

RESEARCH MONOGRAPH . COMPOUND PROFILE

N-Acetylcysteine (NAC)

N-acetyl-L-cysteine; a glutathione precursor used as a mucolytic, the antidote for acetaminophen overdose, and a candidate for neuropsychiatric and metabolic conditions.

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COMPOUND CLASS	Glutathione precursor / mucolytic / antioxidant

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ABSTRACT

N-acetylcysteine (NAC; CAS 616-91-1; molecular formula $C_5H_9NO_3S$; molecular weight 163.20) is the N-acetylated derivative of L-cysteine, approved by the FDA in 1963 as a mucolytic and acetaminophen overdose antidote. Mechanism: NAC is hydrolyzed to L-cysteine, the rate-limiting precursor for glutathione (GSH) biosynthesis; NAC administration rapidly replenishes intracellular GSH. The acetyl group also has direct mucolytic activity through disulfide bond reduction in mucus glycoproteins (the original FDA indication, Mucomyst). In acetaminophen overdose, replenished GSH conjugates the toxic NAPQI metabolite, preventing hepatocellular necrosis. Plasma half-life is approximately 6 hours. Off-label and research uses are extensive: OCD, trichotillomania, gambling disorder, addiction (cocaine, alcohol, cannabis), bipolar disorder, schizophrenia, and as a chemoprotective antioxidant. The clinical evidence is mixed; meta-analyses generally support modest effects in OCD and addictive behaviors. The compound is sold as both a prescription drug (oral, IV, inhaled) and as an OTC supplement. Used as the canonical glutathione precursor in research.

1. Compound Identification

N-Acetylcysteine (NAC) is described as glutathione precursor / mucolytic / antioxidant. N-acetyl-L-cysteine; a glutathione precursor used as a mucolytic, the antidote for acetaminophen overdose, and a candidate for neuropsychiatric and metabolic conditions.

1.1 Class summary

Glutathione precursor / mucolytic / antioxidant

1.2 Subtitle

N-acetyl-L-cysteine; a glutathione precursor used as a mucolytic, the antidote for acetaminophen overdose, and a candidate for neuropsychiatric and metabolic conditions.

2. Abstract

N-acetylcysteine (NAC; CAS 616-91-1; molecular formula $C_5H_9NO_3S$; molecular weight 163.20) is the N-acetylated derivative of L-cysteine, approved by the FDA in 1963 as a mucolytic and acetaminophen overdose antidote. Mechanism: NAC is hydrolyzed to L-cysteine, the rate-limiting precursor for glutathione (GSH) biosynthesis; NAC administration rapidly replenishes intracellular GSH. The acetyl group also has direct mucolytic activity through disulfide bond reduction in mucus glycoproteins (the original FDA indication, Mucomyst). In acetaminophen overdose, replenished GSH conjugates the toxic NAPQI metabolite, preventing hepatocellular necrosis. Plasma half-life is approximately 6 hours. Off-label and research uses are extensive: OCD, trichotillomania, gambling disorder, addiction (cocaine, alcohol, cannabis), bipolar disorder, schizophrenia, and as a chemoprotective antioxidant. The clinical evidence is mixed; meta-analyses generally support modest effects in OCD and addictive behaviors. The compound is sold as both a prescription drug (oral, IV, inhaled) and as an OTC supplement. Used as the canonical glutathione precursor in research.

3. Mechanism of Action

Glutathione precursor; rapidly hydrolyzed to L-cysteine, the rate-limiting amino acid for GSH synthesis. Direct mucolytic activity via disulfide bond reduction.

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

Clinical 600 to 2400 mg per oral administration daily; acetaminophen overdose IV protocol per body weight.

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. Berk M, et al. The promise of N-acetylcysteine in neuropsychiatry. Trends Pharmacol Sci 2013.
2. Atkuri KR, et al. N-Acetylcysteine - a safe antidote for cysteine/glutathione deficiency. Curr Opin Pharmacol 2007.
3. Smilkstein MJ, et al. Efficacy of oral N-acetylcysteine in the treatment of acetaminophen overdose. N Engl J Med 1988.

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