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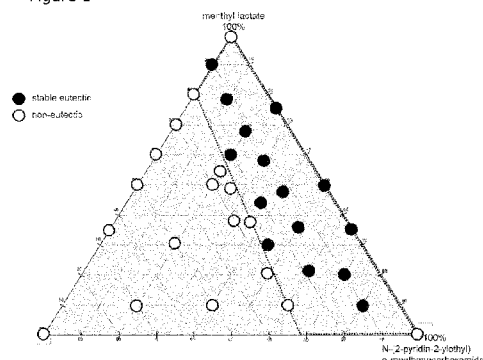
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(54) Title: COOLING COMPOSITIONS

(1)

menthyl lactate	(N-(4-cyanomethylphenyl) p-menthanecarboxamide,	N-(2-pyridin-2-ylethyl) p-menthanecarboxamide
100	0	0
80	20	0
0	31.5	68.5
0	0	100

Figure 1



(57) Abstract: A liquid cooling composition that is a mixture of (N-(4-cyanomethylphenyl) p-menthanecarboxamide, N-(2-pyridin-2-ylethyl) p-menthanecarboxamide and menthyl lactate, the composition being characterized in that, in a triangular ternary phase diagram of (N-(4-cyanomethylphenyl) p-menthanecarboxamide, N-(2-pyridin-2-ylethyl) p-menthanecarboxamide and menthyl lactate, the composition falls within that portion of the diagram bounded by the coordinates of the following table (1). The compositions are stable liquids, able to be stored and easily incorporated into products, and giving superior cooling properties with respect to the same quantities of compounds added as powders.



COOLING COMPOSITIONS

This disclosure relates to cooling compounds and more particularly to compositions of such cooling compounds and to products containing such compositions.

5

Synthetic cooling compounds, that is, compounds that produce a cooling sensation on the skin or the mucous membranes have been long known, and a wide variety of such compounds is now available. A problem with many of these compounds is that, not only are they crystalline solids, but also that they are relatively insoluble in nearly everything, and it is therefore difficult to get sufficient into solution in products utilizing them to produce the desired cooling effect. This has been a particular problem with the recently-introduced (N-(4-cyanomethylphenyl) p-menthanecarboxamide and N-(2-pyridin-2-ylethyl) p-menthanecarboxamide (commercialized respectively as Evercool™ 180 and Evercool™ 190, and hereinafter referred to respectively by the designations “180” and “190”), but other cooling compounds have suffered from the same problem to a greater or lesser extent.

One attempt to get more into solution was described in International publication WO 2007/140783, in which primary and secondary cooling compounds, including the 180 and 190, are combined with non-polar solvents in particular ratios. Mixtures of 180 and 190 are also described in WO 2012/113873, but in connection with lowering the proportion of menthol used in a flavour composition, rather than getting more into solution.

It has now been found that it is possible to combine certain solid cooling compounds to provide a liquid cooling composition that is exceptionally stable on storage and that provides useful cooling properties to a wide variety of products. There is therefore provided a liquid cooling composition that is a mixture of (N-(4-cyanomethylphenyl) p-menthanecarboxamide, N-(2-pyridin-2-ylethyl) p-menthanecarboxamide and menthyl lactate, the composition being characterized in that, in a triangular ternary phase diagram of (N-(4-cyanomethyl-phenyl) p-menthanecarboxamide, N-(2-pyridin-2-ylethyl) p-menthanecarboxamide and menthyl lactate, the composition falls within that portion of the diagram bounded by the coordinates of the following table:

menthyl lactate	(N-(4-cyanomethylphenyl) p-menthanecarboxamide,	N-(2-pyridin-2-ylethyl) p- menthanecarboxamide
100	0	0
80	20	0
0	31.5	68.5
0	0	100

In a particular embodiment, the composition comprises all three materials.

Ternary phase diagrams having the form of a equilateral triangle and depicting a three-
 5 component system with one component per apex representing 100% of one component
 and a line from that apex perpendicular to the opposing side as the axis of that component
 are well known to the art and are standard methods of depicting such compositions.
 Examples may be found in the figures.

10 It is a particular feature of this disclosure that these compositions of cooling compounds
 are room-temperature eutectics, that is, they are liquid without the need for the addition of
 solvent. Not only does this mean reduced expense, but also that it is possible to get into
 products more of 180 and 190, both of which are poorly soluble in the normal solvents of
 the art.

15

A further unexpected advantage is that these compositions remain liquid when stored for
 long periods. This makes manufacture and utilization very easy and allows the provision
 of an excellent cooling effect.

20 A particular embodiment includes the compositions defined on the ternary phase diagram
 as follows:

menthyl lactate	(N-(4-cyanomethylphenyl) p-menthanecarboxamide,	N-(2-pyridin-2-ylethyl) p- menthanecarboxamide
100	0	0
80	20	0
10	30	60
20	0	80

A further particular embodiment is as follows:

menthyl lactate	(N-(4-cyanomethylphenyl) p-menthanecarboxamide,	N-(2-pyridin-2-ylethyl) p- menthanecarboxamide
80	10	10
10	20	60
20	0	80

A further particular embodiment is as follows:

menthyl lactate	(N-(4-cyanomethylphenyl) p-menthanecarboxamide,	N-(2-pyridin-2-ylethyl) p- menthanecarboxamide
20	20	60
40	20	40
50	10	40
20	10	70

5

The compositions are prepared by blending the desired components, heating them until they melt and then allowing the mixture to cool to ambient temperature.

The compositions may be pre-blended and stored. Not only are they liquid, making them
10 easier to add and incorporate into compositions, but they are also remarkably stable.

The compositions may be added to any products in which a cooling effect on the skin or mucous membranes is desired. All three have been certified as GRAS (generally recognized as safe) by the US FEMA (Flavor and Extracts Manufacturers Association),
15 the standard for use in consumable compositions, making them usable in any kind of product taken by mouth.

Non-limiting examples of products include the following:

- 20 - Products that are applied to the oral mucosa, but that are not limited to foodstuffs and beverages taken into the mouth and swallowed, and products taken for reasons other than their nutritional value, e.g. tablets, troches, mouthwash, throat sprays, dentifrices and chewing gums, which may be applied to the oral mucosa for the purpose of cleaning, freshening, healing, and/or deodorising.

- Products that are applied to the skin include, but are not limited to perfumes, toiletries, cosmetic products such as lotions, oils, ointments and bathing agents, applicable to the skin of the human body, whether for medical or other reasons.

5

Particular examples of foodstuffs and beverages include, but are not limited to frozen confectionery such as ice creams and sorbets; desserts such as jelly and pudding; confectionery such as cakes, cookies, chocolates, and chewing gum; jams; candies; breads; tea beverages such as green tea, black tea, chamomile tea, mulberry leaf tea,

10 Rooibos tea, peppermint tea; soups; seasonings; instant beverages; snack foods and the like.

Further examples of products for topical application may include, but are not limited to, skin-care cosmetics such as cleansing tissues, talcum powders, face creams, lotions, tonics and gels; hand creams, hand- and body lotions, anti-cellulite/slimming creams and

15 -lotions, lotions, balms, gels, sprays and creams; sunburn cosmetics including sunscreen lotions, balms, gels, sprays and creams; after sun lotions, sprays and creams; soaps, toothpicks, lip sticks, agents for bathing, deodorants and antiperspirants, face washing creams, massage creams, and the like,

20 Further examples of products that are applied to the oral mucosa may include, but are not limited to, oral care products such as toothpastes, tooth gels, tooth powders, tooth whitening products, dental floss, anti-plaque and anti-gingivitis compositions, mouthwashes, compositions for treatment of nasal symptoms, and the like. The compositions have been found to be particularly useful and effective in such oral care

25 products.

The compositions of the invention may be added to and incorporated into a product base by known methods. Sufficient may be added to provide a cooling effect. The necessary proportion to provide such an effect will naturally depend on the desired cooling effect, but

30 typical weight proportions being from 5 to 5000mg/kg, more particularly from 50 to 1500mg/kg. These are general guidelines, not rigid boundaries, and formulators seeking particular effects may find it possible or even desirable to formulate outside them.

There is therefore also provided a product adapted to provide a cooling effect on the skin or the mucous membranes, the composition comprising a product base and a cooling proportion of a liquid cooling composition as hereinabove described.

- 5 There is also provided a method of providing to a product a cooling sensation for the skin or the mucous membranes, comprising the addition to a product base of a cooling proportion of a liquid cooling composition as hereinabove described.

By "product base" is meant all the components of a product other than the liquid cooling
10 mixture. These can vary considerably, depending on the nature of the product. For example, a consumable product cannot have non-consumable ingredients.

Typical non-limiting examples of components for use in product bases include matrix materials both liquid and solid, including gums, starches and starch derivatives,
15 polysaccharides and polymeric materials both natural and artificial, flavours and fragrances, pigments, dyestuffs and colouring matters, solvents, thickeners, rheology and viscosity modifiers, surfactants and dispersion aids, preservatives, bactericides and fungicides.

- 20 The final product not only has an enhanced cooling effect with respect to the addition of the equivalent amount of powder, but it is also free from the potentially irritant effects of undissolved powders on skin on mucous membranes.

In addition to an enhanced performance, the handling of the liquid blend during
25 manufacture of products is much easier than with powders, a feature that is particularly significant on an industrial scale, in which the handling of powders, especially those of potent cooling compounds, present a potentially considerable irritant problem for workers, as well as a potential explosion hazard.

- 30 The disclosure is further described with reference to the following non-limiting examples.

Figure 1 depicts a ternary phase diagram, defining the outer limits of the claimed range of compositions.

- 35 Figure 2 depicts a further ternary phase diagram, defining a particular embodiment of the claimed range of compositions.

Figure 3 depicts a further ternary phase diagram, defining a particular embodiment of the claimed range of compositions.

- 5 Figure 4 depicts a further ternary phase diagram, defining a particular embodiment of the claimed range of compositions.

The figures are derived from the testing of a range of combinations of the three cooling compounds, the actual results being shown in the following table:

"180" %w/w	"190" %w/w	menthyl lactate %w/w	After Heating to 100°C	On cooling to 20°C	On standing 7days @ 20°C
0	0	100	Liquid	Solid	-
12	10	78	Liquid	Liquid	Liquid + Haze
20	20	60	Liquid	Liquid	Liquid + Haze
12	30	58	Liquid	Liquid	Liquid
50	0	50	Liquid + Solids	-	-
0	50	50	Liquid	Liquid	Liquid
26	26	48	Liquid	Liquid + Solids	-
20	36	44	Liquid	Liquid	Liquid
15	50	35	Liquid	Liquid	Liquid
25	45	30	Liquid	Liquid	Liquid
50	20	30	Liquid + Solids	-	-
10	80	10	Liquid	Liquid	Liquid
30	60	10	Liquid	Liquid	Liquid + Solids
50	40	10	Liquid + Solids	-	-
70	20	10	Liquid + Solids	-	-
100	0	0	Solid	-	-
0	100	0	Liquid	Solid	-

The various combinations were tested by first heating to 100 °C, then again after allowing them to cool to 20 °C and finally observations after standing for 7 days at 20 °C.

The various results are evaluated this:

5 Liquid – most desirable

Liquid + haze – not so desirable, but usable

Liquid + solids – undesirable

Solid – undesirable

Blank – previous result undesirable, so not tested further.

10

It can be seen that the most desirable combinations are liquid and remain liquid over a long period, making them easy to prepare and store.

Example

15 A mouthwash base was prepared by combining the following components...

To samples of the base were added 0.02%w/w of a combination of 180, 190 and menthyl lactate in the weight proportions 15:50:35. In one case, the combination was added as a mixture of the individual solid powders, in the other case as a liquid blend as hereinabove

20 described.

It was noticeable that parts of the solid powders were difficult to dissolve, some proportion not dissolving at all. On the other hand, the liquid blend was easily incorporated into the base, and there is assurance that the blend has been homogeneously distributed through

25 the mouthwash.

The resulting toothpaste formulations were tested by a panel of experienced testers. It was found that the formulations containing the liquid blend gave a noticeably enhanced cooling effect compared with the powders, even though the same proportions were used.

30 It is believed that the difficulty of dissolving the powders was responsible for the lower cooling effect.

In addition, the addition of the liquid blend was much easier than with the powder, and the final product is free from the potentially irritant effects of undissolved powders on skin on

35 mucous membranes.

Claims:

1. A liquid cooling composition that is a mixture of (N-(4-cyanomethylphenyl) p-menthanecarboxamide, N-(2-pyridin-2-ylethyl) p-menthanecarboxamide and menthyl lactate, the composition being characterized in that, in a triangular ternary phase diagram of (N-(4-cyanomethylphenyl) p-menthanecarboxamide, N-(2-pyridin-2-ylethyl) p-menthanecarboxamide and menthyl lactate, the composition falls within that portion of the diagram bounded by the coordinates of the following table:

menthyl lactate	(N-(4-cyanomethylphenyl) p-menthanecarboxamide,	N-(2-pyridin-2-ylethyl) p-menthanecarboxamide
100	0	0
80	20	0
0	31.5	68.5
0	0	100

2. A liquid cooling mixture according to claim 1, in which the mixture within that portion of the diagram bounded by the coordinates of the following table:

menthyl lactate	(N-(4-cyanomethylphenyl) p-menthanecarboxamide,	N-(2-pyridin-2-ylethyl) p-menthanecarboxamide
100	0	0
80	20	0
10	30	60
20	0	80

3. A liquid cooling mixture according to claim 1, in which the mixture within that portion of the diagram bounded by the coordinates of the following table:

menthyl lactate	(N-(4-cyanomethylphenyl) p-menthanecarboxamide,	N-(2-pyridin-2-ylethyl) p-menthanecarboxamide
80	10	10
10	20	60
20	0	80

4. A liquid cooling mixture according to claim 1, in which the mixture within that portion of the diagram bounded by the coordinates of the following table:

menthyl lactate	(N-(4-cyanomethylphenyl) p-menthanecarboxamide,	N-(2-pyridin-2-ylethyl) p- menthanecarboxamide
20	20	60
40	20	40
50	10	40
20	10	70

5. A liquid cooling mixture according to any one of claims 1-4, in which all three components are present in the mixture.
6. A product comprising a product base and a cooling effect-providing proportion of a liquid cooling composition according to claim 1.
7. A product according to claim 6, in which the proportion of liquid cooling composition is from 5 to 5000mg/kg, particularly from 50 to 1500mg/kg
8. A product according to claim 6, in which the product is an oral care product.
9. A method of providing to a product a cooling sensation for the skin or the mucous membranes, comprising the addition to a product base of a cooling effect-providing proportion of a liquid cooling composition according to claim 1.

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Figure 1

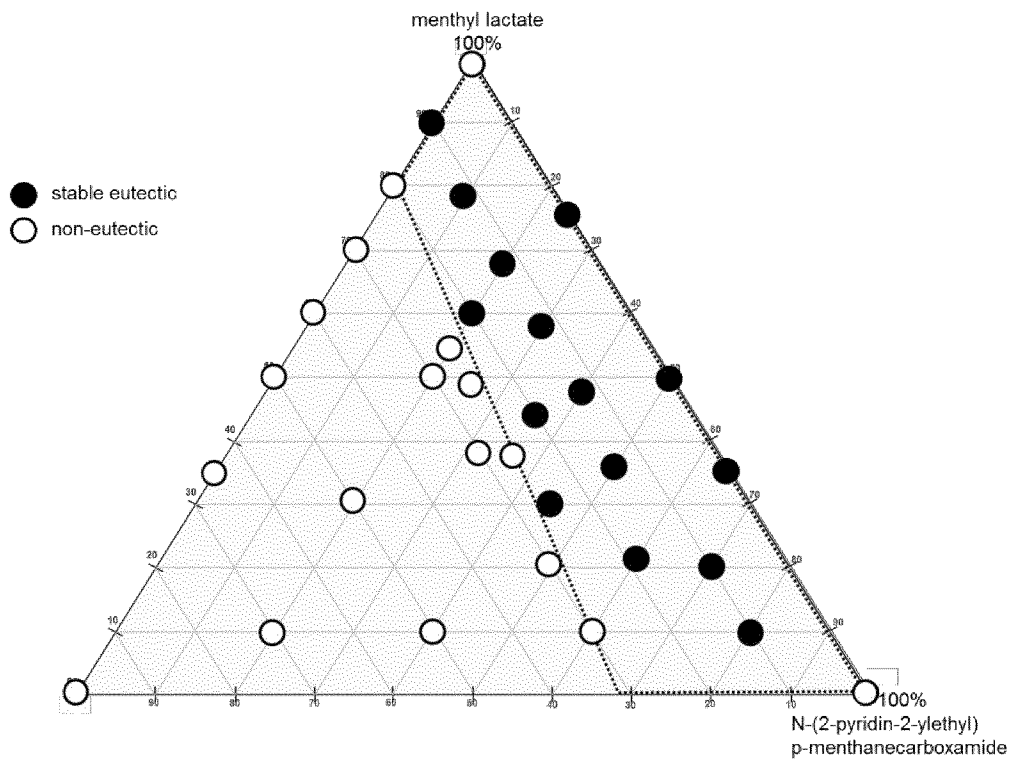
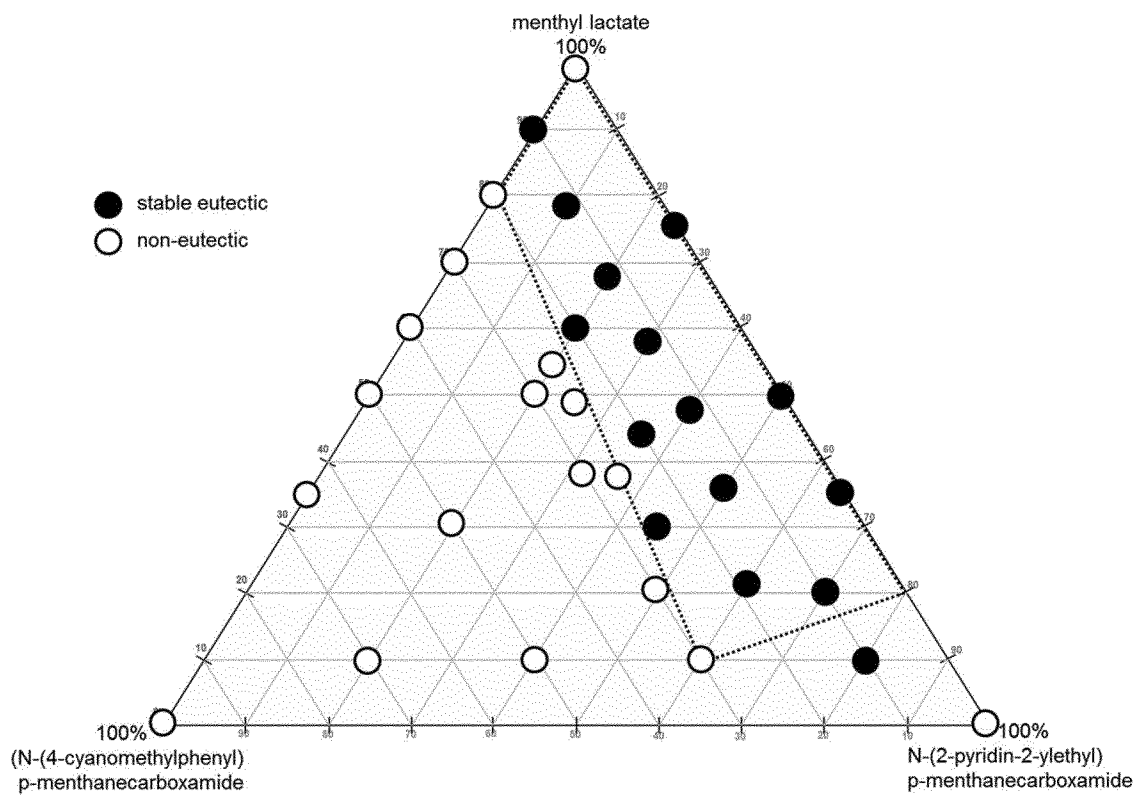


Figure 2



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Figure 3

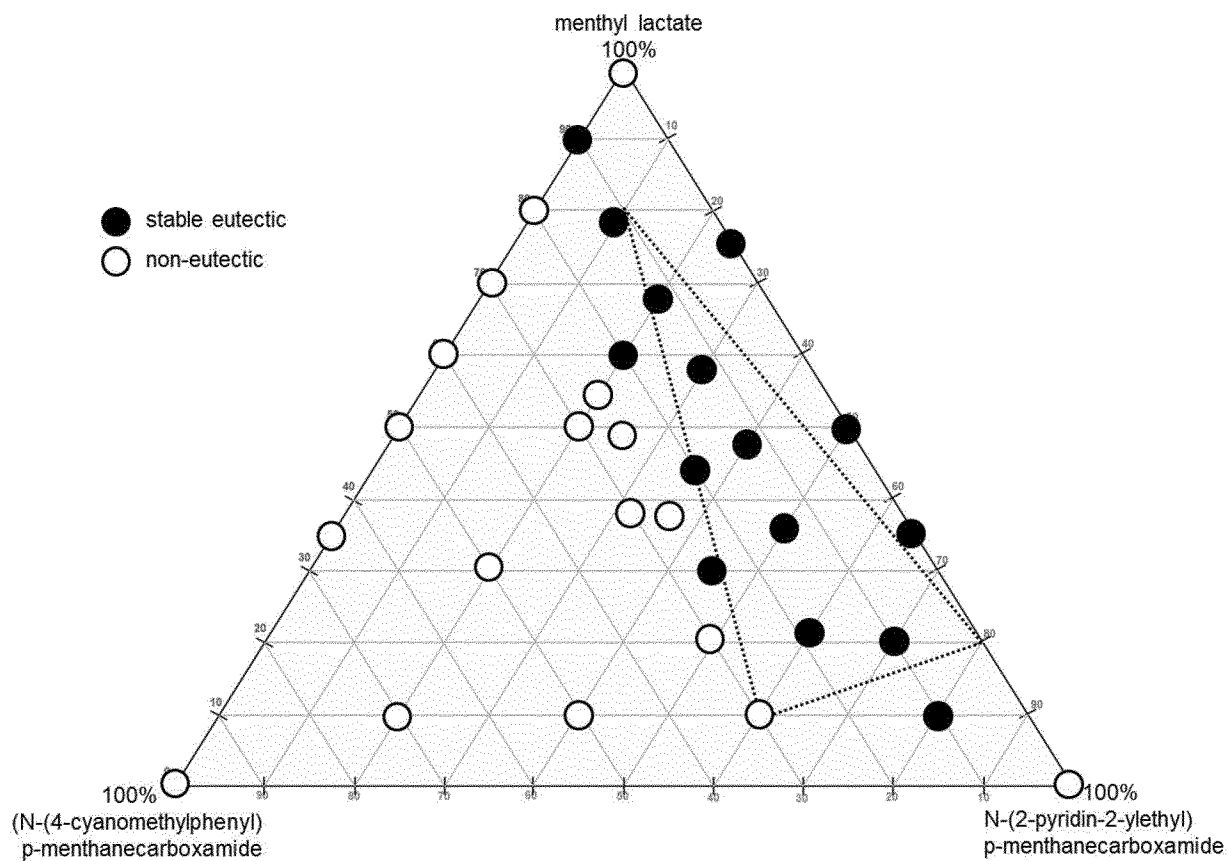
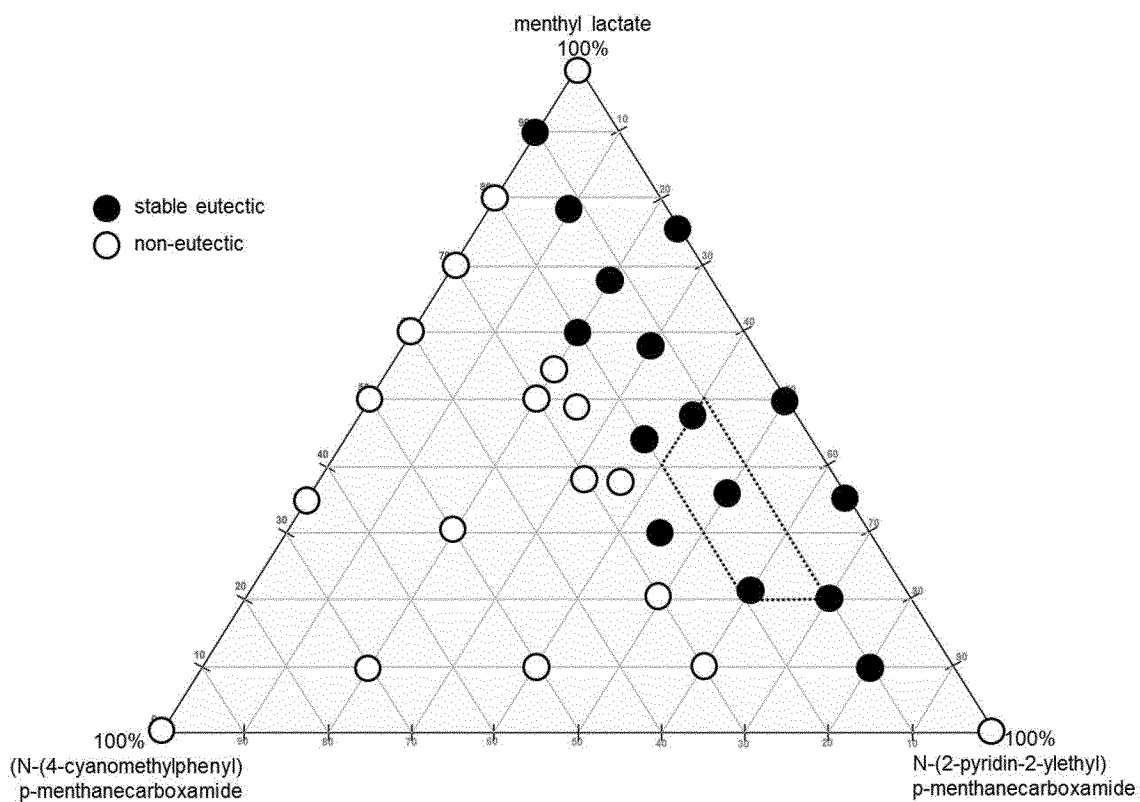


Figure 4



INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2018/054633

A. CLASSIFICATION OF SUBJECT MATTER INV. A61Q11/00 A61K8/42 A61K8/49 A61K8/37 ADD.		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) A61K A61Q		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) EPO-Internal, CHEM ABS Data, WPI Data		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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☒ Further documents are listed in the continuation of Box C. ☒ See patent family annex.		
* Special categories of cited documents : "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international search	Date of mailing of the international search report	
11 April 2018	26/04/2018	
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer Ruckebusch, Virginie	

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Information on patent family members

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