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(54) **Title:** TOPICAL ANESTHETIC FOR RAPID LOCAL ANESTHESIA AND METHOD OF APPLYING A TOPICAL ANESTHETIC

(57) **Abstract:** A topical anesthetic for rapid local anesthesia is provided. The topical anesthetic includes an anesthetic, volatile and non-volatile solvents, and a thickener. In addition, a method is taught for applying the topical anesthetic to the face of a patient without occlusion. The anesthetic is applied topically to an area for injection such that the dermatological procedure (cosmetic injections) can be performed in fifteen minutes.

TITLE

Topical Anesthetic for Rapid Local Anesthesia and Method of Applying a Topical Anesthetic

TECHNICAL FIELD

The invention relates to topical anesthetics and methods for applying such anesthetics.

BACKGROUND ART

Before performing dermatological treatments, the patient is locally anesthetized with topical anesthetics. Existing topical anesthetics used on the face take up to an hour to anesthetize effectively. The delay between application and effective anesthesia causes waiting room delays in a medical office. In addition, an impatient physician may want to begin a procedure before the patient is fully anesthetized

Thus, there exists a need to quicken the action of topical anesthetics.

DISCLOSURE OF INVENTION

It is accordingly an object of the invention to provide a topical anesthetic for rapid (less than one hour) local anesthesia.

With the foregoing and other objects in view there is provided, in accordance with the invention, a topical anesthetic for rapid local anesthesia. The topical anesthetic includes an anesthetic, a volatile solvent, and a non-volatile solvent.

The anesthetic can be a parenteral-local anesthetic such as lidocaine. The anesthetic concentration is four to eight weight percent. Solutions of up to four percent are preferable because the U.S. Food and Drug Administration is expected to limit the concentration for over-the-counter use to four percent of lidocaine.

Parenteral-local anesthetics cause loss of feeling before and during surgery, dental procedures (including dental surgery), or labor and delivery. These medicines do not cause loss of consciousness. Examples of parenteral-local anesthetics include articaine, bupivacaine, chloroprocaine, etidocaine, levobupivacaine, lidocaine, mepivacaine, prilocaine, procaine,

and tetracaine. In the United States, these anesthetics are sold under the following trade names: CARBOCAINE6, CARBOCAINE WITH NEO-COBEFRIN6, CHIROCAINE10, CITANEST FORTE7, CITANEST PLAIN7, DALCAINE5, DILOCAINE5, DURANEST4, DURANEST-MPF4, ISOCAINE6, L-CAINE5, LIDOJECT-15, LIDOJECT-25, MARCAINE2, MARCAINE SPINAL2, NESACAINE3, NESACAINE-MPF3, NOVOCAIN8, OCTOCAINE5, POLOCAINE6, POLOCAINE-MPF6, PONTOCAINE9, SENSORCAINE2, SENSORCAINE-MPF2, SENSORCAINE-MPF SPINAL2, SEPTOCAINE1, XYLOCAINE5, XYLOCAINE-MPF5, and XYLOCAINE-MPF WITH GLUCOSE5. In Canada, the anesthetics are sold under the following trade names: ASTRACAINE 4%1, ASTRACAINE 4% FORTE1, CARBOCAINE6, CITANEST FORTE7, CITANEST PLAIN7, ISOCAINE 2%6, ISOCAINE 3%6, MARCAINE2, NESACAINE-CE3, NOVOCAIN8, OCTOCAINE-505, OCTOCAINE-1005, POLOCAINE6, PONTOCAINE9, SENSORCAINE2, SENSORCAINE FORTE2, ULTRACAINE D-S1, ULTRACAINE D-S FORTE1, XYLOCAINE5, XYLOCAINE TEST DOSE5, and XYLOCAINE 5% SPINAL5.

The non-volatile solvent system includes oleyl alcohol and propylene glycol. Generally, the fatty alcohol can be a C_{10} to C_{14} saturated alcohol, a liquid-at-room-temperature C_{12} to C_{22} mono- or polyunsaturatured or branched chain alcohol, or those same compounds in acid form. The fatty alcohol forms two to six percent of the formulation by weight, and, in particular, four percent by weight of the formulation.

The other non-volatile solvent, propylene glycol or a butane diol with adjacent hydroxyl groups, forms between two and six percent by weight of the formulation.

The formulation includes a volatile, short-chain alcohol such as isopropyl alcohol (IPA) or ethanol. Short-chain alcohols include the isomers of butanol, propanol, ethanol, and methanol. The short-chain alcohol forms between sixty and eighty-five percent by weight of the formulation. A thickener can be added that is soluble in the total solvent system. A suitable thickener is hydroxypropylcellulose (HPC). The thickener can form between two and five tenths and three and five tenths percent by weight of the formulation. The HPC is sold under the trade name KLUCEL.

The formulation also can include a volatile silicone. The preferred volatile silicone is

polydimethylsiloxane. The volatile silicone forms up to twenty-five percent by weight of the formulation. A suitable polydimethylsiloxane is sold under the trademark DOW CORNING 200. Volatile silicone is odorless. In addition, volatile silicone has a low heat of evaporation so it does not create a cold sensation when evaporating after being deposited on the skin.

A thickener can be added to help hold the topical anesthetic on the site of the skin to be anesthetized. Without the thickener, the topical anesthetic would likely run off the skin. Other devices can be used to hold the topical anesthetic on the skin such as a gauze pad.

The invention also encompasses a method applying the topical anesthetic to a face of a patient without occlusion. The above-described topical anesthetic is applied to an injection site (i.e. a surface or area) on the skin of a patient. After approximately fifteen minutes, a dermatological procedure, such as a cosmetic injection, can be performed. The topical anesthetic can also be used as an anesthetic before circumcision. The topical anesthetic not only can be used to anesthetize cosmetic injection sites on or near the face, but any other suitable injection site. The topical anesthetic also can be used to numb any topical pain such as a burn, scrape, or cut.

Other features which are considered as characteristic for the invention are set forth in the appended claims.

As stated, an object of the invention is to provide a topical lidocaine formulation that provides faster local anesthesia than prior-art formulations that include four percent (4%) by weight of lidocaine. A further object is to provide a topical lidocaine formulation producing local anesthesia at least twenty percent (20%) faster than current products and lasts the duration of a subsequent procedure.

The resulting topical lidocaine gel has the following qualities. The topical anesthetic gel is a clear to translucent viscous gel that remains on the area of application while not leaving a film that can be easily wiped off prior to injection.

The topical anesthetic gel provides maximum local anesthesia within fifteen to twenty minutes without occlusion. The local anesthesia allowing for mild-to-deep dermal implantation of dermal fillers such as hyaluronic acid gels (such as those sold under the

trademark RESTYLANE by HA North American Sales AB) and Botulinum Toxin Type A (such as those sold under the trademark BOTOX Purified Neurotoxin Complex by Allergan, Inc.). It is also believed that the topical anesthetic gel provides sufficient local anesthesia for various dermatological office procedures such as skin biopsies and removal of pre-cancerous lesions, moles, etc.

Topical anesthetic formulations that contain four percent by weight of lidocaine have been found to be effective as an external analgesic for topical anesthesia by the Food and Drug Administration (Federal Register, Volume 48, Number 27). The topical anesthetic gel described previously is specially formulated to penetrate intact skin without occlusion, for the rapid relief of pain caused by minor skin irritations, minor burns, minor cuts, and insect bites as well as topical anesthesia for dermatological procedures.

In accordance with the objects of the invention a topical anesthetic gel is provided. The topical anesthetic gel includes lidocaine in concentrations from 1% to 10% by weight in a drug delivery base composed of propylene glycol, unsaturated fatty alcohols, thickeners, isopropyl alcohol and other volatile components that have been proven safe for topical administration.

A typical package is a tube that holds two grams (2.0 g). The tube is single use for application to an individual patient.

Although the invention is illustrated and described herein as embodied in a topical anesthetic for rapid local anesthesia and a method of applying a topical anesthetic, it is nevertheless not intended to be limited to the details shown, because various modifications and structural changes may be made therein without departing from the spirit of the invention and within the scope and range of equivalents of the claims.

The construction and method of operation of the invention, however, together with additional objects and advantages thereof will be best understood from the following description of specific embodiments.

BRIEF DESCRIPTION OF DRAWINGS

Not Applicable.

BEST MODES FOR CARRYING OUT THE INVENTION

Referring now to the composition and the Examples (which are given as non-limiting examples) thereof, there is seen a preferred embodiment of the topical anesthetic (all percentages given throughout the application are weight percentages unless otherwise specified):

4% lidocaine
4% propylene glycol (PG)
4% oleyl alcohol (OA)
3% KLUCEL (HPC)
68% isopropyl alcohol (IPA)
17% Dow Corning 200 volatile silicone (DC200)

The ingredients in the preferred embodiment have been found to make an effective product when in the following approximate ranges:

4%-8%	lidocaine
2%-7%	OA
2%-8%	PG
2.5%-3.5%	KLUCEL
60%-85%	IPA
0%-25%	DC200

The ingredients in the preferred embodiment may be substituted:

OA any saturated C_{10} - C_{14}; any mono or polyunsaturated or branched chain greater than C_{12} that is a liquid at room temperature; acid could replace oleyl alcohol

PG butane diols with adjacent OH groups

KLUCEL any thickener that is soluble in IPA and/or DC200

IPA any safe short-chain alcohol such as ethanol

DC200 other volatile silicones

Fatty alcohols are aliphatic alcohols derived from natural fats and oils. They are the counterparts of fatty acids. They usually (but not always) have an even number of carbon atoms. They find use in the cosmetics and food industry. Fatty alcohols are a common component of waxes, mostly as esters with fatty acids but also as alcohols themselves. Those with common names include:

capryl alcohol (1-octanol) -- 8 carbon atoms

pelargonic alcohol (1-nonanol) -- 9 carbon atoms

capric alcohol (1-decanol, decyl alcohol) -- 10 carbon atoms

1-dodecanol (lauryl alcohol) -- 12 carbon atoms

myristyl alcohol (1-tetradecanol) -- 14 carbon atoms

palmitoleyl alcohol (cis-9-hexadecan-1-ol) -- 16 carbon atoms, unsaturated, $CH_3(CH_2)_5CH=CH(CH_2)_8OH$

isostearyl alcohol (16-methylheptadecan-1-ol) -- 18 carbon atoms, branched, $(CH_3)_2CH\text{-}(CH_2)_{15}OH$

elaidyl alcohol (9E-octadecen-1-ol) -- 18 carbon atoms, unsaturated, $CH_3(CH_2)_7CH=CH(CH_2)_8OH$

oleyl alcohol (cis-9-octadecen-1-ol) -- 18 carbon atoms, unsaturated

linoleyl alcohol (9Z, 12Z-octadecadien-1-ol) -- 18 carbon atoms, polyunsaturated

elaidolinoleyl alcohol (9E, 12E-octadecadien-1-ol) -- 18 carbon atoms, polyunsaturated

linolenyl alcohol (9Z, 12Z, 15Z-octadecatrien-1-ol) -- 18 carbon atoms,

polyunsaturated

elaidolinolenyl alcohol (9E, 12E, 15-E-octadecatrien-1-ol) -- 18 carbon atoms, polyunsaturated

ricinoleyl alcohol (12-hydroxy-9-octadecen-1-ol) -- 18 carbon atoms, unsaturated, diol, $CH_3(CH_2)_5CH(OH)CH_2CH=CH(CH_2)_8OH$

arachidyl alcohol (1-eicosanol) -- 20 carbon atoms

behenyl alcohol (1-docosanol) -- 22 carbon atoms

erucyl alcohol (cis-13-docosen-1-ol) -- 22 carbon atoms, unsaturated, $CH_3(CH_2)_7CH=CH(CH_2)_{12}OH$

lignoceryl alcohol (1-tetracosanol) -- 24 carbon atoms

ceryl alcohol (1-hexacosanol) -- 26 carbon atoms

montanyl alcohol, cluytyl alcohol (1-octacosanol) -- 28 carbon atoms

myricyl alcohol, melissyl alcohol (1-triacontanol) -- 30 carbon atoms

geddyl alcohol (1-tetratriacontanol) -- 34 carbon atoms

Alternatives to the isopropyl alcohol in the formulation could be ethanol.

Propylene glycol, known also by the systematic name propane-1,2-diol, is an organic compound (a diol), usually a tasteless, odorless, and colorless clear oily liquid that is hygroscopic and miscible with water, acetone, and chloroform. It is manufactured by the hydration of propylene oxide.

For the KLUCEL (hydroxypropylcellulose), there are a number of pharmaceutical grades that vary in molecular weight.

For the volatile silicone, there are a number of compounds that are similar.

EXAMPLES

Two lidocaine formulations are being evaluated. Formulation # 1 contains 3% KLUCEL. Formulation # 2 contains 2% KLUCEL.

Both formulations are clear to translucent liquids. Formulation #1 is slightly thicker than Formulation #2 but both are sufficiently viscous so as not to drip when applied.

Product is placed around the area of the lips with a cotton swab and then rubbed into the area.

Patient #1 – Formulation #1 – experienced numbness almost immediately and was able to be injected after 15 minutes exposure. No pain due to the needle stick was noted.

Patient #2 – Formulation #2 - experienced numbness almost immediately and was able to be injected after 15 minutes exposure. Patient indicated that the pain at injection was similar to previous procedures that utilized EMLA. However, previous procedures allowed the EMLA to remain on the skin for over 60 minutes prior to injection.

Patient #3 – Formulation #1 – two applications 15 minutes apart were made. Patient experienced pain on injections similar to previous injections. Again, previous procedures utilized EMLA and greater than 60 minutes exposure.

Patient #4 – Formulations #1 and #2 – Products were applied to the left and right side of the site to evaluate the products side-by-side. Formulation #1 was judged superior by the patient, faster numbness. Injections were made 15 to 20 minutes after application.

Two additional patients were evaluated. Samples were applied as per Patient #4 above. In both cases, Formulation #1 was judged superior. In addition, one patient that required removal of a growth was treated with Formulation #1 and after 15 minutes, had no pain at the site of biopsy.

While various descriptions of the present invention are described above, it should be understood that the various features could be used singly or in any combination thereof. Therefore, this invention is not to be limited to only the specifically preferred embodiments depicted herein.

Further, it should be understood that variations and modifications within the spirit and scope of the invention might occur to those skilled in the art to which the invention pertains. Accordingly, all expedient modifications readily attainable by one versed in the art from the disclosure set forth herein that are within the scope and spirit of the present invention are to be included as further embodiments of the present invention. The scope of the present invention is accordingly defined as set forth in the appended claims.

INDUSTRIAL APPLICABILITY

The invention is applicable in the medical treatment industry, in particular, in the field of dermatology.

SEQUENCE LISTING

Not Applicable.

SEQUENCE LISTING FREE TEXT

Not Applicable.

WHAT IS CLAIMED IS:

1. A topical anesthetic for rapid local anesthesia, comprising:

an anesthetic;

a volatile solvent; and

a non-volatile solvent.

2. The topical anesthetic according to claim 1, further comprising a thickener for holding a mixture of said anesthetic, said volatile solvent, and said non-volatile solvent on a site.

3. The topical anesthetic according to claim 1, wherein said anesthetic is lidocaine.

4. The topical anesthetic according to claim 1, wherein said aesthetic forms from four to eight weight percent of the topical anesthetic.

5. The topical anesthetic according to claim 1, wherein said anesthetic forms up to four percent by weight of the topical anesthetic.

6. The topical anesthetic according to claim 1, wherein said non-volatile solvent includes at least one of oleyl alcohol and propylene glycol.

7. The topical anesthetic according to claim 1, wherein said non-volatile solvent includes a non-volatile solvent selected from the group consisting of a C_{10} to C_{14} saturated alcohol, a liquid-at-room-temperature C_{12} mono- or polyunsaturatured or branched chain alcohol, a C_{10} to C_{14} saturated acid, and a liquid-at-room-temperature C_{12} mono- or polyunsaturatured or branched chain acid.

8. The topical anesthetic according to claim 1, wherein said non-volatile solvent forms between two and seven percent by weight of the topical anesthetic.

9. The topical anesthetic according to claim 1, wherein said non-volatile solvent forms up to 4 percent by weight of the topical anesthetic.

10. The topical anesthetic according to claim 1, wherein said volatile solvent is a short-chain alcohol.

11. The topical anesthetic according to claim 10, wherein said short-chain alcohol includes an alcohol selected from the group consisting of isopropyl alcohol (IPA) and ethanol.

12. The topical anesthetic according to claim 10, wherein said short-chain alcohol forms between sixty and eighty-five eight percent by weight of the topical anestheitc.

13. The topical anesthetic according to claim 10, further comprising a thickener soluble in said short-chain alcohol.

14. The topical anesthetic according to claim 13, wherein said thickener is hydroxypropylcellulose (HPC).

15. The topical anesthetic according to claim 13, wherein said thickener forms between two and five tenths and three and five tenths percent by weight.

16. The topical anesthetic according to claim 14, wherein said HPC is one sold under the trade name KLUCEL.

17. The topical anesthetic according to claim 1, further comprising a volatile silicone.

18. The topical anesthetic according to claim 17, wherein said volatile silicone is polydimethylsiloxane.

19. The topical anesthetic according to claim 17, wherein said volatile silicone forms up to twenty-five percent by weight of the topical anesthetic.

20. The topical anesthetic according to claim 18, wherein said polydimethylsiloxane is sold under the trade name DOW CORNING 200.

21. The topical anesthetic according to claim 17, further comprising a thickener.

22. The topical anesthetic according to claim 21, wherein said thickener is

hydroxypropylcellulose (HPC).

23. The topical anesthetic according to claim 22, wherein said thickener forms between two and five tenths and three and five tenths percent by weight of the topical anesthetic.

24. The topical anesthetic according to claim 22, wherein said HPC is sold under the trade name KLUCEL.

25. A topical anesthetic, comprising:

4% by weight lidocaine;

4% by weight propylene glycol;

4% by weight oleyl alcohol;

3% by weight hydroxypropylcellulose;

17% by weight polydimethysiloxane; and

68% by weight isopropyl alcohol.

26. A method applying the topical anesthetic according to claim 1, which comprises:

applying topically said topical anesthetic to an injection site on skin of a patient; and

waiting at least fifteen minutes.

27. The method according to claim 26, which further comprises injecting the patient on the injection site after the waiting step.

28. The method according to claim 26, wherein the injecting step is performed no later than twenty minutes after the applying step.

29. The method according to claim 26, wherein the injection site is on a face of the patient.

30. The method according to claim 26, which further comprises evaporating said volatile

solvent during the waiting step.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 08/51176

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61L 15/16; A61K 31/24 (2008.04)
USPC - 424/448; 514/536
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC(8) - A61L 15/16; A61K 31/24 (2008.04)
USPC - 424/448; 514/270; 514/304 514/536 514/758

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PUBWEST(PGPB,USPT,USOC,EPAB,JPAB), GOOGLE SCHOLAR: volatile, non-volatile, topical, anesthetic, oleyl alcohol, propylene glycol, isopropanol, ethanol, octadecenol, silicon, polydimethylsiloxane, hydroxypropylcellulose, klucel, lidocaine, dow corning 200, inject, evaporate

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 2003/0027833 A1 (Cleary et al.) 6 Feb 2003 (06.02.2003); para [0013]; [0016]; [0062]; [0063]; [0065]; [0070]; [0118]; Claims 1 and 45	1-3, 6-13, 17-19, 21-23 and 25 --- 24
X --- Y	US 4,091,090 A (Sipos) 23 May 1978 (23.05.1978); col 5, ln 23-35; col 6, ln 57-62; and col 15, ln 35-40 and ln 55-60	1-6, 10, 11 and 13-16 --- 24
X	US 2004/0131665 A1 (Wepfer) 8 Jul 2004 (08.07.2004) para [0021]; [0031]; [0041]; and [0052]	1, 6, 10, 11 and 26-30
X	US 5,534,246 A (Herb et al.) 9 Jul 1996 (09.07.1996) col 4, ln 63-col 5, ln 13; col 5, ln 65-col 6, ln 3; col 11, ln 62-67; and claim 39	1, 17, 18 and 20
A	Material Safety Data Sheet Cyclohexylmethanol, 99%. Fisher Scientific [online] 7 Mar 2006 [retrieved on 20 Apr 2008] Retrieved from the internet URL:<https://fscimage.fishersci.com/msds/46753.htm>.	

☐ Further documents are listed in the continuation of Box C. ☐

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
17 Apr 2008 (17.04.2008)	20 MAY 2008
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774