CLAIMS

1. A water-soluble complex comprising a non-nutritive sugar and a drug compound, which complex comprises:

a molar ratio of up to about 12 moles of the non-nutritive sugar for each mole of the drug compound, wherein the non-nutritive sugar is one or more of ADVANTAME®, NEOTAME®, thaumatin, saccharin, sucralose, Lou Han Guo, aspartame, acesulfame potassium, allulose, rubusoside, dulcoside B, dodecyl-β-D-maltoside, stevioside, or rebaudioside A,

provided that the water-soluble complex has at least a two (2) fold increase in the drug compound water solubility at 20 ºC. as compared to the water solubility of the drug compound not in the water-soluble complex or has one improved pharmacokinetic attribute; and

further, provided that a maximum amount of the non-nutritive sugar in a daily unit dose of the water-soluble complex is no more than about 5 mg/kg, optionally no more than 10 mg/kg of subject weight, and optionally no more than about 280 mg,

wherein the drug compound is for reducing blood glucose in a subject and/or blood A1C, and the drug compound is insulin, an insulin analog, a natural insulin variant, a GLP-1 receptor agonist, an incretin mimetic, a GIP agonist, an amylin agonist, a glucagon agonist, or a salt thereof, and wherein the water-soluble complex optionally further comprises a non-ionic surfactant.

2. The water-soluble complex of claim 1, wherein the drug compound is an insulin analog, insulin, or a natural insulin variant; optionally wherein the insulin analog is insulin ispro, insulin aspart, insulin glulisine, admelog, NPH insulin, insulin isophane, insulin glargine, insulin detemir, or insulin degludec; and optionally wherein the drug compound is a rapid-acting insulin, short-acting insulin, intermediate-acting insulin, long-acting insulin, or an ultra-long-acting insulin.

3. The water-soluble complex of claim 1, wherein the drug compound is a GLP-1 receptor agonist, a GIP agonist, a glucagon agonist, or an amylin agonist, and wherein

optionally:

(a) the GLP-1 receptor agonist is semaglutide, tirzepatide, amycretin, orforglipron, albiglutide, beinaglutide, cagrilintide, CagriSema, CT996, danuglipron, efinopegdutide,

HM15211, lixisenatide, pemvidutide, retatrutide, SCO-094, survodutide, WK2735, mazdutide, PEG-loxenatide (PEX168), liraglutide, dulaglutide, exenatide, or a salt thereof;

(b) the GIP agonist is HM15211, retatrutide, SCO-094, tirzepatide, WK2735, or ZP6590;

(c) the glucagon agonist is efinopegdutide, HM15211, mazdutide, pemvidutide, or survodutide;

or

(d) the amylin agonist is AZD6234, cagrilintide, CagriSema, CT388, a long-acting amylin agonist, amycretin, or ZP8396.

4. The water-soluble complex of any one of claims 1-3, wherein the non-nutritive sugar is rubusoside, rebaudioside A, dodecyl-β-D-maltoside, dulcoside B, or stevioside, and optionally wherein the non-nutritive sugar is rubusoside or stevioside.

5. The water-soluble complex of any one of claims 1 to 4, wherein the water-soluble complex comprises a molar ratio of the drug compound to the non-nutritive sugar of about 1:1 to about 1:10 (drug compound: non-nutritive sugar); optionally a molar ratio of about 2 to about 10 moles of the non-nutritive sugar for each mole of the drug compound; and further optionally a molar ratio of about 3 moles of the non-nutritive sugar for each mole of the drug compound.

6. The water-soluble complex of any one of claims 1 to 5, wherein the water-soluble complex is stable in water at pH 8.5 for at least 2 hours and/or is stable in water at pH 4 for at least 2 hours.

7. The water-soluble complex of any one of claims 1 to 6, wherein the water-soluble complex is in a dried form, optionally wherein the water-soluble complex when dried is stable at 30 °C. for at least 90 days and optionally wherein the dried water-soluble complex is resolubilized in a liquid; and/or wherein the water-soluble complex is formulated as a powder, a tablet, an orally disintegrating tablet, a capsule, a liquid, a gel, a thin film, a lozenge, an effervescent powder or tablet, an emulsion, or for parenteral administration, optionally wherein the water-soluble complex is formulated to be administered intradermally, subcutaneously, intramuscularly, intraperitoneally, intrathecally, intravenously, topically (e.g., a gel, lotion, spray or inhaled form), or as a transdermal patch, and optionally wherein

the water-soluble complex is in the form of a thin film, an effervescent powder or tablet, a syrup, a solution, an elixir, an emulsion, a chewing gum, a lollipop, a sublingual drop, a soft gel, or a tincture.

8. A water-soluble complex comprising a non-nutritive sugar and a drug compound, which water-soluble complex comprises:

a molar ratio of about 1 to 12 moles of the non-nutritive sugar for each mole of the drug compound, wherein the non-nutritive sugar is one or more of ADVANTAME®, NEOTAME®, thaumatin, saccharin, sucralose, Lou Han Guo, aspartame, acesulfame potassium, allulose, rubusoside, dulcoside B, dodecyl-β-D-maltoside, stevioside, or rebaudioside A;

wherein the water-soluble complex is stable in water at pH 8.5 and/or at pH 4.0 for at least 2 hours each;

provided that the water-soluble complex has at least a two (2) fold increase in the water solubility at 20 ºC. as compared to the drug compound water solubility not in the water-soluble complex, and/or at least one improved pharmacokinetic attribute; and

further provided the non-nutritive sugar in a daily unit dose of the water-soluble complex is no more than about 280 mg,

wherein the drug compound is for reducing blood glucose and/or blood A1C in a subject, and is insulin, an insulin analog, a natural insulin variant, a GLP-1 receptor agonist, an incretin mimetic, a GIP agonist, an amylin agonist, a glucagon agonist, or a salt thereof.

9. A method of making a water-soluble complex comprising a non-nutritive sugar and a drug compound, the method comprising the steps of:

a) admixing, one or more solvents, the non-nutritive sugar, and the drug compound in a molar ratio of from about 1 to about 12 moles of the non-nutritive sugar for each mole of the drug compound, wherein formation of the water-soluble complex can be determined by nuclear magnetic resonance spectroscopy (NMR), and wherein the non-nutritive sugar is one or more of ADVANTAME®, NEOTAME®, thaumatin, saccharin, sucralose, Lou Han Guo, aspartame, acesulfame potassium, allulose, rubusoside, dulcoside B, dodecyl-β-D-maltoside, stevioside, or rebaudioside A; and wherein the admixing step is optionally performed with a pharmaceutically acceptable acid and/or a non-ionic surfactant; optionally wherein step a) further comprises a sufficient amount of a pharmaceutically acceptable acid to solubilize and render the reaction mixture homogeneous and clear, and

optionally wherein the pharmaceutically acceptable acid is acetic acid, ascorbic acid, aspartic acid, citric acid, formic acid, fumaric acid, gluconic acid, glutamic acid, glutaric acid, glycolic acid, hydrochloric acid, lactic acid, lauric acid, maleic acid, malic acid, malonic acid, nitric acid, oleic acid, oxalic acid, palmitic acid, propionic acid, salicylic acid, stearic acid, succinic acid, or tartaric acid; and

b) drying the water-soluble complex and dissolving the water-soluble complex in water, and

wherein the drug compound is for reducing blood glucose and/or blood A1C in a subject, and is insulin, an insulin analog, a natural insulin variant, a GLP-1 receptor agonist, an incretin mimetic, a GIP agonist, an amylin agonist, a glucagon agonist, or a salt thereof.

10. The method of claim 9, wherein the drug compound is:

(a) an insulin analog, natural insulin, or an insulin variant, optionally wherein the insulin analog is insulin lispro, insulin aspart, insulin glulisine, admelog insulin, NPH insulin, insulin isophane, insulin glargine, insulin detemir, or insulin degludec, and optionally wherein the drug compound is a rapid-acting insulin, short-acting insulin, intermediate-acting insulin, long-acting insulin, or ultra-long-acting insulin;

(b) a GLP-1 receptor agonist, optionally semaglutide, tirzepatide, amycretin, orforglipron,albiglutide, beinaglutide, cagrilintide, CagriSema, CT996, danuglipron, efinopegdutide, HM15211, lixisenatide, pemvidutide, retatrutide, SCO-094, survodutide, WK2735, mazdutide, PEGloxenatide, liraglutide, dulaglutide, exenatide, or a salt thereof;

(c) a GIP agonist, optionally HM15211, retatrutide, SCO-094, tirzepatide, WK2735, or ZP6590;

(d) a glucagon agonist, optionally efinopegdutide, HM15211, mazdutide, pemvidutide, or survodutide; or

(e) an amylin agonist, optionally AZD6234, cagrilintide, CagriSema, CT388, a long-acting amylin agonist, amycretin, or ZP8396.

11. The method of claim 9 or 10, wherein the water-soluble complex comprises a molar ratio of about 1 to about 10 moles of the non-nutritive sugar for each mole of the drug compound, optionally about 2 to about 5 moles, optionally about 2 to about 4.5 moles, or optionally about 8 moles of the non-nutritive sugar for each mole of the drug compound, and optionally wherein the non-nutritive sugar is rubusoside or stevioside.

12. The method of any one of claims 9 to 11, wherein the method further comprises adding a non-ionic surfactant to the solvent of step a), and/or further comprises drying the dissolved water-soluble complex of step b), optionally wherein drying the water-soluble complex comprises freeze-drying or lyophilizing, optionally wherein the dried water-soluble complex is resolubilized in a liquid, and optionally wherein the dried water-soluble complex is formulated into a pill or a pharmaceutically acceptable liquid.

13. The method of any one of claims 9 to 12, wherein the water-soluble complex is stable in water at pH 8.5 for at least 2 hours and/or is stable in water at pH 4 for at least 2 hours.

14. The water-soluble complex of any one of claims 1 to 8 for use in therapy or as a medicament.

15. The water-soluble complex of any one of claims 1 to 8 for use in the treatment of type 1 diabetes (T1D), type 2 diabetes (T2D), obesity (weight loss reduction), MASH (metabolic dysfunction-associated steatohepatitis), glycemic control, prediabetes, a condition characterized by impaired fasting glucose or impaired glucose tolerance, alpha- and beta-cell dysfunction, and/or a condition having a suboptimal incretin effect.