Claims

1. A stable nanostructured composition comprising:

   (a) nanostructured Candesartan or its pharmaceutically acceptable ester having an average particle size of less than about 500 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 is preferably between 500 nm and 50 nm.

3. The stable nanostructured composition according to claim 1, where the pharmaceutically acceptable ester of Candesartan is the Candesartan Cilexetil.

4. The stable nanostructured composition according to any of claims 1 to 3, where the stabilizers is selected from the group of hydroxypropyl methylcellulose, cellulose acetate phthalate, hydroxypropylcellulose, poly(vinylpyrrolidone), 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 1-ethenyl-2-pyrrolidinone (PVP/VA copolymers), sodium dodecyl benzene sulfonate, tocopheryl polyethylene glycol succinates, polyethoxylated castor oils and its derivateives, polyoxyethylene sorbitan fatty acid esters; polyethylene glycols, polyoxyethylene stearates, methylcellulose, hydroxyethylcellulose, polyvinyl alcohol, 4-(1,1,3,3-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, 30 lysozyme, poly(2-ethyl-2-oxazoline), poly(methyl vinyl ether), random copolymers of vinyl pyrrolidone and vinyl acetate.

5. A process for the preparation of nanostructured Candesartan or its pharmaceutically acceptable ester comprising precipitating nanostructured Candesartan or its pharmaceutically acceptable ester from an appropriate solution of Candesartan or its pharmaceutically acceptable ester comprising one or more stabilizers, if desired in the presence of a pharmaceutically acceptable acid or base, in a continuous flow reactor, preferably in a microfluidic based continuous flow reactor.

6. The process according to claim 5, comprising (1) dissolving Candesartan or its pharmaceutically acceptable ester and optionally one or more stabilizers in a suitable solvent; (2) adding the formulation from step (1) to a solution comprising optionally one or more stabilizer(s) and, if desired, a pharmaceutically acceptable acid or base and (3) precipitating the formulation from step (2).

7. The process according to claim 5 and 6, comprising (1) dissolving Candesartan or its pharmaceutically acceptable ester and optionally one or more stabilizers in a suitable solvent; (2) adding the formulation from step (1) to a solution comprising one or more stabilizer(s) and, if desired, a pharmaceutically acceptable acid or base and (3) precipitating the formulation from step (2).

8. The process according to any of claims 5 to 7 comprising the use of two different solvents miscible with each other, where Candesartan or its pharmaceutically acceptable ester is soluble only in one of them.

9. The process according to any of claim 5 to 8, where the pharmaceutically acceptable ester of Candesartan is the Candesartan Cilexetil.

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

11. Use of stable nanostructured composition according to any of claims 1 to 4 for the preparation of a medicament.

12. Use of stable nanostructured composition according to any of claims 1 to 4 for the treatment of hypertension.

13. The use according to claim 11 or 12, wherein the nanostructured Candesartan or its pharmaceutically acceptable ester or the composition has

- a solubility at least about 0.4836 mg/ml in water,
- instantaneous redispersibility in physiological mediums,
- reduced side effect,
- increased absorption in human gastrointestinal tract,
- faster onset of action,

for decreasing the dosage used.

Claims

1. A stable nanostructured composition comprising:

    (a) nanostructured Candesartan Cilexetil having an average particle size of less than 500 nm; and

    (b) at least one stabilizer,

    wherein the composition is prepared in a continuous flow reactor.

2. The stable nanostructured composition according to claim 1, wherein the continuous flow reactor is a microfluidic based continuous flow reactor.

3. A composition according to claim 1 or 2, wherein the average particle size is preferably between 500 nm and 50 nm.

4. The stable nanostructured composition according to any of claims 1 to 3, where the stabilizers is selected from the group of hydroxypropyl methylcellulose, cellulose acetate phthalate, hydroxypropylcellulose, poly(vinylpyrrolidone), 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 1-ethenyl-2-pyrrolidinone (PVP/VA copolymers), sodium dodecyl benzene sulfonate, tocopheryl polyethylene glycol succinates, polyethoxylated castor oils and its derivateives, polyoxyethylene sorbitan fatty acid esters; polyethylene glycols, polyoxyethylene stearates, methylcellulose, hydroxyethylcellulose, polyvinyl alcohol, 4-(1,1,3,3-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, 30 lysozyme, poly(2-ethyl-2-oxazoline), poly(methyl vinyl ether), random copolymers of vinyl pyrrolidone and vinyl acetate.

5. A process for the preparation of nanostructured Candesartan Cilexetil comprising precipitating nanostructured Candesartan Cilexetil from an appropriate solution of Candesartan Cilexetil comprising one or more stabilizers, if desired in the presence of a pharmaceutically acceptable acid or base, in a continuous flow reactor.

6. The process according to claim 5, wherein the precipitating nanostructured Candesartan Cilexetil is carried out in a microfluidic based continuous flow reactor.

7. The process according to claims 5 or 6, comprising (1) dissolving Candesartan Cilexetil and optionally one or more stabilizers in a suitable solvent; (2) adding the formulation from step (1) to a solution comprising optionally one or more stabilizer(s) and, if desired, a pharmaceutically acceptable acid or base and (3) precipitating the formulation from step (2).

8. The process according to any of claims 5 and 7, comprising (1) dissolving Candesartan Cilexetil and optionally one or more stabilizers in a suitable solvent; (2) adding the formulation from step (1) to a solution comprising one or more stabilizer(s) and, if desired, a pharmaceutically acceptable acid or base and (3) precipitating the formulation from step (2).

9. The process according to any of claims 5 to 8 comprising the use of two different solvents miscible with each other, where Candesartan Cilexetil is soluble only in one of them.

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

11. Use of stable nanostructured composition according to any of claims 1 to 4 for the preparation of a medicament.

12. Use of stable nanostructured composition according to any of claims 1 to 4 in the manufacture of a medicament for the treatment of hypertension.

13. The use according to claim 11 or 12, wherein the nanostructured Candesartan Cilexetil or the composition has

- a solubility at least 0.4836 mg/ml in water,
- instantaneous redispersibility in physiological mediums,
- reduced side effect,
- increased absorption in human gastrointestinal tract,
- faster onset of action,

for decreasing the dosage used.