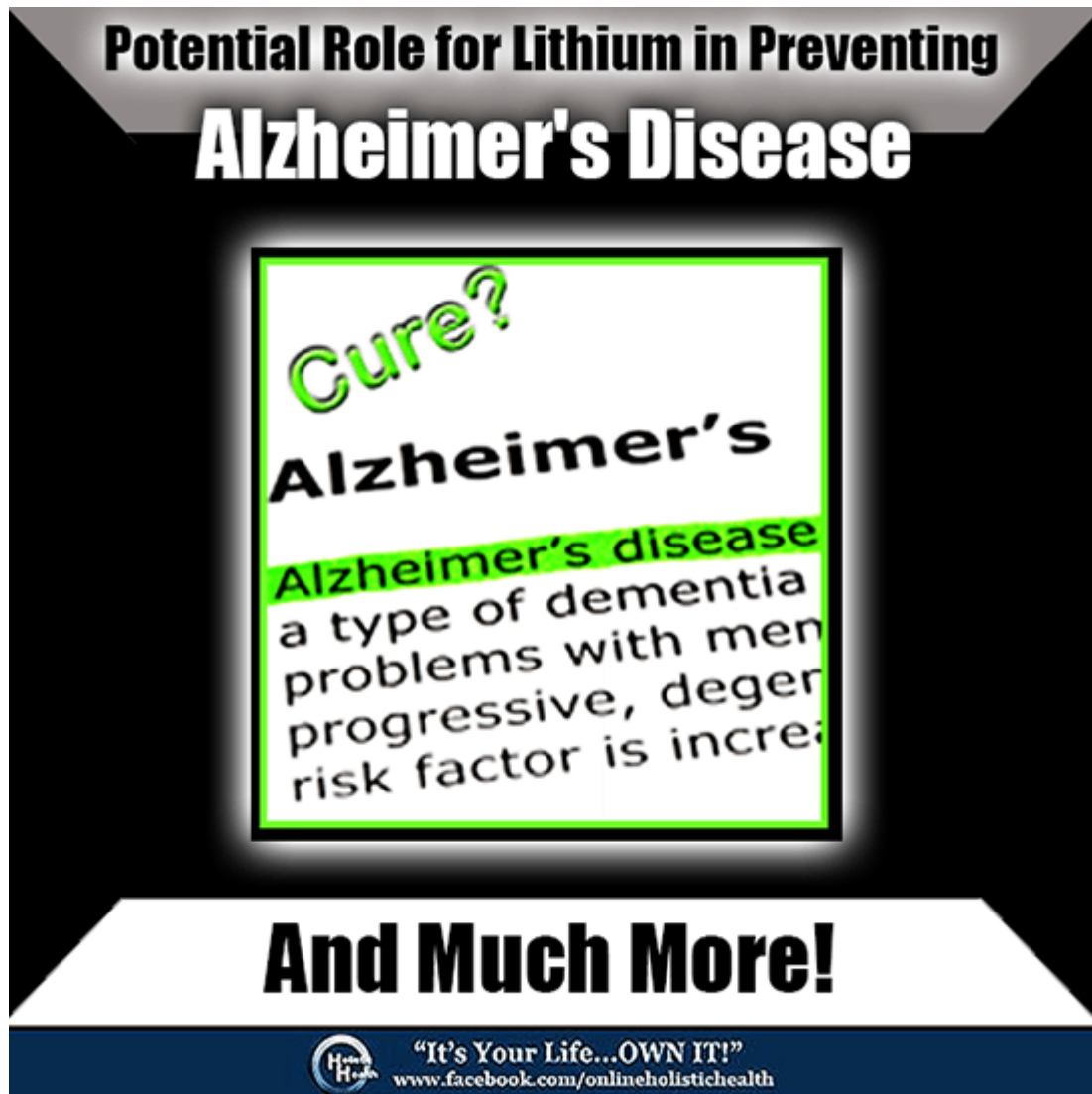


# Cure for Alzheimer's?

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## Potential Role for Lithium (Orotate) in Preventing

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### Alzheimer's Disease

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by Linda Fugate, PhD

Alzheimer's and other neurodegenerative diseases are characterized by the death of brain cells. A research team at Wayne State University School of Medicine recently reported that lithium helps keep brain cells alive, and that it should be investigated as a potential agent in the treatment of Alzheimer's. (1-3)

Lithium is a naturally occurring mineral similar to sodium and potassium. Small amounts are present in most foods. Large amounts are used in the treatment of manic depression-also called bipolar disorder. The Wayne State team was studying lithium's effects on manic depression when they discovered that this remarkable mineral can protect brain cells from premature death. In their Oct. 7, 2000 paper, they reported that lithium may even cause brain cells to regenerate after a loss from disease. (1)

Two proteins are key to lithium's neuroprotective benefits. Bcl-2 (named for the B-cell lymphoma/leukemia-2 gene) protects brain cells from a variety of injuries, including chemical oxidants and ionizing radiation. Lithium is the first substance shown to increase the concentrations of Bcl-2 in brain tissue. On the other hand, a protein you don't want too much of is glycogen synthase kinase 3b (GSK-3b). GSK-3b appears to participate in the production of 'neurofibrillary tangles,' which are a key feature found in Alzheimer's patients. Lithium was shown to reduce the levels of GSK-3b.

The research results came from three sources: humans, rats, and brain cell cultures. The patients all suffered from bipolar disease (manic depression). Magnetic Resonance Imaging (MRI) scans of the brain were performed before and after four weeks of lithium treatment. The researchers were surprised to find that the patients' brain gray matter increased by an average of 3 percent.

In an in vitro study, lithium was shown to increase brain cell survival. When human brain cells were incubated in a lithium solution and then exposed to two different toxins, the lithium-treated cells showed up to a 220 percent increase in survival rate compared to the control groups. (2)

Although there are no published studies on the effect of lithium on Alzheimer's, the Wayne State team suggests that the possibility should be studied. An obvious question is whether manic depressed people who take lithium have a reduced incidence of Alzheimer's. Data are not yet available, since at least nine other drugs can be used to treat manic depression. (4) However, current data show that lithium plays a vital role in maintaining neural health.

## **Benefits of Lithium**

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Lithium offers both short and long term benefits for the health of the nervous system. Dr. Robert Lenox, a psychiatric researcher at the University of Pennsylvania, commented, 'We are currently still at the stage of identifying the pieces of the lithium puzzle; within the next 50 years, we will be putting the puzzle together.' (5) Additionally, Prof. Bjorksten demonstrated that lithium was an effective aluminum chelator and crosslinkage inhibitor. Bjorksten stated that 'lithium continues to be the most effective electrolyte for aluminum detachment.' (6)

## **Lithium in the Diet**

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There is growing evidence that lithium may be an essential mineral in the human diet. Animals on low-lithium diets have shown reproductive problems, shorter life spans, poor lipid metabolism, and behavioral abnormalities. (7-9) In epidemiological studies of humans, low levels of lithium in drinking water have been correlated with a higher incidence of mental hospital admissions, (10) violent crime, suicide, drug addiction, (11) and heart disease. (11) Lithium levels in the scalp hair of violent criminals and heart disease patients have been found to be lower than those in healthy volunteers. (13)

The amount of lithium in a normal diet varies considerably. Some lithium is present in essentially all foods, with the highest concentrations reported in eggs and milk. (14) Water can also be a substantial source. The lithium content of drinking water in the United States ranges from 0.00001 to 0.170 mg/liter, with an average of 0.002 mg/liter. (15,16) El Paso, Texas, has one of the highest concentrations, and is the location most noted as a high-lithium, low-mental illness site. (10,11) One region of Northern Chile has 5 mg/liter lithium in the water, which has been consumed for years without adverse effects reported, and even water with 6 to 12 mg/liter lithium from an industrial outflow has not been shown to cause any obvious problems. (23)

## **Lithium in Medicine and as a Supplement**

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Lithium got a bad reputation in the 1940s, when lithium chloride was tried as a salt substitute for patients on low-salt diets. (Today, potassium chloride is a more accepted salt substitute.) The amount of lithium used for this application was toxic, and even fatal, in some cases. Lithium products were removed from the market, and American doctors rejected the mineral for many years. In 1949, the Australian physician John Cade reported that lithium was an effective treatment for manic depression. It was not until 1970 that the FDA approved its use for medical treatment in the United States. (19) By 1996, lithium was included in a list of 18 elements which might be important for human nutrition.<sup>18</sup> In 1998, the U. S. Department of Agriculture recognized 'moderate' evidence that lithium should be considered an ultra-trace element 'with an established, estimated, or suspected requirement generally indicated by micrograms/day for humans.' (20)

There are 13 minerals commonly found in multi-mineral dietary supplements: calcium, potassium, magnesium, iron, zinc, boron, copper, manganese, iodine, molybdenum, chromium, selenium, and vanadium. Other important minerals in the body are phosphorus and sodium. Daily Values have been established for most of these. There are several types of Daily Values: Recommended Dietary Allowances (RDA), Estimated Safe and Adequate Daily Dietary Intakes (ESADDI), and Dietary Reference Intakes (DRI), which include several types of nutrient recommendations. (21) This hodgepodge of dietary advice was created by the Food and Nutrition Board, a subsidiary of the National Research Council, which is part of the National Academy of Sciences.

These categories represent different levels of knowledge about different nutrients. Lithium does not make any of the lists. However, Forrest Nielsen of the U S Department of Agriculture suggested that lithium and other trace elements should be classified as DAMM nutrients, an acronym for Dietary Allowances of Minuscule Minerals. (18) Actually,

lithium is not that minuscule. It has a low atomic weight, so the milligrams of lithium in the diet or in the body look deceptively low. In terms of atoms, lithium is more abundant in the body than six of the minerals that are commonly taken in supplements.

## Lithium Salts

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Lithium, like sodium, occurs naturally in a number of different salts. Lithium carbonate and lithium citrate are approved as prescription forms of lithium. The citrate and carbonate salts are only slightly soluble in water, and are poorly absorbed by the cells. **Another form of lithium — lithium orotate — is a highly bioavailable form of lithium that is available as an over-the-counter dietary supplement. (24) Because of its superior bioavailability, lower doses of lithium orotate than lithium carbonate (or lithium citrate) may be used to achieve therapeutic brain lithium concentrations and relatively stable serum concentrations. (25)**

Lithium orotate has also been demonstrated to be of benefit in the treatment of alcoholics, and proved useful in alleviating alcohol-related symptoms of liver dysfunction, seizure disorders, headaches, hyperthyroidism, affective disorders. Meniere's syndrome, and liver and lung cancers. (25)

Standard lithium orotate dietary supplements provide 5 mg lithium. This is 1 to 2 percent of the dose provided by prescription forms of lithium.

## Safety Issues

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Bipolar patients commonly take 200 to 400 mg (elemental) lithium per day, which is approximately 1,000 to 2,000 mg lithium carbonate. (18) Because the blood levels of lithium citrate or lithium carbonate that have been demonstrated to be therapeutic are only slightly below the level that has been determined to be toxic, patients who take these prescription forms of lithium require regular blood tests to make sure their serum lithium concentrations stay below the toxic range. Adverse side effects and the inconvenience of frequent blood tests cause many patients to discontinue treatment with these prescription drugs.

## Conclusion

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**Lithium orotate is a safe nutritional supplement that may help to prevent Alzheimer's disease, alcoholism (and related conditions) and other neurodegenerative conditions. Because of its superior bioavailability, lower (and safer) doses of lithium orotate are as effective as the much higher doses found in prescription lithium.**

*(The information in this article is not intended to provide personal medical advice, which should be obtained from a medical professional)*

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