Life Sciences Student Journal

2023, vol1, No2,pp:106-116

Doi:10.22034/LSSJ.2023.89

Herbs in the Time of Crisis: A Comprehensive Review on COVID-19 and Herbal Therapies

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Article Type:
Review Article

Received:1December.2023
Revised: 3 December may . 2023
Accepted:8December.2023
ePublished: 10 December. 2023

Abstract

The COVID-19 pandemic has ignited a global quest for alternative therapeutic strategies, with herbal remedies emerging as compelling candidates. This review explores the potential roles and efficacy of herbal therapies in the context of COVID-19, synthesizing existing research and traditional knowledge to provide a thorough examination of their impact on viral infections, immune modulation, and overall health. Herbal Agents and Antiviral Properties: Examining antiviral herbs like Echinacea, Elderberry, Astragalus, Garlic, Andrographis, Licorice, Olive Leaf, and Cat's Claw reveals potential in combating viral infections. Caution is stressed, considering individual differences and potential interactions with standard treatments. Herbal Compounds and Viral Replication: The review delves into intricate interactions of herbal compounds with viral replication, emphasizing the necessity for rigorous research, including clinical trials, to establish efficacy, safety, and optimal dosages. Explored mechanisms comprise direct antiviral activity, immune modulation, anti-inflammatory effects, interference with cellular signaling pathways, viral protease inhibition, and RNA/DNA polymerase inhibition. Immunomodulatory Effects of Herbal Therapies: The review highlights herbs' bioactive compounds, exploring immune modulation, antioxidant-rich properties, anti-inflammatory effects, support for mucous membranes and skin integrity, direct antiviral and antimicrobial properties, gut health support, respiratory benefits, and adaptogenic properties. Clinical Implications: Herbs for COVID-19 Respiratory Symptoms: Evaluating studies, the review suggests potential benefits of herbal medicine alongside conventional treatment for COVID-19 prevention and respiratory relief. However, conclusive evidence is lacking, necessitating more rigorous trials.

1. Introduction

The COVID-19 pandemic has prompted an urgent exploration of alternative therapeutic strategies, and herbal remedies have emerged as compelling candidates in the search for effective interventions. As the world grapples with the challenges posed by the novel coronavirus, this comprehensive review aims to elucidate the potential roles and efficacy of herbal therapies in the context of COVID-19. By synthesizing existing research and traditional knowledge, we delve into various facets of herbal interventions, providing a thorough examination of their impact on viral infections, immune modulation, and overall health.

1.Herbal Agents and Antiviral Properties:

The search for potent antiviral solutions has reignited curiosity in herbal remedies, blending traditional knowledge with modern scientific inquiry. This segment offers a thorough examination of herbs renowned for their established antiviral attributes, shedding light on their potential importance, particularly in the realm of viral infections like COVID-19. This in-depth exploration underscores the array of tools nature provides in combating viral infections. However, the utilization of these herbs should be approached with care, taking into account individual differences and potential interactions with standard treatments.

1.1. Echinacea (Echinacea purpurea)

Echinacea, renowned for its immune-modulating properties, has emerged as a subject of interest due to its potential antiviral effects. Studies suggest its capacity to stimulate immune cells, potentially reducing the severity and duration of viral infections(1).

1.2. Elderberry (Sambucus nigra)

Abundant in flavonoids, elderberry has demonstrated antiviral activity against respiratory viruses. Its potential to inhibit viral replication and modulate immune responses positions it as a promising candidate for combatting viral infections(2).

1.3. Astragalus (Astragalus membranaceus)

Astragalus, recognized for its immunomodulatory effects, exhibits promise in enhancing the body's natural defense mechanisms against viral infections. Current research suggests a potential role in mitigating symptom severity(3).

1.4. Garlic (Allium sativum):

Garlic, celebrated for its antimicrobial properties, has displayed antiviral effects against a spectrum of viruses. Allicin, a key component, exhibits potent antiviral activity, underscoring garlic's potential in the realm of viral infections(4).

1.5. Andrographis (Andrographis paniculata)

Andrographis, a staple in traditional medicine, boasts antiviral and anti-inflammatory properties. Research suggests its effectiveness against respiratory viruses, with potential applications in managing upper respiratory infections(5).

1.6. Licorice (Glycyrrhiza glabra)

Licorice, containing glycyrrhizin, exhibits antiviral activity against various viruses. Its potential in inhibiting viral replication and modulating immune responses highlights its role as a promising antiviral agent(6).

1.7. Olive Leaf (Olea europaea)

Olive leaf extract harbors compounds with demonstrated antiviral properties. Studies indicate its efficacy against several viruses by inhibiting viral entry, replication, and assembly(7).

1.8. Cat's Claw (Uncaria tomentosa)

Cat's Claw, renowned for its immunomodulatory effects, has exhibited antiviral properties against various viruses. It is suggested to interfere with viral replication, making it a subject of interest in antiviral research(8).

2. Herbal Compounds and Viral Replication: Unveiling Mechanisms of Action

The interaction between herbal compounds and viral replication involves complex mechanisms, and the study of these interactions is an evolving area of research. While herbal compounds may have antiviral properties, it's important to note that the efficacy and safety of such compounds can vary widely(9). Emphasizing the growing interest in herbal compounds for their potential antiviral properties, it is crucial to recognize that the scientific evidence supporting their efficacy and safety can vary. Additionally, the antiviral activity of herbal compounds may be specific to certain viruses, and not all herbal remedies are effective against all types of viruses. Rigorous research, including clinical trials, is needed to establish the efficacy, safety, and optimal dosages of herbal compounds for antiviral purposes. It is always advisable to consult with healthcare professionals before considering the use of herbal supplements, especially in the context of viral infections (10). Here are some general mechanisms of action and examples of herbal compounds that have been studied in the context of viral replication:

2.1.Direct Antiviral Activity:

Some herbal compounds may interfere with the initial stages of viral infection by preventing the virus from entering host cells (Inhibition of Viral Entry). For example, compounds found in green tea, such as epigallocatechin gallate (EGCG), have been studied for their ability to inhibit the entry of certain viruses(11).

For instance, curcumin, derived from turmeric, has been investigated for its potential to inhibit the replication of various viruses(12).

2.2.Modulation of Host Immune Response

Herbal compounds can modulate the host immune response to enhance antiviral defense mechanisms (Immunomodulation). For example, compounds from echinacea and astragalus have been studied for their immunomodulatory effects(13).

2.3. Anti-Inflammatory Effects

Chronic inflammation is often associated with viral infections(Reduction of Inflammation). Some herbal compounds possess anti-inflammatory properties, and by reducing inflammation, they may indirectly impact the viral replication process. Examples include compounds found in ginger and licorice(14).

2.4. Cellular Signaling Pathways

Herbal compounds may interfere with cellular signaling pathways that viruses exploit for their replication. Resveratrol, found in red grapes and wine, has been studied for its potential to disrupt certain signaling pathways associated with viral infections(15).

2.5. Viral Protease Inhibition

Herbal compounds may inhibit viral enzymes, such as proteases, which are essential for viral replication. Some studies have explored the protease inhibition properties of compounds from licorice against certain viruses(16).

2.6. RNA/DNA Polymerase Inhibition:

Compounds from plants like ginkgo biloba have been investigated for their potential to inhibit viral polymerases, enzymes critical for the replication of viral genetic material (17).

3. Immunomodulatory Effects of Herbal Therapies

3.1. Herbs for Immune Modulation and Enhancement

Herbs can enhance the immune response through various mechanisms, thanks to the diverse array of bioactive compounds they contain. Herbs can modulate the activity of immune cells, helping to balance and optimize the immune response. Adaptogenic herbs, like astragalus and ashwagandha, are believed to enhance the body's ability to adapt to stressors and promote immune balance(18). herbs stimulate the production and activity of white blood cells, which are essential components of the immune system. Echinacea, for example, is thought to enhance the function of immune cells like macrophages and lymphocytes(19,20). Antioxidant-rich herbs help combat oxidative stress by neutralizing free radicals in the body. Free radicals can contribute to inflammation and compromise immune function. Herbs such as turmeric, green tea, and rosemary exhibit potent antioxidant effects(21). Chronic inflammation can hinder immune responses. Herbs with anti-inflammatory properties, including ginger, turmeric, and holy basil, may modulate inflammatory pathways and support overall immune health(22). Some herbs support the integrity of mucous membranes and skin (Enhanced Barrier Function), which act as physical barriers against pathogens. Herbs like licorice and aloe vera may contribute to maintaining healthy barriers that prevent the entry of harmful microorganisms(23).

Certain herbs exhibit direct antiviral and antimicrobial properties, helping to combat infections. Garlic, for instance, is known for its antimicrobial effects, and elderberry has been studied for its potential antiviral activity(24). A significant portion of the immune system is located in the gut. Herbs with prebiotic and probiotic properties, such as ginger and turmeric, as well as fermented foods, can support a healthy gut microbiome(Gut Health Support). A balanced gut microbiome positively influences immune function (25,26). Herbs like thyme, oregano, and eucalyptus are traditionally used for their respiratory benefits (Respiratory Health Support). They may help soothe the respiratory tract and support immune responses against respiratory infections(27). Adaptogenic herbs, such as rhodiola and holy basil, may help the body adapt to stress. Chronic stress can weaken the immune system, and adaptogens may contribute to maintaining resilience against stress-related immune suppression(28,29).Some herbs can influence the production and activity of cytokines, which are signaling molecules involved in immune responses. Modulating cytokine levels can contribute to a balanced and effective immune response(30).

3.2. Herbs for Cytokine Storm in COVID-19

Mitigating the cytokine storm associated with severe COVID-19 cases poses a complex challenge, and it's important to acknowledge that specific treatments for COVID-19 are continuously evolving. The term "cytokine storm" denotes an excessive immune response that may contribute to severe inflammation and tissue damage.

herbs, particularly in the context of severe medical conditions like COVID-19. Although these herbs may possess potentially beneficial properties, rigorous scientific studies, such as well-designed clinical trials, are imperative to establish their safety and efficacy in mitigating cytokine storms associated with severe COVID-19 cases(31). Always consult healthcare professionals before contemplating the use of herbs or supplements, especially in the context of severe medical conditions. Healthcare professionals can offer guidance based on the latest evidence and ensure that any interventions are safe and suitable for individual health conditions(32,33). Here are some herbs that have been studied or proposed for their potential in mitigating cytokine storms or modulating the immune response:

Quercetin: Found in foods like onions, apples, and berries, quercetin is a flavonoid with anti-inflammatory and antioxidant properties. Some studies suggest that quercetin may modulate cytokine levels and have potential benefits in respiratory infections(34).

Curcumin (Turmeric): Curcumin, the active compound in turmeric, is known for its anti-inflammatory and antioxidant properties. It has been studied for its potential to modulate immune responses and reduce inflammation, which could be relevant in mitigating cytokine storms(35,36).

Green Tea (Epigallocatechin Gallate - EGCG): Green tea contains EGCG, a polyphenol with anti-inflammatory and antioxidant properties. Some studies suggest that EGCG may help regulate immune responses and reduce inflammation(32,33,37).

Ginger: Ginger has anti-inflammatory properties and has been traditionally used to alleviate respiratory symptoms. Some research indicates that ginger may modulate cytokine production and contribute to anti-inflammatory effects(38,39).

Boswellia (Frankincense): Boswellia extracts contain compounds with anti-inflammatory properties, and they have been studied for their potential to modulate immune responses. Some research suggests that boswellia may influence cytokine production(40,41).

Andrographis paniculata: Andrographis paniculata is an herb traditionally used in Ayurvedic medicine. Some studies suggest that it may have anti-inflammatory properties and could potentially modulate the immune response(42,43).

Astragalus: Astragalus is an adaptogenic herb that has been studied for its immunomodulatory effects. It may have anti-inflammatory properties that could be relevant in mitigating excessive immune responses (44,45).

Root:Licorice root contains glycyrrhizin, which has anti-inflammatory properties. Some studies suggest that licorice may modulate cytokine production and could have potential benefits in inflammatory conditions(46,47).

It's crucial to approach the use of herbs with caution, especially in the context of severe medical conditions like COVID-19. While these herbs may have properties that could be beneficial, rigorous scientific studies, including well-designed clinical trials, are needed to establish their safety and efficacy in mitigating cytokine storms associated with severe COVID -19 cases.

4. Clinical Implications: Herbs for COVID-19 Respiratory Symptoms

Clinical studies have evaluated the use of herbal medicine in combination with conventional treatment for COVID-19 prevention and respiratory symptom relief. However, the evidence is not conclusive and more rigorous trials are needed to confirm the safety and efficacy of these herbal remedies. One systematic review and meta-analysis of 40 randomized controlled trials (RCTs) found that herbal medicine combined therapy was associated with significant improvements in coughing, fever, fatigue, chest CT images, viral conversion rates and times, and C-reactive protein levels compared to conventional treatment alone(48). The most commonly used herbs were eucalyptus, ginger, spiked pepper, garlic, and chamomile. However, the authors acknowledged the limitations of the study, such as the heterogeneity of the trials, the risk of bias, and the lack of long-term follow-up. Another systematic review and meta-analysis of 14 RCTs reported that herbal medicine combined therapy had beneficial effects on clinical symptoms, inflammatory markers, and viral clearance in COVID-19 patients(49). The most frequently used herbs were licorice, astragalus, honeysuckle, and forsythia. However, the authors also noted the low quality of the evidence, the small sample sizes, and the potential publication bias.A news article described some ongoing trials that are testing whether medicinal mushrooms and Chinese herbs can enhance

the immune response and reduce the adverse effects of COVID-19 vaccines(50). Some of the herbs being investigated are reishi, cordyceps, ginseng, andrographis, and scutellaria. The article cited experts who cautioned that the trials are still in early stages and that the results may not be generalizable to different populations and settings. A review article summarized the traditional Chinese herbal medicine (TCM) formulas that have been used in China for the treatment of COVID-19, such as Qingfei Paidu Decoction, Lianhua Qingwen Capsule, and Xuebijing Injection(51). The article explained the rationale and mechanisms of TCM in modulating the immune system, inhibiting viral replication, and alleviating inflammation. The article also discussed the challenges and opportunities of integrating TCM with western medicine in the management of COVID-19. A systematic review and meta-analysis of 11 RCTs evaluated the effect of herbal compounds on coronavirus infections, including COVID-19, SARS, and MERS(52). The review found that herbal compounds had a significant effect on reducing mortality, improving clinical symptoms, and decreasing viral load compared to placebo or standard care. The most effective herbs were glycyrrhizin, baicalin, and quercetin. However, the review also highlighted the limitations of the evidence, such as the low quality of the trials, the inconsistency of the outcomes, and the lack of data on safety and adverse events.

there are some evidence that herbal medicine may have a role in the prevention and treatment of COVID-19 and its respiratory symptoms, but the quality and quantity of the evidence are insufficient to draw definitive conclusions. Therefore, more high-quality and large-scale trials are needed to verify the effectiveness and safety of herbal remedies for COVID-19. Moreover, herbal medicine should not be used as a substitute for conventional treatment, but rather as a complementary therapy under the guidance of a qualified health professional. Some of the examples of traditional herbal remedies and modern medical approaches in covid19 are:

Quinine and its synthetic analogues such as chloroquine or hydroxychloroquine, which are derived from the bark of a Peruvian tree and have been used to treat malaria and other diseases. They are now being revisited for the treatment of covid19 symptoms, as they may have antiviral and anti-inflammatory effects (53).

Artemisinin and its derivatives, which are derived from a Chinese herb and have been used to treat malaria and other diseases. They are now being investigated for the treatment of covid19 symptoms, as they may have antiviral and immunomodulatory effects(54).

Garlic, onion, and other plants that contain sulfur compounds, which have been used to treat tuberculosis and other diseases. They are now being recommended to boost immunity and prevent respiratory infections, as they may have antibacterial and antiviral effects(55).

Ayurvedic preparations, traditional Chinese medicines, and other plant-based products have been used to treat various diseases. They are now being explored as possible therapeutics against covid19, as they may have antiviral, anti-inflammatory, and immunomodulatory effects(56,57).

5. Safety and Quality Considerations

5.1. Herbal Safety

Herbal safety is the practice of using herbal medicines or supplements in a responsible and informed way, taking into account the possible risks and benefits of these natural products(58).

Herbal medicines or supplements are natural compounds from plants' leaves, bark, roots, seeds, or flowers that people can use for medicinal purposes. They may offer therapeutic benefits when people use them as complementary medicine(59).

The FDA is a federal agency that protects public health by regulating drugs, biological products, and medical devices. Herbal medicines or supplements are not regulated as drugs, but as dietary supplements, which have less strict standards of evidence and approval. The FDA does not evaluate or approve herbal products for their quality or effectiveness, but only monitors their safety after they are on the market. The FDA advises consumers to be careful and informed when using herbal products, and to consult their health -care providers before taking them. The FDA also provides online resources and information for consumers. However, herbal medicines or supplements are not subject to regulation by the FDA and, therefore, have not been tested in an FDA-approved clinical trial to prove their effectiveness in the treatment or management of medical conditions(60). This means that there is limited scientific evidence for the safety and efficacy of many plants used in 21st century herbalism, which generally does not provide standards for purity or dosage(61).

these factors can affect the quality and safety of

herbal medicines or supplements are: The true identity of the herbs, which is very important, as some plants may be mislabeled, misidentified, or contaminated with other substances. The growing conditions, age, and preparation of the plants, which can influence the concentration and potency of the active ingredients. The individual variability of the consumers, such as their age, weight, health status, genetics, and metabolism, which can affect how they respond to the herbs. The interactions between the herbs and other drugs, foods, or supplements, which can alter the effects or cause adverse reactions.

5.2. Herbal Quality Control and Standardization in Medicine

Herbal quality control and standardization in medicine are important aspects of ensuring the safety, efficacy, and consistency of herbal products. Herbal quality control and standardization in medicine are important aspects of ensuring the safety, efficacy, and consistency of herbal products. Herbal medicines are derived from plant sources, which may vary in their chemical composition, potency, and quality depending on various factors such as geographical origin, harvesting time, processing methods, storage conditions, and adulteration. Therefore, it is necessary to establish quality parameters and specifications for herbal materials and products, as well as to employ analytical techniques and methods to verify their identity, purity, and content of active ingredients. The following methods and techniques are useful for quality control and standardization of herbal medicines. Organoleptic evaluation: This involves the examination of the herbal material by using the senses of sight, smell, taste, touch, and sometimes hearing. This can help to identify the plant species, part, and form, as well as to detect any signs of deterioration, contamination, or adulteration. Macroscopic and microscopic evaluation: This involves the observation of the external and internal features of the herbal material by using a magnifying glass, a microscope, or a digital imaging system. This can help to confirm the identity of the plant material, as well as to detect any foreign matter, insects, fungal growth, or structural damage.

Physicochemical evaluation: This involves the measurement of various physical and chemical properties of the herbal material, such as moisture content, ash value, extractive value, pH, solubility, density, viscosity, refractive index, optical rotation, melting point, and boiling point. This can help to determine the quality and purity of the herbal material, as well as to indicate the presence of any adulterants or contaminants. Phytochemical evaluation: This involves the detection, identification, and quantification of the chemical constituents of the herbal material, such as alkaloids, flavonoids, tannins, saponins, glycosides, terpenoids, steroids, phenols, and essential oils. This can help to determine the chemical profile and the content of active ingredients of the herbal material, as well as to differentiate between similar or closely related plant species.Chromatographic techniques: These are analytical techniques that separate the components of a mixture based on their different affinities to a stationary phase and a mobile phase. Some of the common chromatographic techniques used for herbal analysis are thin layer chromatography (TLC), high performance liquid chromatography (HPLC), gas chromatography (GC), and supercritical fluid chromatography (SFC). These techniques can help to separate, identify, and quantify the chemical constituents of the herbal material, as well as to compare the fingerprints of different batches or samples of the same herbal product. Biological evaluation: This involves the assessment of the biological activity and pharmacological effects of the herbal material or product, such as antioxidant, anti-inflammatory, antimicrobial, antidiabetic, anticancer, immunomodulatory, and neuroprotective properties. This can help to evaluate the efficacy and safety of the herbal product, as well as to establish the dose-response relationship and the mechanism of action. These are further methods and techniques that are used for quality control and standardization of herbal medicines. They can help to ensure the quality, safety, and efficacy of herbal products, as well as to provide scientific evidence and validation for their use.(62–67).

6. Herbal Preparations and Formulations:

In comparison between herbal traditional and modern formulations, there are many differences and similarities. Herbal traditional formulations are based on the principles and practices of various traditional medical systems, such as traditional Chinese medicine, Ayurveda, Unani, and African traditional medicine. These systems have a holistic view of health and disease and use herbal medicines to balance the body, mind, and spirit. Herbal traditional formulations are usually complex mixtures of multiple plant materials, which may have synergistic or antagonistic effects.

They are often prepared by using traditional methods, such as decoction, infusion, maceration, or extraction. They are usually prescribed by trained practitioners, who consider the individual constitution, symptoms, and environment of the patient. Herbal traditional formulations are often used for the prevention, maintenance, and treatment of various diseases and disorders(68,69). Modern formulations are based on the principles and methods of Western pharmaceutical sciences, which have a reductionist view of health and disease, and use herbal medicines to target specific pathologies or symptoms. Modern formulations are usually standardized extracts or isolated compounds of single or few plant materials, which have well-defined chemical structures and pharmacological activities. They are often prepared by using modern technologies and techniques, such as chromatography, spectroscopy, or mass spectrometry. They are usually tested by using rigorous scientific and ethical standards, such as quality control, pharmacological evaluation, clinical trials, and safety assessment. Modern formulations are often used for treatment, cure, or palliation of various diseases and disorders (Table 1).

Table1, A comparison between herbal traditional and modern formulations

	Advantage	Disadvantage
Traditional Formulations	-Have a long history of use and empirical evidence in different cultures and regions. -Have a holistic approach that considers the whole person and the context of the disease. - Have a wide range of effects and applications that can address multiple aspects of the disease. -Have a low cost and easy availability in many areas.	-Have a lack of quality control, identification, and standardization of the plant materials and products. -Have a lack of scientific validation and regulation of the efficacy and safety of the products. -Have a high variability and unpredictability of the individual doses and responses of the products. -Have a potential for adverse effects, interactions, and contamination of the products.
Modern Formulations	-Have a high degree of quality control, identification, and standardization of the plant materials and products. -Have a high degree of scientific validation and regulation of the efficacy and safety of the products. -Have a high specificity and targeting of the pathologies or symptoms of the disease. -Have a high reliability and reproducibility of the individual doses and responses of the products. -Have a high cost and limited availability in some areas.	-Have a short history of use and limited evidence in different cultures and regions. -Have a reductionist approach that ignores the whole person and the context of the disease. -Have a narrow range of effects and applications that can address only one aspect of the disease.

Conclusion

The manuscript contributes valuable insights into the potential roles of herbal therapies in addressing the challenges posed by COVID-19. It navigates through the complexities of antiviral properties, immunomodulation, clinical implications, safety considerations, and the dynamics between traditional and modern formulations. The comprehensive nature of the review underscores the importance of ongoing research and collaboration between traditional and modern approaches to optimize the potential benefits of herbal therapies in the face of a global health crisis

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