

RESEARCH MONOGRAPH . COMPOUND PROFILE

# Nicotine

*A pyridine alkaloid from tobacco (Nicotiana spp.) with broad nicotinic acetylcholine receptor agonist activity, studied at low doses for cognitive enhancement.*

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## ABSTRACT

Nicotine (CAS 54-11-5; molecular formula C<sub>10</sub>H<sub>14</sub>N<sub>2</sub>; molecular weight 162.23) is a pyridine alkaloid present principally in *Nicotiana tabacum* and other Solanaceae species. The compound is a potent agonist at nicotinic acetylcholine receptors (nAChRs) with affinity that varies by subunit composition: alpha4-beta2 nAChRs (high abundance in CNS) at high affinity, alpha7 nAChRs at moderate affinity, alpha3-containing autonomic nAChRs at moderate affinity. Low-dose nicotine has been studied extensively for cognitive enhancement (improved attention, working memory) in non-smokers; effect sizes are modest but consistent. Smoking cessation pharmacotherapy uses nicotine replacement (gum, patch, lozenge, inhaler, nasal spray) at doses sufficient to relieve withdrawal but lower than typical cigarette smoking exposure. The compound is highly addictive when delivered through rapid-onset routes (smoking, vaping); slower-onset routes (gum, patch) have lower abuse liability. Doses for cognitive applications are typically 1 to 4 mg via gum or lozenge.

# 1. Compound Identification

**Nicotine** is described as nicotinic acetylcholine receptor agonist. A pyridine alkaloid from tobacco (*Nicotiana* spp.) with broad nicotinic acetylcholine receptor agonist activity, studied at low doses for cognitive enhancement.

## 1.1 Class summary

Nicotinic acetylcholine receptor agonist

## 1.2 Subtitle

A pyridine alkaloid from tobacco (*Nicotiana* spp.) with broad nicotinic acetylcholine receptor agonist activity, studied at low doses for cognitive enhancement.

## 2. Abstract

Nicotine (CAS 54-11-5; molecular formula C<sub>10</sub>H<sub>14</sub>N<sub>2</sub>; molecular weight 162.23) is a pyridine alkaloid present principally in *Nicotiana tabacum* and other Solanaceae species. The compound is a potent agonist at nicotinic acetylcholine receptors (nAChRs) with affinity that varies by subunit composition: alpha4-beta2 nAChRs (high abundance in CNS) at high affinity, alpha7 nAChRs at moderate affinity, alpha3-containing autonomic nAChRs at moderate affinity. Low-dose nicotine has been studied extensively for cognitive enhancement (improved attention, working memory) in non-smokers; effect sizes are modest but consistent. Smoking cessation pharmacotherapy uses nicotine replacement (gum, patch, lozenge, inhaler, nasal spray) at doses sufficient to relieve withdrawal but lower than typical cigarette smoking exposure. The compound is highly addictive when delivered through rapid-onset routes (smoking, vaping); slower-onset routes (gum, patch) have lower abuse liability. Doses for cognitive applications are typically 1 to 4 mg via gum or lozenge.

### 3. Mechanism of Action

Nicotinic acetylcholine receptor agonist with subunit-dependent affinity (alpha4-beta2 high, alpha7 moderate, autonomic moderate).

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

1 to 4 mg via gum or lozenge for cognitive applications; higher doses for smoking cessation.

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. Heishman SJ, et al. Meta-analysis of the acute effects of nicotine and smoking on human performance. Psychopharmacology 2010.

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