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Review on Potential of Phytotherapeutics in Fight against COVID-19

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Abstract:- As the oldest and most utilized form of medicine for thousands of years, herbal medicine has an indispensable place within the field of medicine that has been established throughout history. However, with the introduction of allopathic medicine over the last century, herbal medicine has been somewhat phased out of modern practice. This is a grave mistake, especially during a time of medical crisis and more particularly in the time of a pandemic. Plants and their active constituents have a greater complexity and diversity than anything that can be created in a laboratory setting, especially in a short period of time. There is considerable evidence that plant-based medicine - phytotherapeutics - could play a significant role against SARS-CoV-2, and the disease it causes, COVID-19. Following these, the field of phytotherapeutics has already been explored during the outbreak in Wuhan, where traditional Chinese medicine (TCM) was employed during treatment to help improve patient conditions. Moreover, laboratory testing dating back to the original SARS epidemic in 2003 provides concrete evidence that certain plant compounds have a direct antiviral effect on SARS-CoV, and could be potentially utilized against SARS-CoV-2. In addition to these studies, historical evidence from the most deadly pandemic preceding COVID-19, the Spanish Influenza Epidemic, clearly presents that phytotherapeutics as part of a holistic approach can save patient lives. Based on this evidence, phytotherapeutics may be the key to preventing, treating, and even having direct actions against SARS-CoV-2.

Keywords:- *Phytotherapeutics, SARS-CoV-2, COVID-19, plants, herbs, antiviral effect).*

I. INTRODUCTION

The COVID-19 pandemic has shocked the world in numerous ways, resulting in medical professionals, researchers, and government leaders scrambling to find potential treatment methods, vaccines, and cures [1]. Personal protective equipment (PPE) and medical supplies are becoming increasingly difficult to come by [2]. Additionally, while potential drug cures are being explored on a compassion treatment basis, there have already been some unfortunate situations involving the overuse of supposed curative drugs that resulted in significant side effects and even death [3]. As expected in a pandemic of such massive proportions, conventional treatment approaches are beginning to fall short and underperform. Medical staff in hospitals and clinics are put under increasing strain as they have to stretch supplies, work overtime, and make difficult decisions about who to treat and how to treat them [2].

One powerful potential solution to many of these problems may lie within the realm of herbal medicine. Unlike drug cures or supportive methods such as mechanical ventilation which have very specific actions, plant-based therapeutic agents - dubbed phytotherapeutics for concision - have a broad spectrum of potential actions, both remedial and prophylactic [4]. The field of herbal medicine and individual phytotherapeutics have been studied for thousands of years by countless doctors, herbalists, and researchers [5]. However, in current medical practice, herbal medicine plays a much smaller role, which is due in no small part to the severe regulation of herbal medicine that occured in the Western superpowers of Great Britain and the United States following the discovery of antibiotic and steroid drugs [4]. Prior to these restrictions, phytotherapeutics were used extensively by several conventional, as well as herbal, practitioners during the Spanish Influenza Pandemic of 1918. Medical doctors documented a death rate as low as 0.6% in some hospitals, over 15 times lower than the global mortality rate of 4-10%, which is believed to be underreported [5], [6]. Phytotherapeutics were also examined for antiviral properties during the SARS-CoV epidemic of 2003, and several plants and their active constituents were identified as effective antiviral agents [7], [8]. While SARS-CoV-2, which causes COVID-19, is different to the SARS-CoV virus, they both infect cells using the ACE2 target receptor [9]. Many of the phytotherapeutic agents employed in research during the SARS epidemic, whether in the form of whole plants or active constituents, are used in the practice of traditional Chinese medicine (TCM), a medicinal system based on the idea that illness is caused by imbalances within the body that must be brought back into balance through the use of various remedies [4], [10]. TCM has already been employed early in the COVID-19 pandemic, where it was used to manage symptoms and discomfort caused by the SARS-CoV-2 virus [10].

Individual phytotherapeutics could also alleviate the symptoms of COVID-19. The most common symptoms are fever, headache, sore throat, myalgia, chest pain, and overall inflammation which can culminate into cytokine storms [11]. Upper respiratory symptoms are also incredibly common, ranging from mild, such as dry cough, to more severe symptoms such as pneumonia and dyspnea and can

culminate into acute respiratory distress syndrome, or ARDS [10], [12]. Additionally, more information is emerging about digestive symptoms and severe cardiac symptoms caused by the SARS-CoV-2 virus [13], [14]. Each of these symptoms can be treated using traditional herbal remedies [4], [5]. This paper aims to cover a broad spectrum of phytotherapeutics that have been researched previously, either specifically against coronaviruses or for use with specific symptoms that can be seen in a COVID-19 infection. If medical professionals can employ experimental drugs on a compassion basis for patients in critical conditions [10], it should logically follow that they be able to do the same thing with herbs, especially since herbal medicine has existed far longer and extensive evidence to support its efficacy [4], [5].

II. METHODOLOGY

Initially, studies were found that tested the antiviral efficacy of various phytotherapeutics. Studies were included if they directly tested whole plants or active constituents on members of the *Coronaviridae* family, and were not discussed as potential SARS-CoV-2 antivirals if they had antiviral action against another virus family such as *Influenzae*. However, some phytotherapeutics that were not mentioned as direct antivirals against coronaviruses were still included in the symptomatic discussion of COVID-19 and were mentioned as "general antiviral" in combination with the symptoms the herbs treat. Symptoms of COVID-19 were researched extensively, and the main symptoms were pinpointed, which include pneumonia; acute respiratory distress syndrome (ARDS); fever; pain in the forms of myalgia, headache, and chest pain; dry cough; dyspnea; digestive symptoms including nausea, diarrhea, and appetite loss; and cardiac symptoms such as thrombosis [10], [12], [21]. A literature review was then conducted to label phytotherapeutics with direct ability to treat these symptoms. For an herb to be included, it had to either have literature demonstrating its long-standing historical use, studies labeling its active constituents, and/or studies conducted showing its direct efficacy on managing a particular symptom. Potential phytotherapeutics were excluded if there was insufficient evidence to support their use as a traditional remedy. Active constituents for each phytotherapeutic were also recorded. Additionally, two medicinal fungi were reviewed and included for their significant immunomodulatory activities.

III. MAJOR ACTIVE CONSTITUENTS FOUND IN PHYTOTHERAPEUTICS

In order to properly address the discussion of the potential effect of various phytotherapeutics on the SARS-CoV-2, it is essential to understand the general chemical aspect of these beneficial compounds found in plants, such as their chemical classification, composition, structural characteristics, and biosynthetic routes. Natural active constituents can be divided into three main groups: alkaloids, terpenoids and phenolic compounds [15].

A. ALKALOIDS

Alkaloids are pharmacologically potent substances containing nitrogen, found in the form of primary, secondary or tertiary amines. It is the amine functionality that enables alkaloids to have biological activity, through its protonation to form a quaternary system [15]. Alkaloids generally have basic properties, which makes them reactive towards mineral acids to form water-soluble salts, which are often commercially available as pharmaceuticals [15]. The term "alkaloid" itself originates from the word "alkali" indicating their basicity [16].

Alkaloids are synthesised in plants from amino acid precursors and are characterised by the presence of a heterocyclic ring, such as pyrrolidine, piperidine, pyridine, indole, quinoline, isoquinoline, and tropane [16]. Additionally, because amino acids form certain heterocyclic rings through biosynthetic pathways, there are alkaloids derived from ornithine, tyrosine, tryptophan, and nicotinic acid [15]. It has been reported that, in some alkaloids, the nitrogen atom does not derive from an amino acid, and the other biosynthetic pathways include the shikimate, acetate, polyketide and terpenoid metabolic pathways [17]. Notable examples of alkaloids include: coniin, caffeine, nicotine, cocaine, strychnine, atropine, codeine, lycorine, etc [4], [15].

B. TERPENES

Terpenes are the largest and the most diverse group of secondary metabolites, which are most commonly found in plants and fungi. They are structurally marked by a five-carbon unit, upon which their classification is based. The five-carbon unit is biosynthetically derived from isoprene, derived through the mevalonate pathway. By binding of isoprene units together in a head-tail fashion, terpenes with structures of five (hemiterpenes), ten (monoterpenes), fifteen (sesquiterpenes), twenty (diterpenes), thirty (triterpenes) and forty (tetraterpenes) carbon atoms can be formed. Most of the terpene molecules have cyclic structures [18]. Terpenes are very significant for their essential oils and fragrances, and have important applications in aromatherapy, especially monoterpenes and sesquiterpenes of low molecular weight, who are less oxygenated, that are volatile and give essential oils their organoleptic characteristics [19].

One notable example of medicinal application is eucalyptol, which was shown to have an anti-inflammatory and analgesic effect and promotes leukemia cell death [16]. Some other monoterpenes have also shown significant antiviral properties: it has been reported that carvone, geraniol, citral and citronellal have shown antiviral activity towards Herpes Simplex Virus Type 1 (HSV-1) comparable to the effect of acyclovir, the standard drug used to treat the infection [19], along with many other examples.

C. PHENOLIC COMPOUNDS

Phenolic compounds can be most correctly defined as compounds having one or more hydroxyl groups bound to one or more aromatic rings [4]. The classification of phenolic compounds that is widely accepted today was postulated by Harborne and Simmonds in 1964, which is primarily based on the number of carbon atoms and the structural characteristics. The classifications proposed by other researchers are based on either the scope of distribution of these compounds or they are just classified as common or less common [20]. Some of the most common phenolic compound types are listed in Table 1 below.

Structure	Class	Structure	Class
C6	Simple phenolics	C15	Flavanones
C6-C1	Phenolic acids		Flavanols
C6-C3	Cinnamic acids (phenylpropanoids)		Flavans
C6-C3	Coumarins and related compounds		Flavanonols
Polymers or other structures	Lignans, lignins, tannins		Anthocyanins and anthocyanidins

Table 1:- Phenolic compounds classification

Because of the varied structural characteristics, biosynthetic pathways that yield these compounds are specific for every group. For instance, phenylpropanoids are biosynthesized by the shikimate pathway [20], as the C6-C3 structural unit (basis of cinnamic acids, coumarins and flavonoids) is derived from aromatic amino acids phenylalanine and tyrosine, formed through the intermediate called shikimic acid [15]. Phenolic compounds are considered to exhibit strong antioxidant activity, and also anti-cancerogenic, antimicrobial, antiviral and anti-inflammatory effects [20]. Flavonoids are especially held in high regard because of their antioxidant properties, with most notable examples being quercetin, kaempferol, and anthocyanins; they additionally give protection against cardiovascular diseases and age-dependent cell component degeneration by scavenging harmful radicals such as the superoxide anion radical and hydroxyl radicals [15].

IV. POTENTIALLY ANTIVIRAL PLANTS AGAINST CORONAVIRUSES

Several phytotherapeutics have been directly tested for their antiviral properties against *Coronaviridae*, specifically within the domain of blends found in TCM [22], [23]. Individual plants have also shown prowess both in general antiviral activity and specifically against members of *Coronaviridae*, which includes SARS-CoV and SARS-CoV-2 [24]. It is important to make the distinction when describing the antiviral properties of plants whether a specific herb has antiviral capacity against coronaviruses, or just general antiviral capabilities [25].

Astragalus (*Astragalus mongolicus)*, a powerful herb used frequently in TCM, was tested against avian infectious bronchitis virus (AIBV), a member of *Coronaviridae*. The study showed that polysaccharides from astragalus could interfere with viral replication, and the researchers suggested it could be used as an adjuvant for a vaccine designed for AIBV [26]. Astragalus was also tested as part of a TCM blend, which proved to have antiviral action [22]. Many other herbs and phytotherapeutic components were tested during the SARS-CoV epidemic, including glycyrrhizin, an active component of licorice (*Glycyrrhiza glabra*), where it was found to be the most potent viral replication inhibitor of six different compounds researched in one study [27]. The researchers of this particular study also reported that glycyrrhizin inhibited absorption and penetration of the virus, with most absorption inhibition occurring when the compound was administered during and after the absorption period [27], [28].

Another study in 2005 screened more than 200 different TCM extracts for antiviral activity against SARS, and four individual plants were reported to have high antiviral abilities [24]. The most notable species, red spider lily (*Lycoris radiata*), is a plant with a very high content of alkaloids, which are used medicinally [29]. A 2005 study showed that the primary antiviral component of red spider lily is lycorine, an alkaloid known for its antiviral properties; the isolated lycorine from the plant has showed to have a low EC50 concentration at 2.4 μg/mL [24], [30]. However, the study was not able to pinpoint the specific antiviral action of red spider lily or its lycorine isolate. The study also reported two more plants to have potent antiviral action: sweet annie (*Artemisia annua*) and *Pyrrosia lingua*, which showed to have EC50 values of 34.5 and 43.2, respectively [24]. Sweet annie is of interest because it is also antimalarial, and current research indicates that certain compounds with antimalarial action might inhibit SARS-CoV-2 [4], [31]. However, it is not the only member of the *Artemisia* genus that may prove effective against COVID-19, as another study done on 10 clinical isolates of SARS-CoV suggested that *Artemisia apiaceae*, which also has documented antimicrobial properties, could effectively work as an antiviral when used in a TCM extract [28]. *Pyrrosia lingua* is a widely-growing fern with habitats in large portions of Asia, Australia, and Africa, which could make it of interest to researchers and doctors in developing countries needing to explore readily available antivirals, [32]. Chromatography testing proved that it contains notable active constituents [33].

Three other herbs were found to be SARS-CoV 3CL protease inhibitors, as well as being traditionally used to treat pneumonia [23]. The first of these, woad (*Isatis indigotica*), is a traditional TCM herb, the phenolic compounds of which proved to have notable antiviral activity [34]. Japanese nutmeg-yew (Torreya nucifera), and chameleon plant (*Houttuynia cordata*) also possess antiviral action against SARS-CoV related to 3CL protease

inhibition, and chameleon plant has been traditionally used to alleviate respiratory symptoms and treat pneumonia [23], [35]

V. SYMPTOMATIC TREATMENT USING PHYTOTHERAPEUTICS

While SARS-CoV-2 is a novel virus, the symptoms it presents, including upper and lower respiratory symptoms, fever, digestive symptoms, as well as general pain and discomfort [12], have been observed for millenia occurring as part of a variety of infections [4]. Therefore, herbalists, medical practitioners, and researchers have long since identified different phytotherapeutics that can be used to manage these symptoms, and in a time of global pandemic, it may be time to return to these traditional therapies [4], [5], [10]. Even for severe symptoms presented by COVID-19 infections, including pneumonia, there are established phytotherapeutic treatments used for hundreds of years and significant research establishing active constituents of these remedies [4], [5], [34], [35]. Additionally, common herbs found in households that have common use against viral and bacterial infections should be considered for COVID-19 symptomatic management, as they can address a wide spectrum of symptoms including respiratory, cardiac and digestive. These include herbs such as cinnamon (*Cinnamomum* spp.), sage (*Salvia officinalis*), garlic (*Allium sativum)*, and clove *(Eugenia caryophyllata/Syzygium aromaticum*) [4].

Pneumonia

One of the more concerning symptoms of COVID-19 to date is bilateral interstitial pneumonia, which is most often presented with ground glass opacities and a crazy-paving pattern [10], [36]. The mortality rate of those who were diagnosed with pneumonia as a direct result of a COVID-19 infection stands at around 7% [37]. Respirators, ventilators, and basic medical amenities are in short supply around the world as more patients need critical care, which should serve as a call to begin considering alternative methods for treating pneumonia, especially in the early stages of the illness [2], [10]. Phytotherapeutics that can be used to treat pneumonia include herbs commonly found in North America, such as lobelia, boneset, and pleurisy root, which had a history of regular use during the Spanish Flu Pandemic in 1918 by conventional physicians and herbalists alike [5]. Another powerful phytotherapeutic is Ephedra (*Ephedra sinica*), known for its ability to dilate the lungs and airways [4]. However, ephedra contains powerful active constituents such as alkaloids, and should not be taken without direct medical supervision or while pregnant [4], [38].

It is important to note that phytotherapeutics used in the treatment of pneumonia have many other mechanisms of action, including diaphoretic, analgesic, and antispasmodic, helping treat the whole body rather than a single symptom [4], [5]. Additionally, many of the phytotherapeutics used in TCM to treat SARS can manage pneumonia symptoms as well as attack the virus [27], [34], [35]. Since SARS-CoV-2 and the original SARS-CoV do share similarities [39], it is logical to conclude that these treatments could be effectively used for COVID-19 patients. Evidence from the Spanish Flu Pandemic, as well as evidence from studies using TCM on COVID-19 patients, suggests that pneumonia can be treated using herbal treatments, if these treatments are implemented early enough [5], [10].

Fever, pain, and inflammation

For the majority of COVID-19 cases, fevers do not seem to be an overly major problem and many patients can be afebrile in the initial stages of infection [12]. However, when a fever does present, doctors have recommended that patients with COVID-19 not be treated using NSAIDs or ibuprofen except in extreme cases, because researchers have hypothesized that these drugs might worsen the course of infection and increase susceptibility [5], [11]. While acetaminophen/paracetamol is still recommended by most medical professionals to deal with fever, the use of it could mask a fever and keep an infection from being diagnosed properly [40]. Additionally, allowing a fever to run its natural course if it is within a fairly benign range could assist in overcoming infection, even for more critical patients [41]. This would indicate then that the best treatment of most fevers associated with COVID-19 would be to let them run their course; however; phytotherapeutic options with a more gentle afebrile action as opposed to paracetamol or NSAIDs could be considered [4], [5]. The TCM approach to a fever when it presents during the later stages of infection is to use herbs that “clear heat” and detoxify [10]. The process of “clearing heat” can be accomplished by herbs with diaphoretic (or sweat-inducing) action, and many pungent aromatic herbs have this effect [4], [5]. Other phytotherapeutics containing a higher content of sesquiterpene lactones and flavonoids have shown to inhibit signaling pathways that trigger pro-inflammatory cytokines and prostaglandin, reducing fever and pain in patients with various conditions [4], [42], [43]. Other anti-inflammatory herbs with phenolic and flavonoid components can assist in inhibiting pain signaling molecules, including inhibition of Ca++ channels and cytokine production [44], [45], [46].

Dry Cough and Dyspnea

The cough that results from an SARS-CoV-2 infection tends to be very dry and unproductive [10]. Dyspnea is also a common occurrence among COVID-19 patients, usually associated with pneumonia, and can get so severe as to require mechanical ventilation [12]. Plant constituents that can be used to treat cough include alkaloid, terpenoids, tannins, and saponins [47]. Some herbs, including the panacea licorice (*Glycyrrhiza glabra*) and ashwagandha (*Withania somnifera*), have been proven to have an equal or better effect on cough than codeine [47], [48]. Common herbs used to treat upper-respiratory viral infections, such as elderberry (*Sambucus nigra*), echinacea (*Echinacea purpurea*), and garlic (*Allium sativum*) have general antiviral properties and help manage symptoms such as cough during the duration of an illness [49], [50], [51]. It is important to note that these herbs have not been directly tested on SARS-CoV-2, but their general antiviral action in numerous studies make them and other herbs potential

candidates for future research testing the efficacy of phytotherapeutics against COVID-19 infections.

Other phytotherapeutics that are not proven antivirals by nature, but do have a pronounced effect in relieving dry cough and spasms include herbs with demulcent and experoratant mechanisms of action [4], [52]. Marshmallow root (*Althaea officinalis*) contains up to 5% mucilage and 35% starch, as well as other constituents such as flavonoids and tannins, which provide an effective treatment for dry cough [53]. It is also an herb that can be used with infants and children, as it is a highly safe herb [54]. Similar to marshmallow, mullein (*Verbascum* spp.) has expectorant and antispasmodic activities, which comes from constituents such as flavonoids and mucilaginous compounds, as well as glycosides, terpenes, and saponins. Traditionally, it can be used as an infusion to reduce mucus production and make a dry cough more productive by helping expel phlegm [52], [54]. Herbs with terpenoid and phenolic constituents like thymol, menthol, and eucalyptol can also have analgesic, antiseptic, and expectorant properties [4], [20].

Digestive symptoms

Original statistics from early cases of SARS-CoV-2 indicated that digestive symptoms were present to a lesser degree than the typical respiratory symptoms associated with coronavirus, but as the pandemic has progressed, more and more evidence is being presented that digestive symptoms are indeed tell-tale signs of potential SARS-CoV-2 infection [13]. Some patients have even been admitted to hospitals based on digestive symptoms alone, without the presence of fever, and still tested positive for SARS-CoV-2 [55]. Digestive symptoms could include primarily diarrhea and abdominal pain, as well as nausea, vomiting, and loss of appetite [13]. Researchers confirm that digestive symptoms may result due to the fact that ACE2 viral binding receptors can be found in the upper esophagus, ileum, and colon, as well as in the lung [56].

Herbal therapies for digestive symptoms associated with COVID-19 infection can come from the same herbs that are used to treat the more common symptoms, such as fever and respiratory symptoms. Licorice (*Glycyrrhiza glabra*), which has been mentioned in this paper multiple times already, can work as a digestive and appetite stimulant, due to its numerous identified anti-inflammatory components [57]. Yarrow (*Achillea millefolium*) has been traditionally used to treat diarrhea, and it also has a stimulating activity and, though there is a need for more research documenting its active constituents, it has been confirmed to contain alkaloids, flavonoids, and phenolic compounds [43], [58]. Turmeric (*Curcuma longa*) and ginger (*Zingiber officinalis*) have documented anti-nausea and digestion-aiding properties, which is due to their high concentrations of active constituents, such as the very potent constituent curcumin isolated from turmeric [59], [60]. Other aromatic herbs such as garlic (*Allium sativum*) and horseradish (*Armoracia rusticana, syn. Cochlearia armoracia*) can be used as digestive and appetite stimulants [4], [61]. Additionally, marshmallow root (*Althaea officinalis*) is an effective digestive tonic because of its demulcent properties, as well as its high concentration of starch [53].

Cardiac involvement

Many patients with COVID-19 are likely to have a worse prognosis if there is cardiac involvement during infection, and mortality rate due to cardiac involvement is more statistically significant than factors such as diabetes, age, or previously occurring chronic pulmonary and cardiovascular disease [14]. Myocardial injury has been observed as a direct result of a SARS-CoV-2 infection [21]. Some patients have succumbed to thrombosis, as indicated by higher levels of D-dimers obtained from lab analyses [62]. Thus, patients with any potential cardiovascular comorbidities may need an extra level of care and prevention, as well as support during infection [14]. Thankfully, several phytotherapeutics exist that support the overall function of the heart and prevent thrombosis. Arjun (*Terminalia arjuna*) has a history as a heart tonic that goes back thousands of years and notable active constituents [63]. Another herb traditionally used in ayurvedic medicine is broom (*Cystus scoparius*), which grows wildly as a weed in some regions and has a similar, albeit safer, mechanism of action to quinine due to its quinolizidine alkaloids; it has been recommended as a as regulatory treatment and as a treatment for atrial and ventricular fibrillation [4], [64]. Cayenne (*Capsicum annuum*) also has heart-supporting properties, and can help with managing risk factors for COVID-19 infection mortality such as obesity and high blood pressures [46]. The fungi cordyceps (*Cordyceps sinensis*) also has a long history of use in traditional medicine as a cardiac supporting herb that has thrombosis-preventing properties [65].

VI. THE PROPHYLACTIC ACTIONS OF ADAPTOGENIC PHYTOTHERAPEUTICS AND FUNGI

The most obvious example of the significant array of actions a single herb can have upon the body is shown by phytotherapeutics that are adaptogenic in nature. The definition of an adaptogen is a substance that helps the body adapt to different forms of stress [66]. Adaptogens are broadly defined, but must meet three criteria which are widely accepted by herbal practitioners and researchers alike [67]. First of all, they must be non-specific in the role they play within the human body and provide support to the body as a whole during periods of high stress, whether physiological and environmental such as in the case of disease, or psychological [66]. Secondly, when the body encounters these examples of stress, adaptogens must have a clear ability to help bring it back to a state of homeostasis. Thirdly, and most importantly, these substances must be completely non-toxic at normal doses and not interfere with the normal functions of the human body in any way [67]. Adaptogenic status of a plant is established through in vivo studies involving both humans and animals [66]. Adaptogens have a profound stimulating effect on the immune system which aids in producing an effective immune response without the presence of antigens, and affect both extra- and intracellular signaling to modulate

immune and stress response [68]. Phyto-adaptogens mentioned in this paper that show antiviral activity against coronaviruses include plants like astragalus (*Astragalus mongolicus*) and licorice (*Glycyrrhiza glabra)* [26], [27], [66]. Other adaptogens with abilities to manage symptoms associated with COVID-19 include ashwagandha (*Withania somnifera*), holy basil (*Ocimum sanctum*), and echinacea (*Echinacea purpurea*) [4], [47], [50], [67]. While not strictly "phytotherapeutics," adaptogenic fungi including cordyceps and reishi support the cardiac and respiratory systems of the body, as well as having powerful antioxidant and general antiviral activities [65], [69]. Since each adaptogen contains a distinct set of active constituents and components to modulate the immune system, covering them all is beyond the scope of this paper; however, they do tend to contain a wide variety of anti-inflammatory components, including cytokine inhibitors [66], [69]. The importance of adaptogenic phytotherapeutics and therapeutic fungi cannot be overstated, as their use prior to or early in a viral infection, including COVID-19, could potentially lower the risk of sepsis or cytokine storms.

Herb	Latin name	Mode(s) of action	Active constituents (antiviral or anti symptomatic)	Reference
Arjun	*Terminalia arjuna*	Cardiotonic	Flavonoids, phytosterols, tannins, triterpenoid saponins	[4], [63]
Ashwagandha	*Withania somnifera*	Adaptogenic, sedative, tonic	Alkaloids, steroidal lactones	[4], [47],[66]
Astragalus	*Astragalus mongolicus*	Adaptogenic, immune stimulant, antiviral	Isoflavonoids, phytosterols, polysaccharides, triterpene saponins	[4], [26],[66]
Boneset	*Eupatorium perfoliatum*	Diaphoretic, expectorant, antimalarial	Diterpenes, flavonoids, polysaccharides, sesquiterpene lactones	[4], [5]
Broom	*Cytisus scoparius*	Cardiotonic, anti-arrhythmia	Flavonoids, isoflavones, tannins, quinolizidine alkaloids	[4], [64]
Cayenne	*Capsicum annuum*	Stimulant, antispasmodic, analgesic, diaphoretic	Capsaicin, flavonoids, steroidal saponins	[4], [46]
Chameleon plant	*Houttuynia cordata*	Expectorant, antiviral	Hottuynum, phenolic compounds, quinoline alkaloids	[35]
Clove	*Eugenia caryophyllata/Syzygium aromaticum*	Analgesic, antiemetic, antiseptic, antispasmodic, stimulant	Eugenol, gum, methyl salicylate, phenolics, tannins	[4]
Cordyceps*	*Cordyceps sinensis*	Adaptogenic, anti-inflammatory, respiratory tonic	Adenosine, cordycepin, lectins, polysaccharides	[65]
Echinacea	*Echinacea spp.*	Anti-inflammatory, detoxifying, adaptogenic	Alkylamides, caffeic acid esters, polysaccharides	[4], [50]
Elderberry	*Sambucus nigra*	Antiviral, mucus-clearing, anti-inflammatory	Anthocyanins, flavonoids, vitamins	[4], [49]
Ephedra	*Ephedra sinica*	Diaphoretic, bronchioles dilator, stimulant, drying	Flavons, protoalkaloids, saponins, tannins	[4], [38]
Eucalyptus	*Eucalyptus globulus*	Antiseptic, analgesic, expectorant, blood flow stimulant	Flavonoids, phenolics, tannins, resin	[4], [44]
Feverfew	*Tanacetum parthenium*	Anti-inflammatory, analgesic, fever reducing	Alpha-pinene, sesquiterpenes, sesquiterpene lactones	[4], [42]
Garlic	*Allium sativum*	Expectorant, diaphoretic, antiseptic	Allicin, scordinins, selenium, vitamins	[4], [51]
Ginger	*Zingiber officinale*	Anti-inflammatory, antiemetic, antiviral, digestive stimulant	Oleoresin, zingiberene	[4], [60]
Holy basil	*Ocimum sanctum*	Adaptogenic, antispasmodic, analgesic, fever reducing, anti-inflammatory	Eugenol, flavonoids, polyphenols, saponins, triterpenes	[4], [66]
Horseradish	*Armoracia rusticana,*	Digestive stimulant, diaphoretic, expectorant	Flavonoids, glucosinolates, resin, vitamin C	[4], [61]

Japanese nutmeg-yew	*Torreya nucifera*	Antiviral	Biflavonoids, flavones, terpenoids	[23], [70]
Licorice	*Glycyrrhiza glabra*	Expectorant, demulcent, anti-inflam., adrenal support	Isoflavones, phytosterols, polysaccharides, triterpene saponins	[4], [27],[48]
Lobelia	*Lobelia inflata*	Antispasmodic, expectorant, emetic, diaphoretic, respiratory stimulant	Carboxylic acids, piperidine alkaloids	[4], [5]
Marshmallow	*Althaea officinalis*	Demulcent, mucilaginous, soothing	Flavonoids, mucilage, phenolic acids, starch	[4], [53],[54]
Mullein	*Verbascum thapsus*	Antispasmodic, expectorant	Flavonoids, tannins, triterpenoid saponins	[4], [52]
Pleurisy root	*Asclepias tuberosa*	Historically used for pneumonia, analgesic, anti-inflammatory, diaphoretic, digestive	Cardenolides, flavonoids	[4], [5]
Pyrrosia	*Pyrrosia lingua*	Antiviral	Chlorogenic acid, flavonoids	[32]. [33]
Red spider lily	*Lycoris radiata*	Antiviral, antimalarial	Alkaloids (lycorine), minerals	[24],[29],[30]
Reishi*	*Ganoderma lucidum*	Adaptogenic	Lectins, polysaccharides, peptidoglycans, triterpenes	[66]
Sage	*Salvia officinalis*	Expectorant, nervine, astringent, antiseptic	Phenolic compounds, terpenes, tannins	[4]
Sweet annie	*Artemisia annua*	Antiviral, antimalarial, febrifuge	Arteminisin, flavonoids, polyphenols	[4], [31]
Turmeric	*Curcuma longa*	Anti-inflammatory, antiemetic, helps with dizziness	Curcuminoids, phenolic compounds, resin	[4], [59]
Woad/indigo	*Isatis indigotica*	Antiviral, anti-inflammatory	Indigo, indirubin, phenolic compounds	[34]
Yarrow	*Achillea millefolium*	Antispasmodic, diaphoretic, anti-inflammatory, analgesic	Alkaloids, flavonoids, phytosterols, sesquiterpene lactones, terpenes	[4], [43],[58]

Table 2:- List of Active Constituents and Mechanisms of Action (* Fungi; **General Antiviral)

Herb	Immune support	Antiviral	Fever	Pain	Sore throat	Cough	Pneumonia/pleurisy	Shortness of breath	Digestive symptoms	Cardiac support	Reference
Arjun										yes	[4], [63]
Ashwagandha	yes					yes					[4], [47], [66]
Astragalus	yes	yes (SARS)									[4], [26], [66]
Boneset		yes	yes			yes	yes	yes	yes (laxative)		[4], [5]
Broom*										yes	[4], [64]
Cayenne			yes	yes				yes		yes	[4], [46]
Chameleon plant		yes (SARS)		yes (chest)		yes	yes	yes			[35]
Clove		yes**		yes	yes	yes			yes		[4]
Cordyceps*	yes	yes**				yes		possible		yes	[65]
Echinacea	yes	yes**			yes	yes					[4], [50]
Elderberry	yes		possible		yes	yes					[4], [49]
Ephedra		yes (SARS)	yes				yes (dilation of lung airways)	yes (stimulant)			[4], [38]

Eucalyptus				yes	yes	yes	yes	yes			[4], [44]
Feverfew			yes	yes							[4], [42]
Garlic	yes	yes**	yes		yes	yes	possible	possible			[4], [51]
Ginger	yes		yes	yes (stomach)	yes	possible	possible (anti-inflam.)	possible (anti-inflam)	yes		[4], [60]
Holy basil	yes		yes	yes		yes		possible			[4], [66]
Horseradish	yes		yes			yes	possible	yes	yes (stimulant)		[4], [61]
Japanese nutmeg-yew		yes (SARS)									[23], [70]
Licorice		yes (SARS)			yes	yes	possible	possible	yes (laxative and anti-emetic)		[4], [27], [48]
Lobelia			yes			yes	yes	yes	yes (emetic)		[4], [5]
Marshmallow				yes (cough pain)	yes	yes	possible	possible	yes*		[4], [53], [54]
Mullein						yes	possible	yes			[4], [52]
Pleurisy root			yes	yes (chest)		yes	yes	yes	yes		[4], [5]
Pyrrosia		yes (SARS)									[32]. [33]
Red spider lily		yes (SARS)									[24], [29], [30]
Reishi*	yes	yes**						yes			[66]
Sage				yes (throat)	yes	yes	yes	possible	yes		[4]
Sweet annie		yes (SARS)	yes								[4], [31]
Turmeric		yes**		yes		possible	possible (anti-inflam.)	possible	yes		[4], [59]
Woad/indigo		yes (SARS)					yes	possible			[34]
Yarrow			yes	yes		possible	possible	possible	yes		[4], [43],[58]

Table 3:- Potential actions in COVID-19 treatment (* Fungi; **General antiviral – not yet proven for coronaviruses)

VII. CONCLUSION

As SARS-CoV-2 that causes COVID-19 becomes a global threat and spreads rapidly across the globe, solutions that are practical, safe, and low-cost are needed to treat symptoms as well as the virus itself [10]. The field of phytomedicine could provide many potential treatment options that could address COVID-19 in a variety of ways. Several plants have already proven to have antiviral efficacy against the *Coronaviridae* family, specifically SARS-CoV, which is genetically similar to SARS-CoV-2 [22], [23], [24], [27], [28]. Some active constituents that possess antiviral activity have been labeled [24], [70]. Furthermore, many plants have been used for centuries to treat symptoms similar to those presented by COVID-19 infections [4], [5], [64]. It is also important to state that many phytotherapeutics that could have antiviral action against SARS-CoV-2 have already been established to work prophylactically by modulating the immune system, a feat not attainable for many conventional antiviral treatments [66], [67]. While further clinical validation with proper in-vitro, in-vivo, and clinical studies is warranted prior to official clinical recommendation, based on the evidence

already available, phytotherapeutics should present a viable solution to the COVID-19 pandemic.

REFERENCES

[1]. Li, G., & De Clercq, E. (2020). Therapeutic options for the 2019 novel coronavirus (2019-nCoV).
[2]. Ranney, M. L., Griffeth, V., & Jha, A. K. (2020). Critical Supply Shortages—The Need for Ventilators and Personal Protective Equipment during the Covid-19 Pandemic. New England Journal of Medicine.
[3]. FitzGerald, G. A. (2020). Misguided drug advice for COVID-19. Science, 367(6485), 1434-1436.
[4]. Chevallier, A. (2016). Encyclopedia of Herbal Medicine (3rd ed.). New York: Dorling Kindersley Ltd.
[5]. Abascal, K., & Yarnell, E. (2006). Herbal Treatments for Pandemic Influenza: Learning from the Eclectics' Experience. Alternative & Complementary Therapies, 12(5), 214-221
[6]. Johnson, N. P., & Mueller, J. (2002). Updating the accounts: global mortality of the 1918-1920" Spanish" influenza pandemic. Bulletin of the History of Medicine, 105-115.
[7]. Saxena, S. (2005). Glycyrrhiza glabra: medicine over the millennium.
[8]. Elias, R. M., & Câmara, N. O. S. (2012). Bioactive Foods, Nutrients and Herbs in Infectious Diseases. Bioactive Food as Dietary Interventions for Arthritis and Related Inflammatory Diseases: Bioactive Food in Chronic Disease States, 251.
[9]. Ceccarelli, M., Berretta, M., Rullo, E. V., Nunnari, G., & Cacopardo, B. (2020). Editorial–Differences and similarities between Severe Acute Respiratory Syndrome (SARS)-CoronaVirus (CoV) and SARS-CoV-2. Would a rose by another name smell as sweet?. European Review for Medical and Pharmacological Sciences, 24, 2781-2783.
[10]. Jin, Y. H., Cai, L., Cheng, Z. S., Cheng, H., Deng, T., Fan, Y. P., ... & Han, Y. (2020). A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). Military Medical Research, 7(1), 4.
[11]. Favalli, E. G., Ingegnoli, F., De Lucia, O., Cincinelli, G., Cimaz, R., & Caporali, R. (2020). COVID-19 infection and rheumatoid arthritis: Faraway, so close!. Autoimmunity Reviews, 102523.
[12]. Zhang, J., Zhou, L., Yang, Y., Peng, W., Wang, W., & Chen, X. (2020). Therapeutic and triage strategies for 2019 novel coronavirus disease in fever clinics. The Lancet Respiratory Medicine, 8(3), e11-e12.
[13]. Luo, S., Zhang, X., & Xu, H. (2020). Don't overlook digestive symptoms in patients with 2019 novel coronavirus disease (COVID-19). Clinical Gastroenterology and Hepatology.
[14]. Akhmerov, A., & Marban, E. (2020). COVID-19 and the Heart. Circulation Research
[15]. Dewick, P. M. (2010). Medicinal natural products: a biosynthetic approach (3rd ed.). Chichester, U.K.: Wiley.
[16]. Cseke, L. J., Kirakosyan, A., Kaufman, P. B., Warber S. L., Duke, J. A., Brielmann, H. L. (2006). Natural products as plants (2nd ed.). Boca Raton, FL: CRC Press
[17]. Seigler, D. S. (1998). Plant Secondary Metabolism. Boston, MA: Springer US
[18]. Hanson, J. R. (2003). Natural products: the secondary metabolites. Cambridge: Royal Society of Chemistry.
[19]. Roy, D. N. (2019). Terpenoids Against Human Diseases. CRC Press
[20]. Vermerris, W., & Nicholson, R. (2008). Phenolic compound biochemistry. Dordrecht: Springer.
[21]. Hui, H., Zhang, Y., Yang, X., Wang, X., He, B., Li, L., ... & Chen, Y. (2020). Clinical and radiographic features of cardiac injury in patients with 2019 novel coronavirus pneumonia. medRxiv.
[22]. Yang Y, Islam MS, Wang J, Li Y, Chen X. Traditional Chinese medicine in the treatment of patients infected with 2019-new coronavirus (SARS-CoV-2): a review and perspective. International journal of biological sciences. 2020;16(10):1708.
[23]. Lin, L. T., Hsu, W. C., & Lin, C. C. (2014). Antiviral natural products and herbal medicines. Journal of traditional and complementary medicine, 4(1), 24–35. https://doi.org/10.4103/2225-4110.124335
[24]. Li, S. Y., Chen, C., Zhang, H. Q., Guo, H. Y., Wang, H., Wang, L., ... & Li, R. S. (2005). Identification of natural compounds with antiviral activities against SARS-associated coronavirus. Antiviral research, 67(1), 18-23.
[25]. Lin CW, Tsai FJ, Tsai CH, Lai CC, Wan L, Ho TY, et al. Anti-SARS coronavirus 3C-like protease effects of Isatis indigotica root and plant-derived phenolic compounds. Antivir Res. 2005;68:36–42
[26]. Zhang, P., Liu, X., Liu, H., Wang, W., Liu, X., Li, X., & Wu, X. (2018). Astragalus polysaccharides inhibit avian infectious bronchitis virus infection by regulating viral replication. Microbial pathogenesis, 114, 124-128.
[27]. Cinatl, J., Morgenstern, B., Bauer, G., Chandra, P., Rabenau, H., & Doerr, H. W. (2003). Glycyrrhizin, an active component of liquorice roots, and replication of SARS-associated coronavirus. The Lancet, 361(9374), 2045-2046.
[28]. Chen, F., Chan, K. H., Jiang, Y., Kao, R. Y. T., Lu, H. T., Fan, K. W., ... & Guan, Y. (2004). In vitro susceptibility of 10 clinical isolates of SARS coronavirus to selected antiviral compounds. Journal of Clinical Virology, 31(1), 69-75.
[29]. Salachna, P., & Piechocki, R. (2019). Comparison of nutrient content in bulbs of Japanese red spider lily (Lycoris radiata) and golden spider lily (Lycoris aurea), ornamental and medicinal plants. World News of Natural Sciences, 26, 72-79.
[30]. Wang, P., Li, L. F., Wang, Q. Y., Shang, L. Q., Shi, P. Y., & Yin, Z. (2014). Anti-dengue-virus activity and structure–activity relationship studies of lycorine derivatives. ChemMedChem, 9(7), 1522-1533.

[31]. Gautret P, Lagier JC, Parola P, Meddeb L, Mailhe M, Doudier B, Courjon J, Giordanengo V, Vieira VE, Dupont HT, Honoré S. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. International journal of antimicrobial agents. 2020 Mar 20:105949.
[32]. Wei, X., Qi, Y., Zhang, X., Luo, L., Shang, H., Wei, R., Liu, H., & Zhang, B. (2017). Phylogeny, historical biogeography and characters evolution of the drought resistant fern Pyrrosia Mirbel (Polypodiaceae) inferred from plastid and nuclear markers. Scientific reports, 7(1), 12757. https://doi.org/10.1038/s41598-017-12839-w
[33]. Cui, L., Zhang, Y., Shao, W., & Gao, D. (2016). Analysis of the HPLC fingerprint and QAMS from Pyrrosia species. Industrial Crops and Products, 85, 29-37.
[34]. Lin CW, Tsai FJ, Tsai CH, Lai CC, Wan L, Ho TY, Hsieh CC, Chao PD. Anti-SARS coronavirus 3C-like protease effects of Isatis indigotica root and plant-derived phenolic compounds. Antiviral research. 2005 Oct 1;68(1):36-42.
[35]. Lau KM, Lee KM, Koon CM, Cheung CS, Lau CP, Ho HM, et al. (2008) Immunomodulatory and anti-SARS activities of Houttuynia cordata. J Ethnopharmacol. 2008;118:79–85
[36]. Lai CC, Shih TP, Ko WC, Tang HJ, Hsueh PR. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and corona virus disease-2019 (COVID-19): the epidemic and the challenges. International journal of antimicrobial agents. 2020 Feb 17:105924.
[37]. CDC. (2020). COVID View. Centers for Disease Control and Prevention. Retrieved 11 April 2020, from https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview/index.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fcovid-data%2Fcovidview.html.
[38]. Ibragic, S., & Sofić, E. (2015). Chemical composition of various Ephedra species. Bosnian journal of basic medical sciences, 15(3), 21–27. https://doi.org/10.17305/bjbms.2015.539
[39]. Xu, J., Zhao, S., Teng, T., Abdalla, A. E., Zhu, W., Xie, L., ... & Guo, X. (2020). Systematic comparison of two animal-to-human transmitted human coronaviruses: SARS-CoV-2 and SARS-CoV. Viruses, 12(2), 244.
[40]. Day, M. (2020). Covid-19: ibuprofen should not be used for managing symptoms, say doctors and scientists.
[41]. Ray, Juliet J., and Carl I. Schulman. "Fever: Suppress or Let It Ride?" Journal of Thoracic Disease 7, no. 12 (December 2015): E633–36. https://doi.org/10.3978/j.issn.2072-1439.2015.12.28.
[42]. Pareek, A., Suthar, M., Rathore, G. S., & Bansal, V. (2011). Feverfew (Tanacetum parthenium L.): A systematic review. Pharmacognosy reviews, 5(9), 103–110. https://doi.org/10.4103/0973-7847.79105
[43]. Chandler, R. F., Hooper, S. N., & Harvey, M. J. (1982). Ethnobotany and phytochemistry of yarrow, Achillea millefolium, Compositae. Economic botany, 36(2), 203-223.
[44]. Vecchio, M. G., Loganes, C., & Minto, C. (2016). Beneficial and healthy properties of Eucalyptus plants: A great potential use. The Open Agriculture Journal, 10(1).
[45]. Kumar, Manish & Shete, Abhilasha & Akbar, Zafar. (2010). A Review on Analgesic: From Natural Sources.. International Journal of Pharmaceutical & Biological Archives. 1. 95-100.
[46]. Sanati, S., Razavi, B. M., & Hosseinzadeh, H. (2018). A review of the effects of Capsicum annuum L. and its constituent, capsaicin, in metabolic syndrome. Iranian journal of basic medical sciences, 21(5), 439–448. https://doi.org/10.22038/IJBMS.2018.25200.6238
[47]. Nosalova, G., Fleskova, D., Jurecek, L., Sadlonova, V., & Ray, B. (2013). Herbal polysaccharides and cough reflex. Respiratory Physiology & Neurobiology, 187(1), 47–51. doi:10.1016/j.resp.2013.03.015
[48]. Kuang, Y., Li, B., Fan, J., Qiao, X., & Ye, M. (2018). Antitussive and expectorant activities of licorice and its major compounds. Bioorganic & Medicinal Chemistry, 26(1), 278–284. doi:10.1016/j.bmc.2017.11.046
[49]. Krawitz, C., Mraheil, M. A., Stein, M., Imirzalioglu, C., Domann, E., Pleschka, S., & Hain, T. (2011). Inhibitory activity of a standardized elderberry liquid extract against clinically-relevant human respiratory bacterial pathogens and influenza A and B viruses. BMC complementary and alternative medicine, 11, 16. https://doi.org/10.1186/1472-6882-11-16
[50]. Sperber, S. J., Shah, L. P., Gilbert, R. D., Ritchey, T. W., & Monto, A. S. (2004). Echinacea purpurea for prevention of experimental rhinovirus colds. Clinical Infectious Diseases, 38(10), 1367-1371.
[51]. Nantz, M. P., Rowe, C. A., Muller, C. E., Creasy, R. A., Stanilka, J. M., & Percival, S. S. (2012). Supplementation with aged garlic extract improves both NK and γδ-T cell function and reduces the severity of cold and flu symptoms: a randomized, double-blind, placebo-controlled nutrition intervention. Clinical Nutrition, 31(3), 337-344.
[52]. Riaz, M., Zia-Ul-Haq, M., & Jaafar, H. Z. (2013). Common mullein, pharmacological and chemical aspects. Revista brasileira de farmacognosia, 23(6), 948-959.
[53]. Al-Snafi, A. E. (2013). The pharmaceutical importance of Althaea officinalis and Althaea rosea: A review. Int J Pharm Tech Res, 5(3), 1387-1385.
[54]. Franova, S., Nosalova, G., & Mokry, J. (2006). Phytotherapy of cough. Advances in Phytomedicine, 111–131. doi:10.1016/s1572-557x(05)02007-6
[55]. An, P., Chen, H., Jiang, X., Su, J., Xiao, Y., Ding, Y., ... & Lv, X. (2020). Clinical features of 2019 novel coronavirus pneumonia presented gastrointestinal symptoms but without fever onset.
[56]. Dong, Y., Mo, X., Hu, Y., Qi, X., Jiang, F., Jiang, Z., & Tong, S. (2020). Epidemiological characteristics of 2143 pediatric patients with 2019 coronavirus disease in China. Pediatrics.

[57]. Yang, R., Yuan, B. C., Ma, Y. S., Zhou, S., & Liu, Y. (2017). The anti-inflammatory activity of licorice, a widely used Chinese herb. Pharmaceutical biology, 55(1), 5-18.
[58]. Applequist, W. L., & Moerman, D. E. (2011). Yarrow (Achillea millefolium L.): A Neglected Panacea? A Review of Ethnobotany, Bioactivity, and Biomedical Research1. Economic Botany, 65(2), 209–225. doi:10.1007/s12231-011-9154-3
[59]. Dulbecco, P., & Savarino, V. (2013). Therapeutic potential of curcumin in digestive diseases. World journal of gastroenterology, 19(48), 9256–9270. https://doi.org/10.3748/wjg.v19.i48.9256
[60]. Palatty, P. L., Haniadka, R., Valder, B., Arora, R., & Baliga, M. S. (2013). Ginger in the Prevention of Nausea and Vomiting: A Review. Critical Reviews in Food Science and Nutrition, 53(7), 659–669. doi:10.1080/10408398.2011.553751
[61]. Charles, D. J. (2012). Horseradish. In Antioxidant Properties of Spices, Herbs and Other Sources (pp. 347-351). Springer, New York, NY.
[62]. Hunt, B., Retter, A., & McClintock, C. (2020). Practical guidance for the prevention of thrombosis and management of coagulopathy and disseminated intravascular coagulation of patients infected with COVID-19
[63]. Kumar, D. S., & Prabhakar, Y. S. (1987). On the ethnomedical significance of the arjun tree, Terminalia arjuna (Roxb.) Wight & Arnot. Journal of ethnopharmacology, 20(2), 173-190.
[64]. Yarnell E, Abascal K. Botanicals for regulating heart rhythms. Alternative & Complementary Therapies. 2003 Jun 1;9(3):125-9
[65]. Tuli, H. S., Sandhu, S. S., & Sharma, A. K. (2014). Pharmacological and therapeutic potential of Cordyceps with special reference to Cordycepin. 3 Biotech, 4(1), 1–12. https://doi.org/10.1007/s13205-013-0121-9
[66]. Panossian A. Understanding adaptogenic activity: specificity of the pharmacological action of adaptogens and other phytochemicals. Annals of the New York Academy of Sciences. 2017 Aug;1401(1):49-64.
[67]. Liao LY, He YF, Li L, Meng H, Dong YM, Yi F, Xiao PG. A preliminary review of studies on adaptogens: comparison of their bioactivity in TCM with that of ginseng-like herbs used worldwide. Chinese Medicine. 2018 Dec 1;13(1):57.
[68]. Wagner HK. Immunostimulants and adaptogens from plants. InPhytochemistry of medicinal plants 1995 (pp. 1-18). Springer, Boston, MA.
[69]. Wachtel-Galor S, Yuen J, Buswell JA, Benzie IF. Ganoderma lucidum (Lingzhi or Reishi). InHerbal Medicine: Biomolecular and Clinical Aspects. 2nd edition 2011. CRC Press/Taylor & Francis.
[70]. Ryu YB, Jeong HJ, Kim JH, Kim YM, Park JY, Kim D, Naguyen TT, Park SJ, Chang JS, Park KH, Rho MC. Biflavonoids from Torreya nucifera displaying SARS-CoV 3CLpro inhibition. Bioorganic & medicinal chemistry. 2010 Nov 15;18(22):7940-7.