aerosolization characteristics of any individual heating element and the quantity of formulation resting thereon.

Thus the primary objectives of the present invention are to largely mitigate, if not entirely remedy, such disadvantages.

Summary of the Invention

Aspects of the invention are defined in the independent claims. Some optional features of the invention are defined in the dependent claims.

There is provided a first exemplary aerosolisable formulation comprising

- Between 25- 50%, w/w free-base nicotine,
- Between 25-40% w/w of one, or some combination of two or more pharmaceutically and biologically safe mono- or di-carboxylic organic acids,
- Between 50-20% w/w of one or some combination of two or more pharmaceutically and biologically safe liquid excipients, and optionally
- Between 0-5% w/w water.

Preferably the one or more organic acids is selected from one of the following groups of acids:

- Acids containing an aromatic group,
- Hydroxycarboxylic acids, being of the α- (alpha), β- (beta) or ω- (omega) variety, or some other variety,
- Heterocyclic carboxylic acids,
- aromatic carboxylic acids,
- Terpenoid acids,
- Sugar acids;,
- Pectic acids,
- Amino acids,
- Cycloaliphatic acids,
- Aliphatic carboxylic acids, and
- Keto carboxylic acids.

Preferably, the one or more organic acids present in the formulation is one or more of the following (herein otherwise referred to as "List A"):
1-hydroxy-2-naphthoic acid, 2,2-dichloroacetic acid, 2-hydroxyethanesulfonic acid, 2-oxoglutaric acid, 4-acetamidobenzoic acid, 4-aminosalicylic acid, acetic acid, adipic acid, ascorbic acid (L), aspartic acid (L), benzenesulfonic acid, benzoic acid, camphoric acid (+), camphor-10-sulfonic acid (+), capric acid (decanoic acid), caproic acid (hexanoic acid), caprylic acid (octanoic acid), carbonic acid, cinnamic acid, citric acid, cyclamic acid, dodecyl sulfonic 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, isobutyric acid, lactic acid (DL), lactobionic acid, lauric acid, maleic acid, malic acid (- L), malonic acid, mandelic acid (DL), methanesulfonic acid, naphthalene-1,5-disulfonic acid, naphthalene-2-sulfonic acid, nicotinic acid, oleic acid, oxalic acid, palmitic acid, pamoic acid, propionic acid, pyroglutamic acid (- L), salicylic acid, sebacic acid, stearic acid, succinic acid, tartaric acid (+ L), thiocyanic acid, toluenesulfonic acid (p), undecylenic acid.

Most preferably, the one or more acids selected is one of: an Alpha-keto acid (2-oxoacid), a Beta-keto acid (3-oxoacid), and a Gamma-keto acid (4-oxoacid). Alpha-keto acids, such as pyruvic acid, have the keto group adjacent to the carboxylic acid. Beta-keto acids, such as acetoacetic acid, have the ketone group at the second carbon from the carboxylic acid. Gamma-keto acids, such as levulinic acid, have the ketone group at the third carbon from the carboxylic acid.

Most preferably, the formulation includes one of:

- Only one of: lactic acid and benzoic acid,
- Only lactic acid,
- A binary system of two organic acids, one being lactic acid and the other being one of: benzoic acid, salicylic acid, and
- A binary system of two organic acids, one being lactic acid and the other being chosen from List A above, excepting lactic acid.

In the case where the formulation includes a binary system of two organic acids, one of which is lactic acid, the w/w ratio between the two acids is most preferably 1:1.

In the case where the formulation includes a binary system of two organic acids, one being lactic acid, the second acid is most preferably one of: benzoic acid, salicylic acid.

Most preferably the formulation includes only one acid, being lactic acid.

Preferably the one or more excipients present in the formulation is/are selected from the following: Glycerol, Vegetable Glycerin (VG), Propylene Glycol (PG), Polyethylene Glycol (PEG), & trimethylene glycol (TMG).

Most preferably, the formulation includes only a single excipient, being, most preferably, Glycerol.

In one preferred embodiment, there is provided an exemplary nicotine-containing formulation comprising

- 25% w/w freebase nicotine
- 25% w/w of one of: benzoic acid, salicylic acid
- 50% glycerol.

In another preferred embodiment, there is provided an exemplary nicotine-containing formulation comprising

- 25% w/w freebase nicotine
- 16.2% w/w lactic acid solution, said solution consisting of 12% w/w water and 88% lactic acid,
- 1.8% w/w water, and
- 58% w/w glycerol.

In yet another preferred embodiment, there is provided an exemplary nicotine-containing formulation comprising

- 25% w/w freebase nicotine
- 24.3% w/w lactic acid,
- 2.7% w/w water, and
- 48% w/w glycerol.

In yet another preferred embodiment, there is provided an exemplary nicotine-containing formulation comprising

- 25% w/w freebase nicotine
- 13.5% w/w lactic acid,
- 6% w/w of one of: benzoic acid, salicylic acid
- 1.5% w/w water, and
- 54% w/w glycerol.

In yet another preferred embodiment, there is provided an exemplary nicotine-containing formulation comprising

- 25% w/w freebase nicotine
- 13.5% w/w lactic acid,
- 5% w/w of one of: benzoic acid, salicylic acid
- 1.5% w/w water, and
- 55% w/w glycerol.

In yet another preferred embodiment, there is provided an exemplary nicotine-containing formulation comprising

- 34% w/w freebase nicotine
- 16% w/w of a 1:1 molar ratio mixture of lactic acid and benzoic acid, and
- 50% w/w glycerol.

In yet another preferred embodiment, there is provided an exemplary nicotine-containing formulation comprising:

- 46.5% w/w freebase nicotine
- 31.5% w/w of a lactic acid, and
- 22% w/w polyethylene glycol (PEG).

In yet further preferred embodiment, there is provided an exemplary nicotine-containing formulation comprising:

- 45% w/w freebase nicotine
- 32.4% w/w of a lactic acid, and

- 22.6% w/w polyethylene glycol (PEG).

These last 2 embodiments are particularly useful, because such formulations are so viscous at room temperature that they handle more like solids than liquids, and indeed these formulations may satisfy the chemical definition of a solid at room temperature. Thus, not only can such formulations be very easily, repeatably, positionally accurately, and volumetrically precisely applied to a base substrate, but such formulations have negligible wetting characteristics once extant on the substrate surface so there is practically no spreading out of the formulations over the surface of the substrate once applied thereto.

There is further provided a second exemplary aerosolisable formulation comprising

- Between 26-40%, w/w free-base nicotine,
- Between 24-40% w/w of one, or some combination of two or more pharmaceutically and biologically acceptable mono- or di-carboxylic organic acids,
- Between 50-20% w/w of one or some combination of two or more pharmaceutically and biologically acceptable liquid excipients, and optionally
- Between 0-5% w/w water.

There is further provided a third exemplary aerosolisable formulation comprising

- Between 25-55%, w/w free-base nicotine,
- Between 15-35% w/w of one, or some combination of two or more pharmaceutically and biologically acceptable mono- or di-carboxylic organic acids,
- Between 60-10% w/w of one or some combination of two or more pharmaceutically and biologically acceptable liquid excipients, and optionally
- Between 0-5% w/w water.

For the avoidance of doubt, all preferred embodiments and dependent features of the first exemplary aerosolisable formulation detailed above should be considered to apply equally to the second and any further exemplary aerosolisable formulations, adjusted for the increase (in the exemplary aerosolisable formulations subsequent to the first) in the concentration of freebase nicotine, as the case may be. Such preferred embodiments and dependent features have not been repeated here simply in the interests of brevity.

Applicant has advantageously discovered that the formulations prescribed above, and particularly those containing only lactic acid, an aqueous solution thereof, or a mixture thereof with benzoic acid, again either in pure form or in aqueous solution, all exhibit excellent chemical stability as compared to

CLAIMS

1. An aerosolisable formulation comprising

- Between 25-55%, w/w free-base nicotine,
- Between 15-35% w/w of lactic acid, or a combination of lactic acid and one or more pharmaceutically and biologically acceptable mono- or di-carboxylic organic acids,
- between 60-10% w/w of one or some combination of two or more pharmaceutically and biologically acceptable liquid excipients, and optionally
- Between 0-5% w/w water.

2. A formulation according to claim 1 wherein the formulation comprises between 15-35% of a combination of lactic acid and one or more mono- or di-carboxylic organic acids selected from one of the following groups of acids:

- Acids containing an aromatic group,
- Hydroxycarboxylic acids,
- Heterocyclic carboxylic acids,
- aromatic carboxylic acids,
- Terpenoid acids
- Sugar acids;,
- Pectic acids,
- Amino acids,
- Cycloaliphatic acids,
- Aliphatic carboxylic acids, and
- Keto carboxylic acids.

3. A formulation according to claim 1 wherein the formulation comprises between 15-35% of a combination of lactic acid and one or more mono- or di-carboxylic organic acids selected from the following: 1-hydroxy-2-naphthoic acid, 2,2-dichloroacetic acid, 2-hydroxyethanesulfonic acid, 2-oxoglutaric acid, 4-acetamidobenzoic acid, 4-aminosalicylic acid, acetic acid, adipic acid, ascorbic acid (L), aspartic acid (L), benzenesulfonic acid, benzoic acid, camphoric acid (+), camphor-10-sulfonic acid (+), capric acid (decanoic acid), caproic acid (hexanoic acid), caprylic acid (octanoic acid), carbonic acid, cinnamic acid, citric acid, cyclamic acid, dodecyl sulfonic 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, isobutyric acid, lactic acid (DL), lactobionic acid, lauric acid, maleic acid, malic acid (- L), malonic acid,

mandelic acid (DL), methanesulfonic acid, naphthalene-1,5-disulfonic acid, naphthalene-2-sulfonic acid, nicotinic acid, oleic acid, oxalic acid, palmitic acid, pamoic acid, propionic acid, pyroglutamic acid (- L), salicylic acid, sebacic acid, stearic acid, succinic acid, tartaric acid (+ L), thiocyanic acid, toluenesulfonic acid (p), undecylenic acid.

4. A formulation according to claim 1 wherein the formulation comprises between 15-35% of a combination of lactic acid and one or more mono- or di-carboxylic organic acids selected from the following: an Alpha-keto acid (2-oxoacid), a Beta-keto acid (3-oxoacid), and a Gamma-keto acid (4-oxoacid).

5. A formulation according to claim 1 wherein the formulation includes

- A binary system of two organic acids, one being one of lactic acid and the other being one of: benzoic acid, salicylic acid.

6. A formulation according to claim 5 wherein the formulation includes a binary system of two organic acids, one of which is lactic acid, and the molar ratio between the two acids is 1:1, and the overall combined w/w percentage of acid in the formulation is at least 25% w/w.

7. A formulation according to claim 1 wherein the one or more excipients present in the formulation is/are selected from the following: Glycerol, Vegetable Glycerin (VG), Propylene Glycol (PG), Polyethylene Glycol (PEG), and trimethylene glycol (TMG).

8. A formulation according to claim 1 which includes only a single excipient component, being one of Glycerol and Polyethylene Glycol.

9. A formulation according to claim 1 comprising

25% w/w freebase nicotine
24.3% w/w lactic acid,
2.7% w/w water, and
48% w/w glycerol.

10. A formulation according to claim 1 comprising

- 45-46%, w/w free-base nicotine,
- 31-33% w/w of lactic acid,
- 24-21% w/w polyethylene glycol.

11. A formulation according to claim 10 wherein the polyethylene glycol is a high molecular weight polyethylene glycol compound having a molecular weight of 3000.

12. An aerosolisable formulation comprising

- Between 25-50%, w/w free-base nicotine,
- Between 25-40% w/w of lactic acid, or a combination of lactic acid and one or more pharmaceutically and biologically acceptable mono- or di-carboxylic organic acids,
- Between 50-20% w/w of one or some combination of two or more pharmaceutically and biologically acceptable liquid excipients, and optionally
- Between 0-5% w/w water.