

RESEARCH MONOGRAPH . COMPOUND PROFILE

Articaine

The dominant dental local anesthetic in much of Europe and increasingly in North America, distinguished by a thiophene ring enabling rapid plasma esterase hydrolysis.

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COMPOUND CLASS	Amide local anesthetic with thiophene ring (dental)

ABSTRACT

Articaine (methyl 4-methyl-3-(2-propylaminopropanoylamino)thiophene-2-carboxylate; CAS 23964-58-1; molecular formula C₁₃H₂₀N₂O₃S; molecular weight 284.38) is an amide local anesthetic developed by Hoechst in the 1970s and introduced in Germany in 1976 (Ultracain, Septocaine in North America). The compound is structurally distinct among amide local anesthetics in carrying both an amide and a methyl ester linkage on a thiophene ring rather than the dimethylphenyl ring of lidocaine and the pipecoloxylidide family. The methyl ester is rapidly hydrolyzed by plasma esterases to the inactive articainic acid metabolite (plasma half-life approximately 25 minutes, shorter than any other amide), which truncates systemic exposure and reduces accumulation risk during dental procedures requiring repeated infiltration. The thiophene ring confers enhanced bone diffusion, supporting the clinical perception that articaine produces effective infiltration anesthesia of mandibular molar teeth without requiring inferior alveolar nerve block in many cases (a clinical advantage that makes articaine the dominant dental anesthetic in much of Europe). Mechanism is voltage-gated sodium channel block; potency is approximately 1.5-fold that of lidocaine on infiltration. Articaine is sold as a 4 percent solution with epinephrine 1:100,000 or 1:200,000. The principal safety considerations are the same methemoglobinemia risk noted for prilocaine (articaine generates methemoglobin-inducing metabolites though at lower doses than prilocaine, the clinical risk is correspondingly low) and case reports of paresthesia after inferior alveolar nerve block. Maximum recommended dose is 7 mg/kg in adults and 5 mg/kg in children.

1. Compound Identification

Articaine is described as amide local anesthetic with thiophene ring (dental). The dominant dental local anesthetic in much of Europe and increasingly in North America, distinguished by a thiophene ring enabling rapid plasma esterase hydrolysis.

1.1 Class summary

Amide local anesthetic with thiophene ring (dental)

1.2 Subtitle

The dominant dental local anesthetic in much of Europe and increasingly in North America, distinguished by a thiophene ring enabling rapid plasma esterase hydrolysis.

2. Abstract

Articaine (methyl 4-methyl-3-(2-propylaminopropanoylamino)thiophene-2-carboxylate; CAS 23964-58-1; molecular formula C₁₃H₂₀N₂O₃S; molecular weight 284.38) is an amide local anesthetic developed by Hoechst in the 1970s and introduced in Germany in 1976 (Ultracain, Septocaine in North America). The compound is structurally distinct among amide local anesthetics in carrying both an amide and a methyl ester linkage on a thiophene ring rather than the dimethylphenyl ring of lidocaine and the pipecoloxylidide family. The methyl ester is rapidly hydrolyzed by plasma esterases to the inactive articainic acid metabolite (plasma half-life approximately 25 minutes, shorter than any other amide), which truncates systemic exposure and reduces accumulation risk during dental procedures requiring repeated infiltration. The thiophene ring confers enhanced bone diffusion, supporting the clinical perception that articaine produces effective infiltration anesthesia of mandibular molar teeth without requiring inferior alveolar nerve block in many cases (a clinical advantage that makes articaine the dominant dental anesthetic in much of Europe). Mechanism is voltage-gated sodium channel block; potency is approximately 1.5-fold that of lidocaine on infiltration. Articaine is sold as a 4 percent solution with epinephrine 1:100,000 or 1:200,000. The principal safety considerations are the same methemoglobinemia risk noted for prilocaine (articaine generates methemoglobin-inducing metabolites though at lower doses than prilocaine, the clinical risk is correspondingly low) and case reports of paresthesia after inferior alveolar nerve block. Maximum recommended dose is 7 mg/kg in adults and 5 mg/kg in children.

3. Mechanism of Action

Voltage-gated sodium channel block. Plasma esterase hydrolysis of methyl ester drives short systemic half-life. Thiophene ring enhances bone diffusion.

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

7 mg/kg in adults, 5 mg/kg in children. Dental 4 percent with epinephrine 1:100,000 or 1:200,000.

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. Malamed SF, et al. Articaine hydrochloride: a study of the safety. J Am Dent Assoc 2001.
2. Yapp KE, et al. Articaine: a review of the literature. Br Dent J 2011.
3. Kammerer PW, et al. Articaine versus lidocaine in maxillary infiltration anesthesia. J Am Dent Assoc 2012.

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