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(54) **NICOTINE ORAL DELIVERY COMPOSITION**

(57) A nicotine oral delivery composition comprising a source of nicotine and a proflavour compound, wherein the proflavour compound comprises a flavour component and a support component joined by an enzymatically

cleavable bond, wherein the nicotine oral delivery compound is in solid form, and wherein the enzymatically cleavable bond is not a glycosidic bond.

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Description**Field**

5 **[0001]** The present invention relates to a nicotine oral delivery composition which is in solid form. In particular, the present invention relates to a nicotine oral delivery composition comprising a source of nicotine and a proflavour compound comprising a flavour component and a support component joined by an enzymatically cleavable bond, wherein the enzymatically cleavable bond is not a glycosidic bond. The present invention also relates to a nicotine oral delivery product comprising a pouch and a nicotine oral delivery composition enclosed within the pouch and methods of making
10 such products. The present invention also relates to uses of the nicotine oral delivery composition and nicotine oral delivery product.

Background

15 **[0002]** Nicotine oral delivery compositions and products are means of administering nicotine to a user in a pleasurable manner and may be used as an alternative to smoking articles such as cigarettes. Nicotine oral delivery products are typically known as a "smokeless" product and can comprise tobacco material or be tobacco-free.

[0003] Nicotine oral delivery products typically take the form of a nicotine composition enclosed within a pouch. The nicotine oral delivery products are typically placed between the upper or lower gum and lip or cheek of a user and are
20 retained in this position for a certain period of time. In the case of the pouched nicotine oral delivery compositions, saliva passes into the interior of the pouch and components including flavour and nicotine are dissolved and subsequently diffuse into a user's mouth.

[0004] It is desirable to provide a nicotine oral delivery product that effectively delivers nicotine to a user, whilst maintaining a pleasant taste and mouth-feel.

25 **[0005]** Flavour is an important component of the nicotine oral delivery compositions. Flavouring substances are typically volatile compounds with a limited longevity at room temperature. In particular, the lifespan of flavouring substances is typically short, in comparison with the duration of consumption of the nicotine oral delivery composition. As a consequence, the flavour quality and/or intensity of the nicotine oral delivery composition may reduce over time.

[0006] It is desirable to provide a nicotine oral delivery composition that addresses at least one disadvantage of the
30 prior art, whether identified here or elsewhere, or to provide an alternative to existing nicotine oral delivery compositions.

Summary of the Invention

35 **[0007]** According to aspects of the present invention, there are provided a nicotine oral delivery composition and product, a method of forming a nicotine oral delivery product and the use of a nicotine oral delivery composition and/or product to deliver nicotine to a user. Other features of the invention will be apparent from the dependent claims, and from the description which follows.

[0008] According to a first aspect of the present invention, there is provided a nicotine oral delivery composition comprising a source of nicotine and a proflavour compound, wherein the proflavour compound comprises a flavour
40 component and a support component joined by an enzymatically cleavable bond, wherein the nicotine oral delivery composition is in solid form, and wherein the enzymatically cleavable bond is not a glycosidic bond.

[0009] According to a second aspect of the present invention, there is provided a nicotine oral delivery product comprising a pouch and a nicotine oral delivery composition according to any preceding claim contained within the pouch, suitably wherein the pouch is water-insoluble and/or is permeable for saliva.

45 **[0010]** According to a third aspect of the present invention, there is provided a method of making the nicotine oral delivery product according to the second aspect, the method comprising enclosing the nicotine oral delivery composition according to the first aspect in the pouch and sealing the pouch.

[0011] According to a fourth aspect of the present invention, there is provided a use of the nicotine oral delivery composition according to the first aspect or a nicotine oral delivery product according to the second aspect for oral
50 delivery of nicotine.

[0012] According to a fifth aspect of the present invention, there is provided a method for oral delivery of nicotine, the method comprising placing a nicotine oral delivery product according to the second aspect into a user's mouth.

[0013] Features described in relation to the second, third, fourth and fifth aspects may have any of the suitable features and advantages described in relation to the first aspect.

55 **[0014]** Notably, the nicotine oral delivery product of the present invention may effectively deliver nicotine to a user, whilst having a pleasant taste and mouth-feel.

[0015] The compositions, products, uses and methods of the present invention provide an alternative to current nicotine compositions, products, uses and methods. The flavour component, when bonded to a support component, has an

improved stability at ambient temperature when compared to the analogous flavour compound not bonded to a support component. In particular, the support component, which is less volatile than the flavour component, provides stability to the proflavour compound, such that the proflavour compound typically is stable at ambient temperature. The flavour component bonded to the support component thus has an extended lifespan and a longer lasting flavour effect is observed in use. Further, these features allow for the controlled release of flavour and offer an enhanced user experience.

Detailed Description of the Invention

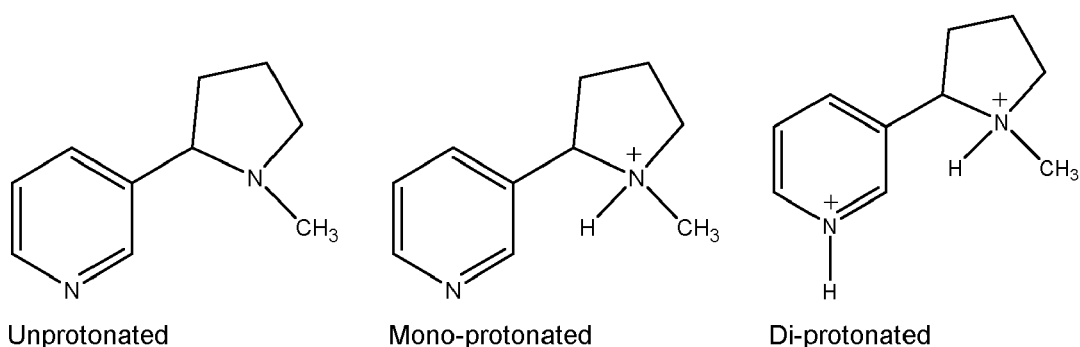
[0016] Unless otherwise stated, the following terms used in the specification and claims have the meanings set out below.

[0017] The first aspect of the invention provides a nicotine oral delivery composition comprising a source of nicotine and a proflavour compound, wherein the proflavour compound comprises a flavour component and a support component joined by an enzymatically cleavable bond, wherein the nicotine oral delivery composition is in solid form, and wherein the enzymatically cleavable bond is not a glycosidic bond.

[0018] The nicotine oral delivery composition comprises a source of nicotine. By "source of nicotine" we mean any source providing nicotine in a form that can be solubilised by saliva. The source of nicotine thus provides and/or delivers nicotine. Therefore nicotine may be described as the "active ingredient" of the composition of the first aspect. The source of nicotine may be any suitable source of nicotine. The source of nicotine may be a pharmaceutically acceptable source of nicotine. It is noted that some sources of nicotine may be completely soluble in saliva, whilst others may remain insoluble but provide nicotine in a form that can be solubilised by saliva. The term "soluble in saliva" and like terms used herein simply refer to a component which has a solubility in saliva that is adequate for its intended use.

[0019] Examples of suitable sources of nicotine include tobacco, nicotine salts, free-base nicotine (otherwise referred to as unprotonated nicotine), stabilised nicotine, and combinations thereof. The source of nicotine may comprise two or more alternative sources of nicotine.

[0020] As a non-limiting example, the nicotine source may be a nicotine salt. Examples of nicotine salts include mono- or di-protonated nicotine. For the avoidance of doubt, unprotonated (or free-base), mono-protonated and di-protonated nicotine each have the following structures:



[0021] For example, when the nicotine oral delivery composition has a pH below about 6, the nicotine salt typically comprises a mixture of mono- and di-protonated nicotine. When the nicotine oral delivery composition has a pH above about 6 and below about 8.5, the nicotine salt typically comprises a mixture of un- and mono-protonated nicotine. When the nicotine oral delivery composition has a pH above about 8.5, the nicotine salt is typically unprotonated nicotine.

[0022] References to tobacco include any part, including leaves, flowers or stems, of any member of the genus *Nicotiana*, and reconstituted material thereof.

[0023] Suitable nicotine salts include, but are not limited to, nicotine hydrochloride, nicotine dihydrochloride, nicotine monotartrate, nicotine bitartrate, nicotine bitartrate dihydrate, nicotine sulphate, nicotine zinc chloride monohydrate and nicotine salicylate, and mixtures thereof.

[0024] Free-base nicotine may be synthetically produced or extracted from tobacco.

[0025] Stabilised nicotine refers to nicotine bound to, adsorbed to, absorbed into, enclosed into or forming a complex or any other non-covalent binding with another component(s). A number of stabilised nicotine combinations are well known in the art. Examples of stabilised nicotine include, but are not limited to, nicotine bound to an ion exchange resin such as a cation exchange resin, for example, Amberlite IRP 64 derived from a copolymer of methacrylic acid and divinylbenzene; nicotine bound to a zeolite; nicotine bound to cellulose and cellulose derivatives (such as microcrystalline cellulose), as well as nicotine bound to starch microspheres and betacyclodextrin inclusion complexes.

[0026] The source of nicotine may comprise tobacco. The source of nicotine may comprise tobacco and a further

source of nicotine, for example a further source of nicotine selected from a nicotine salt, free-base nicotine, stabilised nicotine, or combinations thereof. As will be known by the skilled person, nicotine typically constitutes approximately 0.6 to 3.0% by weight of the dry weight of tobacco.

[0027] The nicotine oral delivery composition of the first aspect of the present invention may be substantially free of tobacco. The nicotine oral delivery composition of the present invention may be completely free of tobacco. The source of nicotine may therefore be selected from a nicotine salt, free-base nicotine, stabilised nicotine, or combinations thereof.

[0028] As used herein, the term "substantially free" means that the material being discussed is present in the composition, if at all, as an incidental impurity. In other words, the material does not affect the properties of the composition. As used herein, the term "completely free" means that the material being discussed is not present in the composition at all.

[0029] Suitably, the source of nicotine is stabilised nicotine. Suitably, the source of nicotine is nicotine polacrilex (nicotine bound to an ion-exchange resin such as Amberlite IRP64 or Purolite C115HMR or Doshion P551).

[0030] The source of nicotine may be present in the nicotine oral delivery composition in any suitable amount. Preferably, the nicotine oral delivery composition comprises from 0.1 to 20 wt% of the source of nicotine, such as from 0.2 to 18 wt%, or even from 0.5 to 15 wt%, of the source of nicotine, based on the total weight of the composition.

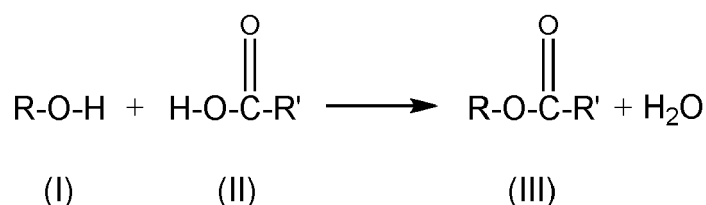
[0031] The source of nicotine may provide from 1 to 40 mg/g of nicotine per nicotine oral delivery composition, calculated as nicotine in the form of free-base nicotine. Preferably, the source of nicotine provides 1 to 40 mg/g, such as 2 to 30 mg/g, of nicotine per nicotine oral delivery composition, calculated as nicotine in the form of free-base nicotine, and more preferably from 3 to 20 mg/g of nicotine per nicotine oral delivery composition, calculated as nicotine in the form of free-base nicotine.

[0032] The nicotine oral delivery composition comprises a proflavour compound. The nicotine oral delivery composition may comprise one or more, for example two or more, proflavour compounds.

[0033] The term "proflavour compound" refers to a compound comprising a flavour component and a support component joined by an enzymatically cleavable bond. In other words, the flavour component and the support component are joined by an enzymatically cleavable bond and thereby form the proflavour compound. The enzymatically cleavable bond is a covalent bond. Suitably the proflavour compound consists essentially of a flavour component and a support component joined by an enzymatically cleavable bond. Suitably the proflavour compound consists of a flavour component and a support component joined by an enzymatically cleavable bond.

[0034] The proflavour compound comprising a flavour component and a support component is suitably formed from the reaction between a flavour compound and a support compound. In other words, a flavour compound and a support compound react to form the proflavour compound, wherein the proflavour compound comprises a flavour component derived from the flavour compound and a support component derived from the support compound. Suitably, the flavour and support components each differ chemically to the flavour and support compounds respectively following their reaction.

[0035] The following Scheme 1 is provided as an example to illustrate what is meant by the terms flavour component, support component, flavour compound and support compound:



Scheme 1

[0036] In Scheme 1, the proflavour compound is an ester compound (III). The ester compound (III) is formed by the reaction of an alcohol (I), which may be termed a flavour compound, and a carboxylic acid (II), which may be termed a support compound. The ester or proflavour compound (III) so formed comprises a flavour component R-O- and a support component -C(O)-R', which components are joined by an enzymatically cleavable covalent bond. Upon cleavage of this bond, the flavour component R-O- and the support component -C(O)-R' may be released to reform and provide the alcohol (or flavour) compound (I) and the carboxylic acid (or support) compound (II).

[0037] In the proflavour compound, the flavour component and the support component are joined by an enzymatically cleavable bond. A flavour compound and a support compound are respectively released following cleavage of the bond between the flavour component and the support component. Therefore, the flavour component is derived from a flavour compound and the support component is derived from a support compound.

[0038] The term "flavour compound" refers to any compound that provides flavour to a user. The proflavour compound releases a flavour compound when the bond between the flavour component and the support component is cleaved. This may occur upon contact of the proflavour compound with a suitable enzyme, such as an enzyme present in saliva. The flavour compound may be pharmaceutically acceptable.

[0039] The term "support compound" refers to any compound with which a flavour compound may react to form a

proflavour compound in which the flavour component is supported and/or stabilised. The support component may act to reduce the volatility of the flavour compound. The support compound may be pharmaceutically acceptable.

[0040] Suitably, unlike the flavour compound, the proflavour compound itself has no flavouring properties. Suitably, the proflavour compound is less volatile at room temperature than the flavour compound, because of the presence of the support component.

[0041] Suitably, the flavouring properties of the flavour compound may be restored by cleavage of the bond between the flavour component and the support component. In the context of the present invention, the proflavour compound therefore acts as a precursor to the flavour compound comprised in the proflavour compound. The release of the flavour compound occurs when the (suitably covalent) bond between the flavour component and the support component is cleaved, for example upon contact with an enzyme.

[0042] As used herein, the term "bonded" means that the flavour component is covalently bonded to the support component to form a proflavour compound. Typically, the proflavour compound comprises a covalent bond that can be cleaved by an enzyme to release a flavour compound.

[0043] Suitably, the enzymatically cleavable bond may be cleaved by reaction with an enzyme present in saliva. Suitably, the enzymatically cleavable bond may be cleaved via a hydrolysis reaction. Suitably, the enzymatically cleavable bond may be cleaved following contact of the proflavour compound with saliva. Suitably, the flavour component is releasable from the support component following contact with saliva.

[0044] Suitably, the enzymatically cleavable bond may be cleaved following contact of the proflavour compound with at least one endogenous enzyme present in saliva. Suitably, the flavour component is releasable from the support component following contact with at least one endogenous enzyme present in saliva.

[0045] Suitably, the enzymatically cleavable bond may be cleaved following contact of the proflavour compound with at least one endogenous enzyme selected from lipases, proteases, esterases, anhydrases and derivatives and mixtures thereof. Suitably, the flavour component is releasable from the support component following contact with at least one endogenous enzyme selected from lipases, proteases, esterases, anhydrases and derivatives and mixtures thereof.

[0046] Suitably, the enzymatically cleavable bond may be cleaved following contact of the proflavour compound with at least one enzyme selected from carboxylesterase, cholesterol esterase, carbonic anhydrase, lipase, choline esterase, salivary α -amylase, and mixtures thereof. Suitably, the flavour component is releasable from the support component following contact with at least one enzyme selected from carboxylesterase, cholesterol esterase, carbonic anhydrase, lipase, choline esterase, salivary α -amylase, and mixtures thereof.

[0047] Suitably, the enzymatically cleavable bond may be selected from an ester bond, an amide bond or an anhydride bond. More suitably, the enzymatically cleavable bond may be an ester bond.

[0048] Suitably, the proflavour compound may be selected from an ester compound, an amide compound, an anhydride compound or a combination thereof. More suitably, the proflavour compound may be an ester compound. The proflavour compound may be an ester compound and the bond between the flavour component and the support component may be an ester bond. Such an ester bond may be cleavable by an esterase enzyme, for example by an enzyme with total salivary esterase activity (TSEA) which includes enzymes selected from carboxylesterase, cholesterol esterase, carbonic anhydrase, lipase and choline esterase. The ester compound is suitably formed by reaction of an alcohol and an acid (for example a carboxylic acid). Such esterification reactions are well known to persons skilled in the art.

[0049] Suitably, when the ester compound is formed by reaction of an alcohol and a carboxylic acid, either the flavour component or the support component is derived from the alcohol and the other of the flavour component and the alcohol component is derived from the carboxylic acid. In other words, the ester compound may be formed by reaction of an alcohol and a carboxylic acid, wherein the alcohol is a flavour or support compound, and the carboxylic acid is the other of the flavour or support compound.

[0050] Suitably, when the ester compound is formed by reaction of an alcohol and a carboxylic acid, the support component is derived from the alcohol and the flavour component is derived from the carboxylic acid.

[0051] When the proflavour compound is an ester compound, the flavour compound released upon cleavage of the ester bond may be a carboxylic acid. In this case, the support compound used to form the ester and released upon cleavage of the ester bond may suitably be an alcohol. Thus, the flavour component may suitably be derived from a carboxylic acid. The carboxylic acid may be any aliphatic or aromatic carboxylic acid. The carboxylic acid may contain one or more carboxylic acid (COOH) functional groups.

[0052] For example, the flavour component may be derived from a polycarboxylic acid, defined herein as a carboxylic acid containing two or more carboxylic acid functional groups. For example, the flavour component may be derived from a di-carboxylic acid or a tri-carboxylic acid. The flavour component may be derived from one or more of oxalic acid, citric acid and malic acid. The flavour component may be derived from a monocarboxylic acid. The flavour component may be derived from a hydroxy-substituted carboxylic acid, defined herein as a compound comprising at least one carboxylic acid functional group and at least one hydroxyl function group, such as an α -hydroxy acid or a phenolic acid. The flavour component may suitably be derived from one or more of vanillic acid and lactic acid. The flavour component may be derived from a fatty acid. The fatty acid may be saturated, unsaturated or a mixture thereof. The flavour component may

suitably be derived from one or more of butyric acid, caproic acid, caprylic acid and lauric acid.

[0053] The flavour component may suitably be derived from a carboxylic acid selected from one or more of vanillic acid, ascorbic acid, citric acid, malic acid, oxalic acid, butyric acid, caproic acid, caprylic acid, lauric acid, tartaric acid, hydroxycinnamic acid, caffeic acid, ferulic acid, p-coumaric acid, hydroxybenzoic acid and lactic acid. For example, the

[0054] When the proflavour compound is an ester compound, the support compound released upon cleavage of the ester bond may be an alcohol. In this case, the flavour compound released upon cleavage of the ester bond may suitably be a carboxylic acid. Thus, the support component may suitably be derived from an alcohol. Suitably, the alcohol may be selected from one or more of a sterol, an aliphatic polyol, and a cationic alcohol. For example, the support component may be derived from an alcohol selected from one or more of glycerol, propylene glycol, cholesterol and choline. For example, the support compound used to form the ester and released upon cleavage of the enzymatically cleavable bond

[0055] The proflavour compound may be an ester compound formed by reaction of an alcohol from which the support component is derived and a carboxylic acid from which the flavour component is derived, wherein the carboxylic acid is selected from one or more of ascorbic acid, citric acid, malic acid, oxalic acid, lactic acid, vanillic acid, butyric acid, caproic acid, caprylic acid and lauric acid, and/or wherein the alcohol is selected from one or more of glycerol, propylene glycol, cholesterol and choline.

[0056] Suitably, when the ester compound is formed by reaction of an alcohol and a carboxylic acid, the flavour component may be derived from the alcohol and the support component may be derived from the carboxylic acid.

[0057] When the proflavour compound is an ester compound, the flavour compound released upon cleavage of the ester bond may be an alcohol. In this case, the support compound released upon cleavage of the ester bond may suitably be a carboxylic acid. For example, the flavour component may be derived from an aliphatic or aromatic alcohol.

[0058] For example, the flavour component may be derived from a phenolic compound, for example phenol or a derivative thereof, such as guaiacol or meta-cresol. Therefore the flavour compound used to form the ester and released upon cleavage of the ester bond may be a phenolic compound, for example phenol or a derivative thereof, such as one or more of guaiacol and meta-cresol. For example, the flavour component may be derived from a terpenoid alcohol, such as a monoterpenoid alcohol, suitably menthol. Therefore the flavour compound used to form the ester and released upon cleavage of the ester bond may be a terpenoid alcohol, such as a monoterpenoid alcohol, suitably menthol. For example, the flavour component may suitably be derived from an alcohol selected from one or more of geraniol, nerol, citronellol, linalool and terpineol, notably α -terpineol. Therefore the flavour compound used to form the ester and released upon cleavage of the ester bond may be an alcohol selected from one or more of geraniol, nerol, citronellol, linalool and terpineol, notably α -terpineol.

[0059] For example, the flavour component may suitably be derived from an alcohol selected from one or more of citronellol, geraniol, farnesol, phenylhexanol, borneol, polysantol, (Z)-3-hexenol, phenethylol, dimethyl benzyl carbinol, menthol, norisoprenoid compounds comprising a hydroxyl group such (as α -ionol, β -ionol and 3-hydroxy- β -ionol) and any derivatives thereof. Therefore the flavour compound used to form the ester and released upon cleavage of the ester bond may be an alcohol selected from one or more of citronellol, geraniol, farnesol, phenylhexanol, borneol, polysantol, (Z)-3-hexenol, phenethylol, dimethyl benzyl carbinol, menthol and norisoprenoid compounds comprising a hydroxyl group (such as α -ionol, β -ionol and 3-hydroxy- β -ionol) and any derivatives thereof. Suitably, the flavour component may suitably be derived from an alcohol selected from one or more of citronellol, geraniol, farnesol, phenylhexanol, borneol, polysantol, (Z)-3-hexenol, phenethylol, dimethyl benzyl carbinol, menthol, α -ionol, β -ionol and 3-hydroxy- β -ionol.

[0060] For example, the flavour component may suitably be derived from menthol. In this case, the flavour compound used to make the ester and released upon cleavage of the ester bond is menthol.

[0061] When the proflavour compound is an ester compound, the support compound used to form the ester and released upon cleavage of the ester bond may be a carboxylic acid. In this case, the flavour compound used to form the ester and released upon cleavage of the ester bond may suitably be an alcohol. For example, the support component may be derived from a hydroxy-substituted carboxylic acid. The support component may suitably be derived from one or more of glyceric acid, carboxylic cholesterol and lactic acid.

[0062] The proflavour compound may be an ester compound formed by reaction of an alcohol from which the flavour component is derived and a carboxylic acid from which the support component is derived, wherein the alcohol is selected from one or more of citronellol, geraniol, farnesol, phenylhexanol, borneol, polysantol, (Z)-3-hexenol, phenethylol, dimethyl benzyl carbinol, menthol, α -ionol, β -ionol and 3-hydroxy- β -ionol and/or wherein the carboxylic acid is selected from one or more of glyceric acid, carboxylic cholesterol and lactic acid.

[0063] When the proflavour compound is an ester compound, the ester compound may be one or more of a glycerol ester, an alkylene glycol ester (such as a propylene glycol ester), a lipid ester (for example a cholesterol ester), a choline

ester, a glyceric acid ester (or glycerate), a carboxylic cholesterol ester, a lactic acid ester, a diglyceride or a triglyceride.

[0064] Suitably, the proflavour compound may be an amide compound. The proflavour compound may be an amide compound and the bond between the flavour component and the support component may be an amide bond. Such an amide bond may be cleavable by an enzyme that can cleave an amide bond, such as amidase.

[0065] The amide compound is suitably formed by reaction of an amine compound and a carboxylic acid. Such reactions are well known to persons skilled in the art.

[0066] Suitably, when the amide compound is formed by reaction of an amine compound and a carboxylic acid, either the flavour component or the support component is derived from the amine compound and the other of the flavour component and the alcohol component is derived from the carboxylic acid. In other words, the amide compound may be formed by reaction of an amine compound and a carboxylic acid, wherein the amine compound is a flavour or support compound, and the carboxylic acid is the other of the flavour or support compound.

[0067] Suitably, when the amide compound is formed by reaction of an amine compound and a carboxylic acid, the support component is derived from the amine compound and the flavour component is derived from the carboxylic acid.

[0068] When the proflavour compound is an amide compound, the flavour compound used to form the amide and released upon cleavage of the amide bond may be a carboxylic acid. In this case, the support compound used to form the amide and released upon cleavage of the amide bond may suitably be an amine compound. The carboxylic acid may be any aliphatic or aromatic carboxylic acid and may contain one or more carboxylic acid (COOH) functional groups. For example, the carboxylic acid may be a polycarboxylic acid (such as a di- or a tri-carboxylic acid) or a monocarboxylic acid. The carboxylic acid may be cinnamic acid. The amine compound may be any compound comprising one or more amino groups, such as a polysaccharide compound containing one or more amino groups. The amine compound may be chitosan. Suitably, the proflavour compound may be an anhydride compound.

[0069] The proflavour compound may be an anhydride compound and the bond between the flavour component and the support component may be an anhydride bond. Such an anhydride bond may be cleavable by an enzyme that can cleave an anhydride bond, such as hydrolase.

[0070] The anhydride compound is suitably formed by reaction of two carboxylic acids. Such reactions are well known to persons skilled in the art.

[0071] Suitably, when the anhydride compound is formed by reaction of two carboxylic acids, both the flavour component and the support component is derived from a carboxylic acid. In other words, the anhydride compound may be formed by reaction of two carboxylic acids, wherein one of the carboxylic acids is a flavour compound and the other carboxylic acid is a support compound.

[0072] For example, the carboxylic acids may be selected from a polycarboxylic acid (such as a di- or a tri-carboxylic acid) and a monocarboxylic acid. Suitable carboxylic acids include glyceric acid, carboxylic cholesterol, lactic acid and fatty acids.

[0073] In one example, the proflavour compound is L-menthyl lactate. In this example, the flavour component and the support component are joined by an ester bond. Thus, upon cleavage of the ester bond, menthol is released as the flavour compound and lactic acid is released as the support compound. The flavour component is suitably derived from menthol and the support component is derived from lactic acid.

[0074] In one example, the proflavour compound is L-menthyl acetate. In this example, the flavour component and the support component are joined by an ester bond. Thus, upon cleavage of the ester bond, menthol is released as the flavour compound and acetic acid is released as the support compound. The flavour component is suitably derived from menthol and the support component is derived from acetic acid.

[0075] In one example, the proflavour compound is citronellyl oleate. In this example, the flavour component and the support component are joined by an ester bond. Thus, upon cleavage of the ester bond, citronellol is released as the flavour compound and oleic acid is released as the support compound. The flavour component is suitably derived from citronellol and the support component is derived from oleic acid.

[0076] Suitably, the support compound is non-volatile at ambient temperature, i.e. the support component has a boiling point, measured at a standard atmospheric pressure of 101325 Pa, of greater than 90°C, for example greater than 120°C, such as greater than 160°C.

[0077] The flavour component is typically derived from a flavour compound that provides the user with a specific flavouring effect.

[0078] Suitably, the flavour component is derived from a flavour compound naturally present in tobacco. The flavour compound may make it possible to amplify the flavour intensity of at least one flavour naturally present in tobacco.

[0079] Suitably, the flavour component is derived from a flavour compound which has a slightly different flavour to at least one flavour naturally present in tobacco (or a "nuanced" flavour). This may be termed as a "congruent pairing element". This type of pairing is intended to amplify a specific tone within the original flavour profile, for example toasted, nutty, fruity, etc.

[0080] Suitably, the flavour component is derived from a flavour compound having a contrasting pairing element with at least one flavour naturally present in tobacco. The flavour compound may be different from the flavouring naturally

present in tobacco. This type of pairing is called contrasting pairing, and it is intended to provide a surprising and unexpected twist in the flavour perception.

[0081] The support compound derived from the support component may provide an effect on the sensory perception of the user. In addition to the taste/aroma perception associated to the release of the flavour compound, a secondary sensory effect (taste or perception) may be expected depending on the choice of the support component and thus the release of the support compound. A mouthfeel perception, for example a coating perception, may be provided by selecting fatty acids as the support compound.

[0082] Examples of proflavour compounds, flavour compounds and their associated flavour perception are summarised in Table 1 below.

Table 1

Examples of Proflavour Compound	Flavour compound	Flavour
Glycerides esters, such as mono-, di- and triglycerides Alkylene glycol esters, such propylene glycol esters Lipidic esters, notably cholesterol esters Choline esters	Carboxylic acids such as: ascorbic acid, citric acid, malic acid, oxalic acid	Acidic/tart taste
Glyceric acid esters Carboxylic cholesterol esters Lactic acid esters	Alcohols, such as: Citronellol Geraniol, farnesol, phenylhexanol Borneol, polysantol (Z)-3-hexenol, phenethylol, dimethyl benzyl carbinol menthol	Fresh, citrus Floral Woody Green, fresh Fresh, sweet
	Carboxylic acids, such as lactic acid	Sour, tart
	norisoprenoid compounds comprising a hydroxyl group, such as: α -ionol, β -ionol, 3-hydroxy- β -ionol and any derivatives thereof	Sweet, floral, woody, fruity
Di, tri-glycerides	Free fatty acids such as: butyric acid, caproic acid, caprylic acid, lauric acid	Pungent, acidic, waxy,

[0083] Suitably, the nicotine oral delivery composition of the first aspect of the present invention comprises from 0.001 wt% to 30 wt% of the proflavour compound, more suitably from 0.01 wt% to 20 wt%, even more suitably from 0.5 wt% to 15 wt% of the proflavour compound, based on the total weight of the composition.

[0084] The nicotine oral delivery composition of the present invention is in solid form. Suitable solid forms include powders and granules, and agglomerates and/or aggregates thereof.

[0085] Powder and granule forms provide a large surface area (with respect to its volume) which allows adherence of particles of the nicotine source thereto. Thus, the overall density of nicotine (which is provided by the source of nicotine) particles is suitably high.

[0086] By "granular form", it should be understood that the components are present in the composition as granules. Typically, upon measurement of particle size distribution of a component in granular form by sieve analysis, the median particle size (i.e. D50) is from 0.2 to 1 mm, such as from 0.5 to 1 mm, or from 0.5 to 0.7 mm.

[0087] It will be appreciated by a skilled person that a component in granular form may be formed by a granulation process, such as wet or dry granulation, during which single discrete particles such as powder particles agglomerate to form larger entities, i.e., granules. The granular form is therefore to be physically distinguished from powder form.

[0088] By "powder form" it should be understood that the components are present in the composition as a powder. Typically, upon measurement of particle size distribution of a component in powder form by sieve analysis, the median particle size (i.e. D50) is less than 1.0 mm, such as less than 0.8 mm.

[0089] The nicotine oral delivery composition of the present invention may further comprise suitable additional components, such as a carrier and/or a filler.

[0090] Suitable carriers and/or fillers will be known to persons skilled in the art. Suitable carriers and/or fillers include, but are not limited to, silica, cellulose, starch, metal oxides and polysaccharides. The carrier and/or filler may be porous. The carrier and/or filler may be non-porous. Suitable examples of fillers include, but are not limited to, cellulose and cellulose derivatives, polysaccharides (such as maltitol), polyols, natural fibres silica, metal oxides (such as titania and zirconia) and mixtures thereof. It is noted that any filler present may also have a secondary function as, for example, a sweetener. Preferably, the composition of the nicotine oral delivery composition of the present invention is free of sugars, due to the impact that they may have on a user's teeth.

[0091] The filler and/or carrier may be present in any suitable amount. Suitably, the nicotine oral delivery composition

of the first aspect of the present invention comprises from 20 to 60 wt%, such as from 30 to 50 wt% of filler, based on the total weight of the composition. For example, the nicotine oral delivery composition of the first aspect of the present invention may comprise a cellulose or a cellulose derivative in any suitable form. The nicotine oral delivery composition of the first aspect of the present invention may comprise microcrystalline cellulose. The term "cellulose derivative" as used herein refers to cellulose which has been modified by virtue of the hydroxyl groups of the compound being partially or fully reacted with one or multiple reagents. Any suitable cellulose derivative may be used.

[0092] Examples of suitable cellulose derivatives include cellulose ethers and cellulose esters. In the production of cellulose ethers, the hydroxyl groups of the cellulose are typically reacted with alkali such as sodium hydroxide, followed by one or more etherifying agents such as methyl chloride, ethyl chloride, ethylene oxide or propylene oxide. Cellulose esters are commonly derived from cellulose through the reaction of the hydroxyl groups with organic acids, anhydrides, or acid chlorides.

[0093] Suitably, the nicotine oral delivery composition of the first aspect of the present invention comprises a cellulose derivative. Preferably, the cellulose derivative is a cellulose ether or cellulose ester. Suitable cellulose ethers include, but are not limited to, alkyl cellulose ethers such as methylcellulose, ethylcellulose and ethyl methyl cellulose; hydroxyalkyl cellulose ethers such as hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxyethyl methyl cellulose, hydroxypropyl methyl cellulose and ethyl hydroxyethyl cellulose; and carboxymethyl cellulose ethers such as carboxymethylcellulose. Suitable cellulose esters include, but are not limited to, organic cellulose esters such as cellulose acetate, cellulose triacetate, cellulose propionate, cellulose acetate-propionate and cellulose acetate-butyrate; and inorganic cellulose esters such as nitrocellulose (cellulose nitrate) and cellulose sulfate.

[0094] The nicotine oral delivery composition of the first aspect of the present invention may further comprise one or more pH adjusting agents. The term "pH adjusting agent" and like terms used herein refers to agents which adjust and regulate the pH of the composition to which they are added. Such agents may be acids and bases, including acidic and alkaline buffering agents. However, the term does not encompass substances that only affect pH by dilution.

[0095] Any pH adjusting agent may be used in the composition of the first aspect of the present invention. Suitable examples of pH adjusting agents include, but are not limited to, carbonates including monocarbonates, bicarbonates and sesquicarbonates of alkaline metals or ammonium such as sodium carbonate, potassium carbonate, potassium bicarbonate, sodium bicarbonate and magnesium carbonate; acetates of alkaline metals or ammonium; glycinate of alkaline metals or ammonium; gluconates of alkaline metals or ammonium, borates of alkaline metals or ammonium, glycerophosphates of alkaline metals or ammonium; citrates of alkaline metals or ammonium; phosphate systems including monohydrogenphosphate, dihydrogenphosphate and trihydrogenphosphate; metal hydroxides such as sodium hydroxide and potassium hydroxide; and mixtures thereof. Suitably, the nicotine oral delivery composition of the first aspect of the present invention comprises one or more pH adjusting agents. Suitably, the one or more pH-adjusting agent is selected from sodium carbonate, potassium carbonate and potassium bicarbonate.

[0096] It will be appreciated by a skilled person that the absorption of nicotine over the mucous membrane in the oral cavity of a user is affected by local pH, i.e., the pH inside and in close proximity to the nicotine oral delivery product in the saliva of the user. Preferably, the one or more pH adjusting agent provides a local pH of 6 or above, such as a pH of from 8 to 10, more preferably 9, when the composition of the nicotine oral delivery product is dissolved or dispersed in aqueous solution such as purified water.

[0097] It will be appreciated by a person skilled in the art that the amount of pH adjusting agent present in the composition affects local pH. The one or more pH adjusting agent may be present in the composition of the first aspect in any suitable amount. Suitably, the nicotine oral delivery composition of the first aspect of the present invention comprises from 0.1 to 18 wt%, for example 1 to 10 wt%, such as from 2 to 8 wt%, of one or more pH adjusting agents, based on the total weight of the composition.

[0098] The nicotine oral delivery composition of the first aspect of the present invention may further comprise one or more sweeteners to enhance the taste and sweetness of flavour provided by the nicotine oral delivery composition. Suitable examples of sweeteners include, but are not limited to, polyols such as xylitol; mono-, di- and tri-polysaccharides such as mannitol and maltitol; natural and synthetic sweeteners such as sucrose, glucose, dextrose, maltose, fructose, saccharin, aspartame, acesulfame including acesulfame K, sucralose, saccharin and cyclamates and mixtures thereof. The one or more sweeteners may be present in the nicotine oral delivery composition of the first aspect of the present invention in any suitable amount. The nicotine oral delivery composition of the first aspect of the present invention may comprise from 0.1 to 15 wt% of one or more sweeteners, based on the total weight of the composition.

[0099] The nicotine oral delivery composition of the first aspect of the present invention may further comprise one or more salts. Any suitable salt may be used, such as sodium chloride (table salt), sodium carbonate, hydrogen carbonate, potassium chloride, potassium sulfate, calcium chloride, monosodium glutamate and sodium malate. The one or more salts may be present in any suitable amount. The nicotine oral delivery composition of the first aspect of the present invention may comprise from 0.1 to 15 wt% of one or more salts, based on the total weight of the composition.

[0100] The nicotine oral delivery composition of the first aspect of the present invention may further comprise one or more gelling agents (gellants). Any suitable gelling agent may be used. Typical gelling agents include natural gums,

starches, pectins, agar-agar and gelatin. The one or more gelling agents may be present in any suitable amount. The nicotine oral delivery composition of the first aspect of the present invention may comprise from 0.1 to 15 wt% of one or more gelling agents, based on the total weight of the composition.

[0101] The nicotine oral delivery composition of the first aspect of the present invention may further comprise one or more humectants. Humectants may also be known in the art as moisturisers or softeners and may be present in the composition of the present invention to control and maintain appropriate moisture levels of the composition. Suitable examples of humectants include, but are not limited to, glycerine, propylene glycol, hexyleneglycol, butylene glycol, polydextrose, sorbitol, maltitol, xylitol, glyceryl triacetate, triethylene glycol and combinations thereof. Suitably, the one or more humectant is selected from glycerol and/or propylene glycol. The one or more humectants may be present in nicotine oral delivery composition of the first aspect of the present invention in any suitable amount. Preferably, the nicotine oral delivery composition of the first aspect of the present invention comprises from 0.1 to 15 wt%, such as from 5 to 15 wt%, of the one or more humectant, based on the total weight of the composition.

[0102] The nicotine oral delivery composition of the first aspect of the present invention may contain water. Suitably, the nicotine oral delivery composition of the first aspect of the present invention may have a water content of from 1 to 55 wt%, such as from 5 to 50 wt%, based on the total weight of the composition.

[0103] Suitably, the nicotine oral delivery composition of the first aspect of the present invention contains less than 15 wt% of water, based on the total weight of the composition. Suitably the composition may be described herein as "dry". Suitably, the nicotine oral delivery composition of the first aspect of the present invention contains more than 35 wt% of water, based on the total weight of the composition. Suitably the composition may be described herein as "moist".

[0104] It will be appreciated by a skilled person that in the context of the present invention additional moisture content may be provided by the one or more humectants and flavours, predominantly the one or more humectants. The term "moisture content" as used herein is meant to refer to the total amount of oven (i.e., at a temperature of from 120 to 300°C) volatile materials in the composition. The moisture content of the nicotine oral delivery composition may be measured using a Mettler Toledo's Moisture Analyzer HB43, a balance with halogen heating technology. The sample is heated to 105 °C. The measurement is stopped when the weight change is less than 1 mg during a 90 seconds period. The moisture content as a weight percentage of the sample is then calculated automatically by the Moisture Analyzer HB43.

[0105] The nicotine oral delivery composition of the first aspect of the present invention suitably has a pleasant taste to the user.

[0106] The nicotine oral delivery composition of the first aspect of the present invention may be enclosed in a water-insoluble pouch, such as completely contained within a water-insoluble pouch.

[0107] A second aspect of the present invention provides a nicotine oral delivery product comprising a pouch and a nicotine oral delivery composition according to the first aspect of the present invention contained within the pouch, suitably wherein the pouch is water-insoluble and/or is permeable for saliva.

[0108] The second aspect of the invention may provide a nicotine oral delivery product comprising a pouch and a nicotine oral delivery composition according to the first aspect of the present invention contained within the pouch, wherein the pouch is water-insoluble and is permeable for saliva. In the nicotine oral delivery product, the nicotine oral delivery composition is sealed within the pouch.

[0109] Suitably, the pouch is a water-insoluble pouch, i.e. the pouch is formed from a water-insoluble material. The pouch may be formed from any suitable material, such as any suitable water-insoluble material.

[0110] Examples of suitable materials from which a water-insoluble pouch may be formed include, but are not limited to, woven or non-woven fabrics such as cotton or fleece; and heat-sealable non-woven cellulose or other polymeric materials such as synthetic, semi-synthetic or natural polymeric agents. The pouch may further comprise components, such as polymers, to bind the materials and facilitate sealing of the pouch. Suitably, the nicotine oral delivery composition of the present invention may be enclosed in a water-insoluble pouch formed from a non-woven material comprising viscose rayon fibres (i.e., regenerated cellulose) and an acrylic polymer that acts as a binder for the non-woven material and provides for heat sealing of the pouch during manufacturing thereof. The water-insoluble pouch is sealed to enclose and retain the composition in the pouch. Preferably, the water-insoluble pouch is heat-treated to seal the composition inside and form the nicotine oral delivery product of the present invention. It will be appreciated that the material of the water-insoluble pouch influences the mouth-feel for the user. It will further be appreciated that the water-insoluble pouch suitably does not dissolve in saliva; is chemically and physically stable; is insoluble in water i.e., incapable of being dissolved in water; and is easily sealable. The water-insoluble pouch of the second aspect of the present invention may provide a semi-permeable membrane which prevents the composition leaving the pouch, but when the product is in use and placed in a user's mouth, is permeable to saliva and dissolved components of the composition including nicotine and flavour components such that they can diffuse therefrom into the user's mouth.

[0111] The nicotine oral delivery product of the second aspect of the invention is suitably intended to be placed in the oral cavity of a user, such as by buccal placement (placing the product between the upper or lower gum and the lip or cheek). The nicotine oral delivery product will therefore be sized and configured to fit comfortably and discreetly in the

user's mouth in this manner. It may have an oblong shape, such as a rectangular shape.

[0112] The nicotine oral delivery composition of the first aspect of the invention may be enclosed in the pouch (for example water-insoluble pouch) of the nicotine oral delivery product of the second aspect of the present invention in any suitable amount. Preferably 50 to 1,000 mg, such as 200 to 800 mg, for example 150 to 700 mg, of the nicotine oral delivery composition is enclosed in the pouch. It will be appreciated that the amount of the nicotine oral delivery composition enclosed in the pouch is selected such that the nicotine oral delivery product remains of an appropriate size. The total weight of the nicotine oral delivery product (both composition and pouch) according to the present invention may be from 0.3 to 1.5 g, such as from 0.3 to 1 g, or even from 0.4 to 0.8 g.

[0113] It has been found by the inventors that the nicotine oral delivery product of the present invention effectively delivers nicotine provided by the source of nicotine to a user. The nicotine oral delivery product of the second aspect of the present invention provides a high perceived nicotine impact. The term "perceived nicotine impact" as used herein refers to the nicotine 'hit' perceived by a user. As discussed above, the local pH of 6 or above, such as from 8 to 10, or even 9, contributes to the absorption of nicotine over the mucous membrane in the oral cavity of a user.

[0114] During use, the nicotine oral delivery product is placed and retained for a period of time in the mouth of a user. This is commonly between the upper or lower gum of the user and the chin or cheek. Once saliva enters the interior of the pouch, it dissolves any components of the composition enclosed therein that are soluble in saliva. Thus, typically the pouch is permeable for saliva. The solubilised components of the composition (including nicotine provided by the source of nicotine and the proflavour compound) diffuse from the pouch in the saliva and into the mouth of the user. Once released from the pouch, the nicotine is bioavailable, i.e., available for absorption over a mucous membrane in the oral cavity of the user. Accordingly, once released from the pouch, nicotine is absorbed over a mucous membrane of the oral cavity of a user into their blood so as to provide nicotine and satisfaction to the user.

[0115] It is noted that the nicotine oral delivery products of the second aspect of the present invention are intended for single use.

[0116] As used herein, the terms "mouth" and "oral cavity" are interchangeable.

[0117] According to a third aspect of the present invention, there is provided a method of making the nicotine oral delivery product according to the second aspect of the present invention, the method comprising enclosing the nicotine oral delivery composition according to the first aspect of the present invention in the pouch and optionally sealing the pouch.

[0118] The method of making the nicotine oral delivery product according to the third aspect of the present invention may comprise the steps of admixing the components of the nicotine oral delivery composition, filling the nicotine oral delivery composition into the pouch (for example water-insoluble pouch), and enclosing the composition in the pouch such that the composition is completely contained within. The pouch is sealed (for example by heat) to enclose and retain the composition therein. Appropriate machines for the manufacture of the nicotine oral delivery products of the present invention will be well known in the art.

[0119] As will be known to those skilled in the art, a pasteurization step may also be used to prolong the shelf-life of the nicotine oral delivery product of the second aspect of the present invention.

[0120] According to a fourth aspect of the present invention, there is provided a use of the nicotine oral delivery composition according to the first aspect or of the nicotine oral delivery product according to the second aspect for oral delivery of nicotine.

[0121] According to a fifth aspect of the present invention, there is provided a method for oral delivery of nicotine, the method comprising placing the nicotine oral delivery composition according to the first aspect or the nicotine oral delivery product according to the second aspect into a user's mouth.

[0122] For a better understanding of the invention, and to show how exemplary embodiments of the same may be brought into effect, reference will be made to the following non-limiting examples.

Examples

Example 1: Suitable Nicotine Oral Delivery Compositions

[0123] Compositions may be prepared according to the details given in Table 2.

[0124] The pH of the compositions will be in the range of 7.5 to 9.5, such that the nicotine is typically in the form of un-protonated (free-base) nicotine and mono-protonated nicotine.

Table 2

Component	Composition 1	Composition 2	Composition 3	Composition 4	Composition 5
Cellulose	30 wt%	30 wt%	25 wt%	25 wt%	-

(continued)

Component	Composition 1	Composition 2	Composition 3	Composition 4	Composition 5
Nicotine	2 wt%	1 wt%	2 wt%	1 wt%	-
Tobacco	-	1 wt%	-	1 wt%	50 wt%
Flavour (menthol)	-	-	-	-	-
Proflavour compound (L-menthyl lactate)	10 wt%	10 wt%	5 wt%	5 wt%	5 wt%
Gelling agent	10 wt%	10 wt%	3 wt%	3 wt%	-
pH regulator	20 wt%	20 wt%	10 wt%	10 wt%	2.5 wt%
Additives*	20 wt%	20 wt%	5 wt%	5 wt%	2.5 wt%
Water	8 wt%	8 wt%	50 wt%	50 wt%	40 wt%

*Additives include sweetener, salt, humectant, binder

Example 2: Flavour detection

[0125] The detection of flavour by user's for proflavour compounds used in this invention follows a two-stage approach, as follows:

Stage 1. Training and familiarization

Training (several months prior to the evaluations)

[0126] A group of naive adult users of nicotine products characterized by their ability to express themselves and for the acuity to detect attributes related to flavour have been recruited, trained, and regularly tested on their capacity to conduct sensory evaluations with high reproducibility.

Familiarization

[0127] On a familiarization session, a group of panel members were presented with selected samples covering all the flavour directions which will be presented later during a blind assessment (stage 2). During this session, a moderator guides the discussion, and encourages the description of the nicotine products tested among the panel members. By the end of this session, a consensus should be achieved as to which attributes are perceived by them, and what is the definition of each attribute.

Stage 2. Product evaluations for flavour detection/recognition or optimization.

[0128] This stage consists of a sensory discrimination test which follows a standard procedure outlined in ISO 13301:2018 (Sensory analysis - Methodology - General guidance for measuring odour, flavour and taste detection thresholds by a three-alternative forced-choice (3-AFC) procedure).

[0129] This procedure involves the testing of a reference sample having a known composition. Such reference sample is known for a characteristic flavour attribute. Each reference sample covers a single specific attribute: i.e., citrus taste, floral taste, woody taste. In addition to this, the reference sample is formulated with the minimum concentration threshold detection. In other words, the reference sample has a flavoring concentration which is clearly perceivable by a trained user. Assessors will be asked to consume each product, and to indicate which one contained the selected flavour.

[0130] This procedure will be performed as a recognition test as follows:

An assessor (panel member) is presented with three samples. One of the samples is the reference sample to validate its perceivable taste/smell. This sample will be used as the positive control.

[0131] An array of other samples containing specific proflavour (PF) compounds will be presented instead of the reference sample in randomized order. Each sample is identifiable with a 3-digit code, and no code should be repeated for any of the samples to be evaluated for the same assessor. Assessors are asked to indicate which sample presented the specific flavour and to single it out. A percentage of flavour detection or recognition can be obtained by simply calculating the number of assessors identifying the sample with PF compounds in the formulation.

[0132] For example, a group of assessors could be asked to identify a "citrus" flavour in two tests as follows:

Test 1	024 (Reference)	598	981
Test 2	492	137	605 (PF sample)

Samples 024 and 605 should be recognized as the citrus flavour. Samples 492, 598, 137 and 981 should be recognized as not a citrus flavour. Test 1 contains the reference sample, known to contain the citrus flavour. Test 2 contains the proflavour sample. If reference sample in test 1 is not singled-out, the flavour identification test fails (the panel member is unable to recognise the flavour in a sample known to contain this flavour). If the proflavour samples in test 2 is not singled-out the test fails: the sample is not recognized to contain the flavour in scope by the panel member. Both samples need to be singled out by >50% of the panel members to conclude that the proflavour sample to pass the test.

[0133] Throughout this specification, the term "comprising" or "comprises" means including the component(s) specified but not to the exclusion of the presence of other components. The term "consisting essentially of" or "consists essentially of" means including the components specified but excluding other components except for materials present as impurities, unavoidable materials present as a result of processes used to provide the components, and components added for a purpose other than achieving the technical effect of the invention. Typically, when referring to compositions, a composition consisting essentially of a set of components will comprise less than 5% by weight, typically less than 3% by weight, more typically less than 1% by weight of non-specified components.

[0134] The recitation of numerical ranges by endpoints includes all integer numbers and, where appropriate, fractions subsumed within that range (e.g. 1 to 5 can include 1, 2, 3, 4 when referring to, for example, a number of elements, and can also include 1.5, 2, 2.75 and 3.80, when referring to, for example, measurements). The recitation of end points also includes the end point values themselves (e.g. from 1.0 to 5.0 includes both 1.0 and 5.0). Any numerical range recited herein is intended to include all sub-ranges subsumed therein.

[0135] For the avoidance of doubt, wherein amounts of components in a composition are described in wt%, this means the weight percentage of the specified component in relation to the whole composition referred to. For example, "wherein the nicotine oral delivery composition comprises from 1 to 15 wt% of the source of nicotine" means that 1 wt% to 15 wt% of the nicotine oral delivery composition is provided by the source of nicotine.

[0136] As used in the specification and the appended claims, the singular forms "a", "an," and "the" include both singular and plural referents unless the context clearly dictates otherwise.

[0137] The optional features set out herein may be used either individually or in combination with each other where appropriate and particularly in the combinations as set out in the accompanying claims. The optional features for each aspect or exemplary embodiment of the invention as set out herein are also to be read as applicable to any other aspect or exemplary embodiments of the invention, where appropriate. In other words, the skilled person reading this specification should consider the optional features for each exemplary embodiment of the invention as interchangeable and combinable between different exemplary embodiments.

[0138] Attention is directed to all papers and documents which are filed concurrently with or previous to this specification in connection with this application and which are open to public inspection with this specification, and the contents of all such papers and documents are incorporated herein by reference.

[0139] All of the features disclosed in this specification (including any accompanying claims, and drawings), and/or all of the steps of any method or process so disclosed, may be combined in any combination, except combinations where at least some of such features and/or steps are mutually exclusive.

[0140] Each feature disclosed in this specification (including any accompanying claims, and drawings) may be replaced by alternative features serving the same, equivalent or similar purpose, unless expressly stated otherwise. Thus, unless expressly stated otherwise, each feature disclosed is one example only of a generic series of equivalent or similar features.

[0141] The invention is not restricted to the details of the foregoing embodiment(s). The invention extends to any novel one, or any novel combination, of the features disclosed in this specification (including any accompanying claims, and drawings), or to any novel one, or any novel combination, of the steps of any method or process so disclosed.

Claims

1. A nicotine oral delivery composition comprising a source of nicotine and a proflavour compound, wherein the proflavour compound comprises a flavour component and a support component joined by an enzymatically cleavable bond, wherein the nicotine oral delivery composition is in solid form, and wherein the enzymatically cleavable bond is not a glycosidic bond.

2. The nicotine oral delivery composition according to claim 1, wherein the enzymatically cleavable bond is cleaved by reaction with an enzyme present in saliva, suitably wherein the enzymatically cleavable bond is an ester bond, an amine bond or an anhydride bond.
- 5 3. The nicotine oral delivery composition according to claim 1 or claim 2, wherein the proflavour compound is an ester compound, an amide compound, an anhydride compound or a combination thereof.
4. The nicotine oral delivery composition according to claim 3, wherein the proflavour compound is an ester compound.
- 10 5. The nicotine oral delivery composition according to claim 4, wherein the ester compound is one or more of a glycerol ester, a propylene glycol ester, a cholesterol ester, a choline ester, a glyceric acid ester (or glycerate), a carboxylic cholesterol ester, a lactic acid ester, a diglyceride and a triglyceride.
- 15 6. The nicotine oral delivery composition according to claim 4 or 5, wherein the ester compound is formed by reaction of an alcohol and a carboxylic acid, wherein either the flavour component or the support component is derived from the alcohol and the other of the flavour component and the support component is derived from the carboxylic acid.
7. The nicotine oral delivery composition according to according to claim 6, wherein the flavour component is derived from the carboxylic acid and the support component is derived from the alcohol.
- 20 8. The nicotine oral delivery composition according to according to claim 7, wherein the carboxylic acid is selected from ascorbic acid, citric acid, malic acid, oxalic acid, lactic acid, butyric acid, caproic acid, caprylic acid and lauric acid, and/or wherein the alcohol is selected from glycerol, propylene glycol, cholesterol and/or choline.
- 25 9. The nicotine oral delivery composition according to claim 6, wherein the flavour component is derived from the alcohol and the support component is derived from the carboxylic acid.
- 30 10. The nicotine oral delivery composition according to claim 9, wherein the alcohol is selected from citronellol, geraniol, farnesol, phenylhexanol, borneol, polysantol, (Z)-3-hexenol, phenethylol, dimethyl benzyl carbinol and menthol, α -ionol, β -ionol or 3-hydroxy- β -ionol and/or wherein the carboxylic acid is selected from glyceric acid, carboxylic cholesterol and lactic acid.
- 35 11. The nicotine oral delivery composition according to any preceding claim, wherein the source of nicotine is selected from the group consisting of nicotine salt, free-base nicotine, stabilised nicotine or a combination thereof.
12. A nicotine oral delivery product comprising a pouch and a nicotine oral delivery composition according to any preceding claim, wherein the pouch is water-insoluble and is permeable for saliva and wherein the nicotine oral delivery composition is contained within the pouch.
- 40 13. A method of making the nicotine oral delivery product according to claim 12, the method comprising enclosing the nicotine oral delivery composition according to any of claims 1 to 11 in the pouch and sealing the pouch.
14. Use of the nicotine oral delivery composition according to any one of claims 1 to 11 or a nicotine oral delivery product according to claim 12 for oral delivery of nicotine.
- 45 15. A method for oral delivery of nicotine, the method comprising placing the nicotine oral delivery product according to claim 12 into a user's mouth.



EUROPEAN SEARCH REPORT

Application Number

EP 23 15 1815

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