

RESEARCH MONOGRAPH . COMPOUND PROFILE

CDP-Choline (Citicoline)

Cytidine 5'-diphosphocholine, an endogenous nucleotide intermediate in phosphatidylcholine synthesis with neuroprotective and cognitive enhancement applications.

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AUTHOR	Kodiac bioLabs Research
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ABSTRACT

Citicoline (cytidine 5'-diphosphocholine, CDP-Choline; CAS 987-78-0; molecular formula $C_{14}H_{26}N_4O_{11}P_2$; molecular weight 488.32) is an endogenous nucleotide intermediate in the Kennedy pathway for phosphatidylcholine biosynthesis. Exogenous citicoline is hydrolyzed in the gut to cytidine and choline, which are absorbed independently and reassembled centrally as needed. The bioavailability profile differs from alpha-GPC: citicoline does not cross the blood-brain barrier intact at therapeutic concentrations; the elevation in central choline derives from increased availability of the precursor pools. The compound is approved as a medicine in many countries (Italy, Spain, Japan, Mexico, much of Latin America) for ischemic stroke, traumatic brain injury, and chronic cerebrovascular disease. Large randomized trials (ICTUS, COBRIT) have produced mixed results; meta-analysis suggests modest benefit in acute stroke recovery and chronic cognitive impairment with effect sizes in the 0.2 to 0.4 range. The compound is sold as a dietary supplement in the United States. Pharmacokinetics: plasma half-life of cytidine and choline components is several hours after dissociation; the CDP-Choline structure itself is not detectable in serum after oral administration. Doses are typically 500 to 2000 mg per day. Excellent safety profile with rare serious adverse events.

1. Compound Identification

CDP-Choline (Citicoline) is described as cholinergic precursor / nucleotide. Cytidine 5'-diphosphocholine, an endogenous nucleotide intermediate in phosphatidylcholine synthesis with neuroprotective and cognitive enhancement applications.

1.1 Class summary

Cholinergic precursor / nucleotide

1.2 Subtitle

Cytidine 5'-diphosphocholine, an endogenous nucleotide intermediate in phosphatidylcholine synthesis with neuroprotective and cognitive enhancement applications.

2. Abstract

Citicoline (cytidine 5'-diphosphocholine, CDP-Choline; CAS 987-78-0; molecular formula $C_{14}H_{26}N_4O_{11}P_2$; molecular weight 488.32) is an endogenous nucleotide intermediate in the Kennedy pathway for phosphatidylcholine biosynthesis. Exogenous citicoline is hydrolyzed in the gut to cytidine and choline, which are absorbed independently and reassembled centrally as needed. The bioavailability profile differs from alpha-GPC: citicoline does not cross the blood-brain barrier intact at therapeutic concentrations; the elevation in central choline derives from increased availability of the precursor pools. The compound is approved as a medicine in many countries (Italy, Spain, Japan, Mexico, much of Latin America) for ischemic stroke, traumatic brain injury, and chronic cerebrovascular disease. Large randomized trials (ICTUS, COBRIT) have produced mixed results; meta-analysis suggests modest benefit in acute stroke recovery and chronic cognitive impairment with effect sizes in the 0.2 to 0.4 range. The compound is sold as a dietary supplement in the United States. Pharmacokinetics: plasma half-life of cytidine and choline components is several hours after dissociation; the CDP-Choline structure itself is not detectable in serum after oral administration. Doses are typically 500 to 2000 mg per day. Excellent safety profile with rare serious adverse events.

3. Mechanism of Action

Hydrolyzed in gut to cytidine + choline; both contribute to phosphatidylcholine resynthesis and acetylcholine production. Indirect cholinergic and membrane-stabilizing effects.

The mechanistic profile described above represents the consensus position from peer-reviewed literature where available; for compounds with sparse formal characterization, this section reflects vendor-grade reports and structurally-related class pharmacology and should be interpreted with appropriate caution.

4. Pharmacokinetics and Routes of Administration

Pharmacokinetic data are summarized within the abstract for compounds with formal Phase 1 records. Compounds without published human pharmacokinetic studies are noted as such; investigators should treat the absence of data as a research limitation.

5. Reported Research Dose Ranges

500 to 2000 mg per day in divided doses.

Doses are scaled from clinical use where the compound is approved as a medicine, from Phase 2/3 trials where development advanced, or from rodent dose-response data scaled by allometric assumptions where the compound has no human clinical record. Investigators should treat dose ranges from research-chemical-grade vendors as starting points for their own pharmacokinetic and tolerability characterization rather than validated dosing recommendations.

6. Sourcing and Quality Verification

Investigators should obtain analytical confirmation of identity (mass spectrometry; for peptides, additionally amino acid analysis or N-terminal sequencing) and purity (HPLC area-percent, ideally greater than 95 percent) on every lot. Vendor certificates of analysis vary in quality; third-party analytical confirmation through independent laboratories (e.g., Janoshik Analytical, Anabolic Lab) is the gold standard for research-grade peptides and small molecules.

For compounds with established pharmaceutical-grade marketing in any jurisdiction, sourcing from the marketed product (where legal and accessible) provides the highest quality assurance.

7. Reconstitution and Handling

Peptides should be reconstituted in bacteriostatic water or sterile water for injection in the volume appropriate to the desired concentration; lyophilized peptides should be allowed to come to room temperature before reconstitution to minimize precipitation. Reconstituted peptides should be stored refrigerated and used within the timeframe specified by the manufacturer (typically 14 to 30 days for bacteriostatic water reconstitutions, shorter for sterile water).

Small molecules: storage conditions vary by compound; consult the certificate of analysis for the specific product. Most are stable at room temperature in dry, dark conditions; oxidation-sensitive compounds (e.g., catecholamine precursors) require cool storage and protection from light.

8. Stack Interaction Considerations

Investigators combining this compound with other research substances should consider receptor-level interactions (additive effects at shared targets), enzyme-level interactions (CYP-mediated drug-drug interactions where applicable), and pharmacodynamic interactions (additive sedation, additive serotonergic activity, additive hemodynamic effects).

The stack interaction section in published monographs of well-characterized compounds is necessarily incomplete for any specific combination; investigators should treat novel combinations with elevated caution and titrate gradually.

9. References

1. Davalos A, et al. Citicoline in the treatment of acute ischaemic stroke (ICTUS): a multicentre RCT. Lancet 2012.
2. Zafonte RD, et al. Effect of citicoline on functional and cognitive status among patients with traumatic brain injury (COBRIT). JAMA 2012.
3. Secades JJ. Citicoline: pharmacological and clinical review. Rev Neurol 2011.

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