Herbal Medicine Interventions

FOR IMMUNE SUPPORT

ARTICLE BY
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The immune system is significantly complex in its physiology and functionality. Maintaining homeostasis involves an intricate interaction between the innate and adaptive immune systems, and the cells, receptors, molecules and chemical substances that comprise these systems.[1]

This complexity also extends to the impact of many factors on immune function, including diet and nutritional status, lifestyle, physical activity levels, age, stress, microbiome composition, and physiological and genetic variability.[2-4]

Herbal medicine can support immune system responses in a variety of ways, including through:

- antioxidant activity
- prebiotic effects
- cytokine production, release and inhibition
- modulation of T and B cells
- stimulation of antibodies
- hypothalamic-pituitary-adrenal axis (HPA) regulation
- antimicrobial actions[5]

The following herbs are researched and valued as interventions for immune health and related conditions through their numerous active constituents and complex actions.

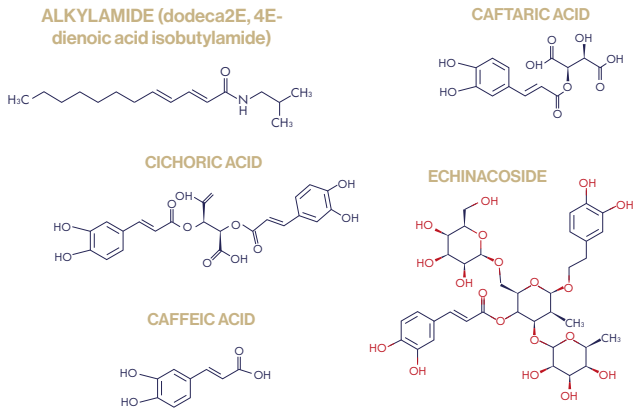
Echinacea (*Echinacea purpurea*)

Native to North America, echinacea is a well-researched immune system supporting herb.[6] The root of *Echinacea purpurea (E.purpurea)* is traditionally used for the relief of common cold symptoms,[7] with scientific evidence supporting this role. Alone or in combination with *Echinacea angustifolia* it also reduces symptoms, severity, and duration of acute respiratory infections (ARI), especially when taken at symptom onset.[6] According to recent research, it may also have preventative effects on severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections.[8]

Active Constituents

The various active constituents attributed to its effect on immunity include the phenolic compounds (caffeic acid esters – chicoric acid, chlorogenic acid, caftaric acid, echinacoside and cynarin), polysaccharides and alkamides.[9,10]

Figure 1. The structure of the active constituents of *Echinacea purpurea*.[11]



As an immune modulator, rather than simply an immune stimulator, echinacea has antiviral, antibacterial, antifungal, antioxidant, lymphatic, anti-inflammatory and immune response adapting effects.[8,9]

Mechanism of Action

This herb exerts its effects on innate and adaptive immune activity through numerous mechanisms:

- modulation of T-cell cytokine response and regulating the production of inflammatory and anti-inflammatory chemokines and cytokines, including:
  - tumour necrosis factor-alpha (TNF-alpha)
  - interleukin- 1 beta (IL-1 beta)
  - nitric oxide (NO)
  - various interleukins (IL-1, IL-6, IL-8, IL-10, IL-12)
  - interferon gamma (IFN-gamma)
- activation of:
  - the endocannabinoid system (ECS), which influences anti-inflammatory cytokines and may decrease cytokine storms and reduce systemic inflammation
- Production and activation of:
  - macrophages
  - monocytes, lymphocytes and leukocytes
- Modulation of dendritic cell activity (essential for regulatory T-cell induction)
- Inhibition of nuclear factor kappa B (NF-kappa B) expression to reduce inflammatory responses and prevent viral receptor binding capacity[8-13]

A novel approach in the way echinacea exerts its immunomodulatory action is through its polysaccharide content, specifically fructans or inulin-type fructans (ITFs). These are already well known as prebiotics and have been shown to elicit a positive response on the immune system directly and indirectly through the gastrointestinal tract.[12]

Andrographis (*Andrographis paniculata*)

Andrographis *(Andrographis paniculata)* also known as the 'King of bitters' has a traditional use in Ayurvedic, Chinese, Thai and many more medicine systems for numerous conditions.[14] Its modern clinical uses include prophylaxis and symptomatic treatment relief of common colds and upper respiratory tract infections (URTIs), uncomplicated sinusitis, bronchitis, pharyngotonsillitis and influenza.[15]

Andrographis has numerous pharmacological effects, including:

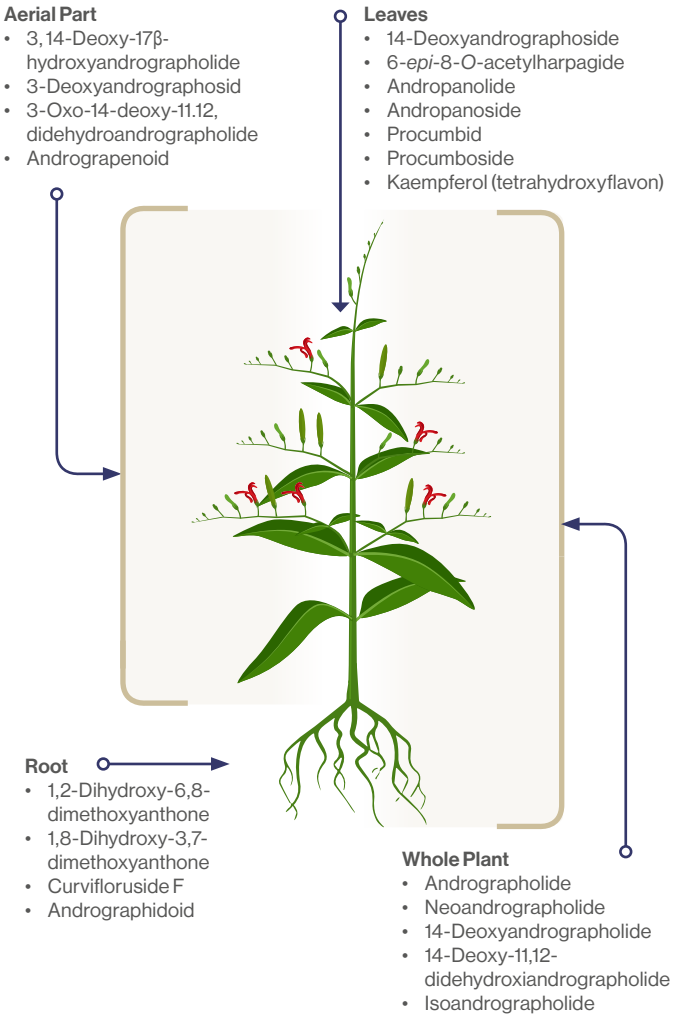
- anti-inflammatory
- antipyretic
- antiviral
- antidiarrhoeal
- antimicrobial
- antioxidant
- hepatoprotection
- adaptogenic activity
- immunomodulatory effect[13,16,17]

Active Constituents

The major constituents of andrographis are diterpene lactones. Of these, the main active constituent considered to be significant for its immune modulatory and anti-inflammatory activity is andrographolide.[13,15]

Evidence shows andrographis improves cough, sore throat and cough duration, and has a statistically significant effect on overall symptoms of acute respiratory tract infections (ARTIs).[16]

Figure 2. Botanical illustration of *Andrographis paniculata*[18]



Mechanism of Action

Animal and in vitro data has found there are many underlying mechanisms that may contribute to the anti-inflammatory, antiviral, and immune effects of andrographis and andrographolide, including:

- lymphocyte production and macrophage phagocytosis
- antibody synthesis and activity
- reduction/inhibition/regulation of:
  - virus replication and structural proteins
  - arachidonic release through phospholipase 2 inhibition
  - pro-inflammatory mediators (TNF-alpha, interferons, interleukins)
  - cyclooxygenase-2 (COX-2) signalling
  - macrophage inflammatory protein (MIP-2) mRNA expression
  - platelet activating factor (PAF)

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- NO-mediated inflammation
- NF-kappa B-mediated inflammation, signalling, translocation and expression
- mitogen-activated protein kinase (MAPK) signalling pathway
- nuclear factor-erythroid 2-related factor 2 (Nrf2)-mediated oxidative stress response signalling pathway proteins
- antioxidant proteins and upregulated expression of heme oxygenase 1 (HO-1)[13,14,16]

Astragalus (*Astragalus membranaceus*)

Astragalus (*Astragalus membranaceus* or Huangqi) is a valued therapeutic herb and the most important Qi tonifying adaptogen in the traditional Chinese medicine system for many health functions, including strengthening the immune system, and supporting metabolism, respiration and elimination.[19]

Active Constituents

Over 200 constituents have been identified in astragalus, with triterpene saponins, flavonoids and polysaccharides being considered the primary active constituents behind its biological actions.[19]

Astragalus has been shown in pharmacological studies to have the following properties:

- antioxidant
- anti-inflammatory
- immunoregulatory
- hepatoprotective
- antiviral
- expectorant
- diuretic[19,20]

Mechanism of Action

Some of the specific mechanisms contributing to its therapeutic immune effects include:

- upregulating antioxidant factors
- activation, migration and monocyte maturation of peripheral blood mononuclear cells (PBMCs)
- modulating the synthesis and expression of inflammatory mediators
- supporting antibody responses, T-cell numbers and lymphocyte activity[19]

Elecampane (*Inula helenium*)

Elecampane (*Inula helenium*) has a long history of use in traditional medicine for respiratory conditions, immune support, bronchitis, colds, bronchial and tracheal catarrh and dry irritating coughs.[21-23]

Active Constituents

The biologically active constituents that have been isolated include coumarins, flavonoids, polysaccharides, fatty acids and saponins. The polysaccharides, known for their immune activity in herbs, contain up to 44% inulin and other pectic substances.[21,24] Elecampane also contains antimicrobial sesquiterpene lactones (SLs) that have been shown in vitro to inhibit staphylococci.[22] One of these SLs, called alantolactone, is attributed to many of the immune and anti-inflammatory effects of this herb.[25]

Mechanism of Action

The actions of elecampane in immunity, may be due to its ability to:

- support T-helper cell 1 (Th1 response)
- enhance phagocytosis
- decrease free radical production
- inhibit pro-inflammatory cytokines and increase anti-inflammatory mediator release
- upregulate Nrf2 activity
- suppress NF-kappa B activation
- control neutrophil chemotaxis to reduce respiratory inflammation[25]

This herb has antitussive, antiseptic, expectorant, diaphoretic and bactericidal properties.[22]

Olive leaf (*Olea europaea*)

Olive leaf (*Olea europaea*) has been used in traditional and folk medicine for respiratory and urinary tract infections, cholesterol and blood sugar reduction, and gastrointestinal disorders.[26]

Active Constituents

The bioactive constituents of olive leaf are secoiridoids, flavonoids, lignans, and phenolic compounds. The secoiridoid, oleuropein is a major contributor to this herb's immune-related actions, with olive leaf having antioxidant, anti-inflammatory, immunomodulatory and antimicrobial effects.[26-28]

Mechanism of Action

Research shows olive leaf can "modulate the human immune system by influencing the production of cytokines or other factors involved in immunological defence in addition to proliferating white blood cells."[29]

Other mechanisms of actions evidenced from its constituents include:

- reducing reactive oxygen species (ROS), TNF-alpha, inflammatory interleukins and mediators[26]
- inhibiting a wide range of bacterial and microbial pathogens (*Escherichia coli, Staphylococcus aureus, Salmonella enteriditis and typhyimurium, Bacillus subtilis and cereus, Klebsiella pneumoniae, Campylobacter jejuni, and Candida albicans, glabrate* and *parapsilosis*)[30]

Elder (*Sambucus nigra*)

Both the fruit and flowers from the elder plant have traditionally been used for many conditions, including treating the common cold and influenza, and for immune system enhancement.[31,32]

Active constituents and mechanism of action

Elder berries contain multiple constituents, with its rich anthocyanin content (makes up around 80% of its polyphenol content) associated with antioxidant and anti-inflammatory effects. Elder berries also have antimicrobial and antiviral properties and can increase cytokines that modulate the immune system. Their antiviral effect is due to inhibition of viral replication, while their antioxidant activity works by regulating antioxidant enzymes and inhibiting ROS to reduce oxidative stress and inflammation.[31,32]

Thyme (*Thymus vulgaris*)

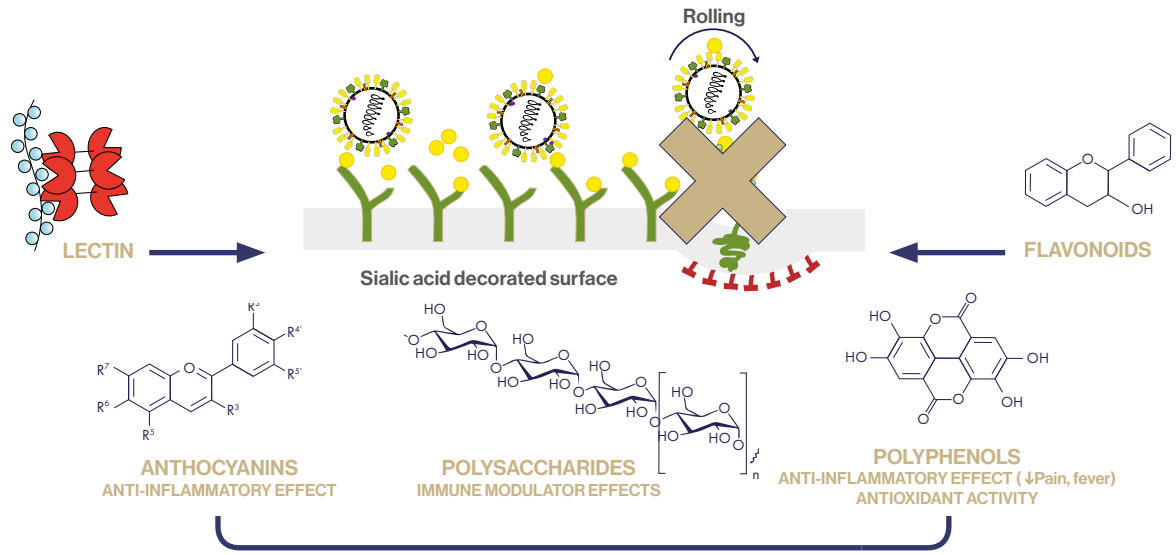
Thyme (*Thymus vulgaris*) has been used in traditional medicine for conditions such as sore throat, bronchitis, bronchial catarrh and whooping cough.[34] This herb has anti-inflammatory, antibacterial, antiviral, antifungal and broad antimicrobial and antioxidant activities.[34,35]

Thyme's immune activities may be due to its ability to:

- scavenge free radicals, chelate metal ions and inhibit oxidative enzymes
- enhance antioxidant enzyme activity (superoxide dismutase, catalase, glutathione peroxidase, glutathione-S transferase)
- support vitamin C, vitamin E and reduced glutathione levels
- decrease production and expression of inflammatory mediators:
  - TNF-alpha
  - IL-1 beta and IL-6
  - increase production of anti-inflammatory IL-10
  - reduce elevations in COX-2, NF-kappa B, inducible nitric oxide (NO) synthase (iNOS), TNF-alpha and NO, when induced by lipopolysaccharides (LPS)
  - inhibition of peroxisome proliferators–activated receptor-gamma (PPAR-gamma)-dependent COX-2 expression
  - inhibition of multiple gram-positive and gram-negative bacteria[34,35]

The phenols thymol and carvacrol are the main constituents that are attributed to the herb's beneficial effects.[34]

Figure 3. Mechanism of action of *S. nigra* for the treatment of cold and flu.[33]



↓ **Fever, cough, muscle ache, headache, nasal congestion, mucus discharge**

↑ **Improvement in clinical symptoms**

↑ **Complete cure after 2 days**

↓ **Mean duration of illness (2.7 days)**

↑ **Improvement the symptoms of flu**

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