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1 Overview

Summary and Quick Facts for Common Cold

- The common cold is the most frequent acute infectious illness in the United States.
- The common cold can be caused by more than 200 subtypes of rhinovirus, influenza viruses, and other common viruses.
- Treatment strategies for the common cold are generally aimed at relieving symptoms and minimizing risk of complications.
- Several nutrients such as vitamin D, zinc lozenges, beta-glucans, and probiotics may help prevent colds and manage symptom duration and intensity.

What is the Common Cold?

The common cold is a viral infection of the upper respiratory tract. Common colds can be caused by over 200 distinct viral pathogens, typically from the rhinovirus, influenza virus, and other common virus families. Because there are so many distinct cold-causing viruses, developing immunity against the common cold is unlikely.

Infection occurs when the virus reaches mucous membranes (eg, eyes, nose, mouth), often via direct contact or respiratory droplets from an infected individual. Colds generally resolve without treatment, and conventional treatments are mostly palliative and aim to shorten the duration of the illness and prevent complications such as a secondary bacterial infection. However, no cold medication is yet known to effectively decrease duration, severity, or risk of complications.

Nutrients such as **probiotics**, **vitamin D**, and **zinc lozenges** may help prevent the common cold and aid the body's immune response.

What are Signs and Symptoms of the Common Cold?

- Nasal swelling and congestion
- Runny nose
- Sore throat
- Coughing and sneezing
- Low-grade fever
- Mild aches

Note: Cold symptoms are usually mild. If symptoms are more severe (eg, high fever, severe body aches, shortness of breath, digestive symptoms), notify a healthcare provider as this may indicate a more serious condition, such as the flu.

What are Ways to Prevent the Common Cold?

- Wash and sanitize hands and surfaces, and avoid touching your eyes, nose, and mouth.
- Gargling with salt water and nasal irrigation may help mechanically remove viruses from mucous membranes.
- Maintain adequate vitamin D levels.
- Humidify air if you are in a low-humidity environment.
- Maintain a healthy lifestyle—avoid smoking, get enough exercise and sleep, and eat a healthy diet such as the Mediterranean diet.

What are Conventional Medical Treatments for the Common Cold?

- **DO NOT take antibiotics for a common cold.**
- Gargling (eg, with salt water) and nasal irrigation may help improve symptoms and reduce duration of the illness.
- Some over-the-counter medications that may help relieve cold symptoms include:
 - Analgesics
 - Decongestants
 - Antihistamines, and others.

Note: Many cold medicines contain the same active ingredients. **ALWAYS read labels** to ensure you do not exceed the recommended dose.

What Nutrients May Be Beneficial for the Common Cold?

- **Probiotics.** Specific probiotics have been shown to reduce incidence and duration of upper respiratory tract infections.
- **Beta-glucans.** These prebiotic fibers may stimulate the body's antimicrobial defense and prevent infection as well as decrease symptoms.
- **Vitamin D.** Regular vitamin D supplementation and maintaining higher vitamin D levels are associated with a decreased risk of seasonal viral infection and acute respiratory infection.
- **Zinc.** Zinc deficiency has been linked to immune impairment and susceptibility to infection; zinc can bolster the body's ability to fight off viruses. Using zinc in the form of a lozenge within 24 hours of symptom onset

may reduce the duration and severity of a cold.

- **Vitamin C.** Vitamin C augments several aspects of the immune system and helps defend against infections. Using vitamin C may reduce the chances of catching a cold and cold duration.
- **Echinacea.** Echinacea may reduce the incidence of colds and sick days, as well as reducing the risk of recurrent infections.

If you are reading this because you have developed symptoms consistent with an acute respiratory infection, it is critical that you act quickly to halt the rapid replication of viruses occurring in your body at this very moment. Go to the nearest health food store or pharmacy and purchase:

1. **Zinc Lozenges:** Dissolve in mouth one lozenge containing 18.75 mg of zinc, in the form of zinc acetate, every 2–3 waking hours up to five times per day until symptoms of acute respiratory infection subside.
2. **Probiotics & Postbiotics:** Take one capsule daily containing *Lactobacillus rhamnosus* CRL-1505 and dried fermentate of *Saccharomyces cerevisiae*.
3. **Black elderberry extract:** Chew one tablet containing 90 mg of black elderberry extract up to eight times daily for five days. Alternatively, take capsules containing 600 mg of black elderberry extract up to 4 times daily for five days.
4. **Lactoferrin:** Take 300 mg of bovine apolactoferrin twice daily.
5. **Garlic:** Take up to 3,600 mg of garlic extract, standardized to 10,000 ppm allicin, in divided doses with meals each day until symptoms subside. Garlic should be taken with food to minimize stomach irritation. Some people prefer using aged garlic extract in divided doses with meals, taken at 3,600-7,200 mg a day.
6. **Vitamin D:** If you do not already maintain a blood level of **25-hydroxyvitamin D** over **50** ng/mL, then take **250 mcg (10,000 IU)** vitamin D the first day and continue for three more days; then reduce the dose to 50–125 mcg (2,000–5,000 IU) vitamin D each day. If you already take 2,000–5,000 IU vitamin D daily, then you probably do not need to increase your intake.
7. **Melatonin:** Take 3–50 mg at bedtime.
8. **Vitamin C:** Take 6,000 – 8,000 mg of vitamin C in divided doses for up to five days and continue with 1,000 mg three times daily thereafter. Alternatively, a liposomal hydrogel form of vitamin C with enhanced bioavailability may be taken at lower doses once daily to achieve high plasma levels through the day. **Note:** Unformulated vitamin C may have a laxative effect at higher doses. This can be partially mitigated by taking it in divided doses during the day.
9. **Cimetidine:** Take 800-1,200 mg cimetidine daily in divided doses. Cimetidine is a heartburn drug that has potent immune-enhancing properties. (It is sold in pharmacies over-the-counter.) **Note:** cimetidine can interact with many drugs and potentially cause adverse effects. Talk with a qualified healthcare provider or pharmacist before starting cimetidine to be sure you do not take any drugs that could interact with cimetidine.

Do not delay implementing the above regimen. Once a respiratory virus infects too many cells, it replicates out of control and strategies like zinc lozenges will not be effective. Treatment must be initiated as soon as symptoms manifest!

2 Introduction

The common cold is a viral infection of the upper respiratory tract that typically causes symptoms such as a runny or stuffy nose, sneezing, coughing, sore throat, and malaise. American adults contract an average of two to three colds per year and children contract as many as eight, making common cold the most frequent acute infectious illness in the United States, as well as the rest of the industrialized world.¹

The common cold is generally a mild, self-limiting, and can be distinguished from more severe infections (eg, influenza) by the absence of digestive, neurological, and severe systemic symptoms. Although some people experience systemic symptoms such as fatigue, headache, fever, and muscle aches, the intensity of these symptoms is milder in those with a common cold.²

Common colds, like other respiratory viral infections, begin when viruses infect the cells lining the upper airways.

Viruses reach the respiratory mucosa by being inhaled into the nose or mouth, or by direct contact, such as when contaminated hands touch the mouth, nose, or eyes. In most cases, the mucosal immune system clears the infection in a few days, causing mild symptoms in the process; however, common colds can exacerbate respiratory conditions like asthma and chronic obstructive pulmonary disease (COPD) and increase vulnerability to secondary infections that can result in rhinosinusitis, influenza, or pneumonia, particularly in smokers, young children, the elderly, those with chronic diseases, and those with weakened immune function.^{6,7}

Stress, sleep disturbance, smoking, allergies, chronic diseases, and use of some medications are associated with more frequent or more severe colds, whereas limiting exposure to respiratory viruses through hygiene can reduce risk and prevent spread of the common cold.^{1,8,9} Engaging in regular moderate-intensity physical activity, getting adequate sleep, and managing stress can help maintain the immune system's ability to mount a balanced response to respiratory viral infections, including those that cause the common cold.³³⁸⁻³⁴⁰ Eating a diet rich in vitamins, minerals, fiber, and phytonutrients supports healthy immune function and may lower the risk of infection.¹³⁻¹⁵

Conventional therapies for the common cold, such as analgesics, non-steroidal anti-inflammatory drugs (NSAIDs), decongestants, and antihistamines, as well as saline nasal irrigation, provide varying degrees of symptom relief but do not shorten the course of the illness.¹⁶ Nasal irrigation and gargling with salt water may reduce viral load and thereby shorten respiratory viral infections, decrease symptom severity, and limit transmission. In addition, a growing body of evidence supports the use of integrative therapies such as probiotics, vitamin D, zinc lozenges, and vitamin C, as well as treatment with medicinal herbs like echinacea, andrographis, and ginseng, for reducing the severity and duration of colds.^{9,18,19} Importantly, antibiotics, which are only effective against bacterial infections, are not indicated for the common cold.^{16,20}

3 Background

More than 200 subtypes of viruses are known to cause the common cold, and new cold-causing viruses are still being identified.^{1,9} Viruses in the rhinovirus family are the most frequent cause, responsible for an estimated 30–50% of colds. Influenza viruses may cause another 5–15%.¹ Viruses in these families can also cause other types of illnesses: for example, rhinoviruses can cause ear infections, sinus infections, and pneumonia,^{21,22} and influenza viruses typically cause flu-like illnesses and are also responsible for some pneumonias.²³

4 Risk Factors

The common cold has long been noted to be more prevalent in winter months in temperate regions. This is due to climate-related changes in viral stability and transmission properties, the immune response, and human behavior (for example, spending more time indoors).³⁰

In addition to seasonality, several other factors increase the likelihood of contracting a cold^{1,8}:

- Lose contact with children, such as in schools and daycare settings
- Asthma and allergic rhinitis (nasal swelling)
- Smoking
- Stress
- Sleep disorders
- Chronic illness
- Medications that suppress immune function, such as prednisone, dexamethasone (Decadron), azathioprine (Imuran), and cyclosporine (Gengraf).

Immune Senescence and Common Cold

The immune system undergoes marked age-related remodeling, known as immune senescence, that gradually weakens the response to infections and leaves the elderly more vulnerable to both acute infections and chronic inflammatory conditions.³² With increasing age, the relative populations of various immune cell types change. For example, immune cells involved in immunological memory and recognition of previously encountered pathogens are typically over-represented and those involved in responsiveness to new antigens are under-

represented. Overall, numbers of exhausted and dysfunctional immune cells grow and expression of inflammation-related genes increases. In this immunosenescent landscape, the response to viral infections like the common cold are less effective at clearing the infection and more likely to result in dysregulated inflammation.^{32,33} Immune senescence is thought to be a major contributing factor to high rates of viral respiratory outbreaks and increased hazards of complications, such as secondary bacterial infections, in long-term care facilities.³⁴

Exercise, eating a healthy diet, and maintaining a healthy body weight can help limit or slow immune senescence. In older individuals, both aerobic and resistance exercise have been found to balance anti-inflammatory and pro-inflammatory immune signaling molecules and improve immune regulation.^{35,36} Healthy eating habits such as those comprising the Mediterranean-like and DASH (Dietary Approaches to Stop Hypertension) diets have been linked to markers of immune responsiveness and reduced inflammation.^{37,38} Calorie restriction, the practice of regularly consuming fewer calories without causing nutrient deficiencies, has been widely shown to have positive effects on immune function in many animal models of aging, and promising health effects have been reported from controlled trials in humans.³⁹⁻⁴² In addition, some evidence suggests integrative therapies such as melatonin,⁴³ cistanche,⁴⁴ Pu-erh tea,⁴⁵ and reishi⁴⁶ may be able to slow or reverse some effects of aging on immune function.

More information is available in Life Extension's [Immune Senescence](#) protocol.

5 Symptoms

Usual symptoms of the common cold include^{1,8}:

- Nasal swelling and congestion
- Runny nose
- Sore throat
- Cough
- Headache
- Low-grade fever
- Muscle aches
- Malaise (general feeling of being unwell)

Notably, these symptoms are mild in individuals with a cold. The presence of digestive symptoms or severe and body-wide symptoms, such as fatigue, fever, body aches, shortness of breath, and malaise, may indicate a more serious infection such as influenza.^{2,33,4}

Table 1: Comparison of Characteristics: Common Cold and Influenza^{1-4,8}

	Common Cold	Influenza
Causative virus(es)	rhinoviruses, influenza viruses, and others	influenza A virus influenza B virus influenza C virus
Site of infection	Upper respiratory tract	Upper and lower respiratory tracts
Incubation period	1–3 days	1–4 days
Onset of illness	Gradual	Abrupt
Duration of illness	Typically 7–10 days	Typically 7–14 days
Severity of illness	Mild	Mild to severe
Symptoms:		
Nasal congestion and runny nose	Characteristic	Common
Sore throat	Characteristic	Common
Cough	Characteristic, usually mild to moderate	Characteristic, can be severe
Headache	Common, usually mild	Common
Fever	Rare, low-grade	Characteristic, can be high

Muscle aches	Uncommon, usually mild	Characteristic, often severe
Malaise/fatigue	Common, usually mild	Characteristic, often severe
Shortness of breath	None	Uncommon
Diarrhea and/or vomiting	None	Uncommon
Loss of sense of smell (without nasal congestion) or taste	None	None
Other neurological symptoms	None	None

6 The Course of the Common Cold

Common cold-causing viruses can be contracted in at least three ways^{1,23}:

- **Direct contact.** Hands are an important route of transmission for common cold-related viruses. When an uninfected person touches an infected person who is actively shedding viruses, or touches surfaces contaminated with shed viruses, they can then transmit the virus to their own respiratory tract by touching their eyes, nose, or mouth.
- **Respiratory droplet.** Respiratory droplets emitted during coughing or sneezing can harbor cold-causing viruses, carrying them short distances. These infectious droplets contribute to cold transmission when inhaled by those in close proximity or land on surfaces and are picked up by hands.
- **Aerosol.** Some exhaled viruses can become suspended in tiny droplets of moisture that linger in the air for long periods of time. Aerosolized viruses can be spread by natural or mechanically induced air currents and thereby infect people farther away from the source.

Although direct contact and respiratory droplet are accepted as major routes of cold virus transmission, the role of aerosol in spreading the common cold has not been well defined and is likely to vary between types of cold-causing viruses.^{1,5} One study in people with respiratory infection due to influenza virus found people with lung (ie, lower respiratory) infections emitted infectious viruses in aerosols during coughing, sneezing, and normal breathing; however, upper respiratory infections were not strong predictors of infectious aerosol emission.⁴⁸ Aerosolized rhinoviruses have also been detected, but whether this is an important mechanism of spread for the common cold is still unclear.⁴⁹

Infection and Incubation

Cold-causing viruses attach and gain entry to upper respiratory epithelial cells (cells that line the respiratory tract) by interacting with molecules on epithelial cell surfaces.²¹ Once inside a cell, the virus releases its genetic material and triggers conversion of cellular activity to support production of viral proteins and viral replication. Newly generated viruses are released into the airway where they can infect nearby cells or be shed through breathing, sneezing, and coughing.

The time from infection to symptom onset is known as the incubation period. The incubation period in cases of the common cold can be as short as 10–12 hours but is usually between one and three days. During this time, the infected person is shedding transmissible virus unknowingly. Once symptoms begin, they typically last between three and 10 days; however, symptoms persist for as long as two weeks in about 25% of individuals, especially smokers and those with weakened immune function. The rate of viral shedding generally coincides with symptom severity, peaking on day two or three of illness, then persisting at a low level for a week or longer, especially in children.¹

Illness and Recovery

Viral infection triggers the release of a wide array of pro-inflammatory molecules, which are responsible for the well-known symptoms of the common cold.^{8,51} Interferons and cytokines produced by infected cells help inhibit infection spread to nearby cells and initiate the immune response. Leukotrienes, bradykinin, and other peptides released as part of the immune response stimulate mucus secretion, vasodilation, and increased blood vessel permeability that lead to nasal congestion and runny nose. In addition, some of these molecules trigger increased acetylcholine signaling in the nervous system, which can further contribute to mucous production, coughing, and

sneezing.^{8,51} Both viral activity and the immune response cause varying degrees of cell damage and disruption to the integrity of the epithelial barrier, leading to increased risk of secondary infections.^{22,51}

Ultimately, the immune response leads to containment of infection, destruction of infected cells, tissue repair, and restoration of homeostasis. In addition, specialized immune cells develop lasting memory that may prevent re-infection by the same virus. Nevertheless, since there are many cold-causing viruses with vast variability in the specific immune response they elicit, recovery from the common cold does not protect against another cold, and many people experience multiple colds in one season.^{1,22}

Complications

For most people, the common cold is a mild and self-limiting illness, but occasionally it progresses to, or exacerbates, a more serious condition. This is more likely in^{6,52}:

- Smokers
- Pregnant women
- Children under 2 years old
- Adults over 60 years old
- Those with asthma, COPD, or other lung conditions
- Those with other chronic diseases, such as heart disease, kidney disease, diabetes, or cancer
- Those whose immune systems are compromised due to a health problem or its treatment

Complications arise when cold-causing viruses infect other regions of the respiratory tract, such as the sinuses (sinusitis), middle ear (otitis media), large bronchial tubes (bronchitis), or lungs (pneumonia). Secondary bacterial infections, which are often more serious, can also affect the sinuses, throat, bronchial tubes, and lungs.^{1,6} Furthermore, the common cold is a frequent trigger of asthma and COPD exacerbations.^{6,53}

Some people experience a lingering cough at the tail end of a common cold, even after other symptoms have long resolved. This post-viral cough, which occurs with no lung involvement, lasts between three and eight weeks. If it persists longer than eight weeks, it is considered a chronic cough. Although the mechanism underlying post-viral cough is not fully understood, hyper-sensitization of the cough reflex by bradykinin and other inflammatory mediators or due to damage to the epithelial barrier is thought to play a major role.^{6,51}

Another possible sequela of the common cold is post-viral acute rhinosinusitis (inflammation of the nasal passages and sinuses). While rhinosinusitis is one of the most frequent features of the common cold, it is considered post-viral if it persists longer than 10 days or worsens after the fifth day of a cold. Its cause appears to be inflammatory in nature, rather than infectious. The risk of secondary bacterial rhinosinusitis is higher in those with post-viral rhinosinusitis.¹⁶

7 Diagnosis

The most important aspect of diagnosing a common cold is ruling out other conditions that could be more serious or treatable.⁵⁴ In general, the presence of characteristic symptoms and absence of indicators of more serious illness are sufficient for diagnosis.^{1,8} Physical exam findings such as nasal mucosal swelling, throat redness, and possibly low-grade fever, along with normal lung sounds, can help secure an uncertain diagnosis.¹

Other serious infections, in their milder manifestations, can also be confused with the common cold. These include influenza and pertussis (whooping cough).¹ A more severe cough, involvement of the lungs, and systemic symptoms like muscle ache, fever, and malaise indicate possible influenza,² and a persistent cough that comes in fits that sometimes induce vomiting and exhaustion, as well as a whooping sound when breathing in, points to pertussis.⁵⁶ Finally, allergic rhinitis (respiratory allergies or hay fever) often mimics a common cold with runny nose and nasal congestion but is more frequently marked by itching of the nasal mucosa or eyes.^{54,57}

The following conditions frequently overlap or share symptoms with the common cold, and a small percentage of cases are due to bacterial infections that may respond to antibiotic therapy:

- **Acute rhinosinusitis.** Swelling of the nasal passages and sinuses, or rhinosinusitis, can occur during or following the common cold. In addition to nasal congestion and discharge, it may be marked by facial pain. Acute rhinosinusitis can be caused by a bacterial infection, but most cases are viral.⁶

- **Acute pharyngitis.** A sore throat is a characteristic symptom of the common cold, but when it is the predominant symptom, it may indicate simple acute pharyngitis. It is estimated that 70–95% of pharyngitis cases are viral, while the rest are bacterial (eg, strep throat).⁶
- **Acute bronchitis.** Bronchitis is an inflammation of the trachea and large bronchial passages, but it does not involve the lungs. Acute bronchitis frequently follows a cold and is characterized by a cough that may be accompanied by chest pain, wheezing, shortness of breath, and breath sounds known as crackles or rales that can be heard during a physical exam.^{6,58} Although most cases are viral, acute bronchitis can be caused by bacterial infection.⁵⁸

In the vast majority of cases, lab tests are not needed to diagnose the common cold.⁵⁴ In rare instances, a procalcitonin level may be useful in confirming the absence of a bacterial infection.¹ Procalcitonin levels have been shown to be elevated in bacterial, but not viral, infections. Monitoring procalcitonin has been proposed as a strategy for distinguishing bacterial from viral respiratory illnesses and guiding decisions around antibiotic prescription.^{59,60} For example, a low procalcitonin level may help secure the diagnosis of common cold and avoid unnecessary antibiotic therapy by ruling out suspected bacterial rhinosinusitis.⁶¹

8 Prevention

Handwashing and Hand Sanitizing

Frequent handwashing is recommended as an important strategy for reducing the spread of cold viruses, as well as pathogenic bacteria.^{9,23,62} Cold-causing viruses have been found to remain viable on skin for as long as two hours.¹ Thorough hand washing can effectively remove viruses, bacteria, fungi, and microbe-harboring soil from hands, thereby preventing self-inoculation via touching the eyes, nose, or mouth, and transmission to others via direct contact or contamination of touched surfaces. Frequent cleaning of high-touch surfaces like doorknobs and faucets may also reduce viral spread.⁶⁴ Respiratory viruses generally remain viable longer on hard surfaces like metal and plastic than on soft, porous surfaces like cloth, paper, and cardboard.^{65,66}

Alcohol-based hand sanitizers may play a role in cold prevention since they can be used in circumstances where hand washing is not possible. The virus-killing action of alcohol, especially ethanol, is effective against several major cold-causing viruses. Rhinoviruses are relatively resistant to alcohol-based hand sanitizers and surface disinfectants²²; nevertheless, the use of an alcohol-based hand sanitizer, along with routine hand washing, has been found to reduce the presence of rhinovirus on hands more than hand washing alone.⁶⁸ Hand sanitizers with alcohol concentrations of 60–95% are more likely to be effective against an array of viruses than those with lower concentrations.

Gargling and Nasal Irrigation

Gargling and nasal irrigation are practices that may mechanically reduce the presence of cold-causing viruses on the upper respiratory mucosa. In a clinical trial that included 387 adults, gargling with tap water three times daily for 60 days during winter was found to lower the incidence of upper respiratory tract infections and was more effective than gargling with iodine.⁶⁹ A trial in children aged 2–6 years found gargling with water or green tea reduced the likelihood of fever, a common symptom of upper respiratory infection in this age group.⁷⁰ Some research also suggests gargling with green tea may reduce the risk of influenza.⁷¹

Maintaining Adequate Vitamin D Levels

Maintaining adequate vitamin D levels may help prevent viral respiratory infections such as the common cold. Vitamin D deficiency has been correlated with increased incidence of colds and flu in multiple studies.^{72,73} In a study that took place in Connecticut, 198 healthy adults were monitored through the winter months; those who maintained vitamin D levels ≥ 38 ng/mL had 2.7 times lower incidence of acute respiratory illnesses and 4.9 times fewer sick days than those whose vitamin D levels were < 38 ng/mL.⁷⁴

Humidification

Ambient air temperature and relative humidity are factors that affect the viability of airborne viruses and function of cells lining the nasal passages. Cooler and drier air conditions may influence the spread of viral respiratory infections both by increasing survival of aerosolized viruses and impairing the ability of the respiratory mucosa to

clear pathogens.⁷⁵⁻⁷⁸ Fluctuating climatic conditions may also be important in determining risk of infections: In a study that included 892 participants in Antarctica, a 3-day period in which both temperature and humidity dropped was found to be correlated with increased incidence of upper respiratory infections caused by rhinoviruses.⁷⁹ A study that evaluated the infectivity of influenza viral particles using simulated coughing in various relative humidities found humidity levels above 40% were associated with reduced infectivity. In this study, viral particles collected 60 minutes after simulated coughing retained about 70–77% infectivity in relative humidity at or below 23%, but retained only 15–22% infectivity at relative humidity at or above 43%.⁸⁰ Observational studies have noted decreased risk of respiratory infections in individuals working or living in environments with relative humidities in the mid-range of 40–60%, versus lower and higher relative humidities.⁸¹

Based on the evidence described in the preceding paragraph, using a humidifier in low-humidity climates may help reduce the risk of respiratory viral infections. Portable humidifiers have been reported to raise room air humidity by 15–20%, and could lower survival of airborne influenza viruses by an estimated 17.5–31.6%.⁸²

9 Treatment

Gargling and nasal irrigation may be helpful as a treatment for common colds.⁸³ An open-label randomized controlled trial with 61 participants found saline nasal irrigation plus gargling, beginning within 48 hours of the onset of cold symptoms, reduced the duration of illness by almost two days, over-the-counter medication use by 36%, and transmission to others in the household by 35%. Nasal swabs indicated those using nasal irrigation and gargling had decreased viral shedding.⁸⁴ In children under 2 years of age with the common cold, the use of saline or seawater nasal drops relieved nasal congestion and improved sleep, nutrition, and strength compared with no nasal drops.⁸⁵

Many people use steam inhalations in the hope of thinning nasal secretions and relieving cold symptoms¹⁹; however, the evidence is mixed. Two clinical trials found nasal delivery of heated humidified air (steam) shortly after symptom onset did not reduce cold symptoms during seven days of monitoring compared with similar delivery of non-humidified room-temperature air,^{86,87} while another controlled trial found two 30-minute treatments with steam one week apart reduced nasal swelling and improved openness of nasal passages compared with placebo treatment.⁸⁸ In addition, a controlled trial found 30-minute steams performed once on the first day and again on the second day after experimental inoculation with a common cold-causing virus had no impact on viral shedding after five days.⁸⁹

There are no medications known to effectively decrease duration, severity, or risk of complications from the common cold. Individuals with moderate-to-severe symptoms may benefit from therapies aimed at symptom reduction, but potential adverse side effects also need to be considered.^{9,20} In particular, cold medications should not be used in children under four years of age, in whom the potential harms outweigh the possible benefits.¹⁹ Antibiotics should not be used to treat uncomplicated common colds, but reserved for cases of secondary bacterial infections.^{20,23}

Table 2: Symptomatic Therapies for the Common Cold

Medication Type	Target Symptoms	Comments
Analgesics (non-steroidal anti-inflammatory drugs [NSAIDs]) and acetaminophen (Tylenol)	Headache Muscle pain Other types of pain Fever	While they may relieve certain symptoms, these medications have been found not to reduce duration or overall symptom score in those with common colds. ⁹⁰
Decongestants (pseudoephedrine and phenylephrine)	Nasal congestion Nasal swelling	Pseudoephedrine may have a small benefit on nasal symptoms, but its sale is restricted in the United States; phenylephrine is less effective and may not be better than placebo. ²⁰
Antihistamines (diphenhydramine [Benadryl])	Nasal swelling Runny nose Sneezing Cough	There is a small likelihood of symptom reduction in the first few days of a cold, but the possible benefit must be weighed against common side effects such as sedation and dry eyes, nose, and mouth. ^{20,91} Combinations

containing an antihistamine and a decongestant, with or without an analgesic, have more evidence indicating benefit.⁹²

Antitussives (dextromethorphan, codeine)	Cough	Evidence supporting dextromethorphan is mixed and benefit, if any, is small ⁹³ ; codeine, an opiate that is not safe in children, has not demonstrated effectiveness in cases of uncomplicated common cold. ^{19,54}
Expectorant (guaifenesin)	Cough	Evidence for guaifenesin's effect on cough associated with the common cold is mixed. ^{19,94}
Anti-asthma Medications (ipratropium [Atrovent] and cromolyn)	Cough Runny nose Nasal congestion	Inhaled ipratropium (an anti-cholinergic) reduces cough and may lead to improvement in those with acute asthma exacerbation. ^{19,95,96} One clinical trial found cromolyn (a mast cell stabilizer), whether inhaled or used as a nasal spray, reduced upper respiratory tract symptoms, especially cough. ⁹⁷ Limited evidence suggests cromolyn use by allergy and asthma patients may reduce common cold risk. ^{98,99}

Cimetidine and the Common Cold

Cimetidine (Tagamet) is an over-the-counter drug that reduces gastric acid secretion by inhibiting a type of histamine receptor (H2 receptors) found in the gastric lining. It is mainly used to treat gastroesophageal reflux disorder (GERD), but is sometimes used to treat gastric and duodenal ulcers and viral warts.¹⁰⁰ Histamine H2 receptors are also found on all types of immune cells, and cimetidine has been shown to modulate immune cell activity. Preclinical studies indicate cimetidine activates monocytes, neutrophils, and other non-specific immune cells, yet inhibits generation of free radicals by neutrophils. This reduces potential tissue damage and uncontrolled inflammation. Cimetidine has also demonstrated the capacity to upregulate natural killer (NK) cells, as well as T and B cells that interact with pathogens via recognition of specific proteins by immune receptors and antibodies.¹⁰¹ Furthermore, cimetidine increases signaling by antiviral cytokines, including interferons, and decreases signaling by immunosuppressive cytokines.^{101,102}

Note: Cimetidine affects the metabolism and clearance of a number of other medications and should be used with caution by those taking drugs for other conditions. For example, cimetidine should not be used by those taking the antiviral drug delavirdine (Rescriptor), bone-building drug risedronate (Actonel), broad-spectrum antibiotics cefuroxime (Zinacef) and cefditoren (Spectracef), or triple therapy for *Helicobacter pylori* infection that includes bismuth, metronidazole (Flagyl), and tetracycline (Sumycin).¹⁰⁴

10 Novel and Emerging Therapies

The development of a **vaccine** to prevent and treat the common cold is hampered by the existence of a myriad of causative viruses and their rapidly mutating nature.¹⁰⁵ The search for effective treatment faces these same challenges, as well as the likelihood that antiviral agents may only be effective if initiated around the time of peak viral replication, which may be before or at the onset of symptoms.⁹ Furthermore, because the common cold is generally mild and self-limiting, there is the possibility that vaccine- or medication-related adverse side effects could be worse than the cold itself.

Capsid-binding agents block the uncoating of viruses and prevent their entry into cells. Capsid-binding drugs such as pleconaril have shown particular promise against respiratory viruses in preclinical research, and researchers are currently seeking antiviral drugs with a similar mode of action as potential treatments for respiratory viral infections.¹⁰⁷⁻¹⁰⁹ In an analysis of results from two randomized placebo-controlled trials that included a combined total of 2,096 patients with the common cold, pleconaril, administered within 24 hours of symptom onset, was found to have shortened the duration of illness by an average of 2.3 days in subjects infected by specific susceptible rhinovirus strains, but did not alter the course of infection in those with non-susceptible viruses. The researchers estimated approximately half of participants were infected with susceptible viruses.¹¹⁰ Pleconaril was

associated with slightly increased risk of mild-to-moderate adverse side effects, including headache, nausea, and diarrhea, in common cold patients.¹¹¹ Pleconaril is not approved for systemic use in the United States as of early 2021, but is used on a compassionate basis of some conditions in infants.¹¹² It is hoped that new antiviral drugs with broader efficacy will be identified.¹⁰⁸

11 Dietary and Lifestyle Interventions

Smoking

One of the most important lifestyle factors influencing risk and severity of the common cold is smoking. Cigarette smoke and nicotine from electronic cigarettes alter the mechanical function of the respiratory lining and dull the cough reflex, making it more difficult to clear pathogens. Smoking and vaping also cause toxic damage to the airway epithelium, disrupt immune activity, and trigger heightened inflammation, further increasing susceptibility to infection.^{7,113-115} Although less is known about vaping, researchers have found cigarette smokers are approximately twice as likely to experience the common cold as non-smokers and have higher rates of complications like pneumonia.⁷ Exposure to secondhand smoke also increases common cold risk: in one study, those with regular secondhand smoke exposure had an almost 60% higher likelihood of becoming sick with a cold.^{7,116} A number of studies suggest smoking is correlated with increased rates of complications of respiratory infections as well.⁷

Exercise

Regular moderate-intensity physical activity is associated with reduced inflammation and stronger antiviral immune activity, while the extremes of physical inactivity and overtraining can weaken immune defenses and raise inflammatory signaling.^{10,118} Some evidence suggests exercise may limit or delay the effects of aging on immune function and help restore competent immune responsiveness in older individuals.¹¹⁹ A review of observational and randomized controlled trials noted engaging in moderate aerobic exercise daily or almost daily lowers the risk of upper respiratory infections like the common cold by approximately 40–50%, and is also associated with shorter upper respiratory illnesses.¹¹⁸ One controlled trial included 115 overweight or obese, sedentary, postmenopausal women who were randomly assigned to an exercise group (45 minutes of moderate intensity exercise five days per week) or a stretching group (45 minutes of stretching once per week) for one year. In the final three months of the trial, the incidence of colds was three times higher in the stretching versus the exercise group.¹²⁰

Sleep

Sleep is vital for healthy immune function, and impaired sleep can disrupt the balance between inflammatory and anti-infection immune activity. Even one night of partial sleep deprivation has been shown to suppress an important aspect of normal immune function for more than four days.¹²¹ In a study that included cold histories from 651 military recruits undergoing basic military training, those who routinely slept less than six hours per night were four times as likely to be diagnosed with an upper respiratory infection than those who slept seven to nine hours per night.¹²² This evidence was supported by a clinical trial in which 164 healthy adults wore devices to assess their sleep duration and continuity for seven days, and were then experimentally exposed to a cold-causing rhinovirus. Those who slept six hours or less per night had a more than four-fold higher risk of developing a cold.¹²³ In a similar study that included 153 healthy adults between age 21 and 55 years old, the odds of developing a cold after rhinovirus exposure were almost three times higher in those who reported sleeping less than seven hours per night compared with those who reported sleeping eight hours or more. Sleep efficiency (percentage of time in bed spent sleeping) is also a factor in the ability to defend against cold viruses. Even among those with good sleep efficiency, decreasing time awake during the night may add to protection: the study described above also noted a 5.5-fold lower risk of a cold in those reporting the highest sleep efficiency (98% or higher) compared with those reporting the lowest sleep efficiency (less than 92%).¹²⁴

Stress Management and Social Support

Chronic psychological stress has been found to increase the risk of upper respiratory tract infections, while social support reduces the risk.¹² One study evaluated stress based on recent stressful life events (eg, death of a spouse or job loss), perceived stress level, and emotional state (eg, anxiety or depression) in 394 healthy volunteers before exposing them to cold-causing viruses and found those with higher stress scores were more likely to

develop colds than those with lower scores.¹²⁵ The same researchers noted persistent interpersonal problems and being under- or unemployed were stressors most closely correlated with a higher chance of developing a cold after virus exposure.¹²⁶ On the other hand, they found having larger and more diverse social networks was associated with lower susceptibility to the common cold.¹²⁷

More recent studies have noted better mental health and lower psychosocial stress levels are associated with lower incidence of acute respiratory infection.^{128,129} One study examined participants' use of an emotional regulating skill called cognitive reappraisal, which is re-interpreting emotional situations in ways that change their emotional impact. The study found those who reported more frequent use of cognitive reappraisal strategies had lower nasal production of inflammatory cytokines and less severe cold symptoms after experimental exposure to rhinovirus.¹³⁰ In another study, 154 participants were assigned to an eight-week mindfulness training group, eight-week exercise training group, or control group and were monitored for common colds during the cold and flu season. The mindfulness group had significantly reduced cold severity and fewer missed days of work compared with the control group. In addition, the mindfulness and exercise groups had fewer colds and shorter cold duration than the control group, but these differences did not reach statistical significance.¹³¹

Diet

A healthy diet that supplies adequate amounts of vitamins A, B complex, C, D, and E, as well as zinc, selenium, magnesium, iron, copper, and omega-3 fatty acids supports normal immune function and defense against respiratory viral infections like the common cold.^{13,132} In an open clinical trial, 128 children with recurring colds and frequent inflammatory complications whose families adopted a traditional Mediterranean diet, a well-established health-promoting dietary pattern, had reduced frequency of infection and medication use at the end of one year.¹³³ In women, higher intake of fruits and vegetables, as sources of vitamin C, has been associated with lower risk of respiratory infection.^{134,135} Kiwifruit in particular has been shown to protect against common colds: a randomized cross-over trial in 32 elderly adults found eating four kiwifruits per day for four weeks reduced the severity and duration of common cold symptoms.¹³⁶

In addition to vitamin C, fruits, vegetables, and other plant foods provide fiber, polyphenols, carotenoids, and other phytochemicals and nutrients that support balanced immune activity and may have direct antiviral effects.^{14,15} Although whole foods are likely to be more beneficial, one randomized placebo-controlled trial found participants who supplemented with encapsulated fruit and vegetable extracts for eight months had 20% fewer days with moderate-to-severe cold symptoms compared with placebo.¹³⁷ Plant-based nitrates, such as those found in beet roots, may also protect against colds by increasing availability of nitric oxide, which is important for healthy epithelial immune function. In one controlled trial, the addition of daily beet juice for seven days reduced the risk of upper respiratory infections in college students during and after final exams, and students with asthma experienced the greatest benefit.¹³⁸ The inclusion of foods high in probiotic bacteria, such as kimchi and yogurt, may also lower the incidence of common colds.¹⁴¹

The Gut Microbiome and the Common Cold

The gut microbiome—the community of microorganisms that inhabit the intestines—plays an essential role in immune regulation. Interactions between gut microbes and gut-associated immune tissue promote the development and maintenance of a well-modulated immune system. In addition, gut microbes help reduce infection and illness by preventing colonization by pathogens, strengthening the intestinal epithelial barrier, and producing anti-inflammatory compounds through fermentation of dietary fibers.¹⁴³

Dysbiosis—an imbalance in the composition of the gut microbiome—can disrupt intestinal barrier function and lead to an inflammatory state, and may reduce immune defenses against viruses, including those that cause the common cold.¹⁴³ Psychological stress, sleep disturbance and circadian rhythm disruption, chronic diseases, and a number of other stressors may have detrimental effects on microbiome health and are also associated with increased risk of common colds.^{1,145} Acute viral respiratory infections can also disturb the microbial balance of the airways and gut thereby increasing vulnerability to secondary infections.¹⁴³ A diet rich in fermentable fiber and supplemental probiotics can help restore a healthy gut microbiome, improving immune function, and possibly lowering the risk of viral upper respiratory infections.¹⁴⁶

The upper respiratory tract also has a substantial and diverse microbiome. Studies indicate microbial residents

of the upper respiratory tract influence respiratory immune function and infection susceptibility, although less is known about this microbial community than the gut microbiome.^{143,148,149}

Alcohol

Chronic heavy use of alcohol has been linked to impaired immune function and increased risk of infectious illnesses and complications. The effect of regular moderate alcohol use, on the other hand, may enhance immunity and lower infection risk.¹⁵⁰ A study that looked at the relationship between alcohol consumption and common cold incidence among 899 men in Japan found higher frequency of alcohol intake (but not amount) was associated with lower odds of having had common colds in the previous year.¹⁵¹ Another study found only wine consumption was associated with reduced risk of common cold, and the association was stronger for red wine.¹⁵²

While this evidence adds common cold to the list of conditions that may be positively impacted by light-to-moderate use of alcohol, especially red wine, there is no compelling evidence to suggest non-drinkers should start drinking alcohol solely for its health benefits.¹⁵⁵ It is important to bear in mind alcohol use, in some cases, leads to excessive use and addiction, which are harmful to health.¹⁵⁵

12 Nutrients

Probiotics

Probiotics can modulate the composition of the gut microbial community and have been shown in multiple studies to improve immune defenses while reducing inflammatory activity. A meta-analysis of 12 randomized controlled trials with a total of 3,720 participants from various age groups found taking probiotic supplements reduced the number and duration of upper respiratory tract infections, resulting in decreased antibiotic use and fewer cold-related missed school days.¹⁴⁶ Another meta-analysis that included data from 11 randomized controlled trials with a total of 2,417 children found probiotic use decreased the risk of both upper and lower respiratory infections.¹⁵⁸

Synbiotics, which contain both probiotic organisms and prebiotic fibers that enhance the growth of beneficial bacteria in the intestines, have also been shown to lower respiratory infection risk: a meta-analysis that included findings from 16 randomized controlled trials with a combined total of more than 10,000 participants found supplementing with synbiotics reduced the incidence of respiratory tract infections by 16%.¹⁵⁹ A series of three trials with a combined total of 721 healthy participants compared the effects of four synbiotic preparations made with mixed strains of *Lactobacillus plantarum* (LP 01 and LP 02), *L. rhamnosus* (LR 04 and LR 05), and *Bifidobacterium lactis* (BL 01), along with a prebiotic (either fructooligosaccharides or galactooligosaccharides), to placebo during three flu seasons. All of the preparations were found to reduce the incidence, severity, and duration of flu-like illnesses, as well as upper respiratory infections generally.¹⁶⁰

A probiotic strain isolated from goat's milk, *L. rhamnosus* CRL1505, was tested in a randomized controlled trial of 298 healthy Argentinian children. The children were given a yogurt containing at least 100 million colony forming units (CFUs) of *L. rhamnosus* CRL1505 five days a week for six months. By the end of the trial, the children in the probiotics group had experienced roughly half the number of total recorded infections compared with those in the placebo group. For specific types of infections, upper respiratory infection incidence was 31% in the probiotic groups versus 69% for placebo; pharyngitis and tonsillitis (28% vs. 72%), and acute diarrhea (26% vs 74%). Children in the probiotic group required less antibiotics and had increased levels of secretory IgA.³⁴² This probiotic is now given to several hundred thousand Argentinian school children every school day.³⁴³

In a placebo-controlled trial in 98 elderly subjects living in nursing homes, taking a supplement providing 3 billion CFUs per day of *L. coryniformis* for two weeks reduced respiratory infection symptoms and influenza-like illness during five months of monitoring.¹⁶¹ A similar trial in 196 nursing home residents found 20 billion CFUs *L. rhamnosus* daily for six months reduced the risk of viral respiratory infections.¹⁶² In 205 healthy volunteers aged 45 years and older, taking 10.8 billion CFUs *L. paracasei* in a yogurt for 12 weeks reduced the risk of upper respiratory tract infection by 45% compared with placebo.¹⁴⁰

In a randomized controlled trial, 152 healthy adults received either *B. animalis* or placebo for 28 days prior to being experimentally exposed to rhinovirus; those given the probiotic had less viral shedding in their nasal

secretions during the five days following exposure.¹⁶³ In a trial that included 136 participants with a history of frequent episodes of common cold and influenza-like illnesses, taking a daily supplement containing at least 63 million CFUs *L. paracasei*, *L. casei*, and *L. fermentium* led to greater reduction in upper respiratory tract infection frequency and enhanced antiviral immune activity compared with placebo.¹⁶⁴ In a 12-week trial that included 96 middle-aged male office workers, 22.4% of those taking 100 billion CFUs *L. casei* in a fermented milk product had an upper respiratory infection versus 53.2% of those receiving a probiotic-free milk product. In addition, the duration of infection episodes was shorter in the probiotic-treated group.¹⁶⁵ Another trial compared the effect of 12 weeks of supplementation with *L. plantarum*, at a dose of 1 billion CFUs per day, to placebo in 109 adults. Those taking the probiotic had reduced frequency of upper respiratory tract infections and duration of nasal symptoms. Furthermore, they showed signs of improved immune regulation, with lower markers of inflammation and oxidative stress.¹⁶⁶

Beta-Glucans

Beta-glucans, found in foods such as whole grains and mushrooms, as well as yeasts and algae, are a common type of prebiotic fiber, indigestible by human enzymes but fermentable via the digestive action of beneficial gut bacteria.^{167,168} Beta-glucans have been found to stimulate antimicrobial defenses through direct actions on intestinal immune tissue and modulate the inflammatory immune response through their ability to improve the health of the gut microbiome.^{167,169,170}

In a placebo-controlled trial in 357 marathon runners, those given a yeast extract supplement providing 250 mg beta-glucan daily had fewer days with upper respiratory symptoms, lower symptom severity, and fewer missed workout days after the marathon than those given placebo.¹⁷¹ The same supplement was found to reduce upper respiratory symptoms and improve mood in a 12-week placebo-controlled trial in 77 women with moderate psychological stress.¹⁷² In a randomized controlled trial in 34 healthy endurance athletes, those who received 367 mg beta-glucan from algae (beta-1,3-glucan) per day for 90 days had fewer and milder upper respiratory symptoms, fewer upper respiratory infection episodes, and fewer sick days than those receiving placebo.¹⁷³ In a 16-week placebo-controlled trial with 299 participants who experienced three or more upper respiratory infections in the previous year, 900 mg beta-glucan (extracted from yeast [beta-1,3-1,6-glucan]) daily reduced severity of upper respiratory infection symptoms.¹⁷⁴ A similar trial with 162 participants found 900 mg of the same beta-glucan supplement per day reduced the incidence of upper respiratory infections by 25% and symptom severity scores by 15%.¹⁷⁵

In 175 children with recurrent respiratory infections, those given supplements containing beta-glucan extracted from mushrooms (dosed according to body weight) had fewer flu-like illnesses and respiratory infections than those given placebo.¹⁷⁶ Similarly, in a study of 52 healthy adults, ingestion of 5 or 10 g of shiitake mushrooms per day for 4 weeks resulted in increased levels of immune cells with the ability to proliferate. Additionally, levels of secretory immunoglobulin A in the saliva were increased, which implies improved gut immunity. The authors of this study attributed the beneficial effects of the mushrooms to compounds found in shiitake mushrooms, including beta-glucans and other compounds (eg, ergothioneine, linoleic acid).¹⁷⁷

Vitamin D

Vitamin D modulates the immune response via receptors on various types of immune cells, supporting antimicrobial immune defenses while limiting inflammatory signaling and promoting tolerance.^{72,178} Vitamin D deficiency has been associated with higher incidence, increased severity, and longer duration of respiratory tract infections in children and adults.^{72,73} Vitamin D deficiency is common in those with chronic pulmonary disease, and restoration of vitamin D sufficiency may help prevent exacerbations, such as those caused by common colds, in people with asthma and COPD.¹⁷⁹ Because vitamin D levels decline and the risk of respiratory infection and complications rise with age, supplementing with vitamin D may also be especially important in the elderly.¹⁸⁰

Clinical research evaluating the effect of vitamin D supplementation has resulted in mixed findings.

Inconsistencies in dosing strategies and differences in selecting participants may be factors hampering a clear understanding of the potential benefits of vitamin D.¹⁸ One clinical trial screened 428 middle-aged and elderly participants and identified 252 with insufficient or deficient vitamin D levels (≤ 75 nmol/L or 30 ng/mL) who were then randomized to receive 400 IU vitamin D daily or placebo for 16 weeks overlapping with cold and flu season.

Those receiving vitamin D had shorter duration and decreased severity of upper respiratory tract infections, and were less likely to develop new colds during weeks 9–12.¹⁸¹ An analysis of data from 124 adults with compromised immune function and a history of frequent respiratory infections who participated in a vitamin D trial found those given 4,000 IU vitamin D daily had a 36% reduced risk of respiratory infections compared with placebo during one year of monitoring.¹⁸² In a placebo-controlled trial with 1,300 participants, supplementing with 14,000 IU vitamin D weekly for eight months lowered incidence of viral respiratory infections in children and adolescents by 19%.¹⁸³

A meta-analysis of findings from 25 randomized controlled trials found daily or weekly vitamin D supplementation reduced the risk of acute respiratory infections, and the effect was stronger in those with low baseline vitamin D levels. Daily doses between 800 and 2,000 IU appeared to be most effective. The analysis further showed treatment regimens that included large boluses (30,000 IU vitamin D or more) did not reduce infection risk.¹⁸⁴ Nevertheless, a controlled trial in nursing home residents found monthly 100,000 IU boluses of vitamin D, in addition to standard daily doses of 400–1,000 IU, resulted in greater respiratory infection prevention than standard daily dosing alone, but was associated with a higher risk of falling (a known adverse side effect of high-dose vitamin D supplementation).¹⁸⁵

Zinc

Zinc has an important role in stimulating the antiviral immune response, and zinc deficiency is marked by compromised immune function and increased vulnerability to viral and other infections.¹⁸⁶

An analysis of pooled findings from six controlled trials found treatment of colds with zinc lozenges can reduce the duration of symptoms by about 2.25 days.¹⁸⁷ A meta-analysis of three randomized controlled trials, in which a total of 199 common cold patients were given 80–92 mg elemental zinc (in the form of zinc acetate lozenges) daily or placebo, beginning within 24 hours of symptom onset, found zinc treatment reduced the duration of illness: by day five, 70% of those receiving zinc had recovered versus 27% of those receiving placebo.¹⁸⁸ In a 2024 Cochrane review of 34 randomized trials, zinc supplementation reduced the duration of symptoms by about 2.4 days when it was used as a treatment for an active cold, albeit with low certainty. Doses and forms of supplemental zinc varied widely in the eight studies included in the symptom duration analysis: most treatment studies used zinc lozenges (often gluconate or acetate) delivering roughly 45–276 mg elemental zinc per day for about 4.5–21 days.¹⁸⁹

Zinc lozenges can cause adverse side effects such as a bad taste in the mouth and nausea.¹⁸⁹ Two placebo-controlled trials have found a zinc nasal gel was also effective for shortening the duration of cold symptoms^{190,191}; however, a zinc nasal spray has not yet been demonstrated to be effective.¹⁹²⁻¹⁹⁴

The use of zinc supplements in cold prevention is less well studied than their use in cold treatment. In a placebo-controlled trial that included 40 U.S. military cadets, those given 15 mg zinc (as zinc gluconate) daily for seven months reported more weeks without any common cold symptoms.¹⁹⁵ Controlled trials in children have found supplementing with 10 mg or 15 mg zinc (as zinc sulfate) daily through the winter months can reduce frequency of common colds and possibly inappropriate use of antibiotics.¹⁹⁶

Vitamin C

As an antioxidant, vitamin C helps reduce tissue-damaging oxidative stress caused by immune cell activation, and studies have shown vitamin C levels drop during infections. Restoring vitamin C concentrations may lead to decreased symptom severity and shorten duration of illness.¹⁹⁷ Vitamin C supplementation may be especially valuable in athletes, since heavy physical exertion increases oxidative stress and may increase the rate of vitamin C depletion.^{18,197}

In a 30-day randomized controlled trial that included 1,444 military recruits, those who received 6,000 mg vitamin C per day had 20% fewer colds than those who received placebo.¹⁹⁸ In a placebo-controlled trial in 28 healthy non-smoking men with marginal vitamin C levels (<45 µmol/L), those given 1,000 mg vitamin C daily for eight weeks had a 45% lower incidence of common colds, and their duration was 59% shorter.¹⁹⁹

Echinacea

Echinacea species (*Echinacea purpurea* and *Echinacea angustifolia*) are used in herbal medicine to boost immune

function and prevent and treat various acute infections. Extracts from echinacea have been found to modulate immune cell activity and reduce inflammatory signaling in preclinical studies. Echinacea has demonstrated antiviral effects against common cold-causing viruses, including rhinoviruses and influenza viruses.²⁰⁵

In a randomized controlled trial with 755 healthy participants who reported a prior history of two or more cold episodes per year, taking 2,400 mg of an alcohol extract of echinacea daily for four months, and increasing the dose to 4,000 mg daily during acute cold symptoms, resulted in fewer cold episodes and fewer total sick days compared with placebo. The rate of recurrent infections in particular was 59% lower in those treated with echinacea.²⁰⁶

Meta-analyses of randomized controlled trials found use of echinacea extracts can reduce the risk of common colds by 17%–22%.^{207,208} One meta-analysis that included six randomized controlled trials with a total of 2,458 participants found echinacea reduced the incidence of recurrent upper respiratory infections by approximately 35%. The analysis also noted echinacea may have a stronger protective effect in individuals with increased susceptibility to colds, such as due to stress or weakened immune function, and alcohol extracts appear to be more effective than pressed juices.²⁰⁹ Investigations into the treatment effects of echinacea have yielded mixed results, with uncertain evidence that it can shorten illness duration or limit symptom severity in individuals with colds.^{207,208}

Pelargonium

Pelargonium (*Pelargonium sidoides*) is a medicinal plant native to South Africa and used for centuries to treat respiratory and gastrointestinal infections.^{210,211} The roots contain numerous compounds with biological activity, and root extracts have demonstrated antiviral, antibacterial, and immune-modulating properties.^{210,212-214} A standardized alcohol extract of pelargonium, EPs 7630, has been approved for use in treating acute respiratory tract infections in some countries in Europe, Asia, and Central and South America, as well as in Australia.^{210,211}

In a randomized controlled trial, 105 adults with common cold symptoms were treated with 120 mg EPs 7630 per day or placebo for 10 days. Those receiving EPs 7630 experienced faster reduction in symptom severity: by day 10, 74% of those treated with EPs 7630 and 25% of those receiving placebo had no or only one symptom remaining.²¹⁵ A similar trial found liquid EPs 7630, at a dose of 60 drops three times daily, was also effective for reducing symptom severity and duration in adult common cold patients.²¹⁶ A meta-analysis of results from five randomized controlled trials that included a total of 833 adults with common colds found treatment with EPs 7630 shortened duration and reduced severity of illness.²¹⁷ Another meta-analysis included six randomized controlled trials with 523 participants aged 6–10 years and found treatment with pelargonium extract reduced symptoms and accelerated recovery in children with acute sore throat, tonsillitis, and bronchitis.²¹⁸ Even in children under six years old, seven clinical trials, including two randomized controlled trials, showed EPs 7630 could be a safe and effective option for treating acute upper respiratory tract infections and bronchitis.²¹⁹

Andrographis

Andrographis (*Andrographis paniculata*) is used in Ayurvedic and traditional Chinese herbal medicine for treating common colds and flu, sore throat, and fever.²²⁰⁻²²² Extracts of andrographis have exhibited immune-stimulating, anti-inflammatory, antiviral, and antibacterial actions in preclinical studies.^{220,222} In healthy volunteers, andrographis was found to increase the number of immune cells in circulation.²²³

A randomized controlled trial included 223 patients with upper respiratory infections who received either 200 mg andrographis daily or placebo during the first five days of illness. The andrographis group had greater improvement in overall symptoms, especially during days three through five.²²⁴ In another placebo-controlled trial in 185 patients with upper respiratory infections, five days of treatment with a combination of andrographis and Siberian ginseng (*Eleutherococcus senticosus*) resulted in reduced overall symptom scores, with headache, nasal symptoms, throat symptoms, and malaise being most impacted.²²⁵ A meta-analysis of findings from 33 randomized controlled trials found andrographis, alone and in herbal combinations, reduced acute respiratory tract infection symptoms, particularly cough and sore throat, as well as duration of illness.²²¹ Another meta-analysis examined findings from six trials and found andrographis was beneficial for treating cough associated with common colds and other upper respiratory tract infections.²²⁶

Ginseng

Several ginseng species, including Korean or red ginseng (*Panax ginseng*), American ginseng (*Panax quinquefolius*), and Chinese ginseng (*Panax notoginseng*), have been studied for their ability to modulate immune function and prevent and treat infections. Although not identical, these ginseng species have similar active constituents and overlap in therapeutic potential.²²⁷ Ginseng extracts have shown antiviral actions against influenza viruses and other cold-causing viruses in preclinical studies. In addition, ginseng has been shown to activate the antiviral immune response while reducing the inflammatory response, possibly by lowering oxidative stress.^{227,228}

A popular commercial product that contains a standardized extract of *Panax quinquefolius* may help prevent and treat colds and flu. A randomized placebo-controlled trial in 323 healthy adults with a history of at least two colds in the previous winter found four months of treatment with 400 mg of the standardized ginseng extract per day reduced the incidence of colds and recurrences, as well as severity and duration of cold symptoms.²²⁹ In another randomized controlled trial, 43 individuals aged 65 years and older took either 400 mg of the standardized ginseng extract per day or placebo for four months. In the second half of the trial, 32% of the ginseng group experienced an acute respiratory illness compared with 62% of the placebo group. In addition, the average duration of symptoms in the ginseng group was 5.6 days versus 12.6 days in the placebo group.²³⁰ A report on two similar trials found this ginseng extract lowered the risk of acute respiratory infections by 89% compared with placebo in elderly residents of long-term care facilities.²³¹ The same standardized extract of ginseng has also been found to be effective for treating upper respiratory infections in children.²³² However, a trial in 293 patients with weakened immune function due to chronic lymphocytic leukemia did not find treatment with this ginseng extract to be effective: although the ginseng-treated group tended to have fewer moderate-to-severe acute respiratory infections, the difference did not reach statistical significance and the total number of respiratory infections was similar in the two groups. The ginseng-treated group had significantly less sore throat compared with placebo.²³³

A 12-week, randomized, placebo-controlled trial evaluated the effect of 100 mg per day of a standardized extract of red ginseng on the incidence of common cold and flu in 227 healthy individuals. All participants were vaccinated against flu in week four of the study. Ginseng-treated participants had a stronger response to the flu vaccine and a 64% lower number of cold and flu cases than participants given placebo.²³⁴ A report on a series of observational studies indicated patients treated with red ginseng were less likely to develop common colds than those not taking ginseng. Red ginseng's possible cold-preventing impact was thought to be related to its ability to improve immunity by increasing stress resilience.²³⁵

Saccharomyces cerevisiae

Saccharomyces cerevisiae (*S. cerevisiae*) is a probiotic yeast that is consumed in fermented foods such as beer and sourdough bread. It has been hypothesized that *S. cerevisiae* and other probiotic yeasts may enhance the immune system by improving the physical barrier of the gastrointestinal system and helping regulate cytokine secretion.²³⁶ A yeast fermentation product derived from *S. cerevisiae* (EpiCor) has been shown to protect against cold and flu-like symptoms in two clinical trials. In a randomized controlled trial of 116 participants who had not received a recent seasonal influenza vaccine, 500 mg EpiCor daily significantly reduced the incidence of common cold or flu-like symptoms compared with placebo. When symptoms were measured individually, EpiCor significantly reduced 10 out of 11 symptoms, with no effect on weakness. Although the duration of symptoms was numerically reduced from 4.25 to 3.59 symptom days with EpiCor, there was no significant difference in duration in this study.²³⁷ When EpiCor was evaluated in 116 recently vaccinated individuals, similar results were reported. EpiCor significantly reduced the incidence of cold or flu-like symptoms as well as the duration of symptoms (from 5.01 to 4.16 days) compared with placebo.²³⁸

Garlic

Garlic (*Allium sativum*) has a long history of use in preventing and treating infections, and has been shown to exert antimicrobial and immune-enhancing effects in numerous studies.²³⁹ In addition to improving the antiviral immune response, sulfur compounds from garlic have demonstrated direct antiviral action.²⁴⁰ In a controlled trial in 120 healthy volunteers, 2.56 grams of aged garlic extract per day for 90 days during cold and flu season resulted in improved immune responsiveness compared with placebo. In addition, aged garlic extract reduced the severity of cold and flu symptoms and number of work days missed due to illness.²⁴¹ A placebo-controlled trial in 146 adults

reported taking 180 mg garlic powder daily for 12 weeks during winter reduced the incidence of common colds by 37% and their duration by 30%.^{239,242} In a controlled trial, 172 children given 600 mg per day of an extended-release preparation of garlic for five months had two- to four-fold reductions in acute respiratory illnesses compared with 468 untreated controls. In a follow-up placebo-controlled trial that included 156 children, taking 300 mg per day of extended-release garlic for five months resulted in a 1.7-fold decrease in acute respiratory illnesses compared with placebo and was more effective than benzimidazole (a compound with possible antiviral effects).^{243,244}

Green Tea

Green tea (*Camellia sinensis*) is a rich source of polyphenols known as catechins. Green tea catechins have demonstrated antiviral actions against cold- and flu-causing viruses in preclinical research.²⁴⁵ In a randomized controlled trial in 108 healthy adults, green tea capsules, taken twice daily for three months, reduced the risk of cold and flu illness lasting two days or longer by 22.9% and the number of days with cold or flu symptoms by 35.6% compared with placebo. In addition, immune cells from those receiving green tea exhibited increased antiviral activity.²⁴⁶ In a controlled trial that included 270 healthcare workers, those receiving 171 mg green tea catechins daily for 12 weeks in the winter had a lower rate of upper respiratory infections (13.1%) than those receiving placebo (26.7%).²⁴⁷ Another trial that included 197 healthcare workers found taking 378 mg tea catechins daily, along with 210 mg theanine (another compound from green tea) daily, for five months resulted in fewer influenza virus infections: 4.1% of catechin-treated participants versus 13.1% of participants receiving placebo.²⁴⁸ A study that included 2,050 elementary school students in Japan found, compared with those who drank less than one cup of green tea per day, children who regularly consumed an average of one to less than three cups per day had a 38% lower risk of influenza virus infection and those who consumed 3–5 cups per day had a 46% lower risk.²⁴⁹ In addition, several clinical trials have noted gargling with green tea has a greater protective effect against influenza virus-related illness than gargling with water alone.⁷¹

Elderberry

Black elder (*Sambucus nigra*) has a long history of traditional use in the treatment of colds and flu.²⁵⁰ It has demonstrated antimicrobial properties and shown specific activity against influenza viruses in the laboratory.^{251,252}

One controlled trial enrolled 312 airline passengers travelling overseas on flights lasting seven hours or longer and staying at their destination for four or more days. The participants were given elderberry extract, at a dose of 600 mg per day for 10 days prior to travel and 900 mg per day during time overseas, or placebo. Those receiving elderberry experienced approximately half as many sick days, and symptom severity scores were less than half as high as in those receiving placebo.²⁵³ Several other placebo-controlled trials reported treatment with elderberry extract, alone or combined with echinacea extract, reduced symptoms, duration, and other medication use in patients with influenza,^{254,255} but one found no effect.²⁵⁶

Enzymatically Modified Rice Bran

Enzymatically modified rice bran is made by fermenting rice bran with enzymes extracted from the shiitake mushroom (*Lentinus edodes*). Through the fermentation process, immunologically active polysaccharides, including one called arabinoxylan, become more bioavailable.²⁵⁷ In a double-blind, placebo-controlled, crossover trial, 36 subjects between 70 and 95 years of age received both 500 mg arabinoxylan and placebo, each for six weeks. Common cold symptom scores were three times higher and duration of symptoms more than twice as long in participants during the placebo phase compared with the arabinoxylan phase. In addition, those with low baseline NK cell activity had a greater increase in NK cell activity during the arabinoxylan phase.²⁵⁸ NK cells clear virus-infected cells and stimulate other aspects of the antiviral immune response.

Arabinoxylan has prebiotic effects and can improve gut microbiome composition by increasing both abundance and diversity of intestinal bacteria. This may, in part, explain how arabinoxylan exerts its positive effects on immune function.²⁵⁹ In addition, arabinoxylan may directly stimulate the activity of a variety of immune cells.²⁶¹ Taking 3 grams of enzymatically modified rice bran daily for eight weeks was found to raise immune cell production of interferon- γ , a cytokine involved in antiviral defense, in healthy volunteers.²⁵⁷ A study in geriatric subjects found taking 500 mg enzymatically modified rice bran daily for 30 days increased NK cell activity.²⁶²

Selenium

Selenium is necessary for human health mainly due to its incorporation into selenoproteins, such as the antioxidant enzymes glutathione peroxidase and thioredoxin reductase.²⁶⁴ Selenoproteins are needed for a successful antiviral immune response, and selenium deficiency has been linked to worse outcomes in acute and chronic viral infections in preclinical research and observational studies.^{265,266}

In a placebo-controlled trial in 192 subjects with a history of recurrent upper respiratory infections, 16 weeks of treatment with a nutritional supplement that contained selenium, as well as vitamins C and D and folic acid, resulted in reduced cold symptom severity and work days missed.²⁶⁷ In a randomized controlled trial in 108 COPD patients, taking a supplement containing selenium, vitamin C, echinacea, and zinc along with usual treatment for seven days during an acute upper respiratory infection led to less severe and shorter COPD exacerbations.²⁶⁸

Vitamin E

Vitamin E has an important role in immune function, partly due to its ability to protect immune cells from oxidative damage. Deficiency of this lipid-soluble antioxidant impairs immune health, and vitamin E supplementation may improve defense against upper respiratory infections, particularly in the elderly.^{269,270} Low vitamin E levels have been correlated with acute and recurrent respiratory tract infections in children.²⁷¹⁻²⁷³ Some studies suggest higher dietary vitamin E intake and supplement use may reduce the risk of upper respiratory infection in adults,^{135,274} but may have no benefit or even cause harm in heavy smokers.²⁷⁵

A clinical trial in 33 elderly individuals found taking a supplement providing 200 mg (180 IU) of dl-alpha-tocopherol (a form of vitamin E) per day for three months improved immune cell function.²⁷⁶ However, in 652 healthy community-based older individuals, 200 IU daily of vitamin E did not decrease the risk of acute respiratory infections and appeared to increase symptom severity.²⁷⁸ Further study is necessary to understand vitamin E's role in upper respiratory infections.

Lactoferrin

Lactoferrin is an iron-binding protein made by cells such as those in secretory glands and activated neutrophils (a type of immune cell). It is found in most body fluids, including tears and breast milk, and lactoferrin derived from bovine whey is frequently used in supplements. Lactoferrin possesses immune-modulating effects, capable of enhancing anti-microbial immune activity while reducing inflammation, and has exhibited a broad spectrum of activity against bacteria, fungi, protozoa, and viruses. Laboratory studies have shown lactoferrin inhibits certain viruses, including some cold-causing viruses and influenza viruses, from binding to cell receptor sites, preventing their entry into host cells, and suppresses viral replication inside infected cells. In addition, lactoferrin sequesters pro-oxidant iron and decreases pro-inflammatory molecules released during the immune response to infection. Because of its immune-modulating and antiviral properties, lactoferrin has even attracted interest as a potential therapy for preventing or treating some severe viral respiratory infections.²⁷⁹

In a randomized controlled trial, 90 subjects with a history of frequent common colds were given either 600 mg per day lactoferrin in a bovine whey extract or placebo for 90 days. There were 48 colds in the lactoferrin group and 112 in the placebo group during the study period, and the total number of cold symptoms was lower in the lactoferrin group.²⁸² Another 90-day controlled trial found lactoferrin supplementation reduced the number of common cold symptoms reported by participants.²⁸³

Cystine and Theanine

L-cystine and L-theanine are non-essential amino acids that appear to modulate immune cell activity by enhancing production of the preeminent antioxidant, glutathione. Glutathione levels are known to decrease as a result of stressors such as intense exercise.²⁸⁴ In a randomized controlled trial, 173 healthy men received either 700 mg L-cystine and 280 mg L-theanine or placebo daily for 35 days. The incidence of common colds was 27.1% in the placebo group, with 23 colds occurring during the trial, while the incidence was 11.4% in the L-cysteine and L-theanine group, with only 10 colds occurring during the trial.²⁸⁵

L-cystine and L-theanine may have especially beneficial effects in preserving strong immune function in athletes. A trial in 16 long-distance runners showed supplementing with L-cysteine and L-theanine (700 mg and 280 mg per day, respectively) for seven days prior to and nine days during a training program suppressed alterations in immune function induced by intense exercise, possibly by reducing exercise-induced oxidative stress and

inflammation.²⁸⁶ Other trials in athletes add to the evidence that L-cysteine and L-theanine supplementation during training reduces inflammation and prevents potentially detrimental changes in immune function.^{284,288}

Quercetin

Quercetin is a flavonoid with anti-inflammatory, antioxidant, and antiviral properties. It is naturally found in foods such as apples, grapes, broccoli, kale, red onions, green tea, and wine. Research suggests quercetin may decrease infection risk, prevent histamine release, and support balanced immune cell activity.^{290,291} Quercetin has been shown to inhibit replication and infectivity of cold-causing viruses and reduce inflammation induced by viral infection.³⁴¹

A randomized, double-blind, placebo-controlled trial of over 1,000 people compared 12 weeks of placebo and quercetin (at 500 and 1,000 mg/day, with 500–1,000 mg vitamin C and 20–40 mg niacin) in reducing rates of upper respiratory tract infections. While there was no significant difference in infection rate for all subjects (aged 18 to 85 years), a separate analysis of physically fit individuals aged 40 years and older found 1,000 mg quercetin daily reduced upper respiratory infection severity and number of sick days reported.²⁹³ A randomized, double-blind, placebo-controlled study in which 40 trained male cyclists were given either quercetin (1,000 mg/day) or placebo one week before, during, and two weeks after a three-day period of intense exercise (three hours of cycling per day) found quercetin significantly reduced upper respiratory infection incidence in the two weeks after intense exercise.²⁹⁴

Fish Oil

Fish oil is rich in omega-3 polyunsaturated fatty acids and is a source of vitamins A and D. Two omega-3 fatty acids from fish, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), have well known anti-inflammatory effects, and evidence suggests metabolites of DHA may have direct antiviral activity.²⁹⁵ In a laboratory model of rhinovirus infection, omega-3 fatty acids reduced the inflammatory response while arachidonic acid (an omega-6 fatty acid) and saturated fatty acids from animal fat increased inflammatory signaling.²⁹⁷ Some studies show higher intake of EPA and DHA during infancy and early childhood is associated with better respiratory health.²⁹⁸ In children, taking cod liver oil plus a multivitamin/mineral supplement was reported to result in reduced doctor visits for upper respiratory infections by 36–58%.²⁹⁹

Vitamin A

Vitamin A has a fundamental role in developing and regulating mucosal immunity, interacting with immune cells and the microbiome to maintain a balanced immune response and promote tolerance.³⁰⁰ Vitamin A deficiency has been linked to increased risk of acute and recurrent respiratory infections, particularly in children.^{271,273} Large trials in populations of children at risk for vitamin A deficiency have shown supplementation can lower childhood illnesses and mortality.³⁰¹ However, it is unclear whether vitamin A supplements are beneficial in treatment of respiratory infections, even in children at risk of deficiency.³⁰²

Cistanche

Cistanche (*Cistanche deserticola*) is a medicinal plant that has been used historically as a remedy for chronic infections and other illnesses. *Cistanche* contains an array of bioactive compounds, some of which have been shown to have antiviral and immunomodulatory properties.^{303,304} In an animal model of aging and immune senescence, cistanche extract was found to reverse indicators of immune dysfunction and extend lifespan.⁴⁴

In a 12-week trial in 25 elderly individuals, taking 100 mg cistanche extract daily in a product that also contained vitamin E, vitamin B6, coenzyme Q10, zinc, and fucoidan, led to improvements in relative numbers and activity of immune cells. There were also improvements in tests of vascular function, and study volunteers reported decreased fatigue.³⁰⁵

Melatonin

Although best known for its role in circadian system regulation, melatonin is also produced by immune cells and participates in activation of antimicrobial defenses, reducing inflammatory signaling, and lowering oxidative stress.³⁰⁷ Melatonin production diminishes with age, contributing to higher oxidative stress, inflammation, and infection susceptibility.³⁰⁹

In light of its safety and anti-inflammatory effects, there is growing interest in the possible preventive and

therapeutic use of melatonin in viral respiratory illnesses such as influenza. The elderly and those with chronic medical conditions, who are at higher risk for severe illness and complications, may benefit most from regular use of 3–10 mg melatonin at bedtime.³³⁷

Astragalus

Astragalus (*Astragalus membranaceus*), known as Huang Qi in traditional Chinese herbal medicine, has been used for centuries as a tonic to prolong life and treat a wide variety of conditions, including infections and fatigue.^{311,312} Its medicinal effects are attributed to immune-stimulating polysaccharides, flavonoids, and saponins found in its roots.^{311,313,314} Preclinical research indicates astragalus extracts can enhance mucosal immunity and activate immune cells, and a pilot trial in humans found an astragalus extract reversed markers of immune senescence.^{311,312,315}

Reishi

Reishi mushroom (*Ganoderma lucidum*) has been used for centuries in traditional Chinese medicine for its health-promoting and anti-aging effects. It contains compounds that improve immune function, increase antioxidant capacity, reduce inflammation, and build defenses against infections and cancer.^{46,316} Its polysaccharides in particular have been found to enhance non-specific immune surveillance, as well as specific pathogen-recognizing immune activity. Reishi may further regulate immune function through its effects on immune tissues and cytokine production.³¹⁷ Extracts from reishi have also demonstrated direct antiviral activity.^{316,318} Because of its broad anti-aging and immune-modulating properties, reishi may reduce the risk of viral respiratory infections, especially in the elderly and those with compromised immune function.

Ellagic Acid

Ellagic acid is a polyphenolic compound found in the peels and seeds of pomegranates as well as in grapes, strawberries, and raspberries. Ellagic acid and other polyphenols have been shown to promote immunity by neutralizing free radicals and protecting cells from oxidative stress. These effects are believed to contribute to anti-inflammatory, anticancer, and antiaging effects.³¹⁹ Extracts of ellagic acid made from crepe myrtles have been shown to have antiviral properties, preventing human rhinovirus infection in laboratory experiments.³²⁰ Ellagic acid has also shown activity against influenza virus, hepatitis C virus, and Zika virus in laboratory models.³²¹⁻³²³ Assessments in humans are needed to determine the effectiveness of ellagic acid for preventing or treating cold and flu-like symptoms.

DHEA

Dehydroepiandrosterone (DHEA) is a steroid hormone synthesized by the adrenal gland that has a complex role in immune regulation and controlling the inflammatory process.³²⁴ DHEA levels decline with age, and this may be a contributing factor in immune senescence.^{325,326}

DHEA supplementation has been found to activate immune cells involved in antiviral defense in preclinical research and clinical trials in elderly subjects.^{325,327} DHEA has also been found to reduce inflammation and protect against lethal viral, bacterial, and parasitic infections in laboratory animals.³²⁸⁻³³¹ Despite its importance in antimicrobial immune activity, levels of DHEA-sulfate (the main circulating form of DHEA) can be diminished during acute severe infections, and some research suggests DHEA levels may be suppressed for two weeks or longer after a critical illness or injury.³³² This is because during physiologic stress, such as infection or trauma, adrenal cortisol production rises at the expense of DHEA production. The resulting high cortisol to DHEA-sulfate ratio has been linked to poor outcomes, especially in individuals whose immune function is already altered by aging.³³³ Clinical trials have shown 50–100 mg DHEA daily for up to one year can have various anti-aging effects.³²⁷

Annona muricata

Annona muricata (*A. muricata*), also known as soursop or graviola, is a tropical tree that produces edible fruit. Its leaves, stems, roots, and fruits have been used in traditional medicine across the globe. The plant contains high levels of flavonoids, alkaloids, and phenolic and lipophilic compounds that are believed to exert antiviral, antioxidant, and anti-inflammatory properties.³³⁴ In laboratory experiments, *A. muricata* extracts have been shown to inhibit the replication of Dengue virus and bacteriophages, which are a viral model for enteroviruses.^{334,335} Rutin

is one of the main flavonoids found in *A. muricata*, and a derivative of rutin (troxerutin) combined with zinc gluconate was shown to reduce the incidence of runny nose in a study of 94 participants with common cold symptoms.³³⁶

Bee Propolis Extract

Propolis is a bee-derived waxy, resinous substance used to seal and protect beehives. Bees produce propolis by processing various plant compounds. Therefore, propolis is a naturally variable product, the composition of which changes depending on factors such as the specific hive, geographical environment, and species of plants used.^{344,345} Propolis has been used in traditional medicine for thousands of years due to its antimicrobial properties.³⁴⁶ In more recent years, propolis has been studied for its antiviral effects, particularly against respiratory viruses.^{347,348} Preclinical studies suggest propolis may exert antiviral effects by hindering viral entry into cells, preventing viral replication, and modulating inflammation.³⁴⁸ Furthermore, propolis appears to have immunomodulating properties, such as increasing antibody production and cytotoxicity of NK cells.³⁴⁸⁻³⁵⁰

Although clinical studies of propolis in preventing or treating common colds are sparse, evidence generally suggests a small but significant effect. In one study, 94 school-age children were randomized to be untreated or given a flavonoid-rich propolis preparation (0.5 mL intranasally for one week each month) during cold season. The treated children experienced fewer symptomatic colds and other upper respiratory infections over the course of the study compared with those who were untreated.³⁵¹ In another study of 50 adults and children presenting with cold symptoms at an ENT clinic, patients were orally administered either 6% propolis in honey (1 gram given three times over the course of the first day of symptoms) or honey alone. The patients given propolis experienced shorter duration of cold symptoms (average 1.96 days to resolution) compared with honey alone (average 4.8 days to resolution).³⁵²

The heterogenous nature of propolis, however, makes it difficult to generalize results across various preparations; some researchers have therefore formulated a standardized propolis extract with reproducible polyphenolic content. In one randomized controlled trial, 122 adults with mild upper respiratory tract infections were treated with an oral propolis spray (Promunel, 2–4 sprays three times daily for a total of 12–24 mg of polyphenols) or a placebo spray for five days. By day three, 83% of subjects taking propolis experienced remission of symptoms compared with 28% in the placebo group.³⁵³ In an unpublished randomized controlled trial, 200 mg Promunel or placebo was given in capsule form twice daily (48 mg total polyphenol content) to 295 healthy adults for 12 weeks.³⁵⁴ Over the course of the study, which took place throughout the winter months, participants taking propolis had:

- 29% fewer upper respiratory tract infections,
- 31% reduced risk of experiencing any upper respiratory symptoms, and
- 34% fewer days of upper respiratory symptoms.

Update History

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