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

[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,

wherein the ionic liquid comprises cholinium as a cationic component, and

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 another aspect of the present disclosure, there is provided a composition disclosed herein, for use in therapy.

[0003] Provided herein, in one 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 examples, the disease or disorder is diabetes. In some examples, the disease or disorder is Type 1 diabetes. In some examples, the disease or disorder is Type 2 diabetes. In some examples, the disease or disorder is non-alcoholic steatohepatitis.

[0005] Provided herein, in another 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 examples, the composition is administered via subcutaneous, intravenous, or oral administration. In some examples, the composition is administered via oral administration. In some examples, the composition is administered as a liquid-filled capsule. In some examples, the composition is administered in a single dose. In some examples, the composition is administered in multiple doses. In some examples, the composition is administered to a mucus membrane.

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

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

CLAIMS

WHAT IS CLAIMED IS:

1. 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,
wherein the ionic liquid comprises cholinium as a cationic component, and

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, 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 and/ or exenatide.

4. The composition of any one of claims 1-3, wherein the ionic liquid comprises an anion selected from the group consisting of cinnamate, hydrocinnamate, malonate, citronellate, octenoate, linoleate, and glutarate.

5. The composition of any one of claims 1-4, 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.

6. The composition of any one of claims 1-5, 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.

7. The composition of any one of claims 1-6, 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.

8. The composition of any one of claims 1-7, wherein the composition is formulated as a liquid-filled capsule, a pill, a caplet, an aerosol spray, or a liquid.

9. The composition of any one of claims 1-8, wherein the composition further comprises a pharmaceutically acceptable excipient.

10. Use of the composition of any one of claims 1-9 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.

11. The use of claim 10, wherein the disease or disorder is diabetes, and the diabetes is Type 1 diabetes or Type 2 diabetes.

12. Use of the composition of claims 1-9 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.

13. The use of any one of claims 10-12, 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.

14. Use of the composition of claims 1-9 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.

15. The use of claim 14, wherein the one or more agents are selected from the group consisting of a nucleic acid, a small molecule, and a polypeptide.

16. The use of claim 14 or 15, 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.

17. The use of any one of claims 14-16, wherein the one or more agents are liraglutide and/or exenatide.

18. A composition of any one of claims 1-9, for use in therapy.