

The proven potential of botanicals in boosting immune health



by Kristen McPhee

A healthy immune system is paramount for living one’s best life. A strong immune system exists in surveillance mode, identifying and eliminating pathogens when they arise without any signs or symptoms of sickness appearing.

This first-line of defense is referred to as the innate immune system response. When a pathogen continues to proliferate, the immune system responds by replicating and activating immune cells, including secreting inflammatory cytokines.¹ This temporary inflammatory state is part of a healthy “adaptive” immune response and is essential to pathogen elimination. Once the pathogen is successfully eliminated, the immune system returns to surveillance mode and the inflammation subsides.

However, an unhealthy chronic inflammatory state develops when the immune system cannot return to surveillance mode due to a weakened or prolonged threat to the immune system. Many diseases are associated with a weakened immune system and chronic inflammation, including atherosclerosis, arthritis, cancer, diabetes, hyperglycemia, metabolic syndrome, obesity and prediabetes.¹

Certainly, adopting a healthier lifestyle, including diet and exercise, is fundamental to good health and the prevention and management of many diseases. In addition, mounting scientific evidence has evaluated the potential of various botanicals for immune health, often validating traditional uses in the process.

Andrographis (*Andrographis paniculata*) is a bitter ayurvedic herb traditionally used to reduce symptoms of upper respiratory tract infections (URTIs) and colds.² In fact, a 2017 systematic review and meta-analysis of 33 randomized controlled clinical trials concluded andrographis significantly improved these symptoms.³ In one randomized, double-blind, placebo-controlled clinical study, andrographis (as AP-Bio from AIDP) reduced URTI symptoms by 52.7% compared to placebo after five days of supplementation with a 200 mg daily dose.⁴ Earlier preclinical studies showed that the mechanisms of action involve stimulating immune cells, or phagocytosis, and inhibiting inflammatory mediators in cases where a weakened immune system has compromised a healthy inflammatory response.^{5,6}



A 2019 meta-analysis of four randomized controlled clinical trials found that black elderberry (*Sambucus nigra*) supplementation was effective in substantially reducing upper respiratory symptom severity and total duration, particularly when used at the onset.⁷ A greater reduction of symptoms was seen in individuals with the flu compared to those with the common cold. These findings support elderberry’s traditional uses and earlier preclinical studies. According to Melanie Bush, director of science, Artemis International, “Mechanistic studies have identified the ability of black elderberry actives to inhibit the attachment of influenza hemagglutinin glycoproteins to host cells,⁸ as

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well as interfere with the release of viral particles from host cells via influenza neuraminidase enzymes⁹ ... high-molecular-weight polysaccharides in black elderberry help to mount an immune response by increasing virus-neutralizing antibodies.”^{10,11}



Aged garlic (*Allium sativum*) extract involves soaking the sliced cloves in an aqueous ethanol solution for up to 20 months. Two randomized, double-blind, placebo-controlled clinical trials showed that 2.56 g per day of aged garlic extract enhanced immune cell function by significantly increasing natural killer (NK) and gamma delta T cells, lymphocytes involved in innate and adaptive immunity, and significantly reducing cold and flu symptoms in healthy subjects after three months.^{12,13} More recently, 3.6 g per day of aged garlic extract reduced obesity-associated chronic inflammation in 51 healthy adults by reducing inflammatory cytokines and modulating the aforementioned lymphocytes (NK and gamma delta T cells) after six weeks.¹ Altogether, these findings suggest that aged garlic extract supports immune health, including cold and flu recovery, at least in part by reducing chronic inflammation.

Preclinical studies have shed light on the mechanisms of olive leaf's (*Olea europaea*) traditional use in lowering fever while further validating its antiviral potential for combating the flu.¹⁴ Olive leaf extract (as Isenolic from Pharmactive Biotech Products) was as effective as the standard pharmaceutical treatment, oseltamivir, in inhibiting the influenza A virus in vitro, with 65% inhibition. Similar to black elderberry, the mechanisms involve inhibiting the neuraminidase enzyme, which ultimately prevents the virus from spreading.

Another olive leaf extract (as Olivactive from Pharmactive Biotech Products) inhibited alpha-glucosidase and alpha-amylase enzymatic activities in vitro, showing its candidacy in balancing glucose levels.¹⁵ This is key to immune health since elevated glucose places individuals at a higher risk of infection.¹⁶ Antioxidants, specifically bioflavonoids, present in olive leaf are thought to play a role.¹⁵

Aligned with olive leaf, citrus flavonoids (as Eriomin from Ingredients by Nature) significantly improved glucose tolerance in 103 prediabetic individuals after 12 weeks in a randomized, double-blind, placebo-controlled clinical trial.¹⁷ Other research has shown that high blood sugar decreases the function of white blood cells and NK cells, both critical to immune health.¹⁸ Further, Eriomin reduced systemic inflammation by reducing multiple inflammatory cytokines.¹⁷



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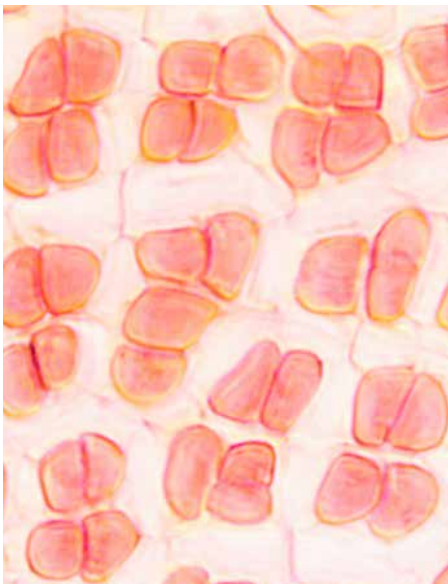


Sevanti Mehta, president of Unibar Corp., pointed to the potential of nutrient-rich maitake mushrooms (*Grifola frondosa*). “What sets them apart from other antioxidant-rich natural ingredients is that they are a unique source of 1,3-1,6 beta-glucans, powerful compounds for immune support,” he stated.

In one clinical study, a maitake 1,3-1,6 beta-glucan-rich extract (3 mg/kg twice daily) demonstrated immune health benefits by significantly increasing neutrophil and monocyte function in 18 subjects with cancer after 12 weeks.¹⁹ A similar maitake preparation showed immunomodulatory effects in 34 postmenopausal women recovering from breast cancer treatment, in part by increasing interleukin (IL)-10 anti-inflammatory cytokine production.²⁰ These findings suggest that maitake may reduce systemic inflammation when a chronic infection, autoimmune state or allergy is present.

Turkey tail (*Trametes versicolor*) is another mushroom of interest for enhancing innate and adaptive immune responses. To understand its unique immunological properties, a 2019 study evaluated the mycelium and the fermented rice flour-based substrate on which it grew, using human peripheral blood mononuclear cells.²¹ Since the fermented substrate is often consumed with the fungal mycelium, it is pertinent to understand the immune health benefits of both.

“Our team found that Turkey tail mycelium had a greater effect on CD69 activation [an early activation marker involved in NK cell function] in lymphocytes and monocytes. The fermented substrate only demonstrated a minor effect on CD69 activation, but had a stronger impact on the induction of several cytokines (including modulatory cytokines, IL-10 and IL-1ra),” concluded Renee Davis, research and development (R&D) director of Fungi Perfecti LLC. Also, both the insoluble beta-glucans and water-soluble components of Turkey tail showed immune-activating effects. Although additional studies are needed, the results suggested the immune health effects of Turkey tail are associated with the whole mycelium and the fermented substrate.



AstraReal astaxanthin is a carotenoid from the alga *Haematococcus pluvialis* that has been shown to support robust immune health through several mechanisms in a number of human and preclinical studies. In one randomized, double-blind, placebo-controlled clinical trial, 8 mg of astaxanthin improved both adaptive and innate immune functions by significantly increasing B and T lymphocyte proliferation and NK cell activity, respectively, after eight weeks in healthy college students.²² In the same study, anti-inflammatory and antioxidant effects were shown by significantly decreasing the chronic inflammation marker CRP, and the DNA oxidative stress marker 8-OHdG, with a 2-mg dose.

Tinofend (from Verdure Sciences), a *Tinospora cordifolia* extract, showed potential for supporting immune health associated with histamine in two randomized, double-blind, placebo-controlled trials. One 300-mg capsule administered three times daily significantly decreased allergic rhinitis



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symptoms in as early as 15 days in 75 adults.²³ Tinofend supports the immune system and combats allergic rhinitis symptoms primarily by stimulating white blood cell activity and reducing eosinophil count, or immune cells which release histamine.²⁴

Although Tinofend has benefits to immune health specifically associated with histamine, Verdure Sciences' Kristen Marshall, marketing, noted "the complexity of the immune system, as well as adaptive and innate responses, challenges the notion that one product or nutritional component will offer the required support for all immune related concerns." As such, Verdure offers additional botanical ingredients like WokVel, a *Boswellia serrata* extract, to use in tandem for robust immune support.

These are but a handful of botanicals offering a complementary solution to a challenged immune system in both healthy and immunocompromised individuals, whether for prevention, symptom management or long-term support. ✨

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References

- 1 Percival SS. "Aged Garlic Extract Modifies Human Immunity." *J Nutr.* 2016;146(2):433S-436S.
- 2 Sagadevan P et al. "Traditional uses of *Andrographis paniculata*: review and perspectives." *Int J Biosci Nanosci.* 2015;2(5):123-131.
- 3 Hu XY et al. "*Andrographis paniculata* (Chuan Xin Lián) for symptomatic relief of acute respiratory tract infections in adults and children: A systematic review and meta-analysis." *PLoS One.* 2017;12(8):e0181780.
- 4 Saxena RC et al. "A randomized double blind placebo controlled clinical evaluation of extract of *Andrographis paniculata* (KalmCold) in patients with uncomplicated upper respiratory tract infection." *Phytomedicine.* 2010;17(3-4):178-185.
- 5 Kumar RA et al. "Anticancer and immunostimulatory compounds from *Andrographis paniculata*." *J Ethnopharmacol.* 2004 Jun;92(2-3):291-295.
- 6 Sheeja K, Shihab PK, Kuttan G. "Antioxidant and anti-inflammatory activities of the plant *Andrographis paniculata* Nees." *Immunopharmacol Immunotoxicol.* 2006;28(1):129-140.
- 7 Hawkins J et al. "Black elderberry (*Sambucus nigra*) supplementation effectively treats upper respiratory symptoms: A meta-analysis of randomized, controlled clinical trials." *Complement Ther Med.* 2019;42:361-365.
- 8 Roschek Jr B et al. "Elderberry flavonoids bind to and prevent H1N1 infection in vitro." *Phytochemistry.* 2009;70(10):1255-1261.
- 9 Swaminathan K et al. "Binding of a natural anthocyanin inhibitor to influenza neuraminidase by mass spectrometry." *Anal Bioanal Chem.* 2013;405(20):6563-6572.
- 10 Kinoshita E et al. "Anti-influenza virus effects of elderberry juice and its fractions." *Biosci Biotechnol Biochem.* 2012;76(9):1633-1638.
- 11 Zakay-Rones Z et al. "Randomized study of the efficacy and safety of oral elderberry extract in the treatment of influenza A and B virus infections." *J Int Med Res.* 2004;32(2):132-140.
- 12 Nantz MP et al. "Supplementation with aged garlic extract improves both NK and $\gamma\delta$ -T cell function and reduces the severity of cold and flu symptoms: a randomized, double-blind, placebo-controlled nutrition intervention." *Clin Nutr.* 2012;31(3):337-344.
- 13 Xu C et al. "Aged garlic extract supplementation modifies inflammation and immunity of adults with obesity: A randomized, double-blind, placebo-controlled clinical trial." *Clin Nutr ESPEN.* 2018;24:148-155.
- 14 Salamanca A et al. "In vitro study of the antiviral activity of Isenolic in MDCK-SIAT1 cells infected with the Influenza A virus." *Nutr. Clin Diet Hosp.* 2018(sup. 1):61.
- 15 Del Castillo MD et al. "Oliveactive inhibits the enzymatic activity in vitro of α -glucosidase and α -amylase." *Nutr. Clin Diet Hosp.* 2018(sup. 1):80.
- 16 Rayfield EJ et al. "Infection and diabetes: the case for glucose control." *Am J Med.* 1982;72(3):439-450.
- 17 Ribeiro CB et al. "Effectiveness of Eriomin in managing hyperglycemia and reversal of prediabetes condition: A double-blind, randomized, controlled study." *Phytother Res.* 2019;33(7):1921-1933.
- 18 Kim JH et al. "Relationship between natural killer cell activity and glucose control in patients with type 2 diabetes and prediabetes." *J Diabetes Investig.* 2019;10(5):1223-1228.
- 19 Wesa KM et al. "Maitake mushroom extract in myelodysplastic syndromes (MDS): a phase II study." *Cancer Immunol Immunother.* 2015;64(2):237-247.
- 20 Deng G et al. "A phase I/II trial of a polysaccharide extract from *Grifola frondosa* (Maitake mushroom) in breast cancer patients: immunological effects." *J Cancer Res Clin Oncol.* 2009;135(9):1215-1221.
- 21 Benson KF et al. "The mycelium of the *Trametes versicolor* (Turkey tail) mushroom and its fermented substrate each show potent and complementary immune activating properties in vitro." *BMC Complement Altern Med.* 2019;19(1):1-14.
- 22 Park JS et al. "Astaxanthin decreased oxidative stress and inflammation and enhanced immune response in humans." *Nutr Metab (Lond).* 2010;7:18.
- 23 Thawani VR et al. "Short term effect of *Tinospora cordifolia* in allergic rhinitis." *The Antiseptic.* 2006;3(4):229-232.
- 24 Badar VA et al. "Efficacy of *Tinospora cordifolia* in allergic rhinitis." *J Ethnopharmacol.* 2005;96(3):445-449.