CLAIMS

1. An orally-disintegrating solid preparation comprising fine granules showing controlled release of a pharmaceutically active ingredient, which has a coating layer comprising a polymer affording a casting film having an elongation at break of 100% - 700%,

wherein said polymer comprises at least methacrylic acid - methyl acrylate - methyl methacrylate copolymer,

wherein the pharmaceutically active ingredient dissolved from the fine granules showing controlled release of the pharmaceutically active ingredient is not more than 10% in 2 hr as expressed by the dissolution rate in a pH 1.2 solution, and not more than 5% in 1 hr as expressed by the dissolution rate in a pH 6.8 solution, and

wherein the fine granules has an average particle size of 500 μm or below.

2. The preparation of claim 1, further comprising a plasticizer, wherein the polymer is an enteric polymer.

3. The preparation of claim 1, wherein the fine granules are obtained by coating fine granules comprising the pharmaceutically active ingredient with a coating layer comprising a polymer affording a casting film having an elongation at break of 100 - 700%.

4. The preparation of claim 3, wherein the fine granules comprising the pharmaceutically active ingredient are enteric fine granules.

5. The preparation of claim 1, wherein the polymer is an enteric polymer.

6. The preparation of any one of claims 3 to 5, wherein the polymer is coated in an amount of 5 - 80wt% of the fine granules

comprising the pharmaceutically active ingredient.

7. The preparation of claim 1, wherein the coating layer is formed on the outermost layer of the fine granules.

8. The preparation of claim 1, further comprising a coating layer comprising a water-soluble sugar alcohol on the outermost layer of the fine granules.

9. The preparation of claim 2, wherein the content of the plasticizer is 1 - 20 wt% of the weight of the solid content of the polymer.

10. The preparation of claim 2, wherein the plasticizer is triethyl citrate.

11. The preparation of claim 4, wherein the enteric fine granules comprising the pharmaceutically active ingredient are pH-dependent controlled release fine granules.

12. The preparation of claim 11, wherein the pH-dependent controlled release fine granules are obtained by coating core granules comprising the pharmaceutically active ingredient with a controlled release film.

13. The preparation of claim 12, wherein the controlled release film comprises a polymer substance that dissolves at not less than pH 6.0 and not more than pH 7.5.

14. The preparation of claim 12, wherein the core granules further comprise a basic inorganic salt.

15. The preparation of claim 12 or 13, wherein the controlled release film is formed via an intermediate coating layer formed on the core granules.

16. The preparation of claim 13, wherein the polymer substance

comprises a mixture of one or more kinds selected from the group consisting of hypromellose phthalate, cellulose acetate phthalate, carboxymethyl ethyl cellulose, methyl methacrylate - methacrylic acid copolymer, methacrylic acid - ethyl acrylate copolymer, hydroxypropyl methylcellulose acetate succinate, polyvinyl acetate phthalate and shellac.

17. The preparation of claim 15, wherein the controlled release film has a polymer substance content of 30 - 100 wt% of the fine granules.

18. The preparation of claim 15, wherein the controlled release film has a polymer substance content of 50 - 100 wt% of the fine granules.

19. The preparation of claim 1, wherein the pharmaceutically active ingredient is unstable to acid.

20. The preparation of claim 19, wherein the pharmaceutically active ingredient unstable to acid is a proton pump inhibitor.

21. The preparation of claim 20, wherein the proton pump inhibitor is lansoprazole or an optically active form thereof or a salt thereof.

22. A method of suppressing breakage of fine granules showing controlled release of a pharmaceutically active ingredient, which are comprised in an orally-disintegrating tablet obtained by tabletting the fine granules and an additive, which method comprises, during production of the tablet, coating the fine granules with a coating layer comprising a polymer affording a casting film having an elongation at break of 100 - 700%,

wherein said polymer comprises at least methacrylic acid - methyl acrylate - methyl methacrylate copolymer,

wherein the pharmaceutically active ingredient dissolved from the fine granules showing controlled release of the pharmaceutically active ingredient is not more than 10% in 2 hr

as expressed by the dissolution rate in a pH 1.2 solution, and not more than 5% in 1 hr as expressed by the dissolution rate in a pH 6.8 solution, and

wherein the fine granules has an average particle size of 500 μm or below.

CLAIMS

1. An orally-disintegrating solid preparation comprising fine granules showing controlled release of a pharmaceutically active ingredient, which has a coating layer comprising a polymer affording a casting film having an elongation at break of 100% - 700%,

wherein said polymer comprising methacrylic acid - methyl acrylate - methyl methacrylate copolymer,

elution of the pharmaceutically active ingredient dissolved from the fine granules showing controlled release of the pharmaceutically active ingredient is not more than 10% in 2 hr as expressed by the dissolution rate in a pH 1.2 solution, and not more than 5% in 1 hr as expressed by the dissolution rate in a pH 6.8 solution, and

the fine granules has an average particle size of 500 μm or below.

2. The preparation of claim 1, further comprising a plasticizer, wherein the polymer is an enteric polymer.

3. The preparation of claim 1, wherein the fine granules are obtained by coating fine granules comprising the pharmaceutically active ingredient with a coating layer comprising a polymer affording a casting film having an elongation at break of 100 - 700%.

4. The preparation of claim 3, wherein the fine granules comprising the pharmaceutically active ingredient are enteric fine granules.

5. The preparation of claim 1, wherein the polymer is an enteric polymer.

6. The preparation of any one of claims 3 to 5, wherein the polymer is coated in an amount of 5 - 80 wt% of the fine granules comprising the pharmaceutically active ingredient.

7. The preparation of claim 1, wherein the coating layer is formed on the outermost layer of the fine granules.

8. The preparation of claim 1, further comprising a coating layer comprising a water-soluble sugar alcohol on the outermost layer of the fine granules.

9. The preparation of claim 2, wherein the content of the plasticizer is 1 - 20 wt% of the weight of the solid content of the polymer.

10. The preparation of claim 2, wherein the plasticizer is triethyl citrate.

11. The preparation of claim 4, wherein the enteric fine granules comprising the pharmaceutically active ingredient are pH-dependent controlled release fine granules.

12. The preparation of claim 11, wherein the pH-dependent controlled release fine granules are obtained by coating core granules comprising the pharmaceutically active ingredient with a controlled release film.

13. The preparation of claim 12, wherein the controlled release film comprises a polymer substance that dissolves at not less than pH 6.0 and not more than pH 7.5.

14. The preparation of claim 12, wherein the core granules further comprise a basic inorganic salt.

15. The preparation of claim 12 or 13, wherein the controlled release film is formed via an intermediate coating layer formed on the core granules.

16. The preparation of claim 15,

wherein the intermediate coating layer comprises one or more kinds of polymers selected from the group consisting of low-substituted hydroxypropyl cellulose, hydroxypropyl cellulose, hypromellose, polyvinylpyrrolidone, polyvinyl alcohol, methylcellulose and hydroxyethylmethylcellulose, and

the amount of the intermediate coating layer is 0.02 - 1.5 parts by weight per 1 part by weight of the core granules comprising the pharmaceutically active ingredient.

17. The preparation of claim 15,

wherein the intermediate coating layer comprises a mixture of low-substituted hydroxypropyl cellulose, hypromellose and D-mannitol, and

the amount of the intermediate coating layer is 0.05 - 1 part by weight per 1 part by weight of the core granules comprising the pharmaceutically active ingredient.

18. The preparation of claim 13, wherein the polymer substance comprises a mixture of one or more kinds selected from the group consisting of hypromellose phthalate, cellulose acetate phthalate, carboxymethyl ethyl cellulose, methyl methacrylate - methacrylic acid copolymer, methacrylic acid - ethyl acrylate copolymer, hydroxypropyl methylcellulose acetate succinate, polyvinyl acetate phthalate and shellac.

19. The preparation of any one of claims 15 to 17, wherein the controlled release film has a polymer substance content of 30 - 100 wt% of the fine granules.

20. The preparation of any one of claims 15 to 17, wherein the

controlled release film has a polymer substance content of 50 - 100 wt% of the fine granules.

21. The preparation of claim 1, wherein the pharmaceutically active ingredient is unstable to acid.

22. The preparation of claim 21, wherein the pharmaceutically active ingredient unstable to acid is a proton pump inhibitor.

23. The preparation of claim 22, wherein the proton pump inhibitor is lansoprazole or an optically active form thereof or a salt thereof.

24. An orally-disintegrating solid preparation comprising (1) fine granules A showing controlled release of a pharmaceutically active ingredient, which has a coating layer comprising a polymer affording a casting film having an elongation at break of 100% - 700%,

wherein said polymer comprising methacrylic acid - methyl acrylate - methyl methacrylate copolymer,

elution of the pharmaceutically active ingredient dissolved from the fine granules A showing controlled release of the pharmaceutically active ingredient is not more than 10% in 2 hr as expressed by the dissolution rate in a pH 1.2 solution, and not more than 5% in 1 hr as expressed by the dissolution rate in a pH 6.8 solution, and

the fine granules A has an average particle size of 500 μm or below, and

(2) fine granules B with a different release rate of a pharmaceutically active ingredient from that of the fine granules of (1).

25. The preparation of claim 24,

wherein the fine granules A showing controlled release of a pharmaceutically active ingredient are pH-dependent controlled

release fine granules having a controlled release film on core granules comprising the pharmaceutically active ingredient,

the controlled release film is formed via an intermediate coating layer formed on the core granules,

the intermediate coating layer comprises one or more kinds of polymers selected from the group consisting of low-substituted hydroxypropyl cellulose, hydroxypropyl cellulose, hypromellose, polyvinylpyrrolidone, polyvinyl alcohol, methylcellulose and hydroxyethylmethylcellulose, and

the amount of the intermediate coating layer is 0.02 - 1.5 parts by weight per 1 part by weight of the core granules comprising the pharmaceutically active ingredient.

26. The preparation of claim 24,

wherein the fine granules A showing controlled release of a pharmaceutically active ingredient are pH-dependent controlled release fine granules having a controlled release film comprising a polymer substance that dissolves at not less than pH 6.0 and not more than pH 7.5 on core granules comprising the pharmaceutically active ingredient,

the controlled release film is formed via an intermediate coating layer formed on the core granules,

the intermediate coating layer comprises one or more kinds of polymers selected from the group consisting of low-substituted hydroxypropyl cellulose, hydroxypropyl cellulose, hypromellose, polyvinylpyrrolidone, polyvinyl alcohol, methylcellulose and hydroxyethylmethylcellulose, and

the amount of the intermediate coating layer is 0.02 - 1.5 parts by weight per 1 part by weight of the core granules comprising the pharmaceutically active ingredient.

27. The preparation of claim 24,

wherein the fine granules A showing controlled release of a pharmaceutically active ingredient are pH-dependent controlled release fine granules having a controlled release

film comprising a polymer substance that dissolves at not less than pH 6.0 and not more than pH 7.5 on core granules comprising the pharmaceutically active ingredient,

the controlled release film is formed via an intermediate coating layer formed on the core granules,

the intermediate coating layer comprises a mixture of low-substituted hydroxypropyl cellulose, hypromellose and D-mannitol, and

the amount of the intermediate coating layer is 0.05 - 1 part by weight per 1 part by weight of the core granules comprising the pharmaceutically active ingredient.

28. The preparation of any one of claims 24 to 27, wherein the pharmaceutically active ingredient of the fine granules A and that of the fine granules B are the same.

29. The preparation of any one of claims 24 to 27, wherein the fine granules B have an average particle size of 500 μm or below.

30. The preparation of any one of claims 24 to 27, wherein the fine granules B are enteric fine granules that dissolve at not less than pH 5.0 and not more than pH 6.0.

31. The preparation of any one of claims 24 to 27, wherein the fine granules B are coated with a coating layer comprising an enteric polymer that dissolves at not less than pH 5.0 and not more than pH 6.0.

32. The preparation of claim 30, wherein the enteric fine granules comprise one or more kinds of aqueous enteric polymer bases selected from hypromellose phthalate, cellulose acetate phthalate, hydroxypropyl methylcellulose acetate succinate, methacrylic acid - ethyl acrylate copolymer, methacrylic acid - methyl acrylate - methyl methacrylate copolymer,

carboxymethyl ethyl cellulose and shellac.

33. The preparation of claim 28, wherein the fine granules B are pH-dependent controlled release fine granules obtained by coating core granules comprising the pharmaceutically active ingredient with a controlled release film comprising a polymer substance that dissolves at not less than pH 6.0 and not more than pH 7.5, wherein the controlled release film is formed via an intermediate coating layer formed on the core granules, and the controlled release film has a polymer substance content of 10 - 70 wt% of the fine granules.

34. The preparation of claim 28, wherein the fine granules A and the fine granules B comprise the pharmaceutically active ingredient at a weight ratio of 1:10 - 10:1.

35. The preparation of any one of claims 24 to 27, further comprising an additive.

36. The preparation of claim 35, wherein the additive comprises a water-soluble sugar alcohol.

37. The preparation of claim 35, wherein the additive comprises a disintegrant.

38. The preparation of claim 35, wherein the fine granules A is comprised at 10 - 50 wt%, the fine granules B is comprised at 10 - 30 wt%, and the additive is comprised at 20 - 80 wt%, each relative to the whole preparation.

39. The preparation of any one of claims 1 and 24 to 27, wherein the total weight of the preparation is 1000 mg or below.

40. The preparation of any one of claims 1 and 24 to 27,

wherein the oral disintegration time is 90 seconds or less.

41. The preparation of any one of claims 24 to 27, which is capable of achieving an average pH in the stomach of not less than 4 at 0.5 hr after oral administration and maintaining said pH or higher pH for 14 hours or longer.

42. The preparation of any one of claims 24 to 27, wherein the pharmaceutically active ingredient is R-lansoprazole or a salt thereof, which reaches the maximum blood drug concentration in 5 hr and maintains the maximum blood drug concentration of not less than 100 ng/mL for 4 hr or longer, when 30 mg of the pharmaceutically active ingredient is administered orally.

43. A method of suppressing breakage of fine granules showing controlled release of a pharmaceutically active ingredient, which are comprised in an orally-disintegrating tablet obtained by tabletting the fine granules and an additive, which method comprises, during production of the tablet, coating the fine granules with a coating layer comprising a polymer affording a casting film having an elongation at break of 100 - 700%,

wherein said polymer comprising methacrylic acid - methyl acrylate - methyl methacrylate copolymer,

elution of the pharmaceutically active ingredient dissolved from the fine granules showing controlled release of the pharmaceutically active ingredient is not more than 10% in 2 hr as expressed by the dissolution rate in a pH 1.2 solution, and not more than 5% in 1 hr as expressed by the dissolution rate in a pH 6.8 solution, and

the fine granules has an average particle size of 500 μm or below.

44. The method of claim 43,

wherein the fine granules showing controlled release of a

pharmaceutically active ingredient are pH-dependent controlled release fine granules having a controlled release film on core granules comprising the pharmaceutically active ingredient,

the controlled release film is formed via an intermediate coating layer formed on the core granules,

the intermediate coating layer comprises one or more kinds of polymers selected from the group consisting of low-substituted hydroxypropyl cellulose, hydroxypropyl cellulose, hypromellose, polyvinylpyrrolidone, polyvinyl alcohol, methylcellulose and hydroxyethylmethylcellulose, and

the amount of the intermediate coating layer is 0.02 - 1.5 parts by weight per 1 part by weight of the core granules comprising the pharmaceutically active ingredient.

45. The method of claim 43,

wherein the fine granules showing controlled release of a pharmaceutically active ingredient are pH-dependent controlled release fine granules having a controlled release film comprising a polymer substance that dissolves at not less than pH 6.0 and not more than pH 7.5 on core granules comprising the pharmaceutically active ingredient,

the controlled release film is formed via an intermediate coating layer formed on the core granules,

the intermediate coating layer comprises one or more kinds of polymers selected from the group consisting of low-substituted hydroxypropyl cellulose, hydroxypropyl cellulose, hypromellose, polyvinylpyrrolidone, polyvinyl alcohol, methylcellulose and hydroxyethylmethylcellulose, and

the amount of the intermediate coating layer is 0.02 - 1.5 parts by weight per 1 part by weight of the core granules comprising the pharmaceutically active ingredient.

46. The method of claim 43,

wherein the fine granules showing controlled release of a pharmaceutically active ingredient are pH-dependent controlled

release fine granules having a controlled release film comprising a polymer substance that dissolves at not less than pH 6.0 and not more than pH 7.5 on core granules comprising the pharmaceutically active ingredient,

the controlled release film is formed via an intermediate coating layer formed on the core granules,

the intermediate coating layer comprises a mixture of low-substituted hydroxypropyl cellulose, hypromellose and D-mannitol, and

the amount of the intermediate coating layer is 0.05 - 1 part by weight per 1 part by weight of the core granules comprising the pharmaceutically active ingredient.