(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) **World Intellectual Property Organization**
International Bureau

(43) **International Publication Date**
03 October 2024 (03.10.2024)

WIPO | PCT

(10) **International Publication Number**
WO 2024/201280 A1

(51) **International Patent Classification:**
A24B 13/00 (2006.01) *A24B 15/28* (2006.01)
A24B 15/16 (2020.01)

(21) **International Application Number:**
PCT/IB2024/052862

(22) **International Filing Date:**
25 March 2024 (25.03.2024)

(25) **Filing Language:** English

(26) **Publication Language:** English

(30) **Priority Data:**
63/456,238 31 March 2023 (31.03.2023) US

(71) **Applicant: NICOVENTURES TRADING LIMITED** [GB/GB]; Globe House, 1 Water Street, London Greater London WC2R 3LA (GB).

(72) **Inventor; and**
(71) **Applicant** *(for US only)*: **ROOHINEJAD, Shahin** [US/US]; 300 Windridge Lane, Apt. 14, Florence, Kentucky 41042 (US).

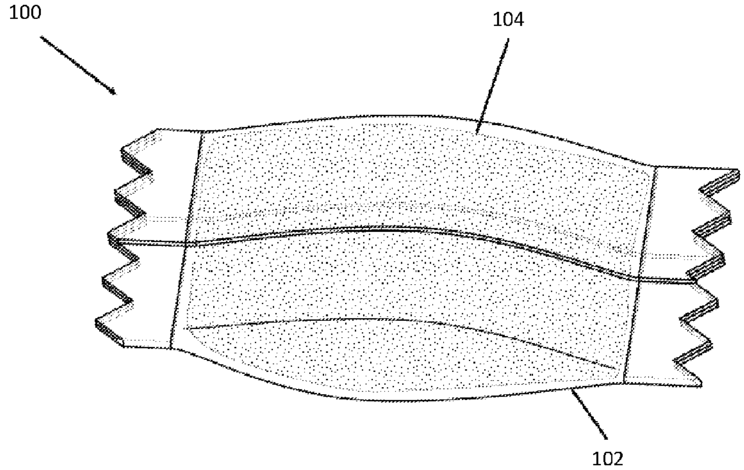
(74) **Agent: BREINING, Scott R.** et al.; Womble Bond Dickinson (US) LLP, Attn: IP Docketing, P.O. Box 570489, Atlanta, Georgia 30357 (US).

(81) **Designated States** *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CV, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IQ, IR, IS, IT, JM, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, MG, MK, MN, MU, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) **Designated States** *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, CV, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SC, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, ME, MK, MT, NL, NO, PL, PT, RO, RS, SE,

(54) **Title:** EMULSIONS FOR NICOTINE ENCAPSULATION

FIG. 1



(57) **Abstract:** The disclosure provides a composition configured for oral use, the composition including an emulsion including a nicotine component, a lipid component, an emulsifying agent, and water; and a filler, wherein the emulsion is adsorbed on the filler, absorbed in the filler, or both.

[Continued on next page]

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SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

- *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*
- *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

Published:

- *with international search report (Art. 21(3))*
- *in black and white; the international application as filed contained color or greyscale and is available for download from PATENTSCOPE*

EMULSIONS FOR NICOTINE ENCAPSULATION

FIELD OF THE DISCLOSURE

The present disclosure relates to compositions intended for human use. The compositions are adapted for oral use and deliver substances such as nicotine, flavors, and/or active ingredients during use. Such compositions may include tobacco or a product derived from tobacco, or may be tobacco-free alternatives.

BACKGROUND

There are many categories of products intended for oral use and enjoyment. For example, oral tobacco products containing nicotine, which is known to have both stimulant and anxiolytic properties, have been available for many years. Conventional formats for so-called "smokeless" tobacco products include moist snuff, snus, and chewing tobacco, which are typically formed almost entirely of particulate, granular, or shredded tobacco, and which are either portioned by the user or presented to the user in individual portions, such as in single-use pouches or sachets. See for example, the types of smokeless tobacco formulations, ingredients, and processing methodologies set forth in US Pat. Nos. 6,668,839 to Williams; 6,834,654 to Williams; 6,953,040 to Atchley et al.; 7,032,601 to Atchley et al.; and 7,694,686 to Atchley et al.; 7,810,507 to Dube et al.; 7,819,124 to Strickland et al.; 7,861,728 to Holton, Jr. et al.; 7,901,512 to Quinter et al.; 8,627,828 to Strickland et al.; 11,246,334 to Atchley, each of which is incorporated herein by reference.

In addition, traditional tobacco materials and non-tobacco materials have been combined with other ingredients to form product formats distinct from traditional smokeless products, with example formats including lozenges, pastilles, gels, and the like. See, for example, the types of products described in US Patent App. Pub. Nos. 2008/0196730 to Engstrom et al.; 2008/0305216 to Crawford et al.; 2009/0293889 to Kumar et al.; 2010/0291245 to Gao et al; 2011/0139164 to Mua et al.; 2012/0037175 to Cantrell et al.; 2012/0055494 to Hunt et al.; 2012/0138073 to Cantrell et al.; 2012/0138074 to Cantrell et al.; 2013/0074855 to Holton, Jr.; 2013/0074856 to Holton, Jr.; 2013/0152953 to Mua et al.; 2013/0274296 to Jackson et al.; 2015/0068545 to Moldoveanu et al.; 2015/0101627 to Marshall et al.; and 2015/0230515 to Lampe et al., each of which is incorporated herein by reference.

There is continuing interest in the development of new types of oral products that deliver advantageous sensorial or biological activity. Such products typically contain flavorants and/or active ingredients such as nicotine, caffeine, botanicals, or cannabidiol. The format of such products can vary and include pouched products containing a powdered or granular composition, lozenges, pastilles, liquids, gels, emulsions, meltable compositions, and the like. See, for example, the types of products described in US Patent App. Pub. Nos. 2022/0160675 to Gerardi et al.; 2022/0071984 to Poole et al.; 2021/0378948 to Gerardi et al.; 2021/0330590 to Hutchens et al.; 2021/0186081 to Gerardi et al.; 2021/0177754 to Keller et al; 2021/0177043 to Gerardi et al.; 2021/0177038 to Gerardi et al.; 2021/0169867 to Holton, Jr. et al.;

2021/0169792 to Holton, Jr. et al.; 2021/0169132 to Holton, Jr. et al.; 2021/0169121 to St. Charles, and 2021/0169122 to St. Charles, each of which is incorporated herein by reference.

BRIEF SUMMARY

Oral products are used by placing a nicotine containing matrix between the cheek and the gum. Nicotine is then released from the product and typically absorbed through the oral mucosa, thereby entering the blood stream where it is circulated systemically. Flavor stability and positive sensory attributes are important elements to a consumer-acceptable oral product.

Accordingly, in one aspect is provided a composition configured for oral use, the composition comprising: an emulsion comprising a nicotine component, a lipid component, an emulsifying agent in an amount by weight of at least 16%, and water; and a filler, wherein the emulsion is adsorbed on the filler, absorbed in the filler, or both.

In some embodiments, the emulsion is a microemulsion comprising droplets having an average size in a range from about 10 to about 500 nm. In some embodiments, the microemulsion comprises droplets having an average size in a range from about 100 to about 300 nm.

In some embodiments, the nicotine component is free base nicotine, a salt of nicotine with an organic acid, or a combination thereof.

In some embodiments, the nicotine component is a salt of nicotine with an organic acid. In some embodiments, the organic acid is benzoic acid, octanoic acid, decanoic acid, heptanesulfonic acid, a menthyl or tocopherol monoester of a dicarboxylic acid, or a combination thereof. In some embodiments, the organic acid is selected from the group consisting of octanoic acid, decanoic acid, benzoic acid, heptanesulfonic acid, and combinations thereof.

In some embodiments, the lipid component comprises diglycerides of medium-chain fatty acids. In some embodiments, the lipid component comprises triglycerides of medium-chain fatty acids.

In some embodiments, the medium-chain fatty acids have from 6 to 10 carbon atoms. In some embodiments, the medium-chain fatty acids have from 6 to 8 carbon atoms. In some embodiments, the medium-chain fatty acids have from 8 to 10 carbon atoms.

In some embodiments, the emulsion comprises from about 20 to about 40% of the lipid component by weight, based on the total weight of the emulsion.

In some embodiments, the emulsifying agent is a non-ionic surfactant. In some embodiments, the emulsifying agent is polyoxyl 40 stearate.

In some embodiments, the emulsion comprises from about 16 to about 30% of the emulsifying agent by weight, based on the total weight of the emulsion.

In some embodiments, the emulsion comprises from about 30 to about 70% water by weight, based on the total weight of the emulsion.

In some embodiments, the emulsion comprises: the emulsifying agent in an amount from about 16 to about 24 percent by weight, based on the total weight of the emulsion; the lipid component in an amount from about 24 to about 36 percent by weight, based on the total weight of the emulsion; and water in an amount from about 40 to about 60 percent by weight, based on the total weight of the emulsion.

In some embodiments, the filler is present in an amount of from about 30% to about 50% by weight of the composition.

In some embodiments, the filler is a cellulose material or cellulose derivative. In some embodiments, the filler is microcrystalline cellulose.

In some embodiments, the composition comprises the emulsion in an amount from about 10 to about 20% by weight, based on the total weight of the composition.

In some embodiments, the composition further comprises one or more flavoring agents, taste modifiers, preservatives, humectants, sweeteners, binders, buffering agents, salts, or mixtures thereof.

In another aspect is provided a pouched oral product comprising a saliva permeable pouch and a composition as disclosed herein incorporated within the pouch.

In some embodiments, the pouched product has a moisture content in a range from about 35 to about 45% by weight, based on the total weight of the pouched product.

In some embodiments, at least about 1 mg of nicotine is released from the pouched product within 30 minutes when stirred at 15 rpm in 900 ml of 12 mM ammonium phosphate (pH 7.4) at 37.0± 0.5°C.

In a still further aspect is provided a process for preparing a composition configured for oral use comprising a microemulsion that comprises a continuous phase and a dispersed phase, the process comprising:

(a) forming a microemulsion in which the continuous phase, the dispersed phase, or both phases contain a nicotine component; and

(b) processing the microemulsion to provide the composition, wherein the continuous phase, the dispersed phase, or both phases comprise an emulsifying agent in an amount of at least 16% by weight, based on the total weight of the emulsion.

In some embodiments, the continuous phase comprises water, and the dispersed phase comprises diglycerides or triglycerides of medium-chain fatty acids having from 6 to 10 carbon atoms. In some embodiments, the continuous phase comprises diglycerides or triglycerides of medium-chain fatty acids having from 6 to 8 or 8 to 10 carbon atoms, and the dispersed phase comprises water.

In some embodiments, the composition further comprises a filler and optionally, other additives; and processing the microemulsion to provide the composition comprises contacting the microemulsion with the filler and other optional additives.

The disclosure includes, without limitations, the following embodiments.

Embodiment 1: A composition configured for oral use, the composition comprising: an emulsion comprising a nicotine component, a lipid component, an emulsifying agent, an emulsifying agent in an amount by weight of at least 16%, and water; and a filler, wherein the emulsion is adsorbed on the filler, absorbed in the filler, or both.

Embodiment 2: The composition of embodiment 1, wherein the emulsion is a microemulsion comprising droplets having an average size in a range from about 10 to about 500 nm.

Embodiment 3: The composition of embodiment 2, wherein the microemulsion comprises droplets having an average size in a range from about 100 to about 300 nm.

Embodiment 4: The composition of any one of embodiments 1-3, wherein the nicotine component is free base nicotine, a salt of nicotine with an organic acid, or a combination thereof.

Embodiment 5: The composition of any one of embodiments 1-4, wherein the nicotine component is a salt of nicotine with an organic acid selected from the group consisting of octanoic acid, decanoic acid, benzoic acid, heptanesulfonic acid, and combinations thereof.

Embodiment 6: The composition of any one of embodiments 1-5, wherein the lipid component comprises diglycerides of medium-chain fatty acids.

Embodiment 7: The composition of any one of embodiments 1-5, wherein the lipid component comprises triglycerides of medium-chain fatty acids.

Embodiment 8: The composition of embodiment 6 or 7, wherein the medium-chain fatty acids have from 6 to 10 carbon atoms.

Embodiment 9: The composition of any one of embodiments 1-8, wherein the emulsion comprises from about 20 to about 40% of the lipid component by weight, based on the total weight of the emulsion.

Embodiment 10: The composition of any one of embodiments 1-9, wherein the emulsifying agent is a non-ionic surfactant.

Embodiment 11: The composition of any one of embodiments 1-10, wherein the emulsifying agent is polyoxyl 40 stearate.

Embodiment 12: The composition of any one of embodiments 1-11, wherein the emulsion comprises from about 16 to about 30% of the emulsifying agent by weight, based on the total weight of the emulsion.

Embodiment 13: The composition of any one of embodiments 1-12, wherein the emulsion comprises from about 30 to about 70% water by weight, based on the total weight of the emulsion.

Embodiment 14: The composition of any one of embodiments 1-13, wherein the emulsion comprises: the emulsifying agent in an amount from about 16 to about 24 percent by weight, based on the total weight of the emulsion; the lipid component in an amount from about 24 to about 36 percent by weight, based on the total weight of the emulsion; and water in an amount from about 40 to about 60 percent by weight, based on the total weight of the emulsion.

Embodiment 15: The composition of any one of embodiments 1-14, wherein the filler is present in an amount of from about 30% to about 50% by weight of the composition

Embodiment 16: The composition of any one of embodiments 1-15, wherein the filler is a cellulose material or cellulose derivative.

Embodiment 17: The composition of any one of embodiments 1-16, wherein the filler is microcrystalline cellulose.

Embodiment 18: The composition of any one of embodiments 1-17, wherein the composition comprises the emulsion in an amount from about 10 to about 20% by weight, based on the total weight of the composition.

Embodiment 19: The composition of any one of embodiments 1-18, further comprising one or more flavoring agents, taste modifiers, preservatives, humectants, sweeteners, binders, buffering agents, salts, or mixtures thereof.

Embodiment 20: A pouched oral product comprising a saliva permeable pouch and the composition of any one of embodiments 1-19 incorporated within the pouch.

Embodiment 21: The pouched product of embodiment 20, having a moisture content in a range from about 35 to about 45% by weight, based on the total weight of the pouched product.

Embodiment 22: The pouched product of embodiment 20 or 21, wherein at least about 1 mg of nicotine is released from the pouched product within 30 minutes when stirred at 15 rpm in 900 ml of 12 mM ammonium phosphate (pH 7.4) at 37.0± 0.5°C.

Embodiment 23: A process for preparing a composition configured for oral use comprising a microemulsion that comprises a continuous phase and a dispersed phase, the process comprising: (a) forming a microemulsion in which the continuous phase, the dispersed phase, or both phases contain a nicotine component; and (b) processing the microemulsion to provide the composition, wherein the continuous phase, the dispersed phase, or both phases comprise an emulsifying agent in an amount of at least 16% by weight, based on the total weight of the emulsion.

Embodiment 24: The process of embodiment 23, wherein the continuous phase comprises water, and the dispersed phase comprises diglycerides or triglycerides of medium-chain fatty acids having from 6 to 10 carbon atoms.

Embodiment 25: The process of embodiment 23, wherein the continuous phase comprises diglycerides or triglycerides of medium-chain fatty acids having from 6 to 10 carbon atoms, and the dispersed phase comprises water.

Embodiment 26: The process of any one of embodiments 23-25, wherein: the composition further comprises a filler and optionally, other additives; and processing the microemulsion to provide the composition comprises contacting the microemulsion with the filler and other optional additives.

These and other features, aspects, and advantages of the disclosure will be apparent from a reading of the following detailed description together with the accompanying drawings, which are briefly described below. The invention includes any combination of two, three, four, or more of the above-noted embodiments as well as combinations of any two, three, four, or more features or elements set forth in this disclosure, regardless of whether such features or elements are expressly combined in a specific embodiment description herein. This disclosure is intended to be read holistically such that any separable features or elements of the disclosed invention, in any of its various aspects and embodiments, should be viewed as intended to be combinable unless the context clearly dictates otherwise.

BRIEF DESCRIPTION OF THE DRAWINGS

Having thus described aspects of the disclosure in the foregoing general terms, reference will now be made to the accompanying drawings, which are not necessarily drawn to scale. The drawings are exemplary only, and should not be construed as limiting the disclosure.

FIG. 1 is a perspective view of a pouched product embodiment according to an example embodiment of the present disclosure, including a pouch or fleece at least partially filled with a composition configured for oral use.

FIG. 2 is a chart showing the release of nicotine over time for a control pouched product comprising nicotine.

FIG. 3 is a chart showing the release of nicotine over time for a pouched product comprising nicotine according to an embodiment of the disclosure.

FIG. 4 is a chart showing the release of nicotine over time for a pouched product comprising nicotine according to an embodiment of the disclosure.

FIG. 5 is a chart showing the release of nicotine over time for a pouched product comprising nicotine according to an embodiment of the disclosure.

FIG. 6 is a chart showing the release of nicotine over time for a pouched product comprising nicotine according to an embodiment of the disclosure.

FIG. 7 is a chart showing the release of nicotine over time for a pouched product comprising nicotine according to an embodiment of the disclosure.

FIG. 8 is a chart showing the release of nicotine over time for a pouched product comprising nicotine according to an embodiment of the disclosure.

FIG. 9 is a chart showing the mouth burning sensation encountered by subjects in a sensory panel for pouched products according to embodiments of the disclosure.

FIG. 10 is a chart showing the throat burning sensation encountered by subjects in a sensory panel for pouched products according to embodiments of the disclosure.

FIG. 11 is a chart showing various sensory attributes encountered by subjects in a sensory panel for pouched products according to embodiments of the disclosure.

DETAILED DESCRIPTION

The present disclosure provides a composition configured for oral use, the composition comprising an emulsion comprising a nicotine component, a lipid component, an emulsifying agent, and water. The composition further includes a filler, and the emulsion is typically adsorbed on the filler, absorbed in the filler, or both.

The present disclosure will now be described more fully hereinafter with reference to example embodiments thereof. These example embodiments are described so that this disclosure will be thorough and complete, and will fully convey the scope of the disclosure to those skilled in the art. Indeed, the disclosure may be embodied in many different forms and should not be construed as limited to the embodiments set forth herein; rather, these embodiments are provided so that this disclosure will satisfy applicable legal requirements.

As used in this specification and the claims, the singular forms "a," "an," and "the" include plural referents unless the context clearly dictates otherwise.

Reference to "dry weight percent" or "dry weight basis" refers to weight on the basis of dry ingredients (i.e., all ingredients except water). Reference to "wet weight" refers to the weight of the mixture including water. Unless otherwise indicated, reference to "weight percent" of a mixture reflects the total wet weight of the mixture (i.e., including water).

Composition

In certain embodiments, the composition configured for oral use as disclosed herein comprises: an emulsion comprising a nicotine component, a lipid component, an emulsifying agent, and water; and a filler, wherein the emulsion is adsorbed on the filler, absorbed in the filler, or both. Each of the individual components of the composition are described further herein below.

Emulsion

The composition configured for oral use as disclosed herein comprises an emulsion. An emulsion is generally defined as a dispersion of minute droplets of one liquid in another liquid in which it is not soluble or miscible. The liquids comprising the emulsion may be described as a continuous phase and a dispersed phase. An emulsion may comprise an oil phase (lipid component) as the continuous phase or the dispersed phase. The emulsion may comprise an aqueous phase as the continuous phase or the dispersed phase. In some embodiments, the emulsion comprises an oil phase as the continuous phase and an aqueous phase as the dispersed phase (i.e., a water-in-oil emulsion). In some embodiments, the emulsion comprises an aqueous phase as the continuous phase and an oil phase as the dispersed phase (i.e., an oil-in-water emulsion).

The size of the droplets present in the emulsion may vary, and the emulsion may be described in terms of the particle size of the droplets. In some embodiments, the emulsion is in the form of a microemulsion. As used herein, the term "microemulsion" refers to s thermodynamically stable, iso-tropic and transparent emulsion of an oil phase and an aqueous phase, which is stabilized by an interfacial film of a suitable surfactant and having a droplet size smaller than 500 nm. The droplets (referred to herein also as particles, e.g., nanoparticles or nanodroplets) are generally solid spheres, and the surfaces of such droplets are amorphous and lipophilic with a negative charge. In some embodiments, the emulsion (such as the microemulsion) as described herein comprises nano-scale particles having an average size from about 10 to about 500 nm, for example, from about 20 to about 300 nm, or from about 40 to about 200 nm. In some embodiments, the average particle size is about 300, about 200, about 100, about 90, about 80, about 70, about 60, about 50 or about 40 nm. In some embodiments, the average particle size is from about 100 to about 300 nm.

The size of particles present in the emulsion (e.g., nanoparticles or nanodroplets) may be determined by quasi-electric light scattering (QELS) as described in Bloomfield, Ann. Rev. Biophys. Bioeng., 10:421-450 (1981), incorporated herein by reference. It may also be measured by correlation spectroscopy that analyzes the fluctuation in scattering of light due to Brownian motion, or by transmission electron microscopy (TEM). The particle sizes may also be measured without any dilution using dynamic light scattering (DLS). The mean particle size is reported as a Z-average, which is the mean hydrodynamic diameter of the particle derived from the cumulative analysis of the intensity of the scattered light.

The emulsion (such as the microemulsion) as described herein may be characterized by reference to a polydispersity index (PDI). Polydispersity indicates the uniformity of droplet size in an emulsion. The higher the value of polydispersity, the lower will be the uniformity of droplet size. The PDI is defined as the ratio of the standard deviation of droplet size to mean droplet size and may be measured by spectrophotometric methods. The PDI of emulsions may also be measured without any dilution using dynamic light scattering (DLS). In some embodiments, it may be advantageous to provide microemulsions with a low polydispersity index, e.g., less than about 0.5. In some embodiments, the microemulsion has a polydispersity index of less than about 0.3.

The emulsion (e.g., microemulsion) as described herein may be characterized by reference to zeta potential. Zeta potential is a measure of the charge on the surface of a droplet in an emulsion. Zeta potential may be measured by Dynamic Light Scattering (DLS), with for example a Zetasizer instrument (Malvern Panalytical, Westborough, MA, USA). In some embodiments, the zeta potential of the droplets is less than about -10 mV. In some embodiments, the zeta potential of the droplets is less than about -20 mV. In some embodiments, the zeta potential of the droplets is less than about -30 mV. In some embodiments, the zeta potential of the droplets is less than about -40 mV. In some embodiments, the zeta potential of the droplets is less than about -50 mV. In some embodiments, the zeta potential of the droplets is from about -100 mV to about -10 mV, such as from about -100 mV to about -20 mV, such as from about -100 mV to about -30 mV, such as from about -100 mV to about -40 mV, such as from about -100 mV to about -50 mV.

In some embodiments, the emulsion (e.g., microemulsion) as described herein is transparent, meaning that the particle is of a size such that light passes through the emulsion without scattering.

Lipid component

The emulsion (e.g., microemulsion) as described herein comprises a lipid component, as either the continuous or dispersed phase. Generally, the lipid component is in the form of an oil. As used herein, the term "oil" refers to any nonpolar chemical substance that is both hydrophobic and lipophilic, and which is a liquid at room temperature. An oil as defined herein may be of animal, vegetable, or petrochemical in origin. Accordingly, any suitable oil may be used to form the emulsion (such as the microemulsion) as disclosed herein, including petroleum-based (e.g., mineral oil) and natural or naturally derived oils (e.g., from plant materials or animal sources).

In some embodiments, the oil is a food grade oil, including fractionated oils. Such oils include, but are not limited to, vegetable oils (e.g., acai oil, almond oil, amaranth oil, apricot oil, apple seed oil, argan oil, avocado oil, babassu oil, beech nut oil, ben oil, bitter gourd oil, black seed oil, blackcurrant seed oil, borage seed oil, borneo tallow nut oil, bottle gourd oil, brazil nut oil, buffalo gourd oil, butternut squash seed oil, cape chestnut oil, canola oil, carob cashew oil, cocoa butter, cocklebur oil, coconut oil, corn oil, cothune oil, coriander seed oil, cottonseed oil, date seed oil, dika oil, egus seed oil, evening primrose oil, false flax oil, flaxseed oil, grape seed oil, grapefruit seed oil, hazelnut oil, hemp oil, kapok seed oil, kenaf seed oil, lallemantia oil, lemon oil, linseed oil, macadamia oil, mafura oil, marula oil, meadowfoam seed oil, mongongo nut oil, mustard oil, niger seed oil, nutmeg butter, okra seed oil, olive oil, orange oil, palm oil, papaya seed oil, peanut oil, pecan oil, perilla seed oil, persimmon seed oil, pequi oil, pili nut oil, pine nut oil, pistachio oil, pomegranate seed oil, poppyseed oil, pracaxi oil, prune kernel oil, pumpkin seed oil, quinoa oil, ramtil oil, rapeseed oil, rice bran oil, royle oil, sacha inchi oil, safflower oil, sapote oil, seje oil, sesame oil, shea butter, soybean oil, sunflower oil, taramira oil, tea seed oil, thistle oil, tigernut oil, tobacco seed oil, tomato seed oil, walnut oil, watermelon seed oil, wheat germ oil, and combinations thereof), animal oils (e.g., cattle fat, buffalo fat, sheep fat, goat fat, pig fat, lard, camel fat, tallow, liquid margarine, fish oil, fish liver oil, whale oil, seal oil, and combinations thereof), and mineral oils. In some embodiments, the oil comprises mineral oil.

In some embodiments, the oil comprises a long chain fatty acid, a monoacylglycerol, a diacylglycerol, a triacylglycerol, or a combination thereof, wherein the acyl group of the acylglycerol is a long chain fatty acid. In some embodiments, the oil may be made up of primarily long-chain triacylglycerols ("LCT"). As used herein, "long chain fatty acid" refers to a carboxylic (CO_2H) acid having an aliphatic carbon chain of from about 11 to about 21 carbon atoms. Likewise, the term "long-chain triacylglycerols" refers to long chain fatty acid triesters of glycerol. The aliphatic carbon chain may be straight or branched. The aliphatic carbon chain may be saturated (i.e., having all sp^3 carbon atoms), or may be unsaturated (i.e., having at least one site of unsaturation). As used herein, the term "unsaturated" refers to the presence of a carbon-carbon, sp^2 double bond in one or more positions within the aliphatic carbon chain. Unsaturated alkyl groups may be mono- or polyunsaturated. The chain lengths of the fatty acids in naturally occurring triglycerides may vary, but is typically 16, 18, or 20 carbon atoms. Representative long chain fatty acids include, but are not limited to, undecylic acid, undecanoic acid, lauric acid, tridecanoic acid, myristic acid, pentadecanoic acid, palmitic acid, margaric acid, stearic acid, nonadecanoic acid, arachidic acid, heneicosanoic acid, α-linolenic acid, stearidonic acid, eicosapentaenoic acid, cervonic acid, linoleic acid, linolelaidic acid, γ-linolenic acid, dihomo-γ-linolenic acid, and arachidonic acid.

In some embodiments, the oil comprises medium-chain fatty acids or mono-, di- or triacylglycerols thereof. wherein the acyl group of the acylglycerol is a medium chain fatty acid. As used herein, "medium chain fatty acid" refers to a carboxylic (CO_2H) acid having an aliphatic carbon chain of from about 6 to about 10 carbon atoms. Likewise, the term "medium-chain triacylglycerols" ("MCT") refers to medium chain fatty acid triesters of glycerol. In some embodiments, the oil comprises medium-chain fatty acid mono, di-, or triacylglycerols. In some embodiments, the medium-chain fatty acid has an aliphatic carbon chain of from about 6 to about 10 carbon atoms. In some embodiments, the medium-chain fatty acid has an aliphatic carbon chain of from about 8 to about 10 carbon atoms. In some embodiments, the medium-chain fatty acid has an aliphatic carbon chain of from about 6 to about 8 carbon atoms.

In some embodiments, the oil may comprise short-chain fatty acids or mono-, di-, or triacylglycerols thereof. As used herein, "short chain fatty acid" refers to a carboxylic (CO_2H) acid having an aliphatic carbon chain of from about 2 to about 6 carbon atoms. Likewise, the term "short-chain triacylglycerols" ("SCT") refers to short chain fatty acid triesters of glycerol.

In some embodiments, the oil comprises fatty acids (e.g., fatty acids or mono, di- or tri- esters thereof with glycerol) with a carbon chain length from about 6 to about 10, such as about 6 to about 8, or about 8 to about 10 carbon atoms. In some embodiments, the oil is a mixture of triglycerides of capric acid and caprylic acid, available as Captex® MCT (Abitec, Columbus, Ohio, USA). In some embodiments, the oil is a mixture of mono- and diglycerides of capric and caprylic acid, available as Capmul® MCM (Abitec, Columbus, Ohio, USA).

In some embodiments, the oil comprises castor oil, corn oil, coconut oil, cod liver oil, evening primrose oil, cottonseed oil, palm oil, rice bran oil, sesame oil, rapeseed oil, canola oil, cocoa butter, linseed oil, olive oil, peanut oil, soybean oil, safflower oil, flaxseed oil, sunflower oil, olive oil, or a combination thereof.

The amount of oil present within the emulsion (e.g., microemulsion) can vary. In some embodiments, the emulsion comprises oil in an amount from about 1% to about 80% by weight, such as from about 5% to about 60% by weight, such as from about 10% to about 50% by weight, or from about 20% to about 40% by weight, based on the total weight of the emulsion. In some embodiments, the lipid component (i.e., oil) is present in the emulsion in an amount from about 24 to about 36% by weight, based on the entirety of the emulsion.

Water

The emulsion (e.g., microemulsion) may comprise water in or as the continuous or dispersed phase; i.e., the emulsion may comprise an aqueous phase. Water may be present as, for example, purified or ultrapure water, saline, buffered saline, or a buffered aqueous phase. The water content of the emulsion may vary according to the desired properties. Typically, the water content will be from about 20% to about 90% by weight, based on the total weight of the emulsion. In some embodiments, the water content is from about 20% to about 90% by weight, such as from about 20 to about 80%, or from about 30% to about 70% by weight, or from about 40% to about 60% by weight, based on the total weight of the emulsion.

Emulsifying agent

Emulsions (e.g., microemulsions) as disclosed herein can comprise one or more emulsifying agents. By "emulsifying agent" is meant a substance which aids in the formation and stabilization of emulsions by promoting dispersion of hydrophobic and hydrophilic (e.g., oil and water) components. In general, emulsifiers are amphiphilic molecules chosen from, for example, nonionic and ionic amphiphilic molecules. The expression "amphiphilic molecule" means any molecule of bipolar structure comprising at least one hydrophobic portion and at least one hydrophilic portion and having the property of reducing the surface tension of water and of reducing the interface tension between water and an oily phase. Emulsifying agents/amphiphilic molecules as provided herein are also referred to as, for example, surfactants and emulsifiers.

In some embodiments, the emulsifying agent comprises neutral, positively charged, or negatively charged natural or synthetic phospholipids molecules. Phospholipids are made up of two fatty acid tails and a phosphate group head, connected via a third molecule, glycerol. Non-limiting examples of natural phospholipids including soybean lecithin, egg lecithin, phosphatidylglycerol, phosphatidylinositol, phosphatidylethanolamine, phosphatidic acid, sphingomyelin, diphosphatidylglycerol, phosphatidylserine, phosphatidylcholine and cardiolipin; synthetic phospholipids including dimyristoylphosphatidylcholine, dimyristoylphosphatidylglycerol, distearoylphosphatidylglycerol and dipalmitoylphosphatidylcholine; and hydrogenated or partially hydrogenated lecithins and phospholipids. Non-limiting examples of synthetic phospholipid derivatives include phosphatidic acid (DMPA, DPPA, DSPA), phosphatidylcholine (DDPC, DLPC, DMPC, DPPC, DSPC, DOPC, POPC, DEPC), phosphatidylglycerol (DMPG, DPPG, DSPG, POPG), phosphatidylethanolamine (DMPE, DPPE, DSPE DOPE), phosphatidylserine (DOPS), PEG phospholipid (mPEG-phospholipid, polyglycerin-phospholipid, functionalized-phospholipid, and terminal activated-phospholipid).

In some embodiments, the emulsifying agent comprises a surfactant, which may be ionic or non-ionic, and which may be hydrophobic or hydrophilic. Examples of hydrophobic surfactants include, but are not limited to, Maisine 35-1, Imwitor 742, Capmul MCM, Capmul PG 12, Lauroglycol 90, Lauroglycol FCC, Caproyl 90, Captex 250, a fatty acid selected from the group consisting of octanoic acid, decanoic acid, undecanoic acid, lauric acid, myristic acid, palmitic acid, stearic acid, oleic acid, linoleic acid, and linolenic acid. As used herein, a hydrophobic surfactant may also be referred to as a poorly water-soluble surfactant or a lipophilic surfactant.

Examples of hydrophilic surfactants may include, but are not limited to, polyoxyethylene sorbitan fatty acid esters, hydrogenated castor oil ethoxylates, PEG mono- and di-esters of palmitic and stearic acids, fatty acid ethoxylates, and combinations thereof.

Examples of suitable surfactants generally include, but are not limited to: polyoxyethylene-sorbitan-fatty acid esters; e.g., mono- and tri-lauryl, palmityl, stearyl and oleyl esters; e.g., products of the type known as polysorbates and commercially available under the trade name Tween®; polyoxyethylene fatty acid esters, e.g., polyoxyethylene stearic acid esters of the type known and commercially available under the trade name Myrj®; polyoxyethylene castor oil derivatives, e.g., products of the type known and commercially available as Cremophors®. Particularly suitable are polyoxyl 35 castor oil (Cremophor®EL) and polyoxyl 40 hydrogenated castor oil (Cremophor®RH40); a- tocopherol, a-tocopheryl polyethylene glycol succinate (vitamin E TPGS), a- tocopherol palmitate and a-tocopherol acetate; PEG glyceryl fatty acid esters such as PEG-8 glyceryl caprylate/caprate (commercially known as Labrasol®), PEG-4 glyceryl caprylate/caprate (Labrafac Hydro WL 1219), PEG-32 glyceryl laurate (Gelucire 44/14), PEG-6 glyceryl mono oleate (Labrafil® M 1944 CS), PEG-6 glyceryl linoleate (Labrafil® M 2125 CS); propylene glycol mono- and di-fatty acid esters, such as propylene glycol laurate, propylene glycol caprylate/caprate; also diethyleneglycol-monoethylether (DGME), commercially known as Transcutol® (Gattefosse, Westwood, N.J.); sorbitan fatty acid esters, such as the type known and commercially available under the name Span® (e.g., Span 85); polyoxyethylene-polyoxypropylene co-polymers, e.g., products of the type known and commercially available as Pluronic® or Poloxamer®; glycerol triacetate; and monoglycerides and acetylated monoglycerides, e.g., glycerol monodicocoate (Imwitor® 928), glycerol monocaprylate (Imwitor® 308), and mono-and di-acetylated monoglycerides.

In some embodiments, the emulsifying agent is a surfactant, a phospholipid, an amphiphilic polysaccharide, an amphiphilic protein, or a combination thereof. In some embodiments, the emulsifying agent is an ionic or non-ionic surfactant. In some embodiments, the emulsifying agent is a non-ionic surfactant. In some embodiments, the emulsifying agent comprises Tween 20, Tween 80, Span 20, Span 40, Span 60, Span 80, lecithin, a hydrocolloid gum, a modified starch, or a combination thereof. In some embodiments, the emulsifying agent is polyoxyl 40 stearate.

The concentration of the emulsifying agent present in the disclosed emulsion (e.g., microemulsion) may vary. The concentration of the emulsifying agent may be in a range of up to about 30% by weight, and is generally present in an amount of at least about 16% by weight, based on the total weight of the emulsion.

In some embodiments, the emulsifying agent is present in the emulsion in an amount from about 16% to about 30%, such as from about 16%, about 17%, about 18%, about 19%, or about 20%, to about 21%, about 22%, about 23%, about 24%, about 25%, about 26%, about 27%, about 28%, about 29%, or about 30%. In some embodiments, the emulsifying agent is present in the emulsion in an amount from about 16 to about 24% by weight, based on the total weight of the emulsion.

As described herein above, the concentration of each of the aqueous phase (e.g., water), lipid component, and surfactant in the emulsion may each vary. The concentration of each component may vary based not only on the nature of the individual component and the desired properties of the emulsion (e.g., microemulsion), but also by the interaction with one another. For example, the phase behavior of a microemulsion containing oil, water, and surfactant can be presented by a ternary or pseudo-ternary phase diagram using a Gibbs triangle in which each corner of the triangle represents 100% of that specific component. To determine suitability of a particular ternary combination for microemulsion formation and stability, the procedure most often carried out is preparation of a series of binary compositions and titration with the third component, evaluating the mixture after each addition. Alternatively, a pseudo-ternary phase diagram can be constructed by preparing samples with different compositions (~100 samples) and defining the phase boundaries in each phase diagram. In this case, each sample should be allowed to equilibrate at room temperature for at least 24 hours before evaluation. Transitions between different phases, as shown in phase diagrams, can be achieved by addition of one of the components (e.g., oil, water, or surfactant), addition of a new component, or changing the temperature. Accordingly, determination of suitable combinations of lipid component, aqueous phase, and emulsifier/surfactant, each as disclosed herein, and the relative concentration of each necessary to form an emulsion (e.g., a microemulsion) having the desired physical properties, is within the capabilities of one of skill in the art.

Hydrophilic component

In some embodiments, a hydrophilic, water-soluble component may be added to the water phase of the emulsion. Such components include, but are not limited to, short chain mono-, di-, and polyhydric alcohols, (e.g., ethanol, benzyl alcohol, glycerol, propylene glycol, propylene carbonate, polyethylene glycol with an average molecular weight of about 200 to about 10,000, diethylene glycol monoethyl ether, and combinations thereof).

Nicotine component

The emulsion (e.g., microemulsion) as described herein comprises a nicotine component, present in the oil phase, the water phase, or both. By "nicotine component" is meant any suitable form of nicotine (e.g., free base or salt) for providing oral absorption of at least a portion of the nicotine present. The source of the nicotine may vary and may be natural or synthetic. Nicotine may be tobacco-derived (e.g., a tobacco extract) or non-tobacco derived (e.g., synthetic or otherwise obtained). Most preferably, the nicotine is naturally occurring and obtained as an extract from a *Nicotiana* species (e.g., tobacco). The nicotine can have the enantiomeric form S(-)-nicotine, R(+)-nicotine, or a mixture of *S*(-)-nicotine and *R*(+)-nicotine. Most preferably, the nicotine is in the form of *S*(-)-nicotine (e.g., in a form that is virtually all S(-)-nicotine) or a racemic mixture composed primarily or predominantly of *S*(-)-nicotine (e.g., a mixture composed of about 95 weight parts *S*(-)-nicotine and about 5 weight parts *R*(+)-nicotine). Most preferably, the nicotine is employed in virtually pure form or in an essentially pure form. Highly preferred nicotine that is employed has a purity of greater than about 95 percent, more preferably greater than about 98 percent, and most preferably greater than about 99 percent, on a weight basis.

Typically, the nicotine component is nicotine free base, a nicotine salt, or a combination thereof. In some embodiments, the nicotine component is nicotine in its free base form.

In some embodiments, at least a portion of the nicotine component can be employed in the form of a salt. Salts of nicotine can be provided using the types of ingredients and techniques set forth in US Pat. No. 2,033,909 to Cox et al. and Perfetti, *Beitrage Tabakforschung Int.*, 12: 43-54 (1983), which are incorporated herein by reference. Additionally, salts of nicotine are available from sources such as Pfaltz and Bauer, Inc. and K&K Laboratories, Division of ICN Biochemicals, Inc. In some embodiments, the nicotine component is a nicotine salt selected from the group consisting of hydrochloride, dihydrochloride, monotartrate, bitartrate, sulfate, salicylate, and nicotine zinc chloride.

In some embodiments, the nicotine component is a salt of nicotine with an organic acid. In some embodiments, at least a portion of the nicotine component can be ion paired with a suitable organic acid, an alkali metal salt thereof, or both. In some embodiments, at least a portion of the nicotine is present in the emulsion in the form of an ion pair with an organic acid or salt thereof, or in the form of a salt with an organic acid. As used herein, the term "organic acid" refers to an organic (i.e., carbon-based) compound that is characterized by acidic properties. Typically, organic acids are relatively weak acids (i.e., they do not dissociate completely in the presence of water), such as carboxylic acids (-CO_2H) or sulfonic acids (-SO_2OH). As used herein, reference to organic acid means an organic acid that is intentionally added. In this regard, an organic acid may be intentionally added as a specific composition ingredient as opposed to merely being inherently present as a component of another composition ingredient (e.g., the small amount of organic acid which may inherently be present in a composition ingredient, such as a tobacco material).

Suitable organic acids will typically have a range of lipophilicities (i.e., a polarity giving an appropriate balance of water and organic solubility). Typically, lipophilicities of suitable organic acids, as indicated by logP, will vary between about 1 and about 12 (more soluble in octanol than in water). In some embodiments, the organic acid has a logP value from about 1 to about 12, e.g., from about 1.0. about 1.5, about 2.0, about 2.5, about 3.0, about 3.5, about 4.0, about 4.5, about 5.0, about 5.5, about 6.0, about 6.5, about 7.0, about 7.5, or about 8.0, to about 8.5, about 9.0, about 9.5, about 10.0, about 10.5, about 11.0, about 11.5, or about 12.0. In specific embodiments, the organic acid has a logP value from about 3.0 to about 8.0, about 10.0, or even 12.0.

In some embodiments, the organic acid is a carboxylic acid or a sulfonic acid. The carboxylic acid or sulfonic acid functional group may be attached to any alkyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl group having, for example, from one to twenty carbon atoms (C_1-C_{20}). In some embodiments, the organic acid is an alkyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl carboxylic or sulfonic acid.

As used herein, "alkyl" refers to any straight chain or branched chain hydrocarbon. The alkyl group may be saturated (i.e., having all sp^3 carbon atoms), or may be unsaturated (i.e., having at least one site of unsaturation). As used herein, the term "unsaturated" refers to the presence of a carbon-carbon, sp^2

double bond in one or more positions within the alkyl group. Unsaturated alkyl groups may be mono- or polyunsaturated. Representative straight chain alkyl groups include, but are not limited to, methyl, ethyl, n-propyl, n-butyl, n-pentyl, and n-hexyl. Branched chain alkyl groups include, but are not limited to, isopropyl, sec-butyl, isobutyl, tert-butyl, isopentyl, and 2-methylbutyl. Representative unsaturated alkyl groups include, but are not limited to, ethylene or vinyl, allyl, 1-butenyl, 2-butenyl, isobutylenyl, 1-pentenyl, 2-pentenyl, 3-methyl-1-butenyl, 2-methyl-2-butenyl, 2,3-dimethyl-2-butenyl, and the like. An alkyl group can be unsubstituted or substituted.

"Cycloalkyl" as used herein refers to a carbocyclic group, which may be mono- or bicyclic. Cycloalkyl groups include rings having 3 to 7 carbon atoms as a monocycle or 7 to 12 carbon atoms as a bicycle. Examples of monocyclic cycloalkyl groups include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, and cyclooctyl. A cycloalkyl group can be unsubstituted or substituted, and may include one or more sites of unsaturation (e.g., cyclopentenyl or cyclohexenyl).

The term "aryl" as used herein refers to a carbocyclic aromatic group. Examples of aryl groups include, but are not limited to, phenyl and naphthyl. An aryl group can be unsubstituted or substituted.

"Heteroaryl" and "heterocycloalkyl" as used herein refer to an aromatic or non-aromatic ring system, respectively, in which one or more ring atoms is a heteroatom, e.g. nitrogen, oxygen, and sulfur. The heteroaryl or heterocycloalkyl group comprises up to 20 carbon atoms and from 1 to 3 heteroatoms selected from N, O, and S. A heteroaryl or heterocycloalkyl may be a monocycle having 3 to 7 ring members (for example, 2 to 6 carbon atoms and 1 to 3 heteroatoms selected from N, O, and S) or a bicycle having 7 to 10 ring members (for example, 4 to 9 carbon atoms and 1 to 3 heteroatoms selected from N, O, and S), for example: a bicyclo[4,5], [5,5], [5,6], or [6,6] system. Examples of heteroaryl groups include by way of example and not limitation, pyridyl, thiazolyl, tetrahydrothiophenyl, pyrimidinyl, furanyl, thienyl, pyrrolyl, pyrazolyl, imidazolyl, tetrazolyl, benzofuranyl, thianaphthalenyl, indolyl, indolenyl, quinolinyl, isoquinolinyl, benzimidazolyl, isoxazolyl, pyrazinyl, pyridazinyl, indolizinyl, isoindolyl, 3H-indolyl, 1H-indazolyl, purinyl, 4H-quinolizinyl, phthalazinyl, naphthyridinyl, quinoxalinyl, quinazolinyl, cinnolinyl, pteridinyl, 4aH-carbazolyl, carbazolyl, phenanthridinyl, acridinyl, pyrimidinyl, phenanthrolinyl, phenazinyl, phenothiazinyl, furazanyl, phenoxazinyl, isochromanyl, chromanyl, imidazolidinyl, imidazolinyl, pyrazolidinyl, pyrazolinyl, benzotriazolyl, benzisoxazolyl, and isatinoyl. Examples of heterocycloalkyls include by way of example and not limitation, dihydroypyridyl, tetrahydropyridyl (piperidyl), tetrahydrothiophenyl, piperidinyl, 4-piperidonyl, pyrrolidinyl, 2-pyrrolidonyl, tetrahydrofuranyl, tetrahydropyranyl, bis-tetrahydropyranyl, tetrahydroquinolinyl, tetrahydroisoquinolinyl, decahydroquinolinyl, octahydroisoquinolinyl, piperazinyl, quinuclidinyl, and morpholinyl. Heteroaryl and heterocycloalkyl groups can be unsubstituted or substituted.

"Substituted" as used herein and as applied to any of the above alkyl, aryl, cycloalkyl, heteroaryl, heterocyclyl, means that one or more hydrogen atoms are each independently replaced with a substituent. Typical substituents include, but are not limited to, -Cl, Br, F, alkyl, -OH, $-OCH_3$, NH_2, $-NHCH_3$, $-N(CH_3)_2$, -CN, $-NC(=O)CH_3$, -C(=O)-, $-C(=O)NH_2$, and $-C(=O)N(CH_3)_2$. Wherever a group is described as "optionally substituted," that group can be substituted with one or more of the above substituents, independently selected for each occasion. In some embodiments, the substituent may be one or more methyl groups or one or more hydroxyl groups.

In some embodiments, the organic acid is an alkyl carboxylic acid. Non-limiting examples of alkyl carboxylic acids include formic acid, acetic acid, propionic acid, butyric acid, valeric acid, caproic acid, heptanoic acid, octanoic acid, nonanoic acid, decanoic acid, undecanoic acid, dodecanoic acid, stearic acid, oleic acid, linoleic acid, linolenic acid, and the like.

In some embodiments, the organic acid is an alkyl sulfonic acid. Non-limiting examples of alkyl sulfonic acids include propanesulfonic acid, heptanesulfonic acid, and octanesulfonic acid.

In some embodiments, the alkyl carboxylic or sulfonic acid is substituted with one or more hydroxyl groups. Non-limiting examples include glycolic acid, 4-hydroxybutyric acid, and lactic acid.

In some embodiments, an organic acid may include more than one carboxylic acid group or more than one sulfonic acid group (*e.g.*, two, three, or more carboxylic acid groups). Non-limiting examples include oxalic acid, fumaric acid, maleic acid, and glutaric acid. In organic acids containing multiple carboxylic acids (e.g., from two to four carboxylic acid groups), one or more of the carboxylic acid groups may be esterified. Non-limiting examples include succinic acid monoethyl ester, monomethyl fumarate, monomethyl or dimethyl citrate, and the like.

In some embodiments, the organic acid may include more than one carboxylic acid group and one or more hydroxyl groups. Non-limiting examples of such acids include tartaric acid, citric acid, and the like.

In some embodiments, the organic acid is an aryl carboxylic acid or an aryl sulfonic acid. Non-limiting examples of aryl carboxylic and sulfonic acids include benzoic acid, toluic acids, salicylic acid, benzenesulfonic acid,and *p*-toluenesulfonic acid.

Further non-limiting examples of organic acids which may be useful in certain embodiments include 2,2-dichloroacetic acid, 2-hydroxyethanesulfonic acid, 2-oxoglutaric acid, 4-acetamidobenzoic acid, 4-aminosalicylic acid, adipic acid, ascorbic acid (L), aspartic acid (L), alpha-methylbutyric acid, camphoric acid (+), camphor-10-sulfonic acid (+), cinnamic acid, cyclamic acid, dodecylsulfuric acid, ethane-1,2-disulfonic acid, ethanesulfonic acid, furoic acid, galactaric acid, gentisic acid, glucoheptonic acid, gluconic acid, glucuronic acid, glutamic acid, glycerophosphoric acid, glycolic acid, hippuric acid, isobutyric acid, isovaleric acid, lactobionic acid, lauric acid, levulinic acid, malic acid, malonic acid, mandelic acid, methanesulfonic acid, naphthalene-1,5-disulfonic acid, naphthalene-2-sulfonic acid, oleic acid, palmitic acid, pamoic acid, phenylacetic acid, pyroglutamic acid, pyruvic acid, sebacic acid, stearic acid, and undecylenic acid.

Examples of suitable acids include, but are not limited to, the list of organic acids in Table 1.

Table 1. Non-limiting examples of suitable organic acids

Acid Name	log(P)*
benzoic acid	1.9
phenylacetic	1.4
p-toluic acid	2.3

ethyl benzoic acid	2.9
isopropyl benzoic acid	3.5
4-phenylbutyric	2.4
2-(4-Isobutylphenyl)propanoic acid	3.5
2-napthoxyacetic acid	2.5
napthylacetic acid	2.7
heptanoic acid	2.5
octanoic acid	3.05
nonanoic acid	3.5
decanoic acid	4.09
9-deceneoic acid	3.3
2-deceneoic acid	3.8
10-undecenoic acid	3.9
dodecandioic acid	3.2
dodecanoic acid	4.6
myristic acid	5.3
palmitic acid	6.4
stearic acid	7.6
cyclohexanebutanoic acid	3.4
1-heptanesulfonic acid	2.0
1-octanesulfonic acid	2.5
1-nonanesulfonic acid	3.1
monooctyl succinate	2.8
tocopherol succinate	10.2
monomenthyl succinate	3
monomenthyl glutarate	3.4
norbixin ((2*E*,4*E*,6*E*,8*E*,10*E*,12*E*,14*E*,16*E*,18*E*)-4,8,13,17-tetramethylicosa-2,4,6,8,10,12,14,16,18-nonaenedioic acid)	7.2
bixin ((2*E*,4*E*,6*E*,8*E*,10*E*,12*E*,14*E*,16*Z*,18*E*)-20-methoxy-4,8,13,17-tetramethyl-20-oxoicosa-2,4,6,8,10,12,14,16,18-nonaenoic acid)	7.5

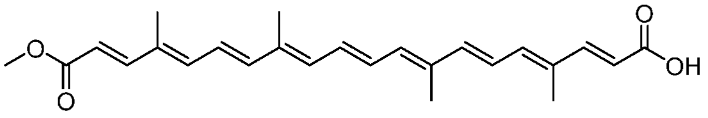
*Values obtained from PubChem or calculated

The selection of organic acid may further depend on additional properties in addition to consideration of the logP value. For example, an organic acid should be one recognized as safe for human consumption, and which has acceptable flavor, odor, volatility, stability, and the like. Determination of appropriate organic acids is within the purview of one of skill in the art.

In some embodiments, the organic acid is a mono ester of a dicarboxylic acid or a poly-carboxylic acid. In some embodiments, the dicarboxylic acid is malonic acid, succinic acid, glutaric acid, adipic acid, fumaric acid, maleic acid, or a combination thereof. In some embodiments, the dicarboxylic acid is succinic acid, glutaric acid, fumaric acid, maleic acid, or a combination thereof. In some embodiments, the dicarboxylic acid is succinic acid, glutaric acid, or a combination thereof.

In some embodiments, the alcohol forming the mono ester of the dicarboxylic acid is a lipophilic alcohol. Examples of suitable lipophilic alcohols include, but are not limited to, octanol, menthol, and tocopherol. In some embodiments, the organic acid is an octyl mono ester of a dicarboxylic acid, such as monooctyl succinate, monooctyl fumarate, or the like. In some embodiments, the organic acid is a monomenthyl ester of a dicarboxylic acid. Certain menthyl esters may be desirable in oral compositions as described herein by virtue of the cooling sensation they may provide upon use of the product comprising the composition. In some embodiments, the organic acid is monomenthyl succinate, monomenthyl fumarate, monomenthyl glutarate, or a combination thereof. In some embodiments, the organic acid is a monotocopheryl ester of a dicarboxylic acid. Certain tocopheryl esters may be desirable in oral compositions as described herein by virtue of the antioxidant effects they may provide. In some embodiments, the organic acid is tocopheryl succinate, tocopheryl fumarate, tocopheryl glutarate, or a combination thereof.

In some embodiments, the organic acid is a carotenoid derivative having one or more carboxylic acids. Carotenoids are tetraterpenes, meaning that they are produced from 8 isoprene molecules and contain 40 carbon atoms. Accordingly, they are usually lipophilic due to the presence of long unsaturated aliphatic chains, and are generally yellow, orange, or red in color. Certain carotenoid derivatives can be advantageous in oral compositions by virtue of providing both ion pairing and serving as a colorant in the composition. In some embodiments, the organic acid is 2E,4E,6E,8E,10E,12E,14E,16Z,18E)-20-methoxy-4,8,13,17-tetramethyl-20-oxoicosa-2,4,6,8,10,12,14,16,18-nonaenoic acid (bixin) or an isomer thereof. Bixin is an apocarotenoid found in annatto seeds from the achiote tree (Bixa orellana) and is the naturally occurring pigment providing the reddish orange color to annatto. Bixin is soluble in fats and alcohols but insoluble in water, and is chemically unstable when isolated, converting via isomerization into the double bond isomer, trans-bixin (β-bixin), having the structure:



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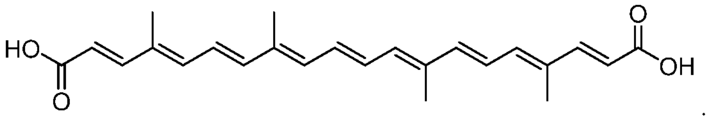
In some embodiments, the organic acid is (2*E*,4*E*,6*E*,8*E*,10*E*,12*E*,14*E*,16*E*,18*E*)-4,8,13,17-tetramethylicosa-2,4,6,8,10,12,14,16,18-nonaenedioic acid (norbixin), a water-soluble hydrolysis product of bixin having the structure:



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In some embodiments, more than one organic acid may be present. For example, the emulsion may comprise two, or three, or four, or more organic acids. Accordingly, reference herein to "an organic acid" contemplates mixtures of two or more organic acids. The relative amounts of the multiple organic acids may vary. For example, the emulsion may comprise equal amounts of two, or three, or more organic acids, or may comprise different relative amounts. In this manner, it is possible to include certain organic acids (e.g., citric acid or myristic acid) which have a logP value outside the desired range, when combined with other organic acids to provide the desired average logP range for the combination. In some embodiments, it may be desirable to include organic acids in the emulsion which have logP values outside the desired range for purposes such as, but not limited to, providing desirable organoleptic properties, stability, as flavor components, and the like. Further, certain lipophilic organic acids have undesirable flavor and or aroma characteristics which would preclude their presence as the sole organic acid (e.g., in equimolar or greater quantities relative to nicotine). Without wishing to be bound by theory, it is believed that a combination of different organic acids may provide the desired ion pairing while the concentration of any single organic acid in the emulsion remains below the threshold which would be found objectionable from a sensory perspective.

In some embodiments, the organic acid is a combination of any two organic acids selected from the group consisting of benzoic acid, a toluic acid, benzenesulfonic acid, toluenesulfonic acid, hexanoic acid, heptanoic acid, decanoic acid, and octanoic acid. In some embodiments, the organic acid is a combination of benzoic acid, octanoic acid, and decanoic acid, or benzoic and octanoic acid. In some embodiments, the emulsion comprises citric acid in addition to one or more of benzoic acid, a toluic acid, benzenesulfonic acid, toluenesulfonic acid, hexanoic acid, heptanoic acid, decanoic acid, and octanoic acid.

In some embodiments, the emulsion comprises an alkali metal salt of an organic acid. For example, at least a portion of the organic acid may be present in the composition in the form of an alkali metal salt. Suitable alkali metal salts include lithium, sodium, and potassium. In some embodiments, the alkali metal is sodium or potassium. In some embodiments, the alkali metal is sodium. In some embodiments, the composition comprises an organic acid and a sodium salt of the organic acid.

In some embodiments, the emulsion comprises benzoic acid and sodium benzoate, octanoic acid and sodium octanoate, decanoic acid and sodium decanoate, or a combination thereof. In some embodiments, the emulsion comprises benzoic acid. In some embodiments, the emulsion comprises benzoic acid and sodium benzoate. In some embodiments, the emulsion comprises sodium benzoate.

In some embodiments, the organic acid may comprise from about 1 to about 5 or more molar equivalents of benzoic acid relative to nicotine, combined with e.g., about 0.2 molar equivalents of octanoic acid or a salt thereof, and 0.2 molar equivalents of decanoic acid or a salt thereof.

In some embodiments, the ratio of the organic acid to the sodium salt (or other alkali metal salt) of the organic acid is from about 0.1 to about 10, such as from about 0.1, about 0.25, about 0.3, about 0.5, about 0.75, or about 1, to about 2, about 5, or about 10. For example, in some embodiments, both an organic acid and the sodium salt thereof are added to the other components of the emulsion, wherein the organic acid is added in excess of the sodium salt, in equimolar quantities with the sodium salt, or as a fraction of the sodium salt. One of skill in the art will recognize that the relative amounts will be determined by the desired pH of the emulsion, as well as the desired ionic strength. For example, the organic acid may be added in a quantity to provide a desired pH level of the emulsion, while the alkali metal (e.g., sodium) salt is added in a quantity to provide the desired extent of ion pairing. As one of skill in the art will understand, the quantity of organic acid (i.e., the protonated form) present in the emulsion, relative to the alkali metal salt or conjugate base form present in the emulsion, will vary according to the pH of the emulsion and the pKa of the organic acid, as well as according to the actual relative quantities initially added to the emulsion.

The amount of organic acid or an alkali metal salt thereof present in the emulsion, relative to the basic amine containing active ingredient (e.g., nicotine), may vary. Generally, as the concentration of the organic acid (or the conjugate base thereof) increases, the percent of nicotine that is ion paired with the organic acid increases. This typically increases the partitioning of the nicotine, in the form of an ion pair, into octanol versus water as measured by the logP (the $\log_{10}$ of the partitioning coefficient). In some embodiments, the emulsion comprises from about 0.05, about 0.1, about 1, about 1.5, about 2, or about 5, to about 10, about 15, or about 20 molar equivalents of the organic acid, the alkali metal salt thereof, or the combination thereof, relative to the nicotine component, calculated as free base nicotine.

In some embodiments, the emulsion comprises from about 2 to about 10, or from about 2 to about 5 molar equivalents of the organic acid, the alkali metal salt thereof, or the combination thereof, to nicotine, on a free-base nicotine basis. In some embodiments, the organic acid, the alkali metal salt thereof, or the combination thereof, is present in a molar ratio with the nicotine from about 2, about 3, about 4, or about 5, to about 6, about 7, about 8, about 9, or about 10. In embodiments wherein more than one organic acid, alkali metal salt thereof, or both, are present, it is to be understood that such molar ratios reflect the totality of the organic acids present.

In certain embodiments the organic acid inclusion is sufficient to provide a pH of the emulsion from about 4.0 to about 9.5, such as from about 4.0 to about 9.0, or from about 4.0 to about 8.5, or from about 4.0 to about 8.0, or from about 4.5 to about 7.5, or from about 4.5 to about 7.0, or from about 5.5 to about 7.0, or from about 4.0 to about 5.5, or from about 7.0 to about 9.5. In some embodiments, the organic acid inclusion is sufficient to provide a composition pH of about 4.0, about 4.5, about 5.0, about 5.5, about 6.0, about 6.5, about 7.0, about 7.5, about 8.0, about 8.5, or about 9.0. In some embodiments, the organic acid inclusion is sufficient to provide an emulsion pH of from about 4.5 to about 6.5, for example, from about 4.5, about 5.0, or about 5.5, to about 6.0, or about 6.5. In some embodiments, the organic acid is provided in a quantity sufficient to provide a pH of the emulsion of from about 5.5 to about 6.5, for example, from about 5.5, about 5.6, about 5.7, about 5.8, about 5.9, or about 6.0, to about 6.1, about 6.2, about 6.3, about 6.4, or about 6.5. In other embodiments, a mineral acid (e.g., hydrochloric acid, sulfuric acid, phosphoric acid, or the like) is added to adjust the pH of the emulsion to the desired value.

In some embodiments, the organic acid is added as the free acid, either neat (i.e., native solid or liquid form) or as a solution in, e.g., water, to the other emulsion components. In some embodiments, the alkali metal salt of the organic acid is added, either neat or as a solution in, e.g., water, to the other emulsion components.

In some embodiments, the organic acid and nicotine) are combined to form a salt, either before addition to the emulsion, or the salt is formed within and is present in the emulsion as such.

In some embodiments, the emulsion comprises nicotine benzoate, alone or with added sodium benzoate, wherein at least a portion of the nicotine and benzoate ions present are in an ion paired form. In some embodiments, the emulsion comprises nicotine benzoate and sodium benzoate.

In some embodiments, the emulsion further comprises a solubility enhancer to increase the solubility of one or more of the organic acid or salt thereof. Suitable solubility enhancers include, but are not limited to, humectants as described herein, such as glycerol or propylene glycol.

In some embodiments, at least a portion of the nicotine can be in the form of a resin complex of nicotine, where nicotine is bound in an ion-exchange resin, such as nicotine polacrilex, which is nicotine bound to, for example, a polymethacrilic acid, such as Amberlite IRP64, Purolite C115HMR, or Doshion P551. See, for example, US Pat. No. 3,901,248 to Lichtneckert et al., which is incorporated herein by reference. Another example is a nicotine-polyacrylic carbomer complex, such as with Carbopol 974P. In some embodiments, nicotine may be present in the form of a nicotine polyacrylic complex.

Typically, the nicotine component (calculated as the free base) is present in a concentration of at least about 0.001% by weight of the composition, such as in a range from about 0.001% to about 10%. In some embodiments, the nicotine component is present in a concentration from about 0.1% w/w to about 10% by weight, such as, e.g., from about 0.1% w/w, about 0.2%, about 0.3%, about 0.4%, about 0.5% about 0.6%, about 0.7%, about 0.8%, or about 0.9%, to about 1%, about 2%, about 3%, about 4%, about 5%, about 6%, about 7%, about 8%, about 9%, or about 10% by weight, calculated as the free base and based on the total weight of the composition. In some embodiments, the nicotine component is present in a concentration from about 0.1% w/w to about 3% by weight, such as, e.g., from about 0.1% w/w to about 2.5%, from about 0.1% to about 2.0%, from about 0.1% to about 1.5%, or from about 0.1% to about 1% by weight, calculated as the free base and based on the total weight of the composition.

The nicotine component may be present in the oil phase (lipid) of the emulsion, the water phase of the emulsion, or both. The distribution of the nicotine component may vary between the phases based on the nature of the nicotine component and the emulsion phases as well as the method of preparation of the emulsion (e.g., microemulsion).

Filler

The composition as disclosed herein comprises a filler. Fillers may fulfil multiple functions, such as enhancing certain organoleptic properties such as texture and mouthfeel, enhancing cohesiveness or compressibility of the product, and the like, depending on the product and the association between the filler and the emulsion. The emulsion as disclosed herein may be associated with the filler in various ways (i.e., in an oral composition comprising an emulsion as disclosed herein). For example, the emulsion (e.g., a microemulsion) may be disposed on the surface of a filler, may be dispersed in or impregnated into (e.g., adsorbed or absorbed) a filler, or a filler and the emulsion may be present in an oral composition without being physically combined or in physical contact (e.g., they may be provided separately and independently within the same product).

In some embodiments, the filler is a porous particulate material and is cellulose-based. For example, the filler may be a non-tobacco plant material or derivative thereof, including cellulose materials derived from such sources. Examples of cellulosic non-tobacco plant material include cereal grains (e.g., maize, oat, barley, rye, buckwheat, and the like), sugar beet (e.g., FIBREX® brand filler available from International Fiber Corporation), bran fiber, and mixtures thereof.

In some embodiments, the filler is a cellulose material selected from the group consisting of maize fiber, oat fiber, barley fiber, rye fiber, buckwheat fiber, sugar beet fiber, bran fiber, bamboo fiber, wood pulp fiber, cotton fiber, citrus pulp fiber, grass fiber, willow fiber, poplar fiber, cocoa fiber, derivatives thereof, and combinations thereof. In some embodiments, the filler is a cellulose material selected from the group consisting of maize fiber, oat fiber, sugar beet fiber, bamboo fiber, wood pulp fiber, cotton fiber, grass fiber, derivatives thereof, and combinations thereof. In some embodiments, the filler is a cellulose material selected from the group consisting of sugar beet fiber, wood pulp fiber, bamboo fiber, derivatives thereof, and combinations thereof.

In some embodiments, the filler is derived from any of maize fiber, oat fiber, barley fiber, rye fiber, buckwheat fiber, sugar beet fiber, bran fiber, bamboo fiber, wood pulp fiber, cotton fiber, citrus pulp fiber, grass fiber, willow fiber, poplar fiber, cocoa fiber, or combinations thereof. In some embodiments, the filler is derived from wood pulp fiber.

In some embodiments, the filler is a cellulose material. One particularly suitable filler for use in the compositions described herein is microcrystalline cellulose ("MCC"). MCC is typically derived from wood pulp fiber. MCC is composed of glucose units connected by a 1-4 beta glycosidic bond and may be synthesized by partially depolymerizing alpha-cellulose, by, for example, reactive extrusion, enzyme mediated depolymerisation, mechanical grinding, ultrasonication, steam explosion and/or acid hydrolysis. The MCC may be synthetic or semi-synthetic, or it may be obtained entirely from natural celluloses. The MCC may be selected from the group consisting of AVICEL® grades PH-100, PH-101, PH-102, PH-103, PH-105, PH-112, PH-113, PH-200, PH-300, PH-301, PH-302, VIVACEL® grades 101, 102, 12, 20 and EMOCEL® grades 50M and 90M, and the like, and mixtures thereof. In some embodiments, the composition comprises MCC as the filler. In some embodiments, the filler is microcrystalline cellulose. The emulsion may be disposed on the surface of the microcrystalline cellulose, or may be dispersed in or impregnated into (e.g., adsorbed or absorbed) the microcrystalline cellulose,

In some embodiments, the filler is a non-tobacco plant material or a derivative thereof. Non-limiting examples of derivatives of non-tobacco plant material include starches (e.g., from potato, wheat, rice, corn), natural cellulose, and modified cellulosic materials. Additional examples of potential fillers include maltodextrin, dextrose, calcium carbonate, calcium phosphate, lactose, mannitol, xylitol, and sorbitol. Combinations of fillers can also be used.

"Starch" as used herein may refer to pure starch from any source, modified starch, or starch derivatives. Starch is present, typically in granular form, in almost all green plants and in various types of plant tissues and organs (e.g., seeds, leaves, rhizomes, roots, tubers, shoots, fruits, grains, and stems). Starch can vary in composition, as well as in granular shape and size. Often, starch from different sources has different chemical and physical characteristics. A specific starch can be selected for inclusion in the composition based on the ability of the starch material to impart a specific organoleptic property to composition. Starches derived from various sources can be used. For example, major sources of starch include cereal grains (e.g., rice, wheat, and maize) and root vegetables (e.g., potatoes and cassava). Other examples of sources of starch include acorns, arrowroot, arracacha, bananas, barley, beans (e.g., favas, lentils, mung beans, peas, chickpeas), breadfruit, buckwheat, canna, chestnuts, colacasia, katakuri, kudzu, malanga, millet, oats, oca, Polynesian arrowroot, sago, sorghum, sweet potato, quinoa, rye, tapioca, taro, tobacco, water chestnuts, and yams. Certain starches are modified starches. A modified starch has undergone one or more structural modifications, often designed to alter its high heat properties. Some starches have been developed by genetic modifications and are considered to be "genetically modified" starches. Other starches are obtained and subsequently modified by chemical, enzymatic, or physical means. For example, modified starches can be starches that have been subjected to chemical reactions, such as esterification, etherification, oxidation, depolymerization (thinning) by acid catalysis or oxidation in the presence of base, bleaching, transglycosylation and depolymerization (e.g., dextrinization in the presence of a catalyst), cross-linking, acetylation, hydroxypropylation, and/or partial hydrolysis. Enzymatic treatment includes subjecting native starches to enzyme isolates or concentrates, microbial enzymes, and/or enzymes native to plant materials, e.g., amylase present in corn kernels to modify corn starch. Other starches are modified by heat treatments, such as pregelatinization, dextrinization, and/or cold-water swelling processes. Certain modified starches include monostarch phosphate, distarch glycerol, distarch phosphate esterified with sodium trimetaphosphate, phosphate distarch phosphate, acetylated distarch phosphate, starch acetate esterified with acetic anhydride, starch acetate esterified with vinyl acetate, acetylated distarch adipate, acetylated distarch glycerol, hydroxypropyl starch, hydroxypropyl distarch glycerol, and starch sodium octenyl succinate.

The amount of filler can vary, but when present, is typically at least about 50 percent by weight of the composition comprising the emulsion, based on the total weight of the composition. A typical range of filler (e.g., a cellulose material, such as microcrystalline cellulose) within the composition can be from about 10 to about 75 percent by total weight of the composition. For example, the filler (e.g., MCC) may be present in the composition in an amount from about 5, about 10, about 15, or about 20, to about 25, about 30, about 35, about 40, about 45, or about 50% by weight of the composition. In some embodiments, the composition comprises microcrystalline cellulose in an amount of from about 10% to about 20% by weight based on the total weight of the composition. In some embodiments, the weight ratio of the filler (such as microcrystalline cellulose) to the emulsion (e.g., microemulsion) may be from about 10:1 to about 1:10, such as from about 5:1 to about 1:5, such as from about 5:1 to about 1:2, such as from about 3:1 to about 1:1, such as from about 2:1 to about 1:1.

The amount of the emulsion in the composition may vary and may be any suitable amount for forming a solid product suitable for oral application. In some embodiments, the emulsion is present in an amount of from about 1% to about 75% by weight of the composition, such as from about 5% to about

60%, such as from about 10% to about 50%, such as from about 15% to about 45%, or such as from about 20% to about 40% by weight, based on the total weight of the composition.

Further components

In some embodiments, the composition as disclosed herein may further comprise additional components, either within the emulsion or within the composition as a whole. The additional components may comprise one or more flavoring agents, taste modifiers, preservatives, humectants, sweeteners, binders, buffering agents, salts, or mixtures thereof. Each of these additional components is further described herein below.

Flavoring agent

In some embodiments, the composition as described herein comprises a flavoring agent. As used herein, a "flavoring agent" or "flavorant" is any flavorful or aromatic substance capable of altering the sensory characteristics associated with the oral product. Examples of sensory characteristics that can be modified by the flavoring agent include taste, mouthfeel, moistness, coolness/heat, and/or fragrance/aroma. Flavoring agents may be natural or synthetic, and the character of the flavors imparted thereby may be described, without limitation, as fresh, sweet, herbal, confectionary, floral, fruity, or spicy.

Flavoring agents may be imitation, synthetic or natural ingredients or blends thereof. Flavoring agents may include naturally occurring flavor materials, botanicals, extracts of botanicals, synthetically obtained materials, or combinations thereof (e.g., tobacco, cannabis, licorice (liquorice), hydrangea, eugenol, Japanese white bark magnolia leaf, chamomile, fenugreek, clove, maple, matcha, menthol, Japanese mint, aniseed (anise), cinnamon, turmeric, Indian spices, Asian spices, herb, wintergreen, cherry, berry, red berry, cranberry, peach, apple, orange, mango, clementine, lemon, lime, tropical fruit, papaya, rhubarb, grape, durian, dragon fruit, cucumber, blueberry, mulberry, citrus fruits, Drambuie, bourbon, scotch, whiskey, gin, tequila, rum, spearmint, peppermint, lavender, aloe vera, cardamom, celery, cascarilla, nutmeg, sandalwood, bergamot, geranium, khat, naswar, betel, shisha, pine, honey essence, rose oil, vanilla, lemon oil, orange oil, orange blossom, cherry blossom, cassia, caraway, cognac, jasmine, ylang-ylang, sage, fennel, wasabi, piment, ginger, coriander, coffee, hemp, a mint oil from any species of the genus Mentha, eucalyptus, star anise, cocoa, lemongrass, rooibos, flax, ginkgo biloba, hazel, hibiscus, laurel, mate, orange skin, rose, tea such as green tea or black tea, thyme, juniper, elderflower, basil, bay leaves, cumin, oregano, paprika, rosemary, saffron, lemon peel, mint, beefsteak plant, curcuma, cilantro, myrtle, cassis, valerian, pimento, mace, damien, marjoram, olive, lemon balm, lemon basil, chive, carvi, verbena, tarragon, limonene, thymol, camphene), flavor enhancers, bitterness receptor site blockers, sensorial receptor site activators or stimulators, sugars and/or sugar substitutes (e.g., sucralose, acesulfame potassium, aspartame, saccharine, cyclamates, lactose, sucrose, glucose, fructose, sorbitol, or mannitol), and other additives such as charcoal, chlorophyll, minerals, botanicals, or breath freshening agents.

Flavorants may further include flavor enhancers, bitterness receptor site blockers, sensorial receptor site activators or stimulators, and trigeminal sensates, As used herein, "trigeminal sensate" refers to a flavoring agent which has an effect on the trigeminal nerve, producing sensations including heating, cooling, tingling, and the like. Non-limiting examples of trigeminal sensate flavoring agents include capsaicin, citric acid, menthol, Sichuan buttons, erythritol, and cubebol. A suitable heat effect agent may be, but is not limited to, vanillyl ethyl ether, and a suitable cooling agent may be, but is not limited to eucalyptol or N-ethyl-p-menthane-3-carboxamide (WS-3).

Flavoring agents may be in any suitable form, for example, liquid such as an oil, solid such as a powder, or gas. In some instances, the flavoring agent may be provided in a spray-dried form or a liquid form. In some embodiments, a liquid flavorant is disposed (i.e., adsorbed or absorbed in or on) a porous particulate carrier, for example microcrystalline cellulose, which is then combined with the other composition ingredients. In some embodiments, one or more flavorants are present within the emulsion, and may be added to the oil phase, the liquid phase, or both phases during preparation of the emulsion. In some embodiments, different flavoants may be provided in the emulsion and in the composition as a whole.

The amount of flavoring agent utilized in the composition can vary, but is typically up to about 10% by weight, and certain embodiments are characterized by a flavoring agent content of at least about 0.1% by weight, such as about 0.5 to about 10%, about 1 to about 5%, or about 2 to about 4% weight, based on the total weight of the composition.

Taste modifiers

In order to improve the organoleptic properties of a composition as disclosed herein, the composition may include one or more taste modifying agents ("taste modifiers") which may serve to mask, alter, block, or improve e.g., the flavor of a composition as described herein. Non-limiting examples of such taste modifiers include analgesic or anesthetic herbs, spices, and flavors which produce a perceived cooling (e.g., menthol, eucalyptus, mint), warming (e.g., cinnamon), or painful (e.g., capsaicin) sensation. Certain taste modifiers fall into more than one overlapping category.

In some embodiments, the taste modifier modifies one or more of bitter, sweet, salty, or sour tastes. In some embodiments, the taste modifier targets pain receptors. In some embodiments, the composition comprises an active ingredient having a bitter taste, and a taste modifier which masks or blocks the perception of the bitter taste. In some embodiments, the taste modifier is a substance which targets pain receptors (e.g., vanilloid receptors) in the user's mouth to mask e.g., a bitter taste of another component (e.g., an active ingredient). Suitable taste modifiers include, but are not limited to, capsaicin, gamma-amino butyric acid (GABA), adenosine monophosphate (AMP), lactisole, or a combination thereof.

In some embodiments, a taste modifier is present within the emulsion, and may be added to the oil phase, the liquid phase, or both phases during preparation of the emulsion. In some embodiments, a taste modifier is present in the emulsion, or within the composition as a whole.

When present, a representative amount of taste modifier is about 0.01% by weight or more, about 0.1% by weight or more, or about 1.0% by weight or more, but will typically make up less than about 10% by weight of the total weight of the composition, (e.g., from about 0.01%, about 0.05%, about 0.1%, or about 0.5%, to about 1%, about 5%, or about 10% by weight of the total weight of the composition).

Salts

In some embodiments, the composition may further comprise a salt (e.g., alkali metal salts), typically employed in an amount sufficient to provide desired sensory attributes to the composition. Non-limiting examples of suitable salts include sodium chloride, potassium chloride, ammonium chloride, flour salt, and the like.

In some embodiments, a salt is present within the emulsion, and may be added to the oil phase, the liquid phase, or both phases during preparation of the emulsion. In some embodiments, a salt is present in the emulsion, or within the composition as a whole.

When present, a representative amount of salt is about 0.5 percent by weight or more, about 1.0 percent by weight or more, or at about 1.5 percent by weight or more, but will typically make up about 10 percent or less of the total weight of the composition, or about 7.5 percent or less or about 5 percent or less (e.g., about 0.5 to about 5 percent by weight).

Sweeteners

In order to improve the sensory properties of the composition according to the disclosure, one or more sweeteners may be added. The sweeteners can be any sweetener or combination of sweeteners, in natural or artificial form, or as a combination of natural and artificial sweeteners. Examples of natural sweeteners include fructose, sucrose, glucose, maltose, mannose, galactose, lactose, stevia, honey, and the like. Examples of artificial sweeteners include sucralose, isomaltulose, maltodextrin, saccharin, aspartame, acesulfame K, neotame, and the like. In some embodiments, the sweetener comprises one or more sugar alcohols. Sugar alcohols are polyols derived from monosaccharides or disaccharides that have a partially or fully hydrogenated form. Sugar alcohols have, for example, about 4 to about 20 carbon atoms and include erythritol, arabitol, ribitol, isomalt, maltitol, dulcitol, iditol, mannitol, xylitol, lactitol, sorbitol, and combinations thereof (e.g., hydrogenated starch hydrolysates). In some embodiments, the sweetener is sucralose, acesulfame K, or a combination thereof.

In some embodiments, a sweetener or combination thereof is present within the emulsion, and may be added to the oil phase, the liquid phase, or both phases during preparation of the emulsion. In some embodiments, a sweetener or combination thereof is present in the emulsion, or within the composition as a whole.

When present, a sweetener or combination of sweeteners may make up from about 0.01 to about 20% or more of the of the composition by weight, for example, from about 0.01 to about 0.1, from about 0.1 to about 1%, from about 1 to about 5%, from about 5 to about 10%, or from about 10 to about 20% by weight, based on the total weight of the composition. In some embodiments, a combination of sweeteners is present at a concentration of from about 0.01% to about 0.1% by weight of the composition, such as about 0.01, about 0.02, about 0.03, about 0.04, about 0.05, about 0.06, about 0.07, about 0.08, about 0.09, or about 0.1% by weight of the composition. In some embodiments, a combination of sweeteners is present at a concentration of from about 0.1% to about 0.5% by weight of the composition, such as about 0.1, about 0.2, about 0.3, about 0.4, or about 0.5% by weight of the composition. In some embodiments, a combination of sweeteners is present at a concentration of from about 1% to about 3% by weight of the composition.

Binding agents

A binder (or combination of binders) may be employed in certain embodiments. Typical binders can be organic or inorganic, or a combination thereof. Representative binders include povidone, sodium alginate, starch-based binders, pectin, carrageenan, pullulan, zein, and the like, and combinations thereof. A binder may be employed in amounts sufficient to provide the desired physical attributes and physical integrity to the composition. The amount of binder utilized in the composition can vary, but is typically up to about 30 weight percent, and certain embodiments are characterized by a binder content of at least about 0.1% by weight, such as about 1 to about 30% by weight, or about 5 to about 10% by weight, based on the total weight of the composition.

Other suitable binders include a gum, for example, a natural gum. As used herein, a natural gum refers to polysaccharide materials of natural origin that have binding properties, and which are also useful as a thickening or gelling agent. Representative natural gums derived from plants, which are typically water soluble to some degree, include xanthan gum, guar gum, gum arabic, ghatti gum, gum tragacanth, karaya gum, locust bean gum, gellan gum, and combinations thereof. When present, natural gum binder materials are typically present in an amount of up to about 5% by weight, for example, from about 0.1, about 0.2, about 0.3, about 0.4, about 0.5, about 0.6, about 0.7, about 0.8, about 0.9, or about 1%, to about 2, about 3, about 4, or about 5% by weight, based on the total weight of the composition.

Humectants

In certain embodiments, one or more humectants may be employed in the composition. Examples of humectants include, but are not limited to, polyols such as glycerin, propylene glycol, and the like. Where included, the humectant is typically provided in an amount sufficient to provide desired moisture attributes to the composition. Further, in some instances, the humectant may impart desirable flow characteristics to the composition for depositing in a mold.

When present, a humectant will typically make up about 5% or less of the weight of the composition (e.g., from about 0.5 to about 5% by weight). When present, a representative amount of humectant is about 0.1% to about 1% by weight, or about 1% to about 5% by weight, based on the total weight of the composition.

Buffering agents

In certain embodiments, the composition of the present disclosure can comprise pH adjusters or buffering agents. Examples of pH adjusters and buffering agents that can be used include, but are not limited to, metal hydroxides (e.g., alkali metal hydroxides such as sodium hydroxide and potassium hydroxide), and other alkali metal buffers such as metal carbonates (e.g., potassium carbonate or sodium carbonate), or metal bicarbonates such as sodium bicarbonate, and the like. Non-limiting examples of suitable buffers include alkali metals acetates, glycinates, phosphates, glycerophosphates, citrates, carbonates, hydrogen carbonates, borates, or mixtures thereof.

In some embodiments, a buffer is present within the emulsion, and may be added to the oil phase, the liquid phase, or both phases during preparation of the emulsion. In some embodiments, a buffer is present in the emulsion, or within the composition as a whole.

Where present, the buffering agent is typically present in an amount less than about 5 percent based on the weight of the composition, for example, from about 0.5% to about 5%, such as, *e.g.,* from about 0.75% to about 4%, from about 0.75% to about 3%, or from about 1% to about 2% by weight, based on the total weight of the composition.

Colorants

A colorant may be employed in amounts sufficient to provide the desired physical attributes to the composition. Natural or synthetic colorants, such as natural or synthetic dyes, food-grade colorants and pharmaceutical-grade colorants may be used. Examples of colorants include various dyes and pigments, such as caramel coloring and titanium dioxide. Natural colorants such as curcumin, beet juice extract, spirulina; also a variety of synthetic pigments may also be used.

In some embodiments, a colorant is present within the emulsion, and may be added to the oil phase, the liquid phase, or both phases during preparation of the emulsion. In some embodiments, a colorant is present in the emulsion, or within the composition as a whole.

The amount of colorant utilized in the composition can vary, but when present is typically up to about 3% by weight, such as from about 0.1%, about 0.5%, or about 1%, to about 3% by weight, based on the total weight of the composition.

Tobacco material

In some embodiments, the composition may include a tobacco material. The tobacco material can vary in species, type, and form. Generally, the tobacco material is obtained from for a harvested plant of the *Nicotiana* species. Example *Nicotiana* species include N. tabacum, N. rustica, N. alata, N. arentsii, N. excelsior, N. forgetiana, N. glauca, N. glutinosa, N. gossei, N. kawakamii, N. knightiana, N. langsdorffi, N. otophora, N. setchelli, N. sylvestris, N. tomentosa, N. tomentosiformis, N. undulata, N. x sanderae, N. africana, N. amplexicaulis, N. benavidesii, N. bonariensis, N. debneyi, N. longiflora, N. maritina, N. megalosiphon, N. occidentalis, N. paniculata, N. plumbaginifolia, N. raimondii, N. rosulata, N. simulans, N. stocktonii, N. suaveolens, N. umbratica, N. velutina, N. wigandioides, N. acaulis, N. acuminata, N. attenuata, N. benthamiana, N. cavicola, N. clevelandii, N. cordifolia, N. corymbosa, N. fragrans, N.

goodspeedii, N. linearis, N. miersii, N. nudicaulis, N. obtusifolia, N. occidentalis subsp. Hersperis, N. pauciflora, N. petunioides, N. quadrivalvis, N. repanda, N. rotundifolia, N. solanifolia, and N. spegazzinii. Various representative other types of plants from the *Nicotiana* species are set forth in Goodspeed, *The Genus Nicotiana*, (Chonica Botanica) (1954); US Pat. Nos. 4,660,577 to Sensabaugh, Jr. et al.; 5,387,416 to White et al., 7,025,066 to Lawson et al.; 7,798,153 to Lawrence, Jr. and 8,186,360 to Marshall et al.; each of which is incorporated herein by reference. Descriptions of various types of tobaccos, growing practices and harvesting practices are set forth in *Tobacco Production, Chemistry and Technology*, Davis et al. (Eds.) (1999), which is incorporated herein by reference.

Nicotiana species from which suitable tobacco materials can be obtained can be derived using genetic-modification or crossbreeding techniques (e.g., tobacco plants can be genetically engineered or crossbred to increase or decrease production of components, characteristics or attributes). See, for example, the types of genetic modifications of plants set forth in US Pat. Nos. 5,539,093 to Fitzmaurice et al.; 5,668,295 to Wahab et al.; 5,705,624 to Fitzmaurice et al.; 5,844,119 to Weigl; 6,730,832 to Dominguez et al.; 7,173,170 to Liu et al.; 7,208,659 to Colliver et al. and 7,230,160 to Benning et al.; US Patent Appl. Pub. No. 2006/0236434 to Conkling et al.; and PCT WO2008/103935 to Nielsen et al. See, also, the types of tobaccos that are set forth in US Pat. Nos. 4,660,577 to Sensabaugh, Jr. et al.; 5,387,416 to White et al.; and 6,730,832 to Dominguez et al., each of which is incorporated herein by reference.

The *Nicotiana* species can, in some embodiments, be selected for the content of various compounds that are present therein. For example, plants can be selected on the basis that those plants produce relatively high quantities of one or more of the compounds desired to be isolated therefrom. In certain embodiments, plants of the *Nicotiana* species (e.g., *Galpao commun* tobacco) are specifically grown for their abundance of leaf surface compounds. Tobacco plants can be grown in greenhouses, growth chambers, or outdoors in fields, or grown hydroponically.

Various parts or portions of the plant of the *Nicotiana* species can be included within a composition as disclosed herein. For example, virtually all of the plant (*e.g.*, the whole plant) can be harvested, and employed as such. Alternatively, various parts or pieces of the plant can be harvested or separated for further use after harvest. For example, the flower, leaves, stem, stalk, roots, seeds, and various combinations thereof, can be isolated for further use or treatment. In some embodiments, the tobacco material comprises tobacco leaf (lamina). The composition disclosed herein can include processed tobacco parts or pieces, cured and aged tobacco in essentially natural lamina and/or stem form, a tobacco extract, extracted tobacco pulp (e.g., using water as a solvent), or a mixture of the foregoing (e.g., a mixture that combines extracted tobacco pulp with granulated cured and aged natural tobacco lamina).

In certain embodiments, the tobacco material comprises solid tobacco material selected from the group consisting of lamina and stems. The tobacco that is used for the mixture most preferably includes tobacco lamina, or a tobacco lamina and stem mixture (of which at least a portion is smoke-treated). Portions of the tobaccos within the mixture may have processed forms, such as processed tobacco stems (e.g., cut-rolled stems, cut-rolled-expanded stems or cut-puffed stems), or volume expanded tobacco (e.g., puffed tobacco, such as dry ice expanded tobacco (DIET)). See, for example, the tobacco expansion processes set forth in US Pat. Nos. 4,340,073 to de la Burde et al.; 5,259,403 to Guy et al.; and 5,908,032 to Poindexter, et al.; and 7,556,047 to Poindexter, et al., all of which are incorporated by reference. In addition, the d mixture optionally may incorporate tobacco that has been fermented. See, also, the types of tobacco processing techniques set forth in PCT WO2005/063060 to Atchley et al., which is incorporated herein by reference.

The tobacco material is typically used in a form that can be described as particulate (i.e., shredded, ground, granulated, or powder form). The manner by which the tobacco material is provided in a finely divided or powder type of form may vary. Preferably, plant parts or pieces are comminuted, ground or pulverized into a particulate form using equipment and techniques for grinding, milling, or the like. Most preferably, the plant material is relatively dry in form during grinding or milling, using equipment such as hammer mills, cutter heads, air control mills, or the like. For example, tobacco parts or pieces may be ground or milled when the moisture content thereof is less than about 15 weight percent or less than about 5 weight percent. Most preferably, the tobacco material is employed in the form of parts or pieces that have an average particle size between 1.4 millimeters and 250 microns. In some instances, the tobacco particles may be sized to pass through a screen mesh to obtain the particle size range required. If desired, air classification equipment may be used to ensure that small sized tobacco particles of the desired sizes, or range of sizes, may be collected. If desired, differently sized pieces of granulated tobacco may be mixed together.

The manner by which the tobacco is provided in a finely divided or powder type of form may vary. Preferably, tobacco parts or pieces are comminuted, ground or pulverized into a powder type of form using equipment and techniques for grinding, milling, or the like. Most preferably, the tobacco is relatively dry in form during grinding or milling, using equipment such as hammer mills, cutter heads, air control mills, or the like. For example, tobacco parts or pieces may be ground or milled when the moisture content thereof is less than about 15 weight percent to less than about 5 weight percent. For example, the tobacco plant or portion thereof can be separated into individual parts or pieces (e.g., the leaves can be removed from the stems, and/or the stems and leaves can be removed from the stalk). The harvested plant or individual parts or pieces can be further subdivided into parts or pieces (e.g., the leaves can be shredded, cut, comminuted, pulverized, milled or ground into pieces or parts that can be characterized as filler-type pieces, granules, particulates or fine powders). The plant, or parts thereof, can be subjected to external forces or pressure (e.g., by being pressed or subjected to roll treatment). When carrying out such processing conditions, the plant or portion thereof can have a moisture content that approximates its natural moisture content (e.g., its moisture content immediately upon harvest), a moisture content achieved by adding moisture to the plant or portion thereof, or a moisture content that results from the drying of the plant or portion thereof. For example, powdered, pulverized, ground or milled pieces of plants or portions thereof can have moisture contents of less than about 25 weight percent, often less than about 20 weight percent, and frequently less than about 15 weight percent.

For the preparation of oral compositions, it is typical for a harvested plant of the *Nicotiana* species to be subjected to a curing process. The tobacco materials incorporated within the composition as disclosed herein are those that have been appropriately cured and/or aged. Descriptions of various types of curing processes for various types of tobaccos are set forth in *Tobacco Production, Chemistry and Technology,* Davis et al. (Eds.) (1999). Examples of techniques and conditions for curing flue-cured tobacco are set forth in Nestor et al., *Beitrage Tabakforsch. Int.,* 20, 467-475 (2003) and US Pat. No. 6,895,974 to Peele, which are incorporated herein by reference. Representative techniques and conditions for air curing tobacco are set forth in US Pat. No. 7,650,892 to Groves et al.; Roton et al., *Beitrage Tabakforsch. Int.,* 21, 305-320 (2005) and Staaf et al., *Beitrage Tabakforsch. Int.,* 21, 321-330 (2005), which are incorporated herein by reference. Certain types of tobaccos can be subjected to alternative types of curing processes, such as fire curing or sun curing.

In certain embodiments, tobacco materials that can be employed include flue-cured or Virginia (e.g., K326), burley, sun-cured (e.g., Indian Kurnool and Oriental tobaccos, including Katerini, Prelip, Komotini, Xanthi and Yambol tobaccos), Maryland, dark, dark-fired, dark air cured (e.g., Madole, Passanda, Cubano, Jatin and Bezuki tobaccos), light air cured (e.g., North Wisconsin and Galpao tobaccos), Indian air cured, Red Russian and *Rustica* tobaccos, as well as various other rare or specialty tobaccos and various blends of any of the foregoing tobaccos.

The tobacco material may also have a so-called "blended" form. For example, the tobacco material may include a mixture of parts or pieces of flue-cured, burley (e.g., Malawi burley tobacco) and Oriental tobaccos (e.g., as tobacco composed of, or derived from, tobacco lamina, or a mixture of tobacco lamina and tobacco stem). For example, a representative blend may incorporate about 30 to about 70 parts burley tobacco (e.g., lamina, or lamina and stem), and about 30 to about 70 parts flue cured tobacco (e.g., stem, lamina, or lamina and stem) on a dry weight basis. Other example tobacco blends incorporate about 75 parts flue-cured tobacco, about 15 parts burley tobacco, and about 10 parts Oriental tobacco; or about 65 parts flue-cured tobacco, about 25 parts burley tobacco, and about 10 parts Oriental tobacco; or about 65 parts flue-cured tobacco, about 10 parts burley tobacco, and about 25 parts Oriental tobacco; on a dry weight basis. Other example tobacco blends incorporate about 20 to about 30 parts Oriental tobacco and about 70 to about 80 parts flue-cured tobacco on a dry weight basis.

Tobacco materials used in the present disclosure can be subjected to, for example, fermentation, bleaching, and the like. If desired, the tobacco materials can be, for example, irradiated, pasteurized, or otherwise subjected to controlled heat treatment. Such treatment processes are detailed, for example, in US Pat. No. 8,061,362 to Mua et al., which is incorporated herein by reference. In certain embodiments, tobacco materials can be treated with water and an additive capable of inhibiting reaction of asparagine to form acrylamide upon heating of the tobacco material (e.g., an additive selected from the group consisting of lysine, glycine, histidine, alanine, methionine, cysteine, glutamic acid, aspartic acid, proline, phenylalanine, valine, arginine, compositions incorporating di- and trivalent cations, asparaginase, certain non-reducing saccharides, certain reducing agents, phenolic compounds, certain compounds having at least one free thiol group or functionality, oxidizing agents, oxidation catalysts, natural plant extracts (e.g., rosemary extract), and combinations thereof. See, for example, the types of treatment processes described in US Pat. Pub. Nos. 8,434,496, 8,944,072, and 8,991,403 to Chen et al., which are all incorporated herein by reference. In certain embodiments, this type of treatment is useful where the original tobacco material is subjected to heat in the processes previously described.

In some embodiments, the type of tobacco material is selected such that it is initially visually lighter in color than other tobacco materials to some degree (e.g., whitened or bleached). Tobacco pulp can be whitened in certain embodiments according to any means known in the art. For example, bleached tobacco material produced by various whitening methods using various bleaching or oxidizing agents and oxidation catalysts can be used. Example oxidizing agents include peroxides (e.g., hydrogen peroxide), chlorite salts, chlorate salts, perchlorate salts, hypochlorite salts, ozone, ammonia, potassium permanganate, and combinations thereof. Example oxidation catalysts are titanium dioxide, manganese dioxide, and combinations thereof. Processes for treating tobacco with bleaching agents are discussed, for example, in US Patent Nos. 787,611 to Daniels, Jr.; 1,086,306 to Oelenheinz; 1,437,095 to Delling; 1,757,477 to Rosenhoch; 2,122,421 to Hawkinson; 2,148,147 to Baier; 2,170,107 to Baier; 2,274,649 to Baier; 2,770,239 to Prats et al.; 3,612,065 to Rosen; 3,851,653 to Rosen; 3,889,689 to Rosen; 3,943,940 to Minami; 3,943,945 to Rosen; 4,143,666 to Rainer; 4,194,514 to Campbell; 4,366,823, 4,366,824, and 4,388,933 to Rainer et al.; 4,641,667 to Schmekel et al.; 5,713,376 to Berger; 9,339,058 to Byrd Jr. et al.; 9,420,825 to Beeson et al.; and 9,950,858 to Byrd Jr. et al.; as well as in US Pat. App. Pub. Nos. 2012/0067361 to Bjorkholm et al.; 2016/0073686 to Crooks; 2017/0020183 to Bjorkholm; and 2017/0112183 to Bjorkholm, and in PCT Publ. Appl. Nos. WO1996/031255 to Giolvas and WO2018/083114 to Bjorkholm, all of which are incorporated herein by reference.

In some embodiments, the whitened tobacco material can have an ISO brightness of at least about 50%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, or at least about 80%. In some embodiments, the whitened tobacco material can have an ISO brightness in the range of about 50% to about 90%, about 55% to about 75%, or about 60% to about 70%. ISO brightness can be measured according to ISO 3688:1999 or ISO 2470-1:2016.

In some embodiments, the whitened tobacco material can be characterized as lightened in color (e.g., "whitened") in comparison to an untreated tobacco material. White colors are often defined with reference to the International Commission on Illumination's (CIE's) chromaticity diagram. The whitened tobacco material can, in certain embodiments, be characterized as closer on the chromaticity diagram to pure white than an untreated tobacco material.

In various embodiments, the tobacco material can be treated to extract a soluble component of the tobacco material therefrom. "Tobacco extract" as used herein refers to the isolated components of a tobacco material that are extracted from solid tobacco pulp by a solvent that is brought into contact with the tobacco material in an extraction process. While a tobacco extract may comprise nicotine, reference to a tobacco extract herein is distinct and different from nicotine, which may also be obtained, e.g., by extraction from tobacco material. In various embodiments, a tobacco material can be treated to extract soluble components of the tobacco material therefrom. Various extraction techniques of tobacco materials can be used to provide a tobacco extract and tobacco solid material. See, for example, the extraction processes described in US Pat. Appl. Pub. No. 2011/0247640 to Beeson et al., which is incorporated herein by reference. Other example techniques for extracting components of tobacco are described in US Pat. Nos. 4,144,895 to Fiore; 4,150,677 to Osborne, Jr. et al.; 4,267,847 to Reid; 4,289,147 to Wildman et al.; 4,351,346 to Brummer et al.; 4,359,059 to Brummer et al.; 4,506,682 to Muller; 4,589,428 to Keritsis; 4,605,016 to Soga et al.; 4,716,911 to Poulose et al.; 4,727,889 to Niven, Jr. et al.; 4,887,618 to Bernasek et al.; 4,941,484 to Clapp et al.; 4,967,771 to Fagg et al.; 4,986,286 to Roberts et al.; 5,005,593 to Fagg et al.; 5,018,540 to Grubbs et al.; 5,060,669 to White et al.; 5,065,775 to Fagg; 5,074,319 to White et al.; 5,099,862 to White et al.; 5,121,757 to White et al.; 5,131,414 to Fagg; 5,131,415 to Munoz et al.; 5,148,819 to Fagg; 5,197,494 to Kramer; 5,230,354 to Smith et al.; 5,234,008 to Fagg; 5,243,999 to Smith; 5,301,694 to Raymond et al.; 5,318,050 to Gonzalez-Parra et al.; 5,343,879 to Teague; 5,360,022 to Newton; 5,435,325 to Clapp et al.; 5,445,169 to Brinkley et al.; 6,131,584 to Lauterbach; 6,298,859 to Kierulff et al.; 6,772,767 to Mua et al.; and 7,337,782 to Thompson, all of which are incorporated by reference herein.

Typical inclusion ranges for tobacco materials can vary depending on the nature and type of the tobacco material, and the intended effect on the final mixture, with an example range of up to about 30% by weight (or up to about 20% by weight or up to about 10% by weight or up to about 5% by weight), based on total weight of the composition (e.g., about 0.1 to about 15% by weight). In some embodiments, the compositions of the disclosure can be characterized as completely free or substantially free of tobacco material (other than purified nicotine as an active ingredient). For example, certain embodiments can be characterized as having less than 1% by weight, or less than 0.5% by weight, or less than 0.1% by weight of tobacco material, or 0% by weight of tobacco material.

Oral care additives

In some embodiments, the composition comprises an oral care ingredient (or mixture of such ingredients). Oral care ingredients provide the ability to inhibit tooth decay or loss, inhibit gum disease, relieve mouth pain, whiten teeth, or otherwise inhibit tooth staining, elicit salivary stimulation, inhibit breath malodor, freshen breath, or the like. For example, effective amounts of ingredients such as thyme oil, eucalyptus oil and zinc (e.g., such as the ingredients of formulations commercially available as ZYTEX® from Discus Dental) can be incorporated into the composition. Other examples of ingredients that can be incorporated in desired effective amounts within the present composition can include those that are incorporated within the types of oral care compositions set forth in Takahashi et al., Oral Microbiology and Immunology, 19(1), 61-64 (2004); U.S. Pat. No. 6,083,527 to Thistle; and US Pat. Appl. Pub. Nos. 2006/0210488 to Jakubowski and 2006/02228308 to Cummins et al. Other exemplary ingredients of tobacco containing-formulation include those contained in formulations marketed as MALTISORB® by Roquette and DENTIZYME® by NatraRx. When present, a representative amount of oral care additive is at least about 1%, often at least about 3%, and frequently at least about 5% of the total dry weight of the composition. The amount of oral care additive within the composition will not typically exceed about 30%, often will not exceed about 25%, and frequently will not exceed about 20%, of the total dry weight of the composition.

Processing aids

If necessary, for downstream processing of the composition, such as granulation, mixing, or molding, a flow aid can also be added to the composition in order to enhance flowability of the composition. In some embodiments, the composition (e.g., melt and chew forms) may be surface treated with anti-stick agents, such as oils, silicones, and the like. Exemplary flow aids include microcrystalline cellulose, silica, polyethylene glycol, stearic acid, calcium stearate, magnesium stearate, zinc stearate, sodium stearyl fumarate, canauba wax, and combinations thereof. In some embodiments, the flow aid is sodium stearyl fumarate.

When present, a representative amount of flow aid may make up at least about 0.5 percent or at least about 1 percent, of the total dry weight of the composition. Preferably, the amount of flow aid within the composition will not exceed about 5 percent, and frequently will not exceed about 3 percent, of the total dry weight of the composition.

Other additives

Other additives can be included in the disclosed composition. For example, the composition can be processed, blended, formulated, combined and/or mixed with other materials or ingredients. The additives can be artificial or can be obtained or derived from herbal or biological sources. Examples of further types of additives include thickening or gelling agents (e.g., fish gelatin), emulsifiers, preservatives (e.g., potassium sorbate and the like), disintegration aids, or combinations thereof. See, for example, those representative components, combination of components, relative amounts of those components, and manners and methods for employing those components, set forth in US Pat. No. 9,237,769 to Mua et al., US Pat. No. 7,861,728 to Holton, Jr. et al., US Pat. App. Pub. No. 2010/0291245 to Gao et al., and US Pat. App. Pub. No. 2007/0062549 to Holton, Jr. et al., each of which is incorporated herein by reference.

Typical inclusion ranges for such additional additives can vary depending on the nature and function of the additive and the intended effect on the final composition, with an example range of up to about 10% by weight, based on total weight of the composition (e.g., about 0.1 to about 5% by weight).

The aforementioned additives can be employed together (e.g., as additive formulations) or separately (e.g., individual additive components can be added at different stages involved in the preparation of the final mixture). Furthermore, the aforementioned types of additives may be encapsulated as provided in the final composition. Example encapsulated additives are described, for example, in WO2010/132444 to Atchley, which has been previously incorporated by reference herein.

Particulate

In some embodiments, any one or more of the filler tobacco material, other composition components, and the overall composition described herein can be described as a particulate material. As used herein, the term "particulate" refers to a material in the form of a plurality of individual particles, some of which can be in the form of an agglomerate of multiple particles, wherein the particles have an average length to width ratio less than 2:1, such as less than 1.5:1, such as about 1:1. In various embodiments, the particles of a particulate material can be described as substantially spherical or granular.

The particle size of a particulate material may be measured by sieve analysis. As the skilled person will readily appreciate, sieve analysis (otherwise known as a gradation test) is a method used to measure the particle size distribution of a particulate material. Typically, sieve analysis involves a nested column of sieves which comprise screens, preferably in the form of wire mesh cloths. A pre-weighed sample may be introduced into the top or uppermost sieve in the column, which has the largest screen openings or mesh size (i.e., the largest pore diameter of the sieve). Each lower sieve in the column has progressively smaller screen openings or mesh sizes than the sieve above. Typically, at the base of the column of sieves is a receiver portion to collect any particles having a particle size smaller than the screen opening size or mesh size of the bottom or lowermost sieve in the column (which has the smallest screen opening or mesh size).

In some embodiments, the column of sieves may be placed on or in a mechanical agitator. The agitator causes the vibration of each of the sieves in the column. The mechanical agitator may be activated for a pre-determined period of time in order to ensure that all particles are collected in the correct sieve. In some embodiments, the column of sieves is agitated for a period of time from 0.5 minutes to 10 minutes, such as from 1 minute to 10 minutes, such as from 1 minute to 5 minutes, such as for approximately 3 minutes. Once the agitation of the sieves in the column is complete, the material collected on each sieve is weighed. The weight of each sample on each sieve may then be divided by the total weight in order to obtain a percentage of the mass retained on each sieve. As the skilled person will readily appreciate, the screen opening sizes or mesh sizes for each sieve in the column used for sieve analysis may be selected based on the granularity or known maximum/minimum particle sizes of the sample to be analysed. In some embodiments, a column of sieves may be used for sieve analysis, wherein the column comprises from 2 to 20 sieves, such as from 5 to 15 sieves. In some embodiments, a column of sieves may be used for sieve analysis, wherein the column comprises 10 sieves. In some embodiments, the largest screen opening, or mesh sizes of the sieves used for sieve analysis may be 1000 μm, such as 500 μm, such as 400 μm, such as 300 μm.

In some embodiments, any particulate material referenced herein (*e.g.*, filler, tobacco material, and the overall composition) can be characterized as having at least 50% by weight of particles with a particle size as measured by sieve analysis of no greater than about 1000 μm, such as no greater than about 500 μm, such as no greater than about 400 μm, such as no greater than about 350 μm, such as no greater than about 300 μm. In some embodiments, at least 60% by weight of the particles of any particulate material referenced herein have a particle size as measured by sieve analysis of no greater than about 1000 µm, such as no greater than about 500 µm, such as no greater than about 400 µm, such as no greater than about 350 µm, such as no greater than about 300 µm. In some embodiments, at least 70% by weight of the particles of any particulate material referenced herein have a particle size as measured by sieve analysis of no greater than about 1000 µm, such as no greater than about 500 µm, such as no greater than about 400 µm, such as no greater than about 350 µm, such as no greater than about 300 µm. In some embodiments, at least 80% by weight of the particles of any particulate material referenced herein have a particle size as measured by sieve analysis of no greater than about 1000 µm, such as no greater than about 500 µm, such as no greater than about 400 µm, such as no greater than about 350 µm, such as no greater than about 300 µm. In some embodiments, at least 90% by weight of the particles of any particulate material referenced herein have a particle size as measured by sieve analysis of no greater than about 1000 µm, such as no greater than about 500 µm, such as no greater than about 400 µm, such as no greater than about 350 µm, such as no greater than about 300 µm. In some embodiments, at least 95% by weight of the particles of any particulate material referenced herein have a particle size as measured by sieve analysis of no greater than about 1000 µm, such as no greater than about 500 µm, such as no greater than about 400 µm, such as no greater than about 350 µm, such as no greater than about 300 µm. In some embodiments, at least 99% by weight of the particles of any particulate material referenced herein have a particle size as measured by sieve analysis of no greater than about 1000 µm, such as no greater than about 500 µm, such as no greater than about 400 µm, such as no greater than about 350 µm, such as no greater than about 300 µm. In some embodiments, approximately 100% by weight of the particles of any particulate material referenced herein have a particle size as measured by sieve analysis of no greater than about 1000 µm, such as no greater than about 500 µm, such as no greater than about 400 µm, such as no greater than about 350 µm, such as no greater than about 300 µm.

In some embodiments, at least 50% by weight, such as at least 60% by weight, such as at least 70% by weight, such as at least 80% by weight, such as at least 90% by weight, such as at least 95% by weight, such as at least 99% by weight of the particles of any particulate material referenced herein have a particle size as measured by sieve analysis of from about 0.01 µm to about 1000 µm, such as from about 0.05 µm to about 750 µm, such as from about 0.1 µm to about 500 µm, such as from about 0.25 µm to about 500 µm. In some embodiments, at least 50% by weight, such as at least 60% by weight, such as at least 70% by weight, such as at least 80% by weight, such as at least 90% by weight, such as at least 95% by weight, such as at least 99% by weight of the particles of any particulate material referenced herein have a particle size as measured by sieve analysis of from about 10 µm to about 400 µm, such as from about 50 µm to about 350 µm, such as from about 100 µm to about 350 µm, such as from about 200 µm to about 300 µm.

Preparation of the composition

Microemulsion preparation

As described herein above, the disclosed compositions comprise an emulsion, such as a micro- or nanoemulsion. In general, forming an emulsion as disclosed herein comprises mixing an oil phase with an aqueous phase, in the presence of an emulsifying agent, so as to form the emulsion. In some embodiments, the emulsion is a microemulsion.

In one aspect is provided a process for preparing a composition configured for oral use comprising a microemulsion that comprises a continuous phase and a dispersed phase, the process comprising:

(a) forming a microemulsion in which the continuous phase, the dispersed phase, or both phases contain a nicotine component as described herein; and

(b) processing the microemulsion to provide the composition.

Microemulsions as disclosed herein can be prepared using low energy processes to break large emulsion droplets into smaller ones. Low energy approaches may rely on the spontaneous formation of tiny oil droplets within systems when the solution or environmental conditions are altered. Heat and sonication may be used, particularly in systems containing non-ionic surfactants.

In some embodiments, the continuous phase comprises water, and the dispersed phase comprises a lipid component as described herein. In some embodiments, the continuous phase comprises a lipid component as described herein, and the dispersed phase comprises water. The continuous phase, the dispersed phase, or both phases comprise an emulsifying agent as described herein, in an amount of at least about 16% by weight, based on the total weight of the emulsion.

In some embodiments, the lipid component is an oil comprising mono, di-, or triglycerides of medium-chain fatty acids having from 6 to 10 carbon atoms.

In some embodiments, forming the microemulsion comprises:

providing an aqueous phase comprising a nicotine component and an emulsifying agent, each as disclosed herein;

providing an oil phase containing a lipid component as described herein;

combining the aqueous phase and the oil phase to form a mixture; and

homogenizing the mixture for a period of time.

One or more of the nicotine component, flavors, and further components as described herein above may be added to the aqueous and/or oil phase, followed by mixing the same with a suitable mixing device.

In some embodiments, (b) processing the emulsion to provide the composition comprises contacting the emulsion (such as a microemulsion) with the filler and optionally other additives in an amount sufficient to form the composition. As described hereinabove, in some embodiments, the filler may be a cellulose material. For example, the filler may be microcrystalline cellulose. In some embodiments, the process further comprises combining the filler (such as a cellulose material, such as microcrystalline cellulose) with further components including, but not limited to, a salt, sweetener, and flavoring agent.

The contacting of the emulsion with the filler may be performed by any appropriate means such that the emulsion is associated with the filler (and any other composition components) by adsorption or adsorption in or on the filler. The manner by which the various components of the composition are combined may vary. As such, the overall mixture of various components (e.g., an emulsion, such as a microemulsion) with e.g., powdered mixture components, such as a filler, may be relatively uniform in nature. The components noted above, which may be in liquid or dry solid form, can be admixed in a pretreatment step prior to mixture with any remaining components of the composition, or simply mixed together with all other liquid or dry ingredients. The various components of the composition may be contacted, combined, or mixed together using any mixing technique or equipment known in the art. Any mixing method that brings the composition ingredients into intimate contact can be used, such as a mixing apparatus featuring an impeller or other structure capable of agitation. Examples of mixing equipment include casing drums, conditioning cylinders or drums, liquid spray apparatus, conical-type blenders, ribbon blenders, mixers available as FKM130, FKM600, FKM1200, FKM2000 and FKM3000 from Littleford Day, Inc., Plough Share types of mixer cylinders, Hobart mixers, and the like. See also, for example, the types of methodologies set forth in US Pat. Nos. 4,148,325 to Solomon et al.; 6,510,855 to Korte et al.; and 6,834,654 to Williams, each of which is incorporated herein by reference. Manners and methods for formulating mixtures will be apparent to those skilled in the art. See, for example, the types of methodologies set forth in US Pat. No. 4,148,325 to Solomon et al.; US Pat. No. 6,510,855 to Korte et al.; and US Pat. No. 6,834,654 to Williams, US Pat. Nos. 4,725,440 to Ridgway et al., and 6,077,524 to Bolder et al., each of which is incorporated herein by reference.

Configured for oral use

Provided herein is a composition configured for oral use. The term "configured for oral use" as used herein means that the composition is provided in a form such that during use, saliva in the mouth of the user causes one or more of the components of the composition (e.g., basic amine, flavoring agents and/or active ingredients) to pass into the mouth of the user. In certain embodiments, the composition is adapted to deliver components to a user through mucous membranes in the user's mouth, the user's digestive system, or both, and, in some instances, said component is a nicotine component or an active ingredient (including, but not limited to, for example, nicotine, a stimulant, vitamin, amino acid, botanical, or a combination thereof) that can be absorbed through the mucous membranes in the mouth or absorbed through the digestive tract when the product is used.

Compositions configured for oral use as described herein may take various forms, including gels, pastilles, gums, chews, melts, tablets, lozenges, granules, powders, and pouches. Gels can be soft or hard. Certain compositions of the disclosure are in the form of solids. Certain compositions can exhibit, for example, one or more of the following characteristics: crispy, granular, chewy, syrupy, pasty, fluffy, smooth, and/or creamy. In certain embodiments, the desired textural property can be selected from the group consisting of adhesiveness, cohesiveness, density, dryness, fracturability, graininess, gumminess, hardness, heaviness, moisture absorption, moisture release, mouthcoating, roughness, slipperiness, smoothness, viscosity, wetness, and combinations thereof.

The compositions of the present disclosure may be dissolvable. As used herein, the terms "dissolve," "dissolving," and "dissolvable" refer to compositions having aqueous-soluble components that interact with moisture in the oral cavity and enter into solution, thereby causing gradual consumption of the composition. According to one aspect, the dissolvable composition is capable of lasting in the user's mouth for a given period of time until it completely dissolves. Dissolution rates can vary over a wide range, from about 1 minute or less to about 60 minutes. For example, fast release compositions typically dissolve and/or release the desired component(s) (e.g., active ingredient, flavor, and the like) in about 2 minutes or less, often about 1 minute or less (e.g., about 50 seconds or less, about 40 seconds or less, about 30 seconds or less, or about 20 seconds or less). Dissolution can occur by any means, such as melting, mechanical disruption (e.g., chewing), enzymatic or other chemical degradation, or by disruption of the interaction between the components of the composition. In other embodiments, the products do not dissolve during the product's residence in the user's mouth.

The compositions as disclosed herein can be formed into a variety of shapes, including pills, tablets, spheres, strips, films, sheets, coins, cubes, beads, ovoids, obloids, cylinders, bean-shaped, sticks, or rods. Cross-sectional shapes of the composition can vary, and example cross-sectional shapes include circles, squares, ovals, rectangles, and the like. Such shapes can be formed in a variety of manners using equipment such as moving belts, nips, extruders, granulation devices, compaction devices, and the like.

In one embodiment, the composition of the present disclosure is in particulate form and is disposed within a moisture-permeable container (e.g., a water-permeable pouch). The composition enclosed in the pouch may be in any desired form. In certain embodiments, the composition is in granular form. Such compositions in the water-permeable pouch format are typically used by placing one pouch containing the composition in the mouth of a human subject/user. Generally, the pouch is placed somewhere in the oral cavity of the user, for example under the lips, in the same way as moist snuff products are generally used. The pouch preferably is not chewed or swallowed unless the pouch composition or materials are ingestible (e.g., dissolvable or dispersible) as described herein below. Exposure to saliva then causes some of the components of the composition therein (e.g., flavoring agents and/or nicotine) to pass through e.g., the water-permeable pouch and provide the user with flavor and satisfaction, and the user is not required to spit out any portion of the mixture. After about 10 minutes to about 60 minutes, typically about 15 minutes to about 45 minutes of use/enjoyment, substantial amounts of the mixture have been ingested by the human subject, and the pouch may be removed from the mouth of the human subject for disposal.

Accordingly, in certain embodiments, the composition as disclosed herein and any other components noted above are combined within a moisture-permeable packet or pouch that acts as a container for use of the composition to provide a pouched product configured for oral use. Certain embodiments of the disclosure will be described with reference to **FIG. 1** of the accompanying drawings, and these described embodiments involve snus-type products having an outer pouch and containing a mixture as described herein. As explained in greater detail below, such embodiments are provided by way of example only, and the pouched products of the present disclosure can include the composition in other forms. The mixture/construction of such packets or pouches, such as the container pouch **102** in the embodiment illustrated in **FIG. 1**, may be varied. Referring to **FIG. 1**, there is shown a first embodiment of a pouched product **100**. The pouched product **100** includes a moisture-permeable container in the form of a pouch **102**, which contains a material **104** comprising a composition as described herein.

Suitable packets, pouches or containers of the type used for the manufacture of smokeless tobacco products are available under the tradenames CatchDry, Ettan, General, Granit, Goteborgs Rape, Grovsnus White, Metropol Kaktus, Mocca Anis, Mocca Mint, Mocca Wintergreen, Kicks, Probe, Prince, Skruf and TreAnkrare. The mixture may be contained in pouches and packaged, in a manner and using the types of components used for the manufacture of conventional snus types of products. The pouch provides a liquid-permeable container of a type that may be considered to be similar in character to the mesh-like type of material that is used for the construction of a tea bag. Components of the mixture readily diffuse through the pouch and into the mouth of the user.

Non-limiting examples of suitable types of pouches are set forth in, for example, US Pat. Nos. 5,167,244 to Kjerstad and 8,931,493 to Sebastian et al.; as well as US Patent App. Pub. Nos. 2016/0000140 to Sebastian et al.; 2016/0073689 to Sebastian et al.; 2016/0157515 to Chapman et al.; and 2016/0192703 to Sebastian et al., each of which are incorporated herein by reference. Pouches can be provided as individual pouches, or a plurality of pouches (e.g., 2, 4, 5, 10, 12, 15, 20, 25 or 30 pouches) can be connected or linked together (e.g., in an end-to-end manner) such that a single pouch or individual portion can be readily removed for use from a one-piece strand or matrix of pouches.

An example pouch may be manufactured from materials, and in such a manner, such that during use by the user, the pouch undergoes a controlled dispersion or dissolution. Such pouch materials may have the form of a mesh, screen, perforated paper, permeable fabric, or the like. For example, pouch material manufactured from a mesh-like form of rice paper, or perforated rice paper, may dissolve in the mouth of the user. As a result, the pouch and mixture each may undergo complete dispersion within the mouth of the user during normal conditions of use, and hence the pouch and mixture both may be ingested by the user. Other examples of pouch materials may be manufactured using water dispersible film forming materials (e.g., binding agents such as alginates, carboxymethylcellulose, xanthan gum, pullulan, and the like), as well as those materials in combination with materials such as ground cellulosics (e.g., fine particle size wood pulp). Preferred pouch materials, though water dispersible or dissolvable, may be designed and manufactured such that under conditions of normal use, a significant amount of the mixture contents permeate through the pouch material prior to the time that the pouch undergoes loss of its physical integrity. If desired, flavoring ingredients, disintegration aids, and other desired components, may be incorporated within, or applied to, the pouch material.

The amount of material contained within each product unit, for example, a pouch, may vary. In some embodiments, the weight of the composition within each pouch is at least about 50 mg, for example, from about 50 mg to about 1 gram, from about 100 to 800 about mg, or from about 200 to about 700 mg. In some smaller embodiments, the weight of the composition within each pouch may be from about 100 to about 300 mg. For a larger embodiment, the weight of the composition within each pouch may be from about 300 mg to about 700 mg. If desired, other components can be contained within each pouch. For example, at least one flavored strip, piece or sheet of flavored water dispersible or water-soluble material (e.g., a breath-freshening edible film type of material) may be disposed within each pouch along with or without at least one capsule. Such strips or sheets may be folded or crumpled in order to be readily incorporated within the pouch. See, for example, the types of materials and technologies set forth in US Pat. Nos. 6,887,307 to Scott et al. and 6,923,981 to Leung et al.; and The EFSA Journal (2004) 85, 1-32; which are incorporated herein by reference.

The moisture content of the pouched product may vary. In some embodiments, the moisture content of the pouched product is in a range from about 35 to about 45% by weight, based on the total weight of the pouched product.

In some embodiments, the pouched product is configured to release varying quantities of nicotine over a period of time when in contact with moisture, e.g., when in contact with saliva in the mouth of a user of the product. In some embodiments, at least about 1 mg of nicotine is released from the pouched product within about 30 minutes when stirred at 15 rpm in 900 ml of 12 mM ammonium phosphate (pH 7.4) at 37.0± 0.5°C. In some embodiments, at least about 1 mg of nicotine is released within about 20 minutes, about 15 minutes, about 10, or about 5 minutes. In some embodiments, at least about 1 mg of nicotine is released in less than about 5 minutes, such as about 4 minutes, about 3 minutes, about 2 minutes, or about 1 minute.

A pouched product as described herein can be packaged within any suitable inner packaging material and/or outer container. See also, for example, the various types of containers for smokeless types of products that are set forth in US Pat. Nos. 7,014,039 to Henson et al.; 7,537,110 to Kutsch et al.; 7,584,843 to Kutsch et al.; 8,397,945 to Gelardi et al., D592,956 to Thiellier; D594,154 to Patel et al.; and D625,178 to Bailey et al.; US Pat. Pub. Nos. 2008/0173317 to Robinson et al.; 2009/0014343 to Clark et al.; 2009/0014450 to Bjorkholm; 2009/0250360 to Bellamah et al.; 2009/0266837 to Gelardi et al.; 2009/0223989 to Gelardi; 2009/0230003 to Thiellier; 2010/0084424 to Gelardi; and 2010/0133140 to Bailey et al; 2010/0264157 to Bailey et al.; and 2011/0168712 to Bailey et al. which are incorporated herein by reference.

Many modifications and other embodiments of the invention will come to mind to one skilled in the art to which this invention pertains having the benefit of the teachings presented in the foregoing description. Therefore, it is to be understood that the invention is not to be limited to the specific embodiments disclosed and that modifications and other embodiments are intended to be included within the scope of the appended claims. Although specific terms are employed herein, they are used in a generic and descriptive sense only and not for purposes of limitation.

EXAMPLES

Aspects of the present invention are more fully illustrated by the following examples, which are set forth to illustrate certain aspects of the present invention and are not to be construed as limiting thereof.

Example 1. General procedure for preparing microemulsions

For making microemulsions, a lipid component (e.g., a mixture of mono- and diglycerides of capric and caprylic acid (Capmul® MCM)) and water were respectively used as the oil phase and the aqueous phase, were mixed in the presence of a surfactant (e.g., polyoxyl 40 stearate). A pseudo-ternary phase diagram was prepared by mixing different amounts of oil phase, water phase, and surfactant (e.g., 0, 10, 20, 30, 40, 50, 60, 70, 80, 90, and 100 grams) in vials at room temperature followed by mixing (e.g., with a vortex mixer). Specifically, the pseudo-ternary phase diagrams were constructed by preparing samples of 100 different compositions to define the phase boundaries in each phase diagram using SigmaPlot software (version 12.3, Systat Software Inc., Chicago, IL, USA). Each sample was further allowed to equilibrate at room temperature for at least 24 h before evaluation and examined again after one week. Depending upon the components used, four different phases were observed in the phase diagrams: (i) a clear liquid region which included a clear or transparent water-in-oil (W/O) microemulsion; (ii) a clear liquid region which included a clear or transparent O/W microemulsion; (iii) a viscous gel; and (iv) a phase-separated mixture where the lipid separated from the aqueous phase to form a separate layer. All selected microemulsions were stored at room temperature and the stability of each sample was assessed by visual inspection in terms of clarity over time.

Example 2. Nicotine benzoate solution in palm oil

A solution of nicotine benzoate in palm oil was prepared. To palm oil (70 g; Confao 5) was added a solution of nicotine benzoate in water (30 g; the aqueous nicotine benzoate solution containing 12% by weight of free base nicotine).

Example 3. Nicotine Polacrilex solution in palm oil

A solution of nicotine Polacrilex in palm oil was prepared. To palm oil (23 g; Confao 5) was added 14 g of nicotine Polacrilex. The nicotine Polacrilex contained 20% nicotine by weight on a free base basis.

Example 4. Solubility determination of nicotine benzoate in medium chain length glycerol esters

The solubility of nicotine benzoate in a mixture of mono- and diglycerides of capric and caprylic acid (Capmul® MCM) was determined by dissolving different percentages by weight (e.g., 5, 10, 15, 20, 25, 30, and 40%) of solid nicotine benzoate in 1 mL of the oil. Samples were blanketed with nitrogen, sonicated for 30 min, then placed in a thermostatic orbital shaker and continuously shaken at 300 rpm for 48 h at 30°C. The equilibrated samples were then transferred to a polyallomer centrifuge bottle and centrifuged at 60,800×g for 15 min to remove undissolved nicotine benzoate. The oil sample with the highest nicotine benzoate solubility (containing 30% nicotine benzoate by weight) and without sedimentation was selected as the oil phase for making microemulsions.

Example 5. Nicotine Polacrilex solution in medium chain length glycerol esters

A solution of nicotine Polacrilex in a mixture of medium-chain length oils was prepared. To 23 g of a mixture of mono- and diglycerides of capric and caprylic acid (Capmul® MCM) was added 14 g of nicotine Polacrilex. The nicotine Polacrilex contained 20% nicotine by weight on a free base basis.

Example 6. Nicotine solution in medium chain length triglycerides

A solution of nicotine in a mixture of medium chain length triglycerides was prepared. To 93 g of a mixture of medium chain length triglycerides (Captex® MCT) was added 7 g of free base nicotine.

Example 7. Nicotine microemulsions

Emulsions of nicotine benzoate, water, oil, and emulsifier were prepared. A solution of 30% by weight of nicotine benzoate in a mixture of mono- and diglycerides of capric and caprylic acid (Capmul® MCM), prepared as in Example 4) was combined with water and polyoxyl 40 stearate in the proportions provided in Table 2. The individual mixtures were placed in vials and mixed at room temperature using a vortex mixer to emulsify. The droplets in the microemulsion had a mean particle size of 259.6 nanometers, and the mean polydispersity index was 0.37.

Table 2. Emulsion components and amounts

% oil phase (nicotine benzoate in MCM)	**% Polyoxyl 40 stearate**	**% Water**
25-35	15-25	45-55

Example 8. Pouched product with nicotine benzoate/palm oil solution

A pouched product comprising 4 mg of nicotine was prepared using the composition formulation provided in Table 3. To the microcrystalline cellulose, salt, hydroxypropyl cellulose, sodium bicarbonate, sodium benzoate, free base nicotine, sweetener, and propylene glycol was added a portion of the water to form a liquid blend. The flavor and nicotine solution were added, and the mixture blended to form the composition. The composition had a moisture content of 15.9%, and a pH of 7. The composition was placed in a fleece pouch and additional water was added. The resulting pouched product weighed 700 mg and contained 500 mg of the composition on a dry weight basis. The pouched product had a moisture content of 41.5%, and a pH of 6.4.

Table 3. Oral pouched product composition components and amounts

Component	**% by weight of composition**
microcrystalline cellulose	36-54
hydroxypropyl cellulose	2-4
sodium chloride	1-1.5
sodium bicarbonate	0.04-0.06

Component	**% by weight of composition**
nicotine, free base	0.4-0.7
nicotine benzoate solution (Example 2)	2-4
sodium benzoate	1-3
water	32-49
sweetener	1-3
propylene glycol	0.5-0.7
flavor	1-2

Example 9. Pouched product with nicotine Polacrilex/palm oil solution

A pouched product comprising 4 mg of nicotine was prepared as in Example 8 but using the composition formulation provided in Table 4. The composition had a moisture content of 15.3%, and a pH of 5.85. The pouched product weighed 700 mg and contained 500 mg of the composition on a dry weight basis. The pouched product had a moisture content of 39.6%, and a pH of 5.66.

Table 4. Oral pouched product composition components and amounts

Component	**% by weight of composition**
microcrystalline cellulose	32-49
hydroxypropyl cellulose	2-4
sodium chloride	1-1.5
sodium bicarbonate	0.04-0.06
Nicotine, free base	0.4-0.7
nicotine polacrilex solution (Example 3)	7.1
sodium benzoate	1-3
water	32-49
sweetener	1-3
propylene glycol	0.5-0.7
flavor	1-2

Example 10. Pouched product with nicotine benzoate in medium chain fatty acid ester solution

A pouched product comprising 4 mg of nicotine was prepared was prepared as in Example 8 but using the composition formulation provided in Table 5. The composition had a moisture content of 17.6%, and a pH of 6.98. The pouched product weighed 700 mg and contained 500 mg of the composition on a dry weight basis. The pouched product had a moisture content of 39.7% and a pH of 6.36.

Table 5. Oral pouched product composition components and amounts

Component	**% by weight of composition**
microcrystalline cellulose	32-49
hydroxypropyl cellulose	2-4
sodium chloride	1-1.5
sodium bicarbonate	0.04-0.06
Nicotine, free base	0.4-0.7
nicotine benzoate in MCM oil solution (Example 4)	8.46
sodium benzoate	1-3
water	32-49
sweetener	1-3
propylene glycol	0.5-0.7
flavor	1-2

Example 11. Pouched product with nicotine Polacrilex in medium chain fatty acid ester solution

A pouched product comprising 4 mg of nicotine was prepared as in Example 8 but using the composition formulation provided in Table 6. The composition had a moisture content of 17.2%, and a pH of 5.57. The pouched product weighed 700 mg and contained 500 mg of the composition on a dry weight basis. The pouched product had a moisture content of 39%, and a pH of 5.6.

Table 6. Oral pouched product composition components and amounts

Component	**% by weight of composition**
microcrystalline cellulose	32-49
hydroxypropyl cellulose	2-4
sodium chloride	1-1.5
sodium bicarbonate	0.04-0.06
nicotine free base	0.4-0.7
nicotine Polacrilex solution in MCM oil (Example 5)	7.1
sodium benzoate	1-3
water	32-49
sweetener	1-3
propylene glycol	0.5-0.7
flavor	1-2

Example 12. Pouched product with nicotine in medium chain length triglyceride solution

A pouched product comprising 4 mg of nicotine was prepared as in Example 8 but using the composition formulation provided in Table 7. The composition had a moisture content of 16.3%, and a pH of 8.54. The pouched product weighed 700 mg and contained 500 mg of the composition on a dry weight basis. The pouched product had a moisture content of 41% and a pH of 8.4.

Table 7. Oral pouched product composition components and amounts

Component	**% by weight of composition**
microcrystalline cellulose	32-49
hydroxypropyl cellulose	2-4
sodium chloride	1-1.5
sodium bicarbonate	0.04-0.06
Nicotine, free base	0.4-0.7
nicotine solution in MCT oil (Example 6)	7.7
sodium benzoate	1-3
water	32-49
sweetener	1-3
propylene glycol	0.5-0.7
flavor	1-2

Example 13. Pouched product with nicotine microemulsion

Pouched products comprising 6 mg of nicotine were prepared using the composition formulation provided in Table 8. To microcrystalline cellulose, salt, hydroxypropyl cellulose, sodium bicarbonate, sodium benzoate, free base nicotine, sweetener, and propylene glycol was added a portion of the water to form a liquid blend. The flavor and nicotine microemulsion of Example 7 were added and the mixture blended to form the composition. The composition had a moisture content of 15.7%, and a pH of 6.97. The composition was placed in fleece pouches and sealed, and water was sprayed onto the pouches to give the desired moisture content. The pouched products each weighed 700 mg and contained 500 mg of the composition on a dry weight basis. The final, moistened pouched products had a moisture content of 41.3%, and a pH of 6.39.

Table 8. Oral pouched product composition components and amounts

Component	**% by weight of composition**
microcrystalline cellulose	35-52
hydroxypropyl cellulose	2-4
sodium chloride	1-1.5
sodium bicarbonate	0.04-0.06

Nicotine, free base	0.4-0.7
nicotine-oil microemulsion (Example 7)	16.52
sodium benzoate	1-3
water	32-49
sweetener	1-3
propylene glycol	0.5-0.7
flavor	1-2

Example 14. Control pouch

A pouched product (Ruby Berry flavor) comprising 4 mg of nicotine was prepared using the composition formulation provided in Table 9. The pouched product weighed 700 mg and contained 490 mg of the composition on a dry weight basis. The pouched product had a moisture content of 45%, and a pH of 5.9.

Table 9. Oral pouched product composition components and amounts

Component	**% by weight of composition**
microcrystalline cellulose	43.5
hydroxypropyl cellulose	3
sodium chloride	1.3
nicotine (free base)	0.55
12% aqueous nicotine benzoate solution	4.48
sodium benzoate	2
water	41
sweetener	2.05
propylene glycol	0.6
flavor	1.5

Example 15. Dissolution rates

The pouches of Examples 8-14 were evaluated for nicotine release versus time. Pouched samples (1 pouch for each replicate) were accurately weighed and added to a dissolution vessel containing 900 ml of dissolution medium (12 mM ammonium phosphate, pH 7.4) at 37°C. The dissolution vessel was transferred to the dissolution apparatus and samples collected according to the parameters in Table 10.

Table 10. Dissolution parameters

Apparatus	708-DS Apparatus1, Baskets
Sampling Station	850-DS
Shaft Speed	15 RPM (0 to 60 min)

Dissolution Temperature	37.0± 0.5°C
Dissolution Volume	900 mL
Sampling Time Points	3,7,11,15,20,30,60 min (15 RPM)
Sample Collection Volume	1.5 mL
Pull volume	2.0 mL (1.5mL sample + 0.5 mL waste drop)
Filter Plate	8-channel 0.45 µm Nylon Filter

Nicotine content of the samples was determined via high performance liquid chromatography (HPLC) analysis with photodiode array detection using the gradient parameters in Table 11. Mobile phase A was 95:5 water:methanol with 0.1% formic acid titrated to pH – 9.5 with ammonium hydroxide (NH_4OH) and mobile phase B was methanol with 0.1% formic acid titrated to pH – 9.5 with ammonium hydroxide. The flow rate was 0.6 mL/min. The column used for the separation was a Waters Xterra Shield RP18 (3 mm x 50 mm) with 3 µm particle size held at 35°C. The run time included high organic wash and re-equilibration of 10 min. The injection volume was 2.5 µL. The PDA detector was set to monitor the wavelength 210 nm. The experimental sample response was plotted against a linear calibration curve generated with standards of known concentration to accurately determine the nicotine content in the samples.

Table 11. Gradient elution parameters

Time (min)	Composition A (%)	Composition B (%)
0.00	83	17
5.75	83	17
5.76	0	100
7.25	0	100
7.26	83	17
10	83	17

Data for the analyses are provided in (**FIGs. 2-8**; Examples 8-14 respectively). With reference to **FIG. 8**, it was observed that the pouched product containing the microemulsion (Example 13) provided more rapid release of the nicotine. Without wishing to be bound by theory, it is believed that such a rapid release profile may be advantageous for enhanced consumer experience in for certain product configurations.

Example 16. Sensory evaluations

The pouches of Examples 8-14 were evaluated in sensory studies with respect to sensations of mouth burning, throat burning, and overall sensory attributes (flavor release, intensity, mouth feel, and the like; **FIGS. 9-11**). The samples were evaluated by 10 panelists (blind test). The mouth and throat burn were evaluated at 0 min (after first placing pouch in mouth), 5 min (hold time), and 15 min (hold time). The panelists were asked to evaluate the flavor release, flavor intensity, moisture and mouth feel/tactile and score the products between 0 (low) to 10 (high). The final result was reported as the mean ± Standard deviation. One-way analysis of variance (ANOVA) was used to evaluate the significant differences ($p < 0.05$) between the samples.

With reference to **FIG. 9** and **FIG. 10**, mouth and throat burning sensations were lower in pouches prepared with oils comprising longer chain length fatty acids (palm and MCM oil; Examples 8 and 10) than those prepared with oils comprising short- to medium-chain length fatty acids (MCT; Example 12). Further, the pouched products prepared with nicotine Polacrilex (Examples 9 and 11) exhibited a lower burning sensation than those prepared with nicotine benzoate (Examples 8 and 10). Without wishing to be bound by any particular theory, it is believed that this reduction in burning sensation may be due to the lower nicotine release rates as observed in **FIG. 4** and **FIG. 6**. Notably, Example 13, the pouched product including the nicotine emulsion, increased the burning sensation in the 4 mg nicotine pouch format (**FIGs. 9** and **10**). Without wishing to be bound by theory, it is believed that the rapid release observed **(FIG. 8)** for the emulsion may be responsible for the enhanced burning sensation.

With reference to **FIG. 11**, in the overall sensory evaluation, no significant differences ($p<0.05$) were observed in the flavor release, flavor intensity, moisture, and mouth feel/tactile properties of pouched nicotine products prepared with the mixture of oil and nicotine benzoate/polacrilex (i.e., nicotine palm oil, nicotine Capmul MCM oil, nicotine MCT oil) or nicotine microemulsion compared to the control pouched product (Example 14).

Overall, the results herein demonstrate that oral pouched products using thermodynamically stable nicotine microemulsions comprising nano-size particles as disclosed herein provide an improved nicotine release profile as compared to oral pouched products containing un-encapsulated (non-microemulsified) nicotine.

CLAIMS

What is claimed is:

1. A composition configured for oral use, the composition comprising:

an emulsion comprising a nicotine component, a lipid component, an emulsifying agent in an amount by weight of at least 16%, and water; and

a filler;

wherein the emulsion is adsorbed on the filler, absorbed in the filler, or both.

2. The composition of claim 1, wherein the emulsion comprises droplets having an average size in a range from about 10 to about 500 nm.

3. The composition of claim 1, wherein the emulsion comprises droplets having an average size in a range from about 100 to about 300 nm.

4. The composition of claim 1, wherein the nicotine component is free base nicotine, a salt of nicotine with an organic acid, or a combination thereof.

5. The composition of claim 1, wherein the nicotine component is a salt of nicotine with an organic acid selected from the group consisting of octanoic acid, decanoic acid, benzoic acid, heptanesulfonic acid, and combinations thereof.

6. The composition of claim 1, wherein the lipid component comprises diglycerides of medium-chain fatty acids.

7. The composition of claim 1, wherein the lipid component comprises triglycerides of medium-chain fatty acids.

8. The composition of claim 6 or 7, wherein the medium-chain fatty acids have from 6 to 8 carbon atoms.

9. The composition of claim 1, wherein the emulsion comprises from about 20 to about 40% of the lipid component by weight, based on the total weight of the emulsion.

10. The composition of claim 1, wherein the emulsifying agent is a non-ionic surfactant.

11. The composition of claim 1, wherein the emulsifying agent is polyoxyl 40 stearate.

12. The composition of claim 1, wherein the emulsion comprises from about 16 to about 30% of the emulsifying agent by weight, based on the total weight of the emulsion.

13. The composition of claim 1, wherein the emulsion comprises from about 30 to about 70% water by weight, based on the total weight of the emulsion.

14. The composition of claim 1, wherein the emulsion comprises:

the emulsifying agent in an amount from about 16 to about 24 percent by weight, based on the total weight of the emulsion;

the lipid component in an amount from about 24 to about 36 percent by weight, based on the total weight of the emulsion; and

water in an amount from about 40 to about 60 percent by weight, based on the total weight of the emulsion.

15. The composition of claim 1, wherein the filler is present in an amount of from about 30% to about 50% by weight of the composition

16. The composition of claim 1, wherein the filler is a cellulose material or cellulose derivative.

17. The composition of claim 1, wherein the filler is microcrystalline cellulose.

18. The composition of claim 1, wherein the composition comprises the emulsion in an amount from about 10 to about 20% by weight, based on the total weight of the composition.

19. The composition of claim 1, further comprising one or more flavoring agents, taste modifiers, preservatives, humectants, sweeteners, binders, buffering agents, salts, or mixtures thereof.

20. A pouched oral product comprising a saliva permeable pouch and the composition of any one of claims 1-19 incorporated within the pouch.

21. The pouched product of claim 20, having a moisture content in a range from about 35 to about 45% by weight, based on the total weight of the pouched product.

22. The pouched product of claim 20, wherein at least about 1 mg of nicotine is released from the pouched product within 30 minutes when stirred at 15 rpm in 900 ml of 12 mM ammonium phosphate (pH 7.4) at 37.0± 0.5°C

23. A process for preparing a composition configured for oral use comprising an emulsion that comprises a continuous phase and a dispersed phase, the process comprising:

(a) forming an emulsion in which the continuous phase, the dispersed phase, or both phases contain a nicotine component;

(b) processing the emulsion to provide the composition, wherein the continuous phase, the dispersed phase, or both phases comprise an emulsifying agent in an amount of at least 16% by weight, based on the total weight of the emulsion.

24. The process of claim 23, wherein the continuous phase comprises water, and the dispersed phase comprises a diglycerides or triglycerides of medium-chain fatty acids having from 6 to 8 carbon atoms.

25. The process of claim 23, wherein the continuous phase comprises a diglycerides or triglycerides of medium-chain fatty acids having from 6 to 8 carbon atoms, and the dispersed phase comprises water.

26. The process of claim 23, wherein the composition further comprises a filler and optionally other additives, and processing the emulsion comprises contacting the emulsion with the filler and optionally other additives to provide the composition.

FIG. 1

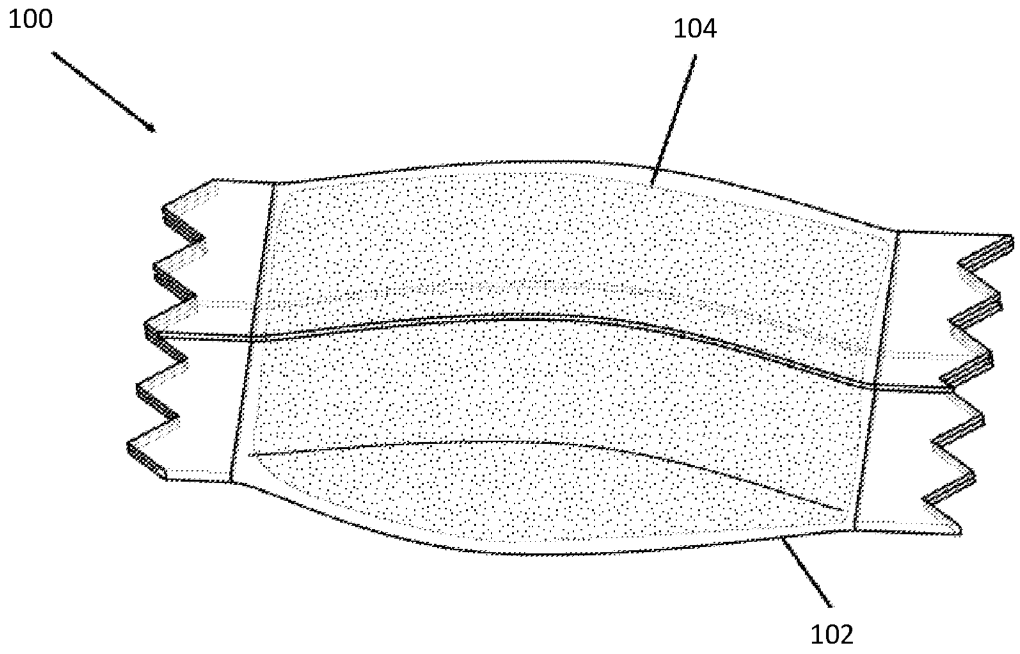
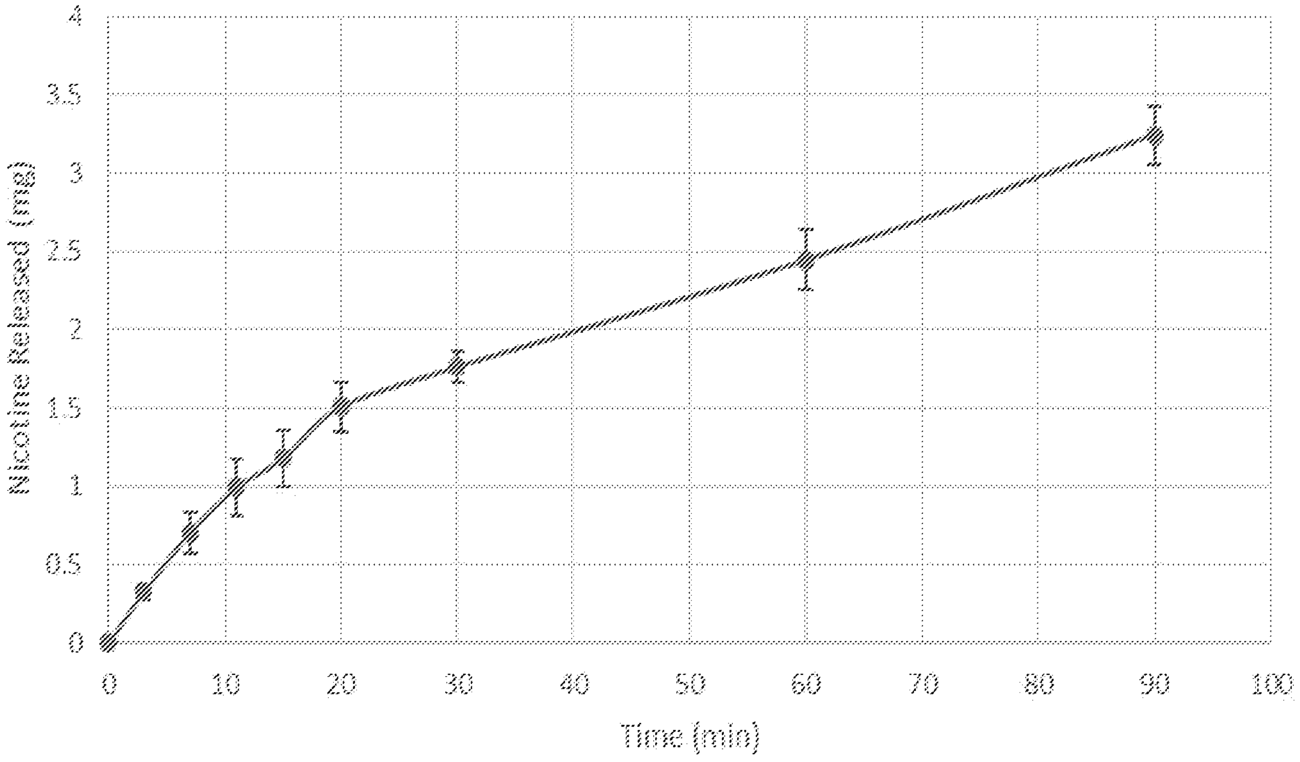
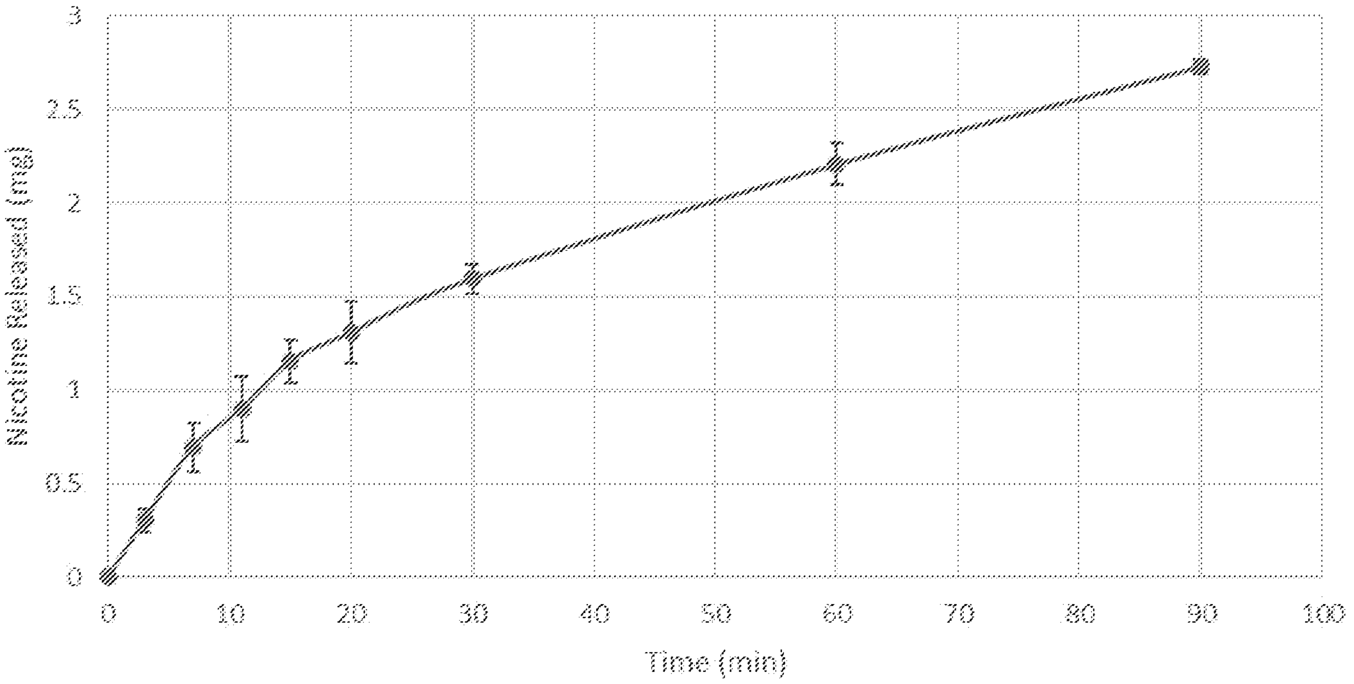


FIG. 2



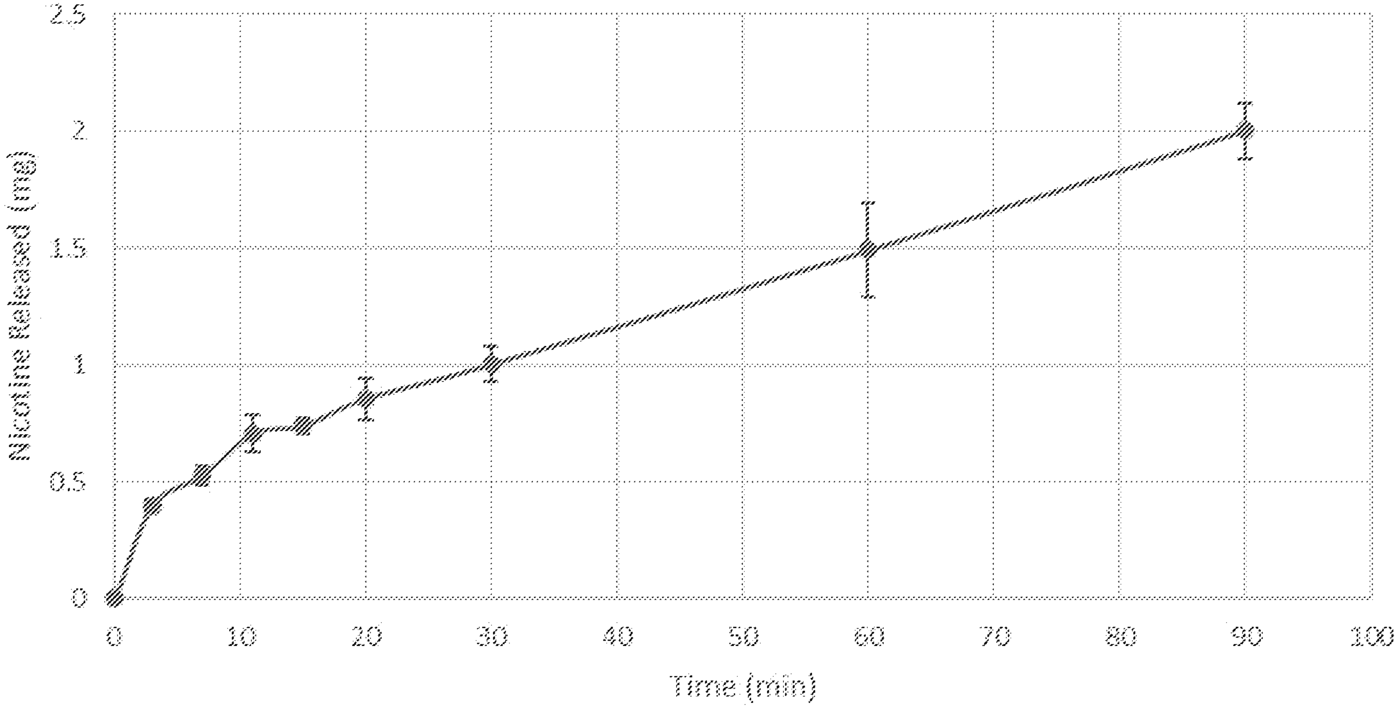
Example 14 (Control)

FIG. 3



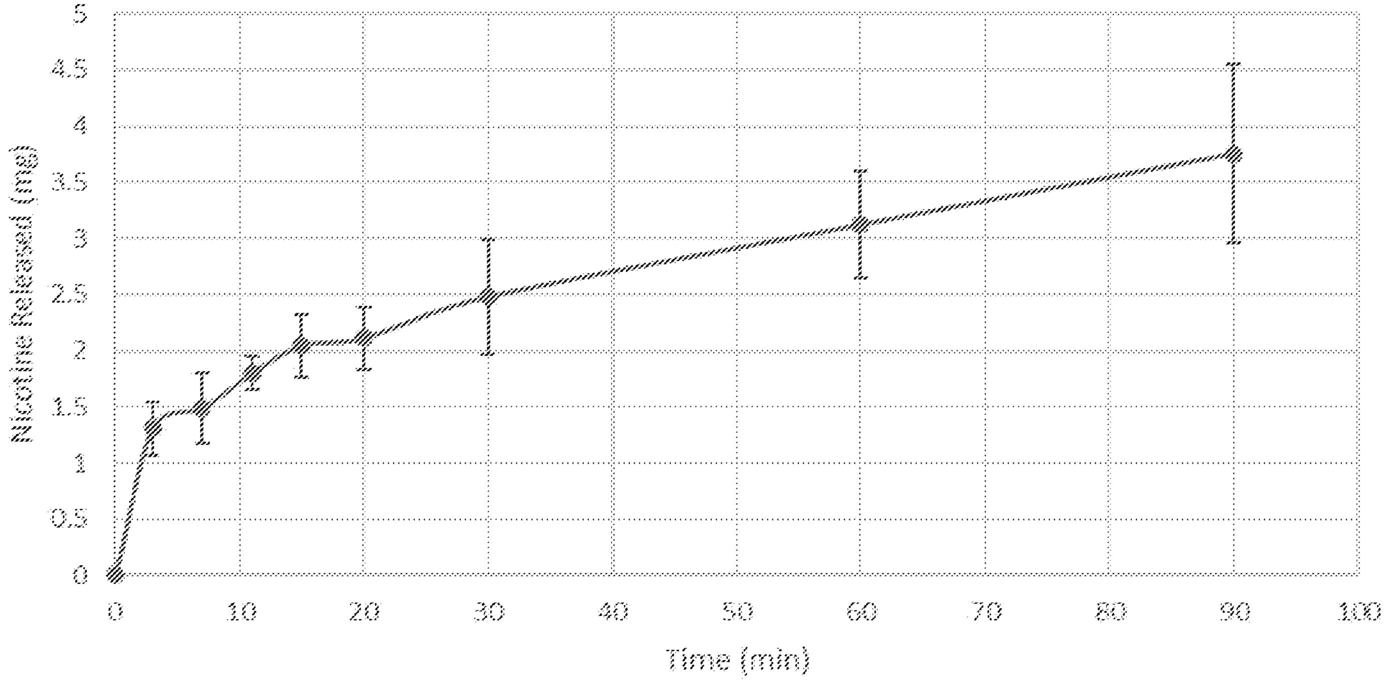
Example 8

FIG. 4



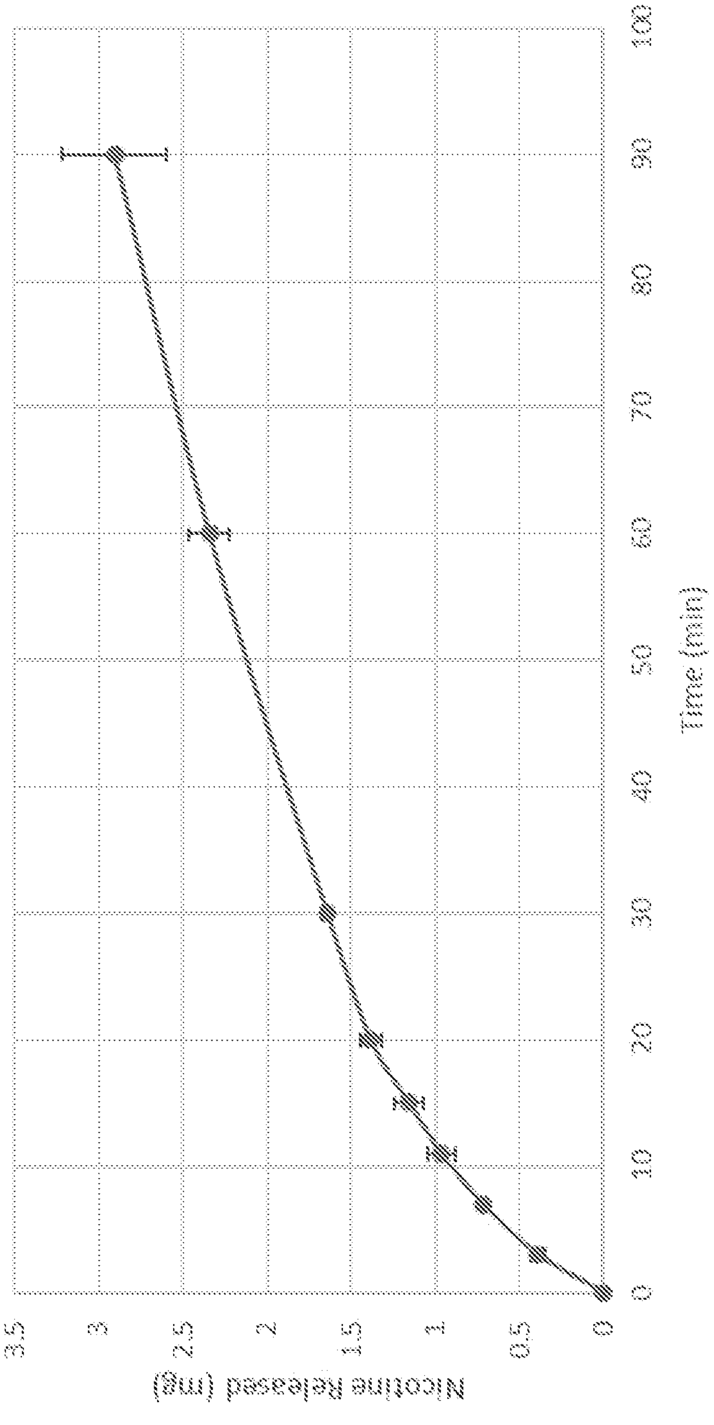
Example 9

FIG. 5



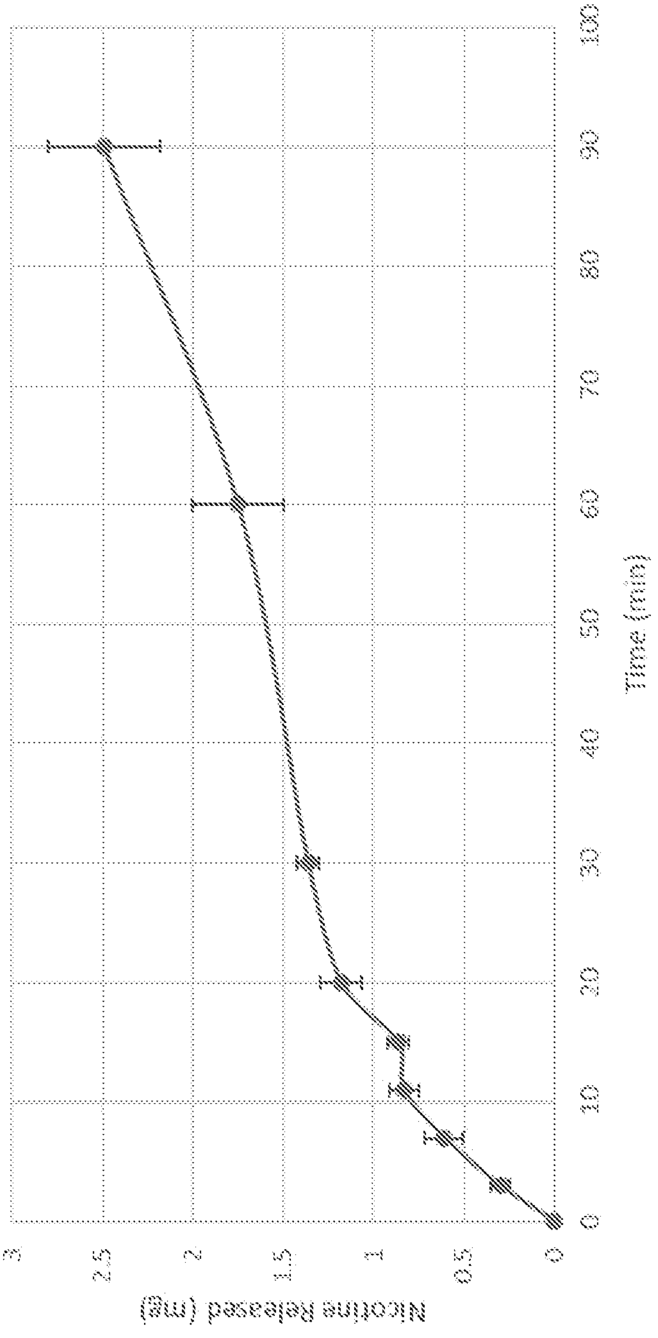
Example 10

FIG. 6



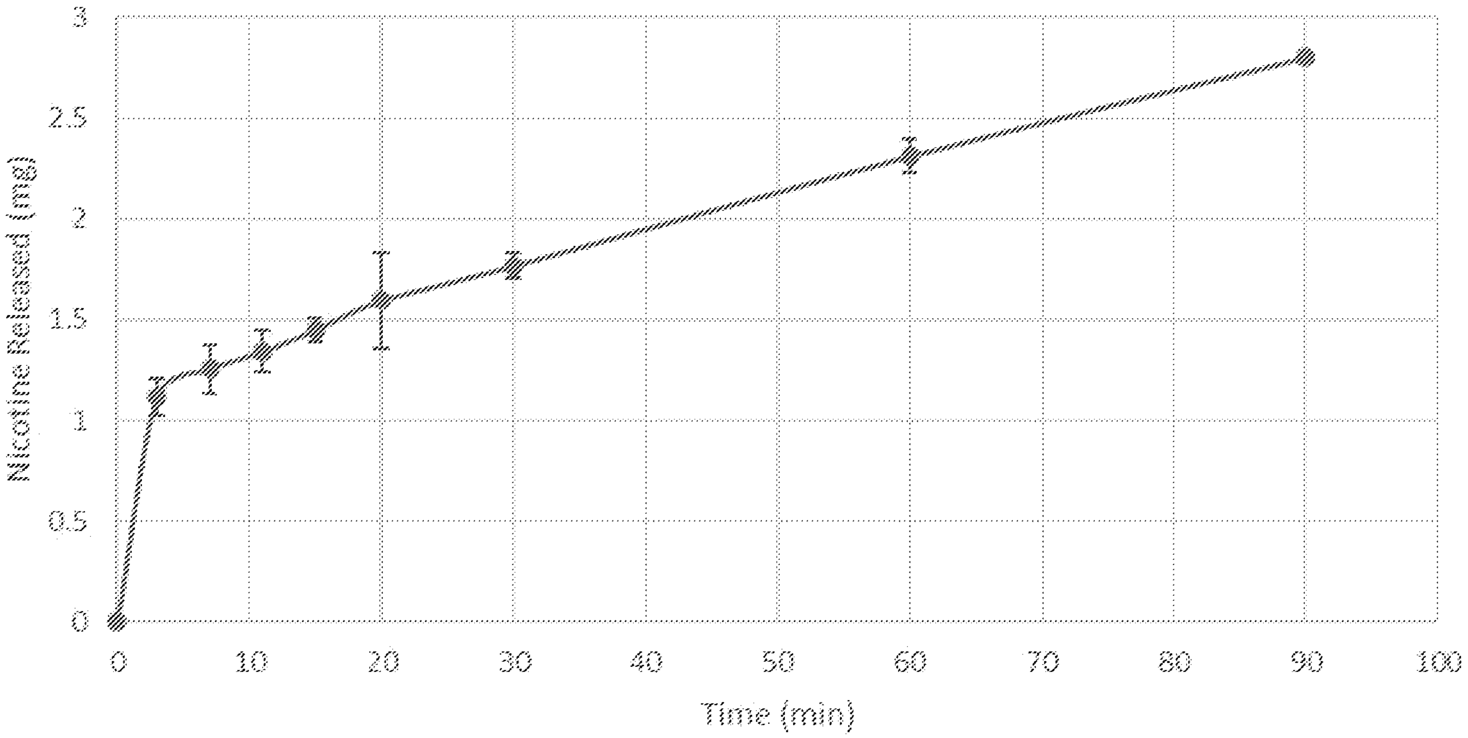
Example 11

FIG. 7



Example 12

FIG. 8



Example 13

FIG. 9

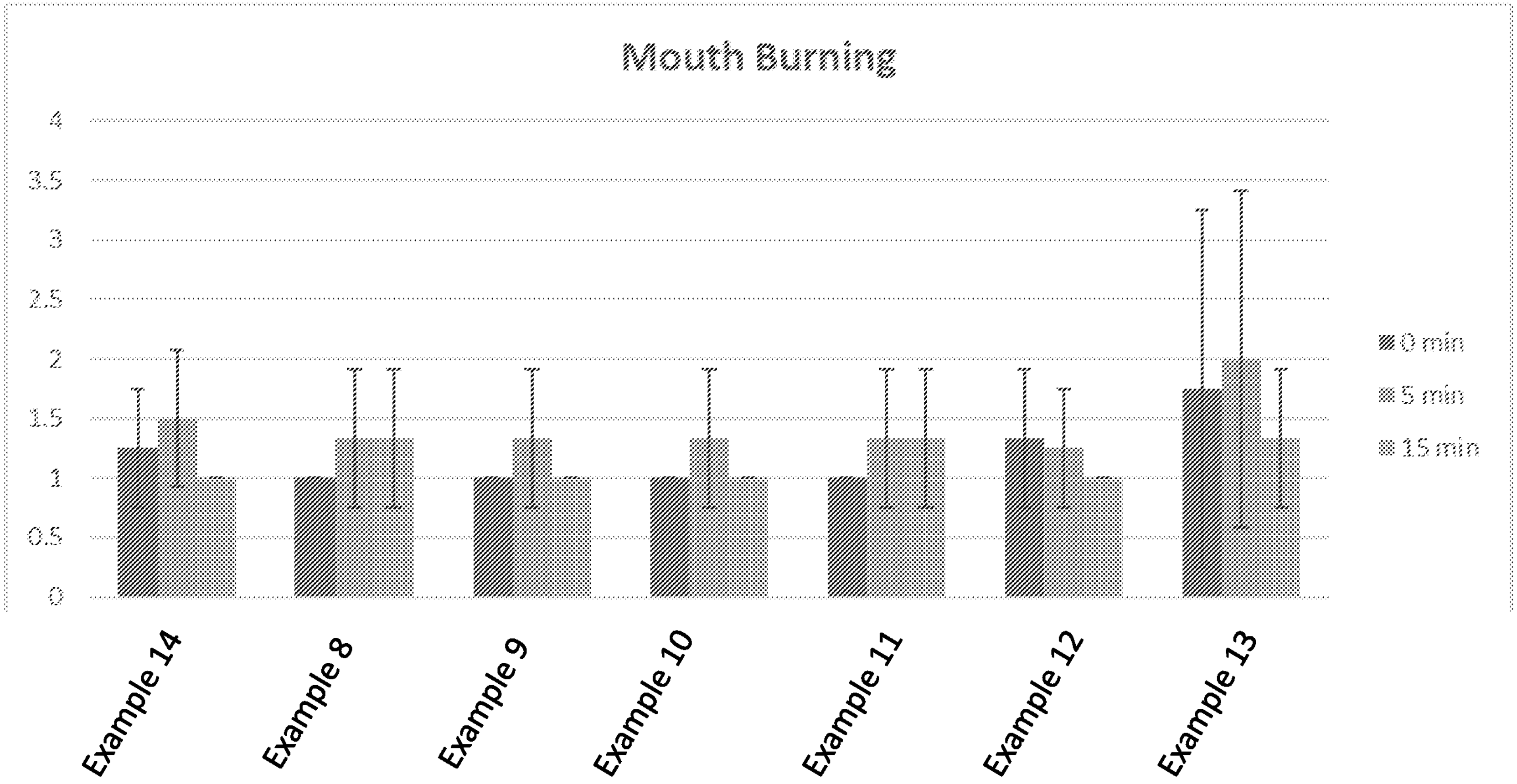

Mouth Burning
4
3.5
3
2.5
2
1.5
1
0.5
0
0 min
5 min
15 min
Example 14
Example 8
Example 9
Example 10
Example 11
Example 12
Example 13

FIG. 10

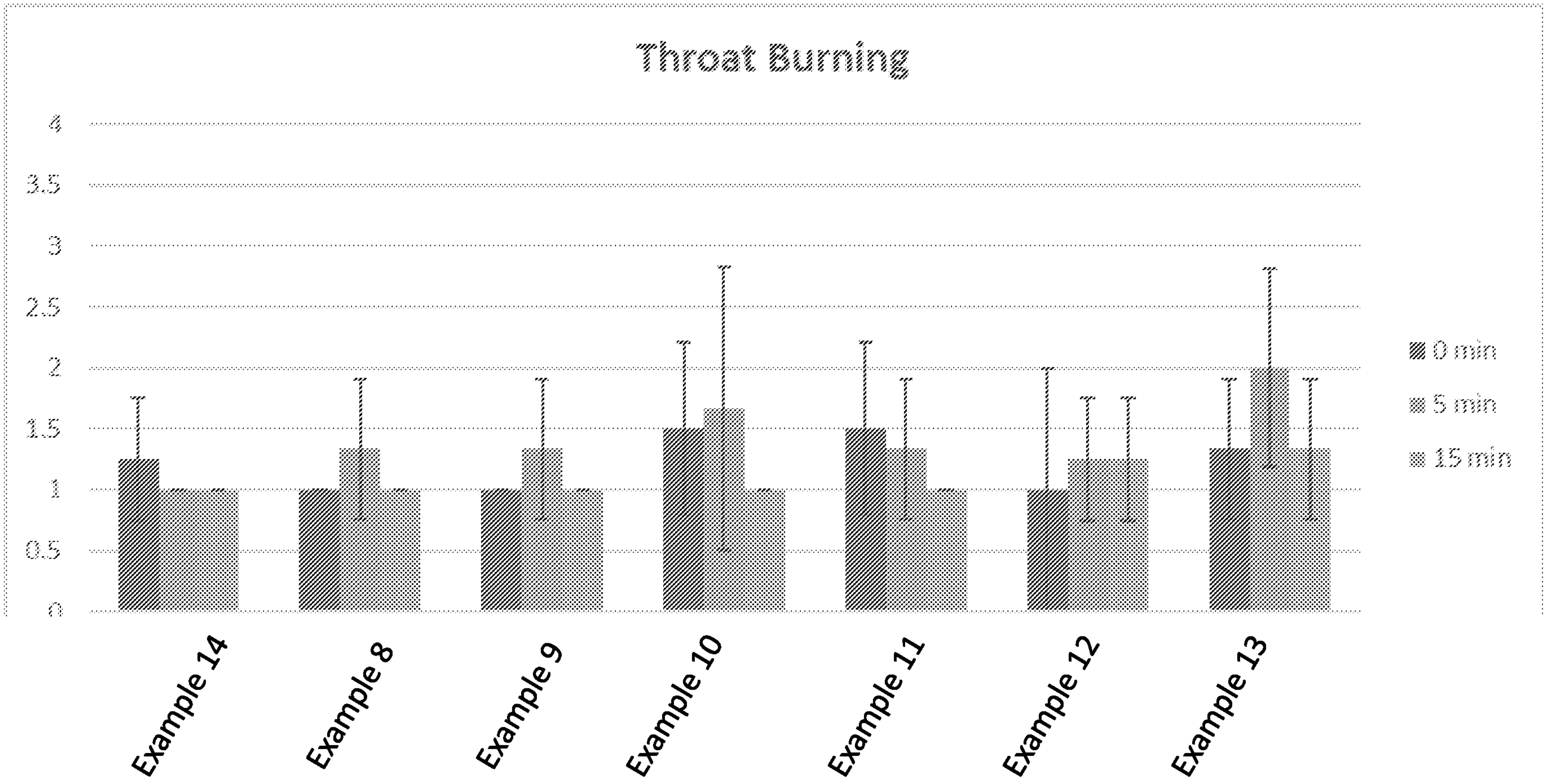
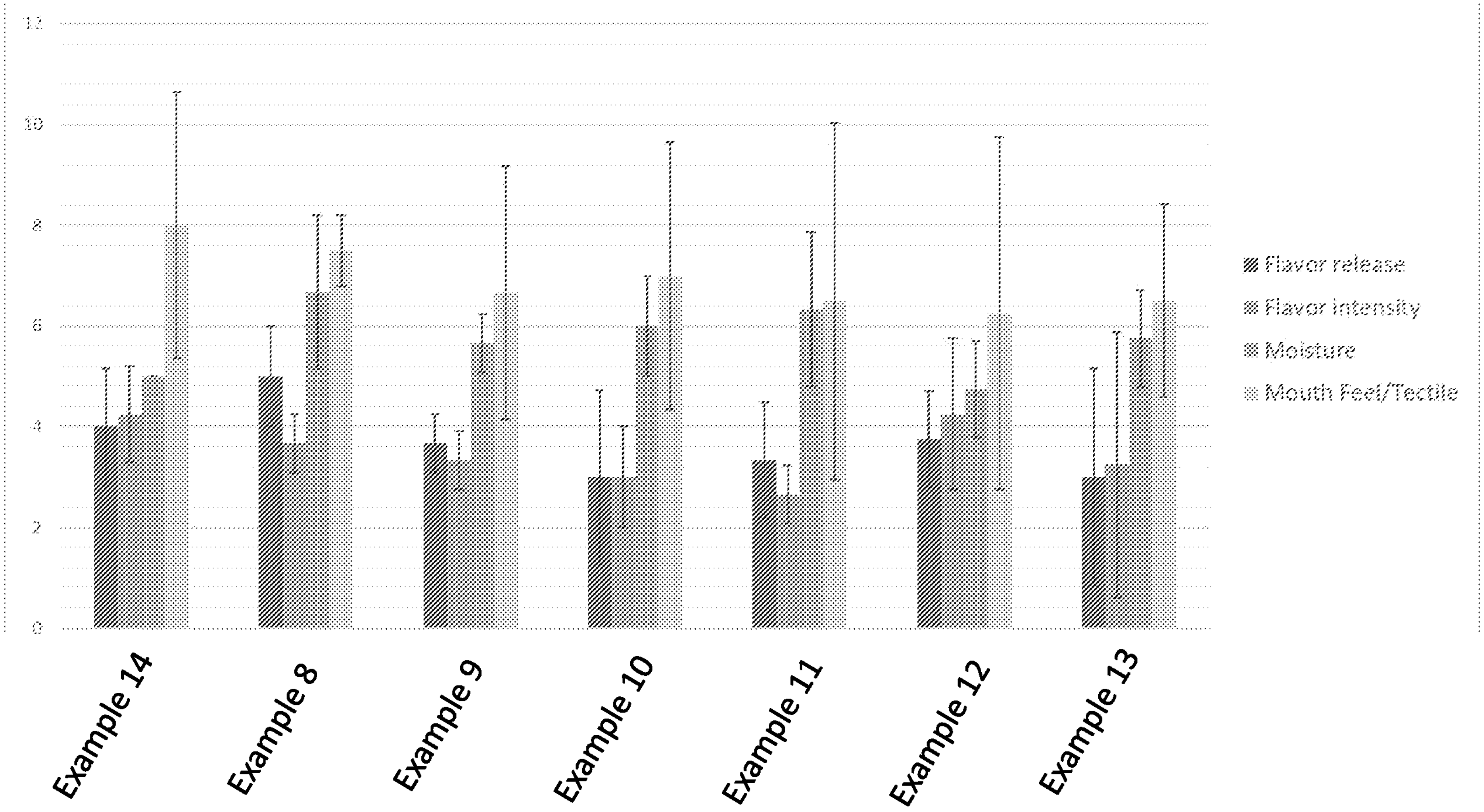

Throat Burning
4
3.5
3
2.5
2
1.5
1
0.5
0
Example 14
Example 8
Example 9
Example 10
Example 11
Example 12
Example 13
▨ 0 min
▨ 5 min
▨ 15 min

FIG. 11


12
10
8
6
4
2
0
Example 14
Example 8
Example 9
Example 10
Example 11
Example 12
Example 13
▨ Flavor release
▨ Flavor intensity
▨ Moisture
▨ Mouth Feel/Tectile

INTERNATIONAL SEARCH REPORT

International application No	PCT/IB2024/052862

A. CLASSIFICATION OF SUBJECT MATTER

INV. A24B13/00 A24B15/16 A24B15/28
ADD.

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)

A24B A61K

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)

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2023/033276 A1 (XU KEYI [US] ET AL) 2 February 2023 (2023-02-02) paragraphs [0003], [0076], [0084], [0092], [0116] - [0118]	1-26
X	CN 114 521 668 A (SHENZHEN YUFOG SCIENCE AND TECH CO LTD) 24 May 2022 (2022-05-24) paragraphs [0007], [0010]; claims 2, 5, 9, 10; example 2	1-26

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

☒ See patent family annex.

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"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

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"&" document member of the same patent family

Date of the actual completion of the international search 10 June 2024	Date of mailing of the international search report 20/06/2024
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer Flügel, Alexander

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IB2024/052862

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2023033276 A1	02-02-2023	CA 3226606 A1	26-01-2023
		EP 4373311 A1	29-05-2024
		US 2023033276 A1	02-02-2023
		WO 2023002439 A1	26-01-2023
CN 114521668 A	24-05-2022	NONE	