



LINUS PAULING INSTITUTE

OREGON STATE UNIVERSITY
RESEARCH NEWSLETTER

WINTER 2021

VITAMIN D AND COVID-19: What you need to know LOOK INSIDE ►

LIPOIC ACID SUPPLEMENTS AND WEIGHT LOSS:

A New Clinical Trial Sheds Light on Potential Benefits

Investigators at the Linus Pauling Institute, along with their collaborators at Oregon Health & Science University, recently published results of a clinical trial using lipoic acid supplements. This study shows that lipoic acid supplements can help some people lose weight.

For over 20 years, scientists and clinicians have explored the potential health benefits of lipoic acid, including its ability to promote healthy aging and mitigate cardiovascular disease.

Researchers at the Linus Pauling Institute have found that lipoic acid reduces oxidative stress, improves detoxification mechanisms, and alters lipid metabolism in animal models. Clinical trials at the Institute have demonstrated the same effects and also suggest that lipoic acid plays a role in maintaining a normal circadian rhythm, otherwise known as the body's internal clock.

What is lipoic acid?

Lipoic acid is a naturally occurring compound produced by both plants and animals. It has a unique chemical structure: it is a medium-chain fatty acid with two sulfur atoms at one end (see illustration on page 4).

Lipoic acid is typically found attached to enzymes, where it acts as an electron carrier. These enzymes are involved in energy and amino acid metabolism in the mitochondria.

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Oregon State University
Linus Pauling Institute



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

On December 9, 2020, Dr. Emily Ho presented "Think Zinc! Fighting Infection and Boosting the Immune System."

The video of this event is available at:
<http://lpi.pub/ZincVideo>

FROM THE DIRECTOR

This is an auspicious year for the Linus Pauling Institute. This year marks the 25th anniversary of the Institute coming to Oregon State University. Also, on February 28, 2021 we will celebrate the 120th birthday of the late Dr. Linus Pauling.

This year, we encourage everyone to challenge their view of nutrition. To achieve optimal health, we need to think about the right time, right dose, and right target in your body – and that recipe for health is likely going to be different depending on your circumstances.

Dr. Pauling dreamed of going in this direction more than 50 years ago, calling this concept "orthomolecular medicine." Science and technology are only now catching up with his vision.

Earlier this year, the National Institutes of Health announced a new strategic plan that has a specific focus on "Precision Nutrition" – a recognition that the relationship between diet and disease is highly complex and individual.

I had the pleasure of joining leaders in the field to share and discuss this topic with the NIH this January. There is a consensus that the one-size-fits-all approach to vitamins, minerals, and other dietary factors needs to be revisited.

At the Institute, we know a highly integrated and holistic approach is needed to find out what foods and dietary supplements (and how much of each) will help achieve the best health. I hope that this priority from the NIH will help us to realize the promise of Dr. Pauling's legacy.

Expect more from me soon on our plans to take personalized nutrition into the next era of the Institute. For now, I hope you enjoy this issue.



IN MEMORIAM

It is with a heavy heart that we announce the death of **Melissa Quin McDougall**, who passed away suddenly on August 23, 2020 in Chatsworth, California.

Melissa was a graduate student working with Dr. Maret Traber at the Linus Pauling Institute from 2011-2017.

Melissa's groundbreaking work at the Institute revolved around the previously uncharacterized effects of vitamin E deficiency on embryonic development. Using zebrafish as a model, she demonstrated the initial consequences of low vitamin E status in the developing embryo, including dramatic effects on survival and overall health.

In 2017, Melissa graduated with her PhD in Molecular Nutrition from Oregon State University and became a registered dietitian nutritionist (RDN). She went on to complete postdoctoral work at Cornell University. In 2019, she was hired by Pharmavite as a nutrition scientist.

As a child, Melissa loved to swim. She participated in synchronized swimming and swam competitively through high school. She loved the theater and had roles in numerous high school productions. Her passions were her family, learning, outdoor activities, and protecting our environment.

Her colleagues at the Institute remember Melissa as an extremely talented scientist and a phenomenal scholar. Melissa's enthusiasm for her work was exemplary. She will be missed by all who had the pleasure of working with her.

In Melissa's memory, her family asks that everyone commits to learning something new and to being a responsible steward of our Earth's resources. They also ask that you please consider making a contribution to one of Melissa's favorite charities: Friends of The Earth; Action for Healthy Kids, Inc.; Feeding America; or your local food bank.

SPONSOR HIGHLIGHT

Dr. Donald Reed, a renowned scientist in antioxidant metabolism, was the first interim director of the Linus Pauling Institute at Oregon State University in 1996, while the Institute was moving from Palo Alto, California to Corvallis, Oregon. He has been a good friend of the Institute ever since.

In 2015, Dr. Reed established the **Caron and Donald Reed Fellowship Fund**. Recognizing that students need extra support at the beginning and end of their graduate careers, Dr. Reed wishes to gift them independence from financial concerns. As a researcher, he appreciates how his fellowship keeps research progressing as students finish their degree requirements.

We are highlighting this important program to encourage others to also support this invaluable graduate fellowship. If supporting young scientists is your passion, please join Dr. Reed in contributing to this fellowship program at <https://lpi.pub/ReedFellows>



“The first year in a graduate student’s career is a very important time. I want to give them the time to learn about the important research at the Linus Pauling Institute without financial worries.”

—Donald Reed, PhD

READER QUESTION

Q. In her webinar on zinc, Dr. Emily Ho said that phytate from seeds can be a problem. I eat pumpkin seeds to get more zinc. What can I do to reduce the effects of phytate?

— From D.B. via email

A. Phytates found in nuts, seeds, grains, and legumes can bind minerals and reduce their absorption in your intestine. One way of reducing phytate content in these foods is to soak them in water. However, most people don't want to eat soggy nuts or seeds, so you can dry or re-roast them afterward. Sprouted foods also are a good source of zinc with minimal amounts of phytate.

Instead of doing the extra work, you could just add another serving of the seeds to your routine. Phytate does not prevent absorption of all zinc, just a fraction of it. The more zinc sources you have in your diet, the less you need to worry about phytate.

— From Dr. Emily Ho

LPI STUDENTS

Recent Graduates

Three graduate students from the Linus Pauling Institute recently defended their PhD dissertations. We wish them great success in the years ahead.



Luying Chen

van Breemen laboratory



Joseph Meeuwssen

Beckman laboratory



Daniel Nosal

van Breemen laboratory

Continued from cover

Your body usually produces adequate amounts of lipoic acid to meet your metabolic needs.

However, something different happens when lipoic acid is taken as a supplement. Often marketed as alpha-lipoic acid, the molecule is found in a free (not enzyme-bound) form. This allows it to take other actions in the body, like stimulating certain types of cell signaling.

Lipoic acid supplements have been shown to stimulate glucose metabolism, antioxidant defenses, and anti-inflammatory responses. For these reasons, lipoic acid has been investigated as a complementary treatment for people with diabetes, heart disease, and age-related cognitive decline.

Changing focus

Over the last few decades, a number of clinical studies on lipoic acid have been completed. However, some researchers – including the Linus Pauling Institute’s resident expert on lipoic acid, Dr. Tory Hagen (see highlight on page 5) – feel that these study designs left some room for improvement.

Lipoic acid trials often focus on people who have a disease diagnosis, such as diabetes. However, the results of those trials are difficult to extrapolate to the general population.

In other words, previous studies do not demonstrate that lipoic acid could help people who do not have pre-existing conditions.

Another issue is the formulation of the supplement. In many research studies, lipoic acid is provided as a racemic mixture that contains two forms of the molecule. This is also the most common form in the marketplace.

However, Dr. Hagen and others advocate using only the *R*-form of lipoic acid because it is the form that is found in nature. There is some evidence that the *R*-form of lipoic acid is better absorbed, has fewer gastrointestinal side effects, and may act on target tissues better than the *S*-form of the molecule.

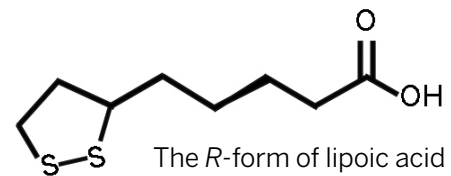
On the other hand, the racemic mixture is less expensive and more stable in a supplement form.

New study, new revelations

Dr. Balz Frei, the former Director of the Linus Pauling Institute, led a team of experts that included Dr. Hagen to design and conduct a better clinical trial on lipoic acid. Recently published in *The Journal of Nutrition*, this study was a joint effort with Oregon Health & Science University.

The study focused on people who were both overweight and had high triglyceride levels without a diagnosed disease. During the study, participants took either 600 mg of *R*-lipoic acid or a matched placebo daily for 24 weeks.

The primary objective of the trial was to see if lipoic acid supplementation could reduce the amount of triglycerides in the blood. In the end, that did not happen – blood triglyceride levels did not change dramatically in either group.



However, many participants taking lipoic acid supplements lost weight during the trial. The lipoic acid group lost 1.7% of their body weight, as compared to the placebo group that did not lose weight.

While that does not appear to be a dramatic weight loss, that number conceals some of the remarkable weight loss seen in some of the study’s subgroups. For example, in female study participants, a 9% reduction in body fat was noted in the lipoic acid group when compared to the placebo group.

The group taking lipoic acid supplements experienced some other benefits. For example, this group had lower urinary F_2 -isoprostane levels, suggesting that they were experiencing less oxidative stress. The participants taking lipoic acid also had lower levels of a protein biomarker called ICAM1, suggesting lower inflammation levels.

Racemic mixtures are 50:50 combinations of the *R*- and *S*- forms of a molecule. For lipoic acid supplements, the racemic mixture is simply called “alpha lipoic acid.” Supplements that contain only the *R*-form of lipoic acid will be labeled as such.

The future of lipoic acid

"Lipoic acid supplements can be beneficial," said Hagen, who served as a lead author on the published study. "But like many dietary supplements, it's possible that these benefits will not be seen by everyone taking them – it is not a perfect panacea."

"Not everyone in the lipoic acid group showed weight loss during the trial," added Dr. Gerd Bobe, principal investigator at the Linus Pauling Institute and one of the study's statisticians. "While this was clearly an improvement over taking a placebo, our study suggests that lipoic acid supplementation has its limitations."

The benefits of lipoic acid supplements do come with drawbacks. In the clinical trial, some of the participants reported frequent heartburn or stomach aches. These symptoms are not uncommon with lipoic acid supplements, especially when taking large doses on an empty stomach.

Cost can also be an issue. Lipoic acid supplements, especially *R*-lipoic acid supplements, can be quite expensive. It can be a costly endeavor to find out that the supplements do not work out for you.

"We need to continue our studies exploring the mechanisms behind the benefits," concluded Hagen. "Otherwise we'll never know why lipoic acid might work for some people and not others."

"Ultimately our goal is to create a more targeted approach to lipoic acid supplementation in the future." 🍷

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RESEARCHER HIGHLIGHT

TORY M. HAGEN, PHD

For nearly three decades, Dr. Tory Hagen has worked to understand how lipoic acid supplements act in the body. His journey began under the mentorship of Dr. Bruce Ames at the University of California, Berkeley. Together, Drs. Hagen and Ames started on the path to understand how and why we age with the hope of learning how to live longer and feel better.

After joining to the Institute in 1998, Dr. Hagen and his team consistently demonstrated the benefits of lipoic acid supplementation for older animals. From maintaining cellular antioxidant levels to cell-signaling pathways, each study found similar results: lipoic acid could make old animals appear like young animals, at least biochemically.

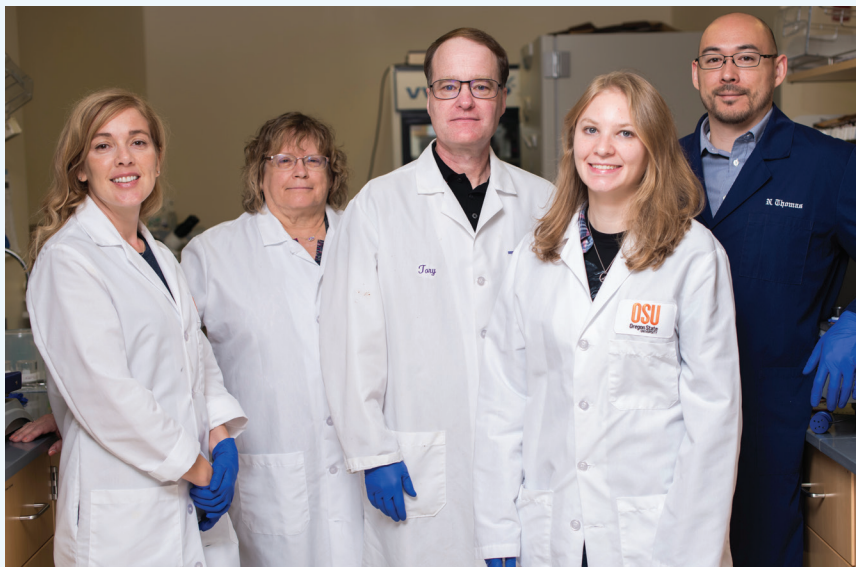
In recent years, Dr. Hagen's focus has transitioned into human studies. Although there are some clinical data demonstrating the utility of lipoic acid in the treatment of diabetes, there is little

evidence for lipoic acid supplements in healthy older adults.

As more research emerges, Dr. Hagen hopes to see an increase in funding for trials focused on older adults. Ultimately, he aims to discover how lipoic acid and other dietary supplements may aid our pursuit of healthy aging.

The Hagen Lab group in 2019: (L-R) Dr. Kate Shay, Judy Butler, Dr. Tory Hagen, Amanda Radke, and Dr. Nicholas Thomas.

Photo Credit: Hannah O'Leary



IMMUNE SUPPORT:

Can multivitamins help?

Why do older adults face an increased risk for micronutrient deficiencies? See the Micronutrient Information Center for more information: <http://lpi.pub/OlderAdults>

As we age, our risk for vitamin and mineral deficiencies increases. While the immune system is complicated, there is no doubt that proper nutrition plays a key role in the immune function.

Research suggests that more than one-third of older adults in the United States, Canada, and Europe falls short of the dietary requirements for at least one micronutrient. These shortfalls can have a big influence on how the body responds to infections.

With this in mind, many have postulated that taking a daily multivitamin supplement might help support the immune system. This may be a low-cost strategy to lower the risk of serious respiratory illness, especially if the supplement contains micronutrients critical to immune function like vitamin C, vitamin D, and zinc.

Dr. Adrian Gombart at the Linus Pauling Institute tested the efficacy of this idea in a recent clinical trial, published last year in the journal *Nutrients*.

Utilizing an over-the-counter multivitamin supplement marketed for immune support, the trial involved 42 healthy older adults, ages 55 to 75 years.

During the trial, study participants refrained from consuming large amounts of zinc, vitamin D, and vitamin C from food and avoided taking any vitamin or mineral supplements. Half of the study participants took the multivitamin once per day, while the other half received an inactive placebo.

Before and after the 12-week study, blood and saliva were collected from participants to examine nutrient levels and biomarkers of immune status. Participants also documented any illnesses that occurred during the study.


Unsurprisingly, the researchers found that blood concentrations of vitamin C and zinc increased in the multivitamin group and not in the placebo group. The multivitamin group also showed fewer symptoms of illness, reported less severe illness, and had shorter duration of illness when compared to the placebo group.

“Although the study was limited to self-reported illness, the differences were striking,” Dr. Gombart noted. “While a similar number of participants from each group reported symptoms, days of sickness in the supplement group were effectively cut in half.”

The research team also measured other immune system indicators to explain these results, but no differences were found.

Overall, this study is encouraging and a timely validation of Dr. Linus Pauling’s message about micronutrients and the immune system. He often advocated for finding the optimal amounts of vitamin C and other nutrients to support the immune system.

Although Dr. Gombart cautions that his study was relatively small, it provides excellent groundwork for new and larger clinical trials to explore the role of multivitamins in the immune system.

Bayer Consumer Care AG funded the study through an Institution Initiated Research grant and provided the supplements used in the study. Bayer had no role in the study’s design, execution, or data interpretation. 

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Photo Credit: Hannah O’Leary



VITAMIN D AND COVID-19:

What you need to know

As the COVID-19 pandemic continues to spread across the world, vitamin D deficiency has emerged as a possible factor in the disease. This is not surprising as vitamin D plays an important role in maintaining a healthy immune system. Vitamin D will likely gain more attention as the winter progresses, a time when respiratory infections are common and vitamin D levels can be low.

At the Linus Pauling Institute, we have been reviewing the available evidence on vitamin D and COVID-19 since the pandemic began. As your source of scientifically accurate information on vitamin D and health, below we present a brief evaluation of the research studies on vitamin D and COVID-19 to help guide you through the pandemic.

How do we know vitamin D is important in COVID-19?

Before the pandemic, we knew that people with low blood concentrations of vitamin D had an increased risk of severe respiratory infection. The current studies simply reinforce that relationship: people hospitalized for COVID-19 also tend to have low blood concentrations of vitamin D.

Vitamin D deficiency appears to also be associated with increased COVID-19 severity, evidenced by advanced progression to pneumonia, increased need for ventilatory support, and a higher mortality risk.

Who is at risk for vitamin D deficiency?

Blood vitamin D concentrations are lower in people who live in higher latitudes, have dark skin, do not spend time out in the sun (or often wear sunblock), are overweight, or simply do not consume enough through their diet. Older adults can also have poor vitamin D status because they do not synthesize it efficiently.

Many experts agree that blood vitamin D concentrations above 30 ng/mL are preferred. People who take regular vitamin D supplements are more likely to have blood vitamin D levels above this threshold, even if they fall into one of the risk groups above.

Will high vitamin D levels prevent COVID-19?

No. Vitamin D is not a shield against viruses – it is only one of many factors that impact your immune response.

In our review of the literature, we noted that there were still people diagnosed with COVID-19 even though their blood levels of vitamin D were above 30 ng/mL or regularly took vitamin D supplements.



What is missing from this information?

Since vaccines rely on a healthy immune response, low vitamin D levels could reduce the effectiveness of a vaccination. We do not yet know if there are any effects of vitamin D levels on mRNA vaccine's efficacy, specifically.

Although vitamin D supplements are of interest in treating COVID-19, there is still very little evidence that taking vitamin D supplements after you get sick will be beneficial. Getting an appropriate amount of vitamin D prior to an infection seems the best course of action.


Currently, there are some clinical trials focused on vitamin D as a COVID-19 treatment, but those data will not be available for many more months.

The takeaway

Vitamin D is an important factor that influences the immune response. The COVID-19 pandemic has only underscored this relationship. Since vitamin D status is associated with disease severity, it is more important than ever to keep your vitamin D levels above 30 ng/mL.

To check your vitamin D levels, blood testing can be done through your physician. However, in the midst of this public health crisis, it is not always feasible to travel to a clinic or hospital to get your blood drawn. Other options for getting blood vitamin D levels checked include at-home blood tests or mobile blood draw services.

In the absence of testing, you still avoid vitamin D deficiency. The Linus Pauling Institute recommends that all adults take 2,000 IU (50 µg) of supplemental vitamin D each day. Daily doses up to 4,000 IU (100 µg) of supplemental vitamin D are generally considered safe for adults.

For detailed information about the published studies on vitamin D and COVID-19, see the Micronutrient Information Center at: <http://lpi.pub/vitDCOVID-19> 



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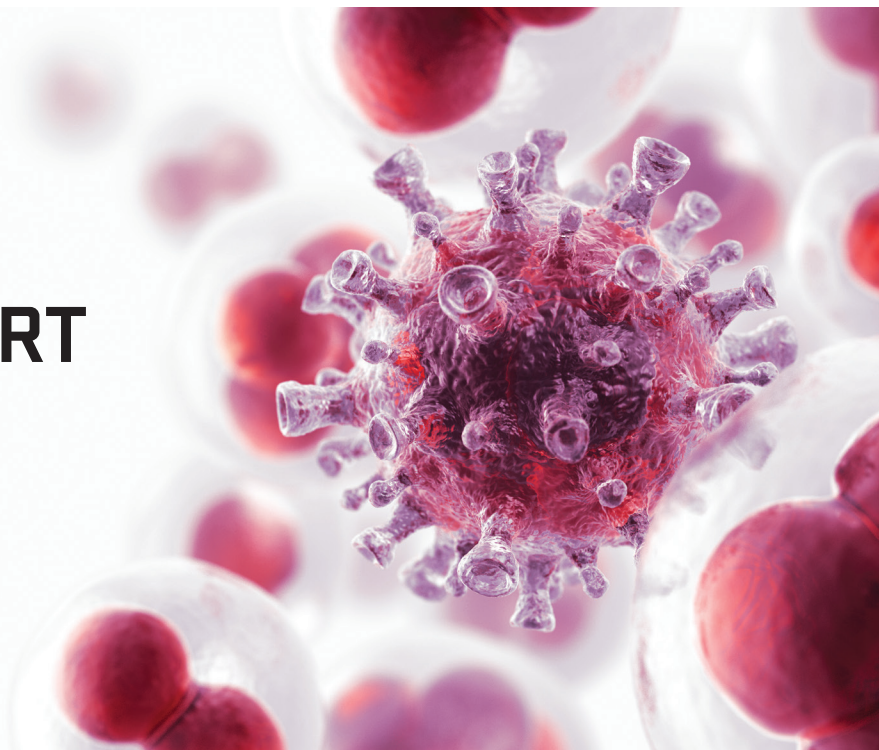
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MULTIVITAMINS: IMPORTANT SUPPORT FOR YOUR IMMUNE SYSTEM?



INSIDE: THE RESULTS OF THE LINUS PAULING INSTITUTE'S LATEST CLINICAL TRIAL