Claims

1. A time controlled, immediate release drug delivery system for oral administration of a first active ingredient to a subject in need thereof, the system comprising

a core comprising 10-60% (w/w) microcrystalline cellulose, 20-70% (w/w) of ~~a filler selected from an organic and/or~~ an inorganic salt as a filler, and 0.1-30 % (w/w) of a first active ingredient; wherein the core further comprises a cross-linked sodium carboxy methylcellulose; and wherein microcrystalline cellulose and crosslinked sodium carboxy methylcellulose are present in a ratio of between about 6:1 (w/w) to 14:1 (w/w), and

a first coating surrounding the core, said first coating comprising a hydrophobic polymer and a hydrophilic substance.

2. The system according to claim 1, wherein the inorganic salt is anhydrous dibasic calcium phosphate or calcium sulphate dihydrate.

3. The system according to claim 1 or claim 2, wherein the core further comprises magnesium stearate.

~~2. The system according to claim 1, wherein said filler is an inorganic salt.~~

~~3. The system according to claim 1 or claim 2, wherein said cellulose is microcrystalline cellulose.~~

~~4. The system according to any one of claims 1-3, wherein said inorganic salt is anhydrous dibasic calcium phosphate.~~

~~5~~4. The system according to any of claims 1-~~4~~3, wherein said delivery system is a tablet.

~~6. The system according to any of the previous claims wherein said core additionally comprises a water-insoluble gel-forming disintegrant comprising cross-linked sodium carboxy-methylcellulose, sodium starch glycolate and/or cross-linked polyvinylpyrrolidone.~~

~~7~~5. The system according to any of the previous claims wherein the hydrophobic polymer of the first coating is ethylcellulose.

~~86~~. The system according to any of the previous claims wherein the hydrophilic substance of said first coating is a water insoluble ~~hydrophylic~~ hydrophilic substance.

~~97~~. The system according to claim ~~86~~, wherein first coating contains pores prior to exposure to an aqueous liquid.

~~108~~. The system according to any of claims 1-~~75~~, wherein the hydrophilic substance of said first coating is a water soluble hydrophilic substance.

~~119~~. The system according to claim ~~108~~, wherein the water soluble hydrophilic substance forms pores in the hydrophobic polymer upon exposure to an aqueous liquid.

~~12. The drug delivery system according to claim 1, wherein the hydrophobic polymer is ethylcellulose and the hydrophilic substance lactose; and wherein the mass ratio of ethylcellulose and lactose is about 1:1.~~

~~13. The drug delivery system according to claim 1, the core further comprising 0.5-6% (w/w) of one or more of a water-insoluble, gel-forming disintegrant.~~

~~14. The drug delivery system according to claim 13, wherein the water-insoluble, gel-forming disintegrant is cross-linked sodium carboxymethyl cellulose.~~

~~15. The drug delivery system according to claim 3, wherein the filler is anhydrous dicalcium phosphate; and wherein the core further comprises a crosslinked sodium carboxy methylcellulose and magnesium stearate; and wherein microcrystalline cellulose and crosslinked sodium carboxy methylcellulose are present in a ratio of between about 6:1 (w/w) to 14:1 (w/w).~~

~~16~~10. The system according to any of the previous claims wherein the first active ingredient is selected from the group consisting of a PDE5 inhibitor, a 5HT1a receptor agonist, and a neutral endopeptidase inhibitor.

~~17~~11. The system according to claim ~~16~~ 10 wherein the PDE5 inhibitor comprises sildenafil.

~~18~~12. The system according to claim ~~16~~ 10 wherein the 5HT1a receptor agonist comprises buspirone.

~~19~~13. A dual drug delivery device, comprising the time controlled, immediate release drug delivery system according to any one of claims 1-~~18~~12, wherein the first coating of the drug delivery system is surrounded by a second coating comprising a second active ingredient.

~~20~~14. The device according to claim ~~19~~13, wherein the second coating comprises hydroxypropylmethylcellulose.

~~21~~15. The device according to claim ~~19~~ 13 or claim ~~20~~14, wherein the second coating provides for immediate delivery of the second active ingredient in the mouth.

~~22~~16. The device according to any of claims ~~19~~13-~~21~~15, wherein the second active ingredient is testosterone or a functional analogue of testosterone.

~~23~~17. The device according to any of claims ~~19~~13-~~22~~16, wherein the second coating comprises a cyclodextrin, or a derivative or polymer thereof.

~~24~~18. The device according to any one of claims ~~19~~13-~~23~~17, wherein the second coating further comprises a flavouring compound.

~~25~~19. The device according to claim ~~24~~18, wherein presence of a flavour indicates that the device is to be held in the mouth.

~~26~~20. The device according to any one of claims ~~19~~13-~~25~~19, wherein an outer surface of the second coating is rougher ~~that~~ than an outer surface of the first coating.

~~27. A method for preparing a dual-delivery drug device comprising a first and a second coating, wherein a roughness of an outer surface of the first coating differs from a roughness of an outer surface of the second coating.~~

~~28~~21. A tablet for sublingual administration of an active ingredient said tablet comprising a core, and a coating (outer coating) on the exterior surface of said

core and optionally a coating that separates said outer coating from said core (separation coating), wherein said outer coating comprises a mixture of

- an active ingredient in amorphous form in an amount of between about 0.1 – 10 mg;

- a coating polymer in an amount of between about 0.25 – 25 mg; and

- water in an amount of between about 0.0 – 10% w/w of the outer coating; and

wherein said core comprises 10-60% (w/w) microcrystalline cellulose, 20-70% (w/w) ~~of a filler selected from~~ of an ~~organic and/or~~ inorganic salt as a filler, and 0.1-30 % (w/w) of a first active ingredient; wherein the core further comprises a cross-linked sodium carboxy methylcellulose; and wherein microcrystalline cellulose and crosslinked sodium carboxy methylcellulose are present in a ratio of between about 6:1 (w/w) to 14:1 (w/w).

22. A tablet according to claim 21, wherein the inorganic salt is anhydrous dibasic calcium phosphate or calcium sulphate dihydrate.

23. A tablet according to claim 22, wherein the core further comprises magnesium stearate.

~~29~~24. A tablet according to any one of claims 21-23~~28~~, wherein said mixture comprises said active ingredient in an amount of between about 0.2 – 5,0 mg; said coating polymer in an amount of between about 0.5 – 12,5 mg; and water in an amount of between about 0.0 – 5% w/w of the outer coating.

~~30~~25. A tablet according to claim ~~28~~21, wherein said mixture further comprises a cyclodextrin or a polyvinylpyrolidone, or a combination thereof in an amount of between 0.25 – 25 mg.

~~31~~26. A tablet according to claim ~~29~~24, wherein said mixture further comprises a cyclodextrin or a polyvinylpyrolidone, or a combination thereof in an amount of between 0.5 – 12,5 mg.

~~32~~27. A tablet according to any one of claims ~~28~~21-~~31~~26, comprising a separation coating that separates said outer coating from said core.

~~33~~28. A tablet according to any one of claims ~~28~~21-~~32~~27, wherein said core and said optional separation coating has a volume of between 50 – 1000 mm^3.

~~34~~29. A tablet according to any one of claims ~~27~~21-~~33~~28, wherein said separation coating comprises a hydrophobic polymer and a hydrophilic substance.

~~35~~30. A tablet according to any one of claims ~~27~~21-~~34~~29, wherein said mixture of said outer coating further comprises a sweetener and/or a flavor.

~~36~~31. A tablet according to any one of claims ~~28~~21-~~35~~30, wherein said separation coating is a pH-independent coating.

~~37~~32. A tablet according to any one of claims ~~28~~21-~~35~~30, wherein said separation coating is a pH-dependent coating, preferably an acid soluble coating or an enteric coating.

~~38~~33. Use of a device according to any one of claims ~~15~~13-~~22~~ 20 or a tablet according to any one of claims ~~28~~21-~~37~~32, in the preparation of a medicament for treatment of male or female: sexual dysfunction, desire dysfunction, or erectile dysfunction, and preferably for use in the treatment of Hypoactive Sexual Desire Disorder.

34. A time controlled, immediate release drug delivery system for oral administration of a first active ingredient to a subject in need thereof, the system comprising

a core comprising 10-60% (w/w) cellulose, 20-70% (w/w) of a filler selected from an organic and/or an inorganic salt, and 0.1-30 % (w/w) of a first active ingredient, and

a first coating surrounding the core, said first coating comprising a hydrophobic polymer and a hydrophilic substance; wherein the hydrophobic polymer is ethylcellulose and the hydrophilic substance is lactose; and wherein the mass ratio of ethylcellulose and lactose is about 1:1.

~~39. A dual drug delivery device according to any one of claims 15-22, the core comprising:~~

~~between 100 mg and 150 mg of microcrystalline cellulose;~~

- between 100 mg and 150 mg of DicalciumPhosphate 0 aq;
- between 25 mg and 100 mg of Sildenafil citrate;
- between 10 mg and 20 mg of Croscarmellose;
- between 1 mg and 2 mg of Magnesiumstearate;

the first coating comprising:

- between 5 mg and 20 mg of ethylcellulose;
- between 5 mg and 20 mg of microcrystalline cellulose with a nominal particle size of about 20 micron and a moisture less than 5.0 %;

the second coating comprising:

- between 1 mg and 2 mg of hydroxypropylmethylcellulose (HPMC) 5cps;
- between 2 mg and 3.5 mg of HydroxyPropyl B-cyclodextrin; and
- between 0.1 mg and 1 mg of Testosterone.

40. A dual drug delivery device according to any one of claims 15-22, the core comprising:

- between 50 mg and 150 mg of microcrystalline cellulose;
- between 150 mg and 250 mg of DicalciumPhosphate 0 aq;
- between 1 mg and 20 mg of Buspirone Hydrochloride;
- between 10 mg and 20 mg of Croscarmellose;
- between 1 mg and 10 mg of Magnesiumstearate;

the first coating comprising:

- between 5 mg and 20 mg ethylcellulose;
- between 10 mg and 50 mg of microcrystalline cellulose with a nominal particle size of about 20 micron and a moisture less than 5.0 %;

the second coating comprising:

- between 1 mg and 2 mg of HPMC 5cps
- between 2 mg and 3.5 mg of HydroxyPropyl B-cyclodextrin; and
- between 0.1 mg and 1 mg of Testosterone.

41. A dual drug delivery device according claim 39 or 40, wherein the second coating further comprises between 1 mg and 2 mg peppermint oil and between 0.5 mg and 1.5 mg of aspartame.