

FACTS FOR HEALTH PROFESSIONALS ABOUT COGNIZIN® CITICOLINE*

Definition

Citicoline is the generic name for synthetic CDP-choline (cytidine diphosphate choline), organic molecule produced endogenously and found in all living cells. CDP-choline 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.

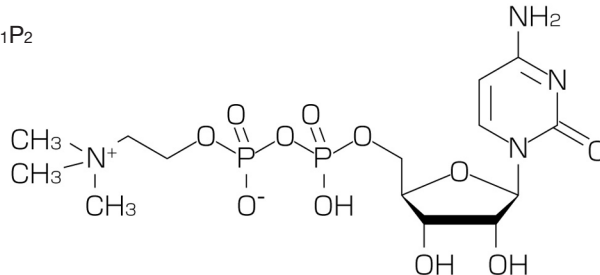
Citicoline is often called a “brain nutrient” because it increases levels of several important neurotransmitters including acetylcholine, dopamine and noradrenaline; helps maintain the integrity of neuronal cell membranes; and increases energy production in the frontal cortex.

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

Chemistry

Molecular formula: C₁₄H₂₆N₄O₁₁P₂

Structural formula:



Sources and metabolism

The diet is not a good source of CDP choline because it 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 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.

Citicoline is available in dietary supplements. high quality brand of pure, natural, stable citicoline is marketed under the brand name, Cognizin® citicoline, 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

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/kgciticoline 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 cats.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 on memory and behavior in elderly people.⁸

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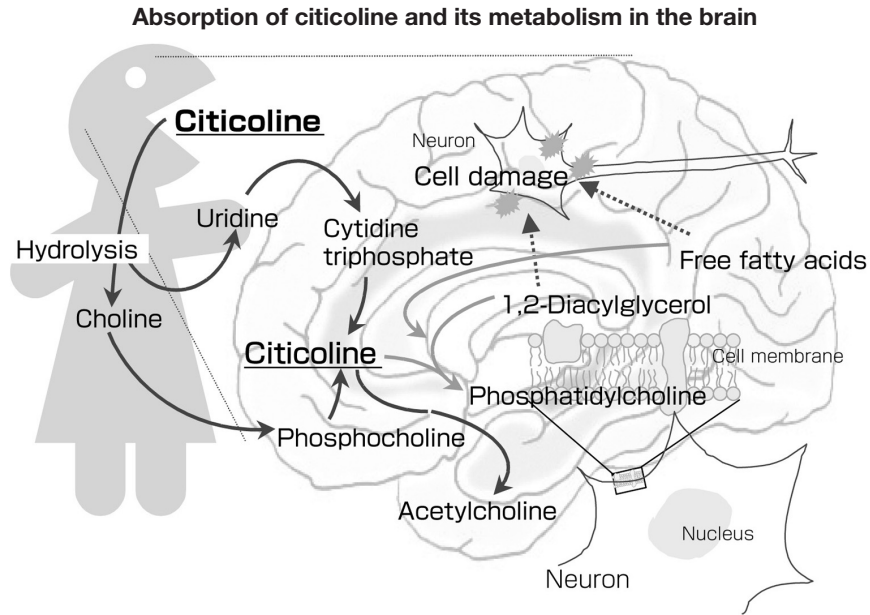
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4. reduces oxidative stress

- 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



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 cognitive 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 per 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

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