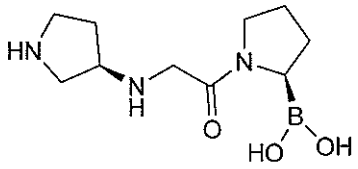
CLAIMS

What is claimed is:

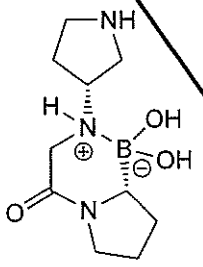
1. A citrate salt solid of a pyrrolidine compound of formula:



or a cyclic isomer thereof, or any mixture of the pyrrolidine compound and the cyclic isomer thereof;

wherein the citrate salt solid is a non-deliquescent solid.

2. The salt solid of claim 1 wherein the cyclic isomer of the pyrrolidine compound is of formula:



3. The salt solid of claim 1 wherein the salt solid is not hygroscopic.

4. A pharmaceutical composition comprising:

(a) the salt solid of claim 1; and

(b) a pharmaceutically acceptable carrier.

5. A method of preparing the pharmaceutical composition of claim 4 comprising mixing a homogenous sample of the salt solid of claim 1 and the pharmaceutically acceptable carrier.

6. A pharmaceutical combination comprising the pharmaceutical composition of claim 4 and further comprising a known second medicament that increases insulin secretion, increases insulin sensitivity, reduces the uptake of sugar from the gastrointestinal tract, enhances the effect of endogenous peptides or proteins that affect glycemic control, provides a replacement for endogenous peptides or proteins that affect glycemic control, or any combination thereof.; or wherein second medicament is an antidiabetic agent.

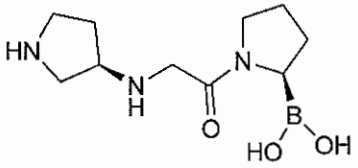
7. The pharmaceutical combination of claim 6, wherein the weight ratio of the citrate salt of the pyrrolidine compound and the antidiabetic agent is from about 0.01:1 to about 200:1.

8. A dosage form comprising a citrate salt of claim 1, wherein the dosage form comprises at least a single effective human dosage of a homogeneous sample of the citrate salt and a pharmaceutically acceptable carrier.

9. A method of making the dosage form of claim 8, comprising combining the homogenous sample of the solid citrate salt of claim 1 and the pharmaceutically acceptable carrier.

10. The citrate salt of claim 1 for treatment of diabetes or of a malcondition in a patient wherein inhibition of DPP-IV is medically indicated.

11. An L-tartrate salt hydrate solid of a pyrrolidine compound of formula:



or a cyclic isomer thereof, or any mixture of the pyrrolidine compound and the cyclic isomer thereof;

wherein the salt hydrate solid is a non-deliquescent hydrate solid.

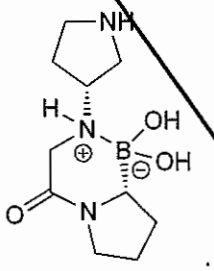
12. The salt hydrate solid of claim 11 comprising about 8–11% water.

13. The salt hydrate solid of claim 11 comprising about 9–10% water.

14. The salt hydrate solid of claim 11 comprising about 2.2–2.6 moles of water per mole of pyrrolidine compound of formula (I) or comprising about 2.2–2.6 moles of water per mole of L-tartaric acid, or both.

15. The salt hydrate solid of any one of claims 11-14 wherein the salt hydrate solid is not hygroscopic.

16. The salt hydrate solid of claim 11 wherein the cyclic isomer of the pyrrolidine compound is of formula:



17. The salt hydrate solid of any one of claims 11-16 wherein the solid does not absorb water from humid air under conditions comprising storage of the solid exposed to air of about 60% relative humidity at 25°C for one month, or for three months, or for six month, or for nine months, or for twelve months.

18. The salt hydrate solid of any one of claims 11-17 wherein the solid does not absorb water from humid air under conditions comprising storage of the solid exposed to air of about 75% relative humidity at 40°C for one month, or for three months, or for six months.

19. A pharmaceutical composition comprising:
(a) the salt hydrate solid of claim 11; and
(b) a pharmaceutically acceptable carrier.

20. A pharmaceutical combination comprising the pharmaceutical composition of claim 19 and further comprising a known second medicament that increases insulin secretion, increases insulin sensitivity, reduces the uptake of sugar from the gastrointestinal tract, enhances the effect of endogenous peptides or proteins that affect glycemic control, provides a replacement for endogenous peptides or proteins that affect glycemic control, or any combination thereof; or the second medicament is an antidiabetic agent.

21. The pharmaceutical combination of claim 20, wherein the weight ratio of the tartrate salt hydrate of the pyrrolidine compound and the antidiabetic agent is from about 0.01:1 to about 200:1.

22. A method of preparing the salt hydrate solid of claim 11 comprising removing substantially all water from an aqueous solution comprising a 1:1 molar mixture of the pyrrolidine compound and L-tartaric acid to provide a substantially anhydrous salt solid, then, allowing the substantially anhydrous solid solid to rehydrate to a water content of 8-11% by exposure to a humid gas.

23. The method of claim 22 wherein prior to removing the water from the aqueous solution, a boronate ester of the pyrrolidine compound, and one molar equivalent of L- tartaric acid, and phenyl boronic acid, are contacted in a water solution, to provide a L-tartrate salt hydrate solid of the compound of the pyrrolidine compound in aqueous solution.

24. The method of claim 22 or 23 wherein the water is removed by spray drying or freeze drying the aqueous solution of the tartrate salt of the pyrrolidine compound to provide an anhydrous solid form of the tartrate salt.

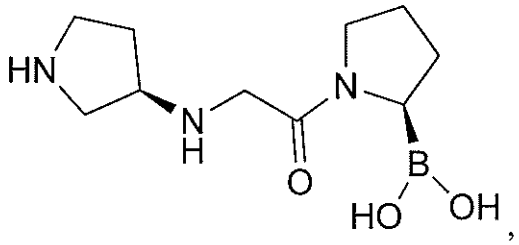
25. A dosage form comprising the tartrate salt hydrate of any of claims 11-17, wherein the dosage form comprises at least a single effective human dosage of a homogeneous sample of the tartrate salt hydrate solid.

26. A method of making the dosage form of claim 25, comprising combining a homogenous sample of the solid tartrate salt solid of any one of claims 11-17 and a pharmaceutically acceptable carrier.

CLAIMS

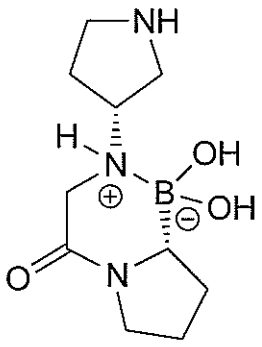
What is claimed is:

1. A solid form of a tartrate salt hydrate of a pyrrolidine compound of formula



,

or a cyclic form thereof of formula



,

or a mixture thereof, wherein the solid form comprises about 8–14% water by weight and is substantially non-hygroscopic when exposed to atmosphere at a relative humidity of up to 40 to 60% at about 25°C.

2. The tartrate salt hydrate solid form of claim 1 wherein the solid form remains a solid upon standing in air at a relative humidity of 40-60% at 25°C for a period of about 100 hours, or a period of about three months, or a period of about six months.

3. The tartrate hydrate solid form of claim 1 wherein the tartrate is the L form.