[0071] In some embodiments, the combined amount of metformin hydrochloride is about 250 mg.

[0072] 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.

[0073] 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 systemic bioavailability.

[0074] In some embodiments, the average systemic bioavailability is less than the average systemic bioavailability of an immediate release metformin formulation having an equivalent amount of metformin. In other embodiments, the average systemic bioavailability is less than 15%.

[0075] In some embodiments, the combined amount of metformin hydrochloride is less than 400 mg.

[0075a] In another aspect, there is provided use of a metformin or a salt thereof in the manufacture of a medicament for lowering blood glucose levels in a patient in need thereof, wherein said medicament comprises an enteric coating formulated to have an onset of release at a pH of about 5.0 or above, such that said metformin or salt thereof is released in the small intestine and provides at least 20% less relative bioavailability of said metformin as measured by plasma area under the curve (AUC) resulting from administration of said medicament compound compared to an immediate release composition having the same amount of said metformin or a salt thereof, wherein said immediate release composition is Glucophage.

[0075b] In another aspect, there is provided use of a metformin or a salt thereof for the manufacture of a medicament for treating a disorder of glucose metabolism in a patient in need thereof, wherein an enteric coating formulated to have an onset of release at a pH of about 5.0 or above, such that said metformin or a salt thereof is released in the small intestine and provides at least 20% less relative bioavailability of said metformin as measured by plasma area under the curve (AUC) resulting from administration of said medicament compound compared to an immediate release composition having the same amount of said metformin or a salt thereof wherein said immediate release composition is Glucophage.

INCORPORATION BY REFERENCE

[0076] 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.

CLAIMS

WHAT IS CLAIMED IS:

1. Use of a metformin or a salt thereof for the manufacture of a medicament for lowering blood glucose levels in a patient in need thereof, wherein said medicament comprises an enteric coating formulated to have an onset of release at a pH of about 5.0 or above, such that metformin or salt thereof is released in the small intestine and provides at least 20% less relative bioavailability of said metformin as measured by plasma area under the curve (AUC) resulting from administration of said medicament compound compared to an immediate release composition having the same amount of said metformin or a salt thereof, wherein said immediate release composition is Glucophage.

2. Use of a metformin or a salt thereof for the manufacture of a medicament for treating a disorder of glucose metabolism in a patient in need thereof, wherein an enteric coating formulated to have an onset of release at a pH of about 5.0 or above, such that said metformin or a salt thereof is released in the small intestine and provides at least 20% less relative bioavailability of said metformin as measured by plasma area under the curve (AUC) resulting from administration of said medicament compound compared to an immediate release composition having the same amount of said metformin or a salt thereof wherein said immediate release composition is Glucophage.

3. The use according to claim 1 or 2, wherein the average systemic bioavailability of said metformin as measured by plasma AUC resulting from administration of said medicament is 30% less than the average systemic bioavailability of said metformin resulting from administration of an immediate release formulation having an equivalent amount of said metformin or salt thereof, wherein said immediate release composition is Glucophage.

4. The use according to claim 1 or 2, wherein the average systemic bioavailability of said metformin as measured by plasma AUC resulting from administration of said medicament is 40% less than the average systemic bioavailability of said

metformin resulting from administration of an immediate release formulation having an equivalent amount of said metformin or salt thereof, wherein said immediate release composition is Glucophage.

5. The use according to claim 1 or 2, wherein the average systemic bioavailability of said metformin as measured by plasma AUC resulting from administration of said medicament is 50% less than the average systemic bioavailability of said metformin resulting from administration of an immediate release formulation having an equivalent amount of said metformin or salt thereof, wherein said immediate release composition is Glucophage.

6. The use according to claim 1 or 2, wherein the average systemic bioavailability of said metformin as measured by plasma AUC resulting from administration of said medicament is 60% less than the average systemic bioavailability of said metformin resulting from administration of an immediate release formulation having an equivalent amount of said metformin or salt thereof, wherein said immediate release composition is Glucophage.

7. The use according to claim 1 or 2, wherein the average systemic bioavailability of said metformin or salt thereof as measured by plasma AUC resulting from administration of said medicament is 70% less than the average systemic bioavailability of said metformin resulting from administration of an immediate release formulation having an equivalent amount of said metformin or salt thereof, wherein said immediate release composition is Glucophage.

8. The use according to claim 1 or 2, wherein said enteric coating is formulated to have an onset of release at a pH of about 5.5 or above.

9. The use according to claim 1 or 2, wherein said enteric coating is formulated to have an onset of release at a pH of about 6.0 or above.

10. The use according to claim 1 or 2~~6~~, wherein said enteric coating is formulated to have an onset of release at a pH of about 6.5 or above.

11. The use according to claim 1 or 2, wherein said enteric coating is formulated to have an onset of release at a pH of about 7.0 or above.

12. The use according to claim 1 or 2, wherein the delayed-release formulation minimizes the circulating plasma concentration of the metformin in the patient below about 0.5 μg/mL.

13. The use according to claim 1 or 2, wherein the delayed-release formulation minimizes the circulating plasma concentration of the metformin in the patient below about 0.25 μg/mL.

14. The use according to claim 1 or 2, wherein said medicament minimizes the plasma C_{max} level of said metformin.

15. The use according to claim 14, wherein the amount of said metformin or salt thereof is about 1000 mg, and wherein the metformin plasma C_{max} in said patient resulting from administration of said medicament is less than about 1000 ng/mL.

16. The use according to claim 1 or 2, wherein said medicament comprises between about 1 mg and about 2000 mg of said metformin or salt thereof.

17. The use according to claim 1 or 2, wherein said medicament comprises between about 100 mg and about 500 mg of said metformin or salt thereof.

18. The use according to claim 1 or 2, wherein said medicament comprises about 500 mg of said metformin or salt thereof.

19. The use according to claim 1 or 2, wherein said medicament comprises about 600 mg of said metformin or salt thereof.

20. The use according to claim 1 or 2, wherein said medicament comprises about 1000 mg of said metformin or salt thereof.

21. The use according to any one of claims 1 to 20, wherein said medicament comprises about 2000 mg of said metformin or a salt thereof.

22. The use according to any one of claims 1 to 20, wherein said metformin or salt thereof is metformin hydrochloride.

23. The use according to any one of claims 1 to 22, wherein an antidiabetic agent selected from: thiazolidinediones, sulfonylureas, meglitinides, alpha-glucosidase inhibitors, DPP-IV inhibitors, incretin mimetics, and SGLT inhibitors or an antiobesity agent is to be further administered.

24. The use according to claim 23, wherein said antidiabetic agent is an SGLT inhibitor.

25. The use according to claim 23, wherein said medicament further comprises an antiobesity agent.

26. The use according to claim 25, wherein said antiobesity agent is lorcaserin.

27. The use according to claim 25, wherein said antiobesity agent is phentermine.

28. The use according to claim 25, wherein said antiobesity agent is a combination of lorcaserin and phentermine.

29. The use according to claim 25, wherein said antiobesity agent is a combination of topiramate and phentermine.

30. The use according to claim 25, wherein said antiobesity agent is a combination of bupropion and naltrexone.

31. The use according to claim 1 or 2, wherein said patient has diabetes.

32. The use according to claim 1 or 2, wherein said medicament releases said metformin or salt thereof downstream of the duodenum.

33. The use according to claim 1 or 2, wherein said medicament releases said metformin or salt thereof downstream of the jejunum.

34. The use according to claim 23, wherein said antiobesity agent or said antidiabetic agent is co-formulated with said metformin or a salt thereof and is to be administered simultaneously in a combined formulation.

35. The use according to claim 34, wherein said combined formulation is provided in the form of a delayed release component coupled with an immediate release component in a unitary dosage form.