

RESEARCH MONOGRAPH . COMPOUND PROFILE

Propofol

An alkylphenol intravenous general anesthetic; the most widely used induction anesthetic and the agent in Michael Jackson's death.

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COMPOUND CLASS	GABA-A receptor positive allosteric modulator (intravenous anesthetic)

ABSTRACT

Propofol (2,6-diisopropylphenol; CAS 2078-54-8; molecular formula $C_{12}H_{18}O$; molecular weight 178.27) is an alkylphenol intravenous general anesthetic developed at ICI (now AstraZeneca) and approved by the FDA in 1989 (Diprivan). The compound is a GABA-A receptor positive allosteric modulator at a unique propofol-binding site distinct from the benzodiazepine, barbiturate, and steroid sites; the result is enhanced GABA-mediated chloride conductance and pronounced CNS depression. Formulation is a 1 percent oil-in-water emulsion (the source of the milky appearance). Plasma half-life is biphasic: rapid distribution (2 to 4 minutes) and slower elimination (3 to 12 hours). Approved indications: induction and maintenance of general anesthesia, sedation in ICU. Misuse for amateur sedation is associated with the death of Michael Jackson (2009). Propofol infusion syndrome (rare) involves metabolic acidosis, rhabdomyolysis, and cardiac failure with prolonged high-dose use. Used as the canonical IV anesthetic in research and clinical practice.

1. Compound Identification

Propofol is described as gaba-a receptor positive allosteric modulator (intravenous anesthetic). An alkylphenol intravenous general anesthetic; the most widely used induction anesthetic and the agent in Michael Jackson's death.

1.1 Class summary

GABA-A receptor positive allosteric modulator (intravenous anesthetic)

1.2 Subtitle

An alkylphenol intravenous general anesthetic; the most widely used induction anesthetic and the agent in Michael Jackson's death.

2. Abstract

Propofol (2,6-diisopropylphenol; CAS 2078-54-8; molecular formula C₁₂H₁₈O; molecular weight 178.27) is an alkylphenol intravenous general anesthetic developed at ICI (now AstraZeneca) and approved by the FDA in 1989 (Diprivan). The compound is a GABA-A receptor positive allosteric modulator at a unique propofol-binding site distinct from the benzodiazepine, barbiturate, and steroid sites; the result is enhanced GABA-mediated chloride conductance and pronounced CNS depression. Formulation is a 1 percent oil-in-water emulsion (the source of the milky appearance). Plasma half-life is biphasic: rapid distribution (2 to 4 minutes) and slower elimination (3 to 12 hours). Approved indications: induction and maintenance of general anesthesia, sedation in ICU. Misuse for amateur sedation is associated with the death of Michael Jackson (2009). Propofol infusion syndrome (rare) involves metabolic acidosis, rhabdomyolysis, and cardiac failure with prolonged high-dose use. Used as the canonical IV anesthetic in research and clinical practice.

3. Mechanism of Action

GABA-A receptor positive allosteric modulator at a unique propofol-binding site; enhances GABA-mediated chloride conductance.

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 induction 1.5 to 2.5 mg/kg IV; maintenance 4 to 12 mg/kg/hour.

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. Kotani Y, et al. The experimental and clinical pharmacology of propofol, an anesthetic agent with neuroprotective properties. CNS Neurosci Ther 2008.
2. Trapani G, et al. Propofol in anesthesia. Mechanism of action, structure-activity relationships, and drug delivery. Curr Med Chem 2000.
3. Kam PC, Cardone D. Propofol infusion syndrome. Anaesthesia 2007.

This monograph is provided for research use only. Not for medical, diagnostic, or therapeutic purposes. Not for human consumption. Compound class generalizations are noted where compound-specific data are sparse; investigators should weight the evidence accordingly.