Claims

1. A method for producing nanoparticles containing tacrolimus or a salt thereof comprising the steps of:
a) providing a solution of tacrolimus or a salt thereof in an organic solvent;
b) providing a liquid non-solvent for tacrolimus or a salt thereof;
c) precipitating nanoparticles containing tacrolimus or a salt thereof by colliding a stream of the organic solvent from a) with the non-solvent stream from b); and
d) isolating the nanoparticles, wherein the nanoparticles have a size of from 10 to 400 nm, and preferably a polydispersity index of ≤ about 0.4.

2. Method according to claim 1, wherein the solvent comprises ethanol, methanol, acetone, and/or tetrahydrofuran.

3. Method according to any one of claims 1 or 2, wherein the non-solvent comprises water.

4. Method according to any one of claims 1 to 3, wherein the solvent and/or the non-solvent further comprises at least one stabilizing agent, preferably polyvinyl pyrrolidone, vinylpyrrolidone-/vinylacetate-copolymer, polyethylenglycol and/or a cellulose derivative such as hydroxypropylmethyl cellulose (HPMC), hydroxypropylmethyl cellulose phthalate (HPMCP), hydroxypropylmethyl cellulose acetate succinate (HPMCAS), hydroxypropyl cellulose (HPC), and/or carboxymethyl cellulose (CMC).

5. Method according to any one of claims 1 to 4, wherein the non-solvent further comprises a non-ionic surfactant and/or an ionic surfactant.

6. Method according to any one of claims 1 to 5, wherein the fluid streams are collided with a velocity of 1 m/sec to 100 m/sec, preferably of 50 m/sec.

7. Method according to any one of claims 1 to 6, wherein the volume ratio of the solvent and the non-solvent is between 1:1 and 1:5.

8. Mucoadhesive buccal film comprising at least one matrix layer containing nanoparticles comprising tacrolimus or a salt thereof and having a particle size of 10 to 400 nm and at least one polymer.

9. Mucoadhesive buccal film according to claim 8, wherein the nanoparticles have a polydispersity index of ≤ about 0.4.

10. Mucoadhesive film according to any of claims 8 – 9, wherein the nanoparticles further comprise at least one stabilizing agent and/or a surfactant.

11. Mucoadhesive film according to any of claims 8 – 10, wherein the at least one stabilizing agent comprises polyvinyl pyrrolidone, vinylpyrrolidone-/vinylacetate-copolymer, polyethylenglycol and/or a cellulose derivative such as hydroxypropylmethyl cellulose (HPMC), hydroxypropylmethyl cellulose phthalate (HPMCP), hydroxypropylmethyl cellulose acetate succinate (HPMCAS), hydroxypropyl cellulose (HPC), and/or carboxymethyl cellulose (CMC).

12. Mucoadhesive buccal film according to any of claims 8 - 11, wherein the at least one polymer comprises hydroxypropylmethyl cellulose, hydroxypropyl cellulose, hydroxyethyl cellulose, pea starch, pullulan, poly(meth)acrylate, polyvinyl caprolactam-polyvinyl acetate-polyethylene glycol graft copolymer, chitosan, gummi arabicum, dextran, dextrin, alginate, polyvinylalcohol, polyvinylpyrrolidone and/or vinylpyrrolidon-vinylacetate-copolymer.

13. Mucoadhesive buccal film according to any one of claims 8 - 12, wherein the at least one matrix layer further comprising at least one adjuvant selected from the group comprising colorants, flavorings, sweeteners, taste masking agents, emulsifiers, enhancers, pH regulators, humectants, preservatives and/or antioxidants.

14. Mucoadhesive buccal film according to any one of claims 8 to 13, wherein the mucoadhesive buccal film comprises one backing layer, which is preferably impermeable for tacrolimus on one side of the at least one matrix layer.

15. Mucoadhesive buccal film according to any one of claims 8 to 14 for use as a medicament, in particular for use in the prophylaxis and/or treatment of solid organ transplant rejection.

16. Mucoadhesive buccal film according to any one of claims 8 to 14 for use as a medicament for treating pediatric patients, in particular for use in the prophylaxis and/or treatment of solid organ transplant rejection in pediatric patients.