component has a pH 5.0 enteric coating. In some instances, the combined amount of metformin from components (a)-(c) is less than 600 mg.

**[00190]** In some embodiments, the excipient in the extended release component is selected from the group consisting of ethylcellulose, hydroxypropylmethylcellulose, hydroxypropylcellulose, polyvinylpyrrolidone, xanthan gum, sodium alginate, polysorbate-80 and mixtures thereof.

**[00191]** In some embodiments, the combined amount of metformin hydrochloride is about 250 mg.

**[00192]** In some embodiments, the dosage form is a bi-layer tablet. In other embodiments, the dosage form is a capsule with the two components as encapsulated mini-tablets.

**[00193]** Also provided herein are pharmaceutical dosage forms comprising (a) a pH 6.5 enterically coated immediate release component comprising metformin hydrochloride and a pharmaceutically acceptable excipient; and (b) a pH 6.5 enterically coated extended release component comprising metformin hydrochloride and a pharmaceutically acceptable excipient; and wherein the metformin hydrochloride has reduced average bioavailability.

**[00194]** In some embodiments, the average bioavailability is less than the average bioavailability of an immediate release metformin formulation having an equivalent amount of metformin. In other embodiments, the average bioavailability is less than 15%.

**[00195]** In some embodiments, the combined amount of metformin hydrochloride is less than 400 mg.

**[00195a]** In one aspect, provided herein is a use of a composition comprising metformin or a salt thereof, in the manufacture of a medicament for lowering blood glucose levels in a subject in need thereof, wherein said composition is adapted to release a therapeutically effective amount of metformin downstream of the stomach, to one or more regions of the intestine.

**[00195b]** In one aspect, provided herein is a Use of a composition comprising metformin or a salt thereof, in the manufacture of a medicament for treating disorders of glucose metabolism in a subject in need thereof, wherein said composition is adapted to release a therapeutically effective amount of metformin downstream of the stomach, to one or more regions of the intestine.

**[00195c]** In one aspect, provided herein is a Use of a composition comprising metformin or a salt thereof, in the manufacture of a medicament for treating a condition associated with a chemosensory receptor in a subject in need thereof, wherein said composition is adapted to

release a therapeutically effective amount of metformin downstream of the stomach, to one or more regions of the intestine, wherein said condition associated with a chemosensory receptor is selected from diabetes, prediabetes, and obesity.

## INCORPORATION BY REFERENCE

**[00196]** 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 FIGURES

**[00197]** Figure 1 shows plasma hormone concentrations, PYY (total) and GLP-1 (active) in response to gastric infusion of bitter receptor ligands.

**[00198]** Figure 2 shows L-cell index of the infusion of bitter receptor ligands as compared to water control.

## DETAILED DESCRIPTION OF THE INVENTION

**[00199]** The present invention relates to methods and compositions for treating conditions associated with a chemosensory receptor, for example, metabolic conditions including obesity.

## CLAIMS

WHAT IS CLAIMED IS:

1. Use of a composition comprising metformin or a salt thereof, in the manufacture of a medicament for lowering blood glucose levels in a subject in need thereof, wherein said composition is adapted to release a therapeutically effective amount of metformin downstream of the stomach, to one or more regions of the intestine.

2. Use of a composition comprising metformin or a salt thereof, in the manufacture of a medicament for treating disorders of glucose metabolism in a subject in need thereof, wherein said composition is adapted to release a therapeutically effective amount of metformin downstream of the stomach, to one or more regions of the intestine.

3. The use according to claim 2, wherein said disorder is hyperglycemia.

4. Use of a composition comprising metformin or a salt thereof, in the manufacture of a medicament for treating a condition associated with a chemosensory receptor in a subject in need thereof, wherein said composition is adapted to release a therapeutically effective amount of metformin downstream of the stomach, to one or more regions of the intestine, wherein said condition associated with a chemosensory receptor is selected from diabetes, prediabetes, and obesity.

5. The use according to any one of claims 1-4, wherein said metformin salt is metformin hydrochloride.

6. The use according to any one of claims 1-5, wherein said one or more regions of the intestine are the duodenum, jejunum, ileum and/or lower intestine.

7. The use according to any one of claims 1-5, wherein said one or more regions of the intestine are the jejunum, ileum and/or lower intestine.

8. The use according to any one of claims 1-7, wherein said composition is adapted to release metformin at an onset of about pH 5.0, about pH 5.5, about pH 6.0, about pH 6.5, about pH 7.0, or combination thereof following administration to a subject.

9. The use according to any one of claims 1-8, wherein said therapeutically effective amount of metformin or salt thereof is about 1 mg to about 2000 mg.

10. The use according to any one of claims 1-8, wherein said therapeutically effective amount of metformin or salt thereof is about 50 mg to about 1000 mg.

11. The use according to any one of claims 1-10, wherein said composition further comprises an antidiabetic agent or an antiobesity agent.

12. The use according to claim 11, wherein said antidiabetic agent is selected from the group consisting of thiazolidinediones, sulfonyureas, meglitinides, alpha-glucosidase inhibitors, DPP-IV inhibitors, incretin mimetics, and SGLT inhibitors.

13. The use according to claim 11, wherein said antiobesity agent is selected from the group consisting of phentermine, fenfluramine, sibutramine, rimonabant, topiramate, zonisamide bupropion, naltrexone, lorcaserin, and orlistat.

14. The use according to any one of claims 1-13, wherein said composition further comprising a chemosensory receptor ligand selected from the group consisting of a sweet

receptor ligand, a bitter receptor ligand, an umami receptor ligand, a fat receptor ligand, a sour receptor ligand and a bile acid receptor ligand.

15. The use according to claim 4, wherein said condition is diabetes or pre-diabetes.

16. The use according to claim 4, wherein said condition is obesity.

17. The use according to any one of claims 1-16, wherein the circulating hormone levels of GLP1 and/or PYY are increased in the subject as compared to circulating hormone levels with a placebo composition.

18. The use according to claim 15, wherein said composition further comprises an antidiabetic agent.

19. The use according to claim 18, wherein said antidiabetic agent is selected from the group consisting of thiazolidinediones, sulfonyureas, meglitinides, alpha-glucosidase inhibitors, DPP-IV inhibitors, incretin mimetics, and SGLT inhibitors.

20. The use according to claim 16, wherein said composition further comprises an antiobesity agent.

21. The use according to claim 20, wherein said antiobesity agent is selected from the group consisting of phentermine, fenfluramine, sibutramine, rimonabant, topiramate, zonisamide bupropion, naltrexone, lorcaserin, and orlistat.

22. The use according to any one of claims 1-4, wherein said composition is adapted to release a therapeutically effective amount of metformin downstream of the duodenum.

23. The use according to any one of claims 1-4, wherein said composition is adapted to release a therapeutically effective amount of metformin downstream of the jejunum.

24. The use according to any one of claims 1-4, wherein said one or more regions of the intestine are the ileum and/or lower intestine.

25. The use according to any one of claims 1-24, wherein said composition is adapted to release about 10% of said metformin in the stomach.