ALKALOID COMPOSITION FOR E-CIGARETTE

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ABSTRACT
An alkaloid composition for an e-cigarette contains a solvent and at least about 25 wt. % anaboline based on the total alkaloid weight of the composition. The alkaloid composition may be contained in a refilling cartridge for an e-cigarette, or in a container as part of a kit for refilling an e-cigarette. The alkaloid compositions disclosed herein feature a balanced form of alkaloids to provide an attractive alternative to smoking tobacco, in which nicotine makes up about 90 wt. % of the total alkaloid content. The alkaloid compositions are characterized by a significant quantity of anaboline, which has lower toxicity than other alkaloids such as nicotine. The alkaloid compositions enable individuals to experience the pleasure-enhancing attributes of conventional cigarette smoking, while avoiding exposure to combusted materials and other potentially hazardous components present in tobacco.
ALKALOID COMPOSITION FOR E-CIGARETTE

CROSS-REFERENCE TO RELATED APPLICATION

[0001] This application claims benefit under 35 U.S.C. §119(e) to U.S. Application No. 61/500,237, filed Jun. 23, 2011, the disclosure of which is hereby incorporated by reference in its entirety.

BACKGROUND

[0002] Combustion of organic materials such as tobacco is known to produce tar and other potentially harmful materials. Electronic cigarettes (or “e-cigarettes”) have been developed as an alternative to traditional cigarettes as a means for volatilizing active components, such as nicotine, for inhalation without combustion, while at the same time providing the user with an oral experience similar to that of traditional cigarette smoking. U.S. Pat. No. 7,832,410 B2 to Hon describes an e-cigarette having a liquid supply bottle in communication with an atomizer for volatilizing a nicotine-containing solution. U.S. Pat. No. 7,726,320 B2 to Robinson et al. discloses a smoking article having an electrically powered aerosol-producing device which heats tobacco contained within the device to generate an aerosol which is described as being similar to tobacco smoke.

[0003] Current e-cigarettes generally use a liquid containing nicotine, a toxic and addictive substance, as the sole active component. It also has been proposed to use so-called whole tobacco alkaloid e-liquid, containing nicotine in proportions similar to those existing in tobacco (e.g., ≥90 wt. % alkaloid content). The art has recognized a need for non-nicotine or reduced-nicotine alternatives to tobacco and tobacco replacement products. See D. K. Hatsukami et al., “Nicotine reduction revisited: science and future directions,” Tobacco Control 19: el-e10 (2010). It would be especially desirable to develop non-nicotine or reduced-nicotine alternatives that more effectively achieve the pleasure-enhancing attributes of traditional cigarette smoking, which in turn may assist smokers in quitting traditional cigarette smoking.

SUMMARY

[0004] Embodiments of the present invention are directed to e-cigarettes, alkaloid compositions for e-cigarettes, and refilling cartridges for e-cigarettes containing certain alkaloid compositions. In one aspect, a refilling cartridge for an e-cigarette contains a liquid alkaloid composition comprising a solvent and at least about 25 wt. % anatabine based on the total alkaloid weight of the composition.

[0005] In another aspect, a kit for refilling an e-cigarette comprises (i) a liquid alkaloid composition comprising a solvent and at least about 25 wt. % anatabine based on the total alkaloid weight of the composition, and (ii) instructions for filling the liquid alkaloid composition into a liquid receptacle of an e-cigarette.

[0006] In another aspect, a method of refilling an e-cigarette includes the steps of (i) providing a liquid alkaloid composition comprising a solvent and at least about 25 wt. % anatabine based on the total alkaloid weight of the composition, and (ii) filling the liquid alkaloid composition into a liquid receptacle of an e-cigarette.

[0007] In yet another aspect, an e-cigarette comprises a cartridge containing a liquid alkaloid composition comprising a solvent and at least about 25 wt. % anatabine based on the total alkaloid weight of the composition. The e-cigarette may be of a single-use or disposable type, or may be refillable with liquid alkaloid compositions to facilitate reuse.

[0008] Other aspects relate to non-tobacco products that contain an alkaloid composition comprising about 25 wt. % to about 95 wt. % anatabine, and about 5 wt. % to about 75 wt. % of a second alkaloid, based on the total alkaloid weight of the composition. The second alkaloid may be nicotine, nor-nicotine, anabasine, or a combination of two or more of them. The non-tobacco product may be in the form of a solid bit of compressed powder, chewing gum, gelcap, capsule, pill, lozenge, or the like.

[0009] The alkaloid compositions disclosed herein feature different ranges of alkaloids to provide an attractive alternative to smoking conventional e-cigarettes, in which nicotine makes up about 90 to 100 wt. % of the total alkaloid content. The disclosed alkaloid compositions are characterized by a significant quantity of anatabine, which has lower toxicity and risk of abuse as compared to other alkaloids such as nicotine. The alkaloid compositions enable individuals to experience the pleasure-enhancing attributes of conventional cigarette smoking, while avoiding exposure to combusted materials and other potentially hazardous components present in tobacco. As a result, individuals may be more likely to quit conventional cigarette smoking.

BRIEF DESCRIPTION OF THE DRAWINGS

[0010] A more complete understanding of the present invention and certain advantages thereof may be acquired by referring to the following detailed description in consideration with the accompanying drawings, in which:

[0011] FIG. 1 is a schematic illustration of one example of an e-cigarette configuration.

DETAILED DESCRIPTION

[0012] Tobacco is among the most chemically complex substances known, with tobacco and tobacco smoke containing more than 8,000 compounds. In addition to nicotine, tobacco contains the minor alkaloids nornicotine, anabasine, and anatabine. While nicotine is regarded as the principal addictive component in tobacco, a variety of other factors also are believed to contribute to tobacco addiction. For example, tobacco smoke has been reported to have a monoamine oxidase (MAO) inhibitory effect. MAO is an enzyme involved in the breakdown of dopamine, a pleasure-enhancing neurotransmitter. See J. S. Fowler et al., “Inhibition of Monoamine Oxidase B in the Brain of Smokers,” Nature (Lond), 379(6567):733 736 (1996); J. Stephenson, “Clues Found to Tobacco Addiction,” Journal of the American Medical Association, 275(16): 1217-1218 (1996). See also Williams et al. U.S. Pat. No. 6,350,479.

[0013] Aspects of the present invention are directed to alkaloid compositions for e-cigarettes which are designed to provide different ranges of alkaloids to more effectively achieve the pleasure-enhancing effects that smokers obtain through smoking traditional cigarettes, while avoiding or reducing exposure to nicotine. In one embodiment, the alkaloid composition comprises at least about 25 wt. % anatabine based on the total alkaloid weight. In some examples, anatabine is the sole alkaloid present in the composition, e.g., anatabine comprises 100 wt. % of the total alkaloid weight. In other examples, up to about 75 wt. % of one or more other alkaloids,
such as nicotine, nornicotine, and/or anabasine, may be present in addition to anatabine. For example, anatabine and nicotine may be combined in a weight ratio (anatabine-to-nicotine) of about 50:1 to about 1:3, or from about 25:1 to about 1:2, from about 10:1 to about 3:2, or from about 5:1 to about 1:1.

[0014] Unless otherwise clear from context, all percentages referred to herein are expressed as percent by weight based on the total weight of the composition.

[0015] Anatabine may be prepared synthetically, such as via a benzophenoneimine pathway as described in co-pending application Ser. No. 12/729,346, filed Mar. 23, 2010, the disclosure of which is incorporated herein by reference in its entirety. Anatabine may be present in the form of a racemic mixture or as isolated enantiomer, e.g., R-(+)-anatabine or S-(−)-anatabine, and/or as one or more pharmaceutically acceptable (or food grade) salts of anatabine. Unless otherwise clear from context, “anatabine” as used herein refers to racemic mixtures of anatabine, enantiomers of anatabine, salt and non-salt forms of anatabine, as well as salt and non-salt forms of anatabine enantiomers. Non-limiting examples of possible salts are described in P. H. Stahl et al., Handbook of Pharmaceutical Salts: Properties, Selection and Use, Weinheim/Zürich: Wiley-VCH, 2002, including salts of 1-hydroxy-2-naphthoic acid, 2,2-dichloroacetic acid, 2-hydroxyethanesulfonic acid, 2-oxoglutaric acid, 4-acetamidobenzoic acid, 4-aminoasacitic acid, acetic acid, adipic acid, ascorbic acid (L), aspartic acid (L), benzenesulfonic acid, benzoic acid, camphoric acid (+), camphor-10-sulfonic acid (+), caprylic acid (decanoic acid), caproic acid (hexanoic acid), caprylyc acid (octanoic acid), carbamic acid, cinnamic acid, citric acid, cycloaminic acid, dodecylosulfonic acid, ethane-1,2-disulfonic acid, ethanesulfonic acid, formic acid, fumaric acid, galactaric acid, gentisic acid, glucoheptonic acid (D), gluconic acid (D), glucuronic acid (D), glutamic acid, glutaric acid, glycerophosphoric acid, glycolic acid, hippuric acid, hydrobromic acid, hydrochloric acid, isobutyric acid, lactic acid (DL), lactobionate, laurate acid, maleic acid, malic acid (−L), malonic acid, mandelic acid (DL), methanesulfonic acid, naphthalene-1,5-disulfonic acid, naphthalene-2-sulfonic acid, nortic acid, nitric acid, oleic acid, oxalic acid, palmitic acid, panoenic acid, phosphoric acid, propionic acid, pyroglutamic acid (−L), salicylic acid, sebacic acid, stearic acid, succinic acid, sulfuric acid, tartaric acid (−L), thioctic acid, toluenesulfonic acid (P), and undecylenic acid.

[0016] As an alternative to synthetic preparation, anatabine may be obtained by extraction from tobacco or other plants, such as members of the Solanaceae family, such as datura, mandrake, belladonna, capsicum, potato, tomato, nicotiana, eggplant, and petunia. A tobacco extract may be prepared from cured tobacco stems, lamina, or both. Flue (bright) varieties of tobacco are often used, i.e., Virginia flue. Other tobacco varieties may be used, such as Burley, dark-fired, and/or other commercial tobacco varieties. Two or more tobacco varieties may be combined to form a blend. In the extraction process, cured tobacco material is extracted with a solvent, typically water, ethanol, steam, or carbon dioxide. The resulting solution contains the soluble components of the tobacco, including alkaloids such as anatabine. Anatabine may be purified using known techniques such as liquid chromatography.

[0017] The amount of anatabine present in the composition may vary depending on factors such as the type of e-cigarette and whether other active components, such as nicotine and/or other alkaloids, are present. By way of example, the amount of anatabine may range from about 0.1 to about 25 mg, from about 0.5 to about 20 mg, or from about 1 to about 10 mg, per total gram of composition.

[0018] As described in co-pending application Ser. No. 12/826,985, compositions containing anatabine were found to be efficacious for the temporary reduction of tobacco cravings, even without the presence of nicotine. Anatabine and other minor alkaloids also have been reported to bind to nicotinic receptors. See “Receptors for Nicotine in the Central Nervous System: 1 Radioligand Binding Studies,” Group Research & Development Centre, British-American Tobacco Co. Ltd. (1984).

[0019] In addition to anatabine, the composition may contain up to about 75 wt. % of one or more other alkaloids, such as nicotine, nornicotine, and/or anabasine, based on the total alkaloid weight. Such alkaloids may be extracted from tobacco or other plant materials and purified using known techniques, and/or prepared synthetically using known synthesis methods. Anatabine and additional alkaloid(s), such as nicotine, may be combined in a weight ratio (anatabine-to-total other alkaloids) of about 50:1 to about 1:3, or from about 25:1 to about 1:2, from about 10:1 to about 3:2, or from about 5:1 to about 1:1.

[0020] The composition typically contains other components such as water, organic solvents, sweetening and/or flavoring agents, and the like. Examples of solvents that are commonly used in liquid compositions for e-cigarettes include polyhydric alcohols such as 1,2-propylene glycol (PG) or PG, monohydric alcohols such as ethanol, ethyl acetate, and the like. The amount of water present typically ranges from about 0.1 to about 10 wt. %, usually from about 0.5 to about 5 wt. %. The amount of organic solvent present typically ranges from about 50 to about 99 wt. %, often from about 75 to about 95 wt. %.

[0021] If desired, one or more flavorants may be added to the composition, non-limiting examples of which include peppermint, menthol, wintergreen, spearmint, propolis, eucalyptus, cinnamon, or the like. The total amount of flavorants typically ranges from about 0.5 to about 15 wt. %, often from about 1 to about 10 wt. %, based on the total weight of the composition.

[0022] The e-cigarette may be of various types of configurations, the details of which form no part of the present invention. In general, e-cigarettes may be of a single-use or disposable type, or may be refillable with liquid alkaloid compositions and/or cartridges containing liquid compositions to facilitate reuse. One example of an e-cigarette is shown in FIG. 1. An air inlet 4 is provided on the external wall of a shell 14 which houses LED 1, cell 2, electronic circuit board 3, normal pressure cavity 5, sensor 6, vapor-liquid separator 7, atomizer 9, liquid-supplying bottle 11, mouthpiece 15, microswitch 16, gas vent 17, and air passage 18. The electronic circuit board 3 has an electronic switching circuit and a high frequency generator. A negative pressure cavity 8 is provided in the sensor 6 and is separated from the sensor 6 by a ripple film. An atomization cavity 10 is provided in the atomizer 9. A retaining ring 13 is provided for locking the liquid-supplying bottle 11 between one side of the liquid-supplying bottle 11 and the shell 14; and an aerosol passage 12 is provided on the other side of the liquid-supplying bottle.
Other details are described in U.S. Pat. No. 7,832,410 B2 to Hon, the disclosure of which is hereby incorporated by reference in its entirety.

[0023] By providing a balanced alkaloid composition containing anatabine as a significant alkaloid component, it is possible to prepare e-cigarettes that reduce cravings for traditional tobacco smoking, while minimizing toxicity and other undesirable side effects associated with nicotine and other tobacco components. The e-cigarette may be used as needed to satisfy cravings, or at intervals such as once daily, twice daily, or three or more times daily, depending on such factors as the concentration of active components and the subject’s physiological conditions.

[0024] In an alternative embodiment, a non-tobacco formulation contains an alkaloid composition comprising about 25 wt. % to about 95 wt. % anatabine, and about 5 wt. % to about 75 wt. % of a second alkaloid, based on the total alkaloid weight of the composition. The second alkaloid may be nicotine, nornicotine, anabasine, or a combination of two or more of them. The non-tobacco product may be in the form of a solid bit of compressed powder, chewing gum, capsule, pill, lozenge, or the like. The term “non-tobacco” means that the product is essentially free of tobacco leaf or tobacco extract, except however that some or all of the alkaloids present in the non-tobacco product may be extracted from tobacco and purified using conventional techniques such as liquid chromatography.

[0025] Additional components ingredients may be added to the non-tobacco products to improve taste or stability. Such additional components include, but are not limited to, sweeteners, natural flavorants, artificial flavorants, colorants, antioxidants, preservatives, chelating agents, viscomodulators, tonicifiers, odorants, opacifiers, suspending agents, binders, thickeners, and mixtures thereof, including, but not limited to, xanthum gum, carboxymethylcellulose, carboxymethylcellulose, hydroxypropylcellulose, methylcellulose, microcrystalline cellulose, starches, dextrins, fermented whey, tofu, maltodextrins, polys (including sugar alcohols, such as sorbitol or mannitol), carbohydrates (e.g., lactose), propylene glycol alginate, gelatin gum, guar, pectin, tragacanth gum, gum acacia, locust bean gum, gum arabic, gelatin, mannitol, natural and/or artificial mint flavors, sucrose, silicon dioxide, stearic acid, hydroxypropyl methylcellulose, magnesium stearate, titanium dioxide, natural glaze, methyl paraben, propyl parabens, triethyl citrate, citric acid, butylated hydroxytoluene (BHT), mono and diglycerides, polysorbate 80, and the like.

[0026] The non-tobacco products may be in a variety of forms, e.g., to be taken orally, such as pills, tablets, capsules, soft gels, gelcaps, liquids, syrups, suspensions, powders, chews, lozenges, gums, bars, etc., or to be administered by other routes, such as parenterally, by inhalation spray, topically, via an implanted reservoir, etc. The alkaloid compositions also can be prepared to be administered in foods or beverages. For example, they can be supplied as a dried or powdered product for reconstitution with water or other suitable vehicle before use (e.g., milk, fruit juice, and the like).

EXAMPLES 1-8

[0027] Alkaloid compositions for e-cigarettes may be prepared by combining the components listed in Table 1 below and mixing to form a solution. Anatabine may be prepared synthetically as described in Examples 1-3 of co-pending application Ser. No. 12/729,346.

TABLE 1

<table>
<thead>
<tr>
<th>Example</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anatabine (mg)</td>
<td>10</td>
<td>8</td>
<td>4</td>
<td>6</td>
<td>7</td>
<td>12</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>Nicotine (mg)</td>
<td>—</td>
<td>4</td>
<td>8</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>—</td>
<td>4</td>
</tr>
<tr>
<td>Nornicotine (mg)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Anabasine (mg)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>—</td>
<td>2</td>
</tr>
<tr>
<td>Polyethylene Glycol (g)</td>
<td>91</td>
<td>90</td>
<td>92</td>
<td>93</td>
<td>92</td>
<td>94</td>
<td>91</td>
<td>90</td>
</tr>
<tr>
<td>Ethyl acetate (g)</td>
<td>0.5</td>
<td>0.5</td>
<td>—</td>
<td>0.5</td>
<td>0.5</td>
<td>0.4</td>
<td>0.5</td>
<td>—</td>
</tr>
<tr>
<td>Water (g)</td>
<td>4</td>
<td>4.5</td>
<td>3.5</td>
<td>4</td>
<td>2.5</td>
<td>3.5</td>
<td>5</td>
<td>4.5</td>
</tr>
<tr>
<td>Flavors (g)</td>
<td>1</td>
<td>1.25</td>
<td>1.5</td>
<td>1</td>
<td>1</td>
<td>1.5</td>
<td>0.75</td>
<td>1.25</td>
</tr>
</tbody>
</table>

[0028] The compositions described in Examples 1-8 may be filled into refilling cartridges for e-cigarettes, or filled into a liquid container that is used as part of a kit for refilling liquid receptacles in e-cigarettes. The compositions alternatively may be filled into a single-use or disposable type of e-cigarette.

[0029] While the invention has been described with respect to specific examples, those skilled in the art will appreciate that there are numerous variations and permutations of the above described systems and techniques that fall within the spirit and scope of the invention as set forth in the appended claims.

What is claimed is:

1. A refilling cartridge for an e-cigarette containing a liquid alkaloid composition comprising a solvent and at least about 25 wt. % anatabine based on the total alkaloid weight of the composition.

2. The refilling cartridge of claim 1, wherein the anatabine is synthetic anatabine.

3. The refilling cartridge of claim 1 wherein anatabine is provided in the form of an extract of a plant selected from the group consisting of tobacco, datura, mandrake, belladonna, capsicum, potato, tomato, nicotiana, eggplant, and petunia.

4. The refilling cartridge of claim 1, wherein the solvent is 1,2-polyethylene glycol.

5. The refilling cartridge of claim 1, wherein the solvent further comprises ethyl acetate.

6. The refilling cartridge of claim 1, wherein the liquid alkaloid composition further comprises an alkaloid selected from the group consisting of nicotine, nornicotine, anabasine, and combinations thereof.

7. The refilling cartridge of claim 1, wherein anatabine comprises at least about 50 wt. % of the total alkaloid weight of the composition.

8. The refilling cartridge of claim 1, wherein anatabine comprises at least about 75 wt. % of the total alkaloid weight of the composition.

9. The refilling cartridge of claim 1, wherein anatabine comprises 100 wt. % of the total alkaloid weight of the composition.

10. An e-cigarette comprising the refilling cartridge of claim 1.
11. A kit for refilling an e-cigarette comprising:
   a liquid alkaloid composition comprising a solvent and at least
   about 25 wt. % anatabine based on the total alkaloid
   weight of the composition; and
   instructions for filling the liquid alkaloid composition into
   a liquid receptacle of an e-cigarette.
12. The kit of claim 11, wherein the liquid alkaloid
   composition further comprises an alkaloid selected from
   the group consisting of nicotine, nornicotine, anabasine, and
   combinations thereof.
13. The kit of claim 11, wherein anabasine comprises at
   least about 50 wt. % of the total alkaloid weight of the
   composition.
14. The kit of claim 11, wherein anatabine comprises at
   least about 75 wt. % of the total alkaloid weight of the
   composition.
15. The kit of claim 11, wherein anatabine comprises 100
   wt. % of the total alkaloid weight of the composition.
16. A method of refilling an e-cigarette comprising
   providing a liquid alkaloid composition comprising a solv-
   ent and at least about 25 wt. % anatabine based on the
   total alkaloid weight of the composition; and
   filling the liquid alkaloid composition into a liquid recept-
   able of an e-cigarette.
17. The method of claim 16, wherein the liquid alkaloid
   composition further comprises an alkaloid selected from
   the group consisting of nicotine, nornicotine, anabasine, and
   combinations thereof.
18. The method of claim 16, wherein anatabine comprises
   at least about 50 wt. % of the total alkaloid weight of the
   composition.
19. The method of claim 16, wherein anatabine comprises
   at least about 75 wt. % of the total alkaloid weight of the
   composition.
20. The method of claim 16, wherein anatabine comprises
   100 wt. % of the total alkaloid weight of the composition.
21. An e-cigarette comprising a cartridge containing a liq-
   uid alkaloid composition comprising a solvent and at least
   about 25 wt. % anatabine based on the total alkaloid weight
   of the composition.
22. The e-cigarette of claim 21, wherein the liquid alkaloid
   composition further comprises an alkaloid selected from
   the group consisting of nicotine, nornicotine, anabasine, and
   combinations thereof.
23. The e-cigarette of claim 21, wherein anatabine
   comprises at least about 50 wt. % of the total alkaloid weight
   of the composition.
24. The e-cigarette of claim 21, wherein anatabine
   comprises at least about 75 wt. % of the total alkaloid weight
   of the composition.
25. The e-cigarette of claim 21, wherein anatabine
   comprises 100 wt. % of the total alkaloid weight of the composi-
   tion.
26. A non-tobacco product containing an alkaloid com-
   position comprising about 25 wt. % to about 95 wt. % anatabine
   and about 5 wt. % to about 75 wt. % of a second alkaloid,
   based on the total alkaloid weight of the composition,
   wherein the second alkaloid is selected from the group con-
   sisting of nicotine, nornicotine, anabasine, and combinations
   thereof; and wherein the product is in a form selected from
   the group consisting of pills, tablets, capsules, soft gels, gel-
   caps, liquids, syrups, suspensions, powders, chews, lozenges, gum,
   bars, inhalation spray, and implanted reservoir.
27. The non-tobacco product of claim 26, wherein the
   second alkaloid is nicotine.
28. The non-tobacco product of claim 26, wherein anatab-
   ine comprises at least about 50 wt. % of the total alkaloid
   weight of the composition.
29. The non-tobacco product of claim 26, wherein anatab-
   ine comprises at least about 75 wt. % of the total alkaloid
   weight of the composition.
30. The non-tobacco product of claim 26, wherein anatab-
   ine comprises about 95 wt. % of the total alkaloid weight
   of the composition.

* * * * *