

Definition

Citicoline is the generic name for synthetic CDP-choline (cytidine diphosphate choline), an organic molecule produced endogenously and found in all living cells. CDP-choline is a precursor for the synthesis of phospholipids that are essential constituents of cell membranes, including phosphatidylcholine, phosphatidylserine, and phosphatidyl-ethanolamine. Because cell membranes have a very high turnover rate, these phospholipids must be continuously synthesized to ensure adequate function of cells.

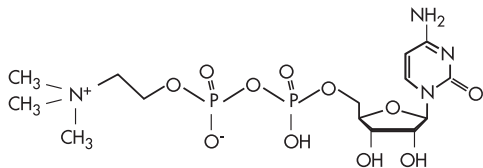
Citicoline is often called a “brain nutrient” because it increases levels of several important neurotransmitters including acetylcholine, dopamine and noradrenaline; helps maintain the integrity of neuronal cell membranes; and increases energy production in the frontal cortex.

The scientific name for citicoline is cytidine 5'-diphosphocholine.

Chemistry

Molecular formula: $C_{14}H_{26}N_4O_{11}P_2$

Structural formula



Sources and metabolism

Diet is not a good source of CDP-choline because the molecule is present in very low amounts in foods. The best sources, liver and brains, are not widely consumed in the United States. Some CDP-choline can be synthesized from dietary choline, which is found in beef, eggs and other foods. Adequate Intake (AI) for choline established by the Food and Nutrition Board of the Institute of Medicine is 550 mg/day for men and 425 mg/day for women.¹ At present there are no nationally representative estimates of intake of either choline or CDP-choline.

This high-quality brand of pure, stable citicoline is marketed under the brand name Cognizin® citicoline, and is manufactured by Kyowa Hakko Bio Co., Ltd. Citicoline is degraded to uridine and choline during intestinal absorption.² These two compounds then pass through the blood-brain barrier to reconstitute citicoline in the brain.³

*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.

Biochemical roles

In the brain, citicoline plays a number of critical roles:

1. Maintains cell integrity through the biosynthesis of structural phospholipids of neuronal membranes
 - In animal experiments, supplementation with 500 mg/kg citicoline for 90 days increased the amount of phosphatidylcholine in the frontoparietal cortex by about 30%.⁴
 - Citicoline was able to significantly increase phosphatidylcholine, sphingomyelin and cardiolipin levels in gerbils.⁵
 - In healthy elderly human subjects, supplementation with 500 mg/day citicoline for 6 weeks was shown by magnetic resonance spectroscopy to stimulate phosphatidylcholine synthesis.⁶
2. Enhances cell signaling by increasing the synthesis of neurotransmitters
 - Citicoline administration in laboratory rats produced a rapid increase in acetylcholine production in the dorsal hippocampus and neocortex, as compared to control animals.
 - Citicoline increases norepinephrine and dopamine levels in the central nervous system.^{8,9}
3. Increases blood flow and brain metabolism
 - Citicoline increased glucose incorporation and metabolism in the brain and increased cerebral blood flow in rats.¹⁰
 - Supplementation of human subjects with 500 mg or 2000 mg Cognizin® citicoline for six weeks enhanced frontal lobe bioenergetics with a 14 percent increase in ATP.¹¹
 - Citicoline supplementation has been shown to improve brain metabolism in various animal models of ischemia/reperfusion and to have positive effects.⁸
4. Reduces oxidative stress
 - Administration of citicoline has been shown in animal models to help reduce oxidative stress in the brain and promote a normal inflammatory response by inhibiting free fatty acid release, decreasing breakdown of the blood-brain barrier, and attenuating arachidonic acid release.⁵
5. Improved attentional focus
 - Healthy, middle-aged women taking 250mg of Cognizin, saw improved attentional focus and inhibition on a test of attention researchers at the Brain Institute at The University of Utah.
 - Participants were evaluated with the Continuous Performance Test II (CPT-II), a measure sensitive to attentional function. Results after supplementation showed individuals receiving either the low or high dose of Cognizin citicoline produced fewer commission errors on the CPT-II compared to the placebo group. Specifically, individuals in the two Cognizin citicoline supplemented groups made fewer errors when responding to non-target stimuli.¹⁴



KYOWA HAKKO USA, INC.

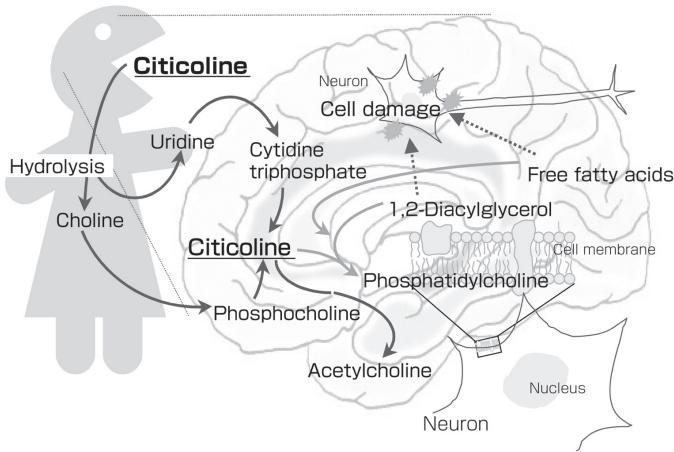
Customer Service: 800.596.9252

info@kyowa-usa.com

600 Third Ave. 19th Floor
New York, NY 10016

Tel: 212.319.5353
Fax: 212.421.1283

www.kyowa-usa.com
www.cognizin.com



Roles in health

The roles of citicoline in supporting brain structure and function suggest possible benefits in cognitive function in aging. Functional benefits demonstrated in human studies include:

- Supplemental citicoline given to certain groups of elderly people resulted in improvements in measurements of memory, attention, behavior, reaction time, relational life, independence and cooperation.⁹
- A meta-analysis of double-blind, randomized human trials on citicoline and cognition concluded that citicoline modestly improves memory and behavioral outcomes.⁸
- Citicoline at a dose of 1,000 mg/day for three months was found to improve verbal memory in a group of healthy older adults who were free of any medical, neurological or psychiatric illness but who had relatively inefficient memories.¹²
- In a study of mentally healthy older adults, supplementation with citicoline significantly improved immediate and short term memory, suggesting beneficial effects on the underlying cognitive processes of memory retrieval and storage.¹³

Safety

Citicoline has been found to have a very low toxicity profile in toxicology studies in animals and humans. In clinical use it has been observed to be safe at doses up to 2000 mg/day. A drug surveillance study analyzed the results of citicoline treatment in more than 2,800 adults and found minor transient adverse effects in approximately five percent of cases, most commonly stomach pain and diarrhea.⁵

References

- ¹ Food and Nutrition Board, Institute of Medicine. National Academy Press, Washington DC, 1998.
- ² Wurtman RJ *et al. Biochem Pharmacol.* 2000; 60(7): 989–92.
- ³ Rao AM *et al. J Neurosci Res.* 1999; 58(5): 697–705.
- ⁴ Lopez-Coviella I *et al. J Neurochem.* 1995; 65(2): 889–94.
- ⁵ Conant R, Schauss AG. *Alt Med Rev.* 2004; 9:1: 17–31.
- ⁶ Babb SM *et al. Psychopharmacology (Berl).* 2002; 161: 248–54.
- ⁷ Dixon CE *et al. J Neurotrauma.* 1997; 14: 161–69.
- ⁸ Fiorvanti M, Yanagi M. *The Cochrane Library*, Oxford, England. 2006; Issue 4.
- ⁹ Secades JJ, Lorenzo JL. *Meth Find Exp Clin Pharmacol.* 2006; 27(Suppl B): 1–56.
- ¹⁰ Watanabe S *et al. Folia Psychiatr Neurol Jpn.* 1975; 29(1): 67–76.
- ¹¹ Silveri MM *et al. NMR Biomed.* 2008; www.interscience.wiley.com DOI: 10.1002/nbm.1281.
- ¹² Spiers PA *et al. Arch Neurol.* 1996; 53: 441–48.
- ¹³ Alvarez XA *et al. Meth Find Exp Clin Pharmacol.* 1997; 19(3): 201–10.
- ¹⁴ McGlade, E. *et al. Food and Nutrition Sciences*, Vol. 3 No. 6, 2012, pp. 769-773. doi: 10.4236/fns.2012.36103.

Cognizin® is a registered trademark of Kyowa Hakko Bio Co., Ltd.

This information is based on data we believe to be reliable. It is intended only as a guide for use at the user's discretion. It cannot be taken as a license to apply for, or infringe on any patents.

Copyright ©2011 Kyowa Hakko Bio Co., Ltd. All Rights Reserved.

*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.

This information is being provided to you for educational and informational purposes only. This information is not intended to be used as marketing materials to consumers. All marketing claims should be cleared by your regulatory counsel.



KYOWA HAKKO USA, INC.

Customer Service: 800.596.9252

info@kyowa-usa.com

600 Third Ave. 19th Floor
New York, NY 10016

Tel: 212.319.5353
Fax: 212.421.1283

www.kyowa-usa.com
www.cognizin.com