

Lithium Synergy



*Bioavailable lithium orotate for natural mood support**

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Lithium Synergy combines lithium orotate, known for its ability to help stabilize mood swings related to depression and other mood disorders, with vitamin B12 (methylcobalamin) and trimethylglycine to support healthy methylation pathways.*

It is estimated that 26% of Americans suffer from mental disorders such as depression or bipolar disorder. Approximately 16% of Americans have been diagnosed with depression at some point in their lifetime. Australian doctor John Cade discovered the role of lithium in controlling bipolar disorder. Lithium orotate was introduced as a supplement by the German physician Dr. Hans Nieper, who used it to improve depression, headaches, migraine, epilepsy, and alcoholism. When salts of lithium are ingested, the lithium ions interact with several neurotransmitters and receptors in the central nervous system, resulting in decreased norepinephrine release and increased serotonin synthesis.

Several studies conducted in various parts of the world have found associations between higher levels of lithium in drinking water and lower rates of mental disturbances and impulsivity, including aggression, homicide, and suicide.¹⁻⁶ Some researchers have posited that impulsivity and violence may be in part "lithium deficiency states."^{7,8} Overall, international clinical practice guidelines recognize lithium as a robust intervention for bipolar disorder and mania, with supportive evidence for managing acute bipolar depression as well as reducing risk of suicide.⁹ Lithium has been called "an underutilized treatment" with regard to mood disorders.¹⁰

Biological Action

Irregularities of intracellular calcium homeostasis have been implicated in the pathophysiology of bipolar disorder. Lithium has been researched for its ability to improve receptor function that allows for better calcium flux in and out of the cell. One of the most studied mechanisms of action is the inositol depletion hypothesis.^{11,12} This hypothesis suggests that lithium's mood-stabilizing effects comes from its ability to inhibit IMPase, an enzyme involved in the recycling and synthesis of inositol, a primary component of the phosphoinositol signaling pathway. Depleting inositol concentrations decreases the amount of phosphoinositide 4,5-bisphosphate (PIP2), a cellular membrane phospholipid that is available for signaling cascades that rely on this pathway.

GSK-3, a serine-threonine kinase that functions as an intermediary in numerous intracellular pathways, is currently receiving interest as a regulator of apoptosis and cellular resilience. Evidence suggests an association between mood disorders and impairments of neuroplasticity and cellular resilience. In rodent and cell-based models lithium demonstrates neuroprotective effects at least partly by inhibiting GSK-3. Inhibiting GSK-3 attenuates or prevents neuronal apoptosis. Lithium has also been shown to increase levels of BDNF (brain derived neurotrophic factor), a compound that supports neuronal survival and synaptic plasticity.¹³ Numerous other mechanisms are currently being explored to further elucidate the biochemical effects of lithium responsible for its mood stabilizing properties, with some researchers speculating that it may one day be considered a micronutrient with a specific recommended intake.¹⁴

Brain Support

Studies show that lithium in general inhibits the atrophy of the hippocampus. Atrophy of the human hippocampus is seen in a variety of psychiatric and neurological disorders including recurrent depression, schizophrenia, bipolar disorder, post-traumatic stress disorder, epilepsy, and Alzheimer's disease. In Alzheimer's disease the hippocampus is one of the first regions of the brain to suffer damage.¹⁵ Mouse models of Alzheimer's disease have shown that oral lithium administration reduces the buildup of beta-amyloid protein fragments, which aggregate into the insoluble amyloid plaques believed to play a role in the pathophysiology of this disease. Increases in BDNF were also observed.^{16,17} A study from Denmark found an inverse association between higher long-term exposure to lithium in drinking water and incidence of Alzheimer's disease or vascular dementia.¹⁸ Research indicates a positive association between lithium treatment and increased brain grey matter volume, suggesting that use of this element "might help maintain brain health even in patients without bipolar disorders and could possibly demonstrate disease modifying properties in neurodegenerative disorders."¹⁹

Other possible applications where lithium orotate may be of benefit*:

- Disruptive behavior disorders in children and adolescents²⁰
- Preventing episodic impulsive aggressiveness²¹
- Protecting the brain from damage by alcohol²²
- Preventing symptoms of Fragile X Syndrome (FXS).²³ FXS is a genetic condition that causes certain forms of autism, learning disabilities, anxiety disorders, and mental retardation.)

Orotates may*:

- Protect the heart from arrhythmias²⁴
- Help reduce heart-attack damage²⁴
- Stimulate production of red and white blood cells²⁴
- Help lower mental stress²⁴

Supplement Facts

Serving Size 1 capsule

Amount Per Serving	% Daily Value	
Vitamin B-12 (as Methylcobalamin)	250 mcg	10417%
Trimethylglycine (TMG)	200 mg	*
Lithium (as Lithium Orotate)	5 mg	*

*Daily Value not established.

Other Ingredients: Cellulose (capsule), dicalcium phosphate, vegetable stearate, silicon dioxide.

Vitamin B12 and Trimethylglycine (TMG)

Observational studies have found as many as 30% of patients hospitalized for depression are deficient in vitamin B12.²⁵ The reasons for the relationship between vitamin B12 deficiency and depression may involve S-adenosylmethionine (SAME). Vitamin B12 is required for the synthesis of SAME, a methyl group donor essential for methylation reactions and subsequently the metabolism of neurotransmitters. SAME deficiency may contribute to depression—a hypothesis supported by several studies that have shown supplementation with SAME improves depressive symptoms.²⁶ The addition of vitamin B12 and TMG helps support healthy methylation pathways.

Lithium Orotate Dosage and Toxicity

Lithium carbonate and lithium citrate have poor toxicity profiles and therefore must be used with caution. They show toxic effects at dosages only slightly higher than the medically effective dose because lithium in these forms is poorly absorbed by the cells of the body. Poor absorption and limited bioavailability necessitate taking high doses of pharmaceutical forms of lithium in order to obtain a satisfactory therapeutic effect. In contrast, the therapeutic dose of lithium orotate is much lower than that of the other lithium salts.²⁷

Recommended Use:

- Take one capsule per day, or as directed by your health care practitioner.

Serum lithium levels should be monitored by a qualified health care practitioner during use.

Cautions:

- This product should not be used to replace any antidepressant medication, including prescription forms of lithium, unless under the direction of a qualified health care practitioner. Lithium Synergy™ should not be used by individuals with significant renal or cardiovascular diseases, severe debilitation, dehydration or sodium depletion, or by individuals who are taking diuretics or ACE inhibitors. Caution should be taken with patients on antihypertensive drugs, anti-inflammatory drugs, analgesic drugs or insulin. Lithium should not be used by pregnant women and breast-feeding mothers. Serum lithium levels should be monitored by a qualified health care provider during use.

For a list of references cited in this document, please visit:

<https://www.designsforhealth.com/techsheet-references/lithium-synergy-references.pdf>

Dosing recommendations are given for typical use based on an average 150 pound healthy adult. Healthcare practitioners are encouraged to use clinical judgement with case-specific dosing based on intended goals, subject body weight, medical history, and concomitant medication and supplement usage.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.

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