

# OVERVIEW

## Compounded Topical Anesthetics in Orthodontics

NEAL D. KRAVITZ, DMD, MS  
JOHN W. GRAHAM, DDS, MD  
JONATHAN L. NICOZISIS, DMD, MS  
JAY GILL, PharmD

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*(Editor's Note: In this regular column, JCO provides an overview of a clinical topic of interest to orthodontists. Contributions and suggestions for future subjects are welcome.)*

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**C**ompounded topical anesthetics are commonly used in orthodontics as an alternative to local infiltration for soft-tissue laser surgery,<sup>1,2</sup> placement of temporary anchorage devices,<sup>3,4</sup> and transmucosal alveolar micro-osteoperforation.<sup>5</sup> Questions remain, however, regarding the consistency of their formulation and the safety of their use. At

present, compounded topical anesthetics are in “regulation limbo”—neither regulated nor unregulated by the U.S. Food and Drug Administration (FDA).<sup>6</sup>

In 2007, a comprehensive review of compounded topical anesthetics in the *Journal of the American Dental Association* examined clinical trials, case reports, descriptive articles, FDA regulations, clinical implications, and legitimate risks associated with their uncontrolled application.<sup>7</sup> This article will serve as a follow-up for orthodontists, providing current information on the creation and packaging of compounded topical anesthetics.



**Dr. Kravitz**



**Dr. Graham**



**Dr. Nicozisis**



**Dr. Gill**

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Dr. Kravitz is a Contributing Editor of the *Journal of Clinical Orthodontics*; an adjunct faculty member, Department of Orthodontics, Washington Hospital Center, Washington, DC; and in the private practice of orthodontics at 25055 Riding Plaza, Suite 110, South Riding, VA 20152; e-mail: nealkravitz@gmail.com. Dr. Graham is a Contributing Editor of the *Journal of Clinical Orthodontics*; an Adjunct Associate Professor, Department of Orthodontics, Arthur A. Dugoni School of Dentistry, University of the Pacific, San Francisco, and the Department of Orthodontics, University of Rochester School of Medicine and Dentistry, Rochester, NY; and in the private practice of orthodontics in Salt Lake City. Dr. Nicozisis is in the private practice of orthodontics in Princeton, NJ. Dr. Gill is a compounding pharmacist and owner, The Compounding Center, Leesburg, VA.

**TABLE 1  
POPULAR COMPOUNDED TOPICAL ANESTHETICS**

<b>Brand Name*</b>	<b>Active Ingredients</b>
TAC 20% Alternate	20% lidocaine, 4% tetracaine, 2% phenylephrine
Profound	10% lidocaine, 10% prilocaine, 4% tetracaine
Profound PET/DēpBlu	10% lidocaine, 10% prilocaine, 4% tetracaine, 2% phenylephrine
Baddest Topical in Town	3% lidocaine, 12.5% prilocaine, 12.5% tetracaine, 3% phenylephrine
Best Topical Ever	12.5% lidocaine, 3% prilocaine, 12.5% tetracaine, 3% phenylephrine

\*Any compounding pharmacy can create any formulation with a prescription.

**Compounded Preparations**

Simply put, a compounded preparation is a custom-made pharmaceutical. Compounding is the process by which the pharmacist or doctor combines, mixes, or alters pharmaceutical ingredients in accordance with a prescription.<sup>8</sup> Compounds are in common usage as intravenous or parenteral medications, anti-inflammatories, antibiotics, soaps, troches, rinses, and topicals. At the most basic level, when you dilute the Listerine bottle at your brushing station with tap water, you are practicing a form of compounding.

Compounding is not the same as drug manufacturing. A compounded preparation is created for the unique needs of an individual patient. Although the separate components of a compounded preparation are commonly manufactured under FDA approval, it is their alteration and combination that make the end product unregulated. Under section 503A of the Food and Drug Administration Modernization Act of 1997, any drug products that are compounded on a customized basis are exempt from the FDA’s approval requirements.<sup>9</sup>

On the other hand, drug manufacturing is defined as the production, preparation, propagation, processing, and packaging of a pharmaceutical for general use.<sup>10</sup> Manufactured drugs are regulated under the Federal Food, Drug, and Cosmetic Act. For example, benzocaine gel is a popular FDA-approved topical anesthetic sold over the counter under brand names such as Anbesol, HurriCaine, Orajel, and Orabase.

The confusion between compounded pharmaceuticals and manufactured drugs is likely due to two factors: the emergence of large, multicenter compounding pharmacies that produce hundreds of custom-made medical, dental, and veterinary medications, and the brand names assigned to compounded pharmaceuticals.

Section 503A states that a pharmacy cannot compound an “inordinate” amount of a preparation before receiving a prescription.<sup>6</sup> “Inordinate” is not defined, but state inspectors generally look to match historical use patterns with the amount of premade preparations on the pharmacy’s shelf. For example, if a pharmacy can show that it typically receives six orders a month for a specific pharmaceutical, it would be allowed to premake the compound in anticipation of those orders. If an inspector saw a 30-gallon drum of the premade preparation, however, it would be a violation of the pharmacy’s 503A status. Where “inordinate” preparation actually becomes an end run around drug-manufacturing regulations is a gray area of pharmacy law.

In addition, a compounded pharmaceutical is sometimes given an attractive brand name that can diminish the product’s individualization and perceived risks. The brand name becomes a form of marketing, inappropriately tying the compounded formulation to a particular pharmacy. Popular brand names of intraoral mucosal compound topical anesthetics include TAC Alternate, Profound, DēpBlu, Baddest Topical in Town, and Best Topical Ever.

## Popular Compounded Anesthetics in Orthodontics

Regardless of brand name, mucosal compound topical anesthetics are relatively similar. Each contains a combination of high-dose anesthetics, including both ester-type (tetracaine) and amide-type (lidocaine and prilocaine), to provide profound numbness, as well as other inactive ingredients for structure and taste. Some formulations also contain vasoconstrictors such as phenylephrine—though it is debatable what this agent truly contributes. Orthodontists should be familiar with a few of the most popular mucosal compounded topical anesthetics (Table 1):

**TAC 20% Alternate**, or TAC Alternate, contains two anesthetic agents (20% lidocaine and 4% tetracaine) and one vasoactive agent (2% phenylephrine). The original TAC, composed of tetracaine, epinephrine (adrenaline), and cocaine, was once commonly used in hospital emergency departments as a dermal topical anesthetic to provide pain relief and vasoconstriction prior to suturing. TAC Alternate is somewhat of a misnomer, since the formulation does not contain cocaine. Its active ingredients are identical to those of LET (lidocaine, epinephrine, and tetracaine), another popular dermal compounded topical anesthetic.<sup>7</sup>

**Profound** is a topical anesthetic gel compounded from three anesthetic agents (10% lidocaine, 10% prilocaine, and 4% tetracaine). Its equal concentration of lidocaine and prilocaine is similar to that of two FDA-approved topical anesthetics: EMLA cream (2.5% lidocaine and 2.5% prilocaine), which provides dermal anesthesia prior to venipuncture, and Oraqix (2.5% lidocaine and 2.5% prilocaine), which is inserted into the gingival sulcus before root planing. Dr. Graham has introduced Profound PET (for “phenylephrine thick”),<sup>11</sup> or Profpet, which adds a vasoactive agent (2% phenylephrine) and methylcellulose for greater viscosity. DēpBlu, another popular compounded anesthetic, was developed by Dr. Jason Cope and has the same active ingredients as those of Profound PET.

**Baddest Topical in Town (BTT)**, is composed of three anesthetics (12.5% prilocaine, 12.5% tetra-

caine, and 3% lidocaine) and a vasoactive agent (3% phenylephrine). BTT was introduced by Dr. Nicozisis for use with Propel transmucosal alveolar micro-osteoperforation.<sup>5</sup> The high concentration of tetracaine provides strong, penetrating anesthesia. Another popular topical compound, the Best Topical Ever, uses similar active ingredients, but reverses the concentration of lidocaine and prilocaine (12.5% lidocaine, 12.5% tetracaine, and 3% prilocaine).

It should be noted that dermal compounded topical anesthetics made for extraoral use should not be applied intraorally. Although the active ingredients may be similar to those of a mucosal compounded topical anesthetic used inside the mouth, the carrier ingredient is different.

## What to Look for in a Compounding Pharmacy

Any compounding pharmacy can create the formulations listed above at the request of a licensed prescriber. When choosing a compounding pharmacy, it is important to ensure that it meets the following criteria:

- Is licensed and in good standing with its state pharmacy board.
- Is accredited by the Pharmacy Compounding Accreditation Board.
- Purchases ingredients from FDA-registered suppliers.
- Documents the Certificate of Analysis on its ingredients.
- Strictly follows U.S. Pharmacopeia (USP)-National Formulary guidelines.

Orthodontists should familiarize themselves with chapters 795 and 797 of the USP Compounding Compendium<sup>8</sup> ([www.usp.org](http://www.usp.org)). Chapter 795 provides guidance on the preparation of nonsterile compounded formulations, including definitions of terms and criteria for compounding each drug. Chapter 797 lists procedures and requirements for compounding sterile preparations. It also describes how to prevent harm to patients from contamination, variability in intended strengths, or ingredients of inappropriate quality.



**Fig. 1** A. Powder anesthetics measured with barcode technology. B. Dry ingredients placed in glass mortar. C. Wetting agents and base mixed with powder anesthetic and vasoconstrictor. D. Bitterness suppressor and flavoring agent added. E. Compounded preparation placed in Unguator jar for mixing. F. Digital balance used to confirm proper weight and amount prior to mixing. G. Unguator jar attached to Unguator machine for blending. H. Compounded preparation placed in ointment mill to further reduce particle size. I. Compounded preparation dispensed from Unguator jar into metered-dose pump.

## The Compounding Process

A compounded topical anesthetic has five primary components: a mixture of powder anesthetics, a powder vasoactive agent, a wetting agent to mix the powders, a base to transport the drug, and ingredients for flavor and color. The dry ingredients and base, distributed to the compounding pharmacy in large plastic containers, are purchased from FDA-registered chemical suppliers such as Letco, Medisca, and the Professional Compounding Centers of America (PCCA). The powder anesthetics and vasoactive agents are pure powders, meaning there are no added ingredients or excipients that could interfere with the compounding process or intended use.

First, the dry ingredients, or active agents, are measured and mixed. In accordance with a prescription, the powder anesthetics and vasoactive agent are scanned using barcode technology and weighed on a digital balance (Fig. 1A). The barcode scanner ensures that the correct ingredient is weighed within a range of  $\pm 3\%$ ; the digital balance, with a scale in 1mg increments, is fully integrated with the compounding software.

After the powder ingredients are titrated by a pharmacist in a glass mortar to reduce the particle size (Fig. 1B), the wet ingredients are added. A wetting agent such as alcohol, propylene glycol, or ethoxydiglycol is applied to moisten the powder into a dough-like consistency, displacing air and



**Fig. 2** Finished compounded anesthetic with proper labeling ready to ship to doctor.

allowing the powder to be easily incorporated into the base (Fig. 1C). Wetting agents also serve to enhance penetration of the active ingredients through the skin or mucous membrane. Next, a cream, gel, or ointment base is added to the mixture as a vehicle to carry the drug. PCCA's plasticized polyethylene-and-mineral-oil gel base is commonly used for topical and oral preparations because it has a soft feel and is completely anhydrous, ideal for water-sensitive active ingredients. Finally, a bitterness suppressor, flavoring, sweeteners, and color dyes to match the flavor (e.g., red for cherry flavor) are added to make the preparation more palatable for the patient (Fig. 1D).

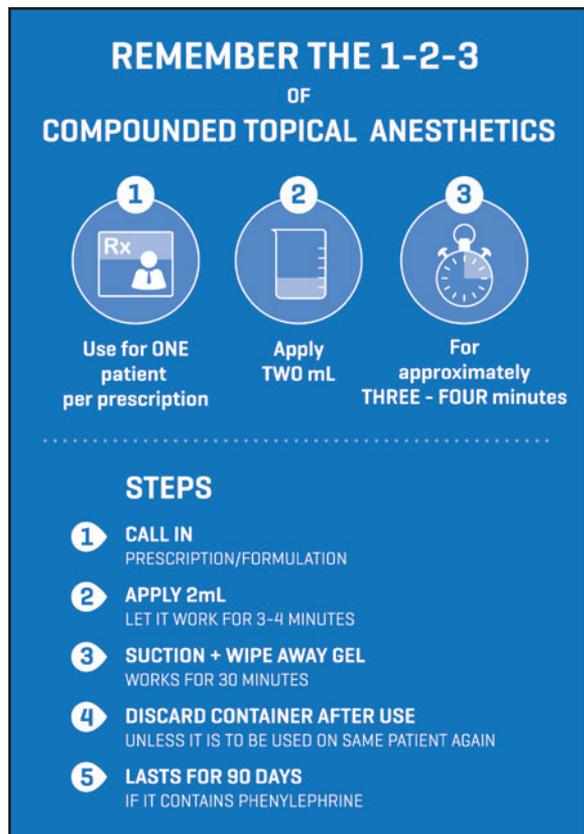
At this point, the mixture may be rough or gritty. To improve its consistency and ensure it is well mixed, it is placed in an Unguator jar, which acts simultaneously as a measuring unit, mixing chamber, storage container, and dispensing vessel (Fig. 1E). After the proper weight and amount of preparation are confirmed on the digital balance (Fig. 1F), the jar is attached to the Unguator machine for high-speed blending (Fig. 1G).

In a final important step to further reduce particle size, the anesthetic is removed from the Unguator jar and placed in an ointment mill, which shears the mixture through a series of rollers (Fig. 1H). Particle size is reduced to less than 20 microns, thus increasing the surface area of the active ingredients. The end product is smooth, consistent, and creamy.

After the anesthetic has been milled, it is dispensed directly from the Unguator jar into a metered-dose pump, a sealed container that deposits .5ml of anesthetic per actuation (Fig. 1I). Each container is then labeled with the compound name, strength, lot number, expiration date, and quantity (Fig. 2).

## Patient Application

In accordance with federal pharmacy law, a compounded topical anesthetic should be applied to a single patient per prescription (Fig. 3). A doctor who stores a jar of compounded topical anesthetic in the office and applies it on multiple patients, regardless of whether a syringe is used to



**Fig. 3** Infographic of key information on compounded topical anesthetics.

extract a single-patient dosage, may be in violation.

The suggested dosage for compounded topical anesthetics is typically 2ml (or four pumps) per patient. The anesthetic should be applied under direct doctor supervision for three to four minutes, although a slightly longer application may be needed for the thicker palatal tissue. After four minutes, the gross amount of anesthetic is removed with high-speed suction, and the tissues are then wiped with gauze to ensure that all anesthetic has been removed. Using a surgical suction tip instead of a large-bore standard suction tip facilitates more complete removal. Prolonged application, particularly around the gingival margin, may lead to tissue irritation and sloughing. Anesthesia occurs rapidly and lasts about 30 minutes.



**Fig. 4** Two formulations of 20% lidocaine, 4% tetracaine, and 2% phenylephrine mixture, both ordered in 2007. Note difference in thickness and mixture quality.

A compounded anesthetic should be stored at room temperature rather than in the office’s laboratory refrigerator. If the anesthetic is contained in a cylindrical jar with a removal top, it should not be exposed to light unnecessarily; phenylephrine makes the topical light-sensitive, with a shelf life of 90 days.<sup>11</sup>

**Potential Risks**

Previous articles have warned of several risks associated with the creation and packaging of compounded topical anesthetics.<sup>6,7</sup> First, they may vary in strength of anesthesia and in composition and quality of mixture (Fig. 4). Second, the containers may be improperly labeled. Finally, many compounding pharmacies continue to package topical anesthetics in tubes or jars rather than metered-dose pumps, which makes accurate dosing difficult. Assuming 2ml of anesthetic per patient, a traditional 30g jar contains 15 patient doses. Clearly, smaller quantities should be prescribed. Moreover, the maximum recommended dosage is unknown, since compounded pharmaceuticals are intended for single-patient usage. They also have a low therapeutic index—in other words, a small difference between the therapeutic dose and the dose at which the preparation becomes toxic. This is critical because many compounding topical anesthetics contain high concentrations of tetracaine, an ester-type anesthetic metabolized in the bloodstream, which can cause anaphylactic shock in a patient who is allergic to para-aminobenzoic acid.

## Conclusion

Compounded topical anesthetics are a useful and valuable adjunct, allowing orthodontists to provide profound mucosal anesthesia for patients who refuse local infiltration. Advances in creation and packaging have mitigated some previous concerns, particularly with regard to consistency, composition, dosing, and labeling. We are unaware of any reports of toxicity from compounded topical anesthetics used intraorally. Nevertheless, they remain unregulated drug products. To ensure the highest safety, compounded topical anesthetics should be applied in minimal doses, under direct doctor supervision, and used on only one patient per prescription.

The products and suppliers listed in this article are trademarks of their respective companies, as follows:

Listerine: McNeil PPC, Inc., Fort Washington, PA; [www.mcneil-consumer.com](http://www.mcneil-consumer.com).

Anbesol: Pfizer, Inc., New York, NY; [www.pfizer.com](http://www.pfizer.com).

HurriCaine: Beutlich Pharmaceuticals, LLC, Waukegan, IL; [www.beutlich.com](http://www.beutlich.com).

Orajel: Church & Dwight Co., Inc., Ewing, NJ; [www.churchdwight.com](http://www.churchdwight.com).

Orabase: Colgate-Palmolive, Co., New York, NY; [www.colgate-palmolive.com](http://www.colgate-palmolive.com).

TAC Alternate: Professional Arts Pharmacy, Lafayette, LA; [www.professionalarts.com](http://www.professionalarts.com).

Profound, DēpBlu: Steven's Pharmacy, Costa Mesa, CA; [www.stevensrx.com](http://www.stevensrx.com).

Baddest Topical in Town: Woodland Hills Pharmacy, Woodland Hills, CA; [www.woodlandhillsparmacy.com](http://www.woodlandhillsparmacy.com).

Best Topical Ever: AAACP/Nueva Vista Dental, Westminster, CA; [www.thebesttopicalever.com](http://www.thebesttopicalever.com).

EMLA cream: AstraZeneca, Wilmington, DE; [www.astrazeneca.com](http://www.astrazeneca.com).

Oraqix: Dentsply Pharmaceutical, York, PA; [www.dentsply.com](http://www.dentsply.com).

Propel: Propel Orthodontics, Briarcliff Manor, NY; [www.propelorthodontics.com](http://www.propelorthodontics.com).

Unguator: GAKO International, Munich, Germany; [www.unguator.com](http://www.unguator.com).

Letco Medical, Decatur, AL; [www.letcomedical.com](http://www.letcomedical.com).

Medisca, Plattsburgh, NY; [www.medisca.com](http://www.medisca.com).

Professional Compounding Centers of America, Houston, TX; [www.pccarx.com](http://www.pccarx.com).

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