

RESEARCH MONOGRAPH . COMPOUND PROFILE

Levobupivacaine

The (S)-enantiomer of bupivacaine, marketed as Chirocaine, with a reduced cardiotoxic and CNS toxic profile relative to the racemate.

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COMPOUND CLASS	Amide local anesthetic (S-enantiomer of bupivacaine)

ABSTRACT

Levobupivacaine ((S)-1-butyl-N-(2,6-dimethylphenyl)piperidine-2-carboxamide; CAS 27262-47-1; molecular formula C₁₈H₂₈N₂O; molecular weight 288.43) is the (S)-enantiomer of bupivacaine, developed by Chiroscience and Purdue and approved by the FDA in 1999 (Chirocaine). The enantioselective pharmacology of bupivacaine motivated separation: the (R)-enantiomer carries the dominant cardiotoxic and CNS toxic burden through higher cardiac sodium channel affinity and slower dissociation, while the (S)-enantiomer produces equivalent neural block with substantially reduced toxic margin. Direct toxicology comparisons in rat and pig models show 30 to 40 percent lower toxic dose ratios for cardiovascular collapse and seizure threshold with levobupivacaine versus racemic bupivacaine at equivalent neural block efficacy. Clinical equivalence trials in epidural, spinal, and peripheral nerve block applications demonstrate non-inferior efficacy with lower incidence of CNS toxicity in inadvertent intravascular dosing. Mechanism is identical to racemic bupivacaine (voltage-gated sodium channel block) with the favorable enantioselectivity at cardiac sodium channels driving the safety advantage. Onset, duration, and maximum recommended doses are similar to bupivacaine; some sources permit slightly higher cumulative levobupivacaine doses (3 mg/kg without epinephrine) reflecting the safety margin. The principal limitation of levobupivacaine is acquisition cost relative to racemic bupivacaine, which has restricted uptake in some markets despite the favorable safety profile. The compound was withdrawn from the US market in 2010 for commercial reasons

but remains available in Europe and Asia. Lipid emulsion rescue is the standard therapy for any LAST event.

1. Compound Identification

Levobupivacaine is described as amide local anesthetic (s-enantiomer of bupivacaine). The (S)-enantiomer of bupivacaine, marketed as Chirocaine, with a reduced cardiotoxic and CNS toxic profile relative to the racemate.

1.1 Class summary

Amide local anesthetic (S-enantiomer of bupivacaine)

1.2 Subtitle

The (S)-enantiomer of bupivacaine, marketed as Chirocaine, with a reduced cardiotoxic and CNS toxic profile relative to the racemate.

2. Abstract

Levobupivacaine ((S)-1-butyl-N-(2,6-dimethylphenyl)piperidine-2-carboxamide; CAS 27262-47-1; molecular formula C₁₈H₂₈N₂O; molecular weight 288.43) is the (S)-enantiomer of bupivacaine, developed by Chiroscience and Purdue and approved by the FDA in 1999 (Chirocaine). The enantioselective pharmacology of bupivacaine motivated separation: the (R)-enantiomer carries the dominant cardiotoxic and CNS toxic burden through higher cardiac sodium channel affinity and slower dissociation, while the (S)-enantiomer produces equivalent neural block with substantially reduced toxic margin. Direct toxicology comparisons in rat and pig models show 30 to 40 percent lower toxic dose ratios for cardiovascular collapse and seizure threshold with levobupivacaine versus racemic bupivacaine at equivalent neural block efficacy. Clinical equivalence trials in epidural, spinal, and peripheral nerve block applications demonstrate non-inferior efficacy with lower incidence of CNS toxicity in inadvertent intravascular dosing. Mechanism is identical to racemic bupivacaine (voltage-gated sodium channel block) with the favorable enantioselectivity at cardiac sodium channels driving the safety advantage. Onset, duration, and maximum recommended doses are similar to bupivacaine; some sources permit slightly higher cumulative levobupivacaine doses (3 mg/kg without epinephrine) reflecting the safety margin. The principal limitation of levobupivacaine is acquisition cost relative to racemic bupivacaine, which has restricted uptake in some markets despite the favorable safety profile. The compound was withdrawn from the US market in 2010 for commercial reasons but remains available in Europe and Asia. Lipid emulsion rescue is the standard therapy for any LAST event.

3. Mechanism of Action

Voltage-gated sodium channel block, identical to racemic bupivacaine with favorable enantioselective profile at cardiac sodium channels reducing cardiotoxicity.

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

Up to 2 mg/kg without epinephrine. Spinal 7.5 to 15 mg, epidural 50 to 150 mg.

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. Bardsley H, et al. Comparison of cardiovascular effects of levobupivacaine and rac-bupivacaine in volunteers. Br J Clin Pharmacol 1998.
2. Foster RH, Markham A. Levobupivacaine: a review. Drugs 2000.
3. McLeod GA, Burke D. Levobupivacaine. Anaesthesia 2001.

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