

RESEARCH MONOGRAPH . COMPOUND PROFILE

Liothyronine (T3)

The active thyroid hormone triiodothyronine; faster-acting and more potent than levothyroxine, used in hypothyroidism, depression augmentation, and metabolic research.

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ABSTRACT

Liothyronine (3,3',5-triiodo-L-thyronine, T3; CAS 6893-02-3; molecular formula C₁₅H₁₂I₃NO₄; molecular weight 650.97) is the active thyroid hormone, marketed as Cytomel for hypothyroidism. The compound binds thyroid hormone receptors (TR-alpha, TR-beta) with approximately 4-fold higher affinity than thyroxine (T4) and produces direct genomic effects on metabolic gene transcription without the conversion delay required for T4. Plasma half-life is 2.5 days, much shorter than T4's 7-day half-life, producing more variable plasma levels but faster onset and offset. Approved for hypothyroidism (alternative or adjunct to levothyroxine), myxedema coma (intravenous), and as a thyroid suppression test. Off-label use in major depressive disorder augmentation (the STAR*D trial-supported strategy of T3 25 to 50 mcg added to a partially-responding antidepressant), fat loss, and bodybuilding cutting cycles. The cardiac risk is the principal limitation: T3 directly increases myocardial oxygen demand, producing tachycardia, atrial fibrillation, and angina at supratherapeutic doses. Used as the canonical T3 reference compound.

1. Compound Identification

Liothyronine (T3) is described as active thyroid hormone (t3). The active thyroid hormone triiodothyronine; faster-acting and more potent than levothyroxine, used in hypothyroidism, depression augmentation, and metabolic research.

1.1 Class summary

Active thyroid hormone (T3)

1.2 Subtitle

The active thyroid hormone triiodothyronine; faster-acting and more potent than levothyroxine, used in hypothyroidism, depression augmentation, and metabolic research.

2. Abstract

Liothyronine (3,3',5-triiodo-L-thyronine, T3; CAS 6893-02-3; molecular formula C₁₅H₁₂I₃NO₄; molecular weight 650.97) is the active thyroid hormone, marketed as Cytomel for hypothyroidism. The compound binds thyroid hormone receptors (TR-alpha, TR-beta) with approximately 4-fold higher affinity than thyroxine (T4) and produces direct genomic effects on metabolic gene transcription without the conversion delay required for T4. Plasma half-life is 2.5 days, much shorter than T4's 7-day half-life, producing more variable plasma levels but faster onset and offset. Approved for hypothyroidism (alternative or adjunct to levothyroxine), myxedema coma (intravenous), and as a thyroid suppression test. Off-label use in major depressive disorder augmentation (the STAR*D trial-supported strategy of T3 25 to 50 mcg added to a partially-responding antidepressant), fat loss, and bodybuilding cutting cycles. The cardiac risk is the principal limitation: T3 directly increases myocardial oxygen demand, producing tachycardia, atrial fibrillation, and angina at supratherapeutic doses. Used as the canonical T3 reference compound.

3. Mechanism of Action

Active thyroid hormone; binds TR-alpha and TR-beta with ~4-fold higher affinity than T4. Direct genomic effects without T4-to-T3 conversion delay.

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 5 to 75 mcg per oral administration daily, in divided doses. Depression augmentation 25 to 50 mcg/day. Off-label fat loss 25 to 75 mcg/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. Wiersinga WM, et al. Combined therapy with levothyroxine plus liothyronine in hypothyroidism. Nat Rev Endocrinol 2014.
2. Aronson R, et al. Triiodothyronine augmentation in the treatment of refractory depression: a meta-analysis. Arch Gen Psychiatry 1996.
3. Joffe RT, et al. Triiodothyronine in depression: a meta-analysis. Psychiatry Res 2010.

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