

RESEARCH MONOGRAPH . COMPOUND PROFILE

# Pregnenolone

*An endogenous steroid hormone synthesized from cholesterol; the precursor of all other endogenous steroid hormones and a neurosteroid in its own right.*

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| AUTHOR         | Kodiac bioLabs Research           |
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## ABSTRACT

Pregnenolone (CAS 145-13-1; molecular formula C<sub>21</sub>H<sub>32</sub>O<sub>2</sub>; molecular weight 316.48) is the metabolic precursor of all endogenous steroid hormones (corticosteroids, mineralocorticoids, gonadal steroids) synthesized from cholesterol by the side-chain cleavage enzyme CYP11A1. Pregnenolone is also a neurosteroid acting at sigma-1 receptors and as a positive allosteric modulator of NMDA receptors at micromolar concentrations. Plasma and CNS pregnenolone decline with age. The compound has been studied for cognitive enhancement, depression, and schizophrenia (where some Phase 2 trials have shown modest effects). The compound is sold as a dietary supplement. Doses are typically 10 to 100 mg per day. Investigators should be aware that pregnenolone elevates downstream steroid hormones (DHEA, cortisol, sex steroids) through metabolic conversion, with potential clinical implications.

# 1. Compound Identification

**Pregnenolone** is described as endogenous neurosteroid precursor. An endogenous steroid hormone synthesized from cholesterol; the precursor of all other endogenous steroid hormones and a neurosteroid in its own right.

## 1.1 Class summary

Endogenous neurosteroid precursor

## 1.2 Subtitle

An endogenous steroid hormone synthesized from cholesterol; the precursor of all other endogenous steroid hormones and a neurosteroid in its own right.

## 2. Abstract

Pregnenolone (CAS 145-13-1; molecular formula  $C_{21}H_{32}O_2$ ; molecular weight 316.48) is the metabolic precursor of all endogenous steroid hormones (corticosteroids, mineralocorticoids, gonadal steroids) synthesized from cholesterol by the side-chain cleavage enzyme CYP11A1. Pregnenolone is also a neurosteroid acting at sigma-1 receptors and as a positive allosteric modulator of NMDA receptors at micromolar concentrations. Plasma and CNS pregnenolone decline with age. The compound has been studied for cognitive enhancement, depression, and schizophrenia (where some Phase 2 trials have shown modest effects). The compound is sold as a dietary supplement. Doses are typically 10 to 100 mg per day. Investigators should be aware that pregnenolone elevates downstream steroid hormones (DHEA, cortisol, sex steroids) through metabolic conversion, with potential clinical implications.

### 3. Mechanism of Action

Sigma-1 receptor activity; NMDA receptor PAM. Precursor for downstream steroid hormone synthesis.

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

10 to 100 mg per day.

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. Marx CE, et al. Pregnenolone as a novel therapeutic candidate in schizophrenia. Mol Psychiatry 2009.

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