IONIC LIQUID FORMULATIONS FOR TREATING DIABETES

RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Patent Application No. 63/073,172 filed on September 01, 2020, U.S. Provisional Patent Application No. 63/154,461 filed on February 26, 2021, and U.S. Provisional Patent Application No. 63/160,575 filed on March 12, 2021, the entire contents of each of which are hereby incorporated by reference.

BACKGROUND OF THE INVENTION

[0002] Diabetes is a metabolic disease characterized by the inability of the pancreas to secrete a level of insulin adequate to maintain a normal level of systemic glucose. Despite advances, there remains a need for novel treatments of diabetes.

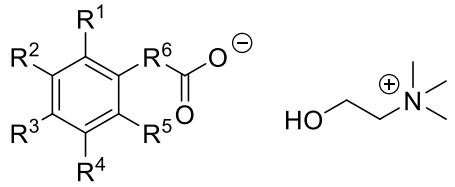
SUMMARY ~~OF THE INVENTION~~

[0002a] In an aspect of the present disclosure, there is provided a composition comprising one or more agents, and an ionic liquid,

wherein the one or more agents are selected from the group consisting of a nucleic acid, a small molecule, and a polypeptide, and

wherein:

(A) (i) the ionic liquid is represented by Formula (I):



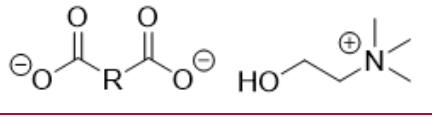
Formula (I),

wherein:

R^1, R^2, R^3, R^4, and R^5 are independently selected from hydrogen, halo, cyano, nitro, amino, C_{1-6}alkoxy, C_{1-6}heteroalkyl, C_{1-6}haloalkyl, C_{1-6}alkyl, C_{2-6}alkenyl, and C_{2-6}alkynyl; and

R^6 is selected from C_{1-6}alkyl, C_{2-6}alkenyl, and C_{2-6}alkynyl;

(ii) the ionic liquid is represented by Formula (II):

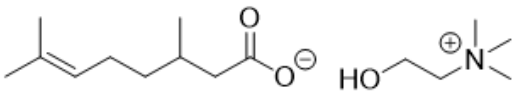


Formula (II),

wherein:

R is selected from C_{1-6}alkyl, C_{2-6}alkenyl, and C_{2-6}alkynyl; or

(iii) the ionic liquid is represented by Formula (III):



Formula (III); or

(B) the ionic liquid comprises an anionic component selected from the group consisting of (R)-α-lipoic acid, 2-(4-isobutylphenyl)propionic acid, 2-(4,4-dimethyl-2-pentanyl)-5,7,7-trimethyloctanoic acid, 2-hexyldecanoic acid, 2-hydroxyhippuric acid, 3,7-dimethyloctanoic acid, 4-methylhexanoic acid, 4-methyloctanoic acid, 4-methylvaleric acid, 5-norbornene-2-carboxylic acid, abietic acid, acetic acid, arachidonic acid, caffeic acid, cinnamic acid, citric acid, citronellic acid, crotonic acid, D-(+)-galactonic acid, decanoic acid, deoxycholic acid, dihydrobenzoic acid, eicosapentanoic acid, ellagic acid, fumaric acid, geranic acid, glutaric acid, glycolic acid, hexanoic acid, hydrocinnamic acid (3-phenylpropionic acid), isovaleric acid, L-(+)-tartaric acid, L-ascorbic acid, L-glutathione reduced, lactic acid, lauric acid, levulinic acid, linoleic acid, linolenic acid, maleic acid, malonic acid, mesaconic acid, nonanoic acid, octanoic acid, oleic acid, p-toluenesulfonic acid, perillic acid, phosphoric acid, pimelic acid, propionic acid, pyroglutamic acid, pyruvic acid, ricinoleic acid, sorbic acid, syringic acid, trans-2-decenoic acid, trans-2-hexenoic acid, trans-2-octenoic acid, trans-3-octenoic acid, trans-7-octenoic acid, trans-ferulic acid, undecanoic acid, vanillic acid, α-ketoglutaric acid, succinic acid, malic acid, mandelic acid, and octenoic acid.

[0002b] In another aspect of the present disclosure, there is provided a use of the composition disclosed herein in the manufacture of a medicament for treating a disease or disorder in a subject in need thereof,

wherein the composition is formulated in an effective amount to treat the disease or disorder in the subject; and

wherein the disease or disorder is diabetes or non-alcoholic steatohepatitis.

[0002c] In a further aspect of the present disclosure, there is provided a use of the composition disclosed herein in the manufacture of a medicament for treating obesity, preventing weight gain, or reducing weight in a subject in need thereof,

wherein the composition is formulated in an effective amount to treat obesity, to prevent weight gain, or to reduce weight in the subject.

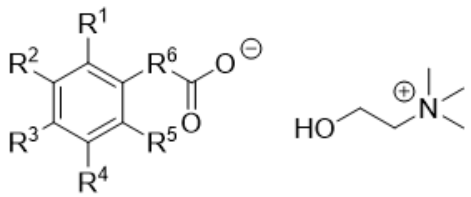
[0002d] In another aspect of the present disclosure, there is provided a use of the composition disclosed herein in the manufacture of a medicament for delivering one or more agents to a subject in need thereof,

wherein the one or more agents are formulated in combination with the composition; and

wherein the delivery of the one or more agents formulated in combination with the composition is more efficient relative to the delivery of the one or more agents formulated without the composition.

[0002e] In a further aspect of the present disclosure, there is provided a composition comprising an ionic liquid, wherein:

(A) (i) the ionic liquid is represented by Formula (I):



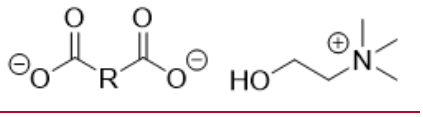
Formula (I),

wherein:

R^1, R^2, R^3, R^4, and R^5 are independently selected from hydrogen, halo, cyano, nitro, amino, C_{1-6}alkoxy, C_{1-6}heteroalkyl, C_{1-6}haloalkyl, C_{1-6}alkyl, C_{2-6}alkenyl, and C_{2-6}alkynyl; and

R^6 is selected from C_{1-6}alkyl, C_{2-6}alkenyl, and C_{2-6}alkynyl;

(ii) the ionic liquid is represented by Formula (II):

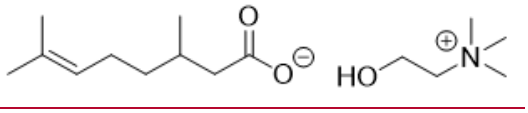


Formula (II),

wherein:

R is selected from C_{1-6}alkyl, C_{2-6}alkenyl, and C_{2-6}alkynyl; or

(iii) the ionic liquid is represented by Formula (III):



Formula (III); or

(B) the ionic liquid comprises an anionic component selected from the group consisting of (R)-α-lipoic acid, 2-(4-isobutylphenyl)propionic acid, 2-(4,4-dimethyl-2-pentanyl)-5,7,7-trimethyloctanoic acid, 2-hexyldecanoic acid, 2-hydroxyhippuric acid, 3,7-dimethyloctanoic acid, 4-methylhexanoic acid, 4-methyloctanoic acid, 4-methylvaleric acid, 5-norbornene-2-carboxylic acid, abietic acid, acetic acid, arachidonic acid, caffeic acid, cinnamic acid, citric acid, citronellic acid, crotonic acid, D-(+)-galactonic acid, decanoic acid, deoxycholic acid, dihydrobenzoic acid, eicosapentanoic acid, ellagic acid, fumaric acid, geranic acid, glutaric acid, glycolic acid, hexanoic acid, hydrocinnamic acid (3-phenylpropionic acid), isovaleric acid, L-(+)-tartaric acid, L-ascorbic acid, L-glutathione reduced, lactic acid, lauric acid, levulinic acid, linoleic acid, linolenic acid, maleic acid, malonic acid, mesaconic acid, nonanoic acid, octanoic acid, oleic acid, p-toluenesulfonic acid, perillic acid, phosphoric acid, pimelic acid, propionic acid, pyroglutamic acid, pyruvic acid, ricinoleic acid, sorbic acid, syringic acid, trans-2-decenoic acid, trans-2-hexenoic acid, trans-2-octenoic acid, trans-3-octenoic acid, trans-7-octenoic acid, trans-ferulic acid, undecanoic acid, vanillic acid, α-ketoglutaric acid, succinic acid, malic acid, mandelic acid, and octenoic acid.

[0002f] In another aspect of the present disclosure, there is provided a composition disclosed herein, for use in therapy.

[0003] Provided herein, in one ~~aspect~~example, is a method of treating a disease or disorder in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a composition comprising an ionic liquid.

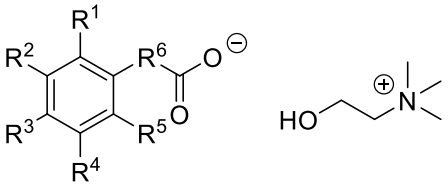
[0004] In some ~~embodiment~~examples, the disease or disorder is diabetes. In some ~~embodiment~~examples, the disease or disorder is Type 1 diabetes. In some ~~embodiment~~examples, the disease or disorder is Type 2 diabetes. In some ~~embodiment~~examples, the disease or disorder is non-alcoholic steatohepatitis.

[0005] Provided herein, in another ~~aspect~~example, is a method of treating obesity, preventing weight gain, or reducing weight in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a composition comprising an ionic liquid.

[0006] In some ~~embodiment~~examples, the composition is administered via subcutaneous, intravenous, or oral administration. In some ~~embodiment~~examples, the composition is administered via oral administration. In some ~~embodiment~~examples, the composition is administered as a liquid-filled capsule. In some ~~embodiment~~examples, the composition is administered in a single dose. In some ~~embodiment~~examples, the composition is administered in multiple doses. In some ~~embodiment~~examples, the composition is administered to a mucus membrane.

[0007] In some ~~embodiment~~examples, the composition comprises the ionic liquid at a concentration of at least 0.1% weight per volume. In some ~~embodiment~~examples, the composition comprises the ionic liquid at a concentration of at least 0.05M. In some ~~embodiment~~examples, the ionic liquid comprises a cation:anion ratio of from about 4:1 to about 1:4.

[0008] In some ~~embodiment~~examples, the ionic liquid is represented by Formula (I):



Formula (I),

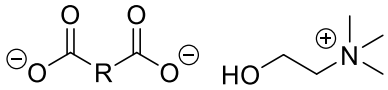
wherein:

R^1, R^2, R^3, R^4, and R^5 are independently selected from hydrogen, halo, cyano, nitro, amino, C_{1-6}alkoxy, C_{1-6}heteroalkyl, C_{1-6}haloalkyl, C_{1-6}alkyl, C_{2-6}alkenyl, and C_{2-6}alkynyl; and R^6 is selected from C_{1-6}alkyl, C_{2-6}alkenyl, and C_{2-6}alkynyl.

[0009] In some ~~embodiment~~examples, at least two of R^1, R^2, R^3, R^4, and R^5 are hydrogen. In some ~~embodiment~~examples, at least three of R^1, R^2, R^3, R^4, and R^5 are hydrogen. In some ~~embodiment~~examples, R^1, R^2, R^3, R^4, and R^5 are hydrogen.

[0010] In some ~~embodiment~~examples, R^6 is selected from C_{1-6}alkyl and C_{2-6}alkenyl. In some ~~embodiment~~examples, R^6 is C_{1-6}alkyl. In some ~~embodiment~~examples, R^6 is C_2alkyl. In some ~~embodiment~~examples, R^6 is C_{1-6}alkenyl. In some ~~embodiment~~examples, R^6 is C_2alkenyl.

[0011] In some ~~embodiment~~examples, the ionic liquid is represented by Formula (II):



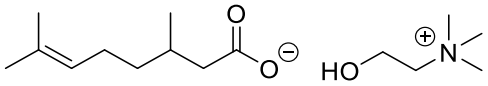
Formula (II),

wherein:

R is selected from C_{1-6}alkyl, C_{2-6}alkenyl, and C_{2-6}alkynyl.

[0012] In some ~~embodiment~~examples, R is C_{1-6}alkyl. In some ~~embodiment~~examples, R is C_1alkyl. In some ~~embodiment~~examples, R is C_3alkyl.

[0013] In some ~~embodiment~~examples, the ionic liquid is represented by Formula (III):



Formula (III).

[0014] In some ~~embodiment~~examples, the ionic liquid comprises a cholinium cation and an anion selected from cinnamate, hydrocinnamate, malonate, citronellate, and glutarate. In some ~~embodiment~~examples, the anion is selected from cinnamate, hydrocinnamate, and citronellate.

[0015] In some ~~embodiment~~examples, the composition further comprises one or more additional agents. In some ~~embodiment~~examples, the one or more additional agents are selected from a nucleic acid, a small molecule, and a polypeptide. In some ~~embodiment~~examples, the one or more additional agents comprise a

nucleic acid. In some ~~embodiment~~examples, the one or more additional agents comprise a small molecule. In some ~~embodiment~~examples, the one or more additional agents comprise a polypeptide.

[0016] In some ~~embodiment~~examples, the one or more additional agents are selected from a glucagon-like peptide (GLP-1), a glucagon-like peptide derivative, and a glucagon-like peptide mimetic. In some ~~embodiment~~examples, the one or more additional agents are selected from liraglutide, exenatide, and semaglutide. In some ~~embodiment~~examples, the one or more additional agents comprise liraglutide.

[0017] In some ~~embodiment~~examples, the one or more additional agents are selected from insulin and pramlintide.

[0018] In some ~~embodiment~~examples, the composition further comprises a pharmaceutically acceptable excipient.

[0019] Provided herein, in another ~~aspect~~example, is a composition comprising an ionic liquid, wherein the ionic liquid comprises choline and hydrocinnamic acid in a 1:2 molar ratio.

[0020] Provided herein, in another ~~aspect~~example, is a composition comprising an ionic liquid, wherein the ionic liquid comprises choline and cinnamic acid in a 1:1 molar ratio.

[0021] Provided herein, in another ~~aspect~~example, is a composition comprising an ionic liquid, wherein the ionic liquid comprises choline and glutaric acid in a 1:1 molar ratio.

[0022] Provided herein, in another ~~aspect~~example, is a composition comprising an ionic liquid, wherein the ionic liquid comprises choline and malonic acid in a 1:1 molar ratio.

[0023] Provided herein, in another ~~aspect~~example, is a composition comprising an ionic liquid, wherein the ionic liquid comprises choline and octenoic acid in a 1:1 molar ratio.

[0024] Provided herein, in another ~~aspect~~example, is a composition comprising an ionic liquid, wherein the ionic liquid comprises choline and octenoic acid in a 1:2 molar ratio.

[0025] Provided herein, in another ~~aspect~~example, is a composition comprising an ionic liquid, wherein the ionic liquid comprises choline and citronellic acid in a 1:1 molar ratio.

[0026] Provided herein, in another ~~aspect~~example, is a composition comprising an ionic liquid, wherein the ionic liquid comprises choline and citronellic acid in a 1:2 molar ratio.

[0027] In some ~~embodiment~~examples, the composition further comprises one or more additional agents. In some ~~embodiment~~examples, the one or more additional agents are selected from a nucleic acid, a small molecule, and a polypeptide. In some ~~embodiment~~examples, the one or more additional agents comprise a nucleic acid. In some ~~embodiment~~examples, the one or more additional agents comprise a small molecule. In some ~~embodiment~~examples, the one or more additional agents comprise a polypeptide.

[0028] In some ~~embodiment~~examples, the one or more additional agents are selected from a glucagon-like peptide (GLP-1), a glucagon-like peptide derivative, and a glucagon-like peptide mimetic. In some

~~embodiment~~examples, the one or more additional agents are selected from liraglutide, exenatide, and semaglutide. In some ~~embodiment~~examples, the one or more additional agents comprise liraglutide.

[0029] In some ~~embodiment~~examples, the one or more additional agents are selected from insulin and pramlintide.

[0030] Provided herein, in another ~~aspect~~example, is a pharmaceutical composition comprising a composition described herein and a pharmaceutically acceptable excipient

INCORPORATION BY REFERENCE

[0031] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference.

BRIEF DESCRIPTION OF THE DRAWINGS

[0032] The novel features of the invention are set forth with particularity in the appended claims. A better understanding of the features and advantages of the present invention will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the invention are utilized, and the accompanying drawings of which:

[0033] **FIG. 1** shows the amino acid sequence of glucagon-like peptide-1 (GLP-1) (SEQ ID NO: 1).

[0034] **FIG. 2** shows the amino acid sequence of Exenatide (SEQ ID NO: 2).

[0035] **FIG. 3** shows the amino acid sequence of Liraglutide (SEQ ID NO: 3).

[0036] **FIG. 4** shows the amino acid sequence of Semaglutide (SEQ ID NO: 4).

[0037] **FIG. 5** shows various ionic liquids which are liquid at room temperature.

[0038] **FIG. 6** shows various ionic liquids which are not liquid at room temperature.

[0039] **FIG. 7** shows the change in blood glucose levels over time following intrajejunal administration of choline-citronellic acid to non-diabetic rats.

[0040] **FIG. 8** shows the change in blood glucose levels over time following administration of choline-octanoic acid and choline-octenoic acid to non-diabetic rats.

[0041] **FIG. 9** shows the change in blood glucose levels over time following administration of citronellic acid to non-diabetic rats.

[0042] **FIG. 10** shows the change in blood glucose levels over time following subcutaneous and oral administration of choline-citronellic acid to non-diabetic rats.

[0043] **FIG. 11** shows the change in blood glucose levels over time following oral administration of choline-citronellic acid to diabetic rats.

[0044] **FIG. 12** shows the change in plasma insulin levels over time following intrajejunal, subcutaneous, and oral administration of choline-citronellic acid to diabetic rats.

CLAIMS

WHAT IS CLAIMED IS:

1. A method of treating a disease or disorder in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a composition comprising an ionic liquid.

2. The method of claim 1, wherein the disease or disorder is diabetes.

3. The method of claim 1 or claim 2, wherein the disease or disorder is Type 1 diabetes.

4. The method of claim 1 or claim 2, wherein the disease or disorder is Type 2 diabetes.

5. The method of claim 1, wherein the disease or disorder is non-alcoholic steatohepatitis.

6. A method of treating obesity, preventing weight gain, or reducing weight in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a composition comprising an ionic liquid.

7. The method of any one of claims 1 to 6, wherein the composition is administered via subcutaneous, intravenous, or oral administration.

8. The method of any one of claims 1 to 7, wherein the composition is administered via oral administration.

9. The method of any one of claims 1 to 8, wherein the composition is administered as a liquid-filled capsule.

10. The method of any one of claims 1 to 9, wherein the composition is administered in a single dose.

11. The method of any one of claims 1 to 9, wherein the composition is administered in multiple doses.

12. The method of any one of claims 1 to 11, wherein the composition is administered to a mucus membrane.

13. The method of any one of claims 1 to 12, wherein the composition comprises the ionic liquid at a concentration of at least 0.1% weight per volume.

14. The method of any one of claims 1 to 12, wherein the composition comprises the ionic liquid at a concentration of at least 0.05M.

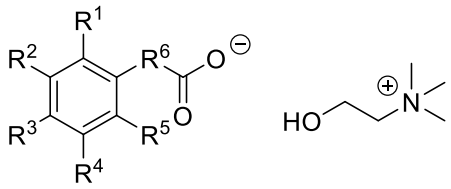
15. The method of any one of claims 1 to 14, wherein the ionic liquid comprises a cation:anion ratio of from about 4:1 to about 1:4.

~~16.~~1. ~~The method of any one of claims 1 to 15~~A composition comprising one or more agents, and an ionic liquid,

wherein the one or more agents are selected from the group consisting of a nucleic acid, a small molecule, and a polypeptide, and

wherein:

(A) (i) the ionic liquid is represented by Formula (I):



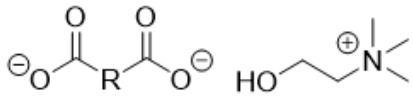
Formula (I),

wherein:

R^1, R^2, R^3, R^4, and R^5 are independently selected from hydrogen, halo, cyano, nitro, amino, C_{1-6}alkoxy, C_{1-}6heteroalkyl, C_{1-}6haloalkyl, C_{1-6}alkyl, C_{2-6}alkenyl, and C_{2-6}alkynyl; and

R^6 is selected from C_{1-6}alkyl, C_{2-6}alkenyl, and C_{2-6}alkynyl;

(ii) the ionic liquid is represented by Formula (II):

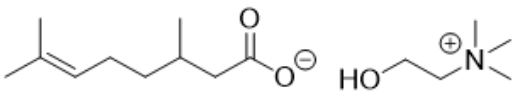


Formula (II),

wherein:

R is selected from C_{1-6}alkyl, C_{2-6}alkenyl, and C_{2-6}alkynyl; or

(iii) the ionic liquid is represented by Formula (III):



Formula (III); or

(B) the ionic liquid comprises an anionic component selected from the group consisting of (R)-α-lipoic acid, 2-(4-isobutylphenyl)propionic acid, 2-(4,4-dimethyl-2-pentanyl)-5,7,7-trimethyloctanoic acid, 2-hexyldecanoic acid, 2-hydroxyhippuric acid, 3,7-dimethyloctanoic

acid, 4-methylhexanoic acid, 4-methyloctanoic acid, 4-methylvaleric acid, 5-norbornene-2-carboxylic acid, abietic acid, acetic acid, arachidonic acid, caffeic acid, cinnamic acid, citric acid, citronellic acid, crotonic acid, D-(+)-galactonic acid, decanoic acid, deoxycholic acid, dihydrobenzoic acid, eicosapentanoic acid, ellagic acid, fumaric acid, geranic acid, glutaric acid, glycolic acid, hexanoic acid, hydrocinnamic acid (3-phenylpropionic acid), isovaleric acid, L-(+)-tartaric acid, L-ascorbic acid, L-glutathione reduced, lactic acid, lauric acid, levulinic acid, linoleic acid, linolenic acid, maleic acid, malonic acid, mesaconic acid, nonanoic acid, octanoic acid, oleic acid, p-toluenesulfonic acid, perillic acid, phosphoric acid, pimelic acid, propionic acid, pyroglutamic acid, pyruvic acid, ricinoleic acid, sorbic acid, syringic acid, trans-2-decenoic acid, trans-2-hexenoic acid, trans-2-octenoic acid, trans-3-octenoic acid, trans-7-octenoic acid, trans-ferulic acid, undecanoic acid, vanillic acid, α-ketoglutaric acid, succinic acid, malic acid, mandelic acid, and octenoic acid.

2. The composition of claim 1, wherein the one or more agents are selected from the group consisting of a glucagon-like peptide (GLP-1) or derivative or mimetic thereof, insulin, and pramlintide.

3. The composition of claim 1 or 2, wherein the one or more agents are liraglutide, exenatide, and/or semaglutide.

4. The composition of any one of claims 1-3, wherein the composition comprises semaglutide, and choline-cinnamic acid.

5. The composition of any one of claims 1-4, wherein the ionic liquid is represented by Formula (I), and wherein:

(i) at least two of R^1, R^2, R^3, R^4, and R^5 are hydrogen;

(ii) at least three of R^1, R^2, R^3, R^4, and R^5 are hydrogen; or

(iii) R^1, R^2, R^3, R^4, and R^5 are hydrogen.

6. The composition of any one of claims 1-5, wherein the ionic liquid is represented by Formula (I), and wherein R^6 is selected from the group consisting of C_{1-6}alkyl and C_{2-6}alkenyl.

7. The composition of any one of claims 1-6, wherein the ionic liquid is represented by Formula (I), and wherein R^6 is C_{1-6}alkyl, C_2alkyl, C_{1-6}alkenyl, or C_2alkenyl.

8. The composition of any one of claims 1-4, wherein the ionic liquid is represented by Formula (II), and wherein R is C_{1-6}alkyl, C_1alkyl, or C_3alkyl.

9. The composition of any one of claims 1-8, wherein the ionic liquid comprises a cholinium cation.

10. The composition of any one of claims 1-9, wherein the ionic liquid comprises a cholinium cation and an anion selected from the group consisting of cinnamate, hydrocinnamate, malonate, citronellate, octenoate, linoleate, and glutarate.

11. The composition of any one of claims 1-10, wherein the ionic liquid comprises choline-hydrocinnamic acid, choline-cinnamic acid, choline-glutaric acid, choline-malonic acid, choline-octenoic acid, choline-linoleic acid, or choline-citronellic acid.

12. The composition of any one of claims 1-11, wherein:

(i) the composition comprises the ionic liquid at a concentration of at least 0.1% weight per volume;

(ii) the composition comprises the ionic liquid at a concentration of at least 0.05M; and/or

(iii) the ionic liquid comprises a cation:anion molar ratio of from about 4:1 to about 1:4.

13. The composition of any one of claims 1-12, wherein the ionic liquid comprises:

(i) choline and hydrocinnamic acid in a 1:2 molar ratio;

(ii) choline and cinnamic acid in a 1:1 molar ratio;

(iii) choline and glutaric acid in a 1:1 molar ratio;

(iv) choline and malonic acid in a 1:1 molar ratio;

(v) choline and octenoic acid in a 1:1 molar ratio;

(vi) choline and octenoic acid in a 1:2 molar ratio;

(vii) choline and citronellic acid in a 1:1 molar ratio; or

(viii) choline and citronellic acid in a 1:2 molar ratio.

14. The composition of any one of claims 1-13, wherein the composition is formulated as a liquid-filled capsule, a pill, a caplet, an aerosol spray, or a liquid.

15. The composition of any one of claims 1-14, wherein the composition further comprises a pharmaceutically acceptable excipient.

16. Use of the composition of any one of claims 1-15 in the manufacture of a medicament for treating a disease or disorder in a subject in need thereof,

wherein the composition is formulated in an effective amount to treat the disease or disorder in the subject; and

wherein the disease or disorder is diabetes or non-alcoholic steatohepatitis.

17. The use of claim 16, wherein the disease or disorder is diabetes, and the diabetes is Type 1 diabetes or Type 2 diabetes.

18. Use of the composition of claims 1-15 in the manufacture of a medicament for treating obesity, preventing weight gain, or reducing weight in a subject in need thereof,

wherein the composition is formulated in an effective amount to treat obesity, to prevent weight gain, or to reduce weight in the subject.

19. The use of any one of claims 16-18, wherein:

(i) the composition is formulated for administration via subcutaneous, intravenous, or oral administration, or for administration to a mucus membrane; and/or

(ii) the composition is formulated for administration in a single dose or in multiple doses.

20. Use of the composition of claims 1-15 in the manufacture of a medicament for delivering one or more agents to a subject in need thereof,

wherein the one or more agents are formulated in combination with the composition; and

wherein the delivery of the one or more agents formulated in combination with the composition is more efficient relative to the delivery of the one or more agents formulated without the composition.

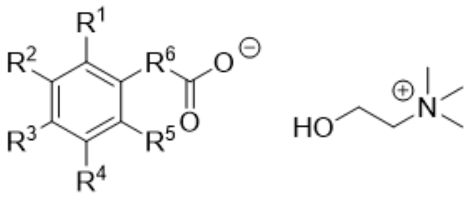
21. The use of claim 20, wherein the one or more agents are selected from the group consisting of a nucleic acid, a small molecule, and a polypeptide.

22. The use of claim 20 or 21, wherein the one or more agents are selected from the group consisting of a glucagon-like peptide (GLP-1) or derivative or mimetic thereof, insulin, and pramlintide.

23. The use of any one of claims 20-22, wherein the one or more agents are liraglutide, exenatide, and/or semaglutide.

24. A composition comprising an ionic liquid, wherein:

(A) (i) the ionic liquid is represented by Formula (I):



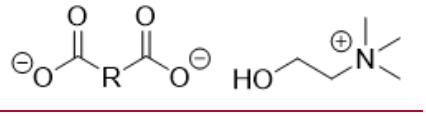
Formula (I),

wherein:

R^1, R^2, R^3, R^4, and R^5 are independently selected from hydrogen, halo, cyano, nitro, amino, C_{1-6}alkoxy, C_{1-6}heteroalkyl, C_{1-6}haloalkyl, C_{1-6}alkyl, C_{2-6}alkenyl, and C_{2-6}alkynyl; and

R^6 is selected from C_{1-6}alkyl, C_{2-6}alkenyl, and C_{2-6}alkynyl;

(ii) the ionic liquid is represented by Formula (II):

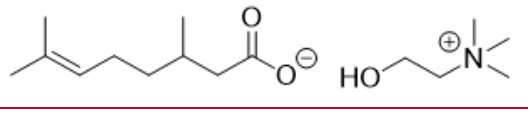


Formula (II),

wherein:

R is selected from C_{1-6}alkyl, C_{2-6}alkenyl, and C_{2-6}alkynyl; or

(iii) the ionic liquid is represented by Formula (III):



Formula (III); or

(B) the ionic liquid comprises an anionic component selected from the group consisting of (R)-α-lipoic acid, 2-(4-isobutylphenyl)propionic acid, 2-(4,4-dimethyl-2-pentanyl)-5,7,7-trimethyloctanoic acid, 2-hexyldecanoic acid, 2-hydroxyhippuric acid, 3,7-dimethyloctanoic acid, 4-methylhexanoic acid, 4-methyloctanoic acid, 4-methylvaleric acid, 5-norbornene-2-carboxylic acid, abietic acid, acetic acid, arachidonic acid, caffeic acid, cinnamic acid, citric acid, citronellic acid, crotonic acid, D-(+)-galactonic acid, decanoic acid, deoxycholic acid, dihydrobenzoic acid, eicosapentanoic acid, ellagic acid, fumaric acid, geranic acid, glutaric acid, glycolic acid, hexanoic acid, hydrocinnamic acid (3-phenylpropionic acid), isovaleric acid, L-(+)-tartaric acid, L-ascorbic acid, L-glutathione reduced, lactic acid, lauric acid, levulinic acid, linoleic acid, linolenic acid, maleic acid, malonic acid, mesaconic acid, nonanoic acid, octanoic acid, oleic acid, p-toluenesulfonic acid, perillic acid, phosphoric acid, pimelic acid, propionic acid, pyroglutamic acid, pyruvic acid, ricinoleic acid, sorbic acid, syringic acid, trans-2-decenoic acid, trans-2-hexenoic acid, trans-2-octenoic acid, trans-3-octenoic acid, trans-7-octenoic acid, trans-ferulic acid, undecanoic acid, vanillic acid, α-ketoglutaric acid, succinic acid, malic acid, mandelic acid, and octenoic acid.

25. A composition of any one of claims 1-15 or 24, for use in therapy.

~~17. The method of claim 16, wherein at least two of R^1, R^2, R^3, R^4, and R^5 are hydrogen.~~

~~18. The method of claim 17, wherein at least three of R^1, R^2, R^3, R^4, and R^5 are hydrogen.~~

~~19. The method of claim 18, wherein R^1, R^2, R^3, R^4, and R^5 are hydrogen~~

~~20. The method of claim 16, wherein R^6 is selected from C_{1-6}alkyl and C_{2-6}alkenyl.~~

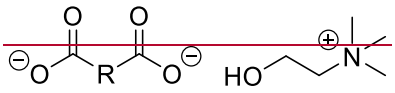
21. The method of claim 20, wherein R^6 is C_{1-6}alkyl.

22. The method of claim 21, wherein R^6 is C_2alkyl.

23. The method of claim 20, wherein R^6 is C_{1-6}alkenyl.

24. The method of claim 23, wherein R^6 is C_2alkenyl.

25. The method of any one of claims 1 to 15, wherein the ionic liquid is represented by Formula (II):



Formula (II),

wherein:

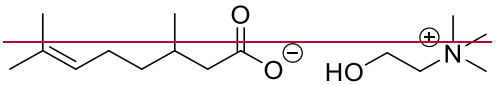
R is selected from C_{1-6}alkyl, C_{2-6}alkenyl, and C_{2-6}alkynyl.

26. The method of claim 25, wherein R is C_{1-6}alkyl.

27. The method of claim 26, wherein R is C_1alkyl.

28. The method of claim 26, wherein R is C_3alkyl.

29. The method of any one of claims 1 to 15, wherein the ionic liquid is represented by Formula (III):



Formula (III).

30. The method of any one of claims 1 to 15, wherein the ionic liquid comprises a cholinium cation and an anion selected from cinnamate, hydrocinnamate, malonate, citronellate, and glutarate.

31. The method of claim 30, wherein the anion is selected from cinnamate, hydrocinnamate, and citronellate.

32. The method of any one of claims 1 to 31, wherein the composition further comprises one or more additional agents.

33. The method of claim 32, wherein the one or more additional agents are selected from a nucleic acid, a small molecule, and a polypeptide.

34. The method of claim 33, wherein the one or more additional agents comprise a nucleic acid.

35. The method of claim 33, wherein the one or more additional agents comprise a small molecule.

36. The method of claim 33, wherein the one or more additional agents comprise a polypeptide.

37. The method of claim 32, wherein the one or more additional agents are selected from a glucagon-like peptide (GLP-1), a glucagon-like peptide derivative, and a glucagon-like peptide mimetic.

38. The method of claim 37, wherein the one or more additional agents are selected from liraglutide, exenatide, and semaglutide.

39. The method of claim 38, wherein the one or more additional agents comprise liraglutide.

40. The method of claim 32, wherein the one or more additional agents are selected from insulin and pramlintide.

41. The method of any one of claims 1 to 40, wherein the composition further comprises a pharmaceutically acceptable excipient.

42. A composition comprising an ionic liquid, wherein the ionic liquid comprises choline and hydrocinnamic acid in a 1:2 molar ratio.

43. A composition comprising an ionic liquid, wherein the ionic liquid comprises choline and cinnamic acid in a 1:1 molar ratio.

44. A composition comprising an ionic liquid, wherein the ionic liquid comprises choline and glutaric acid in a 1:1 molar ratio.

45. A composition comprising an ionic liquid, wherein the ionic liquid comprises choline and malonic acid in a 1:1 molar ratio.

46. A composition comprising an ionic liquid, wherein the ionic liquid comprises choline and octenoic acid in a 1:1 molar ratio.

47. A composition comprising an ionic liquid, wherein the ionic liquid comprises choline and octenoic acid in a 1:2 molar ratio.

48. A composition comprising an ionic liquid, wherein the ionic liquid comprises choline and citronellic acid in a 1:1 molar ratio.

49. A composition comprising an ionic liquid, wherein the ionic liquid comprises choline and citronellic acid in a 1:2 molar ratio.

~~50. The composition of any one of claims 42 to 49, further comprising one or more additional agents.~~

~~51. The composition of claim 50, wherein the one or more additional agents are selected from a nucleic acid, a small molecule, and a polypeptide~~

~~52. The composition of claim 51, wherein the one or more additional agents comprise a nucleic acid.~~

~~53. The composition of claim 51, wherein the one or more additional agents comprise a small molecule.~~

~~54. The composition of claim 51, wherein the one or more additional agents comprise a polypeptide.~~

~~55. The composition of claim 50, wherein the one or more additional agents are selected from a glucagon-like peptide (GLP-1), a glucagon-like peptide derivative, and a glucagon-like peptide mimetic.~~

~~56. The composition of claim 55, wherein the one or more additional agents are selected from liraglutide, exenatide, and semaglutide.~~

~~57. The composition of claim 56, wherein the one or more additional agents comprise liraglutide.~~

~~58. The composition of claim 50, wherein the one or more additional agents are selected from insulin and pramlintide.~~

~~59. A pharmaceutical composition comprising the composition of any one of claims 42 to 49 and a pharmaceutically acceptable excipient.~~