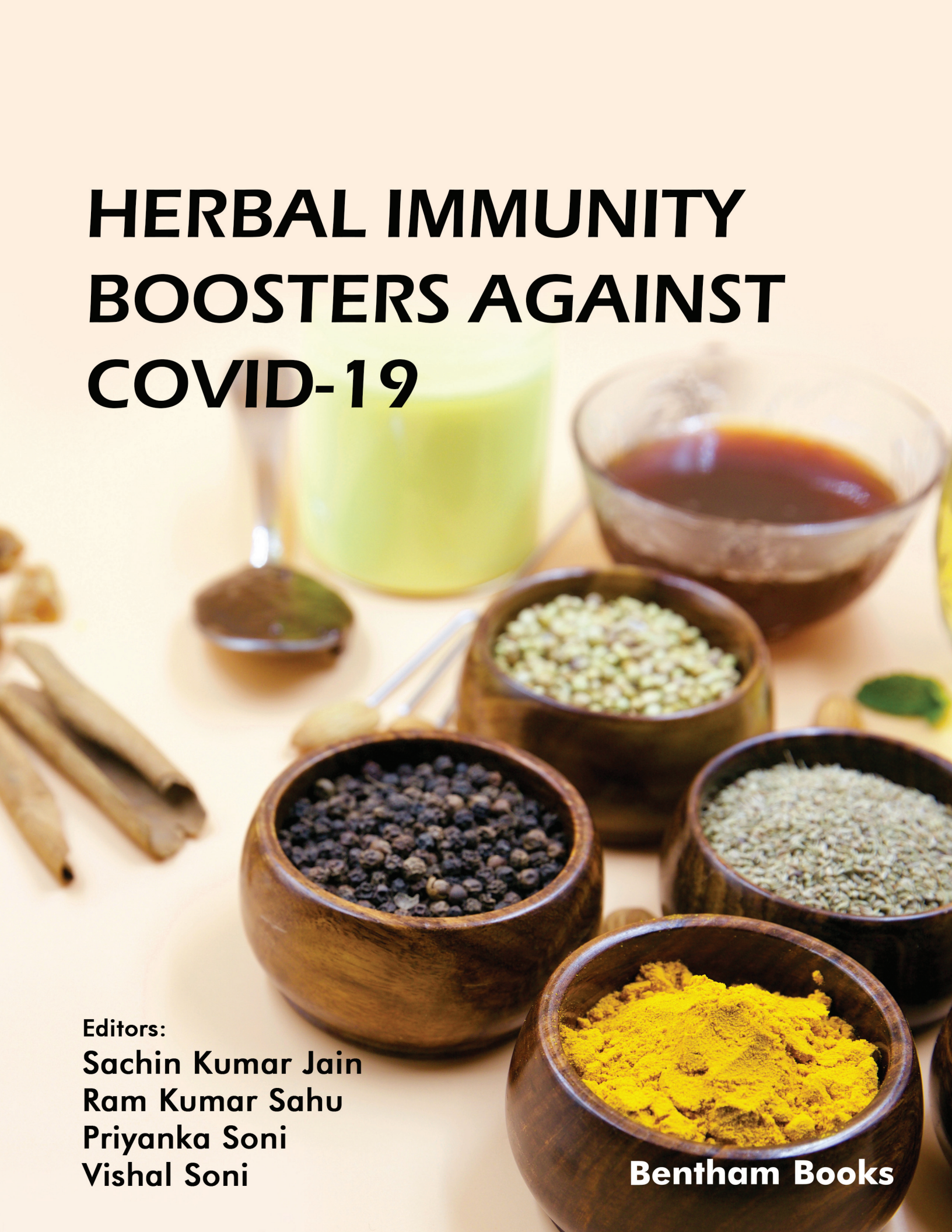


HERBAL IMMUNITY BOOSTERS AGAINST COVID-19



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PREFACE

The book is an exclusive version of the instructive matter on Herbal Immunity Boosters for Covid-19. The herbal immunity booster is basically an emerging field that discusses potential preparations to diminish the severity of the infection caused by Covid-19. Currently, the effective treatment of COVID-19 is lacking. Hence it is imperative for individuals to use such type of food supplements which boost their immune systems. In this concern, the ideal technique is to fortify immunity naturally by using medicinal plants. Whereas, immunity booster deals with the remarkable protection mechanism against loads of bacteria, viruses, fungi, toxins and parasites when entering the body. Additionally, other signaling pathways are recognized that are responsible for the regulation of the pathogenesis of infections and non-infectious diseases due to lower immunity. It also deals with the exploration of functional and nutraceutical foods for preserving body homeostasis which is essential to maintain immunity. Therefore, plants or herbs having immunomodulating properties should be included in the diet, and we should explore novel therapeutic opportunities to improve immunity against diseases. This book contains immense knowledge about Herbal Immunity Boosters for Covid-19 with respect to the mode of action, modulation of signaling pathways, regulatory aspects, safety, food supplements and drug delivery for better function of the immune system. In addition, drug development issues, adaptation to clinical use, market prospects and industrial commercialization too come under the concept of Herbal Immunity Boosters for Covid-19. The book not only focuses on theoretical knowledge but also considers practical aspects. The book is very beneficial for students and researchers across the globe that are indulged in the reading and investigation of Herbal Immunity Boosters for Covid-19, thereby, spreading awareness all over the globe and promoting anticipated trends in the field of Herbal Immunity Boosters. The major objective of this initiative is to bring into light the entire fundamental concept. This book also includes different types of procedures and herbal medicines to increase and treatment and immunity of Covid-19.

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Origin of COVID-19

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Abstract: Coronavirus is a type of virus that is surrounded by non-segmented, single-stranded, positive-sense RNA genomes that reproduce in the cytoplasm. The size of the coronavirus is usually 80-120 nm. It was discovered in Wuhan, China in December 2019, and it was termed 2019 nCoV or COVID-19. The coronavirus is encased in a lipid bilayer and it possesses several proteins. These proteins are surrounded in the envelope of a virus; whereas, in the viral RNA, N-protein shows interactions and it can be found on the outer surface of the viral particle, forming the nucleocapsid. The spike protein is identified as the leading protein and mediates the entrance inside the host body that would cause SARS-CoV-2 syndrome. The spike protein has two spheres namely S1 and S2. The receptor that is attached to the S1 and further S2 is responsible for fusion. In the past, the most severe types of virus which had resulted in large-scale pandemics were SARS (in 2002–2003) which occurred in Guandong Province, China. Meanwhile, Saudi Arabia had experienced the Middle East respiratory syndrome (MERS) in 2012. The virus in the 1960s was commonly identified in birds and mammals; mostly in rats, camels, cats and bats. SARS-CoV-2 causative agents belong to the genus β -Coronavirus. Coronavirus can be classified into four genera such as α , β , γ , and δ coronavirus. Alpha and beta coronaviruses are found in mammals such as bats. Gamma coronaviruses would primarily infect birds and affect mammalians, whereas delta coronaviruses would infect both birds and mammals. This chapter highlights the origin, historical background, the classification of the coronavirus as well as providing the conceptual information on various treatment approaches for COVID-19.

Keywords: β -Coronavirus, Coronavirus, MERS-CoV, SARS-CoV, SARS-CoV-2, Spike Protein.

1. INTRODUCTION

Coronavirus is a chief pathogen that principally infects the respiratory tract of humans. Previous coronavirus outbreaks (CoVs) have shown syndromes of the

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Middle East respiratory syndrome (MERS)-CoV as well as a severe acute respiratory syndrome (SARS)-CoV. These syndromes were alarming to the world's population due to the infections they had caused [1]. SARS-CoV first appeared in 2002, followed by (MERS-CoV) and the novel coronavirus in 2012 and 2019, respectively. COVID-19, which was recently discovered, is the fifth known pandemic since the 1918 flu pandemic [2]. Coronaviruses are viruses enclosed with non-segmented, single-stranded, positive-sense RNA genomes that reproduce in the cytoplasm and they are typically 80-120 nm in size. COVID-19 was first identified in December 2019 in Wuhan, China, and was later referred to as 2019 nCoV or COVID-19 [3]. The SARS-CoV virus is a member of the Coronaviridae family, specifically the orthocoronaviridae subfamily and the order Nidovirales. The size range of the RNA genome lies between 26 to 32 kb. A helical nucleocapsid encompasses the DNA, which is surrounded by a lipid bilayer that is derived from the host [4]. Membrane (M), Spike (S), envelope (E) and nucleocapsid (N) are proteins found on the surface of the coronavirus (N). The S protein is the primary viral entry point [5]. The S protein is a large, Type-I transmembrane protein with 1160 amino acids for avian infectious bronchitis virus (IBV) and 1400 amino acids for feline coronavirus (FCoV). In the S protein, two domains namely S1 and S2 were discovered. The two domains S1 and S2 would recognize the host receptor and act for further fusion, respectively [6]. Once it is attached to the receptor, the envelop spike proteins would enter the host body directly through the cell surface and *via* the endocytosis fusion process. The massive conformational changes in the spike protein would determine the virus-host membrane fusion. Coronavirus has the appearance of a crown in an electron microscope and it is due to the presence of the glycoprotein spikes on its cover [7]. The MHV receptor was first discovered in 1991 and it was identified as the leading coronavirus binding receptor as it would allow the MHV to infect cells by binding them to the CEACAM1 molecule [8]. CEACAM1 is a part of the immunoglobulin superfamily and it is classified as a Type-I transmembrane protein. The multifunctional protein CEACAM1 plays a major role in the adhesion and cell signalling. Human coronaviruses consist of seven strains namely Human Coronavirus OC43 (HCoV-OC43), MERS-CoV, SARS-CoV (HCoV-NL63, New Heaven Coronavirus), Human Coronavirus HKU1, Human Coronavirus 229E (HCoV-229E), HCoV-EMC as well as the new strain that is identified as the Wuhan coronavirus which is known to be extremely dangerous and currently spreading widely worldwide (known as SARS-CoV-2 or COVID-19). Coronavirus Humanoid viruses, such as HCoV-229E, -NL63, -OC43 and -HKU1 are common in the humanoid population and they would display severe infection in the human respiratory tract at every age group. Alpha coronaviruses consist of HCoV-229E and NL63 while beta coronaviruses include OC43 and HKU1 [9]. The binary human viruses (HCoV-229E and HCoV-NL63) that are

identified as the alpha coronavirus can infect animals and cause severe illness. The amino peptidase N (APN) protein is present in the host and acts as a receptor for HCoV-229E [10]. The Type II transmembrane protein CD13 is termed an APN protein that originates on the respiratory and intestinal epithelial cells. The APNs are Zn^{2+} dependent proteases and they have the capability to break down the protein of N terminal neutral amino acids. Furthermore, the beta SARS-CoV is able to bind to the carbohydrates that are presented in a galectin fold-like structure found in the S1 NTD. The SARS-CoV was first discovered in 2002 and the (ACE-2) receptor was responsible for the virus [11]. Type I main membrane protein is a mono-carboxypeptidase that hydrolyzes angiotensin II and it is found in a substantial fraction of ACE2 receptors expressed in lung tissue. When a coronavirus infects the host, the calcium-dependent (C-type) lectins are predicted. Humans, mammals and birds are all afflicted by the coronavirus infection in humans as it affects the respiratory tract, the gastrointestinal tract, the hepatic system and the nervous system. Acute and persistent infections are both possible [12]. The α , β , γ , and δ are four different types of coronaviruses in which the alpha and beta are responsible for infections. Acute lung injury is caused by H5N1, SARS-CoV and H1N1 while acute respiratory distress syndrome (ARDS) could cause failure and death of the pulmonary region. The following are two possibilities that are likely to explain the creation of novel coronaviruses: a) natural selection in an animal host prior to and after zoonotic transmission and b) natural selection in humans after zoonotic transmission. Clinical types and risk factors are highly variable, resulting in scientific data ranging from asymptomatic to lethal. The basic symptoms of coronavirus include: cough, sore throat, breathlessness, fever, and the patient must be quarantined for 2-14 days after infection. Following the (H1N1), 1957 (H2N2), 1968 (H3N2) and 2009 Pandemic flu (H1N1), the WHO had declared a new coronavirus outbreak pandemic on March 11, 2020 [13] (Fig. 1).

CHAPTER 2**COVID-19: Sign, Symptoms and Transmission****Saket Singh Chandel^{1,*}, Deepshikha Verma² and Vipinchandra Bhaskarrao Pande³**

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Abstract: COVID-19, which is caused by SARS-CoV-2, was first reported in Wuhan, China in late 2019. Till date, over 12.1 million people have contracted the disease across 221 countries in the world. The global fatality rate is about 6.2% thus far, and as of May 26th 2020, the highest confirmed cases were recorded in the USA, Brazil, Russia, Spain, UK, Italy and France. Several attempts to fight against the virus are taken by the World Health Organization (WHO) as well as other health agencies in various countries with reported confirmed cases. The present study has reviewed COVID-19 with respect to the clinical symptoms and signs, as well as factors that could exacerbate COVID-19 condition and transmission amongst people. Recent reports and studies have found the disease status to be of the predominantly mild condition and to a lesser extent, a critical/severe status. COVID-19 presents several clinical manifestations with symptoms such as fever, dry cough, fatigue, dizziness, anorexia, headache, expectoration, dyspnea, chest tightness, abdominal pain, diarrhea and nausea. Studies have observed age, obesity, smoking and drinking habit, immune system condition, human selectivity and reactivity as factors that can aggravate the disease condition, while poverty, fake news, non-validated scientific claims, and perception/illiteracy have been reported as risk components that could enhance the transmission of the viral infection. This study concludes by suggesting the appropriate methods to combat the factors discussed.

Keywords: Co-Morbidities, COVID-19, Global Pandemic, Immune System, Public Health, SARS-CoV-2.

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1. INTRODUCTION

In early January 2020, there were several global news concerning the emergence of a novel coronavirus in Wuhan, Hubei Province, China. Prior to that time, specifically towards mid-December 2019, there were cases of unknown pneumonia in the province reported. It rapidly became a major source of concern to the Chinese Government and its health institutions. Consequently, an etiological study was launched to curtail its spread. According to Kakodkar *et al.* (2020), China's CDC discovered a virus called novel coronavirus 2019 (2019-nCoV) and it was colloquially referred to as "Wuhan Coronavirus" on 7th January, 2020 [1].

The causative agent responsible for the disease was identified as Severe Acute Respiratory Syndrome (SARS-CoV-2) by scientists. By the end of January 2020, WHO had declared 2019-nCoV a public health emergency. The cases were increasing in China, before the virus had spread to other nations and territories across various continents of the world. During this period, the WHO had closely monitored the situation and the name of the disease was given as Coronavirus Disease 2019 with a short name of COVID-19 by 11th February, 2020. Authors had attributed the renaming of the "Wuhan Coronavirus" as SARS-CoV-2 as an attempt to de-stigmatize the association of the virus with respect to the geographic locality and in relation to the disease symptomatology [1]. By 11th March 2020, COVID-19 was declared a global pandemic.

Presently, the disease has spread to over 221 countries and territories. The major means of the virus transmission include person to person, making contact with SARS-Cov-2 contaminated surfaces as well as having exposure to and inhalation of droplets released by SARS-Cov-2 patients through aerosolization. The disease has been reported to affect the respiratory tracts which would lead to coughing, sneezing, difficulty in breathing or shortness of breath and pneumonia among others [2].

Information obtained from the Worldometer website as of March 16, 2021, 10:38 GMT has shown that over 12.1 million people have contracted the disease across 221 countries in the world to date. The total numbers of confirmed deaths, recovered and discharged cases were 2,672,766; 100,107,434 and 97,434,668 respectively. Among the active cases currently (20,687,790), 99.6% and 0.4% are in mild and critical conditions, respectively. Presently (Till 16th March, 2021), the number of nations with the highest cases are in this order USA (30,138,586), Brazil (11,525,477), India (11,409,831), Russia (4,400,045), UK (4,263, 527), France (4,078,133), Italy (3,238,394) and Spain (3,195,062), while the countries with the highest death rates are in the order; USA (548,013), Brazil (279,602),

Mexico (194,944), India (158,892), UK (125,580), Italy (102,499), Russia (92,494), France (90,762), Germany (74,115) and Spain (72,424). China is ranked as the 86th nation with the highest number of confirmed cases (90,062) while India and Nigeria are ranked 3rd and 73rd, respectively. India had 11,146,371 confirmed cases, 158,892 deaths, 11,027,543 discharged cases, 223,396 active cases and 8,944 cases in critical condition, while the most populated nation in Africa (Nigeria) had 160,895 confirmed cases, 2,016 deaths, 145,752 discharged cases, 13,127 active cases and 10 in critical condition [2].

A large number of deaths have been recorded as a result of the global pandemic of COVID-19 in which most of the deaths were individuals with underlying health conditions. It is opined that chronic medical conditions would commonly occur in combination which is also known as comorbidities [3]. Researchers have reported that comorbidity is related to adverse health effects, more intricate clinical management and increased cost of health care. It is difficult to accurately define the relationship between a disease and its comorbidities [4]. Furthermore, the nature and prevalence of the comorbidities are mainly swayed by their epidemiology in the patients' area of origin. Most comorbidities of a disease often influence its clinical manifestations and may cause uncertainties in their diagnosis.

Effective management of chronic medical conditions with comorbidities is accrued with multifaceted treatment procedures, therefore, entails suitable self-care by the patients of all comorbid conditions. This can be made possible by understanding the underlying mechanisms, the causative agent of the diseases as well as their interactions [4]. The coexistence of other infectious comorbidities in patients with life-threatening ailments has been recorded in the literature. Studies have shown that most people that had died from COVID-19 had suffered from other health conditions. The comorbidity rate of COVID-19 patients is at least 74.4% and 58.8% of it are from various parts of the pandemic area [5, 6]. Some of the common health conditions associated with COVID-19 include chronic obstructive pulmonary/lung disease, cardiovascular diseases, diabetes, hypertension, chronic liver and kidney disease, malignant tumor, and bacteria co-infection among others [7 - 12].

Therefore, this study is aimed at reviewing the factors that could aggravate the condition and transmission as well as increasing the awareness of the severity status of the disease.

A Silver Lining for Covid 19: Nutraceuticals and Plant Secondary Metabolites

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Abstract: There are some confines to the worldwide disease instigated by the novel coronavirus disease 2019 (COVID19), for now, a vaccine or treatment is available. According to SAGE, the Pfizer-BioNTech, COVID-19 mRNA vaccine is safe and effective. Vaccination is not recommended for certain populations due to contraindications, lack of availability, or inadequate data. Individuals with a background of grave allergies, pregnant women, and foreign travellers who are not part of a prioritized group, and children under the age of 16 are all cautioned against getting the vaccine. This necessitates the use of some alternatives that strengthen the immune system. The new therapies and medications provide our bodies with a window duration that aids in the creation of adaptive ion channels. The human immunity system is made up of various body organs and cells that work together with a symphony to defend the host from foreign particles such as viruses, bacteria, fungi, parasites, and so on. To synthesize various types of immune cells, our body needs a broad range of small amounts (vitamins and minerals) and large amounts (carbohydrate, protein, and fat) nutrients. Certain established prehistoric herbs that improve immunity include garlic, basil leaves, and black pepper. The following chapter includes a list of immune-supporting nutraceuticals (such as omega-3 fats, glucans, amino acids, probiotics, vitamins, and minerals) and plant's secondary metabolites, as well as the impression of their supplementation in boosting the body's immunity to make it able to combat COVID-19.

Keywords: Alkaloids, Amino Acids, COVID 19, Coronavirus, Flavonoids, Herbal Extract, Immunity Booster.

1. INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a communicable ailment instigated by the Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. Firstly, it was discovered in Wuhan, China, in December 2019 and has meanwhile blow-

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out internationally, resulting in a pandemic [2]. On average 7.3 million cases stayed registered across 188 countries and territories as of June 10, 2020, resulting in more than 413,000 deaths [3]. As of March 3, 2021, the virus had infected 115 million people worldwide, with 2.54 million people dying as a result of the disease. COVID-19 is a highly contagious, critical illness characterized by Pneumonia and Acute respiratory distress syndrome (ARDS). Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), like Middle East respiratory syndrome coronavirus (MERS-CoV) and SARS-CoV-1, comes under the Coronaviridae family and causes the disease. The virus's genome is positive-sense Ribonucleic acid (RNA), which codes for 26 proteins that help the virus survive, replicate as well as propagate in the host. The virus is spread by contact with infected people's aerosol droplets [4]. Coronaviruses are encased viruses with a positive-sense genome of single-stranded RNA (+ssRNA). These viruses are members of the Coronaviridae family and subfamily Coronavirinae, which contaminate birds and mammals through its spike (S) glycoprotein and the virus binds to angiotensin-converting enzyme 2 (ACE2) receptors on cells [5]. S1 and S2 are the two domains of the S protein. S1 binds to the peptidase domain of ACE2, known as the receptor-binding domain (RBD), and membrane fusion is catalyzed by S2, allowing genetic material to be released inside the cells [6]. Individuals' immune status and the occurrence of underlying medical conditions, may influence the beginning of the clinical disease and its progression to a serious level. Dry cough (67 percent), fever (88 percent), exhaustion (38 percent), myalgias (14.9 percent), and dyspnoea (18.7%) are the most common clinical symptoms. Other symptoms comprise headache, sore throat, rhinorrhoea, and gastrointestinal symptoms. Pneumonia is a serious infection indicator. COVID-19 has complicated the pathogenesis that includes the conquest of the host's antiviral and innate immune responses, oxidative stress initiation, and a “cytokine storm” that results in acute lung damage, tissue fibrosis, and pneumonia [7]. Vaccines and other treatments are now currently available, although they have certain limitations. According to the Strategic advisory group of experts on immunization (SAGE), the Pfizer-BioNTech COVID-19 mRNA vaccine is safe and effective. Vaccination is not recommended for certain populations due to contraindications, a lack of availability, or inadequate data. The vaccine is not recommended for people who have a background of serious allergies or who are pregnant, international travellers who are not part of a prioritized group, and children under 16.

COVID-19 is more common in pregnant women than in non-pregnant women, and COVID-19 has been related to an increased risk of preterm birth. The World Health Organisation (WHO), however, does not suggest vaccination of pregnant women at this time due to a lack of evidence.

Vaccination may be given to a breastfeeding woman who is part of a group (*e.g.*, health workers) that has been recommended for vaccination. Breastfeeding should not be interrupted following vaccination, according to the WHO [8].

This necessitates the use of some alternatives that strengthen the immune system. The current therapy and medication are providing our bodies a window of opportunity for the production of adaptive immunity against COVID-19. Nutrition should be on top priority, particularly. Since our immune system is the only thing standing between us and this novel coronavirus-19 (Fig. 1). In this situation, the WHO issued certain guidelines for obtaining vital nutrients during the pandemic in order to maintain good health [9].

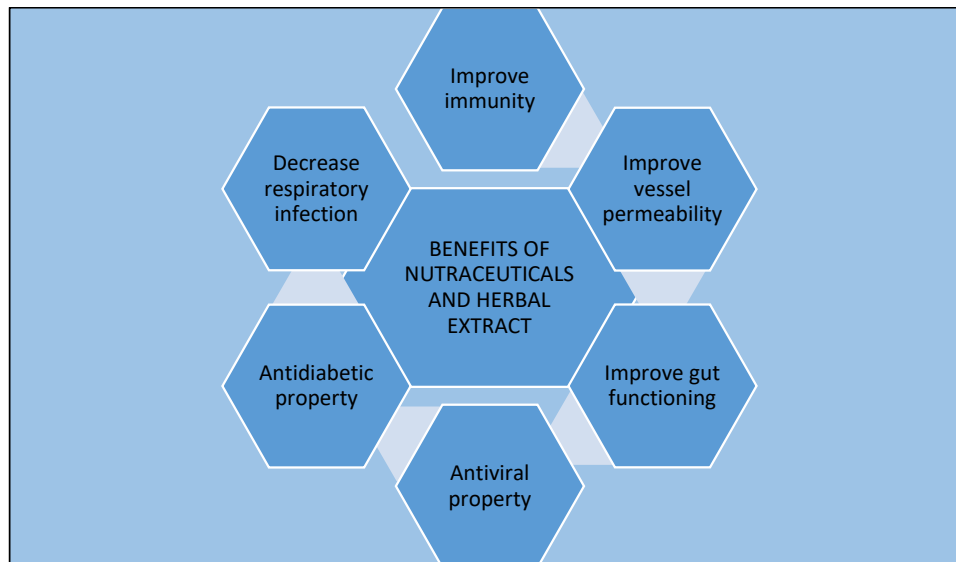


Fig. (1). Diagrammatic representation showing the favourable effects of nutraceuticals and herbal extracts in COVID-19.

Immune cells need adequate energy with macronutrients and micronutrients, serving as co-factors of the growth, articulation, and maintenance of the immunity system. The role of balanced food in the immune system has been extensively recognized, and the effect of various food components on specific aspects of immune function has been extensively researched (Fig. 2). It is generally accepted that an individual's nutritional status affects their immune ability, which can be taken as a proportion of a satisfactory diet [10].

Risk Factors of Covid-19 Enhancing Transmission and Aggravating Patient's Condition

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Abstract: For the last couple of years, novel coronavirus or SAR-CoV-2 is a severe threat to the world. This new strain of coronavirus emerged on 14th December 2020 and has been infecting many parts of the population around the world to date. These viral spikes will bind with the angiotensin-converting enzymes. Many clinical studies conducted have highlighted the association between cardiovascular diseases and COVID-19. It increases the mortality rate, the risk of injury in myocardial, acute coronary syndromes and thromboembolism. COVID-19 has produced some risk factors such as age and gender as well as comorbidities. Coronavirus may pose several challenges for oncology patients. Among cancer patients, severe respiratory and systemic infection are evident specifically among immunosuppressed and ageing patients. Cancer is said to worsen due to COVID-19 as it is linked with inflammatory burst and lymphopenia. This study has discussed the risk factors in COVID-19 transmission, factors that can aggravate it and clinical interactions between the cardiovascular system. Furthermore, several drugs that have been administered against the virus are believed to affect the patients.

Keywords: Cancer and Cardiovascular System, COVID-19, Risk Factors.

1. INTRODUCTION

The world had ceased in December 2019 when the coronavirus outbreak was first reported in Wuhan, China. From then on, the virus had spread all over the world and it was declared a global pandemic, affecting every country in the world. The effects of the virus remain unprecedented on public health [1, 2] as well as on

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social and economic activity. The number of confirmed cases around the world would increase every day over the last six months. Till date, there is no definitive prevention available across the world. The genus *beta coronavirus* mainly caused COVID-19 [3, 4]. The other two corona viruses which also have contributed to the pandemic are Severe Acute Respiratory Coronavirus(SAR-COV) and the Middle East Respiratory Syndrome Coronavirus (MERS-CoV). COVID-19 causes a respiratory infection as well as signs of pneumonia and acute respiratory distress syndrome (ARDS) [5, 6]. This is because these coronaviruses would trigger cytokine storm like tumour necrosis, IL- β , and IL-6 which are released by the immune system, causing multiorgan failure. Furthermore, coagulations in a substantial proportion among patients could take place, leading to thromboembolic events. The biological features have shown that 79.6% of genomic sequence is identified [7, 8]. It shows that both the diseases may enter the body in the same way, triggering the binding of viral spike (S) protein to ACE2 in the host cells. Clinical data shows that the susceptibility to COVID-19 is strongly associated with cardiovascular diseases. This has been observed among a large number of COVID-19 patients which further increases the comorbidities and mortality rate of the virus [9, 10]. Moreover, it can also result in myocardial injury, acute coronary syndrome and thromboembolism. Children too have been affected by COVID-19. The virus could cause hyper inflammatory shock, cardiac dysfunction and coronary vessel abnormalities [11, 12]. There is a bidirectional interaction between the cardiovascular system and COVID-19. This mechanism however is quite elusive. *De novo* cardiovascular damage is developed in a subclinical disorder. ACE2 surface protein plays the most important role in the virus entry. Pathophysiology plays the most crucial role in the development of therapies. There have been around 45 to 50 million of coronavirus cases and the virus has killed around 1.2 to 1.5 million people. Symptoms such as dyspnea, respiratory frequency, blood oxygen saturation and arterial pressure are commonly seen among patients. Some cases of COVID-19 have also shown respiratory failure and mechanism ventilation, shocks as well as coagulopathy. The utilisation of immunopathology is helpful for the identification of clinician patients with a higher risk as they may require prioritised treatment due to rapid progression and adverse outcomes of the infection [13 - 15]. As for demographic risk factors, age, sex and ethnicity complication play an important role as well. Some risk factors would lead to the high risk of the illness. This is because, the cellular serine protease (TMPRSS2) is formed, thus implicating cancer and viral infections. The ACE2 is expressed in alveolar cells type 2. It is also present in the endothelial and smooth muscle cells. The paucisymptomatic and asymptomatic forms depict a substantial fraction in COVID-19 with comorbidities [16, 17] which include acute respiratory failure, cytokine storm, prothrombotic, organ dysfunction and even death. Cancer patients are more susceptible to COVID-19 as compared to non-

cancer patients as a risk factor like cancer has shown high prevalence to the virus. However, as respiratory failure is one of the symptoms of the virus, hematology lung and breast cancers are considered more vulnerable than other types of cancer. In lieu to this, the virus has mostly affected lung cancer patients. There are several countries that have reported cases of cancer patients with traces of small amount of COVID-19 infection. Cancer prevalence however is not associated with infection risk as lung carcinoma is visible in CT scan manifestations. Other than that, gender, obesity and congestive heart failure are also considered as risk factors. In relation to COVID-19, race and ethnicity are believed to be risk factors as well with Hispanic and Black people are the most affected race and ethnicities with this disease [18 - 20]. Furthermore, the Veneto region has shown higher number of cases and death related to COVID-19. The comorbidities also would increase for former smokers and chemotherapy patients. At older age, the haematological malignancies are the diagnosis of myeloid leukaemia and the cell neo plasma associated would be worsening [21, 22]. Metastatic or stage IV carcinomas patients are more likely to contract COVID-19. Moreover, the severity of the cancer treatment also contributes to the risk factor of the virus. In a multivariate analysis of patients, age and immune inhibitor treatment are also associated with COVID-19 in which about 2.5% of patients are tested positive. It remains unclear whether cancer has higher risk factor or cancer associated risks depend on the demography. However, it is apparent that the combination of cancer diagnosis and COVID-19 is far more dangerous with a risk of death.

2. COVID-19 BIOLOGY (GENOME, GENE AND PROTEINS)

Genomic sequencing is done to understand the characteristics of COVID-19 which would help to evaluate the structure of the viral protein. Coronavirus belongs to the family of single-stranded RNA envelope which is highly pathogenic for human beings. MERS-COV is considered as highly pathogenic coronavirus as well. Both of these coronaviruses are originated from bats. SARS-COV-2 is 80% similar to SARS-CoV and 97% similar to bat coronavirus (RaTG13). Based on the homology of genomic sequences, the biological features are also similar to SARS-CoV. ACE2 receptor is utilised by both infections to enter into the host cells. Meanwhile, dipeptidyl peptidase is used in MERS-CoV. The crown like structure formed contains four types of proteins which are known as (S) spike, (E) envelope, (M) membrane and a (N) nucleocapsid [25 - 27] (Fig. 1). N proteins would surround the viral genome in a positive sense. Both genome and mRNA would function as a single-stranded rRNA. α , β , γ and δ are shown in coronavirus in which α and β coronaviruses have infected humans. *Beta coronavirus* is the genus from SARS-CoV, MERS-CoV and SARS-CoV-2. The genome sequence of COVID-19 is approximately 30kb in length, consisting of ORFs (open reading

Indian Expedition against Covid-19 through Traditional Drugs

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Abstract: COVID-19 was a menace to India's densely populated country. The entire globe is dealing with the same problem, but India is fighting it in its own unique way, namely *via* the use of ancient traditional medicines. Every country used to shut down as a first line of defence to safeguard its population; the whole globe came to a halt during the epidemic, and people were confined to their homes. A preparation program was needed to prepare their country and reconstruct their medical institution in the event of a pandemic. The entire globe is paying tribute to all of the corona warriors for their selfless commitment and unwavering care for patients during this critical period. The Indian government has also taken some swift moves to combat the sickness by employing certain traditional medicines. Many researchers went to considerable lengths not just to give therapy but also preventative strategies. Immunity has been proven to be the most critical factor in the illness. This chapter tries to highlight the most important traditional medications utilised by Indians from ancient times. Indians employ a variety of spices in their cooking, many of which are high in chemical elements that can help with a variety of ailments. When Ayurveda has been called upon, it has demonstrated its usefulness several times. The usage of traditional medications in every home is well documented in the Indian system. Since ancient times, the customary approach has been shown to be reliable and applicable. Many ailments have been categorised and evidence-based information has been provided by Indian literature such as the Ayurvedic Pharmacopeia and Chark Samhita. It also reflected the immunity level of Indians and they explored the uses of these traditional drugs in the dosage form *i.e.* kadha, Chwanpras, *etc.* The expedition showed great reflection in terms of the recovery rate of patients *i.e.* 97.15 percent, deaths were also minimized as compared to developed countries in terms of the population ratio.

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Keywords: Ayurveda, Chark Samhita, Immunity, Traditional drugs.

1. INTRODUCTION

COVID-19 has not only affected the people but it deteriorated the economic conditions of countries too. Globally many people lost their jobs due to lockdown but that was the need of the hour. We will not forget this pandemic time and it would be a black chapter in history. People were locked down in their houses and they were in a fearful state while being in social gatherings. During this pandemic, students were silent and educational institutes closed. The disease started in Wuhan China in December 2019 and spread globally within a short period. Nobody has the answer to the treatment's concern; every country was looking for its best scientific efforts. India a religious country with a huge population started its expedition for COVID-19 in its traditional way. Indian people use many herbal drugs on day to day basis. While writing this book, it is a matter of pleasure that a huge vaccination program is running in India. India is also amongst those countries that are manufacturing vaccines for the whole world.

Indian government started some new programs to strengthen the health facilities in many COVID-19 hospital setups in each district. The aim was to maximize the testing protocols, for that many labs were established specifically for COVID-19 testing, and today India is testing approx 10 lacks cases daily through these labs. The self-reliant program is also running for the health care segment also. Many startup programs have also been initiated which are playing an important role in building the economy as well as improving the patient's status.

1.1. Disease Etiology

Corona virus is an enveloped and single-stranded RNA virus. They are zoonotic in nature and can transmit from animals to humans. They are largely classified as alpha, Beta, Gama, and Delta Corona virus with their different genomic structures. Some research suggests that alpha and Beta Corona virus cause infection only in mammals. Human Coronaviruses such as 229E and NL63 are responsible for common cold and cough and belong to α Corona virus. Hemagglutinin esterase is a glycoprotein that helps viruses with attack mechanisms. Several coronaviruses do have envelope-associated hemagglutinin-esterase protein (HE), which helps in the attachment and destruction of certain sialic acid receptors that are found on the host cell surface.

Coronavirus contains a spike protein that has a multifunctional molecular machinery that helps in Coronavirus entry into host cells. Based on a structural

study, it has been revealed that the mechanism is based on binding to the receptor on the host cell surface through its S1 subunit and then through the S2 subunit, it fuses viral and host membranes.

1.2. Regulation of Spike Protein

The life cycle of the virus and, host consists of these steps *i.e.* attachment to the site, penetration, biosynthesis, growth, and release. When binding occurs to the host receptor, it moves inside the host cells through endocytosis or by membrane fusion thereby starting replication. The viral mRNA plays an important role in the biosynthesis of viral proteins which mature and are released. Structural studies suggest that corona viruses have a spike (S), membrane (M), envelope (E), and nucleocapsid (N). Spike has a transmembrane glycoprotein that protrudes to the viral surface and shows multiplicity of Corona virus. There are two functional subunits *i.e.* S1 subunit which has the binding ability to the host cell receptor where S2 subunit is for penetration of the viral cellular membranes, according to some previous research work Angiotensin-converting enzyme 2 identified as a regulating receptor for SARS-Cov [1]. Studies based on structure and function implicated that these spike proteins bind to ACE2 [2 - 4]. These ACE2 are mostly found in the lungs where they play an important role in the disease.

1.3. Indian Traditional Drugs

India is linked with the use of traditional medicine since ancient times. The basic knowledge of these systems gained through literature can be seen in each household. Indian traditional medicinal system is unique and the oldest in the world.

Traditional systems of medicines played a crucial role in the development of the global healthcare system. Traditional medicine is useful in diverse health-related practices and approaches, divine knowledge, skills, and practices related to plants, and minerals. Indian civilization is wide-ranging having versatile cultural aspects and is one of the oldest for mankind. Indian traditional medicinal system is one of the oldest traditional medicinal systems in the world. India has distinctive characteristics and well-acclaimed traditional systems of medicine *i.e.* Ayurveda, Unani, Siddha, Yoga, naturopathy, and homeopathy, however, homeopathy is not an indigenous system and came into existence in India in the eighteenth century, it completely integrated into the Indian civilization and got improved like any other traditional medicinal system and it is believed as part of Indian Systems of Medicine. The unani system originated in Greece, and later it was introduced in India by Arabs.

Herbal Therapy for COVID-19

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Abstract: The Covid-19 epidemic is presently ravaging the world, claiming the lives of countless people. This health crisis is well recognised to be caused by SARS-CoV-2 infection, and the problem has yet to be remedied. Many modern doctors and researchers feel that a person's disease resistance ability is critical in battling viral infections. If used appropriately, herbal therapy can be a game changer in this case, since herbal drugs significantly boost or modify immune function, enhancing resistance to microbial infections. These drugs alter the cellular immune response, enhance immunity, impart antioxidant effect, raise IgG antibody production, activate macrophages, have anti-inflammatory and analgesic properties, and so relieve symptoms and reduce viral infection pathology development. Herbal medicine can also aid in the prevention of viral infections by blocking virus entrance and replication in the host cell. Due to their vast therapeutic capabilities, Curcumin, Shunthi, Bhumi-amalki, Guduchi, Yashtimadhu, Pippali, and Haritaki, among other drugs, can be examined for their efficiency and safety against viral infection. The potential uses of herbal medicine as a supplementary and alternative treatment for SARS-CoV-2 illness were reviewed in this chapter. However, further research into the effects of herbal treatment in COVID-19 is needed.

Keywords: COVID-19, Health, Herbal therapy, Herbal therapy COVID-19, Immunity, Infection.

1. INTRODUCTION

As seen by the current situation, in which people all over the world are battling a new pandemic coronavirus disease, the history of human civilization has witnessed both wealthy advancement and different health calamities (COVID-19). The COVID-19 disease transmitted from humans to humans and was labeled a pandemic even after its initial period of occurrence. Due to its high rate of transmission and severity, COVID-19 is considered a current global health problem, with the medical community investing major efforts in combating it.

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This disorder is caused by the invasion of the zoonotic bacteria “severe acute respiratory syndrome coronavirus 2” (SARS-CoV-2) [1 - 3].

SARS-CoV-2 is an enveloped RNA virus that spreads by close contact and respiratory droplets when an infected person coughs or sneezes. The contaminated surface can also act as a source of transmission when a person contacts it before contacting his or her nose, mouth, or eyes [2 - 4].

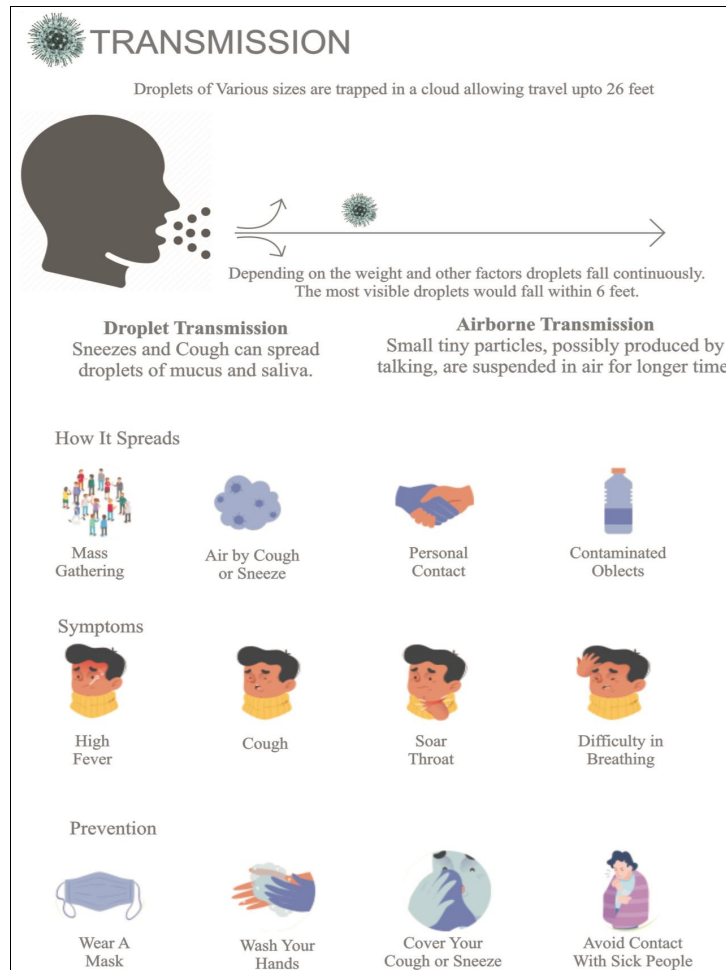


Fig. (1). Transmission, Symptoms and Prevention of COVID-19 Disease.

SARS-CoV-1 (2003), MERS-CoV (2012), and SARS-CoV-2 (2019) are three of the most common “respiratory syndrome coronaviruses” that are also lethal (4). SARS-CoV-2, which exhibits clinical symptoms comparable to those found in

earlier respiratory syndrome coronaviruses, is connected to the current COVID-19 pandemic. The most frequent signs and symptoms are fever, cough, shortness of breath, and sore throat; however, muscular soreness and headache are also prevalent. Bilateral pneumonia, severe respiratory distress, and multi-organ failure, among others, are disease-related consequences that are important causes of death. Other signs of sickness include a loss of taste and smell, however, these only appear in the later stages of the disease [5, 6]. Fig. (1) depicts general considerations about COVID-19 disease propagation, symptoms, and prevention.

Frequent hand washing with soap, maintaining general and respiratory hygiene, avoiding frequent touching of the nose, eye, and face, disinfecting the floor or objects, wearing masks, avoiding close contact with the infected people, maintaining social distance, and using alcohol-based hand sanitizer are some of the preventive measures recommended by medical science. Pharmaceuticals such as favipiravir and Chloroquine, among others, are already used in conjunction with plasma treatment for illness management; however, vaccines are thought to have more favourable results, and scientists anticipate that the drugs will reach the experimental phase [1 - 4].

Researchers are presently concentrating their efforts on finding COVID-19 therapies, which include investigating the antiviral effects of botanicals and natural medications. Herbs have been reported to have antiviral effects against the SARS-CoV-2 virus [7]. Herbs are also thought to improve immunity, making them a vital part of the viral illness prevention strategy. However, it is important to establish the effectiveness and safety of herbal treatment against COVID-19 using experimental models. Herbs contain antiviral and immune-boosting qualities, thus they can help prevent SARS-CoV-2 illness from progressing and spreading. Herbal therapy can also be used as adjuvant and adjunct therapy in combination with standard COVID-19 therapies. Antiviral activity of plants or plant-based extracts has been found in trials against Coronavirus, Enterovirus, Dengue virus, Influenza virus, HIV, and Hepatitis B [1 - 3].

1.1. Herbal Therapy as a COVID-19 Treatment Option

Synthetic antivirals and immunomodulators failed to provide an appropriate therapeutic response against COVID-19, and emergency vaccination usage has yet to be licensed in certain countries, and even if it is, vaccine availability to the general public within a reasonable time period remains a challenge. As a result, alternative, supplemental, and adjuvant therapy techniques for COVID-19 infection prevention and treatment are needed. Fortunately, traditional medical practitioners established the efficiency of natural treatments even against severe viral illness, and herbal therapy may be useful in the treatment of COVID-19 (Fig.

Herbal Immune-Booster for COVID-19

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Abstract: Medicinal plants always play a vital role by enhancing immunity and protecting us against different infections caused by microorganisms like fungi, bacteria, and viruses. The complex immune protection mechanism produces limitless cells or chemicals to control the spectrum of infectious agents and diseases caused by them. Medicinal plants contain different immunomodulatory constituents that amplify or inhibit the components present in the immune system. In India, people have used numerous medicinal plants and plant products since ancient times to boost the immune system and maintain its normal functioning capacity. Traditional herbaceuticals can boost body defense and improvise our health to survive better. In the last two years, the COVID-19 pandemic became a significant health concern. The healthcare system and scientists are fighting generously to save people. Existing medical facilities are not enough to beat the pandemic condition; therefore, the search for alternative remedies is gaining attention. Indeed, public health measures and the immune-boosting process are considered crucial approaches to dwindle the threat and mortality caused by infection. This chapter highlighted immune boosters from plant sources that can play an essential role as an alternative approaches to managing the current pandemic scenario.

Keywords: Immune System, Medicinal Plant, Herbal Booster, Pandemic, COVID-19.

1. INTRODUCTION

The immune system is an integral part of the body, consisting of complex cellular elements that secrete chemicals to conserve the integrity of the body against

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peripheral infection. The exact function of the immune system is to balance and avoid the incidence of the enormous disorders caused by infectious agents. Immunomodulators can be natural or synthetic substances that can suppress or trigger innate and adaptive immune mechanisms [1].

Infectious diseases are very fast-spreading diseases caused by various microorganisms such as viruses, bacteria, fungi, protists, and other pathogenic agents. Pathogenic agents can cause disease by different disease-spreading conditions like coughing, sneezing, and physical contact. Contaminated water, exchanged body fluids, and droplet contaminations also play important roles in such a process. The innate immune system is the initial or first-line defense of the human body against invading pathogens, nonspecific. The innate immune systems are not activated against any particular pathogen but can provide a total defense. Skin is considered a physical barrier and can exert nonspecific defense against invading pathogens. Enzymes present in saliva, mucus, and tears exert defense by digesting invading microorganisms like bacteria. In response to the pathogen's entry into the body, the innate immune mechanism is activated in the initial stage [2].

Entry and spread of pathogenic microorganisms lead to an inflammatory response as a part of the defense mechanism that causes the flow of white blood cells in infected tissues. White blood cells (phagocytes) include neutrophils and protect us by engulfing and destroying bacteria. The immune system also secretes certain chemicals that maintain the body temperature and induce fever. Fever can slow down or stop pathogen's growth and thus help enhance immune responses in the body. Once pathogens invade our body without responding to innate immune defenses, an adaptive immune response gets activated to defend the same [2].

The primary cells of the immune system are known as lymphocytes and can be divided into two types, *i.e.*, B-lymphocyte cell and T-lymphocyte cell. Bone marrow produces B-lymphocyte cells, and maturation of B-lymphocyte takes place in the bone marrow itself. T-lymphocyte cells are also produced in the bone marrow but mature in the thymus. Humoral immunity is the aspect of immunity that consists of serum antibodies produced by plasma cells and exert their function throughout the body. Humoral immunity begins its action when an antibody of B-lymphocyte cell binds with a pathogen, and B-lymphocyte cell presents the pathogen in front of the helper T cell. Activated B cells also rapidly grow to produce plasma cells, which can release antibodies into the blood. Memory B cells are the specialized cells to store information about the pathogen to have future immunity [3].

2. OUTBREAK OF CORONAVIRUS IN THE 21ST CENTURY

COVID-19 pandemic disease has become a global concern in the 21st century; mortality rises regardless of existing medical facilities [4]. Highly communicable COVID-19 is responsible for a large number of morbidities and mortalities around the globe. Non-availability of vaccines until the early part of 2021 or scarcity of adequate vaccines around the world worsens the situation. In the 21st century, viral diseases are becoming more active throughout the world. In the last two decades, the world has witnessed serious infections caused by SARS-CoV, MERS-CoV, and different influenza viruses [5]. In the present scenario, COVID-19 can be considered the world's 3rd most dangerous disease for humans, spreading very fast to all parts of the world. Reports showed that approximately 213 countries are infected with coronavirus [6]. Experts confirmed its clinical characteristics, and it is pretty similar to a pneumonia condition. In March 2020, the World Health Organisation (WHO) announced COVID-19 as a pandemic [7]. COVID-19 disease is caused by the virus named SARS-CoV-2, coined by the International Committee on Taxonomy of Viruses [7]. SARS-CoV has sequence homology with the bat coronavirus and spike glycoproteins present in the virus of SARS play an important role in invading and transmitting the infection from human to human [8]. The spreading capacity of the novel coronavirus and its diagnosis are relatively different from the SARS-CoV virus. The nucleotide patterns of the SARS-CoV virus and their receptor binding sites are unique [9].

The government, WHO, and other healthcare organizations are working together to stop the spread of viral infection. Minimizing the physical contact, isolation, and screening of infected people during the initial stages of infection and sanitization are vital approaches to control the spread of COVID-19. The viral infection can transmit from person to person through the saliva or nose discharge of an infected patient. Manufacturing industries are producing tonnes of masks, and sanitizers to prevent or control the situation [10]. Drugs are in the clinical trial stage, and no specific medicines are available to treat the disease condition yet. Some existing drugs available in the market, like Lopinavir, Chloroquine, Nitazoxanide, Ritonavir, *etc.*, are used to reduce disease progression and balance the virusload [7].

It was observed that COVID-19 virus infection develops in people with weak immune systems, such as older people or people with comorbidities. Certain beneficial bacteria that live in our gut protect us against a spectrum of diseases. The growth of beneficial intestinal bacteria can be increased through the intake of healthy plant-based foods. According to WHO, the COVID-19 virus is similar to different coronavirus types in morphological and chemical compositions [11]. New strains of COVID-19 became a challenge for the healthcare system. It was

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