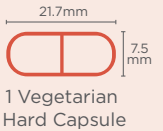


Immunitone Plus™



Relieves symptoms and duration of common colds and flu

OVERVIEW

- > Comprehensive herbal and nutrient complex to support a healthy immune system.
- > Convenient capsule dosage form for enhanced compliance.

Active Ingredients (per vegetarian hard capsule)	
<i>Andrographis paniculata</i> (Andrographis) extract dry conc. std.	166.67 mg
From min dry leaf	8.33 g
Standardised to Andrographolide	41.67 mg
<i>Echinacea purpurea</i> (Echinacea) extract dry conc.	83.33 mg
From dry root	500 mg
<i>Astragalus membranaceus</i> (Astragalus) extract dry conc.	11.11 mg
From dry root	333 mg
<i>Sambucus nigra</i> (Elder Berry) extract dry conc.	9.52 mg
From dry fruit	333.2 mg
<i>Cordyceps sinensis</i> (Cordyceps) extract dry conc.	16.67 mg
From dry hyphae	50 mg
<i>Lentinula edodes</i> (Shiitake) fruiting body powder	16.67 mg
<i>Grifola frondosa</i> (Maitake) fruiting body powder	16.67 mg
<i>Ganoderma lucidum</i> (Reishi) fruiting body powder	16.67 mg
Larix arabinogalactan	33.33 mg
Lauric acid	33.33 mg
Zinc amino acid chelate	75 mg
Equiv. zinc	15 mg

Pack Size	90
Serving Per Pack	30 serves

Excipients
Hypromellose
Maltodextrin
Purified water
Magnesium stearate
Colloidal anhydrous silica

Directions for Use
Take 3 capsules per day or as professionally prescribed.

Allergen Information
No added: gluten, dairy, lactose, nuts or soy.

Warnings
<ul style="list-style-type: none"> • Andrographis may cause allergic reactions in some people. If you have a severe reaction (such as anaphylaxis), stop use and seek immediate medical attention. • Andrographis may cause taste disturbance including loss of taste. If you develop any adverse symptoms, stop use and seek medical advice. • Contains zinc which may be dangerous if taken in large amounts or for a long period. • Do not take while on warfarin therapy without medical advice. • Not to be used in children under two years of age without medical advice. • If symptoms persist, seek advice from a healthcare professional.

Designed and packed in Australia from imported ingredients.



No Added Gluten



No Added Dairy



No Added Seeds



No Added Nuts



No Added Soy



EDUCATION

Healthy immunity requires an appropriate, integrated response to infections by the complex combination of cells, tissues and organs that comprise the immune system.^{1,2} The internal presence of a pathogen (bacteria, viruses, fungi) initially activates the non-specific mechanisms of the innate immune system to attempt infection elimination.^{3,4} If not cleared by the innate immune response, a range of specific functional mechanisms of the adaptive immune system (involving B and T cells) are mobilised to remove the infectious pathogen.^{3,4}

Upper respiratory tract infections (URTI's) are highly prevalent and considered to be a significant health concern for both generally healthy and immune-compromised population groups.^{5,6} Exposure to a complex combination of endogenous (host) and exogenous factors can impair the immune system's capacity to respond effectively. (See Table 1) This results in pathogenic (bacterial, viral) attachment and colonisation to upper respiratory mucosa and the subsequent onset of infection (rhinitis, pharyngitis, laryngitis) and its associated symptoms (cough, sore throat, runny nose, nasal congestion, headache, fever, sneezing).^{5,6}

Table 1: Modifiable factors associated with adverse immune system function.⁷⁻¹²

Lifestyle factor	Effect on immune system
Dietary and nutrient intake patterns: <ul style="list-style-type: none"> - insufficient macronutrients - excessive or imbalanced macronutrients - micronutrient deficiencies - 'Western-style' dietary intake (processed 'fast' foods, high sugar, low fibre and nutrient density) 	<ul style="list-style-type: none"> • chronic inflammation (an abnormal immune response) • modifies gastrointestinal microbiome and intestinal permeability (influences immunity and inflammation) → impairs innate and adaptive immune activity (further elevates inflammation) → suppresses immune functions (cell-mediated immunity, complement system, phagocyte function, cytokine synthesis, mucosal secretory antibody response and affinity)
Physical activity: <ul style="list-style-type: none"> - sedentary lifestyle - excessive frequency/intensity 	<ul style="list-style-type: none"> • chronic inflammation (an abnormal immune response) • altered innate and adaptive immunity (immune overactivation) → increased risk and severity of infectious illnesses
Body composition: <ul style="list-style-type: none"> - obesity - overweight 	<ul style="list-style-type: none"> • adipose tissue-derived chronic inflammation • altered innate and adaptive immunity (immune overactivation) → increased incidence and severity of infectious illnesses
Chronic stress: <ul style="list-style-type: none"> - physical - psychological 	<ul style="list-style-type: none"> • chronic cortisol elevation • chronic inflammation • suppression of immune cell activity • altered innate and adaptive immunity → increased risk and severity of infectious illnesses
Sleep: <ul style="list-style-type: none"> - prolonged disruption 	<ul style="list-style-type: none"> • increases chronic inflammation • induces immune impairment → increased risk of infectious illness
Alcohol: <ul style="list-style-type: none"> - excessive 	<ul style="list-style-type: none"> • altered innate and adaptive immunity • promotes pro-inflammatory state → increased risk and severity of infectious illness
Tobacco: <ul style="list-style-type: none"> - smoking - chewing 	<ul style="list-style-type: none"> • impairs innate and adaptive immunity • disrupts immune homeostasis • induces chronic inflammation (an abnormal immune response) → increased risk and severity of infectious illness

(Trivedi 2020, Marcos 2003, Morey 2015, Park 2021, Christ 2019, Del Frel 2020)

Overall, the evidence demonstrates that healthy immunity requires a multifaceted approach including minimising exposure to all modifiable factors (as outlined in Table 1).⁷ In addition, particular therapeutic nutrients and herbs have been shown to benefit immune system functionality via a range of mechanisms.

Andrographis

Andrographis has been used in Traditional Chinese Medicine (TCM) for centuries. Clinical investigations attribute its therapeutic benefits primarily to the andrographolides constituent.^{13,14} A broad range of human clinical studies and meta-analyses have confirmed that andrographis effectively reduces symptoms associated with acute respiratory tract infections such as common colds and flu.^{15,17} Mechanisms responsible for these therapeutic effects include significant antibacterial, antiviral, anti-inflammatory and antioxidant activity along with modulation of innate and adaptive immune function.^{3,15-18}

Echinacea

Echinacea has a long history of use in traditional Native American medicine and by Eclectic physicians for a range of medicinal purposes. Considered to have immune supportive, depurative, anti-inflammatory actions, the main active components are the polysaccharides, caffeic acid derivatives, alkylamides (alkamides), phenolics and terpenes.^{14,19} The well-established benefits of echinacea for supporting innate and adaptive immune function are based on multiple mechanisms including antiviral, antibacterial, antioxidant, anti-inflammatory effects. It also promotes immune cell proliferation and activity (natural killer, dendritic, monocyte and T-cells) and modulates the gastrointestinal microbiome.^{3,14,19,20}

Astragalus

Astragalus is one of the oldest herbs recorded and used within the traditional Chinese medicinal. The primary active constituents are considered to be the saponins, flavonoids and polysaccharides.^{22,23} They support immune function via multiple mechanisms including regulating immune cell signalling, proliferation and activity (B- and T-lymphocytes, macrophages, natural killer and dendritic cells) and immunoglobulin secretion and modulating the gastrointestinal microbiome.^{22,23} Astragalus also has antiviral (modulating cell proliferation and cellular superoxide dismutase and malonaldehyde concentrations) and antibacterial activity.²¹⁻²⁴

Elderberry

Demonstrated to reduce upper respiratory symptoms associated with the common cold, elderberry supports immunity via antioxidant, antiviral (blocks viral capacity to infect host cells), antibacterial and immune supportive mechanisms (promotes immune cell synthesis of pro-[IL-1 beta, TNF-alpha, IL-6, IL-8] and anti-inflammatory cytokines (IL-10)).^{13,25}

Medicinal mushrooms (Cordyceps, Shiitake, Maitake & Reishi)

Medicinal mushrooms cordyceps, shiitake, maitake and reishi have a long history of use in TCM for their significant health-giving properties.²⁶⁻³¹ Extensive in vitro and in vivo investigations have demonstrated underlying immune-modulatory mechanisms.

Cordyceps has been shown to regulate inflammation (cytokine and chemokine release and inflammatory signalling), promote immune cell proliferation and activity and increase gastrointestinal secretory immunoglobulin (sIgA) secretion.^{26,32,33}

Lentinula has also been shown to support both innate and adaptive immunity by supporting immune cell proliferation and activation (macrophages, T-helper and natural killer cells) and supporting gastrointestinal immunity (sIgA synthesis).^{27,34}

Maitake supports immunity by regulating immune cells activation and proliferation (macrophages, natural killer and cytotoxic T-cells), modulating cytokine signalling and expression, inhibiting viral replication and antibacterial activity.^{28,30,35}

Reishi also aids immunity by modulating immune cells activity (B- and T-lymphocytes, macrophages, natural killer cells), antioxidant and antimicrobial mechanisms.^{31,36,37}

Larix arabinogalactans

There is a long history of humans ingesting arabinogalactans in the diet and recent clinical investigations have demonstrated the beneficial effect of larix arabinogalactans on the common cold.^{38,39} This is attributed to a range of immune modulatory mechanisms involving both innate and adaptive immunity including supporting the proportion of CD8+ T-suppressor cells, regulating lymphocyte proliferation, macrophage phagocytic and natural killer cell activity, maintaining immune-cell pro-inflammatory cytokine release (tumour necrosis factors-alpha (TNF- α), Interleukin-1 beta (IL-1 β) and Interleukin-6 (IL-6)) and modulating the gastrointestinal microbiome.³⁸⁻⁴⁰

Lauric acid

Lauric acid supports immune function via a range of mechanisms including inhibition of pathogen maturation and binding to host cells, regulation of B and T-cell activity (activation, expression, pro-inflammatory cytokine release) as well as antimicrobial and antiviral activity.⁴¹⁻⁴⁴

Zinc

Zinc is an essential mineral required for normal innate and adaptive immune growth and development and supports immune function by regulating a healthy response to infection.⁴⁵⁻⁴⁷ Despite its importance for normal immune function, zinc deficiency is relatively common, particularly in the elderly, vegans, vegetarians and individuals with intestinal malabsorption issues.^{47,48} This has significant consequences for susceptibility to infection, with both marginal and severely deficient levels associated with impaired immune cell (macrophages, neutrophils, B-, T and NK cells), complement and cytokine proliferation, concentration, function and viral response capacity.^{45,47-49}

Figure 1: Responses involved in innate and adaptive immunity.

Fast and nonspecific responses, occurring against all factors identified as nonself, are involved in innate immunity; conversely, adaptive immunity is a highly specific, complex and slow response mediated by T and B lymphocytes, which release antigen-specific antibodies and cytokines. Immunomodulators can directly affect innate and adaptive response or the factors involved, thus leading to immunostimulant or immunosuppressive effects.

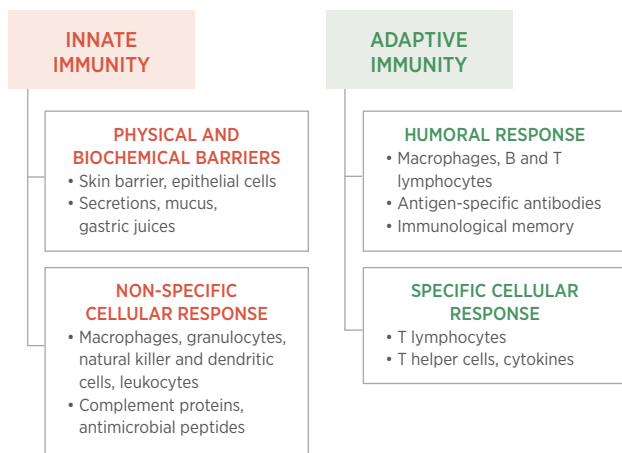


Figure 2: The innate and adaptive immune responses to pathogens.

After breaching a barrier, a pathogen must first survive the activities of preformed antimicrobial agents (products of innate immunity). Usually the damaged tissue produces molecules that activate innate immune cells (induced innate immunity) to attack the pathogen. If this is not sufficient to clear the infection, then the adaptive immune system is activated with the activation of cytotoxic T cells and antibody-producing plasma cells.

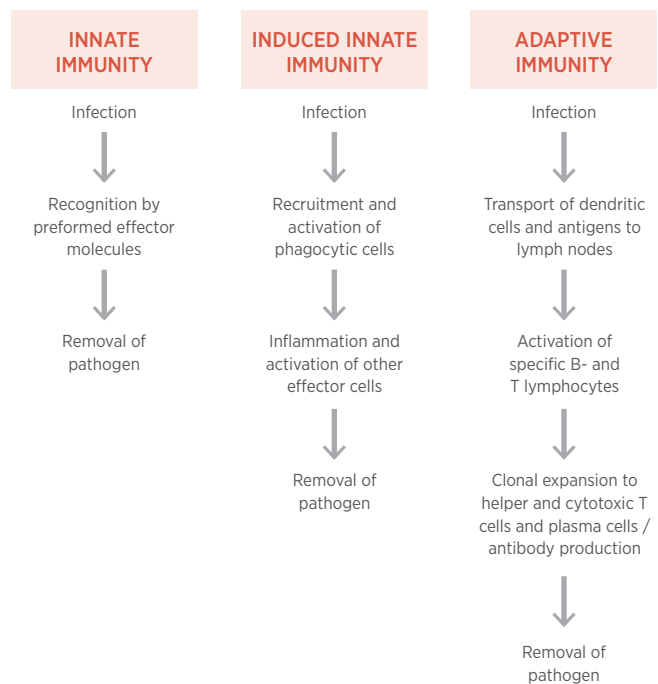


Table 2: Comparison of the innate and adaptive immune response.

	Innate/ induced innate	Adaptive
Response time	Hours	Days
Specificity	Limited specificity and restricted to small number of structures	Highly specific to diverse antigens, improves during the course
Response to repeat infection	Secondary response identical to primary response; no memory	Has memory, secondary response is more rapid and aggressive than primary response

Designs for Health Quality Guarantee

Designs for Health medicines that are listed on the Australian Register of Therapeutic Goods will display an AUSTL number on the label. Listed medicines in Australia need to be manufactured according to legislated standards set out in Therapeutic Goods Order 101. TGO101 legislation sets out minimum quality standards for medicines supplied in Australia that display an AUSTL number. It mandates testing for:

- Impurities such as heavy metals (including lead, mercury, cadmium and arsenic), pesticides and residual solvents.
- Dissolution (to ensure the capsule will dissolve once taken).
- Uniformity (to ensure that every capsule is the same).

Final assay testing is also performed to ensure that what we have on the label is in each capsule, and microbiological testing is performed to ensure that no microbial contamination has occurred during the encapsulation and packing process.