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Issue 4

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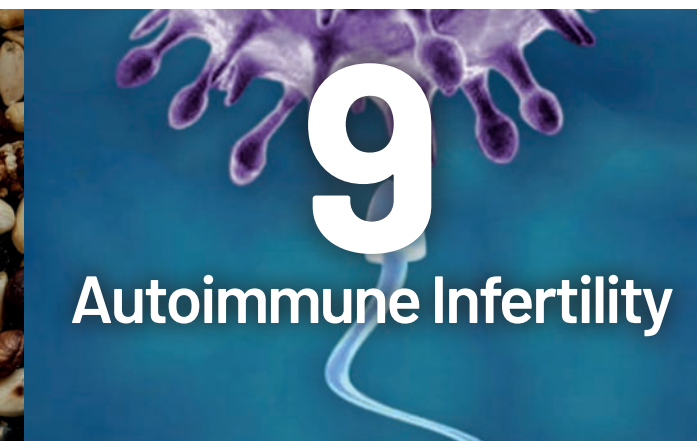


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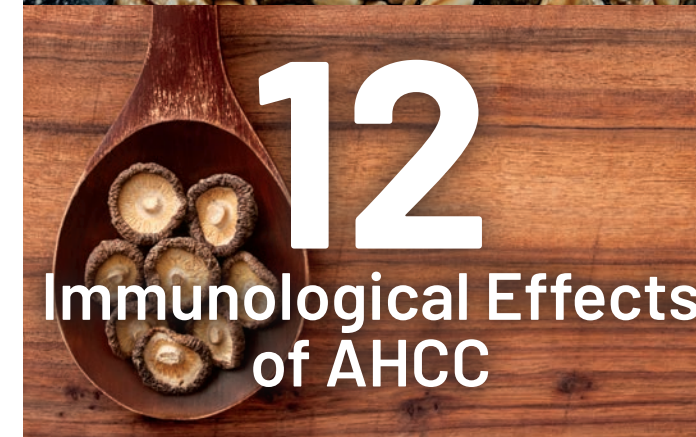
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Zinc and Copper for Immune Health



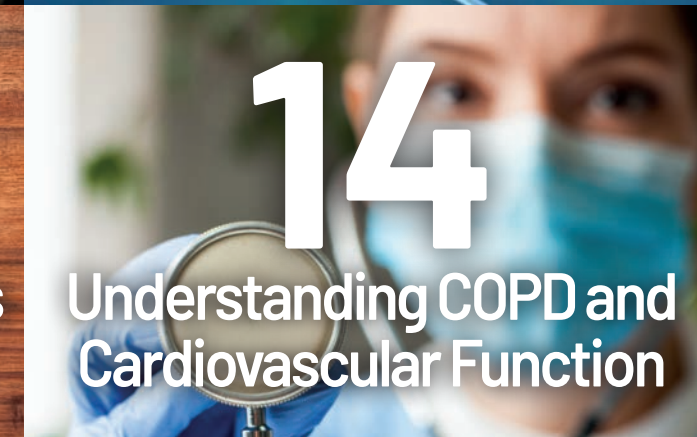
9

Autoimmune Infertility



12

Immunological Effects of AHCC



14

Understanding COPD and Cardiovascular Function



16

Plant Extracts with Activity Against Herpes Simplex Viruses

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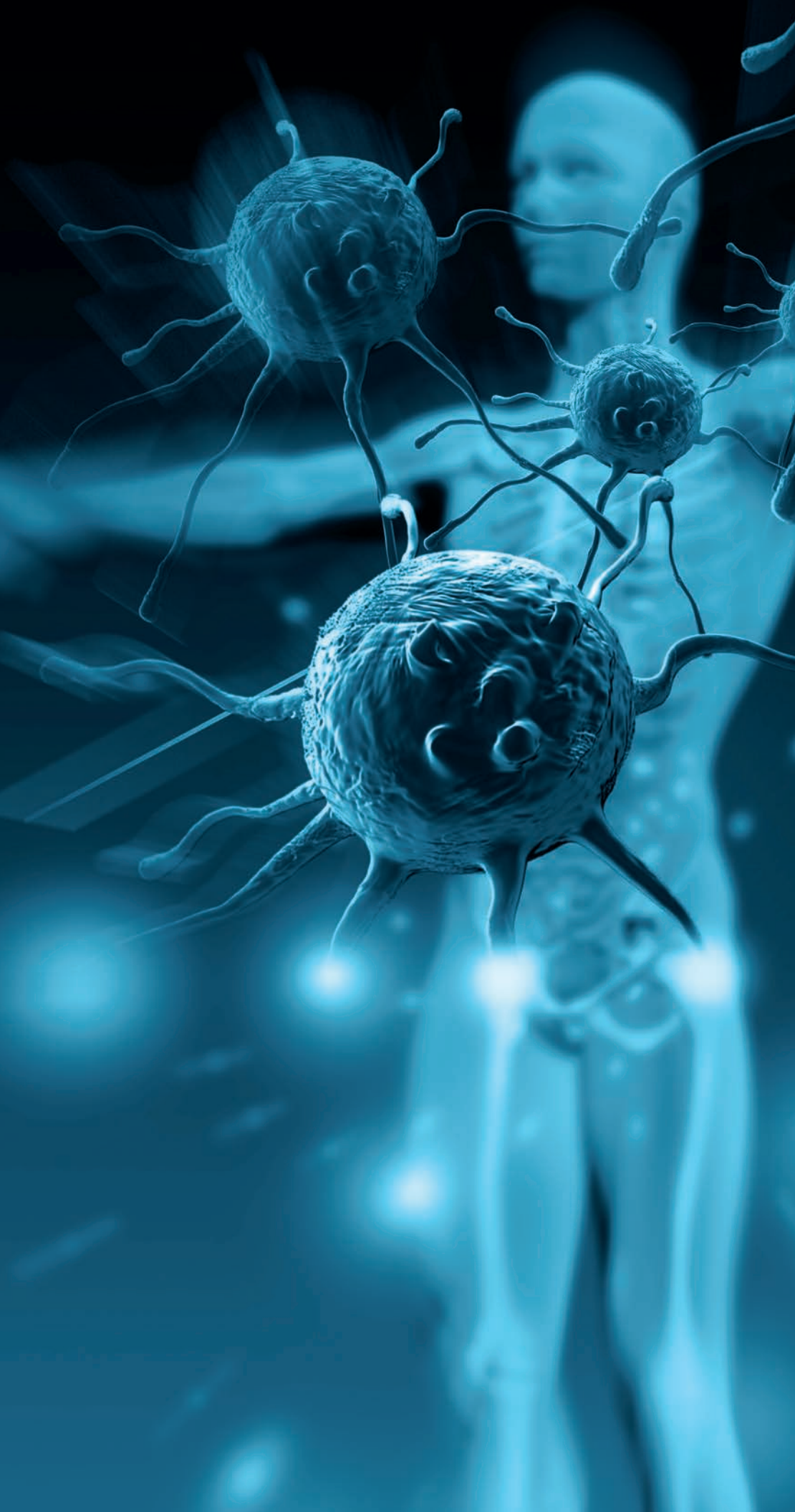
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Zinc And Copper For Immune Health

By Christine Ramos

The need to protect ourselves against pathogens has become more prevalent given the sweeping coverage of the COVID-19 pandemic. Immune health is top of mind for most people, as is the desire to strengthen one's immune system. Keeping the immune system strong starts with leading a healthy lifestyle - eating well, exercising, getting adequate sleep, minimizing stress and alcohol, quitting smoking and maintaining a healthy weight.

Despite our best efforts, stressful situations still arise and our diets can lack diversity, both of which can diminish our nutrient stores which are vital for proper immune function. Various micronutrient deficiencies have been implicated in compromised immune health. It has been established that our complex immune system needs multiple specific micronutrients including vitamins A, D, C, E, B6, folate, zinc, copper and selenium.¹ All of these play a vital and often synergistic role in every stage of the immune response.

Here we look at zinc and copper specifically, how they support immune system health, have a love/hate relationship with each other and why balance between the two is essential for optimal immune function.

Zinc for Immune Health

Zinc is an essential nutrient that must be obtained via food or supplementation. It is required for a myriad of roles in the body, affecting the development and integrity of the innate and adaptive immune system.

Lacking zinc levels in children have been associated with impaired growth, motor development and neuropsychological functioning.² Zinc deficiency can play an important role in the aging process and in the etiology of age-related chronic illnesses such as atherosclerosis, degenerative diseases of the nervous system, immune dysfunction and cancer.³

Zinc affects multiple aspects of the immune system from the skin barrier to gene regulation within lymphocytes.⁴ As a nutritionally fundamental trace element, it is essential for the structure and function of numerous macromolecules, including enzymes regulating cellular processes and cellular signaling pathways. It modulates immune response and exhibits antioxidant and anti-inflammatory activity.⁵ It is crucial for normal development and function of cells mediating innate immunity, neutrophils (white blood cells that kill and digest bacteria that help fight infections and heal wounds), and NK cells (Natural Killer cells help to limit the spread of microbial infections and subsequent tissue damage).

One 2020 meta-analysis combed through 660 studies looking at micronutrient supplementation and its effects on the common cold, extracting data from 20 human clinical trials to conclude that zinc supplementation may reduce common cold duration by 2.25 days.⁶ Particularly for older adults, another study showed that zinc supplementation significantly reduced the risk of infections and positively promotes immune response.⁷

Copper for Immune Health

Copper's crucial role in our health has often been overlooked. Copper is also an essential trace mineral that is necessary for survival. It is found in all body tissues particularly the liver, brain, heart, kidneys and skeletal muscle. It plays a key role in making red blood cells, maintaining nerves cells and the immune system. It also helps the body form collagen and elastin (key building blocks for bones and connective tissues). It also aids iron absorption, contributing to energy production. Considering how vital it is, it's a wonder that it is not discussed as often.

This lack of talk about it may be attributed to the fact that copper deficiency is rare in comparison to zinc deficiency. However, over supplementation with zinc can result in copper deficiency as the two have an antagonistic relationship.

Friends or Foes?

Zinc and copper are antagonists because they work against one another to compete for binding sites.⁸ Excess zinc can lead to a copper deficiency and vice versa. When an imbalance occurs, this can lead to health problems.

Both copper and zinc are needed for an antioxidant called superoxide dismutase (SOD) that helps to fight free radicals and reduce oxidative stress.⁹ Research shows that during times of chronic inflammation and poor health, there is often an imbalanced copper to zinc ratio (high copper: low zinc). A 2017 study found that decreased levels of zinc, reduced activity of the SOD enzyme and a higher copper to zinc ratio were all associated with higher inflammation in IBD patients.¹⁰ This reduction in SOD activity relates to a lower ability to scavenge free radicals, which can lead to excessive oxidative stress.

High copper and low zinc ratios have also been associated with anxiety,¹¹ Alzheimer's disease,¹² heart failure,¹³ and sleep disturbances.¹⁴

Finding Zinc and Copper Balance

A balanced copper to zinc ratio helps support immune function, fight infection and keep inflammatory processes balanced too. Zinc and copper work together to perform their many beneficial tasks, which is why we want to ensure we're consuming sufficient amounts of both within our diet but also, retaining an ideal ratio.

Research suggests that these dynamic minerals are most compatible when hovering in the range of an 8:1 to 12:1 zinc-copper ratio. For example, someone consuming roughly 15 mg of zinc per day would require about 1.5 mg of copper. In nature, this correlation is almost flawlessly observed in animal protein sources where levels of zinc and copper occur in balanced quantities. Other foods with the best zinc to copper ratios include oysters, sesame seeds, cashew nuts, and sunflower seeds. Foods in the nuts, seeds, and legume families often are rich sources of both zinc and copper, and they also have many other benefits. For those obtaining these micronutrients in supplement form, do ensure that they contain the correct balance.

As with all things in life, balance is key.



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Autoimmune Infertility

By Dr. Sarah Zadek ND

Autoimmunity has become a subset of unexplained infertility and subfertility, affecting the ability to get pregnant as well as the ability to maintain a pregnancy. Disorders that have a negative impact on fertility such as endometriosis, PCOS and premature ovarian failure have all been linked to autoimmunity.¹ Many autoimmune (AI) conditions can go unnoticed and undiagnosed for years. Symptoms can be vague or completely absent until we're well into our reproductive years. For these reasons, those who have had multiple pregnancy losses often are screened for AI antibodies.

Autoimmunity refers to the ability of the immune system to target and/or attack the body's own tissues. Normally, the immune system uses antibodies to tag foreign cells or particles so that other immune cells can destroy or remove them. But the body can also produce antibodies that tag its own, healthy normal cells and their components. Fertility and pregnancy can be affected in multiple areas: AI activities could deplete the number of follicles (premature eggs) in the ovaries; it could reduce the uterine lining's ability to allow implantation; and could affect blood flow of the placenta during pregnancy. There are other autoantibodies that can attack the hormones that help eggs to develop, and antibodies that attack sperm.

That said, a person can have autoantibodies and still be able to get pregnant and have a healthy live birth. The presence of antibodies just increases the risk of there being an issue. It also identifies that there is dysfunction within the immune system and to look for this in other areas. It's very common, when a person has one AI disorder, to actually have many. It's for this reason that doctors screen for other AI diseases if one has already been diagnosed.

Celiac disease is an AI disease that is often caught earlier since it is so disruptively symptomatic with chronic diarrhea and abdominal pain. In Celiac disease the immune system attacks the gut lining, causing inflammation and destroying the protective intestinal barrier, leading to increased permeability. This allows bacteria and other pathogens, as well as food antigens to get into the bloodstream where the immune system learns to attack these things that it wouldn't normally see. Celiac disease is associated with infertility because of nutrient deficiencies due to a damaged intestinal lining, but also because it predisposes an individual to other abnormal immune responses.

Ovarian Autoimmunity

Premature ovarian insufficiency (POI) is defined by ovaries that contain a significantly diminished number of follicles earlier in reproductive age (unlike the decreased follicle/egg reserve that occurs with age >40 years, or with menopause). Anti-ovarian antibodies are found in about 30-67% of cases of POI.¹ Destruction of ovarian cells causes a decrease in estrogen production, prevents follicle growth, and leads to a drastic decrease in follicles.

It's possible to have antibodies that act against ovarian cells, the corpus luteum (the pouch that envelops the egg during development and produces progesterone), and placental cells. The incidence of this form of autoimmunity occurs in less than 10% of POI cases, but there are other AI conditions that are also associated with POI including AI thyroid conditions, diabetes, systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), Sjogren's syndrome, pernicious anemia, vitiligo and chronic yeast infections (candidiasis).²

These AI conditions themselves have not been shown to cause POI, but instead serve as a marker of immune dysfunction or other AI antibodies that can affect hormone regulation and overall reproductive function.

Antiphospholipid Autoimmunity

Phospholipids are found in the membranes of our cells. The presence of antiphospholipid (APL) antibodies, including anticardiolipin antibodies, has been shown to cause thrombosis, or clotting, which can increase the likelihood of a pregnancy loss. This type of clotting dysfunction is different than other clotting disorders. Commonly associated with SLE, APL syndrome increases the receptivity of endothelial adhesion molecules and promotes the aggregation of platelets.³ Since the diagnosis of APL syndrome occurs on average around 35 years, it's often missed until women try to conceive and find they need medical fertility assistance.

APL antibodies can interfere with the implantation of an embryo into the uterine lining (the endometrium). These antibodies affect the process of endometrial decidualization when the endometrial cells transform into specialized cells necessary for implantation and placental development. Failure of these local cells to properly remodel arteries will prevent adequate maternal blood flow, and therefore fresh oxygen, from reaching the placenta and the embryo or fetus. It can also cause damage to the placenta itself.

APL antibodies can also stimulate embryonic cells themselves to secrete inflammatory molecules and can block the development of new blood vessels in the uterine lining, further inhibiting blood flow, preventing thickening of the uterine lining and proper placental blood flow.

The rate of miscarriage is about 52% when APL antibody levels are greater than 90% of the normal population values.³ Other fetal complications with the presence of APL antibodies include pre-term birth, intrauterine growth restriction (from insufficient placental blood flow), recurrent pregnancy loss, and stillbirth.³

Thyroid Autoimmunity

It is well established that thyroid dysfunction can negatively affect reproduction. Hypothyroidism can affect the timing and secretion of luteinizing hormone (LH) pulses which determines the release of an egg for ovulation. This can therefore cause ovulatory disorders, failure to ovulate, or to have a menstrual period. It has also been associated with decreased success in IVF cycles when compared to women with normal thyroid function (euthyroid).⁴

The presence of elevated thyroid antibodies, including anti-thyroperoxidase (TPO) and anti-thyroglobulin (TG) doesn't always coincide with hypothyroidism and commonly occurs in euthyroid cases. Having elevated levels of thyroid antibodies has been associated with increased rates of miscarriage and recurrent pregnancy loss and is the most common AI condition in women of reproductive age.⁵

Thyroid antibodies could have multiple effects that lead to poorer reproductive outcomes. First, they could decrease thyroid function, slowly causing an elevation in TSH (thyroid stimulating hormone), leading to full-blown hypothyroidism. Secondly, the presence of autoantibodies tells us the body is facilitating improper immune responses which could cause the body to reject a pregnancy.

One study involving 3593 women showed that those who had positive thyroid antibodies had an increased rate in preterm birth and fetal respiratory distress.⁴ The risk of spontaneous miscarriage and preterm birth increased by about three to five times in those with elevated antibodies.

In a 2011 meta-analysis, compared to those who were antibody-negative, having positive thyroid antibody levels increased the risk of unexplained infertility or subfertility, miscarriage, recurrent pregnancy loss, preterm birth and maternal postpartum thyroiditis.⁶ One of the studies included in this analysis showed that the rate of miscarriage increased from 8.4% to 17% when

thyroid antibodies were present, regardless of thyroid hormone levels or maternal age.⁷

In a more recent meta-analysis, having TPO antibodies, regardless of euthyroid/hypothyroid status, led to a significantly increased risk of preterm birth.⁸ A 2020 study by Inagaki found an increased rate of miscarriages in euthyroid women within six months of trying to conceive in those with thyroid antibodies (18% vs 12% for TPO, and 17% vs 22% for TG) compared to those without.⁹

However, compared to those who conceived spontaneously, having a pregnancy loss after IVF was not associated with increased thyroid antibodies. It seems as though those who undergo IVF with Intracytoplasmic sperm injection (ICSI) have different outcomes to those that conceive spontaneously or with timed intercourse. In ICSI studies, there don't seem to be any significant difference in pregnancy rate or miscarriage rate in euthyroid women with positive thyroid antibodies compared to those who are antibody negative.⁵

Although it's important to identify the specific cause(s) of subfertility or infertility, finding one type of autoantibody or having been previously diagnosed with an AI condition helps us to understand that there may be multiple areas of immune dysfunction. Having a problem in one area could mean there are similar problems in other areas including the ovaries and uterus. But this also doesn't automatically mean that having an AI condition will prevent you from getting pregnant and having a healthy baby. It means that normal function of our hormonal and reproductive systems may be at risk and that this should be an area of investigation. It also provides direction when someone has experienced multiple losses without previous AI investigation.

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Immunological Effects of AHCC

By Krista Powell



A well functioning immune system is critical to our overall health. It protects us from pathogens like viruses, bacteria and toxins. There are steps we can all take to support immune function like eating nutritious foods, exercising regularly, getting adequate sleep and managing stress effectively. However, our immune systems can be weakened by a wide range of factors from autoimmune conditions to age, to certain medications or treatments like chemotherapy.

Shiitake mushrooms are among the most popular edible mushrooms in the world. To cooks, they are known for their delicious taste, versatility in recipes and satisfying meaty texture. However, shiitake mushrooms have an abundance of other health benefits that can be derived from ingesting the mushroom itself or a supplement that contains one of its extracts. So, even if you dislike the flavour or texture of mushrooms in general, you can still reap the benefits of this potent fungus.

Mushrooms and fungi have been used in medicine for thousands of years. They have been used traditionally to provide immune support, treat and prevent infections, protect the liver and offset the negative effects of stress. There are many different varieties of mushrooms that have demonstrated beneficial effects like boosting the immune system.

Mushrooms contain specific compounds called alpha and beta-glucans that are responsible for the immune-stimulating actions. The most well-studied types of mushrooms are *Coriolus versicolor*, *Agaricus blazei*, *Grifola frondosa* (aka Maitake) and *Ganoderma lucidum* (aka Reishi).¹ While these mushrooms have many benefits on their own, there is extensive research supporting a more refined mushroom extract called Active Hexose Correlated Compound (AHCC) that comes from the shiitake mushroom family. This extract is a blend of mushrooms that are grown and fermented together before the active components are extracted.

AHCC is a potent antioxidant and has the unique ability to stimulate the immune system, which is important in controlling inflammation and infection and regulating healthy cell growth. AHCC is widely used in Japan for its immune boosting properties, as well as for its ability to fight the formation of abnormal cells. It has been researched by over 30 academic institutions worldwide and used in over 700 clinics as an accompaniment to chemotherapy or radiation.

The primary way that AHCC delivers its beneficial effects is by stimulating and balancing the immune system. The studies found it increased a specific

part of the immune system that targets microbes for destruction. These specialized immune cells are called macrophages, T-cells, dendritic cells and natural killer cells.² This broad spectrum of action is very important to recreate immune balance while blood cells are able to recognize and attack irregular cells or harmful bacteria. The immune effects of AHCC have been applied to microbial infections as well.

AHCC exerts its influence on the immune system in a process that directly involves the white blood cells.² This process naturally encompasses biochemical processes that have multiple roles that overlap with one another, but if it were to be described in a step-by-step manner, it would likely look something like this:

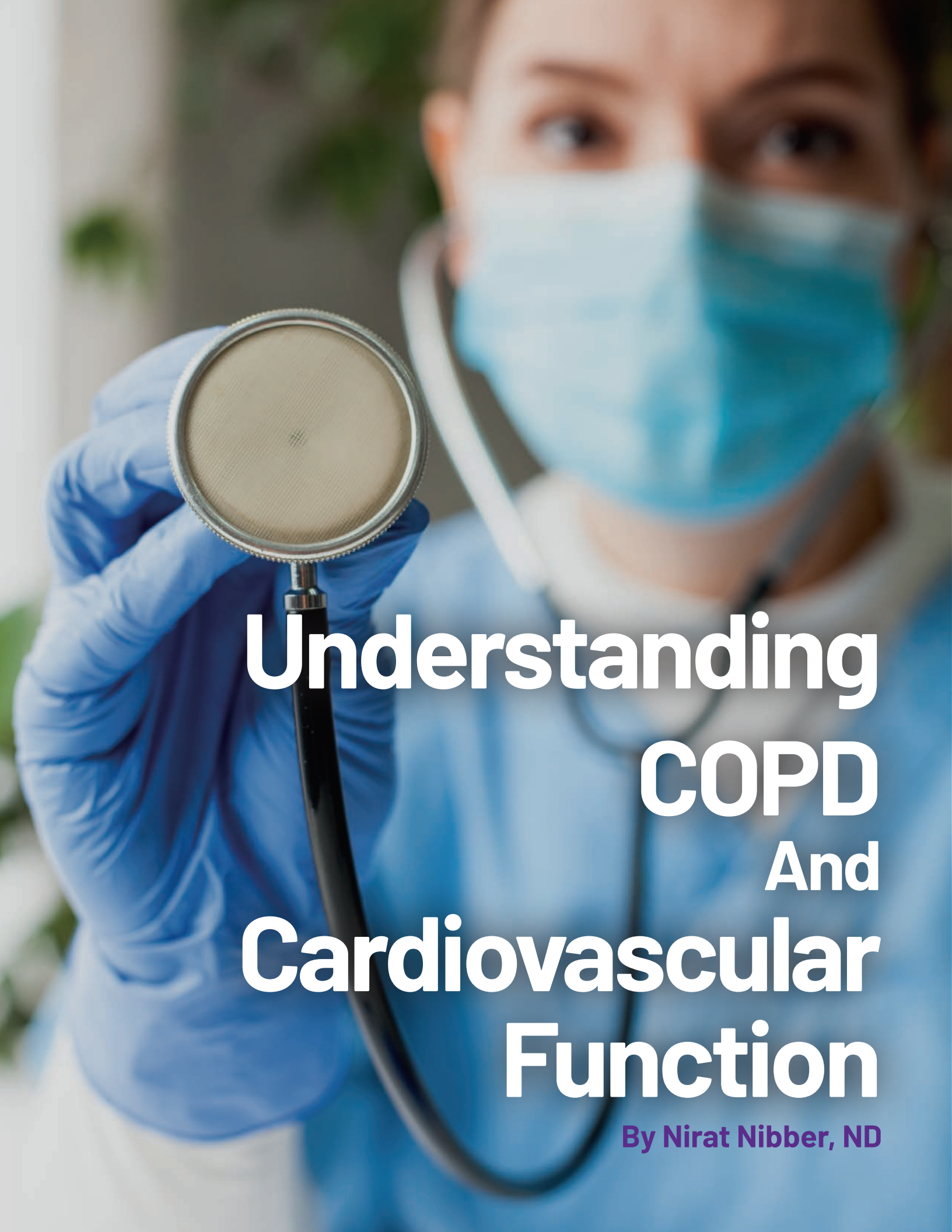
1. An antigen enters the human bloodstream
2. Immune cells begin to produce signalling proteins called interferon in response
3. Interferon binds to macrophages and triggers their activation
4. Macrophages then produce interleukins (secreted proteins and signal molecules)
5. Interleukins stimulate the T cells to assist in the production of antibodies and hypersensitivity reactions
6. The result of the combined efforts of these cells is the destruction and removal of the original invading antigen

AHCC has a broad range of effects on the immune system including natural killer and T cells. These effects are produced by directly modulating the numbers and functions of these cells as well as by increasing the capacity to promote T cell function. The effects of AHCC on natural killer and T cells also appear to have positive effects on infections, inflammation and irregular cell growth.

Years of research and practical use show that AHCC is safe and effective. It has no toxicity and side effects are very rare. AHCC is recommended for anyone with diminished immune function, those undergoing chemotherapy, as well as for people looking to improve immune function to fight off viral or bacterial infections.

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Understanding COPD And Cardiovascular Function

By Nirat Nibber, ND

Key Terms:

Pulmonary: Refers to the lung.¹

Compliance: Refers to the ability of the lungs to stretch, otherwise known as the distensibility. Offering insight into how stretchy or flexible lung tissue is.¹

Lung volumes: These measurements which include the tidal volume, inspiratory and expiratory reserve volume, residual volume and dead space provide insight into the specific amounts of air moving in and out with inhalation and exhalation.²

Lung capacities: These values are derived from the lung volume measurements and provide valuable insight into the physiological limit for air intake by the lungs.²

FEV1: This measurement is important because it measures how much air can be blown out or expired in one second after a full inhalation and should be about 80% of the total amount of air that can be forcibly expired (known as FVC).²

Sputum: Saliva and mucous found in the respiratory tract.¹

Dyspnea: Shortness of breath.¹

Nitric oxide (NO): NO is a simple molecule with wide-ranging effects throughout the body as it acts as a cellular signaling molecule. Transmitting messages between the body's cells. It is particularly important for cardiovascular function as it signals the dilation or opening of blood vessels to increase and redirect blood flow to areas in need.³

Chronic obstructive pulmonary disease (COPD) is a progressive lung disease that is characterised by diminished lung function.⁴ This can be due to either damage to bronchial tubes, known as airway disease, or due to the destruction of the air spaces in the lungs, known as emphysema, or both may be occurring.⁴ The chronic nature of COPD means there are the episodic exacerbations of symptoms such as breathlessness and cough. The frequency, intensity and characteristics of these exacerbations varies significantly from patient to patient. Despite varying presentations, all individuals with COPD demonstrate some degree of airflow limitation on breathing tests.⁴

COPD affects 3.6-11.7% of the worldwide population, though a significant portion of those cases (approximately 30%) are mild to moderate severity.^{5,6}

Signs and Symptoms

Cytokines are small protein molecules that play a key role in cell As mentioned above COPD has many manifestations three cardinal symptoms are⁴:

- Chronic cough that is worse in the morning
- Sputum associated with the cough. Sputum production greater than three tablespoons per day may be seen. Mucous may be clear to white, though during acute exacerbations, production may increase and become more purulent
- Dyspnea or unrelieved shortness of breath which occurs at rest or after minimal exertion. This is often the most distressing symptom for patients with anxiety about dyspnea worsening the sensation. It may also result in exercise intolerance which can in turn lead to greater risk for exacerbations and comorbidities

Measuring lung function²

Pulmonary or lung function can be assessed using several tools that assess lung capacity, distensibility and gas exchange. The most common is called spirometry. This test measures the volume of air the lungs can hold and how forcefully air can be emptied out. It can be relatively easily administered in clinical settings. Exercise testing may also be conducted to assess the cause of dyspnea.

Clinical assessment using spirometry, as well as imaging and blood tests are also available to confirm diagnosis. Spirometry is considered the most effective and accessible in office tool to assess for lung function (see inset.) COPD patients demonstrate airflow restrictions with decreased FEV1 measurements which gets worse during the acute episodes.^{4,10} Imaging with CT scans can also show the changes in the thickness of airway walls and the pulmonary artery both of which would mean progression of the disease.⁵ Pulmonary function tests also demonstrate that during exercise in COPD patients the ratio between the ventilation (VE) and carbon dioxide production (VE/VCO₂) is elevated indicative of pulmonary inefficiencies⁸. Another important marker is the elevated expiratory nitric oxide (eNO) a key mediator in vascular function.⁹

While mild versions of the above symptoms may persist in stable COPD, these are usually punctuated with "episodes" where all symptoms become worse.^{4,10} These include and should be monitored closely:

- Chest pain or tightness that is unrelieved at rest
- Fever and chills
- Wheezing
- Worsening dyspnea when laying down requiring the patient to remain upright
- Elevated heart rate
- Cyanosis or turning blue which can be seen on lips, nail beds or skin
- Confusion
- Bloody or rust coloured sputum
- Muscle wasting and weight loss may also occur

How COPD Develops

While the exact causes of COPD are difficult to pinpoint there is a strong association with high "inhalation exposure."^{4,11} Inhalation exposure refers of course to individuals who are regularly exposed to toxic chemicals that can be inhaled. This includes tobacco smoke,

vaping, second hand smoke, excessive air pollution and can include seasonal irritants such as pollens. Exacerbations of COPD can also arise due to bacterial or viral infections, lack of physical activity, and secondary to heart conditions.⁴

But how does inhalation exposure lead to the obstructive lung disease? We know that in COPD the airway restriction triggers dysfunction in the vasculature found in the lungs.⁸ So, the blood flow to the lungs as well as the capillaries where gas exchange occur are negatively impacted. This diminished capillary blood flow and gas exchange capacity causes the dyspnea. This also explains the decline in FEV1 and increase in eNO.^{8,9}

Obstructive vs Restrictive lung diseases⁷

Chronic obstructive lung disease

- These diseases arise from an airflow limitation due to an obstruction or blockage resulting in an overinflation (high residual volume) of the lungs ahead of the obstruction
- These disorders are not fully reversible once the obstruction has been removed due to tissue damage or increased lung compliance. Akin to an overinflated balloon- when the air is let out the balloon is stretched and overly lax
- Hyperinflated lungs mean there is more difficulty blowing air out resulting in expiratory wheezing
- Examples include end stage of severe asthma, emphysema and chronic bronchitis

Interstitial (Restrictive) lung disease

- This classification refers to lung diseases that have restricted expansion of the lungs, or poor lung compliance
- A key feature is that the restriction is due to inflammatory infiltration of the lung tissue that causes damage and scarring eventually leading to fibrosis
- The restrictive disease results in a smaller lung volume with decreased compliance

Historically healthcare practitioners would differentiate severe manifestations of emphysema versus chronic bronchitis based on the patients who present as “pink puffers” or “blue bloaters.” However, this has become a much more nuanced discussion. In the past emphysema was thought to only be the result of damage due to smoking (hence the “puffers.”) Though now it is known that many more environmental inhalation triggers can trigger the hyperinflation of lung tissue. These toxins are particularly harmful in individuals with Alpha-1 antitrypsin (AAT) deficiency. AAT is an important protein that prevents the enzyme elastin from degrading normal tissue. This deficiency plus the smoke from cigarettes appears to induce emphysema.¹² Over time these patients develop compensatory mechanisms to the lack of oxygen.¹⁰ One of which is the increased production of red blood cells (RBC) via increased erythropoietin output by the kidneys. This results in elevated RBC levels thus the “pink” moniker as well as a barrel chest, pursed lips and slow forced expiration.¹⁰

Meanwhile chronic bronchitis generally presented in the past as a “blue bloaters” because the compensatory mechanisms are not activated as they are with emphysema due to the inconsistent nature of the symptoms.¹³ Infections or chemical irritants can cause the bronchitis and must present with a chronic cough with sputum for at least three months in at least two consecutive years for diagnosis.^{5,13} Because it comes and goes the trigger to increase RBCs is not activated and results in insufficient oxygen transport to tissues resulting in a cyanotic appearance. Patients also experience an increase pulmonary pressure which over time

can increase the stress on the right side of the heart, known as cor pulmonale.¹³ Further these patients appear more bloated due to this heart failure related fluid build-up. This is extremely serious and requires consistent medical care as individuals are more susceptible to serious complications of any lung infection.

Prevention and Management

While COPD is not curable there are management options that can reduce exacerbations, progression and more serious sequelae. Treatments include a combination of medications as well as lifestyle interventions.¹⁴ Including smoking cessation, gradual and consistent exercise. Medications for acute concerns such as short and long-acting bronchodilators may be required. Eventually as the disease progresses patients may consider corticosteroid and surgical options with their doctors.¹⁴

With mild to moderate cases a key goal is to prevent these acute exacerbations and improve gas exchange. Three important approaches are:

1. Decrease inhalation exposures: One of the first recommendations a newly diagnosed patient will hear is to immediately cease smoking if relevant.^{4,11} For those that do not smoke an environmental assessment of inhaled toxins would be helpful. Clear out any industrial spray, increase ventilation in living spaces, purchase air purifiers and avoid areas with poor air quality.¹⁴
2. Improve immune response: We know that bacterial and viral infections can trigger an exacerbation with the most common viral cause as the common cold (rhinovirus.) Further, the more acute episodes an individual with COPD has the less “stable” they become and speeds up loss of lung function.¹⁰ Thus, it is important to improve overall immune function by way of regular sleep, stress reduction and diets with protein, zinc, vitamin C. Vitamin D may be a helpful adjunct depending on baseline levels or risk of deficiency. Patients should consider risk mitigation such as distancing, short term mask usage, and any required vaccinations when available as they are more vulnerable to severe outcomes.
3. Optimise pulmonary blood flow and circulation: A recent study from 2021 found that patients with mild COPD increased exercise tolerance, reduced dyspnea and overall improved oxygen uptake after receiving inhaled NO.¹⁵ This is a promising development as it treats the underlying cause of diminished gas exchange by increasing microvascular circulation. Of course, additional research is needed to understand the impact on preventing exacerbations, but this study offers a promising new therapy to add to the arsenal of treatments.

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Andrographis


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Plant Extracts with Activity Against Herpes Simplex Viruses

By Chantal Ann Dumas, ND

Herpes simplex virus type 1 (HSV-1) and herpes simplex virus type 2 virus (HSV-2) are highly prevalent in humans, with global infections ranging 70 and 10% of the world population, respectively.¹ HSVs are characterized by lifelong infections and sporadic recurrences which may manifest either symptomatically or asymptotically. Although HSVs can produce severe disease in humans, such as life-threatening encephalitis and blindness, the most common symptoms are skin and mucosal lesions in the oro-facial (herpes labialis) and the genital areas (herpes genitalis).² The vesicular ulcers associated with herpes viruses may be painful with a burning sensation, ultimately impacting the quality of life of the affected individuals. They gradually dry out into crusts, and they may last up to 14 days during primary infections and approximately 10 days during recurrences in the absence of treatment.³ The lesions contain high amounts of infiltrating leukocytes (a type of white blood cell) and viral particles (virions) that can be shed onto others through mucosae body fluids.⁴

Unfortunately, there are no cure for HSV-1 or HSV-2 infections.⁵ However, antiviral medications such as acyclovir, penciclovir, and famciclovir are commonly used to prevent and treat outbreaks. While these drugs can prevent severe HSV infection, they are not very effective in addressing skin manifestations.⁶ At most, they only reduce the duration of the lesions by a few days.⁷ Resistance to antivirals has begun to emerge and is a source of concern.⁸

Natural compounds, including botanical extracts, with antiviral properties are a welcome complement or alternative to them.

Aloe vera

Aloe vera (*Aloe barbadensis*) contains more than 75 different compounds and has been used traditionally to treat skin problems such as burns, wounds, and anti-inflammatory processes.⁹ This well-known botanical also exhibits other therapeutic properties including anticancer, antioxidant, antidiabetic, and antihyperlipidemic.¹⁰ Moreover, it has been previously reported to have anti-inflammatory, antibacterial, and antiviral effects.¹¹ Zandi et al. studied aloe vera gel's inhibitory effect on HSV-1 growth in Vero cell line and concluded the gel could be a useful topical treatment for oral HSV-1 infections without any significant toxicity.¹²

Boswellia serrata

Boswellia serrata oleo-gum-resin (BSE) possesses a strong traditional background of treating diverse skin ailments including infection.¹³ Goswami et al. investigated the antiviral activity of a methanol extract of BSE and one of its major constituents β -boswellic acid (BA) against HSV-1 along with the underlying mechanism of action involved. The results showed that BSE and BA nearly completely inhibited HSV-1.14 According to the researchers, BSE and BA exert their inhibitory effect through the modulation of NF- κ B and p38 MAPK pathway.

Mentha piperita

Reichling et al. studied peppermint (*Mentha piperita*) extract against acyclovir-sensitive HSV-1 and acyclovir-resistant HSV-1 at different dilutions.¹⁵ All dilution extracts were effective, even low concentrations of 0.01% almost completely reduced viral infectivity. Moreover, when the extracts were tested against acyclovir-resistant HSV-1, all 80% ethanolic extracts demonstrated complete plaque reduction of both strains and fully suppressed viral infectivity. The authors conclude that the 80% ethanolic extracts of *M. piperita* exhibit antiherpetic mechanism of action and constitutes a promising candidate for treatment of HSV infections.

Essential oils

Essential oils, especially those extracted from plants belonging to the Verbenaceae and Labiatae families, have been shown to exert antiviral activity against HSVs. For instance, essential oils obtained

from the leaves of lemon balm (*Melissa officinalis*) demonstrated activity against both HSVs.¹⁶ *M. officinalis* extracts are also studied extensively. For example, two human trials, carried out by Wolbling et al. demonstrated the efficacy of a cream containing 1% dried extract of *M. officinalis* on HSV lesions.¹⁷

In a very interesting study, Brezani et al. identified twelve compounds isolated from the leaves and twigs of *Eucalyptus globulus* which were found to have antiviral activity against HSV-1 and HSV-2 and even outperformed acyclovir.¹⁸

Algae-Derived Compounds

Many studies have reported the existence of algae with bioactive compounds that display potent antiviral activity against numerous viruses, including HSVs.¹⁹ For example, a study performed in Brazil by Ribeiro et al. reported that four species of algae had significant antiviral activity against both, HSV-1 and HSV-2.²⁰ The extracts of green alga *Styopodium zonale* (Ochrophyta), *Ulva fasciata*, *Codium decortatum* and red alga *Laurencia dendroidea* all exhibited antiviral activity mediated by different compounds, including fatty acids and sesquiterpenes.

Conclusion

Herpes simplex are lifelong infections with sporadic recurrences which can negatively impact the quality of life of the person afflicted by them. Antiherpetic drugs provide limited results, they can have serious side-effects and be responsible of drug-resistance. Consequently, it is important to find safe and efficient natural alternatives. Some have been cited in this article, but it is important to remember to address our immune system and our health as a whole and to incorporate pertaining dietary and lifestyle modifications, including proper stress management to achieve optimal result. Another important point to consider is that the initiation of any treatment in the very early stages of the infection is generally most effective.

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