Claims

1. A stable nanostructured Telmisartan composition comprising:

(a) nanostructured Telmisartan having an average particle size of less than about 600 nm; and

(b) at least one stabilizer,

wherein the composition is prepared in a continuous flow reactor, preferably in a microfluidic based continuous flow reactor.

2. A composition according to claim 1, wherein the average particle size of is between 600 nm and 50 nm, preferably between 200 nm and 50 nm.

3. The composition according to claim 1 or 2 wherein the stabilizer is selected from the group of hydroxypropyl methylcellulose, hydroxypropylcellulose, poly(vinylpyrrolidone), sodium dodecyl sulfate, sodium lauryl sulfate, gelatin, dextran, stearic acid, glycerol monostearate, cetostearyl alcohol, sorbitan esters, polyoxyethylene castor oil derivatives, poly(meth)acrylate-based polymers and copolymers , acetic acid ethenyl ester polymer with l-ethenyl-2-pyrrolidinone (PVP/VA copolymers), sodium dodecyl benzene sulfonate, tocopheryl polyethylene glycol succinates, polyethoxylated castor oils and its derivatives, polyoxyethylene sorbitan fatty acid esters; polyethylene glycols, polyoxyethylene stearates, methylcellulose, hydroxy ethylcellulose, cellulose acetate phthalate, polyvinyl alcohol, 4-(l,l,3,3- tetramethylbutyl)-phenol polymer with ethylene oxide and formaldehyde, poloxamers; poloxamines, which is a tetrafunctional block copolymer derived from sequential addition of propylene oxide and ethylene oxide to ethylenediamine; PEG-phospholipid, PEG-cholesterol, PEG-cholesterol derivative, PEG-vitamin A, PEG-vitamin E, lysozyme, poly(2-ethyl-2-oxazoline), poly(methyl vinyl ether), random copolymers of vinyl pyrrolidone and vinyl acetate.

4. The composition according to any of claims 1 to 3, where the composition contains additional stabilizer which is hydroxyl-propyl-cellulose derivatives, or combination of two stabilizers of Claim 3 and/or lauryl trimethyl ammonium chloride, alkylbenzyl methyl ammonium chloride, alkylbenzyl dimethyl ammonium bromide, benzyl trimethylammonium bromide.

5. Process for the preparation of nanostructured Telmisartan composition according to any of claims 1 to 4, comprising precipitating nanostructured Telmisartan from a solution of Telmisartan comprising optionally one or more stabilizer, if desired in the presence of a pharmaceutically acceptable acid in a continuous flow reactor, preferably in a microfluidic based continuous flow reactor.

6. Process according to claim 5, comprising (1) dissolving Telmisartan and one or more stabilizers in a suitable solvent; (2) adding the formulation from step (1) to a solution comprising optionally one or more stabilizers and if desired a pharmaceutically acceptable acid and (3) precipitating the formulation from step (2).

7. Process according to claim 5, comprising (1) dissolving Telmisartan and optionally one or more stabilizers in a suitable solvent; (2) adding the formulation from step (1) to a solution comprising one or more stabilizers and if desired a pharmaceutically acceptable acid and (3) precipitating the formulation from step (2).

8. Process according to claim 5, comprising (1) dissolving Telmisartan and one or more stabilizers in an alkali-hydroxide solution; (2) adding to the solution of step (1) a solution of a pharmaceutically acceptable acid comprising optionally one or more stabilizers and (3) precipitating the formulation from step (2).

9. Process according to claims 7 or 8, comprising (a) using two different solvents miscible with each other, where Telmisartan is soluble only in one of them, or (b) using the same solvent in the two steps, where Telmisartan forms nanostructured particles, practically, with the restriction that the applied polyelectrolyte and/or stabilizers is soluble in the solvents used.

10. A pharmaceutical composition comprising a nanostructured Telmisartan composition according to any of claims 1 to 4 together with pharmaceutically acceptable auxiliary materials.

11. A pharmaceutical composition according to claim 10, wherein the composition is free of sodium-hydroxide content.

12. Use of nanostructured composition of claims 1 to 4 for preparation of a medicament.

13. Use of nanostructured composition according to any of claims 1 to 4 or a pharmaceutical composition according to claim 10 or 11 for the treatment hypertension.

14. The use according to claim 13, wherein the composition has at least one property from the following group:

- a solubility at least about 0.4 mg/ml in water,
- instantaneous redispersibility in physiological mediums,
- reduced food and side effect,
- increased absorption in human gastrointestinal tract,
- faster onset of action
- decreased variability,

for decreasing the dosage used.

Claims

1. A stable nanostructured Telmisartan composition comprising:

(a) nanostructured Telmisartan having an average particle size of less than about 600 nm; and

(b) at least one stabilizer,

wherein the composition is prepared in a continuous flow reactor, preferably in a microfluidic based continuous flow reactor.

2. A composition according to claim 1, wherein the average particle size of is between 600 nm and 50 nm, preferably between 200 nm and 50 nm.

3. The composition according to claim 1 or 2 wherein the stabilizer is selected from the group of hydroxypropyl methylcellulose, hydroxypropylcellulose, poly(vinylpyrrolidone), sodium dodecyl sulfate, sodium lauryl sulfate, gelatin, dextran, stearic acid, glycerol monostearate, cetostearyl alcohol, sorbitan esters, polyoxyethylene castor oil derivatives, poly(meth)acrylate-based polymers and copolymers , acetic acid ethenyl ester polymer with l-ethenyl-2-pyrrolidinone (PVP/VA copolymers), sodium dodecyl benzene sulfonate, tocopheryl polyethylene glycol succinates, polyethoxylated castor oils and its derivatives, polyoxyethylene sorbitan fatty acid esters; polyethylene glycols, polyoxyethylene stearates, methylcellulose, hydroxy ethylcellulose, cellulose acetate phthalate, polyvinyl alcohol, 4-(l,l,3,3- tetramethylbutyl)-phenol polymer with ethylene oxide and formaldehyde, poloxamers; poloxamines, which is a tetrafunctional block copolymer derived from sequential addition of propylene oxide and ethylene oxide to ethylenediamine; PEG-phospholipid, PEG-cholesterol, PEG-cholesterol derivative, PEG-vitamin A, PEG-vitamin E, lysozyme, poly(2-ethyl-2-oxazoline), poly(methyl vinyl ether), random copolymers of vinyl pyrrolidone and vinyl acetate.

4. The composition according to any of claims 1 to 3, where the composition contains additional stabilizer which is hydroxyl-propyl-cellulose derivatives, or combination of two stabilizers of Claim 3 and/or lauryl trimethyl ammonium chloride, alkylbenzyl methyl ammonium chloride, alkylbenzyl dimethyl ammonium bromide, benzyl trimethylammonium bromide.

5. Process for the preparation of nanostructured Telmisartan composition according to any of claims 1 to 4, comprising precipitating nanostructured Telmisartan from a solution of Telmisartan comprising optionally one or more stabilizer, if desired in the presence of a pharmaceutically acceptable acid in a continuous flow reactor, preferably in a microfluidic based continuous flow reactor.

6. Process according to claim 5, comprising (1) dissolving Telmisartan and one or more stabilizers in a suitable solvent; (2) adding the formulation from step (1) to a solution comprising optionally one or more stabilizers and if desired a pharmaceutically acceptable acid and (3) precipitating the formulation from step (2).

7. Process according to claim 5, comprising (1) dissolving Telmisartan and optionally one or more stabilizers in a suitable solvent; (2) adding the formulation from step (1) to a solution comprising one or more stabilizers and if desired a pharmaceutically acceptable acid and (3) precipitating the formulation from step (2).

8. Process according to claim 5, comprising (1) dissolving Telmisartan and one or more stabilizers in an alkali-hydroxide solution; (2) adding to the solution of step (1) a solution of a pharmaceutically acceptable acid comprising optionally one or more stabilizers and (3) precipitating the formulation from step (2).

9. Process according to claims 7 or 8, comprising (a) using two different solvents miscible with each other, where Telmisartan is soluble only in one of them, or (b) using the same solvent in the two steps, where Telmisartan forms nanostructured particles, practically, with the restriction that the applied polyelectrolyte and/or stabilizers is soluble in the solvents used.

10. A pharmaceutical composition comprising a nanostructured Telmisartan composition according to any of claims 1 to 4 together with pharmaceutically acceptable auxiliary materials.

11. A pharmaceutical composition according to claim 10, wherein the composition is free of sodium-hydroxide content.

12. Use of nanostructured composition of claims 1 to 4 for preparation of a medicament.

13. Use of nanostructured composition according to any of claims 1 to 4 or a pharmaceutical composition according to claim 10 or 11 in the manufacture of a medicament for the treatment of hypertension.

14. The use according to claim 13, wherein the composition has at least one property from the following group:

- a solubility at least about 0.4 mg/ml in water,
- instantaneous redispersibility in physiological mediums,
- reduced food and side effect,
- increased absorption in human gastrointestinal tract,
- faster onset of action
- decreased variability,

for decreasing the dosage used.