CLAIMS

1. Pharmaceutical composition for prolonged release of trimetazidine, wherein:
   - an inner phase comprises trimetazidine;
   - an outer layer comprises a retardant and an anti-agglomerant.

2. Composition according to claim 1, characterised in that the retardant is selected from ethylcellulose, cellulose acetate, cellulose acetate butyrate, cellulose acetate propionate, cellulose acetate phthalate, hydroxypropyl methylcellulose acetate succinate and/or polymethacrylates.

3. Composition according to claim 1, characterised in that the anti-agglomerant is selected from talc, colloidal silicon dioxide, magnesium stearate, stearic acid and/or sodium fumaryl stearate.

4. Composition according to claim 1, characterised in that the outer layer comprises a plasticiser.

5. Composition according to claim 4, characterised in that the plasticiser is selected from acetyl tributyl citrate, glycerol triacetate, acetyl triethyl citrate, acetyl ethyl citrate, diethyl sebacate, dibutyl sebacate, ethyl and dibutyl phthalate, polyethylene glycol, glycerol and/or propylene glycol.

6. Composition according to claim 1, characterised in that the percentage of retardant is strictly less than 9 % of the total weight of the inner phase.

7. Composition according to claim 1, characterised in that the percentage of retardant is between 5.5 % and 8 % inclusive of the total weight of the inner phase.

8. Composition according to claim 1, characterised in that the percentage of anti-agglomerant is between 25 % and 200 % inclusive of the weight of the retardant.

9. Composition according to claim 4, characterised in that the percentage of plasticiser is between 5 % and 50 % inclusive of the weight of the retardant.

10. Composition according to claim 1, characterised in that the inner phase comprises a binder.

11. Composition according to claim 10, characterised in that the binder is selected from hydroxypropyl methylcellulose, hydroxypropylcellulose, maltodextrin, polyvinylpyrrolidone and/or microcrystalline cellulose.

12. Composition according to claim 1, characterised in that the trimetazidine is coated onto a core.

13. Composition according to claim 12, characterised in that the core is composed of sucrose, sucrose and starch, or microcrystalline cellulose.

14. Composition according to claim 1, characterised in that the trimetazidine is in the form of the dihydrochloride.

15. Composition according to claim 1, characterised in that it contains 80 mg of trimetazidine dihydrochloride.

16. Composition according to claim 1, characterised in that the outer layer comprises:

- from 5.5 % to 30 % of acetyl tributyl citrate relative to the weight of the retardant;
- from 5 % to 8 % of ethylcellulose relative to the total weight of the inner phase;

- from 100 % to 200 % of talc relative to the weight of the retardant.

17. Composition according to claim 12, characterised in that the inner phase comprises:

- from 15 % to 40 % of neutral core relative to the total weight of the composition;
- from 35 % to 70 % of trimetazidine relative to the total weight of the composition;
- from 1 % to 15 % of hydroxypropyl methylcellulose relative to the total weight of the composition.

18. Composition according to claim 1, characterised in that it contains 80 mg of trimetazidine dihydrochloride, 36.677 mg of neutral minigranules, 6.40 mg of hydroxypropyl methylcellulose, 1.2 mg of acetyl tributyl citrate, 8 mg of ethylcellulose and 12 mg of talc.

19. Pharmaceutical composition according to any one of claims 1 to 18, characterised in that the level of *in vitro* dissolution of the composition is from 8 % to 28 % of the trimetazidine released by 4 hours and from 37 % to 57 % of the trimetazidine released by 8 hours and more than 75 % of the trimetazidine released by 24 hours and is selected so that the therapeutically efficacious plasma concentration of trimetazidine obtained *in vivo* is prolonged over 24 hours following administration of the pharmaceutical composition.

20. Process for manufacture of a composition according to any one of claims 1 to 19, characterised in that it comprises the following steps:

a) coating neutral cores with trimetazidine and a binder;

b) coating the minigranules obtained in a) with a retardant, a plasticiser and an anti-agglomerant;

c) filling of the coated minigranules obtained in b) and lubricated.

21. Pharmaceutical composition according to any one of claims 1 to 19 for use in the prophylactic treatment of angina pectoris, in the course of chorioretinal disorders and also for the treatment of vertigo of vascular origin.

WHAT WE CLAIM IS:

1. Pharmaceutical composition for prolonged release of trimetazidine, wherein:
   - an inner phase comprises trimetazidine coated onto a core;
   - an outer layer comprises a retardant and an anti-agglomerant.

2. Composition according to claim 1, characterised in that the retardant is selected from ethylcellulose, cellulose acetate, cellulose acetate butyrate, cellulose acetate propionate, cellulose acetate phthalate, hydroxypropyl methylcellulose acetate succinate and/or polymethacrylates.

3. Composition according to claim 1, characterised in that the anti-agglomerant is selected from talc, colloidal silicon dioxide, magnesium stearate, stearic acid and/or sodium fumaryl stearate.

4. Composition according to claim 1, characterised in that the outer layer comprises a plasticiser.

5. Composition according to claim 4, characterised in that the plasticiser is selected from acetyl tributyl citrate, glycerol triacetate, acetyl triethyl citrate, acetyl ethyl citrate, diethyl sebacate, dibutyl sebacate, ethyl and dibutyl phthalate, polyethylene glycol, glycerol and/or propylene glycol.

6. Composition according to claim 1, characterised in that the percentage of retardant is strictly less than 9 % of the total weight of the inner phase.

7. Composition according to claim 1, characterised in that the percentage of retardant is between 5.5 % and 8 % inclusive of the total weight of the inner phase.

8. Composition according to claim 1, characterised in that the percentage of anti-agglomerant is between 25 % and 200 % inclusive of the weight of the retardant.

9. Composition according to claim 4, characterised in that the percentage of plasticiser is between 5 % and 50 % inclusive of the weight of the retardant.

10. Composition according to claim 1, characterised in that the inner phase comprises a binder.

11. Composition according to claim 10, characterised in that the binder is selected from hydroxypropyl methylcellulose, hydroxypropylcellulose, maltodextrin, polyvinylpyrrolidone and/or microcrystalline cellulose.

12. Composition according to claim 1, characterised in that the core is composed of sucrose, sucrose and starch, or microcrystalline cellulose.

13. Composition according to claim 1, characterised in that the trimetazidine is in the form of the dihydrochloride.

14. Composition according to claim 1, characterised in that it contains 80 mg of trimetazidine dihydrochloride.

15. Composition according to claim 1, characterised in that the outer layer comprises:

- from 5.5 % to 30 % of acetyl tributyl citrate relative to the weight of the retardant;
- from 5 % to 8 % of ethylcellulose relative to the total weight of the inner phase;
- from 100 % to 200 % of talc relative to the weight of the retardant.

16. Composition according to claim 12, characterised in that the inner phase comprises:

- from 15 % to 40 % of neutral core relative to the total weight of the composition;
- from 35 % to 70 % of trimetazidine relative to the total weight of the composition;
- from 1 % to 15 % of hydroxypropyl methylcellulose relative to the total weight of the composition.

17. Composition according to claim 1, characterised in that it contains 80 mg of trimetazidine dihydrochloride, 36.677 mg of neutral minigranules, 6.40 mg of hydroxypropyl methylcellulose, 1.2 mg of acetyl tributyl citrate, 8 mg of ethylcellulose and 12 mg of talc.

18. Pharmaceutical composition according to any one of claims 1 to 17, characterised in that the level of *in vitro* dissolution of the composition is from 8 % to 28 % of the trimetazidine released by 4 hours and from 37 % to 57 % of the trimetazidine released by 8 hours and more than 75 % of the trimetazidine released by 24 hours and is selected so that the therapeutically efficacious plasma concentration of trimetazidine obtained *in vivo* is prolonged over 24 hours following administration of the pharmaceutical composition.

19. Process for manufacture of a composition according to any one of claims 1 to 18, characterised in that it comprises the following steps:

a) coating neutral cores with trimetazidine and a binder;

b) coating the minigranules obtained in a) with a retardant, a plasticiser and an anti-agglomerant;

c) filling of the coated minigranules obtained in b) and lubricated.

20. Pharmaceutical composition according to any one of claims 1 to 17 for use in the prophylactic treatment of angina pectoris, in the course of chorioretinal disorders and also for the treatment of vertigo of vascular origin.

21. Use of a pharmaceutical composition according to any one of claims 1-19 in the manufacture of a medicament for use in the prophylactic treatment of angina pectoris, in the course of chorioretinal disorders and also for the treatment of vertigo of vascular origin.

22. A pharmaceutical composition according to claims 1-18, substantially as herein described with reference to any example thereof.

23. A process according to claim 19, substantially as herein described with reference to any example thereof.

24. A use according to claim 21, substantially as herein described with reference to any example thereof.