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Immunity in a viral world: The role of nutrients and herbs



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The unprecedented and rapid spread of the SARS-CoV-2 (COVID-19) virus has forced most of us to change the way we conduct our daily lives in a very short time. It's also made us rethink the way we look after ourselves and how to stay healthy under these unusual and often stressful circumstances.

Being a novel virus, no proven treatment or preventative therapy exists at this stage. This has forced scientists around the world to work at an unprecedented pace to develop a vaccine, effective treatments and accurate rapid testing methods. To date, several antiviral medications and other drugs are showing promise, however research results are likely to be months away.

Until this highly infectious virus is better understood, limiting community exposure through social distancing or isolation where appropriate, and practicing good hygiene are our most important weapons to limit the spread. Fortunately, these things are accessible to everyone, it just takes patience, discipline and planning.

Besides these measures, many people are asking what they can do to improve immune system competence and remain healthy during this unpredictable time. In particular those in the higher-risk categories such as the elderly, and people with diabetes, hypertension or compromised immune function.

As countries start to flatten the curve through social distancing and hygiene measures, there is also discussion around long-term approaches to keeping infection rates at a manageable level since global eradication seems unlikely. This means many individuals will eventually come into contact with this highly infectious virus over an extended period of time.

To be ready to mount an optimal response if exposed and enhance recovery, people need to be actively working towards reaching and maintaining healthy immune function for the long-term.

Besides preparedness for exposure to COVID-19, people are also enquiring about the role of nutrition in other respiratory viruses such as influenza and the common cold which have been prevalent for a long time. Fortunately, nutritional influences on the immune system have broad effects on both innate and adaptive (acquired) immunity and herbal medicines have broad pharmacological activities of value in treating common symptoms and hastening recovery from common respiratory infections.

This review provides an overview of the evidence indicating a role for various nutrients and herbal medicines in the prevention, management or treatment of viral respiratory tract infections.

As COVID-19 is a novel virus, there has been relatively little investigation into the use of nutritional supplements or herbal medicines directly treating the virus. Probably the most active country investigating herbal treatments remains China, however as of the time of writing, research was still in preliminary stages. As always, clinicians are advised to use their professional judgement when interpreting and applying the information and be aware of their local regulations and country guidelines.

The role of nutrition in immunity

It's well known that diet and nutrition have significant impacts on immune system competence and determine the risk and severity of infections. Importantly, there are bi-directional relationships between nutrition, immunity and infection-meaning a change in one of these components has an impact on the others. In other words, **not only will nutritional deficiency adversely affect immune function but chronic or severe infections can adversely affect the body's nutritional status.**

As a consequence, individuals should strive for optimal nutrition before infection and need to consider nutrient replenishment during and afterwards to aid in recovery and restore optimal levels.

The main nutrients essential for immuno-competence are: vitamin A,C,D,E and zinc. Others include: B vitamins, folic acid iron and selenium.

Medicinal herbs can also play an important role.

Blackmores Institute best practice guidelines

Nutrition can have significant impact on immune system competence and determine the risk and severity of respiratory tract infections (RTIs). When developing an optimal nutrition treatment plan, a clinician's approach should consider the following three phases:

- **Phase 1: Protection and prevention**
- **Phase 2: Treatment of symptoms or infection**
- **Phase 3: Recovery and care**

Vitamin C

Vitamin C is so well known, it has virtually achieved celebrity status, but does it therapeutically live up to its reputation? It has shown effectiveness in reducing the incidence and duration of infections like the common cold as well as playing a role in critical care.

Vitamin C is important for immune cell function and is a cofactor for many enzymes. It increases neutrophil phagocytosis and chemotaxis, affects macrophage migration, enhances T and NK cell proliferation and modulates their function, and may increase antibody formation in lymphocytes. It reduces inflammation and limits tissue damage which is associated with the immune response.

Respiratory tract infections of viral origin such as the common cold, are caused by a host of different viruses including rhinovirus, coronavirus and influenza.^{1,2} Studies have shown that supplementation with vitamin C reduces incidence of the common cold in children, the physically active and those with marginal vitamin C deficiency. **A review of 31 study comparisons with 9745 common cold episodes found that regular supplementation slightly reduced the duration of cold symptoms.**³ The same review identified a large trial with adults which reported benefits using an 8 gm dose at the onset of symptoms, and a further two therapeutic trials reported benefits using a five-day supplementation approach.

Younger children can also benefit from supplementation. A meta-analysis of eight randomised-controlled trials (RCTs) showed that vitamin C supplementation reduced the duration of upper respiratory tract infection by 1.6 days and in children under six years, further benefits were achieved with the addition of the herbal medicine, echinacea.⁴

Vitamin C in critical care?

In recent years, numerous researchers have investigated a potential role for vitamin C in managing critically ill patients in intensive care units (ICU). Studies have found that vitamin C levels are depleted in critically-ill patients

despite receiving standard ICU nutrition and that septic shock patients have significantly depleted vitamin C levels compared with non-septic patients. This is likely a result of increased metabolism due to the enhanced inflammatory response observed in septic shock.⁵

Vitamin C supplementation reduced the length of stay in ICU according to a 2019 meta-analysis analysing results from 18 controlled trials with a total of 2004 patients. In 12 trials with 1766 patients, vitamin C reduced the length of ICU stay on average by 7.8% and in six trials, orally administered vitamin C (1-3 gm daily) reduced the length of ICU stay by 8.6%.⁶

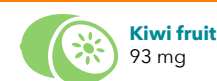
The body of evidence further suggests vitamin C supplementation can also reduce ventilation time in ICU. According to the same 2019 meta-analysis, three trials in which patients needed mechanical ventilation for over 24 hours, vitamin C shortened the duration of mechanical ventilation by 18.2%.⁶

Furthermore, a larger meta-analysis published this year found that vitamin C shortened the length of mechanical ventilation on average by 14%.⁷ The authors of this latest review, which included eight trials of 685 patients, described the evidence as strong, identifying vitamin C as most beneficial for patients with the longest ventilation which corresponded to the most severely ill patients. In five trials including 471 patients requiring ventilation for over 10 hours, a dosage of 1-6 gm daily of vitamin C shortened ventilation time on average by 25%.

Whilst very promising, none of these studies included critically ill patients with COVID-19 so effects are uncertain in this population.

Probably due to the early outbreak of COVID-19 in Wuhan, research with vitamin C in this population has commenced in China. A recent 2020 article in 'Medicine in Drug Discovery' indicates that high dose intravenous vitamin C at doses between 2-10 gm per day given over 8-10 hours had benefits in moderate to severe COVID-19 patients, improving the oxygenation index.⁸ Further research results are anticipated in coming months as more investigation is conducted.

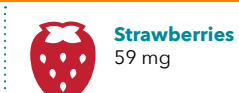
| Good food sources: (Vitamin C per 100 g) |



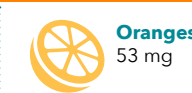
Kiwi fruit
93 mg



Red capsicum
59 mg



Strawberries
59 mg



Oranges
53 mg

Those most at risk of deficiency: Cigarette smokers, individuals with diabetes, people who don't consume fresh fruit and vegetables on a regular basis, the elderly, chronic alcoholism

Place in practice:

Overall, vitamin C supplementation is best started before the onset of infection as a long-term preventative strategy. As the body does not store vitamin C, regular daily intake is required. It is also important to replenish depleted stores during and after infection.

Evidence-informed dosage for RTIs:

Prevention:	≥ 200 mg/day ³
During infection:	≥ 2000 mg/day ⁹
Recovery:	≥ 200 mg/day ³



Evidence-based nutrient interventions



Zinc

Zinc is well known for its effects on skin and wound healing. It has also demonstrated antiviral activity against a range of viral infections, with clinical trials showing it can shorten the duration of colds.

Zinc is an essential trace element involved in many biochemical activities throughout the body. As there is no specialised zinc storage system in the body, it must be consumed on a regular basis or else zinc deficiency can rapidly develop. In regard to immunity, studies have shown that zinc deficiency profoundly alters both innate and adaptive immunity.¹⁴ Additionally, a body of evidence built over 50 years demonstrates the antiviral activity of zinc against a variety of viruses by numerous mechanisms such as inhibition of viral replication.¹⁰

Unfortunately, **zinc deficiency is surprisingly common, with an estimated prevalence of 17-20% globally.** Whilst more common in Asia and Africa, deficiency also occurs in high income countries, most frequently in the elderly, vegans, vegetarians and people with inflammatory bowel disease. Deficiency is also possible with high alcohol consumption, after major surgery and as a result of ongoing diarrhoea. A diet high in phytate, such as corn, rice and cereals, is also problematic because phytate is a natural zinc chelator resulting in significantly reduced zinc absorption.¹⁰

Zinc supplementation has been tested as a means of treating various viral infections, including respiratory infections. One meta-analysis of 17 trials involving 2121 participants showed that oral zinc formulations may shorten the duration of symptoms of the common cold.¹¹

Similarly, a systematic review of 16 clinical trials investigating the role of zinc supplements for the common cold found a significant reduction in the duration of disease with active treatment but no major change to the severity of common cold symptoms. Zinc intake also led to a significant reduction in the incidence of developing a cold, school absence and prescription of antibiotics.¹²

Place in practice:

Zinc should be a part of an ongoing preventative approach to maintaining optimal immune function.

Protection dose ranges from 30-200 mg daily for adults - popular forms include oxide, amino acid chelate, gluconate.

Evidence-informed dosage for RTIs:

During infection: lozenges > 75 mg/day¹³

| Good food sources: (Zinc per 100 g) |



Oysters
61 mg



Beef
11 mg



Pumpkin seeds
8 mg



Soy (Tofu)
2 mg

Those most at risk of deficiency: Vegans, vegetarians, the elderly, people with inflammatory bowel disease or high alcohol intake.



Vitamin D

Vitamin D, known as the sunshine vitamin, is particularly important in current times with so many of us staying indoors. It has been shown to have protective effects, reducing the incidence of RTIs.

Whilst vitamin D is an essential vitamin required for the absorption of calcium and bone development, the discovery of vitamin D receptors in tissues and cells beyond the musculoskeletal system indicates broad ranging effects on health and function in other areas. One of the most salient effects is on immune cells as many possess vitamin D receptors.¹⁴

Numerous experimental studies have shown vitamin D is an important modulator of both innate and adaptive immunity. It can stimulate innate immune responses and inhibit production of pro-inflammatory cytokines (IL-6, IL-8, IL-12, IFN- γ , TNF- α) which help eliminate invading bacteria and viruses, whereas the regulatory effect of vitamin D on T cells can be useful under a number of conditions such as T-cell-mediated autoimmune inflammatory diseases.¹⁴

Population based studies have found an association between low 25-(OH)D levels and chronic diseases including infections.¹⁵ More specifically, vitamin D deficiency has been shown to be independently associated with increased risk of viral acute respiratory infection (ARI) in a number of observational studies.

Conversely, **clinical trials demonstrate that vitamin D supplementation reduces the risk of developing acute RTIs by 12-75%¹⁷**, depending on the study you select.¹⁶⁻²⁰ A meta-analysis of 25 RCTs provides strong evidence that taking vitamin D supplements over the susceptible months provide benefits across all age groups, including school children, and in people with pre-existing disease.¹⁷

As more people are staying at home or working indoors during this pandemic period, there's a significant risk of vitamin D levels reducing and the need to consider supplementation. This is particularly relevant to the elderly who have reduced ability to absorb vitamin D from dietary sources and are at risk of deficiency.

| Good food sources: (Vitamin D per 100 g) |



Salmon
16.7 mcg



Eggs
2.2 mcg



Fortified foods
varying amounts

Those most at risk of deficiency: Vegans and vegetarians; the elderly, those not exposed to sufficient sunlight.

Place in practice:

Ensuring adequate vitamin D levels should be part of a long-term approach to good immune function. The cholecalciferol form (D3) of vitamin D yields a 70% greater increase in serum 25(OH)D than ergocalciferol (D2) which is naturally found in fungi, yeasts and mushrooms. Therefore, the D3 form of supplement will give the quickest response.

Evidence-informed dosage for RTIs:

Prevention: Adults: 50 mcg (2000 IU)/day²¹

*Consider vitamin D testing to determine most appropriate dose

Evidence-based nutrient interventions

A Vitamin A

*Vitamin A has been termed the 'anti-inflammatory' vitamin due to its widespread influence on the immune system.*²³

Vitamin A is a term used to describe a group of fat-soluble retinoids, including retinol, retinal and retinyl esters. It is an essential vitamin in the support of immune function, vision, reproduction and cellular communication. Adequate stores of vitamin A are crucial for both innate and adaptive immunity and for maintaining the integrity of epithelial and mucous membranes which function as the 'front line' of defence against pathogens. Being an integral part of the mucus layer of both the respiratory tract and the intestine, vitamin A promotes mucin secretion and improves the innate immune function associated with these tissues.²²

Vitamin A plays a crucial role in the differentiation and maturation of the cells of the innate immune system, including macrophages and neutrophils, which initiate the immediate responses to infection. It is also required for adaptive immunity where it plays a role in the development of T-helper cells and B-cells.

A deficiency in vitamin A is associated with increased mortality from infectious diseases in many parts of the world, particularly among infants, young children and pregnant women.^{24,25} Deficiency impairs the normal regeneration of mucosal barriers damaged by infection, and impairs the function of neutrophils, macrophages, and natural killer cells, contributing to increased mortality. As such, maintaining adequate vitamin A status is not just important for first line defence but also recovery after infection.

| Good food sources |



Cod-Liver Oil, Eggs and orange coloured vegetables such as carrots, pumpkins and sweet potato (as beta carotene).

Place in practice:

In practice, vitamin A supplementation is only required in cases of frank deficiency. It's important to take extra care when dosing with this vitamin as high doses taken over extended periods can cause cumulative toxicity. In many countries, there are also restrictions on doses to be used during pregnancy.

Recommended Dietary Intakes (RDI) in retinol equivalents (RE) for general health:

Men 14+ years: 900 mcg RE/day (3000 IU/day)

Women 14+ years: 700 mcg RE/day (2330 IU/day)

Pregnancy 14+ years: 700 - 800 mcg RE/day (2330 - 2660 IU/day)

Lactation 14+ years: 1100 mcg RE/day (3660 IU/day)

E Vitamin E

Vitamin E is an antioxidant which helps to protect the body's cells from free radical damage. It is found in high concentrations in immune cells and has been shown to positively support immune function.

It plays a central role in protecting cell membranes against lipid peroxidation. Importantly, vitamin E concentrations are much higher in immune cells compared to other cells in blood and it plays a key role in immunocompetence.²⁶

It's been established that vitamin E deficiency impairs immune function and conversely, vitamin E supplementation has a beneficial effect, particularly in the elderly with compromised immune function.

Clinical studies have found vitamin E supplementation doses ranging from 200 mg - 880 mg daily significantly improve immune response after several months. Plasma levels reaching 25 µmol/L appear necessary to achieving this result, which will necessitate oral doses of at least 200 mg/day.¹⁴

The form found in nature is d-alpha tocopherol, which is also the form with the highest bioavailability and therefore the preferred form for use in supplements.

| Food sources |



Cold-pressed vegetable oils, especially safflower oil, nuts and seeds, spinach, kale, sweet potatoes, yams, egg yolk, liver, soya beans, asparagus and dairy products such as butter and milk.

Those most at risk of deficiency: Deficiency is very rare. Patients with fat malabsorption (in cholestasis where there is low bile flow).²⁷

Place in practice:

Vitamin E needs to be taken for several months to improve the immune response. The d-alpha tocopherol form offers the best bioavailability.

Evidence-informed dosage for RTIs:

200 IU - 800 IU/day

* As always, consider benefit/risks of using high doses



Evidence-based nutrient interventions



Probiotics

Probiotics are live microorganisms well known to offer a wide variety of health benefits. As we better understand these microscopic power houses it's apparent that a healthy, diverse intestinal and respiratory tract microbiome is important for optimal immune function and can influence the clinical course of infection.

Human research has shown that probiotics reduce the incidence and duration of RTIs, the number of antibiotic courses required, and days absent from work according to two meta-analyses published by the York Health Economics Consortium (YHEC) and Cochrane Group.^{28,29}

Multiple benefits have also been reported in children ranging in age from newborn to 18 years. Probiotic supplementation with *Lactobacillus rhamnosus GG*, *Lactobacillus acidophilus* and *Bifidobacterium bifidum* effectively reduced the incidence and recovery time of acute RTIs in children according to a systematic review and meta-analysis of 23 RCTs. It also found that probiotic treatment significantly decreased the number of subjects having at least one RTI episode and that children supplemented with probiotics experienced fewer days of


RTIs compared with children who had taken a placebo. Notably, the treated children had fewer days absent from day care/school.³⁰


Interestingly, **a bi-directional relationship exists between the microbiome, immunity and infection.**

Not only does the microbiome play a role in mounting immune responses, but it is also disrupted by the presence of infection.

| Good food sources, expressed as colony-forming units (CFUs) |

 **Yoghurt**
200 g
100 million -
1 billion CFUs

 **Sauerkraut**
1 cup
3 billion CFUs

 **Natto**
1 g
1 million -
1 billion CFUs



Place in practice:

In practice, it's important to consider the strain and the dose when deciding which probiotic can be useful as not all have benefits in RTIs. It should be considered another important tool in our long-term approach to good immunity.

Evidence-informed dosage:

During infection and for recovery:

$\geq 10^9$ CFUs/day (*Lactobacillus rhamnosus GG*, *Lactobacillus acidophilus*, *Bifidobacterium bifidum*)^{9,30}

Evidence-based medicinal herb interventions



Andrographis

Andrographis (Andrographis paniculata) is a medicinal herb that originates from India and is used traditionally in Ayurvedic and traditional Chinese medicine, mainly for fevers and acute infections.

Andrographis treatment effectively relieved symptoms and reduced the duration of acute RTIs in both adults and children according to a systematic review and meta-analysis of 33 RCTs.³¹ **Specifically, treatment with andrographis improved symptoms of cough and sore throat compared to placebo, and shortened duration of cough, sore throat and sick leave/time to resolution.**

A closer look at the studies reveals the use of different concentrations of andrographolide, depending on the indication. For example, doses ranged from a daily dose of andrographis extract containing 15.75 mg of andrographolide for URTIs, 225 mg for bronchiectasis, and up to 1200 mg for pharyngo-tonsillitis.

A 200 mg daily dose of a specific *Andrographis paniculata* extract showed a positive impact in patients with uncomplicated URTIs in a further double-blind, placebo-controlled trial. Those receiving the andrographis treatment experienced significant symptom reduction after three days, with reduced cough, headache, sore throat and sleep disturbances in comparison to the placebo group which got worse over time.³²

Andrographis exhibits anti-pyretic, anti-inflammatory, and antibacterial and antiviral properties according to mechanistic studies conducted in vitro.⁹ Many of these effects have also been demonstrated clinically.

A novel way to identify potential treatment candidates in medicine is by using computational methods to screen hundreds of synthetic and natural molecules for potential activity of relevance. This approach has been applied to the search for SARS-CoV-2 (COVID-19) treatments. Interestingly, one such study identified several Andrographis compounds and derivatives as potentially effective against important targets on SARS-CoV-2 such as 3-chymotrypsin-like protease (3CLpro), RNA-dependent RNA polymerase (RdRp) and papain-like protease (PLpro).³³ Whilst promising, clinical testing is still required to confirm efficacy.

Place in practice:

Overall, andrographis is a powerful herb which is best suited to managing symptoms and should be used at the first onset of infection, rather than long-term use.

Evidence-informed dosage:

During infection: 100 mg twice daily of a standardised extract³²



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Evidence-based medicinal herb interventions



Echinacea

Echinacea (Echinacea angustifolia/purpurea) is well known for its beautiful flower and is a go-to herb for many herbalists. It is more than just a pretty face however, showing effectiveness in reducing the risk of RTIs and helping to decrease the duration of disease.

Echinacea is a medicinal herb that exhibits anti-inflammatory, antibacterial and antiviral properties.⁹ It also demonstrates immunomodulatory activity and is an extremely popular herbal medicine for the prevention and treatment of respiratory tract infections. Clinical research has been conducted with liquid extracts, pressed juices and solid dose forms.

Echinacea extracts reduce the risk of recurrent respiratory infections by 35% according to a meta-analysis of six RCTs.³⁴ In this report, ethanolic extracts provided superior effects over pressed juices and increased dosing during acute episodes further enhanced these effects.

Of note, echinacea halved the risk of recurrent respiratory infections in people with higher susceptibility, psychological stress or with compromised immune

function. Similar preventive effects were observed with virologically confirmed recurrent infections. Echinacea treatment also reduced the frequency of complications including pneumonia, otitis media/externa, and tonsillitis/pharyngitis.

A more recent report, which included three meta-analyses of RCTs, found a **22% reduced risk of upper respiratory tract infections using echinacea** and a slight non-significant reduction in the average duration of illness.³⁵ The safety of echinacea treatment was also confirmed. Whilst this is promising, not every trial was positive, likely due to the heterogeneity of study methodology and extracts used in the studies.

Place in practice:

Echinacea can be used both for prevention as a long-term strategy as well as at the onset of infection. The reason for use will dictate the dosage required.

Evidence-informed dosage:

Prevention: 2400 mg (dry root equiv.)/day⁹

At first sign of cold: 3825 mg (dry root equiv.)/day⁹



Pelargonium

Pelargonium (Pelargonium sidoides) is a medicinal herb traditionally used in southern Africa for respiratory tract illnesses. Studies show it has a role in numerous RTIs to reduce symptoms, hasten recovery and even reduce time away from work and school.

Over the last few decades, pelargonium has been the focus of multiple clinical trials, mainly conducted in Europe, building up a strong body of evidence to support its use in both adults and children.

The efficacy of *Pelargonium sidoides* preparation EPs 7630 in children, adolescents, and adult patients with acute bronchitis (AB), acute rhinosinusitis (ARS), and acute tonsillopharyngitis (ATP) was demonstrated in a 2007 meta-analysis of 10 RCTs. **The study showed Pelargonium (EPs 7630) was superior to placebo in reducing both symptom severity and time until complete recovery for all indications investigated.**³⁶

Significant advantages were also observed for time until the onset of a meaningful treatment effect, global therapy outcome, and days off work, school, or kindergarten. In AB, efficacy could also be shown for both subsets defined by age. No serious adverse drug reactions were reported in any trial and it as well tolerated. In ARS, all trials included adults only, whereas studies in ATP had been conducted with children only.³⁶

A more recent review (2018) of 8 RCTs confirmed that EPs 7630 significantly reduces symptoms associated with acute bronchitis, acute tonsillopharyngitis and acute RTIs in children as compared to controls. One study involving asthmatic children and adolescents with acute RTI demonstrated a significant symptom-alleviating effect and a possibly reduced number of asthma attacks. In immunocompromised children with acute upper RTI, an alleviating effect of EPs 7630 was shown. All RCTs reviewed reported good safety and tolerability of EPs 7630.³⁷

These positive results were further reinforced by a 2019 meta-analysis of 6 RCTs including children. The review concluded that pelargonium treatment not only reduced symptom burden but also accelerated recovery. It included data from a total of 523 children aged 6-10 years and suffering from non-β-haemolytic streptococcal ATP or from AB. Compared to placebo, EPs 7630 reduced the cumulative dose of paracetamol in 5 out of the 6 trials, by an average of 244 mg.

Importantly, a significant number of children were able to return to school more quickly if receiving active treatment (74.4%) compared to placebo (30.2%).³⁸

The same year, a further meta-analysis confirmed benefits in adults with the common cold. A total of 833 patients were included in 5 RCTs which had a treatment period of ten days. Significant differences for total Cold Intensity Score (CIS) at day 5 and again at day 10 favouring EPs 7630 were observed when compared to placebo.³⁹

More specifically, a higher proportion of patients experienced substantial improvement and complete remission with active treatment. Additionally, people treated with EPs 7630 missed fewer days at work, used less paracetamol and had an improved sleep quality. Once again, this review found no serious adverse reactions and that treatment was well tolerated.³⁹

The preparation EPs 7630 appears to primarily target enveloped viruses such as human coronavirus strain HCo-229E, influenza A virus subtype H1N1 and human respiratory syncytial virus (RSV).⁴⁰

Place in practice:

In practice, pelargonium is a very well tolerated herb. Due to its ability to provide significant symptom relief combined with antiviral properties, pelargonium is best suited to use at the time of infection.

Evidence-informed dosage: Pelargonium EPs 7630³⁷

During infection: Adults: 30 drops (1.35 ml) 3 times/day

Children: 6-12 years: 20 drops (0.9 ml) 3 times/day

Children: 2-5 years: 10 drops (0.45 ml) 3 times/day



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Evidence-based medicinal herb interventions



Garlic

Garlic is the ultimate kitchen cupboard remedy and has been used extensively around the world for centuries. It is favoured in cooking for its flavour enhancing properties, and is a common remedy in both eastern and western traditional medicine for managing mild RTI symptoms.

Garlic is a pungent herb that possess antimicrobial and immune-enhancing properties. It is a popular herbal medicine for managing symptoms such as nasal congestion, often combined with horseradish. Several RCTs have demonstrated the efficacy of garlic supplementation in reducing the severity and duration of symptoms associated with URTIs.^{41,42}

An allicin-containing garlic supplement reduced the frequency of the common cold and accelerated recovery compared to placebo in a double-blind, placebo-controlled trial of 146 volunteers. People were randomised to receive a placebo or a garlic supplement once daily over a 12-week period and asked to self-report on symptoms. The people receiving garlic treatment reported significantly fewer colds than

the placebo group (24 vs 65) and the placebo group recorded significantly more days challenged virally and a significantly longer duration of symptoms (5.01 vs 1.52 days).⁴¹

Another RCT of 120 healthy subjects found that treatment with aged garlic extract supplements (2.56 g/d) enhanced immune cell proliferation after 45 days compared to placebo. After 90 days of supplementation, illness diary entries showed that although the incidence of colds and flu were not statistically different, garlic treatment did reduce illness severity. This was noted by a reduction in the number of symptoms reported, reduced sick days and the number of work/school days missed due to illness (58% fewer than placebo).⁴²

Place in practice:

The results suggest that long-term supplementation with aged garlic extract may enhance immune cell function and that this may be responsible, in part, for reduced severity of colds and flu.

Evidence-informed dosage:

During infection: ≥ 2.56 g (allicin-containing aged garlic)/day for 12 weeks⁴²



Elderberry

Elderberry is another traditional herbal medicine which has been used to treat symptoms of respiratory infections such as the common cold and flu.

Scientific evidence confirms its role in reducing upper respiratory tract symptoms.⁴³ According to one RCT involving air travellers, elderberry extract reduced the length of duration of the common cold compared to placebo and significantly reduced symptom severity, but had no effect on prevention, suggesting its role should remain as an acute treatment.⁴⁴

More recently, pre-clinical research indicates antiviral and antibacterial activity against a range of pathogenic micro-organisms including human influenza virus A.⁴⁵

One study identified that oral use of concentrated elderberry juice stimulated immune responses as observed by suppressed viral replication in the bronchoalveolar lavage fluids (BALFs) and increased levels of influenza-virus-specific neutralising antibody in the serum, as well as the level of secretory IgA in BALFs and faeces. In vitro research also demonstrates that a standardised elderberry liquid is active against human pathogenic bacteria as well as influenza viruses.⁴⁶

A 2019 meta-analysis of four clinical trials confirms that elderberry supplementation, taken at the onset of viral, upper respiratory symptoms, substantially reduces overall symptom duration and severity.⁴³

Whilst symptomatic treatment is effective in both cases of common cold and influenza, symptom relief is more pronounced with influenza virus according to this review.

For safety, raw berries are not the recommended therapeutic option as they contain plant toxins called cyanogenic glycosides. Levels of these naturally occurring phytochemicals are decreased when exposed to heat and evaporation so it's important that elderberry products are prepared appropriately to minimise risk.

Overall, the evidence for the use of elderberry is still emerging,.

Place in practice:

In practice, it is best suited to use at the first sign of infection rather than prevention.

Evidence-informed dosage:

At first sign of symptoms take 15 ml of elderberry syrup four times a day for five days.

| Environmental and Lifestyle Factors |

Herbal medicines and nutritional supplements can play an important role but should not be used as a stand-alone approach to optimal health and enhanced immune function. The frontline measures of social distancing and good hygiene remain the gold standard for COVID-19 precautions.

However, it's important not to forget the advantages other healthy lifestyle measures can afford. Paying attention to consuming a consistently good diet, getting sufficient sleep, regular exercise and managing stress levels are also necessary for a holistic approach to immune system support.


A role for multivitamins


A good quality multivitamin should be considered in the recovery phase because infection can draw on the body's stores of nutrients and a loss of appetite is common during infection. This will provide broad based nutritional support to replenish the body's nutritional status back towards optimal levels.





Usage guidelines

The following tables provide usage guidelines and recommend the most appropriate phase for the ingredients to be administered.


		Protection and prevention	Treatment of symptoms or infection	Recovery and care
 Vitamin C	Phase	*	*	*
	Dosage	Prevention: ≥ 200 mg/day Treatment: ≥ 2000 mg/day (oral); 1 g - 6 g/day (I.V.) Recovery: ≥ 200 mg/day		
	Safety	Regarded as safe to use when taken at the recommended doses		
	Adverse effects	High doses can cause loose bowels or mild diarrhoea in some people		
	Interactions	Please visit: www.blackmoresinstitute.org/interactions/vitamin-c		
	Risk of deficiency	Cigarette smokers, diabetics, people who don't consume fresh fruit and vegetables on a regular basis		
	Practice tips	<ul style="list-style-type: none"> If using chewable tablets, look for sugar free options. Rinse mouth with water after finished chewing If taking high doses, consider taking in divided doses (e.g. one in the morning and one at night) to reduce chance of gastrointestinal discomfort 		


		Protection and prevention	Treatment of symptoms or infection	Recovery and care
 Vitamin D	Phase	*		
	Dosage	Prevention: Adults: 50 mcg (2000 IU)/day		
	Safety	Regarded as safe to use when taken at the recommended doses		
	Adverse effects	Orally well-tolerated		
	Interactions	Please visit: www.blackmoresinstitute.org/interactions/vitamin-d3		
	Risk of deficiency	Vegans and vegetarians; the elderly, those not exposed to sufficient sunlight		
	Practice tips	<ul style="list-style-type: none"> Best to take in divided doses e.g. 1000 IU twice daily Elderly and/or people who are living and working indoors for long periods are at a greater risk of deficiency and should consider supplementation 		


		Protection and prevention	Treatment of symptoms or infection	Recovery and care
 Zinc	Phase	*	*	
	Dosage	Treatment: ≥ 75 mg/day zinc (as acetate or gluconate), taken as a lozenge in divided doses Prevention: 30-200 mg /day for adults - popular forms include oxide, amino acid chelate, gluconate		
	Safety	Regarded as safe to use when taken at the recommended doses		
	Adverse effects	High doses of zinc (100-150 mg/day) may interfere with copper metabolism and cause hypercuprinaemia, red blood cell microcytosis and neutropenia		
	Interactions	Please visit: www.blackmoresinstitute.org/interactions/zinc		
	Risk of deficiency	Vegans, vegetarians, the elderly, people with inflammatory bowel disease		
	Practice tips	<ul style="list-style-type: none"> Best tolerated when taken with meals High doses can induce nausea or gastrointestinal discomfort, consider taking in divided doses Drinking coffee and taking iron supplements can reduce zinc absorption. Separate doses by 2 hours 		

		Protection and prevention	Treatment of symptoms or infection	Recovery and care
 Vitamin A	Phase	*	*	
	Recommend Daily Intake (RDI)	Australian guidelines for general health: Men 14+ years: 900 mcg RE/day (3000 IU/day) Women 14+ years: 700 mcg RE/day (2330 IU/day) Pregnancy 14+ years: 700 - 800 mcg RE/day (2330 - 2660 IU/day) Lactation 14+ years: 1100 mcg RE/day (3660 IU/day)		
	Safety	<ul style="list-style-type: none"> Vitamin A supplements only required in cases of frank deficiency High doses over extended periods of time can cause cumulative toxicity Doses of greater than 10,000 IU/day should be used with caution 		
	Adverse effects	Best tolerated when taken with meals		
	Interactions	Please visit: www.blackmoresinstitute.org/interactions/vitamin-a		
	Risk of deficiency	Very low risk		
	Practice tips	<ul style="list-style-type: none"> Avoid long-term use Not recommended in pregnancy (in some countries) 		


Usage guidelines

		Protection and prevention	Treatment of symptoms or infection	Recovery and care
 Vitamin E	Phase	*		
	Dosage	Prevention: ≥ 200 mg/day (300IU of d alpha tocopherol, natural vitamin E/day)		
	Safety	Regarded as safe to use in doses of up to 1000 mg/day		
	Adverse effects	Generally very well tolerated		
	Interactions	Please visit: www.blackmoresinstitute.org/interactions/vitamin-e		
	Risk of deficiency	<ul style="list-style-type: none"> Deficiency is very rare. Patients with fat malabsorption (in cholestasis where there is low bile flow) 		
	Practice tips	<ul style="list-style-type: none"> Vitamin E needs to be taken for several months to improve the immune response The d-alpha tocopherol form offers the highest bioavailability so is preferred form for use in supplements 		


		Protection and prevention	Treatment of symptoms or infection	Recovery and care
 Multivitamin	Phase	*		*
	Dosage	Typically one a day but check label		
	Safety	Generally regarded as safe		
	Adverse effects	Well tolerated		
	Interactions	Please visit: www.blackmoresinstitute.org/interactions for individual ingredients.		
	Practice tips	<ul style="list-style-type: none"> Best to take a multivitamin in the morning Drinking coffee or tea at the same time can reduce mineral absorption. Aim to separate by 1-2 hours 		


		Protection and prevention	Treatment of symptoms or infection	Recovery and care
 Probiotics	Phase	*	*	*
	Dosage	Treatment and recovery: ≥10 ⁹ CFUs/day (<i>Lactobacillus rhamnosus GG</i> , <i>Lactobacillus acidophilus</i> , <i>Bifidobacterium bifidum</i>)		
	Safety	<ul style="list-style-type: none"> Regarded as safe to use when taken at the recommended doses May not be suitable for individuals with small intestine bacterial overgrowth (SIBO), unless used post-antibiotic treatment 		
	Adverse effects	May cause transient gastrointestinal symptoms such as bloating and abdominal discomfort. However, this is uncommon		
	Interactions	Please visit: https://www.blackmoresinstitute.org/interactions		
	Practice tips	<ul style="list-style-type: none"> Make sure your supplement contains evidence-based strains Best taken with meals Store appropriately 		


Herbal Interventions Table


		Protection and prevention	Treatment of symptoms or infection	Recovery and care
 Andrographis	Phase		*	
	Dosage	At onset of symptoms: <ul style="list-style-type: none"> 100 mg twice daily of a standardised extract (providing 60 mg andrographolide/day) Higher doses required (up to 1200 mg) for pharyngo-tonsillitis 		
	Safety	<ul style="list-style-type: none"> Regarded as safe to use when taken at the recommended doses Insufficient evidence to determine safety in pregnancy Contraindicated in individuals with an allergy to the acanthus family of plants Caution: If patient experience urticaria, gastrointestinal distress or other allergic symptoms discontinue immediately 		
	Adverse effects	Dose-related. Oral doses greater than the tolerable upper limit of 2 g/day can increase the risk of and gastrointestinal upsets		
	Interactions	Please visit: www.blackmoresinstitute.org/interactions/andrographis		
	Practice tips	<ul style="list-style-type: none"> Not recommended in pregnancy Large doses may cause gastrointestinal discomfort, nausea, loss of appetite and/or taste 		

Usage guidelines

		Protection and prevention	Treatment of symptoms or infection	Recovery and care
 Echinacea	Phase	*	*	
	Dosage	Prevention: 2400 mg (dry root equiv.)/day At first sign of cold: 3825 mg (dry root equiv.)/day		
	Safety	<ul style="list-style-type: none"> Regarded as safe to use when taken at the recommended doses Insufficient evidence to determine safety in lactation Contraindicated in individuals with an allergy to the daisy family of plants 		
	Adverse effects	<ul style="list-style-type: none"> Slight risk of transient, reversible and self-limiting gastrointestinal symptoms and rashes No adverse events associated with use in pregnancy 		
	Interactions	Please visit: www.blackmoresinstitute.org/interactions/echinacea		
	Practice tips	<ul style="list-style-type: none"> While can be used for prevention, dosage should be increased at first sign of symptoms Best taken in divided doses 		

		Protection and prevention	Treatment of symptoms or infection	Recovery and care
 Garlic	Phase	*	*	
	Dosage	Treatment: ≥2.56 g (allicin-containing aged garlic)/day		
	Safety	<ul style="list-style-type: none"> Regarded as safe to use when taken at the recommended doses Contraindicated in individuals with an allergy to the onion family of plants 		
	Adverse effects	May cause transient mild gastrointestinal symptoms such as bloating, reflux, flatulence. Garlic odour and breath may occur		
	Interactions	Please visit: www.blackmoresinstitute.org/interactions/garlic		
	Practice tips	<ul style="list-style-type: none"> While garlic can be consumed through diet, aged garlic is a popular supplement choice as it will not cause garlic scented breath after consumption Avoid high doses in patients with bleeding abnormalities High dose garlic may increase the risk of bleeding during surgery. Discontinue 2 weeks prior 		

		Protection and prevention	Treatment of symptoms or infection	Recovery and care
 Pelargonium	Phase		*	
	Dosage (EPs 7630)	Treatment: Adults: 30 drops (1.35 ml) 3 times/day Children: 6-12 years: 20 drops (0.9 ml) 3 times/day Children: 2-5 years: 10 drops (0.45 ml) 3 times/day		
	Safety	<ul style="list-style-type: none"> Regarded as safe to use when taken at the recommended doses Contraindicated in individuals with an allergy to the geranium family of plants 		
	Adverse effects	<ul style="list-style-type: none"> Very rare adverse effects have been reported with pelargonium root medicines Mild side effects limited to gastrointestinal symptoms and rashes 		
	Interactions	Please visit: www.blackmoresinstitute.org/interactions/pelargonium		
	Practice tips	<ul style="list-style-type: none"> Mild adverse effects may include gastrointestinal complaints or allergic skin reactions with pruritus and urticaria Treatment duration should not exceed one week for acute bronchitis and three weeks for acute sinusitis 		

		Protection and prevention	Treatment of symptoms or infection	Recovery and care
 Elderberry	Phase		*	
	Dosage	Treatment: At first sign of RTI: Take 15 ml of elderberry syrup four times a day for five days		
	Safety	Generally, well tolerated		
	Adverse effects	May interact with some immunosuppressant medications		
	Practice tips	<ul style="list-style-type: none"> Best suited for use at first sign of infection Raw berries are not the recommended therapeutic option as they contain plant toxins called cyanogenic glycosides. Levels of these naturally occurring phytochemicals are decreased when exposed to heat and evaporation so it's important that elderberry products are prepared appropriately to minimise risk 		

Immunity in a viral world: The role of nutrients and herbs

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