

LINUS PAULING INSTITUTE

OREGON STATE UNIVERSITY
RESEARCH NEWSLETTER

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VITAMIN D, ZINC, AND COVID-19

COVID will likely be a global public health concern for years to come. Thankfully, clinicians and researchers have developed various public health protocols, vaccines, and treatment options that reduce the likelihood of serious illness and death from COVID. In addition, we now have emerging information about the role that micronutrients might play in complementing these strategies.

At the Linus Pauling Institute, we believe that this is important to share the current state of the science to help you make informed decisions about your health. Therefore, we continually monitor the latest scientific evidence regarding micronutrients and COVID.

This article focuses on vitamin D and zinc, and future newsletters will highlight other micronutrients.

VITAMIN D

Rationale: Although its role in immunity is still a burgeoning area of research, vitamin D is known to have multiple effects on the production, development, and regulation of immune cells. Vitamin D also plays a role in cell barrier functions and the production of antimicrobial peptides.

Additionally, the immunomodulatory properties of vitamin D can help control an overactive immune system and reduce immune deficiencies. This makes vitamin D important for diseases in which an overactive immune response can result in sustained and undesirable inflammation, such as COVID.

Lastly, low blood vitamin D concentrations increase the risk of contracting respiratory tract infections.

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Oregon State University
Linus Pauling Institute

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Emily Ho, PhD
Endowed Chair and Director,
Linus Pauling Institute

**Our Linus Pauling Day
webinar on vitamin C
can be viewed at:**
lpi.pub/VitaminC2022

FROM THE DIRECTOR

The new year at the Linus Pauling Institute is off to a great start! At the time of this writing, we have just celebrated Linus Pauling Day, our annual commemoration of the life and achievements of Dr. Linus Pauling.

On February 28, 2022 – Dr. Linus Pauling's 121st birthday – the Institute hosted a webinar called *Beyond the Common Cold: Elucidating the Roles of Vitamin C in Health*.

This online webinar featured Dr. Jeanne Drisko (who joined us last year for our Linus Pauling Day event) and Dr. Qi Chen, both from the University of Kansas Medical Center. We plan on bringing you highlights from this webinar in our next issue.

Our next webinar will be on dietary indoles, cruciferous vegetables, and cancer, featuring over 30 years of research at Oregon State University. This will be presented by Dr. David E. Williams, University Distinguished Professor and the Linus Pauling Institute Helen P. Rumbel Professor for Cancer Prevention (see details below).

As always, we encourage you to register for the event even if you cannot attend live – registered guests get first access to the video recording and all other webinar materials.

Lastly, we have recently re-established the Director's Circle at the Linus Pauling Institute. The Director's Circle is a group of trusted thought leaders who have a vested interest in our future. Its members primarily serve as an advisory board to me, and they also work as advocates to promote the activities and mission of the Institute within their networks.

You will be hearing from our Director's Circle members in the near future. If you are interested in learning more about this group, please contact me. We are always looking for more people to take an active interest in the Institute.

As always, stay happy and healthy.
Talk to you again soon,

Emily Ho

THE LINUS PAULING INSTITUTE PRESENTS

TROUT, MICE, RATS, AND HUMANS ALL AGREE: BRUSSELS SPROUTS CAN PREVENT CANCER

April 21, 2022

11 am - 12 pm Pacific

Register online at

<https://lpi.pub/Williams2022>



Oregon State University
Linus Pauling Institute



Dr. David E. Williams
Linus Pauling Institute

BROCCOLI FAQ

In December 2021, Dr. Emily Ho provided the last webinar of our 25th anniversary series, *Cancer Fighter: Harnessing the Power of Broccoli*. The response to her webinar and broccoli sprout growing demonstration was amazing, and we appreciate the enthusiastic feedback. Due to time constraints, we were unable to answer all of your questions during the event. Therefore, in lieu of our normal “Reader Question” section, we are summarizing common questions from the webinar with answers provided by Dr. Ho. Enjoy!

Why focus on broccoli or broccoli sprouts?

Broccoli is an abundant source of glucoraphanin, which can be transformed into a molecule called sulforaphane by the enzyme myrosinase, also present in broccoli.

Researchers believe that sulforaphane is a potent anti-cancer molecule, as I talked about in the webinar.

Is it bad to cook broccoli?

No, but just be aware that the myrosinase enzyme is destroyed by heat. Light cooking is fine. Try steaming it for 5 minutes. As long as there is some crunch left in the vegetable, you are probably getting some – if not most – of the sulforaphane you would get when eating the raw vegetable.

Don't worry too much if they are slightly overcooked. All cruciferous vegetables have vitamins, minerals, and fiber that are not only resilient to cooking but also have benefits against cancer. Getting some vegetables in any way is good for your health.

Do broccoli sprouts cause the same intestinal gas issues as eating cruciferous vegetables?

Unfortunately, they can. All cruciferous vegetables contain a carbohydrate called raffinose that our bodies can't digest. If you have problems with intestinal gas after eating sprouts, the best thing you can do is to eat smaller servings.

Over time, you may be able to eat more sprouts as the bacteria in your intestine adjust. You could take over-the-counter gas relief products to help in the meantime.

Thankfully, as I mentioned in the webinar, broccoli sprouts have much higher amounts of glucoraphanin per weight than the mature broccoli plant. Even if you are eating small amounts of sprouts, you can still get some of the cancer-fighting compounds.

Can other seeds be used instead of broccoli?

Broccoli seeds have the most glucoraphanin content, though kohlrabi seeds contain a moderate amount. There is much less in the seeds of cabbage, kale, Brussels sprouts, and other cruciferous vegetables.

If I put broccoli sprouts in my smoothies, will that work the same as chewing?

Yes and no. While chopping up the broccoli sprouts releases glucoraphanin and myrosinase, sulforaphane is not very stable. It might react with some of the other ingredients of your smoothie or start to oxidize, making it less effective.

If you are going to put broccoli sprouts into a smoothie, be sure to drink it as soon as possible. You can also freeze a purée of broccoli sprouts in small “shots” that can be added to a smoothie just before you drink it. These will thaw quickly, allowing you to drink them right away – we do this in our clinical studies!

Are broccoli supplements a good alternative to eating broccoli or sprouts?

They can be. One challenge is that you need active myrosinase to get sulforaphane from these supplements. Sometimes the enzyme is still active in the supplements, but it's hard to know for sure.

Our research trials have shown that supplements cannot match sprouts in terms of sulforaphane production, even if extra myrosinase is added. However, getting some is better than none – supplements are a good alternative if you cannot tolerate eating broccoli or broccoli sprouts.

Can we just eat the seeds instead of the sprouts?

Yes, but make sure to grind them up first. Otherwise, the myrosinase and glucoraphanin might not come into contact with each other. Be warned: they might not be very tasty. Many commercial supplements use broccoli seed as their source, rather than sprouts.

How long do the seeds last?

Seeds from cruciferous vegetables last at least three years but possibly as many as five. To extend their lifespan, keep the seeds dry and cold. For our research studies, we keep ours in the freezer – it's the best way to preserve their glucoraphanin content. 🌱

Missed the webinar?
You can still catch it online at:
lpi.pub/BrocVsCancer

Vitamin D status

Vitamin D status is assessed by measuring 25-hydroxyvitamin D levels in the bloodstream.

Low vitamin D status is defined as a blood concentration below 20 ng/mL. The threshold for deficiency is below 12 ng/mL. Studies vary on which level was used to categorize subjects with low vitamin D status.

COVID Data: Available evidence from observational studies confirms that low vitamin D status is associated with an increased risk of contracting COVID. Additional evidence suggests that low vitamin D status increases the risk of severe illness and death due to COVID.

A limitation of these studies is that blood vitamin D concentrations were often measured at inconsistent times, either before or after people developed COVID. This makes the relationship more of an inference rather than a direct connection.

Ultimately, the data clearly indicate that low vitamin D status should be avoided both prior to and during a COVID infection.

Can vitamin D supplements help people who have already contracted COVID? The data on this topic are not very clear.

Observational studies can only suggest that a dietary supplement will improve clinical outcomes. There are only a few small experimental studies designed to test the impact of vitamin D supplements on COVID. These studies suggest that vitamin D supplements reduce the rate of intubation and the length of hospital stay in COVID patients with no effect on mortality.

Four large randomized controlled trials investigating vitamin D supplements are underway in the US, Canada, Mexico, and the UK. At the conclusion of these trials, there should be a better understanding of how the use of vitamin D supplements can influence COVID outcomes.

Bottom Line: Of all the vitamins and minerals studied in the prevention and treatment of COVID, vitamin D is the most promising. However, the lack of large experimental studies makes specific recommendations difficult.

In general, vitamin D supplements are useful for correcting an existing deficiency. This helps lower the risk of respiratory tract infections – and this was true before the pandemic. It is best to take daily vitamin D supplements rather than taking supplements once an infection is underway.

The Linus Pauling Institute recommends that healthy adults take 2,000 IU (50 mcg) of supplemental vitamin D daily. There are few food sources of vitamin D.

The goal is to maintain blood concentrations of vitamin D at or above 30 ng/mL, so it is a good idea to follow up with vitamin D testing. If you do not reach vitamin D blood concentrations of 30 ng/mL with 2,000 IU daily, you could consider taking additional vitamin D supplements. Some individuals need vitamin D in excess of this amount in order to reach target blood concentrations, especially if their vitamin D status is low.

The tolerable upper intake level for adults is set at 4,000 IU of vitamin D per day. Yet, in healthy people, adverse effects of taking vitamin D supplements are unlikely at intake levels lower than 10,000 IU/day.

For optimal results, consult your physician to measure your blood vitamin D concentration and discuss a supplementation strategy, if needed.

Vitamin D testing

Vitamin D blood tests are standard laboratory tests available from a medical provider. There are also over-the-counter tests that can help you determine your blood vitamin D concentration.

TYPES OF CLINICAL STUDIES ON MICRONUTRIENTS AND COVID

Meta-Analyses or Systematic Reviews: These are analyses of multiple clinical studies on a topic, typically using pre-defined criteria to evaluate study quality. Considered the highest quality evidence available, these analyses are often used to inform recommendations on health. At the moment, few analyses of this type exist concerning vitamins and minerals in the treatment of COVID.

Experimental Studies: This is a type of clinical trial where researchers actively control study variables and introduce an intervention such as supplementation. These studies are considered more valuable since they can directly test causation. Randomized controlled trials are one example of an experimental study. We are still awaiting the results from several larger trials that use micronutrients in the treatment of COVID.

Observational Studies: This is a type of study where researchers analyze available data obtained from a group of people with limited control of study variables. As these studies only support associations, they are considered the least powerful type of clinical research. Currently, observational studies make up the majority of published clinical research on micronutrients and COVID.

SOURCES OF ZINC

Oysters (6 medium): 25-50 mg

Beef (3 ounces): 5-9 mg

Turkey (3 ounces): 3 mg

Cashews (1 ounce): 1.6 mg

Chickpeas (½ cup): 1.2 mg

For more, see the Micronutrient Information Center page on zinc:
lpi.pub/ZincSources



ZINC

Rationale: Zinc has multifold roles in the immune system, including antioxidant, anti-inflammatory, and anti-viral properties important for a healthy immune response. Like vitamin D, zinc has immunomodulatory properties.

Zinc deficiency increases the risk of developing one or more deficits in the immune system, such as poor production of T-cells and B-cells. People with low zinc status are also more likely to have higher markers of inflammation in response to a viral infection.

COVID Data: There are only a few observational studies on zinc and COVID patients. They suggest that patients with severe COVID are more likely to have lower blood zinc concentrations than people with mild or moderate symptoms.

Observational studies have also associated zinc supplementation with improved recovery time in COVID patients, but experimental studies have not reproduced this result. **In general, the evidence on zinc supplementation is very weak and not particularly informative.**

In COVID trials on zinc supplements, people who took high amounts of zinc reported more stomach aches, nausea, and heartburn in the treatment groups than in the controls. These are known side effects of excessive zinc consumption.

As with vitamin D, several randomized controlled trials on zinc in the treatment of COVID are ongoing.

Bottom Line: There is no evidence to support taking zinc supplements to prevent a COVID infection. There is also no good evidence to suggest zinc supplements are effective in the treatment of COVID. However, there are few studies available using zinc supplements alone.

The Linus Pauling Institute recommends that men consume 11 mg of zinc per day and women consume 8 mg of zinc per day. Make sure to include zinc-rich foods in your diet (see examples above).

The tolerable upper intake level for zinc is set at 40 mg per day, so getting too much zinc from food alone is rarely a problem.

If you do not eat any zinc-rich foods, you may need a supplement to meet your needs. Try not to exceed 40 mg of zinc per day.

While the use of zinc supplements in doses above 40 mg per day for a short period of time (such as a few days) is not a concern for health, zinc interferes with copper absorption. Consuming more than 40 mg of zinc every day for several weeks can result in low copper levels in the body.

While taking zinc lozenges is shown to be effective against common cold symptoms, they have not yet been properly evaluated in the treatment of COVID. 🧐

Limitations of clinical trials on zinc

Blood concentrations of zinc are a poor indicator of how much zinc a person consumes, except in the case of severe deficiency. There is currently no good marker for inadequate zinc status. This limitation may prevent researchers from detecting associations of zinc status and COVID outcomes.

Zinc lozenges

For more about zinc lozenges in the treatment of the common cold, see the Micronutrient Information Center:
lpi.pub/ZincLozenge

For the list of scientific articles reviewed here, see: lpi.pub/COVIDrefs

DIET AND OPTIMUM HEALTH ONLINE:

The Linus Pauling Institute's Conference Goes Virtual

With the restrictions on gathering during the pandemic, the Linus Pauling Institute opted to hold a series of virtual conference sessions instead of our in-person biennial conference in 2021.

This virtual conference, *Diet and Optimum Health Online*, hosted sessions focused on healthy aging, the microbiome, and immunity.

Below, we briefly summarize the conference sessions. A more in-depth summary and links to some of the recordings can be found at lpi.pub/DOH2021

Dietary Components and Healthspan: Honoring the Work of Bruce Ames

The first session of the conference was dedicated to extending the healthspan, a concept we introduced in our cover article in the Fall 2021 *LPI Research Newsletter*. The career of **Dr. Bruce Ames** was the theme of the presentations. Dr. Ames has contributed immensely to our understanding of the role of dietary factors in healthy aging.

Dr. Janet King focused her presentation on good nutrition for older adults. Dr. King worked with Dr. Ames on clinical trials with zinc, demonstrating how low dietary zinc could lead to the accumulation of DNA damage.

DNA damage does not often have immediate effects on the body. However, it can lead to serious long-term consequences if uncorrected. Inadequate zinc intake has been associated with an increased risk of cancer and other chronic ailments. This is a good example of Dr. Ames' Triage Theory (see right).

Dr. José Ordovás spoke about understanding individual nutrition needs. He introduced the concept of personalized nutrition – a recognition that people are unique, so nutrition recommendations for vitamins, minerals, and other dietary factors should be tailored to the individual.

Dr. James Kirkland gave an update on his trials with senolytic compounds, including dietary factors like quercetin and fisetin. Senolytic compounds are those that can destroy senescent cells. More about cellular senescence and senolytics can be found in the Fall 2021 *LPI Research Newsletter*.

Dr. Kirkland presented his work using senolytics to treat various age-related conditions, with a special emphasis on new trials in diabetes. This approach echoes Dr. Ames' work looking for dietary factors that could be used to extend the healthspan.

During his career, Dr. Bruce Ames developed a concept he called **Triage Theory**. This theory posits that the body will ration vitamins, minerals, and other compounds if the supply is low, prioritizing immediate survival over long-term health. This accelerates the diseases of aging.

According to this theory, replenishing the body with micronutrients that are in short supply will combat the aging process. In addition, other non-essential dietary compounds could delay the deleterious effects of aging and extend the healthspan.

For more about Dr. Ames and his contributions to nutrition and aging, see lpi.pub/AmesVideo

DIET AND OPTIMUM HEALTH ONLINE

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Diet and Optimal Health: The Role of the Gut Microbiome

The second session of *Diet and Optimum Health Online* examined the influence of diet and dietary factors on the composition of our gut microbiome. This session not only focused on dietary components that feed healthy gut bacteria but also on the health benefits associated with manipulating the types and amounts of microorganisms living in our intestine.

Two presentations focused on the influence of fiber on the composition of the gut microbiota. **Dr. Hannah Holscher** began by speaking about the fibers in plants and the types of bacteria that prefer to consume them. Since certain bacterial families are linked to good health, it is now possible to design interventions with specific foods or fiber supplements to determine if they elicit the desired health benefits.

Dr. Jens Walter reviewed the complex relationships surrounding fiber supplements and changes to the gut microbiome. In clinical trials, both fermentable and non-fermentable fiber supplements had beneficial properties. The use of fermentable corn bran fiber supplements was associated with improved insulin sensitivity, increased satiety, and beneficial changes to the gut microbiome. On the other hand, the use of non-fermentable cellulose fiber supplements reduced inflammation despite the absence of detectable changes to the gut microbiome.

Dr. Leigh Frame's presentation highlighted the production of short-chain fatty acids by bacteria, which can happen during the fermentation of fibers. Small clinical trials show that short-chain fatty acids have been associated with increased gut motility, appetite regulation, and obesity prevention. However, larger experimental trials are needed to understand the role of short-chain fatty acids in health.

Dr. Fred Stevens spoke about the effect of gut bacteria on bile acid metabolism and how this may lead to health benefits. In particular, he discussed his research on xanthohumol and its influence on the gut microbiota – a topic that was covered in more detail in the Fall 2021 *LPI Research Newsletter*.

Dietary Factors for a Healthy Immune System

The final session of the conference focused on the role that diet and supplements can play in combating inflammation and infection. This session was timely, as the information presented by the speakers touched on ways that diet and dietary supplements may influence COVID outcomes.

Dr. Adrian Martineau reviewed the current data on vitamin D status and COVID. Dr. Martineau also spoke about the ongoing trials relating vitamin D status to the risk of COVID infection and the immune response to COVID immunization. He stressed that more information on this topic will be published very soon.

Dr. Mette Berger spoke about the micronutrient status of critical care patients. She noted that many people admitted to the ICU often have a low blood concentration of one or more vitamins and minerals. Extended hospitalization often exacerbates these deficits, which can be accelerated by increasing levels of inflammation. Strategies designed to address micronutrient needs are likely to improve outcomes in critical care patients.

Dr. Simin Meydani discussed the importance of maintaining adequate micronutrient status in the elderly. While good nutrition helps older individuals maintain a proper immune response, it is very commonly overlooked. Dr. Meydani's group has worked on several studies using vitamin, mineral, and botanical supplements to help reduce inflammation levels and lower the risk of contracting infections in older adult populations.

Lastly, **Dr. Philip Calder** spoke about EPA and DHA – the omega-3 fatty acids most abundant in fish oil – and their role in blunting an overactive immune response. He reviewed the data showing positive effects of DHA supplementation on allergic responses, respiratory illness, and arthritic pain. Dr. Calder also spoke about DHA supplements' potential to improve chronic pain issues. 🌱

THE NEXT DIET AND OPTIMUM HEALTH CONFERENCE?

The next Diet and Optimum Health conference is tentatively scheduled for Fall 2023 at Oregon State University in Corvallis, Oregon. Notifications will be sent to all previous conference attendees when dates have been finalized.

If you would like to be added to the notifications list, email us at lpi@oregonstate.edu



Oregon State University
Linus Pauling Institute

**LINUS PAULING INSTITUTE
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INSIDE: ARE VITAMIN D AND ZINC USEFUL IN THE FIGHT AGAINST COVID-19?



JOIN US FOR DAM PROUD DAY!

April 27, 2022

Dam Proud Day is Oregon State University's annual day of giving. The Linus Pauling Institute is raising donations for the **Simone and Balz Frei Graduate Fellowship Fund** in support of young nutrition scientists. Help make this day a success!

Want to know more?

See <http://lpi.pub/DamProud> for more information or contact Andrew.Norwood@osufoundation.org