



# Small Mineral, Big Promise

*The New Case for Lithium in Brain Health*

Last August, a research paper published in the journal *Nature* by scientists from Harvard University Medical School generated a lot of buzz. Their study found that a particular form of lithium, called lithium orotate, slowed cognitive decline and disease progression and reversed Alzheimer's disease (AD) in mice.

It's no wonder the lithium study made headlines. While there are some approved disease-modifying treatments for people with mild cognitive impairment or early-stage AD, their effect is modest and they come with a risk of brain bleeding and swelling. Despite decades of significant research efforts, there is still no cure for AD.

### COULD TAKING LITHIUM OROTATE AS A SUPPLEMENT REALLY BE AN EFFECTIVE TREATMENT FOR NOT JUST SLOWING AND PREVENTING AD PROGRESSION BUT ALSO FOR REVERSING ESTABLISHED DISEASE IN PEOPLE?

We reviewed the evidence and spoke to a scientist who conducts lithium research to put the study findings in context and learn more about the pros and cons of lithium orotate supplementation.

## ABOUT LITHIUM

Lithium is a naturally occurring metal found in soil, rocks, seawater, and mineral springs. Many high-tech products with rechargeable batteries, such as cell phones and electric cars, contain lithium.

Lithium is found in trace amounts in many different foods. Tomatoes, potatoes, cereals, cabbage, and some types of mineral water are the best food sources, according to a review published in *Biological Trace Element Research* in July 2018. The amount varies by geographic area where food is grown. Lithium is not listed on product nutrition labels or on tables of recommended nutrients published by Canadian or U.S. health authorities, so it's difficult to know how much we consume.

The mood-altering benefits of lithium have been known since at least the 19th century. It was first used to treat mania in 1871 at the Bellevue Hospital Medical College in New York City.

Since 1949, a prescription form of lithium called lithium carbonate has been used as a treatment for bipolar disorder, especially for alleviating acute mania and manic episodes. Lithium carbonate therapy is also known to reduce the risk of suicide in people living with bipolar disorder and schizophrenia.

It's hard to imagine today that an early recipe of the soft drink 7Up contained lithium. Launched in 1929 as Bib-Label Lithiated Lemon-Lime Soda, it was marketed with the slogan "Dispels hangovers...takes the 'ouch' out of grouch."

The drink was later renamed 7Up Lithiated Lemon Soda, and then just 7UP. The "7" in the brand name was thought to refer to the atomic weight of lithium or the number of ingredients, and the "up" alluded to its mood-lifting benefit. 7UP has not contained lithium since 1948.

## THE HARVARD STUDY

The Harvard study was conducted by a team of scientists led by Dr. Bruce Yankner, professor of genetics and neurology in the Blavatnik Institute at Harvard Medical School. They began by measuring trace levels of about 30 metals in brain tissue and blood donated from people who were cognitively healthy, those who had mild cognitive impairment, and those with advanced AD.

Lithium was present in the brain tissue of all groups, including healthy people who had never taken it as a treatment. However, levels varied greatly between groups: cognitively healthy donors had much higher lithium levels than those with mild cognitive impairment or advanced AD.

The researchers replicated their findings using samples from multiple brain banks. These findings also tracked with population studies, such as a Danish population study published in *JAMA Psychiatry* in 2017 that found a higher, long-term exposure to lithium in drinking water was associated with a lower incidence of AD and vascular dementia.

Next, Dr. Yankner and his team fed the mice a lithium-restricted diet to mimic the lower levels they had observed in donors who had AD. Restricting lithium resulted in neuroinflammation and accelerated the formation of amyloid plaques and structures resembling neurofibrillary tangles in the mice.

Lithium depletion also impaired the ability of immune cells, called microglia, to degrade amyloid, and also caused a loss of synapses, axons, and myelin sheath covering in neurons - all clear signs of AD. Finally, lowering lithium altered the activity of genes associated with AD risk, including *APOE*.

What happened next was even more surprising. →

## PROVIDING THE MICE WITH LITHIUM OROTATE IN THEIR DRINKING WATER REVERSED DISEASE-RELATED BRAIN DAMAGE AND RESTORED MEMORY FUNCTION, EVEN IN OLDER MICE WITH FEATURES OF ADVANCED AD.

Additionally, the researchers found that maintaining stable lithium levels in early life prevented healthy mice from developing AD.

"I was very excited to see the Harvard study results. They have shone a bright light on lithium orotate that I hope will encourage more research," said Dr. Lane Bekar, associate professor of anatomy, physiology, and pharmacology at the University of Saskatchewan's College of Medicine.

## LITHIUM CARBONATE VS. LITHIUM OROTATE

Dr. Bekar has studied lithium orotate in mouse models to understand how and why it holds promise as a better option than lithium carbonate for brain health and the treatment of brain disorders. He explained that there is a huge difference between lithium carbonate and lithium orotate.

"Lithium carbonate, the prescription medication, is given at high doses to deliver a sufficient quantity to the brain. When lithium carbonate dissolves in the stomach, the lithium enters most cells in the body," he said.

"People taking lithium carbonate are monitored closely with blood work because it has a narrow therapeutic window. When the dose is too low, there are no mood stabilization benefits. When it's too high, people experience nausea, tremors, seizures, and potentially life-threatening kidney and thyroid toxicity," said Dr. Bekar.

"By contrast, lithium orotate stays bound to its carrier, the orotate component, that can actively cross the blood-brain barrier. When brain cells incorporate the orotate as part of their usual biochemistry, the lithium is released."

**LITHIUM OROTATE, THEREFORE, CAN BE TAKEN AT MUCH LOWER DOSES THAN LITHIUM CARBONATE, ABOUT 100 OR 1,000 TIMES LOWER, WHICH HAVE NOT BEEN ASSOCIATED WITH ANY TOXICITIES, ACCORDING TO NUMEROUS STUDIES TO DATE.**

Dr. Bekar's work, published in 2023 in *Journal of Psychiatric Research*, showed how lithium orotate reaches brain cells more selectively than lithium carbonate in mouse models of mania. "After lithium is liberated inside brain cells, it targets a

protein called GSK3-beta somewhat selectively, like throwing a dart. By contrast, lithium carbonate is more like dumping a big bucket of lithium in the body and hoping some will hit GSK3-beta in the brain," he explained.

GSK3-beta is involved in AD disease processes. Several cell and animal studies have shown that lithium treatment can decrease amyloid beta plaques and tau tangles, in part by inhibiting GSK3-beta.

## SHOULD YOU TAKE LITHIUM OROTATE?

Lithium orotate is sold as an over-the-counter supplement online and at pharmacies in the United States. While it is possible to find some online retailers in Canada, Health Canada issued a warning in 2017 that lithium orotate sold online is unauthorized and may pose serious health risks because it has not been assessed for safety, effectiveness, or quality.

Part of the challenge of determining whether lithium orotate supplementation is needed is that levels are hard to measure with current methods. "The available clinical test for lithium identifies lithium carbonate, which is detectable because it's given in high doses. You would have to take a lot of lithium orotate daily for it to elevate blood levels enough to be detectable in the currently available clinical blood test. Mineral analysis in hair may be a more sensitive and accessible option," said Dr. Bekar. "The biggest contributors to lithium deficiency are caffeine and a high-salt diet. As a diuretic, caffeine increases the rate at which the body excretes lithium."

***Salt and lithium compete for the same transporters, so with a high-salt diet, more lithium gets excreted and less gets where it needs to go.***

After the news about lithium orotate as a potential treatment for AD broke last August, there were several social media posts on the topic. People worried about developing dementia or

According to the Alzheimer's Association, nearly three in five Americans said they would accept moderate or very high levels of risk with taking medication to slow the progression of AD in its early stages.

caring for others living with dementia posted questions and touted its benefits. Here is a sample of some Facebook posts:

*My loved one is my 85-year-old mum with mixed dementia. I've been reading about the benefits of lithium orotate for Alzheimer's patients and just wondered if anyone here has their loved one on lithium and their feedback on it.*

*My mom recently died of Alzheimer's after battling it for 10 years. Her father also died of Alzheimer's in his early 60s. I recently found out my APOE status is 3/4, which increases my risk. Additionally, I did a hair mineral analysis, and my lithium level was ZERO. So, I started taking 10 mg of lithium orotate nightly. Research I've seen says that lithium orotate at a low dose (5-10 mg) is very safe. I'm just not going to take a chance, and 3-5 years or longer for clinical trials is too long to wait. I'm already in my mid-60s, and that's when my mom was diagnosed. I'm doing it.*

*Certain types of lithium, in much smaller doses, are actually available as a supplement, and they are used for very different reasons than "old school" lithium. While the dosages are tiny, the potential benefits are not exactly minor (unless you consider brain health and longevity inconsequential!). I've been taking lithium faithfully for 50 years - it's the one supplement I won't miss taking!*

Dr. Yankner advised caution about the implications of his study. "You have to be careful about extrapolating from mouse models, and you never know until you try it in a controlled human trial. But so far, the results are very encouraging," he said in a Harvard Medical School press release.

On a personal note, Dr. Bekar shared that he takes lithium orotate (5 mg/day), and while he is optimistic about lithium orotate's potential, he is also cautious.

"Studies to date have not shown any toxicity at lower doses. However, I'm not a clinician, so I can't recommend whether people should take it."

**“There is an urgent need for more basic and clinical studies investigating its efficacy, especially as more and more people are already taking it as a nutraceutical.”**

## STAY TUNED

Researchers at Massachusetts General Hospital initiated a Phase 2 clinical trial of AL001, a product made by Alzamend Neuro, in April 2025. AL001 is a proprietary formulation described as a combination of a modest amount of lithium together with proline and salicylate, according to a press release from the hospital.

The investigators will compare brain lithium levels between AL001 and lithium carbonate in healthy people and those with AD. They will measure brain lithium levels using a head coil created by Tesla Dynamic Coils BV.

The product may deliver lithium more effectively to the brain, minimizing kidney and thyroid side effects associated with lithium carbonate and potentially eliminating the need for drug monitoring.

While AL001 contains a different format of lithium than lithium orotate, the results of this study may advance the field.

Pending positive outcomes from more research, Dr. Bekar sees a future where a microdose of lithium orotate could be included in multivitamin and mineral supplements, similar to vitamin D.

*If you are considering taking lithium orotate or giving it to a loved one, speak to a doctor first to make sure it's appropriate. 🌱*

