

An Overview of the Application of Green Nature Deep Lung Support, a Natural Product With Herbal Source in Medicine

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Abstract

Background: The use of natural resources, especially medicinal plants, for treating and improving the quality of life has roots as far back as human history. The extensive abilities of plants and the ease of access have led to the use of these huge natural resources in modern medicine. The present study focused on reviewing the component properties of the Green Nature Deep Lung Support as one of the medicinal products with a natural source. Furthermore, while examining some plants' effects on viral respiratory infections, the scientific bases supporting these claims were discussed as well.

Methods: Data were collected by searching keywords such as "drug development", "herbal medicine", "infectious disease", "natural product", and "SARS-CoV-2" in Medline, Embase, and Web of Science databases. The main texts of all related articles were reviewed after reviewing the titles of the articles and their abstracts.

Results: The use of herbal medicines for the treatment and control of viral respiratory infections has been of interest in the past. The effects and benefits of a wide variety of antiviral herbs have been discussed. Green Nature Deep Lung Support product with the extract of plants such as *Eriobotrya japonica*, *Fritillaria cirrhosa*, *Taraxacum Officinale*, *Andrographis paniculata*, and *Echinacea purpurea* can be effective in improving respiratory and inflammatory symptoms of various diseases.

Conclusion: The herbal extracts used in Green Nature Deep Lung Support product have anti-inflammatory and immune-modulating properties and can be influential as a potential treatment in diseases such as COVID-19 that are affected by a cytokine storm.

Keywords: Drug development, Herbal medicine, Infectious disease, Natural product, SARS-CoV-2

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Introduction

The outbreak of COVID-19 around the world has been one of the most challenging issues in human society, which has caused the loss of many lives in a short period. During the last 10 years, our world has experienced other similar infectious diseases, whose negative consequences have affected various dimensions of human societies. However, the prevalence and mortality caused by COVID-19 are higher and more severe than these diseases. Vaccination is the most promising approach for controlling COVID-19.¹ The performance of many of these vaccines is the transfer of complementary DNA or mitochondrial DNA (mRNA) through liposomes or adenovectors, stimulating the

production of spike protein and the neutralization of immunoglobulin G antibodies.²

Although many reports have been published on the positive role of vaccines in reducing the number of patients requiring hospitalization and the burden of COVID-19 infection, this method has also limitations. Investigations have shown that the titer of vaccine antibodies is associated with a significant decrease after the third month.³ On the other hand, vaccinated people are not completely immune, and the possibility of contracting COVID-19 and transmitting the disease to other people still exists. In addition, the mutation created in the spike protein by the virus prevents the correct and



targeted functioning of vaccines. Another limitation in the use of vaccines is that vaccines may not be effective in immunocompromised people.⁴

Therefore, choosing a treatment approach consisting of auxiliary treatments to control the proliferation of the virus and prevent the deterioration of the disease can be considered the most efficient method. The use of nutritional supplements and herbal medicines can prevent damage caused by widespread systemic inflammation caused by COVID-19 by strengthening the immune system.⁵ It can be mentioned that medicinal herbs and natural products are among the most trusted products in this field. In the past, flavonoid compounds, alkaloids, and polyphenols obtained from plants and mushrooms have been used to strengthen the immune system and using their anti-inflammatory properties.⁶ Many of these compounds can control the proliferation of the virus and inflammatory responses.⁶ Some of the bioactive compounds derived from plants have been taken into consideration to control SARS-CoV-2 respiratory infection, including thymoquinone, a-hederin, and nigellidine (obtained from *Nigella sativa*)⁷, quercetin (obtained from *Ginkgo biloba* and green tea), and ellagic acid (obtained from *Moringa oleifera*).⁸ Further, due to its anti-thrombosis and anti-platelet aggregation effect, *Panax ginseng* is one of the medicinal plants that has been successfully utilized in the treatment of COVID-19.⁹ The curcumin, quercetin, luteolin, piperine, and epigallocatechin-3-gallate compounds obtained from *Polygonum cuspidatum* also played a positive role in the treatment of COVID-19 due to their ability to control the cytokine storm and prevent pulmonary fibrosis.¹⁰

Therefore, considering the importance of using these natural resources, the present study aims to review the function of plant extracts used in the Green Nature Deep Lung Support supplement as a natural product that can be effective in improving respiratory diseases.

Methods

The data of this study have been obtained by reviewing English language articles published in the field of herbal natural products in Medline, Embase, and Web of Science databases from 1995 to 2022. Several keywords were searched, including “Drug development”, “Herbal medicine”, “Infectious disease”, “Natural product”, and “SARS-CoV-2”. A total of 253 articles were obtained, of which only 197 articles were accessible in full text. Among them, 127 articles were excluded from the study due to the lack of an understanding of the provided information, and 73 articles were evaluated carefully (Figure 1).

Results

Andrographis Paniculata

Antibiotics are typically used to treat respiratory infections, but due to resistance to antibiotics, herbal sources can play an effective role in the treatment of these diseases as an auxiliary treatment. *A. paniculata* is a herbaceous plant of the *Acanthaceae* family that is found in the tropical and

subtropical regions of Asia, Southeast Asia, and India and is known as the king of bitters. Although people of different regions know this plant by different names.¹¹ The extract of this plant, known as andrographolide, has relative solubility in water, and the use of ethanol, chloroform, and ether increases the solubility of this extract. The chemical formula of this substance is C₂₀H₃₀O₅. This extract can be obtained by using a 1:1 mixture of dichloromethane and methanol and then by recrystallization, andrographolide is directly separated from the extract.¹² *Andrographolide* has various properties and is found in all parts of the plant, especially the leaves (Figure 2).¹³ During the last two decades, due to the high variety of the properties of this plant extract, researchers have been attempting to obtain wider biological properties of this plant extract by combining andrographolide with other substances. Investigations have demonstrated that the aqueous or ethanol extract of andrographolide causes a decrease in blood glucose levels in streptozotocin-diabetic and healthy rats.¹⁴ Furthermore, this substance can interact with many intracellular components as a bipolar compound and create different biological responses. For example, studies have revealed that *A. paniculata* polysaccharides with andrographolide improve diabetic nephropathy.¹⁴

According to studies, *A. paniculata* and its derived compounds have antioxidant properties. The aqueous extract of *A. paniculata* reduces glutathione by increasing the activity of antioxidant enzymes such as catalase, superoxide dismutase, and glutathione-transferase. This extract prevents lipid peroxidation by reducing thiobarbituric-acid-reactive levels in the liver and kidneys of diabetic rats.¹⁵

The expression of the inducible isoforms of nitric oxide (NO) synthase and cyclooxygenase-2 (COX-2) causes excessive production of NO and prostaglandin E2 and

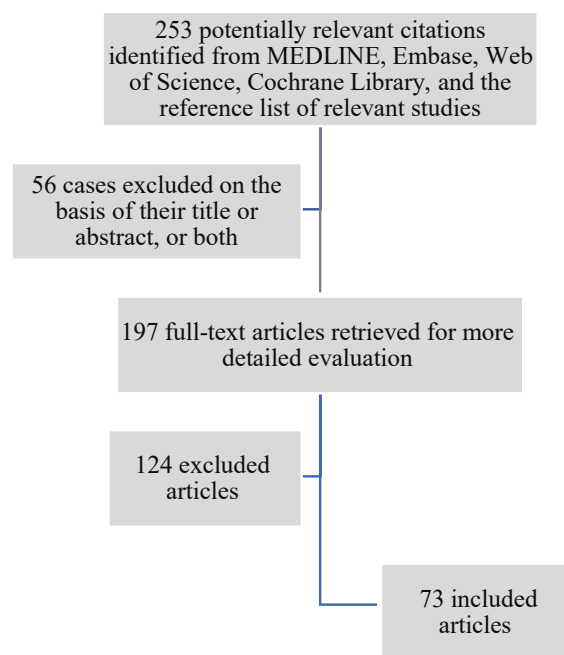


Figure 1. Diagram of Study Steps

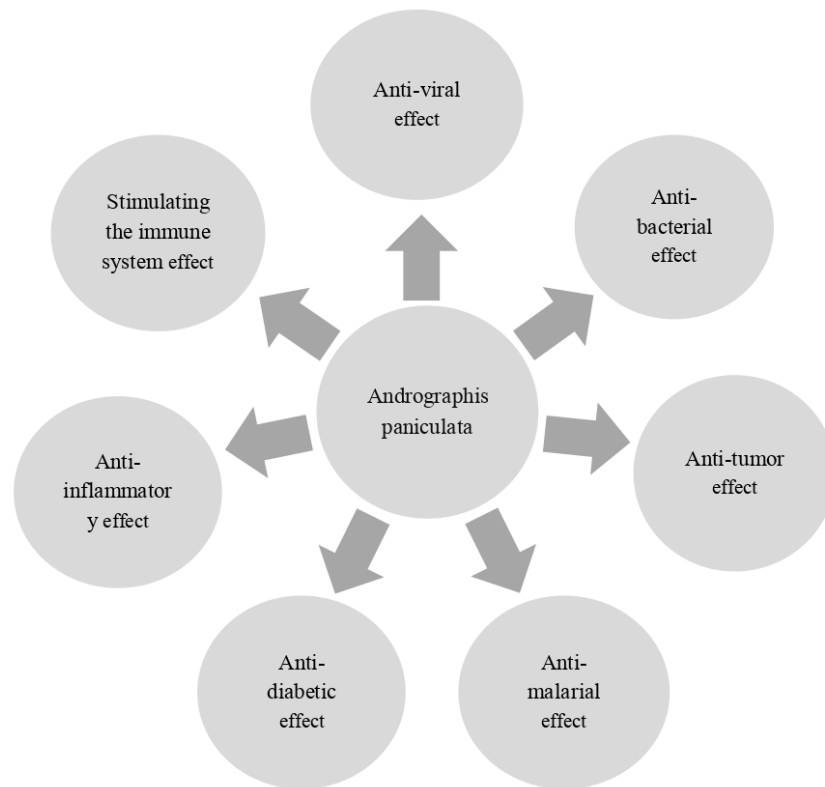


Figure 2. Pharmacological Effects of *Andrographis paniculata*

drives inflammatory processes of macrophages. The release of pro-inflammatory cytokines by macrophages stimulated with lipopolysaccharide (LPS) induces the inducible isoforms of NO synthase, thus increasing NO production. Investigations have shown that the methanol extract of *A. paniculata* and andrographolide inhibits NO production by LPS in a concentration-dependent manner.¹⁶ Examining the effect of the andrographolide extract on mice demonstrated that this substance can inhibit LPS-induced NO production in RAW 264.7 mouse cell lines. The use of this extract in rats causes the maximum contractile response of the thoracic aorta to phenylephrine to be restored after incubation with LPS, decreasing the average arterial blood pressure. *Andrographolide* also suppresses interleukin (IL)-2 production and T-cell proliferation in a mixed lymphocytic reaction and inhibits dendritic cell maturation and antigen presentation.¹⁷ Several studies have been published on the use of this plant extract, some of which are presented in Table 1.

Echinacea

Echinacea is a plant from the *Asteraceae* family, which includes 11 species of herbaceous and flowering plants. More than 800 products and herbal medicines containing *echinacea* (herbal medicines, including homeopathic medicines) are currently available on the market.²⁸ Three commercial varieties of this plant include *Echinacea purpurea*, *Echinacea pallida*, and *Echinacea Angustifolia*, whose antibacterial and antiviral properties have been well-established previously. Additionally, the use of these plants is of special interest due to their anti-inflammatory

properties and modulation of the immune system.²⁹ Aqueous, alcoholic, and polysaccharide extracts from all parts of the plant, including roots and aerial parts, have the above properties on the cells.³⁰ *Echinacea*'s active components, including glycoproteins, high molecular weight polysaccharides, phenolic compounds, caffeic acid derivatives, and alkamides, can induce transcription and modulate immune pathways.³¹ However, using this plant in a situation where the body is in the inflammatory response phase suppresses the immune function.

Echinacea's inflammatory response through the secretion of inflammatory mediators such as tumor necrosis factor-alpha (TNF-a) and IL-1 beta (IL-1b) and increased phagocytosis by macrophages, resulting in the release of NO, is activated. NO is a signal for the activation of macrophages against various microbes and tumor cells, but when it is produced in excess, it can be harmful to host tissues as well. Therefore, the production of these inflammatory mediators is regulated by the anti-inflammatory mechanisms of factors such as IL-4 and IL-10.³²

Echinacea has also anti-cancer effects. The investigation of the effect of using this plant in patients with advanced cancers with extensive metastases has shown that in a number of patients, after immunotherapy, and low-dose cyclophosphamide and thymostimulin, slight clinical and immunological improvements were observed with the use of *E. purpurea*. In addition, this compound can increase the activity of lymphokine-activated killer cells in patients with advanced liver cancer.³³ However, the effect of *echinacea* immune modulation cannot be separated

Table 1. A Summary of Previous Studies on the Properties of the *Andrographis paniculata* Extract

| Type of Activity | Authors | Article Title | Performance |
|------------------------------------|--------------|--|---|
| Antioxidant activity | Lin et al | Antioxidant, antioedema, and analgesic activities of <i>Andrographis paniculata</i> extracts and their active constituent andrographolide | Evaluation of the antioxidant activity of <i>Andrographis paniculata</i> water extract showed that this extract increases the activity of antioxidant defense enzymes such as catalase, superoxide dismutase, and glutathione-transferase while decreasing glutathione content. Therefore, this extract has free radical inhibition, xanthine oxidase inhibition, and anti-lipid peroxidation activities. In addition, this extract is anti-edema and anti-pain. ¹⁸ |
| Diabetes control | Xu et al | Synergetic effect of <i>Andrographis paniculata</i> polysaccharide on diabetic nephropathy with andrographolide | Examination of the andrographolide extract in rats demonstrated that A water-soluble polysaccharide together with andrographolide increases body weight and creatinine clearance rate while decreasing creatinine and urea nitrogen levels in the serum, serum urea, blood glucose, and urinary albumin excretion. This combination can improve the metabolic abnormalities of diabetic rats and prevent or delay the progression of diabetic renal complications, which may be useful as a therapeutic agent to inhibit the progression of diabetes. ¹⁹ |
| Anti-inflammatory activity | Chiou et al | Mechanisms of the suppression of inducible nitric oxide synthase (iNOS) expression in RAW 264.7 cells by andrographolide | Andrographolide prevented the production of NO caused by LPS and decreased the expression of iNOS in the RAW 264.7 mouse macrophage cell line. Further, the administration of andrographolide to rats restored the maximum contractile response of the thoracic aorta to phenylephrine and decreased the mean arterial blood pressure of rats. ²⁰ |
| Anti-cancer activity | Shi et al | Inhibition of cell-cycle progression in human colorectal carcinoma Lovo cells by andrographolide | Andrographolide prevents cell cycle progression in human colorectal cancer Lovo cells by stopping the G1-S phase and inhibits the activity of Cyclin D1/Cdk4 and/or Cyclin A/Cdk2 and Rb phosphorylation by expressing p53, p21 and p16. ²¹ |
| Immunomodulatory activity | Qin et al | Andrographolide inhibits the production of TNF- α and IL-2 in lipopolysaccharide-stimulated macrophages: Role of mitogen-activated protein kinases | Andrographolide decreases TNF- α , IL-12a, and IL-12b mRNA levels. Moreover, this extract can reduce the production of TNF- α and IL-12p70 proteins. Andrographolide prevents ERK1/2 MAP kinase activity and can prevent LPS-induced TNF- α production by suppressing ERK1/2 signaling. ²² |
| Hepatoprotective activity | Singha et al | Protective activity of andrographolide and arabinogalactan proteins from <i>Andrographis paniculata</i> Nees. against ethanol-induced toxicity in mice | Examining the toxicity caused by ethanol in mice and evaluating liver and kidney tissues using andrographolide revealed that treating mice with andrographolide and arabinogalactan proteins can minimize the toxicity caused by ethanol. These compounds have bioactive substances that are responsible for protecting the liver against ethanol toxicity. ²³ |
| Antimicrobial activity | Zaidan et al | In vitro screening of five local medicinal plants for antibacterial activity using the disc diffusion method | Aqueous extract of andrographolide leaves has antimicrobial activity against Gram-positive <i>Staphylococcus aureus</i> , methicillin-resistant <i>Staphylococcus aureus</i> , and Gram-negative <i>Pseudomonas aeruginosa</i> . ²⁴ |
| Antiviral activity | Tang et al | Screening of anti-dengue activity in the methanolic extracts of medicinal plants. | <i>Andrographis paniculata</i> methanolic extract has antiviral activity against DENV1-infected Vero E6 cells. ²⁵ |
| Effects on cardiovascular disease | Awang et al | Cardiovascular activity of labdane diterpenes from <i>Andrographis paniculata</i> in isolated rat hearts. | The dichloromethane extract of <i>Andrographis paniculata</i> Nees can significantly reduce coronary perfusion pressure and heart rate and cause vasodilation. ²⁶ |
| Inhibition of platelet aggregation | Lu et al | Suppression of novel NF- κ B signaling by andrographolide with a novel mechanism in human platelets: Regulatory roles of the p38 MAPK-hydroxyl radical-ERK2 cascade | Andrographolide is a novel NF- κ B inhibitor that has potent antiplatelet activity by activating the endothelial cyclic GMP pathway of NO (eNOS). This combination has the potential to treat thromboembolic disorders and can be considered for the treatment of various inflammatory diseases. ²⁷ |

Note. TNF- α , Tumor necrosis factor-alpha; IL, Interleukin; MAOK, Mitogen-activated protein kinases; NF- κ B, nuclear factor- κ B; LPS, lipopolysaccharide.

from other factors and more and more detailed studies are needed in this regard.

Another application of the *E. purpurea* extract is to improve the severity and duration of various upper respiratory infections such as bronchitis and viral infections such as human and avian influenza viruses, H1N1-type IV, H3N2-type IV, rhinoviruses, and herpes.³³ Investigations represented that inulin-type fructans and other fructans are the main immune system-modulating components found in plant extracts.³⁴ What is important in this context is the preparation quality of *echinacea* products. Herbal products obtained from *echinacea* are among the best-selling herbal medicines for the treatment and prevention of respiratory infections.³⁵ The function of these products includes a set of anti-inflammatory, antiviral, and immunomodulatory activities.

Eriobotrya japonica

Eriobotrya japonica is an evergreen plant native to subtropical regions, which originates from southeast China. The medicinal use of this plant goes back thousands of years, and its extract has been used to treat cough, chronic bronchitis, inflammation, diabetes, and cancer in traditional Chinese medicine.³⁶ In recent years, scientific evidence has confirmed the active medicinal compounds in the extract of this plant. The extracts obtained from different organs of *E. japonica* have different compounds. For example, studies have shown that the leaves and flowers of this plant contain significant amounts of phenols and triterpenes. The fruit of this plant has valuable compounds such as carotenoids, flavonoids, sugars, organic acids, and various vitamins, and the kernel also contains various minerals, types of protein, and tannin.³⁷

Eriobotrya japonica leaves have long been used in

traditional Chinese medicine to treat ailments such as cough, chronic bronchitis, and asthma. In addition to leaves, the seeds and fruits of this plant have anti-inflammatory activities.³⁸ Many lung diseases are caused by inflammation caused by polysaccharides. Studies have demonstrated that the *E. japonica* extract enriched with triterpenes, especially ursolic acid, has anti-inflammatory activity in mice.³⁹ Examining the effect of the seed extract of this plant on mice undergoing chemotherapy with mucositis indicated that the use of this extract significantly controlled mucositis, epithelial damage, and bacterial infection.⁴⁰ The anti-inflammatory effect of the extract obtained from *E. japonica* is applied through the reduction of pro-inflammatory mediators such as TNF- α , IL-6, IL-8, IL-1 β , iNOS, COX-2, and the increase of anti-inflammatory cytokines such as IL-10, followed by the inhibition of NF- κ B activation and mitogen-activated protein kinase signaling pathway.³⁹

Other cytotoxic active compounds isolated from *E. japonica* extract are:

- Ursolic and oleanolic acids: Inhibition of Molt 4B human lymphoid cell proliferation⁴¹
- Procyanidin oligomers: Inhibition of human salivary gland tumor cells and human squamous cell carcinoma⁴²
- Epicatechin, procyanidin C-1, procyanidin B-2, and procyanidin oligomer: Inhibitory effect on HSC-2 cells⁴²
- δ -oleanolic acid, 3-O-(E)-p-coumaroyl tormentic acid, ursolic acid, and betulinic acid: Inhibitory effect on human HL60 cells and the inhibition of DNA topoisomerase I.⁴³
- Euscaphic acid: Antitumor effect on mouse tumor caused by the 7,12-DMBA initiator and tissue-type plasminogen promoter.⁴⁴

Fritillaria

Fritillaria is a plant native to the temperate regions of the Northern Hemisphere, which is often detected in Central Asia, the Mediterranean region, and North America. In China, twelve species of this plant are used as natural medicines for respiratory diseases.⁴⁵ Alkaloids in different species of *Fritillaria* have different properties such as antitussive, antiasthmatic, *chronic obstructive pulmonary disease* (COPD) control, and expectorant effects. In addition, the extract of this plant has potential anti-inflammatory, anti-hypertensive, anti-tumor, and bacteriostasis effects.⁴⁶

Studies have shown that the substances obtained from this plant can be effective for treating coughs without phlegm or chronic coughs.⁴⁷ According to *Fritillaria* properties, including anti-cough, anti-pneumonia, expectorant, anti-inflammatory, antioxidant, and anti-asthma effects, it can be considered a suitable option for treating respiratory diseases and improving disorders such as cough, phlegm, bronchial inflammation, adult respiratory distress syndrome, and COPD. Furthermore, it seems that alkaloids present in some species of this plant, considering the effect on the biological processes effective in the inflammatory response, can be considered a potential treatment for respiratory infections such as the emerging COVID-19 infection^{48,49} (Figure 3).

Several species of *Fritillaria* have anticancer activities in cases such as oral, ovarian, and endometrial keratinocytes, glioblastoma, human promyelocytic leukemia cells, and prostate cancer. One of the active compounds found in many species of *Fritillaria* is Peimine, which has the effect of reversing drug resistance in tumor cells. Investigating the mechanism of this steroidal alkaloid has represented that the expression of P-glycoprotein in drug-resistant cells is inhibited by increasing the concentration of Peimine.⁴⁵

Different species of *Fritillaria* also have anti-

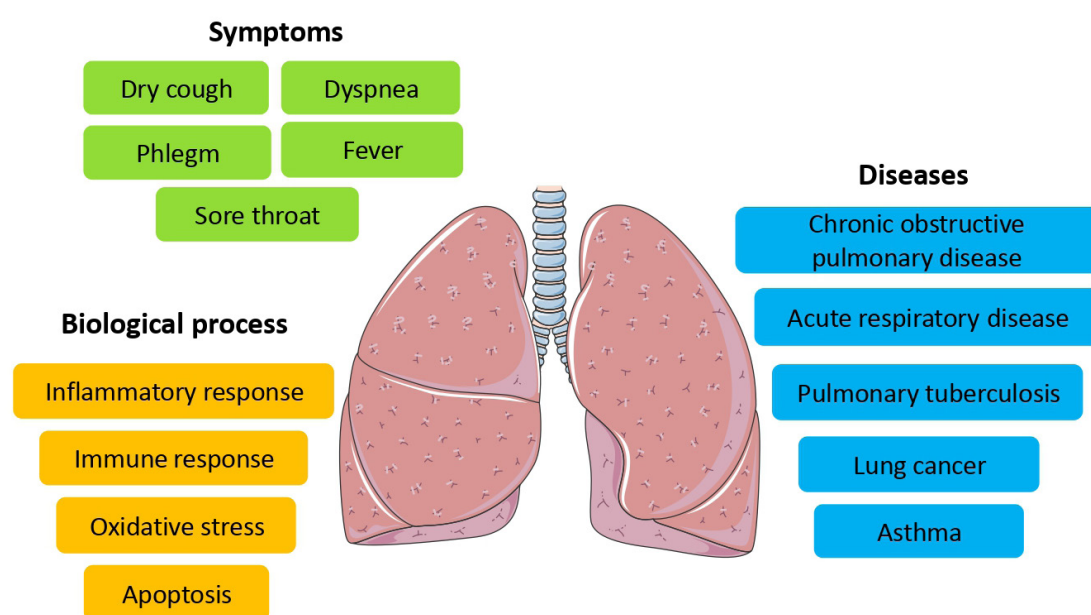


Figure 3. Summary of Pulmonary Diseases, Symptoms, and Biological Pathways Affected by *Fritillaria*.⁴⁸

inflammatory activities. A study on the ethanol extract of two species, *Fritillaria cirrhosa* and *F. pallidiflora*, revealed that consumption of this extract prevents ear edema in mice. Based on previous studies, *F. cirrhosa* alkaloids also prevented acetic acid-induced capillary permeability, and carrageenan-induced edema and suppressed inflammatory cell recruitment and cytokine production in the bronchoalveolar lavage fluid of mice. *Fritillaria* bulbs play their anti-inflammatory role by influencing signaling pathways. These pathways include the inhibition of NF- κ B, downregulation of inflammatory cytokines, and inhibition of mitogen-activated protein kinases⁵⁰ (Figure 4). Extracts obtained from some species of *Fritillaria* have antihypertensive properties. For example, the aqueous extract of *F. ussuriensis* prevents blood pressure caused by NG-nitro-L-arginine methyl ester by increasing vascular NO production and improving kidney function.⁴⁶

Another interesting function of *Fritillaria* is the anticholinesterase activity in some species. Additionally, water and ethanol extracts of this plant have antibiotic activities. For example, *F. thunbergii* has an inhibitory effect against six strains of *Helicobacter pylori*.⁴⁵ In addition to antibiotic activities, some species have antiviral properties. Antiviral effects against the H1N1 influenza virus have been observed in *F. thunbergii* species.⁵¹

Scutellaria baicalensis

Scutellaria baicalensis is a flowering plant from the Lamiaceae family that is native to East Asia and can be found in many European countries. The decoction of the root of this plant, known as Huang-Qin in China, has long been used by the people of this region as a traditional medicine to treat colds and pneumonia.⁵¹ Studies have shown that this plant can be effective in treating hepatitis B and C.⁵³ Fufang is another compound derived from this plant that can increase the life span of patients with bronchial squamous cell cancer and non-small-cell lung cancer.⁵⁴ The *S. baicalensis* extract can also be effective in the treatment of brain tumors,⁵⁵ prostate cancer, and head and neck squamous cell carcinoma⁵⁵. The action of the aqueous root extract of this plant is through changing

the expression of *Bcl* genes and increasing the inhibitory activity of cyclin-dependent p27 kinase, reducing the expression of the *c-myc* oncogene and thus inducing apoptosis.⁵⁷ Some bioactive compounds found in the *Scutellaria* root extract that have anti-cancer activity are as follows⁵⁸:

- Baicalein: Preventing the growth of lymphoma and myeloma cells
- Wogonoside: Having anticancer effects on acute myeloid leukemia cell lines, increased transcription of phospholipid scramblase 1, and cell cycle regulator and differentiation-related genes

Scutellaria baicalensis has antibacterial and antiviral properties. So far, the antibacterial effect of this plant has been proven on *Escherichia coli*, *Salmonella anatum*, *Bacillus cereus*, *Listeria monocytogenes*, and *Staphylococcus aureus*.⁵⁹ Baicalin can play an anti-HIV-1 role so that only 2 μ g/mL of this substance can inhibit up to 90% of reverse transcriptase.⁶⁰

Today, researchers are attempting to increase the biosynthesis of bioactive flavones such as baicalein, baicalin, wogonin, and wogonoside in *S. baicalensis* with the help of new technologies. Next-generation sequencing technologies have identified structural genes such as 6-hydroxylase, 8-O-methyltransferase, and 7-O-glucuronosyltransferases responsible for the biosynthesis of flavones.⁶¹

Taraxacum officinale

Taraxacum officinale, commonly known as dandelion, is a herbaceous plant of the *Asteraceae* family that is found in different regions such as Asia, Europe, and North America. In the past, the leaves and young parts of this plant were used as food due to the presence of valuable substances such as fiber, minerals, vitamins, and essential fatty acids.⁶² In addition, the chemical substances in the flowers, leaves, stems, and roots of this plant, including carotenoids, flavonoids, phenolic acids, sesquiterpene lactones, polysaccharides, triterpenes, and sterols have led to the medicinal use of this plant.⁶³ *Taraxacum* has different species, among which *T. officinale* has been

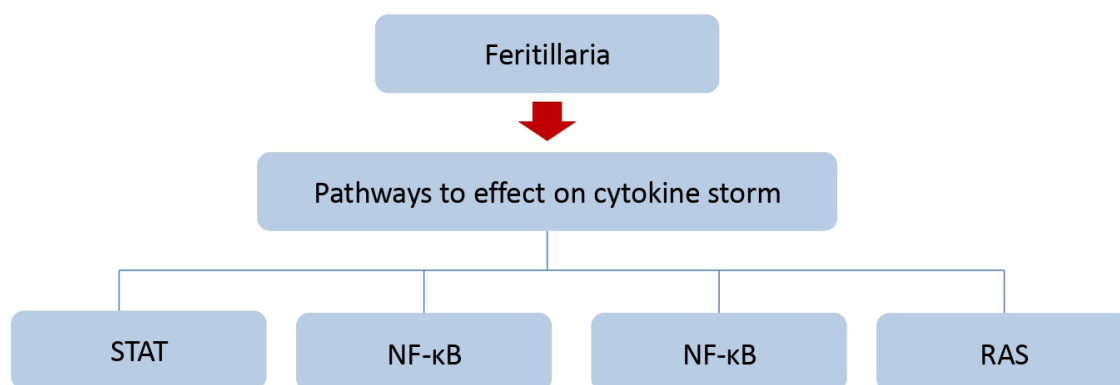


Figure 4. *Fritillaria* Pathway for the Treatment of Respiratory Diseases. Note. STAT: Signal transducer and activator of transcription (STAT) protein, NF- κ B: Nuclear factor kappa-light-chain-enhancer of activated B cells, MAPK: Mitogen-activated protein kinases, RAS: Renin-angiotensin system

studied more due to its various medicinal uses.

Taraxacum officinale has been utilized since the 15th century due to its diuretic properties.⁶⁴ The extract of this plant has also played a significant role in the treatment and control of renal diseases.⁶⁵ After the 16th century, the properties of *T. officinale* in protecting the liver were confirmed, and it was introduced as one of the safest and most practical herbal medicines.⁶⁶ Further, *T. officinale* leaf extract is effective in the treatment of disorders such as non-alcoholic fatty liver, protection against sodium, and liver damage caused by dichromate.⁶⁷

Taraxacum officinale extract can also help strengthen the immune system through processes such as increasing NO, increasing cytokine production, and activating anti-apoptotic *Bax/Bcl-2* signaling.⁶⁸

The antiviral function of the *T. officinale* extract is performed by inhibiting the transcription and reverse replication of human immunodeficiency virus type 1.⁶⁹ In addition, the extract of this plant has antiviral activity against influenza, hepatitis B and C, and DENV2.⁷⁰

Studies indicate that *dandelion* extract can be considered a potential treatment option for inflammatory processes and tissue damage caused by SARS-CoV-2 infection. As mentioned, the various properties of this plant are valuable due to its bioactive compounds (Table 2). Research has shown that during the process of a cytokine storm caused by COVID-19, taraxasterol contained in this plant can prevent the activation of the inflammatory cycle and subsequent tissue damage by inhibiting interferon-gamma, IL-6, and IL-1B. Cichoric acid in dandelion also reduces lung damage caused by LPSs. Further, cichoric acid inhibits the production of pro-inflammatory cytokines such as TNF- α , IL-6, and IL-1 β by reducing the number of neutrophils and macrophages.⁷¹

Investigations demonstrated that in viral infections of the respiratory system, the damage of epithelial cells due to viral attack is aggravated with simultaneous bacterial infection and mucosal dysfunction. This process has been confirmed in influenza but not yet in COVID-19. *Dandelion* ethyl acetate extract can inhibit the growth of Gram-positive and Gram-negative bacteria and can thus prevent simultaneous bacterial infection and deteriorate disease conditions.

Olea europaea

Olea europaea is an evergreen tree of the *Oleaceae* family that is native to tropical and subtropical regions and has long been used in traditional medicine as a diuretic, lowering blood pressure and improving urinary and bladder infections.⁷² The most common use of this plant is its oil, which has diverse and amazing properties. In traditional medicine, the combination of *O. europaea* oil with lemon juice is utilized to treat gallstones.⁷³ The oral consumption of the leaves of this plant is considered for the treatment of stomach and intestinal diseases and as a mouth cleaner.⁷⁴ Further, the decoction of its leaves and dried fruit is applied for diarrhea and treatment of respiratory and urinary tract infections.⁷⁵

Conclusion

Nowadays, many clinical and laboratory studies revealed that, unlike conventional modern medicines, the use of medicinal plants is often non-toxic or with extremely low toxicity due to their natural origin and long-term use as traditional medicines.

However, it cannot be hidden that many problems can also occur for various reasons such as toxicity due to long-term use, possible medicinal and herbal interactions, and incorrect identification of herbal species. With the spread of COVID-19, due to the limited access to resources and treatment processes, the use of herbal medicines received special attention, and the role of pharmacists was highlighted more than before. On the other hand, the knowledge of pharmacists has been one of the important points to provide efficient drug resources according to patients' needs. Therefore, the use of herbal medicines with the help of herbal doctors was considered in all countries. These herbal medicinal resources have worked effectively in reducing the symptoms and treating many patients.

Considering the many cases mentioned in the main text of the article about some medicinal plants and their effect on the treatment cycles of upper respiratory tract diseases, it can be indicated that using a suitable formula to combine these plants can have a more positive effect. Our studies demonstrate that some products in the drug market, including Deep Lung Support, have this feature. Therefore, it is suggested that while developing a study method to investigate the effect of such drugs, a study

Table 2. Examples of Pharmacological Activity and Bioactive Compounds in Dandelion

| Activity | Sample of Bioactive Compound | Process |
|------------------------------------|--------------------------------|--|
| Anti-inflammation | Taraxasterol and cichoric acid | Inhibiting pro-inflammatory mediators such as IFN and IL-6 |
| Anti-cancer | Chlorogenic acid | Destroying free radicals, preventing DNA damage, inhibiting the induction of carcinogenesis, and increasing the proliferation of cells, including cytotoxic T lymphocytes, natural killer cells, and macrophages |
| Cardioprotection | Ferulic acid | Inhibiting apoptosis |
| Effective in HIV treatment | Chicoric acid | Increasing life expectancy and preventing co-morbidities |
| Prevent reproduction of SARS-CoV-2 | Sinapic acid | Targeting the viral envelope protein |

Note. HIV: Human immunodeficiency virus; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; IFN: Interferon; IL: Interleukin.

in the form of a clinical trial should be proposed as well. What is clear is the profound and amazing impact of the potential that lies within nature.

Ethics statement

Not applicable.

Disclosure of funding source

None.

Conflict of interests declaration

None to declare.

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