

Lithium sulfate

CAS: 10377-48-7

MF: Li_2SO_4

FW: 109.9

Solubility: soluble in water (1 part in 2.6 parts of water); almost insoluble in alcohol.

Li^+

MW: 6.94

Major uses

Lithium (Li) is used in psychiatry for the treatment of mania, endogenous depression and psychosis; and also for treatment of schizophrenia. Usually lithium carbonate (Li_2CO_3) is applied, but sometimes lithium citrate ($\text{Li}_3\text{C}_6\text{H}_5\text{O}_7$), lithium sulfate, or lithium oxybutyrate are used as alternatives [1, 2].

Li has also industrial use, e.g. in alloys, as a catalytic agent, and as a lubricant [3].

Human toxicity

Poisoning is categorized as being acute, chronic (when the patient was taking drug therapeutically), or acute-on-chronic. Daily therapeutic oral doses of lithium carbonate or lithium citrate range from 600 mg to 2400 mg [4].

The symptoms of intoxication include nausea, vomiting, diarrhea, drowsiness, weakness, ataxia, blurred vision, tinnitus and seizures. At the severe intoxication, CNS depression, cardiac arrhythmias, epileptic seizures, blood circulation collapse, hypotension, kidney failure, coma, and death can occur [4, 5].

The therapeutic blood plasma level of Li is between 4.2 and 9.7 mg/l; the toxic level is about 14 mg/l; and the lethal level is exceeding 35 mg/l [6].

Carcinogenicity: Li and its salts are not classified as a human carcinogens.

Kinetic data

Absorption: Gastrointestinal absorption of lithium salts is rapid (within a few minutes) and complete following oral administration of tablets or the liquid form of lithium salt [2].

Kinetics is biphasic [7].

Bioavailability: over 95% [5].

Volume of distribution: 0.6 l/kg [5].

Distribution: lithium diffuses quickly into the liver and kidney, but up to 8-10 days is required to reach equilibrium between serum and brain, bone and muscle (reviewed in [5]).

Therapeutic peak plasma levels are reached within 30 min to 2 h; in overdose situation – up to 72 h [5].

The plasma half-life at the overdose situation can vary between 30 and 100 h [2].

Plasma-protein binding: <10% [5].

Elimination half-life: 3-12 h; 8-65 h at the overdose situation [7].

Passage of blood-brain barrier is restricted [7]. Distribution of Li to the brain can be delayed up to 24 h [8].

Li passes freely through the placenta membrane [9].

Metabolism and excretion

Li is not metabolized.

Because Li chemical similarity to sodium (Na^+) and potassium (K^+), it may interact or interfere with biochemical pathways for these substances and displace these cations from intra- or extracellular compartments of the body [2].

Li seems to be transported out of nerve and muscle cells by the active sodium pump, although inefficiently [9].

Excretion is predominantly by the kidney: about 80% of Li is reabsorbed at the proximal renal tubule [2]. At the therapeutic doses, approximately 97% of a single dose of Li is excreted in the urine within 10 days [4].

Mechanisms of action

Li produces many metabolic and neuroendocrine changes, but no conclusive evidence favors one particular mode of action [2]. For example, Li interacts with neurohormones, particularly the biogenic amines, serotonin (5-hydroxy tryptamine) and norepinephrine, which provides a probable mechanism for the beneficial effects in psychiatric disorders, e.g. manias (reviewed in [10]).

In the CNS, Li affects nerve excitation, synaptic transmission, and neuronal metabolism [10]. Li stabilizes serotonergic neurotransmission [2].

Li may influence water balance in the body by reducing the capacity of the renal tubule to react to vasopressin [11].

Partial substitution for Na^+ and K^+ ions by Li^+ ion can, possibly, disturb energy processes in the cells [7].

The exact mechanisms of poisoning are still poorly understood.

Target organs: CNS, kidney, cardiovascular system [7].

References

1. Wikipedia, The Free Encyclopedia (Google, via internet).
2. Haddad, L.M., Winchester, J.F. (1990) *Clinical Management of Poisoning and Drug Overdose*. 2nd ed., pp. 656-665. W.B. Saunders Company.
3. *Casarett and Doull's Toxicology (The Basis Science of Poisons)* (1986) Klaassen, C.D., Amdur, M.O., Doull, J., eds., pp. 621-622, Macmillan Publishing Company.
4. Baselt, R.C. (1982) Lithium. In: *Disposition of Toxic Drugs and Chemicals in Man*. 2nd ed., pp. 434-436. Davis, California: Biomedical Publications.
5. Ellenhorn, M.J., Schonwald, S., Ordog, G., Wasserberger, J. (1997) *Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning*, 2nd ed., pp. 1579-1583. Williams & Wilkins.
6. Winek, C.L. (1994) Drug and chemical blood-level data. *Winek's Toxicological Annual*, Pittsburgh. Allegheny County Department Laboratories.

7. Ekwall, B., Clemedson, C., Crafoord, B., Ekwall, Ba., Hallander, S., Walum, E., Bondesson, I. (1998) MEIC evaluation of acute systemic toxicity. Part V. Rodent and human toxicity data for the 50 reference chemicals. *ATLA* 26, 571-616.
8. Chen, K.P., Shen, W.W., Lu, M.L. (2004) Implication of serum concentration monitoring in patients with lithium intoxication. *Psychiat Clin Neurosci* 58, 25-29.
9. Shou, M. (1976) Pharmacology and toxicology of lithium. *Annu Rev Pharmacol* 16, 231-243.
10. Poisindex, Thomson Micromedex (2005).
11. Stokinger, H.E. (1981) Lithium, Li. In: *Patty's Industrial Hygiene and Toxicology*, 3rd ed., pp. 1728-1739, New York: Interscience.

***Written by Ada Kolman, December 2005; revised March 2007
ada.kolman@telia.com***