

Lithium Orotate: Mood, Alzheimer's, and Aging

I read a lot of studies on health and genetics, and I keep finding research on the mineral lithium popping up. Topics such as circadian rhythm dysfunction, Alzheimer's disease, telomere length, type 2 diabetes, and obesity... all linking to lithium?

The rest of this article explains the research showing the importance of this mineral in our health and longevity.

There is a stigma, at least in my mind, around lithium, and I've hesitated at times to write about it. Funny, isn't it, that no one has hesitation about talking about other minerals such as magnesium or potassium. I'll let you read through the research overview and decide for yourself.

Contents:

Recent scientific research on lithium and health

Is Lithium Orotate the same as lithium (prescription)?

Safety studies specific to lithium orotate:

Research on Alzheimer's Disease and Lithium:

Research studies on lithium and Alzheimer's disease:

Telomeres, aging, and lithium:

The anti-inflammatory action of lithium:

Obesity, Diabetes, Thyroid, and Natural Lithium:

Suicide levels decrease as natural lithium levels increase:

How does lithium work in the brain?

GSK-3 β and Circadian Rhythm:

Prevention of lead toxicity:
Toxicity of lithium:
Side effects of Lithium Orotate:
Lifhacks:
Related Articles and Genes:

Recent scientific research on lithium and health

Minerals are needed by the body in the right amount, and it is important to look at the safety and health effects before supplementing with any mineral.

Lithium is a mineral that can be naturally found in food and drinking water. It is also available in low dose supplemental form (lithium orotate).

Is Lithium Orotate the same as lithium (prescription)?

First, let's look at the different types and amounts of lithium being referenced in the research studies. Quite a range exists – from natural levels found in water to high levels in prescription meds.

For a lot of people, lithium brings to mind the prescription medication for bipolar disorder. This is almost always in the form of lithium carbonate.

Prescription doses of **lithium carbonate** are around 900-1200 mg/day, although this can vary based on the individual. For lithium carbonate, there is about 18.8 mg of elemental lithium per 100mg of lithium carbonate. Thus, a 900mg dose would give about **170 mg elemental lithium**.[\[ref\]](#)

Lithium orotate usually comes as a 120 mg supplement giving about **5mg of elemental lithium**. Some companies also offer 10mg or 20 mg supplements doseages.

The amount of **natural lithium that we get in foods and drinking water** varies based on the mineral content of the soil, with estimates of up to **3 mg/day**.

A *provisional* recommended daily allowance (RDA) of 1 mg/day is recommended.[\[ref\]](#)

Breaking down the numbers: For an average person, a standard lithium orotate (5mg elemental lithium) supplement would be around twice the normal daily consumption from food and water, while the prescription dosages are closer to 80 to 100 times normal daily intake.

Safety studies specific to lithium orotate:

A 2021 study investigated the safety of using lithium orotate as a supplement. The researchers found that there were no genotoxic effects, meaning that it won't damage DNA. In this animal study, researchers found no adverse effects and no organ damage. The highest dose tested in animals was 400 mg/kg/day with no observable adverse effects (NOAEL).[\[ref\]](#)

Research on Alzheimer's Disease and Lithium:

A 2017 study investigated Alzheimer's rates and natural lithium levels in the drinking water in Texas.[\[ref\]](#) In [an article about the study](#) (much quicker read than the full paper), the lead author of the study explains the findings.

Essentially, water samples from almost all of the counties in Texas were tested for their **natural levels of the mineral lithium**, which varies depending on the concentration in rock and soil.

Alzheimer's rates have risen everywhere, but the researchers found that Texas counties with higher levels of lithium in the groundwater had less of an increase in Alzheimer's rates compared with counties that had lower levels of lithium.

In other words, the epidemiology here points to lithium in the ground water being protective against Alzheimer's. At least slightly.

The study results are not a total surprise since previous studies linked lithium to a decreased risk of dementia, but it is a great confirmation at a large scale population level. Additionally, observational studies show patients taking prescription lithium are at a lower risk of dementia.

Research studies on lithium and Alzheimer's disease:

A number of studies have looked at the effect of very low doses of lithium as an Alzheimer's treatment or prevention option.

- A 2015 review in the Journal of Alzheimer's Disease analyzed the data from three **randomized placebo-controlled clinical trials** of lithium for treating Alzheimer's patients. The trials found that lithium "**significantly decreased cognitive decline as compared to placebo**".[\[ref\]](#)
- An October 2017 article in JAMA Psychiatry details a nationwide study in Denmark on the exposure to lithium in drinking water and the incidences of dementia. This was a large study, with 73,000+ dementia patients and 733,000+ people without dementia as the control. The study found a **decreased rate of dementia** in people with naturally higher levels of lithium in their water (measured since 1986).[\[ref\]](#)[\[ref\]](#)
- A March 2018 animal study looked into the **mechanisms of how** lithium chloride lowers the risk of Alzheimer's. It found that **lithium increased the clearance of soluble β -amyloid** from the brain. In mice genetically bred to be a model of human Alzheimer's, lithium chloride restored the clearance of soluble β -amyloid to the levels of normal mice. One big thing to note from this study is that lithium chloride did not affect β -amyloid that had formed plaque already.[\[ref\]](#)
- A study in 2015 looked at the effects of **microdoses of lithium** on a mouse model of Alzheimer's disease. The study found small doses of lithium carbonate in the drinking water of mice carrying the genes for Alzheimer's disease caused a "decreased number of senile plaques, no neuronal loss in cortex and hippocampus and increased BDNF density in the cortex when compared to non-treated transgenic mice." This was a follow-up study to the human study in 2013 which showed that microdoses of **lithium stopped the cognitive decline** in Alzheimer's patients.[\[ref\]](#)[\[ref\]](#)

You may be wondering at this point *why aren't doctors handing out low dose lithium to everyone at risk for Alzheimer's*.

I think the quick answer is that it isn't the 'standard of care' with enough clinical trials backing it up. Lithium is a cheap, natural mineral with no money in it for funding the clinical trials. There seems to be a couple of 'novel' low-dose formulations in the works by pharmaceutical companies, though.[\[ref\]](#)[\[ref\]](#)[\[ref\]](#)

Telomeres, aging, and lithium:

Telomeres are the sequences of DNA found at the ends of each chromosome. This sequence protects the ends of the chromosome from deterioration.

An example often given for telomeres is to think of them like the plastic on the end of shoelaces that protects the shoelace from fraying.

When cells undergo cellular reproduction (mitosis), a little bit of the telomere shortens. Thus, **telomere length** is considered to be a **biomarker of cellular aging**. Shorter telomere length has associations with several age-related chronic diseases including Alzheimer's.

A recent transgenic mouse study found **lithium carbonate treatment leads to longer telomere** length in mice bred to have Alzheimer's disease.[\[ref\]](#) Interestingly, the normal mice had no effect on telomere length from lithium, the telomere lengthening was only found in the Alzheimer's mice. Couple this information with a meta-analysis showing that Alzheimer's patients have shorter telomeres.[\[ref\]](#)

A human study looked at telomere length in patients with bipolar disorder. The study found that patients with bipolar disorder (not on lithium) and their relatives had shorter telomeres lengths than healthy, unrelated people. More interestingly, patients with bipolar disorder treated with lithium had longer telomere lengths than non-lithium-treated patients with bipolar disorder as well as relatives of bipolar patients.[\[ref\]](#)

Telomere length is a **new field of investigation** for researchers looking into so many different topics of aging, longevity, and disease. I don't think the handful of studies on telomere lengthening from lithium can really lead to a conclusion on aging. But I look forward to seeing what future studies tell us on the topic.

The anti-inflammatory action of lithium:

Lithium exerts anti-inflammatory effects on the body — as well as pro-inflammatory effects under specific conditions.

Since the 1970s, it's been known that lithium inhibits prostaglandin synthesis and COX2 in some parts of the brain. While there is some debate on the topic, the majority of studies also point to lithium decreasing the production of **TNF- α** , a pro-inflammatory

cytokine.[ref]

Anti-inflammatory stack: A recent cell study looked at the potential of lithium plus caffeine, theobromine, and catechin on the innate immune system and inflammation. The results showed that stacking lithium with caffeine, theobromine, and catechin was more effective as an anti-inflammatory than using them separately.[ref] Theobromine is found in chocolate and tea, and catechins are also found in tea.

Another recent study looked at the anti-inflammatory effects of lithium on cells containing the SOD2 genetic variant rs4880. The study found that those with rs4880 alanine allele (G/G for 23andMe) had more of an anti-inflammatory response than those with the valine allele (A/A for 23andMe).[ref] This was a cell study though, so it is hard to know how well this translates to the whole body.

Members: [Log in and select your data file](#) Not a member? [Join now](#).

Check your genetic data for **rs4880** (23andMe v4, v5; AncestryDNA):

- G/G: more of an anti-inflammatory response from low dose lithium
- A/G: typical response
- A/A: typical response

Members: *Your genotype for rs4880 is —.*

Obesity, Diabetes, Thyroid, and Natural Lithium:

What surprised me about the Nov. 2017 study about Alzheimer's was that Texas counties with higher levels of lithium in their water also had lower levels of obesity and diabetes.[ref] I was surprised by this because one of the side effects of long-term, high-dose lithium carbonate usage is an increased risk of hypothyroidism and possible weight gain.

Part of the explanation for the high levels of lithium in water correlating to lower levels of obesity and diabetes may be due to the positive effects on circadian rhythm. Another possible connection between lithium, obesity, and T2D may be an effect on blood glucose levels. In mice, certain levels of lithium reduced non-fasting blood glucose levels.[\[ref\]](#)

Suicide levels decrease as natural lithium levels increase:

A number of studies have investigated the link between lithium in the drinking water and its effect on overall mood — such as aggression (violent crime rate) and suicide.

A **meta-analysis of 15 different studies** shows that areas with higher lithium concentrations in their drinking water have lower suicide rates.[\[ref\]](#) The meta-analysis concludes:

“This synthesis of ecological studies, which are subject to the ecological fallacy/bias, supports the hypothesis that there is a protective (or inverse) association between lithium intakes from public drinking water and suicide mortality at the population level. Naturally occurring lithium in drinking water may have the potential to reduce the risk of suicide and may possibly help in mood stabilisation, particularly in populations with relatively high suicide rates and geographical areas with a greater range of lithium concentration in the drinking water.”

Related article: [Lithium orotate, genetics, vitamin B12, and mood](#)

How does lithium work in the brain?

For a long time, exactly how lithium worked for bipolar patients was not understood. (This is unsurprising since quite a few psychiatric medications were used for decades without fully understanding how they work – or don’t work – for people.)

Studies over the past decade or two have shed light on the neurobiological mechanisms of lithium. Genetic studies have further increased that knowledge.

One effect of chronic, low-dose lithium is an **increase in BDNF**, which is a protein that promotes the growth of nerve cells.[\[ref\]](#)

The American Chemical Society published a great overview of the neuroprotective effects of lithium.[\[ref\]](#) One of the effects of lithium is its **inhibition of GSK-3 β (glycogen synthase kinase-3 beta)**, which is involved in neuronal cell development and energy metabolism. Genetic mutations of GSK-3 β increase the risk of bipolar disease.

Lithium ions compete with sodium and magnesium ions in the body for binding sites in certain circumstances. Researchers think that the inhibitory effect on GSK-3 β might be due, in part, to lithium binding to a site normally occupied by magnesium. Lithium isn't regulated the way other minerals are in the body, and some researchers think that at higher levels, it can take the place of other minerals.[\[ref\]](#)

One action of GSK-3 β is its inhibition of glycogen synthase, which is an enzyme involved in the reaction that takes excess glucose and turns it into glycogen for storage. Thus inhibiting GSK-3 β increases glycogen synthesis and increases insulin sensitivity.[\[ref\]](#)[\[ref\]](#)

GSK-3 β and Circadian Rhythm:

Our body's core circadian clock runs by a couple of core genes expressed during the day and a couple of core circadian genes that rise at night. It is this daily rise and fall of gene expression that drives our internal daily cycles of waking and sleeping, body temperature changes, hormone rhythms, and energy metabolism. This is referred to as your circadian rhythm.

GSK-3 β is involved in phosphorylation of both the daytime and nighttime **core circadian genes**.

Genetic variants that change our circadian rhythm have links with an increased risk for bipolar disorder.

People with bipolar disorder who respond well to lithium therapy have changes in their circadian gene expression when they take lithium.[\[ref\]](#)[\[ref\]](#)[\[ref\]](#)[\[ref\]](#)

The link between Alzheimer's disease and circadian disruption is strong, so lithium may play a role here also.[\[ref\]](#)

Prevention of lead toxicity:

A recent article hypothesized that some of the benefits reported for higher lithium levels in the drinking water (lower suicide rate, lower homicide, and crime rates) could be due to lithium mitigating the effects of lead toxicity. "Animal studies demonstrated that lithium pre-treatment mitigates lead toxicity."[\[ref\]](#)

Toxicity of lithium:

If you have questions on any mineral supplement, talk with your doctor or health care provider for medical advice.

Many consider lithium to be an **essential trace element**. Completely eliminating lithium from the body causes a decline in fertility, higher mortality rates, and behavioral abnormalities.[\[ref\]](#)

But, like all substances, there is an upper limit on what you can take.

Patients taking lithium carbonate or lithium chloride for mood stabilization show a variety of side effects, depending on dosing. (e.g. around 170 mg elemental lithium). Most patients taking prescription lithium carbonate need blood tests done at regular intervals to determine their serum lithium levels. Plasma lithium levels above 1.2 mM cause nausea, diarrhea, and tremors.[\[ref\]](#)

Other side effects noted by patients taking prescription levels of lithium chloride include increased thirst and urination, weight gain, and mental dullness. It was theorized that bipolar patients taking lithium may drink more calories due to increased thirst, thus causing weight gain.[\[ref\]](#) Other side-effects of higher doses of lithium include increased risk of kidney problems and hypothyroidism.

Lithium orotate, as a supplement, comes in much lower doses than prescription lithium for bipolar disorder. There is one [case report](#), though, of nausea and mild tremor from a teenager taking 18 tablets of a supplement that contained 100mg of lithium orotate.

As stated at the beginning of this article, a recent toxicity study using lithium orotate showed no genotoxic effects and no adverse effects on organs at a fairly high dose.

Side effects of Lithium Orotate:

There aren't any recent research studies or case reports (other than the one above) on lithium **orotate** side effects, so this section is n=1 personal experiences and, well, internet hearsay.

A couple of people that I've talked with have reported that lithium may make them tired, less peppy than normal, or even a little sleepy during the day.

An [article from a holistic doctor](#) who suggests lithium orotate to most of his patients notes that very few report any side effects. He does suggest taking lithium orotate before bed instead of during the day. This makes sense in light of the circadian rhythm effects via GSK-3B inhibition.

A study from 1986 on using lithium orotate for alcoholism listed minor side effects to the treatment (which included other supplements along with lithium orotate) as loss of appetite, mild apathy, and muscle weakness.[\[ref\]](#)

Lifehacks:

If you have medical questions, talk with your doctor – especially if you are on any medications or if pregnant or nursing – before supplementing with lithium orotate.

Supplement Doses: Lithium orotate is available as a natural supplement in many health food stores and online (Amazon). You can get it in doses from 5 mg to 20 mg.

Anti-inflammatory: The study on stacking lithium with caffeine, theobromine, and catechin for an increased anti-inflammatory effect was interesting. If you are considering this combo, a good source of theobromine is **cacao nibs**. Catechins, theobromine, and caffeine are found in **green tea**.

Related Articles and Genes:

[A little lithium orotate and B12 make the world a happier place... for some people.](#)

Let me cut to the chase: *for some people*, supplementing with lithium orotate helps with anxiety, mood, and anger issues and *for others*, lithium orotate supplements will have little or no noticeable effect on mood.

[Rapamycin, mTOR, and Your Genes](#)

Rapamycin is an antibiotic that is used as an immunosuppressant, an anti-cancer agent, and (possibly) to prevent some of the signs of aging.

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Debbie Moon is the founder of Genetic Lifehacks. Fascinated by the connections between genes, diet, and health, her goal is to help you understand how to apply genetics to your diet and lifestyle decisions. Debbie has a BS in engineering and an MSc in biological sciences from Clemson University. Debbie combines an engineering mindset with a biological systems approach to help you understand how genetic differences impact your optimal health.

