

RESEARCH MONOGRAPH . COMPOUND PROFILE

Benzocaine

The simplest ester local anesthetic, used as a topical mucous membrane anesthetic and the principal ingredient in over-the-counter sore-throat lozenges.

DOCUMENT	KDC-MN-1317
ISSUED	2026-05-10
REVISION	1.0
AUTHOR	Kodiac bioLabs Research
COMPOUND CLASS	Ester local anesthetic (topical only)

ABSTRACT

Benzocaine (ethyl 4-aminobenzoate; CAS 94-09-7; molecular formula $C_9H_{11}NO_2$; molecular weight 165.19) is an ester-class local anesthetic, structurally the simplest member of the para-aminobenzoate family (the primary aminobenzoate ester directly esterified to ethanol, lacking the diethylamino-ethanol group of procaine). The simpler structure produces a lipophilic, water-poorly-soluble compound suitable only for topical mucous membrane anesthesia; the absence of the tertiary amine restricts utility for infiltration and regional anesthesia. Benzocaine is the principal active ingredient in over-the-counter throat lozenges (Cepacol), oral analgesic gels (Anbesol, Orajel), topical preparations for hemorrhoidal and minor wound use, and topical ENT and bronchoscopy preparation. Mechanism is voltage-gated sodium channel block in surface nerve fibers contacted topically. Onset is rapid (15 to 60 seconds on mucous membranes); duration is 5 to 15 minutes. The principal safety concern is dose-dependent methemoglobinemia, more pronounced than with prilocaine, that has driven FDA boxed warnings against benzocaine spray and gel use in infants and limited topical doses in children and adults. The mechanism is hepatic conversion of benzocaine to nitroso and N-hydroxy metabolites that oxidize hemoglobin iron to the ferric state. Clinical methemoglobinemia is reported with topical mucosal application of as little as 250 mg in vulnerable individuals; the risk is amplified in G6PD deficiency, infancy (low NADH-methemoglobin reductase activity), and concurrent oxidant drug exposure. Methylene blue is the rescue therapy. The FDA advised in 2018 against benzocaine teething gels in infants under 2 years.

1. Compound Identification

Benzocaine is described as ester local anesthetic (topical only). The simplest ester local anesthetic, used as a topical mucous membrane anesthetic and the principal ingredient in over-the-counter sore-throat lozenges.

1.1 Class summary

Ester local anesthetic (topical only)

1.2 Subtitle

The simplest ester local anesthetic, used as a topical mucous membrane anesthetic and the principal ingredient in over-the-counter sore-throat lozenges.

2. Abstract

Benzocaine (ethyl 4-aminobenzoate; CAS 94-09-7; molecular formula $C_9H_{11}NO_2$; molecular weight 165.19) is an ester-class local anesthetic, structurally the simplest member of the para-aminobenzoate family (the primary aminobenzoate ester directly esterified to ethanol, lacking the diethylamino-ethanol group of procaine). The simpler structure produces a lipophilic, water-poorly-soluble compound suitable only for topical mucous membrane anesthesia; the absence of the tertiary amine restricts utility for infiltration and regional anesthesia. Benzocaine is the principal active ingredient in over-the-counter throat lozenges (Cepacol), oral analgesic gels (Anbesol, Orajel), topical preparations for hemorrhoidal and minor wound use, and topical ENT and bronchoscopy preparation. Mechanism is voltage-gated sodium channel block in surface nerve fibers contacted topically. Onset is rapid (15 to 60 seconds on mucous membranes); duration is 5 to 15 minutes. The principal safety concern is dose-dependent methemoglobinemia, more pronounced than with prilocaine, that has driven FDA boxed warnings against benzocaine spray and gel use in infants and limited topical doses in children and adults. The mechanism is hepatic conversion of benzocaine to nitroso and N-hydroxy metabolites that oxidize hemoglobin iron to the ferric state. Clinical methemoglobinemia is reported with topical mucosal application of as little as 250 mg in vulnerable individuals; the risk is amplified in G6PD deficiency, infancy (low NADH-methemoglobin reductase activity), and concurrent oxidant drug exposure. Methylene blue is the rescue therapy. The FDA advised in 2018 against benzocaine teething gels in infants under 2 years.

3. Mechanism of Action

Voltage-gated sodium channel block. Topical only. Methemoglobinemia from hepatic generation of nitroso and N-hydroxy metabolites.

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

Topical mucous membrane 1 to 20 percent; bronchoscopy 100 to 200 mg total maximum.

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. Vallurupalli S, Manchanda S. Benzocaine-induced methemoglobinemia. Chest 2011.
2. FDA Drug Safety Communication: Methemoglobinemia warning. May 2018.
3. Guay J. Methemoglobinemia related to local anesthetics: 242 episodes. Anesth Analg 2009.

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.