



US 20220071270A1

(19) **United States**(12) **Patent Application Publication**
SCHALLER et al.(10) **Pub. No.: US 2022/0071270 A1**(43) **Pub. Date: Mar. 10, 2022**(54) **LIQUID NICOTINE FORMULATION****Publication Classification**(71) Applicant: **Philip Morris Products S.A.**,
Neuchatel (CH)(51) **Int. Cl.***A24B 15/167* (2006.01)*A24F 40/42* (2006.01)*A24F 40/10* (2006.01)*A61K 31/465* (2006.01)*A61K 9/00* (2006.01)(72) Inventors: **Jean-Pierre SCHALLER**, Neuchatel
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Neuchatel (CH)(52) **U.S. Cl.**CPC *A24B 15/167* (2016.11); *A24F 40/42*(2020.01); *A61K 9/0078* (2013.01); *A61K**31/465* (2013.01); *A24F 40/10* (2020.01)(73) Assignee: **Philip Morris Products S.A.**,
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(57)

ABSTRACT(21) Appl. No.: **17/419,442**

A liquid nicotine formulation for an aerosol-generating system is provided, the liquid nicotine formulation including: water and one or more water-miscible solvents, the liquid nicotine formulation having a water content of greater than or equal to about 30 percent by weight and a water-miscible solvent content of greater than or equal to about 10 percent by weight, a ratio of the weight percent water content to a weight percent water-miscible solvent content of the liquid nicotine formulation being greater than or equal to about 1, the liquid nicotine formulation having a glycerine content of greater than or equal to about 6 percent by weight, and the liquid nicotine formulation having at least one of: a water content of greater than or equal to about 45 percent by weight, and a combined water and water-miscible solvent content of greater than or equal to about 70 percent by weight.

(22) PCT Filed: **Dec. 31, 2019**(86) PCT No.: **PCT/EP2019/087193**

§ 371 (c)(1),

(2) Date: **Jun. 29, 2021**(30) **Foreign Application Priority Data**

Dec. 31, 2018 (EP) 18215964.0

Dec. 31, 2018 (EP) 18215966.5

Dec. 31, 2018 (EP) 18215969.9

Dec. 31, 2018 (EP) 18215976.4

Dec. 31, 2018 (EP) 18215983.0

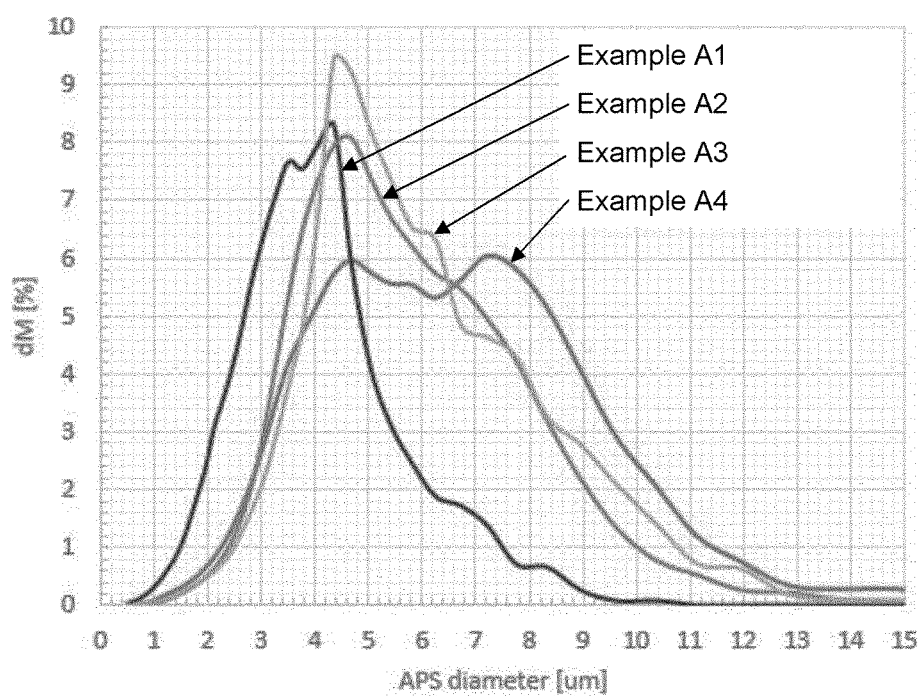


Figure 1A

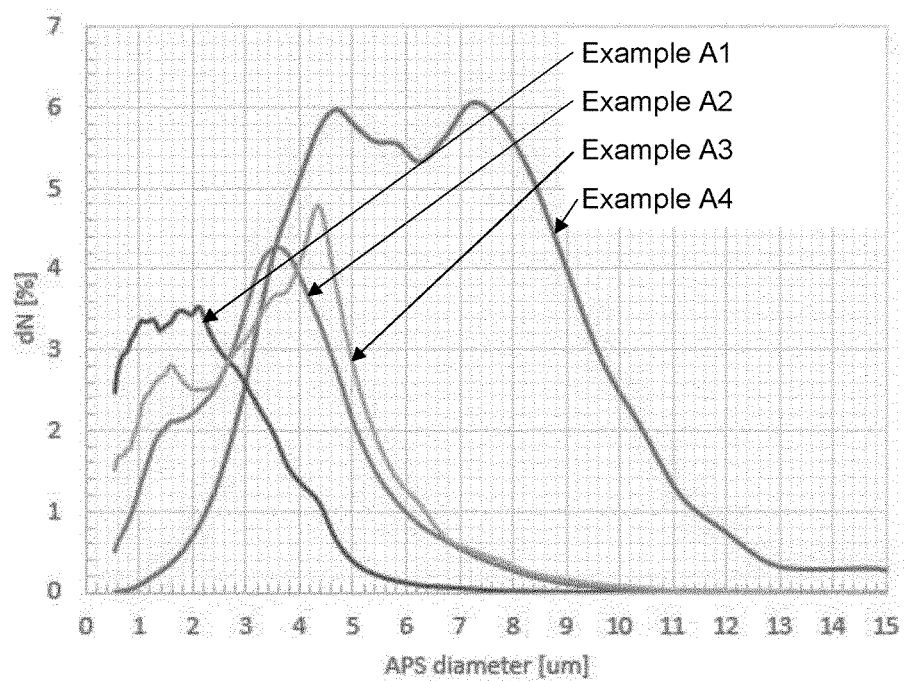


Figure 1B

LIQUID NICOTINE FORMULATION

[0001] The invention relates to a liquid nicotine formulation for use in an aerosol-generating system. In particular, the invention relates to a liquid nicotine formulation for use in an aerosol-generating system comprising a non-thermal atomiser. The invention also relates to a cartridge for an aerosol-generating system comprising the liquid nicotine formulation and an aerosol-generating system comprising the liquid nicotine formulation and an atomiser configured to generate an aerosol from the liquid nicotine formulation.

[0002] Aerosol-generating systems for delivering nicotine to a user that comprise an atomiser configured to generate an inhalable aerosol from a liquid nicotine formulation are known. Some known aerosol-generating systems comprise a thermal atomiser such as an electric heater that is configured to heat and vaporise the liquid nicotine formulation to generate an aerosol. Other known aerosol-generating systems comprise a non-thermal atomiser that is configured to generate an aerosol from the liquid nicotine formulation using, for example, impinging jet, ultrasonic or vibrating mesh technologies.

[0003] In such aerosol-generating systems, pulmonary delivery of the inhalable aerosol generated from the liquid nicotine formulation is important for user palatability and satisfaction. Nicotine adsorption through the pulmonary alveoli is rapid and efficient. By contrast, nicotine adsorption in the upper airways is slower and less efficient. Nicotine adsorption in the upper airways may also undesirably be perceived by a user as having a sensorial harshness and induce mouth and throat irritation.

[0004] The lung deposition characteristics and hence efficacy of the inhalable aerosol generated from the liquid nicotine formulation depend on the particle or droplet size of the aerosol. Typically, a small particle or droplet size is desired to maximise pulmonary nicotine delivery and retention. In particular, it is believed that a particle or droplet size of less than or equal to about 5 micrometres in diameter may be desirable to maximise pulmonary delivery.

[0005] To enhance pulmonary nicotine delivery and retention, it would be desirable to provide a liquid nicotine formulation for use in an aerosol-generating system that facilitates generation of an aerosol having a small droplet size. For example, it would be desirable to provide a liquid nicotine formulation for use in an aerosol-generating system that facilitates generation of an aerosol having a particle or droplet size of less than or equal to about 5 micrometres in diameter.

[0006] According to the invention there is provided a liquid nicotine formulation for use in an aerosol-generating system, the liquid nicotine formulation comprising water and one or more water-miscible solvents, wherein the liquid nicotine formulation has a water content of at least about 30 percent by weight and wherein the ratio of the weight percent water content to the weight percent water-miscible solvent content of the liquid nicotine formulation is greater than or equal to about 1.

[0007] According to the invention there is also provided a cartridge for use in an aerosol-generating system, the cartridge containing a liquid nicotine formulation comprising water and one or more water-miscible solvents, wherein the liquid nicotine formulation has a water content of at least about 30 percent by weight and wherein the ratio of the weight percent water content to the weight percent water-

miscible solvent content of the liquid nicotine formulation is greater than or equal to about 1.

[0008] According to the invention there is further provided an aerosol-generating system comprising: a liquid nicotine formulation comprising water and one or more water-miscible solvents, wherein the liquid nicotine formulation has a water content of at least about 30 percent by weight and wherein the ratio of the weight percent water content to the weight percent water-miscible solvent content of the liquid nicotine formulation is greater than or equal to about 1; and an atomiser configured to generate an aerosol from the liquid nicotine formulation.

[0009] As used herein with reference to the invention, the term "liquid nicotine formulation" describes a liquid formulation comprising nicotine.

[0010] As used herein with reference to the invention, the term "nicotine" describes nicotine, nicotine base or a nicotine salt. In embodiments in which the liquid nicotine formulation comprises a nicotine base or a nicotine salt, the amounts of nicotine recited herein are the amount of free base nicotine or amount of protonated nicotine, respectively.

[0011] As used herein with reference to the invention, the term "water-miscible solvent" describes a compound other than water or an organic acid that is liquid at 20° C. and mixes with water in all proportions to form a homogenous solution.

[0012] Unless stated otherwise, percentages by weight of components of the liquid nicotine formulation recited herein are based on the total weight of the liquid nicotine formulation.

[0013] In combination, a water content of at least about 30 percent by weight and a weight percent water content greater than or equal to the weight percent water-miscible solvent content facilitates generation of an inhalable aerosol having a small particle or droplet size when the liquid nicotine formulation according to the invention is used in an aerosol-generating system. This may advantageously enhance pulmonary nicotine delivery and retention.

[0014] Use of the liquid nicotine formulation according to the invention in an aerosol-generating system comprising a non-thermal atomiser is particularly advantageous.

[0015] In combination the water and one or more water-miscible solvents in the liquid nicotine formulation according to the invention may advantageously help to dissolve and stabilise polar components and ionic components of the liquid nicotine formulation.

[0016] The liquid nicotine formulation may comprise natural nicotine or synthetic nicotine.

[0017] The liquid nicotine formulation may have a nicotine content of greater than or equal to about 0.5 percent by weight.

[0018] Preferably, the liquid nicotine formulation has a nicotine content of greater than or equal to about 1 percent by weight. More preferably, the liquid nicotine formulation has a nicotine content of greater than or equal to about 1.5 percent by weight.

[0019] The liquid nicotine formulation may have a nicotine content of less than or equal to about 10 percent by weight. The liquid nicotine formulation may have a nicotine content of less than or equal to about 8 percent by weight.

[0020] Preferably, the liquid nicotine formulation has a nicotine content of less than or equal to about 5 percent by

[0059] The liquid nicotine formulation may have a combined water and water-miscible solvent content of greater than or equal to about 80 percent by weight or greater than or equal to about 85 percent by weight.

[0060] Preferably, the liquid nicotine formulation has at least one of a water content of greater than or equal to about 45 percent by weight and a combined water and water-miscible solvent content of greater than or equal to about 70 percent by weight. That is, preferably the liquid nicotine has a water content of greater than or equal to about 45 percent by weight, or a combined water and water-miscible solvent content of greater than or equal to about 70 percent by weight, or a water content of greater than or equal to about 45 percent by weight and a combined water and water-miscible solvent content of greater than or equal to about 70 percent by weight.

[0061] Preferably, the one or more water-miscible solvents are one or more water-miscible polyhydric alcohols.

[0062] As used herein with reference to the invention, the term “water-miscible polyhydric alcohol” describes a polyhydric alcohol that is liquid at 20° C. and mixes with water in all proportions to form a homogenous solution.

[0063] According to a preferred embodiment of the invention there is provided a liquid nicotine formulation for use in an aerosol-generating system, the liquid nicotine formulation comprising water and one or more water-miscible polyhydric alcohols, wherein the liquid nicotine formulation has a water content of at least about 30 percent by weight and wherein the ratio of the weight percent water content to the weight percent water-miscible polyhydric alcohol content of the liquid nicotine formulation is greater than or equal to about 1.

[0064] According to a preferred embodiment of the invention there is also provided a cartridge for use in an aerosol-generating system, the cartridge containing a liquid nicotine formulation comprising water and one or more water-miscible polyhydric alcohols, wherein the liquid nicotine formulation has a water content of at least about 30 percent by weight and wherein the ratio of the weight percent water content to the weight percent water-miscible polyhydric alcohol content of the liquid nicotine formulation is greater than or equal to about 1.

[0065] According to a preferred embodiment of the invention there is further provided an aerosol-generating system comprising: a liquid nicotine formulation comprising water and one or more water-miscible polyhydric alcohols, wherein the liquid nicotine formulation has a water content of at least about 30 percent by weight and wherein the ratio of the weight percent water content to the weight percent water-miscible polyhydric alcohol content of the liquid nicotine formulation is greater than or equal to about 1; and an atomiser configured to generate an aerosol from the liquid nicotine formulation.

[0066] As used herein with reference to the invention, the term “water-miscible polyhydric alcohol” describes a polyhydric alcohol that is liquid at 20° C. and mixes with water in all proportions to form a homogenous solution.

[0067] Preferably, the liquid nicotine formulation has a water-miscible polyhydric alcohol content of greater than or equal to about 5 percent by weight. More preferably, the liquid nicotine formulation has a water-miscible polyhydric alcohol content of greater than or equal to about 10 percent by weight. For example, the liquid nicotine formulation may have a water-miscible polyhydric alcohol content of greater

than or equal to about 15 percent by weight, greater than or equal to about 20 percent by weight or greater than or equal to about 25 percent by weight.

[0068] The liquid nicotine formulation may have a water-miscible polyhydric alcohol content of less than or equal to about 50 percent by weight.

[0069] Preferably, the liquid nicotine formulation has a water-miscible polyhydric alcohol content of less than or equal to about 45 percent by weight. More preferably, the liquid nicotine formulation has a water-miscible polyhydric alcohol content of less than or equal to about 40 percent by weight. For example, the liquid nicotine formulation may have a water-miscible polyhydric alcohol content of less than or equal to about 35 percent by weight.

[0070] The liquid nicotine formulation may have a water-miscible polyhydric alcohol content of between about 5 percent by weight and about 50 percent by weight.

[0071] Preferably, the liquid nicotine formulation has a water-miscible polyhydric alcohol content of between about 5 percent by weight and about 45 percent by weight. For example, the liquid nicotine formulation may have a water-miscible polyhydric alcohol content of between about 5 percent by weight and about 40 percent by weight or between about 5 percent by weight and about 35 percent by weight.

[0072] The liquid nicotine formulation may have a water-miscible polyhydric alcohol content of between about 10 percent by weight and about 50 percent by weight.

[0073] More preferably, the liquid nicotine formulation has a water-miscible polyhydric alcohol content of between about 10 percent by weight and about 45 percent by weight. For example, the liquid nicotine formulation may have a water-miscible polyhydric alcohol content of between about 10 percent by weight and about 40 percent by weight or between about 10 percent by weight and about 35 percent by weight.

[0074] The liquid nicotine formulation may have a water-miscible polyhydric alcohol content of between about 15 percent by weight and about 50 percent by weight, between about 15 percent by weight and about 45 percent by weight, between about 15 percent by weight and about 40 percent by weight or between about 15 percent by weight and about 30 percent by weight.

[0075] The liquid nicotine formulation may have a water-miscible polyhydric alcohol content of between about 20 percent by weight and about 50 percent by weight, between about 20 percent by weight and about 45 percent by weight, between about 20 percent by weight and about 40 percent by weight or between about 20 percent by weight and about 35 percent by weight.

[0076] The liquid nicotine formulation may have a water-miscible polyhydric alcohol content of between about 25 percent by weight and about 50 percent by weight, between about 25 percent by weight and about 45 percent by weight, between about 25 percent by weight and about 40 percent by weight or between about 25 percent by weight and about 35 percent by weight.

[0077] The liquid nicotine formulation may have a combined water and water-miscible polyhydric alcohol content of greater than or equal to about 50 percent by weight or greater than or equal to about 50 percent by weight.

[0078] Preferably the liquid nicotine formulation has a combined water and water-miscible polyhydric alcohol content of greater than or equal to about 60 percent by weight.

For example, the liquid nicotine formulation may have a combined water and water-miscible polyhydric alcohol content of greater than or equal to about 65 percent by weight. More preferably the liquid nicotine formulation has a combined water and water-miscible polyhydric alcohol content of greater than or equal to about 70 percent by weight. Most preferably, the liquid nicotine formulation has a combined water and water-miscible polyhydric alcohol content of greater than or equal to 75 percent by weight.

[0079] The liquid nicotine formulation may have a combined water and water-miscible polyhydric alcohol content of greater than or equal to about 80 percent by weight or greater than or equal to about 85 percent by weight.

[0080] Preferably, the ratio of the weight percent water content to the weight percent water-miscible polyhydric alcohol content of the liquid nicotine formulation is greater than or equal to about 1.5.

[0081] That is, preferably, the weight percent water content of the liquid nicotine formulation is at least about 1.5 times the weight percent water-miscible polyhydric alcohol content of the liquid nicotine formulation.

[0082] The ratio of the weight percent water content to the weight percent water-miscible polyhydric alcohol content of the liquid nicotine formulation may be greater than or equal to about 2, greater than or equal to about 3, greater than or equal to about 4 or greater than or equal to about 5.

[0083] That is, the weight percent water content of the liquid nicotine formulation may be at least about 2 times the weight percent water-miscible polyhydric alcohol content of the liquid nicotine formulation, at least about 3 times the weight percent water-miscible polyhydric alcohol content of the liquid nicotine formulation, at least about 4 times the weight percent water-miscible polyhydric alcohol content of the liquid nicotine formulation or at least about 5 times the weight percent water-miscible polyhydric alcohol content of the liquid nicotine formulation.

[0084] Preferably, the ratio of the weight percent water content to the weight percent of water-miscible polyhydric alcohol content of the liquid nicotine formulation is less than or equal to about 9, more preferably less than or equal to about 8.

[0085] That is, preferably the weight percent water content of the liquid nicotine formulation is less than or equal to about 9 times the weight percent water-miscible polyhydric alcohol content of the liquid nicotine formulation. More preferably, the weight percent water content of the liquid nicotine formulation is less than or equal to about 8 times the weight percent water-miscible polyhydric alcohol content of the liquid nicotine formulation.

[0086] The ratio of the weight percent water content to the weight percent water-miscible polyhydric alcohol content of the liquid nicotine formulation may be less than or equal to about 7.

[0087] That is, the weight percent water content of the liquid nicotine formulation may be less than or equal to about 7 times the weight percent water-miscible polyhydric alcohol content of the liquid nicotine formulation.

[0088] Preferably, the ratio of the weight percent water content to the weight percent water-miscible polyhydric alcohol content of the liquid nicotine formulation is between about 1 and about 9. For example, ratio of the weight percent water content to the weight percent water-miscible polyhy-

dric alcohol content of the liquid nicotine formulation may be between about 1 and about 8 or between about 1 and about 7.

[0089] More preferably, the ratio of the weight percent water content to the weight percent water-miscible polyhydric alcohol content of the liquid nicotine formulation is between about 1.5 and about 9. For example, the ratio of the weight percent water content to the weight percent water-miscible polyhydric alcohol content of the liquid nicotine formulation may be between about 1.5 and about 8 or between about 1.5 and about 7.

[0090] The ratio of the weight percent water content to the weight percent water-miscible polyhydric alcohol content of the liquid nicotine formulation may be between about 2 and about 9. For example, the ratio of the weight percent water content to the weight percent water-miscible polyhydric alcohol content of the liquid nicotine formulation may be between about 2 and about 8 or between about 2 and about 7.

[0091] The ratio of the weight percent water content to the weight percent water-miscible polyhydric alcohol content of the liquid nicotine formulation may be between about 3 and about 9. For example, the ratio of the weight percent water content to the weight percent water-miscible polyhydric alcohol content of the liquid nicotine formulation may be between about 3 and about 8 or between about 3 and about 7.

[0092] The ratio of the weight percent water content to the weight percent water-miscible polyhydric alcohol content of the liquid nicotine formulation may be between about 4 and about 9. For example, the ratio of the weight percent water content to the weight percent water-miscible polyhydric alcohol content of the liquid nicotine formulation may be between about 4 and about 8 or between about 4 and about 7.

[0093] The ratio of the weight percent water content to the weight percent water-miscible polyhydric alcohol content of the liquid nicotine formulation may be between about 5 and about 9. For example, the ratio of the weight percent water content to the weight percent water-miscible polyhydric alcohol content of the liquid nicotine formulation may be between about 5 and about 8 or between about 5 and about 7.

[0094] Preferably, the one or more water-miscible polyhydric alcohols are selected from the group consisting of 1,3-butanediol, glycerine, propylene glycol, and triethylene glycol.

[0095] More preferably, the one or more water-miscible polyhydric alcohols are selected from the group consisting of glycerine and propylene glycol.

[0096] Most preferably, the one or more water-miscible polyhydric alcohols are selected from the group consisting of vegetable glycerine and propylene glycol.

[0097] According to a preferred embodiment of the invention there is provided a liquid nicotine formulation for use in an aerosol-generating system, the liquid nicotine formulation comprising water and one or more water-miscible polyhydric alcohols selected from the group consisting of glycerine and propylene glycol, wherein the liquid nicotine formulation has a water content of at least about 30 percent by weight and wherein the ratio of the weight percent water content to the weight percent water-miscible polyhydric alcohol content of the liquid nicotine formulation is greater than or equal to about 1.

[0098] According to a preferred embodiment of the invention there is also provided a cartridge for use in an aerosol-generating system, the cartridge containing a liquid nicotine formulation comprising water and one or more water-miscible polyhydric alcohols selected from the group consisting of glycerine and propylene glycol, wherein the liquid nicotine formulation has a water content of at least about 30 percent by weight and wherein the ratio of the weight percent water content to the weight percent water-miscible polyhydric alcohol content of the liquid nicotine formulation is greater than or equal to about 1.

[0099] According to a preferred embodiment of the invention there is further provided an aerosol-generating system comprising: a liquid nicotine formulation comprising water and one or more water-miscible polyhydric alcohols selected from the group consisting of glycerine and propylene glycol, wherein the liquid nicotine formulation has a water content of at least about 30 percent by weight and wherein the ratio of the weight percent water content to the weight percent water-miscible polyhydric alcohol content of the liquid nicotine formulation is greater than or equal to about 1; and an atomiser configured to generate an aerosol from the liquid nicotine formulation.

[0100] Preferably, the liquid nicotine formulation has a combined glycerine and propylene glycol content of greater than or equal to about 5 percent by weight. More preferably, the liquid nicotine formulation has a combined glycerine and propylene glycol content of greater than or equal to about 10 percent by weight. For example, the liquid nicotine formulation may have a combined glycerine and propylene glycol content of greater than or equal to about 15 percent by weight, greater than or equal to about 20 percent by weight or greater than or equal to about 25 percent by weight.

[0101] The liquid nicotine formulation may have a combined glycerine and propylene glycol content of less than or equal to about 50 percent by weight.

[0102] Preferably, the liquid nicotine formulation has a combined glycerine and propylene glycol content of less than or equal to about 45 percent by weight. More preferably, the liquid nicotine formulation has a combined glycerine and propylene glycol content of less than or equal to about 40 percent by weight. For example, the liquid nicotine formulation may have a combined glycerine and propylene glycol content of less than or equal to about 35 percent by weight.

[0103] The liquid nicotine formulation may have a combined glycerine and propylene glycol content of between about 5 percent by weight and about 50 percent by weight.

[0104] Preferably, the liquid nicotine formulation has a combined glycerine and propylene glycol content of between about 5 percent by weight and about 45 percent by weight. For example, the liquid nicotine formulation may have a combined glycerine and propylene glycol content of between about 5 percent by weight and about 40 percent by weight or between about 5 percent by weight and about 35 percent by weight.

[0105] The liquid nicotine formulation may have a combined glycerine and propylene glycol content of between about 10 percent by weight and about 50 percent by weight.

[0106] More preferably, the liquid nicotine formulation has a combined glycerine and propylene glycol content of between about 10 percent by weight and about 45 percent by weight. For example, the liquid nicotine formulation may have a combined glycerine and propylene glycol content of

between about 10 percent by weight and about 40 percent by weight or between about 10 percent by weight and about 35 percent by weight.

[0107] The liquid nicotine formulation may have a combined glycerine and propylene glycol content of between about 15 percent by weight and about 50 percent by weight, between about 15 percent by weight and about 45 percent by weight, between about 15 percent by weight and about 40 percent by weight or between about 15 percent by weight and about 30 percent by weight.

[0108] The liquid nicotine formulation may have a combined glycerine and propylene glycol content of between about 20 percent by weight and about 50 percent by weight, between about 20 percent by weight and about 45 percent by weight, between about 20 percent by weight and about 40 percent by weight or between about 20 percent by weight and about 35 percent by weight.

[0109] The liquid nicotine formulation may have a combined glycerine and propylene glycol content of between about 25 percent by weight and about 50 percent by weight, between about 25 percent by weight and about 45 percent by weight, between about 25 percent by weight and about 40 percent by weight or between about 25 percent by weight and about 35 percent by weight.

[0110] The liquid nicotine formulation may have a combined water, glycerine and propylene glycol content of greater than or equal to about 50 percent by weight or greater than or equal to about 55 percent by weight.

[0111] Preferably, the liquid nicotine formulation has a combined water, glycerine and propylene glycol content of greater than or equal to about 60 percent by weight. For example, the liquid nicotine formulation may have a combined water, glycerine and propylene glycol content of greater than or equal to about 65 percent by weight. More preferably the liquid nicotine formulation has a combined water, glycerine and propylene glycol content of greater than or equal to about 70 percent by weight. Most preferably, the liquid nicotine formulation has a combined water, glycerine and propylene glycol content of greater than or equal to 75 percent by weight.

[0112] The liquid nicotine formulation may have a combined water, glycerine and propylene glycol content of greater than or equal to about 80 percent by weight or greater than or equal to about 85 percent by weight.

[0113] Preferably, the ratio of the weight percent water content to the combined weight percent glycerine and propylene glycol content of the liquid nicotine formulation is greater than or equal to about 1.5.

[0114] That is, preferably, the weight percent water content of the liquid nicotine formulation is at least about 1.5 times the combined weight percent glycerine and propylene glycol content of the liquid nicotine formulation.

[0115] The ratio of the weight percent water content to the combined weight percent glycerine and propylene glycol content of the liquid nicotine formulation may be greater than or equal to about 2, greater than or equal to about 3, greater than or equal to about 4 or greater than or equal to about 5.

[0116] That is, the weight percent water content of the liquid nicotine formulation may be at least about 2 times the combined weight percent glycerine and propylene glycol content of the liquid nicotine formulation, at least about 3 times the combined weight percent glycerine and propylene glycol content of the liquid nicotine formulation, at least

[0136] Preferably, the liquid nicotine formulation comprises one or more water-immiscible solvents.

[0137] As used herein with reference to the invention, the term “water-immiscible solvent” describes a compound that is liquid at 20° C. and has a water solubility at 20° C. of less than or equal to about 100 mg/ml.

[0138] Unless stated otherwise, water solubility values recited herein are the water solubility measured based on the preliminary test of OECD (1995), *Test No. 105: Water Solubility*, OECD Guidelines for the Testing of Chemicals, Section 1, OECD Publishing, Paris, <https://doi.org/10.1787/9789264069589-en>. In a stepwise procedure, increasing volumes of distilled water are added at 20° C. to 0.1 g of the sample (solid substances must be pulverized) in a 10 ml glass-stoppered measuring cylinder. However, when the substance is an acid, the sample is added to the distilled water in the first step. After each addition of an amount of water, the mixture is shaken for 10 minutes and is visually checked for any undissolved parts of the sample. If, after addition of 10 ml of water, the sample or parts of it remain undissolved, the experiment is continued in a 100 ml measuring cylinder. The approximate solubility is given in Table 1 below under that volume of water in which complete dissolution of the sample occurs.

[0139] When the solubility is low, a long time may be required to dissolve a substance and at least 24 hours should be allowed. If, after 24 hours, the substance is still not dissolved, the measuring cylinder is placed for at 40° C. in an ultrasound bath for 15 minutes and another 24 hours allowed (up to a maximum of 96 hours). If the substance is still not dissolved, the solubility is considered to be below the limit value or not soluble.

TABLE 1

ml of water in which 0.1 g of sample is soluble	0.1	0.5	1	2	10	100	>100
Approximate solubility (mg/ml)	>1000	1000 to 200	200 to 100	100 to 50	50 to 10	10 to 1	<1

[0140] The one or more water-immiscible solvents may advantageously help to dissolve and stabilise non-polar components of the liquid nicotine formulation.

[0141] The one or more water-immiscible solvents may reduce the hygroscopicity of an aerosol generated from the liquid nicotine formulation when used in an aerosol-generating system. This may advantageously reduce or prevent increases in the particle or droplet size of the aerosol when inhaled by a user as a result of adsorption of water in the respiratory tract.

[0142] Preferably, the liquid nicotine formulation comprises water, one or more water-miscible polyhydric alcohols and one or more water-immiscible solvents.

[0143] More preferably, the liquid nicotine formulation comprises water, one or more water-miscible polyhydric alcohols selected from the group consisting of glycerine and propylene glycol, and one or more water-immiscible solvents.

[0144] When used in an aerosol-generating system, the liquid nicotine formulation generates an aerosol comprising dual-phase particles or droplets comprising a water-miscible phase and a water-immiscible phase. This may advantageously reduce nicotine adsorption in the upper airways and enhance pulmonary nicotine delivery and retention. Without

wishing to be bound by theory, the improvement in pulmonary nicotine delivery and retention is believed to be due to coating or enveloping of the water-miscible phase by the water immiscible phase. This is believed to reduce nicotine evaporation and adsorption in the upper airways.

[0145] Preferably, the liquid nicotine formulation has a water-immiscible solvent content of greater than or equal to about 1 percent by weight. More preferably, the liquid nicotine formulation has a water-immiscible solvent content of greater than or equal to about 2 percent by weight. For example, the liquid nicotine formulation may have a water-immiscible solvent content of greater than or equal to about 4 percent by weight, greater than or equal to about 6 percent by weight or greater than or equal to about 8 percent by weight.

[0146] The liquid nicotine formulation may have a water-immiscible solvent content of less than or equal to about 40 percent by weight.

[0147] Preferably, the liquid nicotine formulation has a water-immiscible solvent content of less than or equal to about 35 percent by weight. More preferably, the liquid nicotine formulation has a water-immiscible solvent content of less than or equal to about 30 percent by weight. For example, the liquid nicotine formulation may have a water-immiscible solvent content of less than or equal to about 25 percent by weight, less than or equal to about 20 percent by weight or less than or equal to about 15 percent by weight.

[0148] The liquid nicotine formulation may have a water-immiscible solvent content of between about 1 percent by weight and about 40 percent by weight.

[0149] Preferably, the liquid nicotine formulation has a water-immiscible solvent content of between about 1 per-

cent by weight and about 35 percent by weight. For example, the liquid nicotine formulation may have a water-immiscible solvent content of between about 1 percent by weight and about 30 percent by weight, between about 1 percent by weight and about 25 percent by weight, between about 1 percent by weight and about 20 percent by weight or between about 1 percent by weight and about 15 percent by weight.

[0150] The liquid nicotine formulation may have a water-immiscible solvent content of between about 2 percent by weight and about 40 percent by weight.

[0151] More preferably, the liquid nicotine formulation has a water-immiscible solvent content of between about 2 percent by weight and about 35 percent by weight. For example, the liquid nicotine formulation may have a water-immiscible solvent content of between about 2 percent by weight and about 30 percent by weight, between about 2 percent by weight and about 25 percent by weight, between about 2 percent by weight and about 20 percent by weight or between about 2 percent by weight and about 15 percent by weight.

[0152] The liquid nicotine formulation may have a water-immiscible solvent content of between about 4 percent by weight and about 40 percent by weight or between about 4

percent by weight and about 35 percent by weight. For example, the liquid nicotine formulation may have a water-immiscible solvent content of between about 4 percent by weight and about 30 percent by weight, between about 4 percent by weight and about 25 percent by weight, between about 4 percent by weight and about 20 percent by weight or between about 4 percent by weight and about 15 percent by weight.

[0153] The liquid nicotine formulation may have a water-immiscible solvent content of between about 6 percent by weight and about 40 percent by weight or between about 6 percent by weight and about 35 percent by weight. For example, the liquid nicotine formulation may have a water-immiscible solvent content of between about 6 percent by weight and about 30 percent by weight, between about 6 percent by weight and about 25 percent by weight, between about 6 percent by weight and about 20 percent by weight or between about 6 percent by weight and about 15 percent by weight.

[0154] The liquid nicotine formulation may have a water-immiscible solvent content of between about 8 percent by weight and about 40 percent by weight or between about 8 percent by weight and about 35 percent by weight. For example, the liquid nicotine formulation may have a water-immiscible solvent content of between about 8 percent by weight and about 30 percent by weight, between about 8 percent by weight and about 25 percent by weight, between about 8 percent by weight and about 20 percent by weight or between about 8 percent by weight and about 15 percent by weight.

[0155] Preferably, the one or more water-immiscible solvents comprise one or more partially water-soluble solvents.

[0156] As used herein with reference to the invention, the term “partially water-soluble solvent” describes a compound that is liquid at 20° C. and has a water solubility at 20° C. of between about 20 mg/ml and about 100 mg/ml.

[0157] The one or more partially water-soluble solvents may have a maximum carbon chain length of less than or equal to 12. For example, the one or more partially water-soluble solvents may have a maximum carbon chain length of less than or equal to 10.

[0158] Suitable partially water-soluble solvents include, but are not limited to polysorbate 80, triacetin and triethyl citrate.

[0159] Preferably, the one or more water-immiscible solvents comprise one or more water-insoluble solvents.

[0160] As used herein with reference to the invention, the term “water-insoluble solvent” describes a compound that is liquid at 20° C. and has a water solubility at 20° C. of less than or equal to about 5 mg/ml.

[0161] The one or more water-insoluble solvents may have a maximum carbon chain length of less than or equal to 30. For example, the one or more water-insoluble solvents may have a maximum carbon chain length of less than or equal to 20, less than or equal to 18, less than or equal to 16, less than or equal to 14 or less than or equal to 12.

[0162] Suitable water-insoluble solvents include, but are not limited to oleic acid and MIGLYOL® (mixture of decanoyl- and octanoyl glycerides).

[0163] More preferably, the one or more water-immiscible solvents comprise one or more partially water-soluble solvents and one or more water-insoluble solvents.

[0164] Preferably, the liquid nicotine formulation comprises one or more water-soluble organic acids.

[0165] As used herein with reference to the invention, the term “water-soluble organic acid” describes an organic acid having a water solubility at 20° C. of greater than or equal to about 500 mg/ml.

[0166] The one or more water-soluble organic acids may advantageously bind nicotine in the liquid nicotine formulation through formation of one or nicotine salts.

[0167] The one or more nicotine salts may advantageously be dissolved and stabilised in the water and the one or more water-miscible solvents. In embodiments in which the liquid nicotine formulation comprises water, one or more water-miscible solvents and one or more water-immiscible solvents, this may advantageously reduce nicotine adsorption in the upper airways and enhance pulmonary nicotine delivery and retention as discussed above.

[0168] More preferably, the liquid nicotine formulation comprises one or more water-soluble carboxylic acids.

[0169] Suitable water-soluble carboxylic acids include, but are not limited to, acetic acid, citric acid, lactic acid, levulinic acid, malic acid, malonic acid and pyruvic acid.

[0170] Most preferably, the liquid nicotine formulation comprises lactic acid.

[0171] Preferably, the liquid nicotine formulation has a water-soluble organic acid content of greater than or equal to about 2 percent by weight. More preferably, the liquid nicotine formulation has a water-soluble organic acid content of greater than or equal to about 3 percent by weight.

[0172] Preferably, the liquid nicotine formulation has a water-soluble organic acid content of less than or equal to about 8 percent by weight. More preferably, the liquid nicotine formulation has a water-soluble organic acid content of less than or equal to about 6 percent by weight.

[0173] Preferably, the liquid nicotine formulation has a water-soluble organic acid content of between about 2 percent by weight and about 8 percent by weight. For example, the liquid nicotine formulation may have a water-soluble organic acid content of between about 2 percent by weight and about 6 percent by weight.

[0174] More preferably, the liquid nicotine formulation has a water-soluble organic acid content of between about 3 percent by weight and about 8 percent by weight. For example, the liquid nicotine formulation may have a water-soluble organic acid content of between about 2 percent by weight and about 6 percent by weight.

[0175] The liquid nicotine formulation may be a substantially uncaffeinated liquid nicotine formulation.

[0176] As used herein with reference to the invention, the term “substantially uncaffeinated liquid nicotine formulation” describes a liquid nicotine formulation having a caffeine content of less than 0.5 percent by weight. For example, the liquid nicotine formulation may have a caffeine content of less than about 0.4 percent by weight, less than about 0.3 percent by weight or less than about 0.2 percent by weight.

[0177] The liquid nicotine formulation may be a substantially caffeine-free liquid nicotine formulation.

[0178] As used herein with reference to the invention, the term “substantially caffeine-free liquid nicotine formulation” describes a liquid nicotine formulation having a caffeine content of less than about 0.1 percent by weight.

[0179] The liquid nicotine formulation may be a caffeine-free liquid nicotine formulation.

[0180] As used herein with reference to the invention, the term “caffeine-free liquid nicotine formulation” describes a liquid nicotine formulation having a caffeine content of 0 percent by weight.

[0181] As used herein with reference to the invention, the term “caffeine” describes caffeine or a caffeine salt. When referring to a caffeine salt, the amounts of caffeine recited herein are the amount of caffeine cation.

[0182] The liquid nicotine formulation may comprise one or more flavourants. Suitable flavourants include, but are not limited to, menthol.

[0183] Preferably, the liquid nicotine formulation has a flavourant content of less than or equal to about 4 percent by weight. More preferably, the liquid nicotine formulation has a flavourant content of less than or equal to about 3 percent by weight.

[0184] According to the invention there is also provided a cartridge for use in an aerosol-generating system, the cartridge containing a liquid nicotine formulation according to the invention.

[0185] The cartridge may comprise an atomiser configured to generate an aerosol from the liquid nicotine formulation.

[0186] A cartridge containing the liquid nicotine formulation and an atomiser configured to generate an aerosol from the liquid nicotine formulation may be referred to as a “cartomiser”.

[0187] The atomiser may be a thermal atomiser.

[0188] As used herein with reference to the invention, the term “thermal atomiser” describes an atomiser that is configured to heat the liquid nicotine formulation to generate an aerosol.

[0189] The cartridge may comprise any suitable type of thermal atomiser.

[0190] The thermal atomiser may comprise a heater and a liquid transport element configured to transport liquid nicotine formulation to the heater.

[0191] The liquid transport element may comprise a capillary wick. The heater may comprise a heater coil.

[0192] The thermal atomiser may comprise an electric heater. For example, the thermal atomiser may comprise an electric heater comprising a resistive heating element or an inductive heating element.

[0193] Preferably, the atomiser is a non-thermal atomiser.

[0194] As used herein with reference to the invention, the term “non-thermal atomiser” describes an atomiser that is configured to generate an aerosol from the liquid nicotine formulation by means other than heating.

[0195] The cartridge may comprise any suitable type of non-thermal atomiser.

[0196] For example, the non-thermal atomiser may be an impinging jet atomiser, an ultrasonic atomiser or a vibrating mesh atomiser.

[0197] According to the invention there is further provided an aerosol-generating system comprising a liquid nicotine formulation according to the invention and an atomiser configured to generate an aerosol from the liquid nicotine formulation.

[0198] The atomiser may be a thermal atomiser.

[0199] The aerosol-generating system may comprise any suitable type of thermal atomiser.

[0200] The thermal atomiser may comprise a heater and a liquid transport element configured to transport liquid nicotine formulation to the heater.

[0201] The liquid transport element may comprise a capillary wick. The heater may comprise a heater coil.

[0202] The thermal atomiser may comprise an electric heater. For example, the thermal atomiser may comprise an electric heater comprising a resistive heating element or an inductive heating element.

[0203] Preferably, the atomiser is a non-thermal atomiser.

[0204] The aerosol-generating system may comprise any suitable type of non-thermal atomiser.

[0205] For example, the non-thermal atomiser may be an impinging jet atomiser, an ultrasonic atomiser or a vibrating mesh atomiser.

[0206] The aerosol-generating system may comprise: a cartridge according to the invention containing the liquid nicotine formulation; and an aerosol-generating device comprising a housing defining a device cavity configured to receive at least a portion of the cartridge.

[0207] The aerosol-generating system may comprise: a consumable cartridge according to the invention containing the liquid nicotine formulation; and a reusable aerosol-generating device comprising a housing defining a device cavity configured to receive at least a portion of the cartridge.

[0208] The aerosol-generating device may comprise a battery and control electronics.

[0209] The aerosol-generating system may comprise: a cartridge according to the invention containing the liquid nicotine formulation and the atomiser; and an aerosol-generating device comprising a housing defining a device cavity configured to receive at least a portion of the cartridge.

[0210] The aerosol-generating system may comprise: a cartridge according to the invention containing the liquid nicotine formulation; and an aerosol-generating device comprising a housing defining a device cavity configured to receive at least a portion of the cartridge and the atomiser.

[0211] For the avoidance of doubt, features described above in relation to one aspect of the invention may also be applicable to other aspects of the invention. In particular, features described above in relation to the liquid nicotine formulation of the invention may also relate, where appropriate, to the cartridge of the invention and the aerosol-generating system of the invention. Similarly, features described above in relation to the cartridge of the invention may also relate, where appropriate, to the aerosol-generating system of the invention, and vice versa.

[0212] Embodiments of the invention will now be described, by way of example only, with reference to the following examples and accompanying drawings, in which:

[0213] FIGS. 1A and 1B show the aerodynamic size distribution of aerosols generated from a liquid nicotine composition according to the invention using four aerosol-generating systems comprising non-thermal atomisers.

EXAMPLES

[0214] Four liquid nicotine formulations according to the invention (Examples A, B, C and D) were prepared having the compositions shown in Table 2.

TABLE 2

Example	A	B	C	D
Nicotine (% by weight)	2.7	2.7	2.7	2
Water (% by weight)	80	60	60	31

TABLE 2-continued

Example		A	B	C	D
Vegetable Glycerine (% by weight)	water-miscible polyhydric	8.7	25	25	31
Propylene Glycol (% by weight)	alcohol	1.5	4.2	4.2	0
(Water):(Glycerine and Polypropylene Glycol)		92:10	12:5	12:5	1:1
Triacetin (% by weight)	partially water- soluble solvent	0.9	2	2	0
Triethyl Citrate (% by weight)		2	2	10	30
Polysorbate 80 (% by weight)		0	0	0	1
Lactic Acid (% by weight)	water-soluble organic acid	4.3	4.3	4.3	3
Flavourants (% by weight)		0	0	0	2

[0215] Aerosols were generated from the liquid nicotine composition according to the invention of Example A using the four aerosol-generating systems comprising non-thermal atomisers shown in Table 3. The aerodynamic size distributions of the aerosols were measured using an Aerodynamic Particle Sizer® (APS™) Model 3321 spectrometer from TSI Incorporated. The results are shown in FIGS. 1A and 1B.

TABLE 3

Example	Non-thermal aerosol-generating system
Example A1	Impinging jet nebulizer (nozzle opening: 10 micrometres; driving force: 51N)
Example A2	OMRON Healthcare MicroAIR U100 passive mesh nebulizer (driven by 50 Vpp at 177 kHz with 2 Hz modulation; mesh hole diameter: about 4 micrometres; mesh hole to hole distance about 60 micrometres)
Example A3	Air Wick® Essential Mist Diffuser active mesh nebulizer (120-180 kHz; mesh hole diameter: 4-8 micrometres)
Example A4	Surface Acoustic Wave (SAW) device (double engine operation with each side driven by 600 mVpp at 42.122 MHz with 500 Hz modulation)

[0216] FIG. 1A shows the differential mass concentration (dM) against aerodynamic diameter (APS diameter) of the aerosols and FIG. 1B shows the particle differential number concentration (dN) against aerodynamic diameter (APS diameter) of the aerosols.

[0217] As shown by FIGS. 1A and 1B, use of the liquid nicotine composition according to the invention of Example A in the four aerosol-generating systems advantageously generates aerosols exhibiting a small droplet size.

1.-15. (canceled)

16. A liquid nicotine formulation for an aerosol-generating system, the liquid nicotine formulation comprising:

water and one or more water-miscible solvents,

wherein the liquid nicotine formulation has a water content of greater than or equal to about 30 percent by weight and a water-miscible solvent content of greater than or equal to about 10 percent by weight,

wherein a ratio of the weight percent water content to a weight percent water-miscible solvent content of the liquid nicotine formulation is greater than or equal to about 1,

wherein the liquid nicotine formulation has a glycerine content of greater than or equal to about 6 percent by weight, and

wherein the liquid nicotine formulation has at least one of:
a water content of greater than or equal to about 45 percent by weight, and

a combined water and water-miscible solvent content of greater than or equal to about 70 percent by weight.

17. The liquid nicotine formulation according to claim 16, wherein the ratio of a weight percent water content to the weight percent water-miscible solvent content of the liquid nicotine formulation is less than or equal to about 8.

18. The liquid nicotine formulation according to claim 16, wherein the ratio of the weight percent water content to the weight percent water-miscible solvent content of the liquid nicotine formulation is greater than or equal to about 1.5.

19. The liquid nicotine formulation according to claim 16, wherein the liquid nicotine formulation has a water-miscible solvent content of less than or equal to about 40 percent by weight.

20. The liquid nicotine formulation according to claim 16, wherein the liquid nicotine formulation has a combined water and water-miscible solvent content of at least about 75 percent by weight.

21. The liquid nicotine formulation according to claim 16, wherein the one or more water-miscible solvents are one or more water-miscible polyhydric alcohols.

22. The liquid nicotine formulation according to claim 16, further comprising one or more water-immiscible solvents having a water solubility at 20° C. of less than or equal to about 100 mg/ml,

wherein the liquid nicotine formulation has a water-immiscible solvent content of greater than or equal to about 2 percent by weight.

23. The liquid nicotine formulation according to claim 22, wherein the one or more water-immiscible solvents comprise one or more partially water-soluble solvents having a water solubility at 20° C. of between about 20 mg/ml and about 100 mg/ml and one or more water-insoluble solvents having a water solubility at 20° C. of less than or equal to about 5 mg/ml.

24. The liquid nicotine formulation according to claim 16, further comprising one or more water-soluble organic acids, wherein the liquid nicotine formulation has a water-soluble organic acid content of at least about 2 percent by weight.

25. A cartridge for an aerosol-generating system, the cartridge containing a liquid nicotine formulation according to claim 16.

26. The cartridge according to claim 25, further comprising an atomiser configured to generate an aerosol from the liquid nicotine formulation.

27. An aerosol-generating system, comprising:

a liquid nicotine formulation according to claim 16; and
an atomiser configured to generate an aerosol from the liquid nicotine formulation.

28. The cartridge according to claim **26**, wherein the atomiser is a non-thermal atomiser.

29. The aerosol-generating system according to claim **28**, wherein the atomiser is a non-thermal atomiser.

30. The cartridge according to claim **26**, wherein the atomiser is a thermal atomiser comprising a heater and a liquid transport element configured to transport liquid nicotine formulation to the heater.

31. The aerosol-generating system according to claim **27**, wherein the atomiser is a thermal atomiser comprising a heater and a liquid transport element configured to transport liquid nicotine formulation to the heater.

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