

RESEARCH MONOGRAPH . COMPOUND PROFILE

Levothyroxine (T4)

*Synthetic thyroxine; the standard
hypothyroidism treatment and the most
prescribed drug in the United States.*

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ABSTRACT

Levothyroxine (3,3',5,5'-tetraiodo-L-thyronine, T₄; CAS 51-48-9; molecular formula C₁₅H₁₁I₄NO₄; molecular weight 776.87) is synthetic L-thyroxine, the principal thyroid hormone produced by the thyroid gland. Approved by the FDA from 1955 (multiple manufacturers; brands include Synthroid, Levoxyl, Tirosint). The compound is a prohormone: T₄ is converted by deiodinases (D1, D2) to active T₃ in target tissues. The prohormone strategy provides smoother plasma levels than direct T₃ administration, reflecting the long T₄ half-life (approximately 7 days). Approved indications include primary, secondary, and tertiary hypothyroidism; thyroid cancer suppression therapy; goiter; and myxedema coma. Levothyroxine is the most prescribed drug in the United States by prescription count. Plasma half-life is approximately 7 days; absorption is impaired by food, calcium, iron, and proton pump inhibitors, requiring administration on an empty stomach with at least 4-hour spacing from interfering substances. Used as the canonical T₄ reference compound.

1. Compound Identification

Levothyroxine (T4) is described as thyroid prohormone (t4). Synthetic thyroxine; the standard hypothyroidism treatment and the most prescribed drug in the United States.

1.1 Class summary

Thyroid prohormone (T4)

1.2 Subtitle

Synthetic thyroxine; the standard hypothyroidism treatment and the most prescribed drug in the United States.

2. Abstract

Levothyroxine (3,3',5,5'-tetraiodo-L-thyronine, T4; CAS 51-48-9; molecular formula C₁₅H₁₁I₄NO₄; molecular weight 776.87) is synthetic L-thyroxine, the principal thyroid hormone produced by the thyroid gland. Approved by the FDA from 1955 (multiple manufacturers; brands include Synthroid, Levoxyl, Tirosint). The compound is a prohormone: T4 is converted by deiodinases (D1, D2) to active T3 in target tissues. The prohormone strategy provides smoother plasma levels than direct T3 administration, reflecting the long T4 half-life (approximately 7 days). Approved indications include primary, secondary, and tertiary hypothyroidism; thyroid cancer suppression therapy; goiter; and myxedema coma. Levothyroxine is the most prescribed drug in the United States by prescription count. Plasma half-life is approximately 7 days; absorption is impaired by food, calcium, iron, and proton pump inhibitors, requiring administration on an empty stomach with at least 4-hour spacing from interfering substances. Used as the canonical T4 reference compound.

3. Mechanism of Action

Synthetic T4 prohormone; converted to active T3 by deiodinases in target tissues. Smoother plasma levels than direct T3 administration owing to long half-life.

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 25 to 200 mcg per oral administration daily, on empty stomach. Rodent studies 5 to 50 mcg/kg/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. Garber JR, et al. Clinical practice guidelines for hypothyroidism in adults. Thyroid 2012.
2. Hennessey JV. The emergence of levothyroxine as a treatment for hypothyroidism. Endocrine 2017.
3. Liwanpo L, Hershman JM. Conditions and drugs interfering with thyroxine absorption. Best Pract Res Clin Endocrinol Metab 2009.

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