

RESEARCH MONOGRAPH . COMPOUND PROFILE

Citalopram

A racemic phthalane SSRI; the most selective for SERT over NET in clinical use.

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COMPOUND CLASS	Selective serotonin reuptake inhibitor

ABSTRACT

Citalopram (1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-2-benzofuran-5-carbonitrile; CAS 59729-33-8; molecular formula C₂₀H₂₁FN₂O; molecular weight 324.39) is a bicyclic phthalane SSRI developed at H. Lundbeck in Denmark and approved in Europe in 1989 and by the FDA in 1998 under the trade name Celexa. The compound is sold as the racemate; the (S)-enantiomer (escitalopram) accounts for essentially all SERT inhibitory activity, while the (R)-enantiomer is largely inactive but may attenuate the (S)-enantiomer's binding through allosteric SERT interaction. SERT affinity ((S)-enantiomer): K_i approximately 1 nM; selectivity over NET and DAT exceeds 1000-fold, making citalopram the most selective SSRI in clinical use. Plasma half-life is 33 to 37 hours; hepatic metabolism via CYP2C19, CYP3A4, and CYP2D6 produces minimally active metabolites. The compound is associated with dose-dependent QTc prolongation (FDA boxed warning issued 2011), with the maximum recommended dose reduced from 60 mg to 40 mg as a result. Used as the canonical selective SERT inhibitor in mechanism studies and as a reference compound in SSRI structure-activity work.

1. Compound Identification

Citalopram is described as selective serotonin reuptake inhibitor. A racemic phthalane SSRI; the most selective for SERT over NET in clinical use.

1.1 Class summary

Selective serotonin reuptake inhibitor

1.2 Subtitle

A racemic phthalane SSRI; the most selective for SERT over NET in clinical use.

2. Abstract

Citalopram (1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-2-benzofuran-5-carbonitrile; CAS 59729-33-8; molecular formula C₂₀H₂₁FN₂O; molecular weight 324.39) is a bicyclic phthalane SSRI developed at H. Lundbeck in Denmark and approved in Europe in 1989 and by the FDA in 1998 under the trade name Celexa. The compound is sold as the racemate; the (S)-enantiomer (escitalopram) accounts for essentially all SERT inhibitory activity, while the (R)-enantiomer is largely inactive but may attenuate the (S)-enantiomer's binding through allosteric SERT interaction. SERT affinity ((S)-enantiomer): K_i approximately 1 nM; selectivity over NET and DAT exceeds 1000-fold, making citalopram the most selective SSRI in clinical use. Plasma half-life is 33 to 37 hours; hepatic metabolism via CYP2C19, CYP3A4, and CYP2D6 produces minimally active metabolites. The compound is associated with dose-dependent QTc prolongation (FDA boxed warning issued 2011), with the maximum recommended dose reduced from 60 mg to 40 mg as a result. Used as the canonical selective SERT inhibitor in mechanism studies and as a reference compound in SSRI structure-activity work.

3. Mechanism of Action

Selective high-affinity SERT inhibition; (S)-enantiomer is the active component. Racemic mixture; (R)-enantiomer is largely inactive with possible allosteric attenuation of (S) binding.

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 10 to 40 mg per oral administration daily. Rodent studies 1 to 20 mg/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. Hyttel J. Citalopram: pharmacological profile of a specific serotonin uptake inhibitor with antidepressant activity. Prog Neuropsychopharmacol Biol Psychiatry 1982.
2. Sanchez C, Hyttel J. Comparison of the effects of antidepressants and their metabolites on reuptake of biogenic amines. Cell Mol Neurobiol 1999.
3. Cooke MJ, Waring WS. Citalopram safety and risk of QT interval prolongation. Toxicol Rev 2013.

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.