Sustained Release of Topical Anesthetics

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A composition and method to alleviate oral mucosal discomfort and irritation in an orthodontic patient. A wax matrix containing less than 15% analgesic/anesthetic agent such as benzocaine and excipients enhanced and extended release of the analgesic/anesthetic agent compared to known art formulations. The composition exhibited desirable aesthetic properties, was easy to apply, and the relatively lower concentration of active agent provided enhanced safety.

22 Claims, 2 Drawing Sheets
References Cited

OTHER PUBLICATIONS


Fig. 1

![Graph showing Avg Absorbance at 284 nm vs. Avg Conc of Benzocaine in uM]

\[ y = 0.0192x - 0.0089 \]
\[ R^2 = 0.9985 \]

Fig. 2

![Graph showing Avg % Drug Released vs. Time in min]

\[ y = 0.101x + 3.726 \]
\[ R^2 = 0.9717 \]
SUSTAINED RELEASE OF TOPICAL ANESTHETICS

This application claims priority to co-pending U.S. application Ser. No. 61/721,567 filed Nov. 2, 2012 which is expressly incorporated by reference herein in its entirety.

The discomfort and irritation of the oral mucosa that an orthodontic patient experiences during treatment is caused by friction between the oral mucosa and the orthodontic brackets. Administering painkillers or applying a commercially available non-medicated orthodontic wax over the brackets are options for orthodontic patients. However, orthodontic wax simply prevents friction and avoids further irritation, but does not reduce discomfort.

Commercially available non-medicated waxes for use in orthodontics include, e.g., GUM® Orthodontic Wax. Commercially available medicated products contain, for the most part, 20% benzocaine. “Dent’s Extra Strength Toothache Gum” (Grandpa Brands, Erlanger, KY) is advertised as a medicated wax to place in an exposed tooth cavity or as a protective cover for a chipped tooth. There was a voluntary product recall (May 2012) due to excessive benzocaine levels in some lots.

The disclosed method and composition is an orthodontic wax matrix that provides sustained release of an analgesic/anesthetic agent, also termed “active”, that is used in to alleviate oral mucosal discomfort, with the analgesic/anesthetic agent present in the matrix at a concentration that is relatively lower compared to known formulations. In one embodiment, the analgesic/anesthetic agent is benzocaine, which is the ethyl ester of para-aminobenzoic acid (PABA). In one embodiment, benzocaine is present in the matrix at a concentration from 0.1% up to less than 15%. In one embodiment, the disclosed method and composition is an orthodontic wax that contains an analgesic/anesthetic agent at a concentration lower than that previously used, and at least one excipient that provides sustained release of the analgesic/anesthetic agent from the wax matrix over at least eight hours. The composition is applied to an orthodontic bracket or brace of an orthodontic patient to relieve discomfort up to 24 hours.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 illustrates a calibration curve for the optical measurement of varying concentrations of benzocaine in an artificial saliva simulant by absorbance spectroscopy at 284 nm. FIG. 2 illustrates the time release of benzocaine from an exemplary composition into an artificial saliva simulant, as determined by measurements using absorbance spectroscopy at 284 nm.

FIG. 3 illustrates an exemplary composition applied to an orthodontic bracket or brace affixed to a tooth of a patient.

DETAILED DESCRIPTION

As used herein, all percentage concentrations are weight/weight. As used herein, all concentration ranges are inclusive in that the upper and lower values are included within the range, and in that all sub-ranges within the range are encompassed. For example, and by way of illustration only, a range of 0%-10% concentration of a component includes the absence of that component (0%), and every concentration up to and including 10% (e.g., 0.01%-10%, 0.1%-10%, 0.2%- 10%, 0.1%-9.9%, 0.1%-9.8%, and so on).

In one embodiment, the formation contains xanthan gum as a sustained release agent, and benzocaine (each from Spectrum) as the analgesic/anesthetic agent. In one embodiment, this formulation additionally contains microcrystalline wax (Koster Keunen), glycercyl monostearate, heavy mineral oil, PEG 1500, and Tween 80.

Tables 1A and 1B show exemplary formulations.

<table>
<thead>
<tr>
<th>TABLE 1A</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ingredients</strong></td>
</tr>
<tr>
<td>Microcrystalline wax</td>
</tr>
<tr>
<td>Glyceryl monostearate</td>
</tr>
<tr>
<td>Heavy mineral oil</td>
</tr>
<tr>
<td>PEG 1500</td>
</tr>
<tr>
<td>Benzocaine</td>
</tr>
<tr>
<td>Tween 80</td>
</tr>
<tr>
<td>Xanthan gum</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>TABLE 1B</th>
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</thead>
<tbody>
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<td><strong>Ingredients</strong></td>
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<td>Glyceryl monostearate</td>
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<td>Heavy mineral oil</td>
</tr>
<tr>
<td>PEG 1500</td>
</tr>
<tr>
<td>Benzoic acid</td>
</tr>
<tr>
<td>Tween 80</td>
</tr>
<tr>
<td>(Polysorbate 80)</td>
</tr>
<tr>
<td>Xanthan gum</td>
</tr>
</tbody>
</table>

As shown above, in embodiments, excipients are added to improve product characteristics. In general, in the above formulation of anesthetic/analgesic agent, the microcrystalline wax provides a matrix; glycercyl monostearate has known properties as an emollient, solubilizing agent, stabilize and sustained-release ingredient; heavy mineral oil has known properties as an emollient, lubricant, and oleaginous vehicle making the wax softer and less rigid; polyethylene glycol-1500 (PEG 1500) enhances matrix hydrophilicity; Tween 80 (Polysorbate 80) serves as a wetting/dispersing/suspending agent in lipophilic bases; and xanthan gum is a stabilizing agent and suspending agent, as described in the Handbook of Pharmaceutical Excipients (7th Edition, London: Pharmaceutical Press, 2012), the relevant sections of which are expressly incorporated by reference herein in their entirety.

The following Instruments were used in evaluations: Mettler AE 200 weighing balance, 4802 UV/Vis double beam spectrophotometer, and Hanson Vision Elite 8 dissolution apparatus.

Microcrystalline wax was melted in a beaker placed in a water bath maintained at 90°C. Once melted, glycercyl monostearate was added, followed by 250 μL heavy mineral oil with mechanical stirring. At about the same time, PEG 1500 was added in another beaker placed in a water bath maintained at 90°C, and stirred using a magnetic stirrer at 80 rpm. Benzocaine was added in portions every 2.5 min over a period of 12.5 min waiting for each addition to solubilize before adding the next. Tween 80 was added with continuous stirring and heat. Xanthan gum was then added in 0.25 g quantities over a period of two min while increasing stirring to 150 rpm. The wax mixture was poured into the PEG-drug mixture over two to three min while stirring at 200 rpm and stirred for an additional five min. The two mixtures were stirred mechanically with visual inspection. As soon as the wax began to solidify, the mixture was poured into a mold.

The formulation of Table 1A was assessed for an in vitro benzocaine release profile from the wax using an artificial saliva formulation that was prepared according to Table 2.
The in vitro benzocaine release study used the artificial saliva formulation containing potassium phosphate monobasic (KH$_2$PO$_4$), sodium phosphate dibasic (Na$_2$HPO$_4$), potassium bicarbonate (KHC$_2$O$_3$), sodium chloride (NaCl), magnesium chloride hexahydrate (MgCl$_2$·6H$_2$O), calcium chloride (CaCl$_2$), citric acid anhydrous, dilute hydrochloric acid (HCl), methanol, and MilliQ filtered water (resistivity=18.0 megaohms). Each ingredient was weighed and was ground before weighing. The final pH of the solution was adjusted to 6.7 using dilute HCl.

A standard curve of benzocaine was prepared. One mg benzocaine was dissolved in 20 mL methanol to make a stock solution. The stock solution was used to make 5 mL of increasing concentrations of benzocaine in artificial saliva (5 µM, 10 µM, 15 µM, 20 µM, 25 µM, 30 µM, 35 µM, 40 µM, 45 µM, 50 µM, 55 µM, and 60 µM). Absorbance of each concentration was measured at 284 nm using a UV/Vis double beam spectrophotometer. The cuvette was washed 3-4 times with water between each measurement. Each measurement was performed in triplicate, with the average absorbance of each concentration used to generate the standard curve.

A Hansson Vision Elite 8 dissolution apparatus was used for the in vitro benzocaine release study. Degassed artificial saliva was the dissolution medium (900 mL). The paddle speed was 50 rpm and the water bath was maintained at 37°C. Five mL of medium was withdrawn at each time point (0 min, 30 min, 60 min, 120 min, 180 min, 240 min, 300 min, 360 min, 420 min, 480 min, and 77 hours) and replaced by an equal volume of warm artificial saliva. Sinkers were used to place about 150 mg benzocaine wax in each basket.

The results of a standard benzocaine curve prepared in artificial saliva formulation are reported in Table 3 and shown in FIG. 1. As the data show, this formulation had an average of 56% percent benzocaine released into the artificial saliva medium after eight hours. This release rate was more than twice that obtained for a previous first-generation formulation described in U.S. Pat. No. 6,074,674 (the '674 patent) which is expressly incorporated by reference herein in its entirety. The '674 patent formulation was 7.1% tragacanth, 70.9% microcrystalline wax, 2.0% Span 80, and 20.0% benzocaine. The '674 patent formulation had an in vitro release of only 22.7% benzocaine released into the medium after eight hours.

This difference was unexpected. Without being limited to a specific theory, and with all other variables being equal, Fick’s Law of Diffusion would predict a greater release of analgesic/anesthetic agent from a matrix that contains a higher concentration of the analgesic/anesthetic agent. From the results shown herein, however, a greater percent of benzocaine was released from the disclosed formulation that contained a relatively lower benzocaine concentration, compared to that in the '674 patent. Specifically, the analgesic/anesthetic agent that was released from the formulation now disclosed was 11.3% at 1 hr, 16.6% at 2 hr, 18.8% at 3 hr, 23.8% at 4 hr, 29.7% at 5 hr, 39.8% at 6 hr, 48.3% at 7 hr, and 56.0% at 8 hr. The analgesic/anesthetic is released in one embodiment up to 24 h.

In embodiments using a sustained release agent, xanthum gum provided both a good release rate and a good product aesthetic appearance. Without being bound by a specific theory, this may be due to the structure of the xanthum gum
compound, its hydrophilic characteristic, and its emulsifying property that may facilitate saliva penetration of the wax matrix and release of the analgesic/anesthetic. Xanthium gum is used in oral and topical pharmaceutical formulations, cosmetics, and foods as a suspending agent, stabilizing agent, thickening agent, and emulsifying agent. It is non-toxic, compatible with most other pharmaceutical ingredients, and has good stability and viscosity properties over a wide pH and temperature range. It has been used to prepare sustained-release matrix tablets. Such properties are known, as described in the following references, each of which is expressly incorporated by reference herein in its entirety: Jansson P E, Kenne L, Lindberg B. Structure of extracellular polysaccharide from Xanthomonas campestris. Carbohydr Res 1975; 45: 275-282; Melton L D, Mindt L, Rees D A, Sanderson G R. Covalent structure of the polysaccharide from Xanthomonas campestris: evidence from partial hydrolysis studies. Carbohydr Res 1976; 46: 245-257; Dhopheshwarkar V, Zatz J L. Evaluation of xanthan gum in the preparation of sustained-release matrix tablets. Drug Dev Ind Pharm 1993; 19: 999-1017.

Compared to the '674 patent formulation containing a relatively higher 15%-25% concentration of analgesic/anesthetic, the formulations disclosed herein have a lower concentration of analgesic/anesthetic agent. This results in enhanced patient safety and ease of regulatory approval, while also providing an enhanced release profile for increased efficacy. The formulations disclosed herein have an improved aesthetic appearance, facilitating patient use and compliance, and are more similar to unmedicated waxes, and less similar to the tragacanth-containing wax described in the '674 patent with a yellow appearance. The increased percentage of the wax matrix assists in retaining a wax-like character; sufficiently flexible to be broken off of a wax strip and applied to an orthodontic bracket without crumbling or falling apart, as shown in FIG. 3. This increases both patient acceptability, as well as formulation retention on orthodontic brackets. In use, the wax is applied to the bracket. It will then be in contact with the mucosa as the gums lay against the teeth. Without the wax, the mucosa falls against the metal bracket; this is the source of irritation to the mucosa. The wax will stay on the metal bracket because the wax is malleable. The wax will be molded onto the part of the bracket that protrudes and is in contact with the mucosa.

The ingredients that may be used in embodiments of the formulation are as follows:

Analgesic/anesthetic agents, also termed active agents, include benzocaine, lidocaine, novocaine, procaine, butane, dyclonine, prilocaine, tetracaine, adrenaline/epinephrine, and cocaine; LET which is a combination of lidocaine and prilocaine; TAC which is a combination of tetracaine, adrenaline/epinephrine, and cocaine; and maintaining its integrity after incorporation of all active ingredients, and encouraging after application in the mouth, may be used. Thus, any wax or combination of commercially available natural or synthetic waxes and including but not limited to the following may be used: anionic emulsifying wax, bleached wax, carnauba wax, cetyl esters wax, hard wax, microcrystalline wax, nonionic emulsifying wax, refined wax, white wax, white beeswax, yellow wax, yellow beeswax. In one embodiment, the wax is microcrystalline wax.

In one embodiment, a non-ionic polymer is selected from the group consisting of sodium carboxymethyl cellulose, CARBOPOL® ETD 2001, resin, tragacanth, poly(ethylene oxide), methylethelcellulose, hydroxy-propylmethylethelcellulose, karya gum, cellulose, soluble starch, gelatin, poly(vinyl pyrrolidone), poly (ethylene glycol) 8000, poly(ethylene glycol) 4000, poly(vinyl alcohol), and combinations thereof. In one embodiment, the non-ionic polymer is PEG 1500.

In one embodiment, the surfactant is selected from the group consisting of sorbitol monolaurate, polysorbate 80, Span 80, Tween 80, and combinations thereof. In one embodiment, the surfactant is polysorbate 80 (Tween 80).

In one embodiment, the formulation contains one or more swelling agents, emulsifiers, surfactants, and/or wetting agents, each described in the Handbook of Pharmaceutical Excipients. These may be included to optimize or otherwise alter the release of active, e.g., benzocaine, from the wax matrix, e.g., alginic acid (also known as E404, KELACIL™, L-gulo-D-mannoglycuronan, polymannuronic acid, PROTACID®, SATIALGINE H88®); bitonate (also known as ABAGE®, E558, MAGNABRITE®, mineral soap, POLARLEG®, soap clay, taylorite, VEGUM® H5, wilkinit); calcium alginate (also known as alginic acid calcium salt, Algin, CA33, cale algin, calcium polyamminurate, Calginate, E404, KALTOSTAT®); carboner (also known as ACRITAMER®, acrylic acid polymer, CARBOPOL®), carboxy polymethylene, polyacrylic acid, carboxyvinyl polymer, PEMULLEN®, CARBOPOL® Ultras); carboxymethylcellulose calcium (also known as calcium carboxymethylcellulose, calcium CMC, ECG 505, NYMCELL® ZSC); carboxymethylcellulose sodium (also known as AKUCELL®, AQUASORB®, BLANOSE®, cellulose gum; CMC sodium); cellulose acetate phthalate (also known as acetyl phthalyl cellulose, AQUACOAT® CPD, CAP, cellulose acetate butyrate, 1,2-dicarboxylate, cellulose acetate hydrogen 1,2-benzenedicarboxylate, cellulose acetate hydrogen phthalate, cellulose acetate monophthalate, cellulose acetophthalate, cellulose acetylphthalate); Ceratonia (also known as Algaroba, carob bean gum, carob flour, ceratonia gum, ceratonia siliqua, ceratonia siliqua gum, Cheshire gum, E410, gumme de caroube, locust bean gum, Meyprofluer, St. John’s bread); croscarmellose sodium (also known as AC-DC-SOL™ crosslinked carboxymethylcellulose sodium, EXPROC™ modified cellulose gum, NYMCELL® ZSN, PHARMACEL® X1, PRIMELLOSE®, SOLUTAB®, VIVASOL®); crospovidone (also known as crosslinked povidone, E1202, KOLLIDON® CL, KOLLIDON® CL-M, POLYPLASDONE® XL, POLYPLASDONE® X-10, polyvinylpyrrolidone, PVPP, 1-vinyl-2-pyrrolidinone homopolymer); gelatin (also known as BYACOM™, CRYOGEL®, gelatin, INSTAGEL™, SOLUGEL™); glyceryl monooleate (also known as ALDO® MO, ATLASS® G-695, CAPMUL® G M, glycerol-1-octate, glycerol mono-oleate, KESSCO® M G, Ligailub, mono-olein, MONOMULS® 90-018, mono-olein, a-mono-olein glycerol, PECEOL®, PRIOLUBE® 1408, STEPAN® G M, TEGIN®); guar gum (also known as E412, GALACTOSOL™, guar flour, jaguar gum, Meyproagt, MEYPRO DOR™, Meyprofin); hectorite (also known as Hector clay, HECTABRITE® AW, HECTABRITE® DP, Ghassoulite, LAPONITE®, SHCa-1, Strese & Hofmann’s Hectorite); hydroxyethyl cellulose (also known as CELLOSE® HEC, cellulose hydroxyethyl ether, cellulose hydroxyethyl cellulose, ethylhydroxy cellulose, ethylene, HEC, HE cellulose, 2-hy-
dicroxyethyl cellulose ether, hydroxyethyl ether cellulose, hydroxyethyl starch, hyetellose, NATROSOL®, oxycellulose, Tylose PHA); hypromellose (also known as BENECOL®, MPAC, E464, hydroxypropyl methylcellulose, HPMC, METHOCEL®, methylcellulose propylene glycol ether, methyl hydroxypropylcellulose, METOLOS®, TYLEPOL®); hypromellose acetate succinate (also known as ATOAT®, ATOAT® AS-IH/FI, ATOAT® AS-LF/LG, ATOAT® AS-MF/MG, cellulose 2-hydroxypropyl methyl ether acetate succinate, HPMCAS); hypromellose phthalate (also known as cellulose phthalate hydroxypropyl methyl ether, HPMCp, hydroxypropyl methylcellulose benzene-1,2-dicarboxylate, 2-hydroxypropyl methylcellulose phthalate, methylhydroxypropylcellulose phthalate); kaolin (also known as Argilla, oolite, China clay, E559, kaolinite, Lion, porcelain clay, Sim 90, weissert, white bole); magnesium aluminum silicate (also known as aluminosilicate acid magnesium salt, aluminum magnesium silicate, Carrisorb, GELSORB® MAGNABRITE®, magnesium aluminosilicate, magnesium aluminum silicate colloidal, magnesium aluminum silicate complex colloidal, NEUSILINE®, Pharmosorb, silicic acid aluminum magnesium salt, Veegum); methylecellulose (also known as BENECOL®, CULMINAL® MC, E461, METHOCEL®, METOLOSE®); polacrilin potassium (also known as AMBERLITE® IRP-88, poliacrylic acid polymer with divinylbenzene potassium salt, polacrilin kall); polycarbophil (also known as NOVEO® AA-1); poloxylene oxide (also known as POLYXON®, polyoxirane, polyoxyethylene); polyethylene glycol ethers (also known as ACRYL-EZE®, ACRYL-EZE® MP, EASTACRYL® 30 D, EUDRAGIT® K, KOLLICOAT® MAE 30 D, KOLLICOAT® MAE 30 DP; polymeric methacrylates; USP/NF non-proprietary names are Amnonio methacrylate polymer, methacrylate copolymer, methacrylic acid copolymer, methacrylic acid polymer dispersion; saponite (also known as Afrodit, alumina, auxite, cathkinite, ferroan saponite, grifithite, licianite, lucianite); sodium starch glycolate (also known as Amido, amidon, amilo, amylum, Alkanol1618, Tego Alkanol 6855); cetrimide (also known as C16-alkylpyridinium chloride, CEPACOL®, Cepanol chloride, Cetamin, cetyl pyridinium chloride; Dobedian, hexadecyldropyridinium chloride, 1-hexadecylpyridinium chloride, Medilave, Pristac; Pyrispet); diethanolamine (also known as bis(hydroxyethyl)amine, DEA, diethylyamine, 2,2-dihydroxyethylamine, diolamine, 2,2-imidodithanol); docosane sodium (also known as bis(2-ethylhexyl) sodium sulfosuccinate, dioctyl sodium sulfosuccinate, DSS, sodium dioctyl sulfosuccinate, sulfobutanesulfonic acid, bis(2-ethylhexyl) ester sodium salt); glycerol monostearate (also known as CAP-MUL® GMS-50, CUTINA® GMS, 2,3-dihydroxypropyl octodecanolate, glycerine monostearate, glycerin monostearate, glycerol monostearate, glycerol stearate, glycerol stearate, GMS, IMWITOR® 191, IMWITOR® 900, KESSSCOTM GMS, Lipo GMS 410, Lipo GMS 450, Lipo GMS 600, monoester with 1,2,3-propanetriol, monoester, MYVAPLEX™ 600P, MVYVAEXTM, 1,2,3-propanetriol octodecanate, Protachem GMS-450, Ritau GMS, stearic acid monoster with glycerol, stearic monoglyceride, STEPAN® GMS, TEGIN®, TEGIN® 505, TEGIN® 515, TEGIN® 4100, TEGIN® M, UNIMATE® GMS); lactic acid (also known as C-1297, dodecanoic acid, docic acid, dodecyl acid, n-dodecanic acid, HYDROFOL® acid 1225, HYDROFOL® acid 1295, HYSTREN® 9512, laurosestic acid, Neot-fat 12, Neot-fat 12-43, NINOL® AA62 Extra, 1-undecanecarboxylic acid, vulvic acid, Wecoline 1295); lecitin (also known as E322, egg lecitin, LSC 5050, LSC 6040, mixed soybean phosphatides, olevolicin, PHOSAL® 53 MCT, PHOSPHOLIPON® 100 H, soybean lecitin, soybean phospholipids, Sternum, vegetable lecitin); Macrogol 15 hydroxystearate (also known as 12-hydroxystearic acid polymer with alpha-hydroxyhydroxopoly(oxy-1,2-ethanediyl), polyethylene glycol 600 12-hydroxystearate, SOLUTOL® HS 15); medium-chain triglycerides (also known as BERGABEST®, caprylic/capric triglyceride, CAPTEX® 300, CAPTEX® 355, CRODAMOL® GTC/C, glycerol tricaprylate/caprate, LABRAFAC® 90, MCT oil, MIGLYOL® 810, MIGLYOL® 812, MYRITOL® NUBEES® M5, Nesatol, oleum neutral, oleum vegetale terme, thin vegetable oil, Waglirol 3 9280); monoethanolamine (also known as Δ-aminoethyl alcohol, colamine, ethylolamine, β-hydroxyethylamine, 2-hydroxyethanol); myristic acid and its salts (also known as EDENOR® C14 98-100, n-tetradecanoic acid, 1-tridecanecarboxylic acid); palmitic acid and its salts (also known as cetayc acid, EDENOR® C16 98-100, EMERSOL® 140, EMERSOL® 143, n-hexadecanoic acid, hexadecylic acid, HYDROFOL® HYSTREN® 9016, INDUSTREN® 4516, 1-pentadecanecarboxylic acid, hexadecanoic acid sodium salt, palmitic acid sodium salt, sodium hexadecanoate, myrcyl palmitate); Poloxamer (also known as Lutrol, MONOLAN™, PLURONIC®, poloxaxol, polyethylene-propylene glycol copolymer, polyoxyethylene-polyoxypropylene copolymer, Supronic, SYNERONIC®); polyoxyethylene alkyl ethers (synonyms applicable to polyoxyethylene alkyl ethers are BR®4, CREMOPHOR® A, CYCLOGOL™ 1000, EMILIAN® KB, EMILIAN® KM, EMULGENT® ETHYLHON™ C, macrogol ethers, MARLOWET®, PLURAFAC™, PROCOL®, Ritoleth, Ritox, Texofor A, Volpo); polyoxyethylene castor oil derivatives (also known as ACCON®, ARLATONE®, CREMOPHOR®, ETOSAC®, EUMULGIN®, JEECHEM®, LIPOCEL®, MAPEG®, MARLOWET®, NIKKOL®, Protachem, SIMULSOL®); polyoxyethylene sorbitan fatty acid esters (also known as Tweens, polysorbates of varying molecular weight); polyoxyethylene stearates (also known as ethoxylated fatty acid esters, macrogol stearates, MARLOSOL®; PEG fatty acid esters, PEG stearates, polyoxyethylene glycol stearates, poly(oxy-1,2-ethanediyl) a-hydroxy-1-hydroxystearate,}
monostearate, heavy mineral oil, PEG talline wax, 2.7% glyceryl monostearate, known as may be provided in another type of carrier for self-application 25 bate; sorbic acid potassium salt); sodium lauryl sulfate (also up to patient in need thereof, the method comprising applying a patient in need thereof, the method comprising applying a potassium (E,E)-hexa-2,4-dienoate, potassium (E,E)-sorbic acid potassium salt); sodium lauryl sulfate, sodium dodecyl sulfate, sodium laurilsulfate, sodium monododecyl sulfate, sodium monolauryl sulfate, TEXAPON® K12P; sorbitan esters (sorbitan fatty acid esters) (also known as Spans); stearic acid and its salts (also known as cetylec acid, crocadic, E570, EDENOR®, EMERSOL®, HYSTRENE®, INDUSTRENE®, KARTACID™ 1895, Pearl Steric, PRISTERENE®, stereophonic acid, Tegostearic); triethanolamine (also known as TEA, Tealan, triethyolamine, trihydroxytriethylamine, tris (hydroxyethyl)lamine); triethyl citrate (also known as citric acid ethyl ester, CITROFLEX® 2, CITROFOL™ AI, E1505, HYDAGEN® CAT, TEC). The embodiments shown and described in the specification are only specific embodiments of the inventor who is skilled in the art and thus are not limiting in any way. Various changes, modifications, or alterations may be made or resorted to without departing from the spirit of the invention or the scope of the following claims. As only two examples, additional actives may be incorporated into the formulation to provide additional medicinal effects, and/or the formulation may be provided in another type of carrier for self-application to the orthodontic bracket.

What is claimed is:

1. A method of alleviating orthodontic discomfort in a patient in need thereof, the method comprising applying a pharmaceutically acceptable composition of a wax, from 0.01% to less than 15% of an analgesic/anesthetic agent, and up to 30% xanthum gum to provide to the patient under conditions to alleviate orthodontic discomfort for at least eight hours and up to 24 hours after the application.

2. A method of alleviating orthodontic discomfort in a patient in need thereof, the method comprising applying a pharmaceutically acceptable composition of wax, glyceryl monostearate, heavy mineral oil, PEG 1500, Tween 80, from 0.01% to less than 15% of an analgesic/anesthetic agent, and up to 30% xanthum gum.

3. A method of alleviating orthodontic discomfort in a patient in need thereof, the method comprising applying a pharmaceutically acceptable composition of 83% microcrystalline wax, 2.7% glyceryl monostearate, 1.0% heavy mineral oil, 5% PEG 1500, 5% analgesic/anesthetic agent, 0.3% Tween 80, and 3% xanthum gum, the composition applied to an oral mucosal surface of the orthodontic patient under conditions to alleviate the orthodontic discomfort.

4. A method of alleviating orthodontic discomfort in a patient in need thereof, the method comprising applying a pharmaceutically acceptable composition of 50%-99% microcrystalline wax, 0%-10% glyceryl monostearate, 0%-30% heavy mineral oil, 0%-30% PEG 1500, 0.01%-14.99% analgesic/anesthetic agent, 0%-10% Tween 80, and 0.1%-30% xanthum gum, the composition applied to an orthodontic bracket or brace of the orthodontic patient under conditions to alleviate orthodontic discomfort.

5. The method of claim 1, the composition comprising from 50%-99% microcrystalline wax.

6. The method of claim 1, the composition comprising 83% microcrystalline wax.

7. The method of claim 1, the composition further comprising up to 10% glyceryl monostearate.

8. The method of claim 1, the composition further comprising up to 30% heavy mineral oil.

9. The method of claim 1, the composition further comprising up to 30% PEG 1500.

10. The method of claim 1, the composition further comprising up to 10% Tween 80.

11. The method of claim 1, the composition comprising 5% analgesic/anesthetic agent.

12. The method of claim 1, wherein the analgesic/anesthetic agent is benzocaine.

13. The method of claim 1, wherein the applying step applies the composition to an orthodontic bracket or brace affixed to at least one tooth of a patient.

14. The method of claim 1, wherein the applying step applies the composition to an oral mucosal surface in a patient.

15. An extended release pharmaceutically acceptable composition comprising microcrystalline wax, glyceryl monostearate, heavy mineral oil, PEG 1500, Tween 80, less than 15.0% of an analgesic/anesthetic agent, and up to 30% xanthum gum, the composition having an in-vitro release of the analgesic/anesthetic agent of about 28% to about 56% over eight hours.

16. The composition of claim 15, the composition comprising from 50%-99% microcrystalline wax.

17. The composition of claim 15, the composition further comprising up to 10% glyceryl monostearate.

18. The composition of claim 15, the composition further comprising up to 30% heavy mineral oil.

19. The composition of claim 15, the composition further comprising up to 30% PEG 1500.

20. The composition of claim 15, the composition further comprising up to 10% Tween 80.

21. The composition of claim 15, the composition comprising 5% analgesic/anesthetic agent.

22. The composition of claim 15, wherein the analgesic/anesthetic agent is benzocaine.

* * * * *