LITHIUM OROTATE

1. The pioneer of orotate supplementation was world famous physician Hans Nieper of Germany. Lithium orotate was one of his standard orotate compounds (along with calcium, magnesium, potassium, and zinc orotates).

2. Nieper claimed that lithium orotate was beneficial for a broad range of neurological conditions such as depression, migraines, epilepsy, and alcoholism. Lithium orotate was also part of his "liver orotate" --- the combined lithium orotate + calcium orotate. --- Liver orotate was, according to Nieper's research, particularly beneficial in alcoholism --- protecting from fatty liver disease, alcoholic hepatitis and alcoholic cirrhosis.

   Nieper HA. The clinical applications of lithium orotate. A 2 years study. Agressologie. 1973;14(6):407-11.

3. We have received questions from NUTRI-SPEC practitioners and their patients regarding the lithium orotate in Activator. Some are expressing alarm that there is a "drug" in Activator. Some are (legitimately) alarmed because they have heard of the terrible side effects of lithium salts (generally lithium carbonate, but also sometimes lithium chloride) used as a psychiatric drug for bipolar disorder and for mania. The standard dose of lithium carbonate for those with bipolar disorder is (6 x 300 mg tablets daily = 1800 mg/day = 300 mg of lithium), which is 150 times the amount of lithium in Activator!!! So be assured, there is no pharmacological effect of the lithium orotate in Activator.

4. There are studies supporting Nieper's claim that lithium orotate has physiological (not necessarily pharmacological) effects different from lithium as lithium carbonate or chloride used as a psychiatric drug.

   Smith DF. Lithium orotate, carbonate and chloride: pharmacokinetics, polyuria in rats. Br J Pharmacol, 1976. ----- This study of lithium (in pharmacological doses) showed that lithium administered as orotate did not have the extreme effects on kidney and posterior pituitary function that derive from lithium carbonate and chloride. The rats taking lithium carbonate and chloride developed polydipsia and polyuria --- effects that were caused by lithium orotate only in much, much larger doses. The protective effect was attributed to the action of the orotate anion. [But since we are not using lithium orotate in pharmacological doses, we have no real concern about drug-induced side effects anyway.]

   Kling, MA, et al. Rat brain and serum lithium concentrations after acute injections of lithium carbonate and orotate. J Pharm Pharmacol, 1978.

----- This study showed that lithium orotate is far superior to carbonate in crossing the blood-brain barrier. The 24-hour brain concentration of lithium after lithium orotate was approximately 3 times greater than after lithium carbonate. ----- These data suggest that lower doses of lithium orotate than the (frequently toxic) doses of lithium carbonate used for psychiatric therapies may achieve therapeutic brain lithium concentrations.

5. For our purposes, we see this study as evidence supporting Nieper's claim that orotates preferentially enter mesenchymal cells over parenchymal cells. Nieper theorized that orotates probably release a chelated mineral at the membrane of mitochondria, microsomes, and lysosomes, and that orotates show a special affinity for cells in which the metabolism involves the pentose phosphate pathway. Examples include the glia of the brain, the blood-brain barrier, the liver, vascular walls and cartilage.

6. Lithium orotate is useful as the main pharmacologic agent for the treatment of alcoholism. Furthermore, it is more beneficial than lithium carbonate in alcoholism.

   Sartori HE. Lithium orotate in the treatment of alcoholism and related conditions. Alcohol, 1986.

7. Lithium is being researched as a possible preventative in amyotrophic lateral sclerosis and in Alzheimer's.

   Group, et al. Lithium in patients with amyotrophic lateral sclerosis: a phase 3 multicenter, randomized, double-blind, placebo-controlled trial. Lancet Neurol, 2013.

   Fornai, et al. Autophagy and amyotrophic lateral sclerosis: The multiple roles of lithium. Autophagy, 2008.

   Noble, et al. Inhibition of glycogen synthase kinase-3 by lithium correlates with reduced taupathy and degeneration in vivo. Proc Natl Acad Sci USA, 2005.

   Engel, et al. Lithium, a potential protective drug in Alzheimer's disease. Neurodegener Dis, 2008.

   Nunes, et al. Chronic microdose lithium treatment prevented memory loss and neurohistopathological changes in a transgenic mouse model of Alzheimer's disease. PLoS One, 2015. ----- From the abstract: "Both lithium and treated transgenic groups and lithium treated non-transgenic mice showed no memory disruption. Transgenic mice treated with lithium from age two months showed decreased number of senile plaques, no neuronal loss, in cortex and hippocampus, and increased BDNF density in

cortex when compared to non-treated transgenic mice." --- Note that this was a "microdose" supplementation regimen of these mice --- a dose nowhere near the pharmacological dose used for treating bipolar disorder.

8. What do we mean when we say that the 2 mg of lithium in Activator is a "nutritional" quantity? The amount of lithium obtained from a healthy diet can be as high as 5 mg daily. Lithium is found in significant concentrations in meat, fish and poultry, as well as in grains and vegetables. In some areas, the drinking water is also a significant source of lithium. So, the 2 mg of lithium as orotate in Activator is neither a pharmacological dose, nor a mega-supplemental dose.

9. Is lithium nutritionally essential?

   Schrauzer GN. Lithium: occurrence, dietary intakes, nutritional essentiality. J Am Coll Nutr, 2002. "----- In studies conducted from the 1970s to the 1990s, rats and goats maintained on low lithium rations were shown to exhibit higher mortalities as well as reproductive and behavioral abnormalities. In humans, defined lithium deficiency diseases have not been specifically defined by the FDA --- but low lithium intakes from water supplies are associated with increased rates of suicides, homicides, and the arrest rates for drug use and other crimes. Lithium plays an especially important role during early fetal development as evidenced by the high lithium content of the embryo during the early gestational period. The biochemical mechanisms of action of lithium appear to be multifactorial and are intercorrelated with the functions of several enzymes, hormones and vitamins, as well as with growth and transforming factors."