmeg, basil, bay leaf, and black pepper, among other things. In cells, it suppresses the activity of COX-2 and TNF-. It also prevents NF-B from becoming activated. It also inhibits the expression of pro-inflammatory cytokines in macrophages. Its anti-inflammatory mechanism mode is active due to its inhibitory effect on prostaglandin generation and neutrophil/macrophage chemotaxis [23].

Garlic: Newer research suggests that garlic essential oil may be a helpful natural antivirus option for preventing CoV attacks on the human body, while additional research is needed. The inhibitory effect of the organosulfur compounds found in garlic essential oil on the host receptor ACE2 protein in the human body has been confirmed using a molecular docking technique. This is a significant discovery about individual garlic compounds' coronavirus resistance on the SARS-CoV-2 main protease (PDB6LU7) protein; seventeen organosulfur compounds, accounting for 99.4% of the garlic essential oil constituents, had remarkable interactions with the amino acids of the ACE2 protein and the main protease PDB6LU7.

Glycyrrhizin: (a saponin made up of triterpenes)-Due to its beneficial pharmacological effects, such as downregulating pro-inflammatory cytokines, binding ACE2, obstructing intracellular reactive oxygen species (ROS) accumulation, thrombin inhibition, provoking endogenous interferon, and inhibiting the extra formation of airway exudates, it may be a potential therapeutic option for COVID19.

Jinhua Qinggan: Honeysuckle, gypsum, ephedra (honey), bitter almond, baicalin, forsythia, fritillaria, burdock seed, artemisia annua, mint, and licorice are all found in Jinhua Qinggan granules. In clinical practice, Jinhua Qinggan has been utilized as an adjuvant therapy for COVID-19. Fever, cough, weariness, sputum, and anxiety were greatly reduced when Jinhua Qinggan was added [19].

Kaempferol: Kaempferol is a flavonoid found in foods including spinach, cabbage, kale, beans, tea, and broccoli that has been shown to have antioxidant and anti-inflammatory properties. Several research have looked into how effective these flavanols are at blocking the 3a ion channel created by ORF 3a-coded proteins, reducing viral generation and release from host cells. This capacity allows the body's immune system to change in order to combat the viral infection. Because the benefits of kaempferol can be limited by the autoxidation process, the dosage must be large and modified according to the circumstance [18].

Lianhua Qingwen granules: contain forsythia, honeysuckle, ephedra, bitter almond, gypsum, isatis, mianma guanzhong, houttuynia cordata patchouli, rhubarb, rhodiola rosea, menthol, and licorice, and is a TCM compound preparation based on the principle of plague prevention and cure. It can prevent inflammation-induced lung tissue damage by inhibiting the release of inflammatory mediators.

Linalool-is a monoterpene that can be extracted from coriander leaves. Cinnamon, rosemary, basil, cardamom, and thyme all contain it. Infected mice's IL-1, IL-18, TNF-, and IFN- expression levels were reduced [23].

Monolaurin- Piperine: An amide alkaloid obtained from black, white, and long pepper extracts' fruits. It has been found to have anti-inflammatory, anti-viral, analgesic, anti-convulsant, and anti-cancer biological and pharmaceutical therapeutic properties. Inflammatory disorders such as asthma, Alzheimer's disease (AD), Parkinson's disease, arthritis, gastritis, and endometritis are also treated with it. Piperine's anti-inflammatory activities inhibit inflammatory signaling in chronic diseases via NF-B, MAPK, AP-1, COX-2, NOS-2, IL-1, TNF-, PGE2, and STAT3 [23].

Quercetin: A flavonoid present in a variety of foods, including onions, grapes, shallots, tea, tomatoes, and a variety of seeds, nuts, flowers, barks, and medicinal botanicals such as Ginkgo biloba, Hypericum perforatum, and Sambucus canadensis. It has antioxidant, anti-inflammatory, and antiviral properties, with some preliminary evidence of anticancer benefits. These effects are related to lipid peroxidation inhibition, platelet aggregation inhibition, lipopolysaccharide-induced tumor necrosis factor production in macrophages, and lipopolysaccharide-induced IL-8 production in lung cells [18].

Reduning: Honeysuckle, gardenia, and artemisia annua are used to make Reduning. Pharmacological effects of the injection include antipyretic, anti-inflammatory, and antiviral properties. Anti-inflammatory, antiviral, and immunomodulatory properties of reduning injection The method of action could involve IL-17, C-type lectin receptor, HIF-1, and other pathways operating on IL-6, CASP3, MAPK1, CCL2, and other targets via the IL-17, C-type lectin receptor, HIF-1, and other pathways. Reduning has been shown to be effective in the treatment of lung damage and cardiovascular disease [19].

Shenfu: Red ginseng and black monkshood are used to make Shenfu, which is extensively used to treat cardiovascular and cerebrovascular illnesses. It can also be used alone or in combination with other medications to treat severe pneumonia, sepsis, multiple organ failure, and malignancies. Shenfu reduces the levels of pro-inflammatory cytokines TNF-, IL-6, IL-8, procalcitonin, and hypersensitivity CRP in the serum of sepsis patients, improving therapeutic benefits. Shenfu can lower IL-6 levels, raise the amount of CD3 +, CD4 +, and CD8 + -T cells in the peripheral blood, and maintain the pro-inflammatory/anti-inflammatory balance, all of which improve sepsis therapy efficacy [19].

Shengmai: Red ginseng, ophiopogon japonicas, and schisandra chinensis make up Shengmai. Clinically, Shengmai has been utilized to treat cardiovascular and cerebrovascular illnesses.

Shenmai: Red ginseng and ophiopogon japonicus make up Shenmai. It's used to treat conditions like coronary artery disease, viral myocarditis, chronic pulmonary artery disease, and neutropenia. Saponins, sugars, amino acids, flavonoids, lignans, organic acids, and other chemicals are the major components of Shenmai injection. When administered as an adjuvant treatment for severe pneumonia, Shenmai can lower inflammatory factors, raise anti-inflammatory factors, and lower the quantity of white blood cells, C - reactive protein, and procalcitonin [19].

Shufeng Jiedu granules: To treat acute upper respiratory tract infections. Polygonum cuspidatum, forsythia, radix isatidis, bupleurum, radix, verbena, reed root, and licorice are among the granules. Shufeng Jiedu's anti-inflammatory properties are linked to the down-regulation of NF-kB mRNA expression and suppression of the MAPK/NF-kB signaling pathway [19].

Sulforaphane: The active anti-inflammatory ingredient in mustard leaf extract is sulforaphane. Isothiocyanate is a kind of isothiocyanate (group of sulfur-containing organic compounds). Sulforaphane inhibited the human immunodeficiency virus (HIV) infection in macrophages via regulating the transcription of the regulator Nrf2. In HIV-infected cells, sulforaphane inhibited infection before the development of long terminal repeat (2-LTR) viral DNA rings [23].

Tanreqing: Scutellaria baicalensis, bear bile powder, goat horn, honeysuckle, and forsythia make up Tanreqing. Tanreqing contains quercetin and luteolin, which have anti-influenza a virus action in vitro. Quercetin has been shown in studies to lower TGF-1, -SMA, and TNF- expression, block rat alveolar cell death, and diminish inflammation and fibrosis destruction in rat lung tissue. Baicalin inhibits the expression of TNF- and IL-1, which can minimize inflammatory damage to lung tissue [19].

Thymoquinone: The monoterpene substance thymoquinone is present in the seeds of black cumin. It has anti-oxidant, anti-inflammatory, anti-cancer, immunomodulatory, anti-viral, and anti-bacterial properties, among other things.

Xingnaojing: Musk, turmeric, borneol, gardenia, and other components make up Xingnaojing. Acute poisoning, viral encephalitis, craniocerebral damage, acute cerebrovascular disease, pulmonary encephalopathy, pneumonia, respiratory failure, and sepsis are all common clinical uses. During the adjuvant therapy of ventilator-associated pneumonia, Xingnaojing can suppress the overexpression of serum CRP, IL-6, and TNF-. It can also lower the risk of an inflammatory reaction and harm to several organ functions [19].

Xin-Ji-Er-Kang (XJEK): Is a traditional Chinese herbal medicinal combination made up of fourteen different herbs, including Panax ginseng C.A. Mey., Astragalus Mongolic Bunge, Ophiopogon japonicus (Thunb). Ker Gawl., and Polygonatum odoratisms (Mill). Clinical trials and laboratory studies have revealed that it protects against “Xiong-Bi” disease, viral myocarditis, and toxic myocarditis. XJEK efficiently lowers blood pressure and may diminish vascular oxidative stress, as well as ACh-induced relaxation and endothelial dysfunction [20].

Xiyanping: The major ingredient of Xiyanping is an andrographolide substance. In COVID-19 patients, Xiyanping can reduce inflammation and relieve symptoms like cough, fever, and

rales in the lungs. Reducing viral replication and infection, inhibiting concurrent bacterial infections, increasing body immunity, and enhancing liver function and cardiovascular damage are some of the other advantages [19].

Xuebijing: Safflower, red peony, chuanxiong, salvia miltiorrhiza, and angelica make up Xuebijing. Sepsis, systemic inflammatory response syndrome, and multiple organ dysfunction syndromes are among the conditions for which it is prescribed (MODS). In China, Xuebijing is commonly used to treat severe pneumonia, chronic obstructive pulmonary disease, acute respiratory distress syndrome, and other life-threatening illnesses [19].

Summary and Discussions

The novel Coronavirus (COVID-19), which arose in late 2019, has become a global threat. This virus quickly spread over the world due to its great transmissibility, creating serious health problems. There are currently no specific treatments that effectively block the virus, and developing new medications takes about ten years of research. In-silico, in-vitro, and in-vivo techniques were used to explore a variety of natural cures and chemicals, including alkaloids, terpenes, flavonoids, and benzoquinones. Despite the vast amount of data obtained by a computational approach, experimental proof is rarely available. As a result, naturally occurring compounds with a broad antiviral range could provide a safe, effective, and low-cost platform for discovering new SARS-CoV-2 treatments. However, before moving further with human clinical trials, further well-designed animal studies investigating the mechanism of action, pharmacokinetics, and safety profile of plant complexes and their separated bioactive components are required. Many experimental attempts to treat COVID-19 inflammatory and cardiac alterations with natural treatments have yielded positive outcomes. However, because of the low methodological quality, small sample size, and small number of trials on particular herbs, these findings should be interpreted with caution. Concerns about coronavirus illness 2019 (COVID-19) have sparked interest in dietary supplements and complementary and alternative therapy. These treatments and therapies are advertised as having the ability to boost or promote the body's natural immune function. Consumers may be made to believe that these products or therapies assist the body fight illnesses like COVID-19 by improving immune function. There is, however, no proof that "immune boosters" or other supplements may prevent, treat, or cure COVID-19 or other viral illnesses. The United States Food and Drug Administration (FDA) continues to issue warning letters to companies marketing fake COVID-19 prevention, treatment, mitigation, diagnosis, or cure products. The following FDA website (https://www.fda.gov) has a list of companies who have received such warning letters from the FDA. Finally, randomized controlled trials must be conducted to determine the genuine therapeutic benefits and side effects of herbal therapies in the treatment of myocarditis.

References

1. Guzik TJ, Mohiddin SA, Dimarco A, Patel V, Savvatis K, Berg FMM, et al. COVID-19 and the cardiovascular system: implications for risk assessment, diagnosis, and treatment options. Cardiovasc Res. 2020; 116: 1666-1687.
2. Amruta N, Chastain WH, Paz M, Solch RJ, Brown ICM, Befeler JB, et al. SARS-CoV-2 mediated neuroinflammation and the impact of COVID-19 in neurological disorders. Cytokine Growth Factor Reviews. 2021; 58: 1-15.
3. Li X, Wang L, Yan S, Yang F, Xiang L, Zhu J, et al. Clinical characteristics of 25 death cases infected with COVID-19: a retrospective review of medical records in a single medical center, Wuhan. China. 2020; 94: 128-132.
4. Oudit GY, Crackower MA, Backx PH, Penninger JM. The Role of ACE2 in cardiovascular physiology. Trends Cardiovascular Med. 2003; 13: 93-101.
5. Buja LM, Zehr B, Lelenwa L, Ogechukwu E, Zhao B, Dasgupta A, et al. Clinico pathological complexity in the application of the universal definition of myocardial infarction. Cardiovascular Pathol. 2020; 44: 107153.
6. Geng YJ, Wei ZY, Qian HY, Huang J, Lodato R, Castriotta RJ, et al. Pathophysiological characteristics and therapeutic approaches for pulmonary injury and cardiovascular complications of coronavirus disease 2019. Cardiovascular Pathol. 2020; 47: 107228.
7. World health Organization. WHO global report on traditional and complementary medicine? 2019.
8. FDA. Complementary and alternative medicine products and their regulation by the food and drug Administration: draft Guidance for Industry 2007.
9. Madjid M, Naeini PS, Solomon SD. Potential effects of coronaviruses on the cardiovascular system: A review. JAMA Cardiol. 2020; 5: 831-840.
10. Augoustides JG. Cardiovascular consequences and considerations of coronavirus Infection-Perspectives for the Cardiothoracic Anesthesiologist and intensivist during the coronavirus Crisis. J Cardithoracic Vascular anesthesia. 2020; 34: 1713-1716.
11. Herbal Medicinal Products. European Medicines Agency.
12. Liu J, Zheng X, Tong Q, Li W, Wang B, Sutter K, et al. Overlapping and discrete aspects of the pathology and pathogenesis of the emerging human pathogenic coronaviruses SARS-CoV, MERS-CoV, and 2019-nCoV. J Med Virol. 2020; 92: 491-494.
13. Omrani M, Keshavarz M, Ebrahimi SN, Mehrabi M. Potential natural products against respiratory viruses: a perspective to develop Anti-COVID-19 Medicines. Front Pharmacol. 2021; 17: 586993.
14. Rangachari M, Mauermann N, Marty RR, Dirnhofer S. T-bet negatively regulates autoimmune myocarditis by suppress-ing local production of interleukin 17. J Exp Med. 2006; 203: 2009-2019.
15. Tajbakhsh A, Hayat SMGH, Taghizadeh H, Akbari A. COVID-19 and cardiac injury clinical manifestations, biomarkers, mechanisms, diagnosis, treatment, and follow up. Expert Review of Anti-infective Therapy. 2021; 19: 345-357.

16. Ren LW, Hong Y, Zhou GJ, Xing LX. Histopathologic Findings in the Explant Lungs of a Patient With COVID-19 Treated With Bilateral Orthotopic Lung Transplant. Transplantation. 2020; 104: 329-331.
17. Pastor N, Collado MC, Manzoni P. Phytonutrient and Nutraceutical Action against COVID-19: Current Review of Characteristics and Benefits. Nutrients. 2021; 13: 464.
18. Luo E, Zhang D, Luo H, Liu B, Zhao K, Zhao Y, et al. Treatment efficacy analysis of traditional Chinese medicine for novel coronavirus pneumonia (COVID-19): An empirical study from Wuhan, Hubei Province, China. Chin. Med. 2020; 15: 34.
19. Wang C, Sun S, Ding X. The therapeutic effects of traditional chinese medicine on COVID-19: a narrative review. Int J Clin Pharm. 2021; 43**:** 35-45.
20. Wang XY, Huang GY, Lian FZ, Pan M. Protective effect of Xin-Ji-Er-Kang on cardiovascular remodeling in high-salt induced hypertensive mice: Role of oxidative stress and endothelial dysfunction. Biomedicine Pharmacotherapy. 2019; 115.
21. Nie P, Meng F, Zhang J, Wei X, Shen C. Astragaloside IV Exerts a Myocardial Protective Effect against Cardiac Hypertrophy in Rats, Partially via Activating the Nrf2/HO-1 Signaling Pathway. Oxid Med Cell Longev. 2019.
22. Ghazaleh JS, Hekmatnia A, Nasrollahzadeh M, Shafiei N. SARS-CoV-2 (COVID-19): New discoveries and current challenges. Applied Sci. 2020; 10: 3641.
23. Elengoe A. Indian spices boost the immune system against COVID-19. The Annals of the University of Dun area De Jos of Galati. Fascicle VI Food Technol. 2020; 44: 189-206.