Poly (I:C) has been formulated with several bioadhesive polymers that can prolong the residence time on the nasal epithelium and provide a more effective and controllable stimulation of the innate immune system.

The current invention provides the identification of a unique formulation that could be stored almost indefinitely at room temperature and which retains its innate immune system-stimulating activity.
The current inventive formulation contains water-soluble carriers and has the advantage of low viscosity characteristics.
When pea starch is used in the formulation of the composition comprising Poly (I:C), such composition shows surprisingly a less sticky behavior to the inside of a vial, tube or device (like sprays) when such vials, tubes or devices must be filled with the inventive composition compared to any other starch used for the same purpose. The technical advantage is that more precisely the dosage of said Poly (I:C) can be administered to the patient in need, since less composition will stick to the inner side of the nasal spray device accordingly.
In addition the formulation enhances the efficacy of Poly (I:C) and permits much less frequent dosing with even greater TLR3 stimulating activity.

The invention relates to a microparticle, consisting of polyinosinic acid, polycytidylic acid, water, and one or more carrier polymers selected from pea starch, pregelatinized potato starch, microcrystalline cellulose, and hyaluronate.

The invention relates to a microparticle wherein the microparticle consists essentially of polyinosinic acid, polycytidylic acid, water, and one or more carrier polymers selected from pea starch, potato starch, microcrystalline cellulose, and hyaluronate.

The invention relates to a composition comprising a plurality of microparticles as described herein.

The invention relates to a composition as described herein, for use in medicine.

The invention relates to use of a composition as described herein, in the manufacture of a medicament for treating or inhibiting a respiratory viral infection, or prophylaxing against a respiratory virus.

The invention relates to use of a composition as described herein, in the manufacture of a medicament for prophylacting against a viral infection of the respiratory tract.

The invention also relates to use of a composition in the manufacture of a medicament for preventing upper respiratory infections by nasal administration of the composition, wherein

the composition comprises a plurality of microparticles;

the microparticles comprise polyinosinic acid, polycytidylic acid, and one or more carrier polymers comprising pea starch, pregelatinized potato starch, microcrystalline cellulose, or hyaluronate.

The invention also relates to a nasal delivery device comprising a composition, wherein

the composition comprises a plurality of microparticles;

the microparticles comprise polyinosinic acid, polycytidylic acid, and one or more carrier polymers comprising pea starch, pregelatinized potato starch, microcrystalline cellulose, or hyaluronate.

The invention also relates to use of a composition as disclosed herein, for the manufacture of a medicament for activating an innate immune response.

The invention therefore relates to a composition comprising micro particles of polyinosinic–polycytidylic acid (Poly (I:C)) and a carrier polymer selected from the group pea starch, pregelatinized potato starch, lactose, microcrystalline cellulose, hyaluronate or glucosamine. For hyaluronate its sodium salt is preferred while for glucosamine the N-acetyl-D-glucosamine form is preferred for the purpose of the invention. Micro particles are particles with an average particle size between 0.1 µm and 100 µm. Preferably the carrier polymer is starch obtained from the plant genus Lathyrus more specifically from peas.
Poly (I:C)-carrier-polymer microspheres, or also so-called micro particles, comprised in the composition are produced by means of a particle formation process such as a spray-dry process.
The ratio Poly (I:C) / pea starch according to the invention ranges from 1/200 (w/w) to 1 / 0.1 (w/w), but preferably from 1/100 (w/w) to 1/1 (w/w) and even more preferably from 1/100 (w/w) to 1/5 (w/w) while a ratio Poly (I:C) / pea starch between 1/12 and 1/9 (w/w) is most preferred. The same ranges and ratios apply for the other carriers mentioned according to the invention.

The D_v50 (= volume based 50% cumulative undersize of the particle) of the micro particle in the composition according to the invention ranges from

Claims

1. A microparticle, consisting of polyinosinic acid, polycytidylic acid, water, and one or more carrier polymers selected from pea starch, pregelatinized potato starch, microcrystalline cellulose, and hyaluronate.

2. The microparticle of claim 1, wherein the microparticle is produced by a spray-dry particle formation process.

3. The microparticle of claims 1 or 2, wherein the average chain length of each of the polyinosinic acid and polycytidylic acid is approximately 300 bases to 6,000 bases, or the average molecular weight of the combination of the polyinosinic acid and the polycytidylic acid is approximately 180 kDa to 3,600 kDa.

4. The microparticle of claim 3, wherein the ratio of the combination of polyinosinic acid and polycytidylic acid to carrier polymer ranges from 1/200 (w/w) to 1/0.1 (w/w).

5. The microparticle of any preceding claim, wherein the ratio of the combination of polyinosinic acid and polycytidylic acid to carrier polymer in the microparticle is 1/100 (w/w) to 1/1 (w/w).

6. The microparticle of any preceding claim, wherein the ratio of the combination of polyinosinic acid and polycytidylic acid to carrier polymer in the microparticle is 1/100 (w/w) to 1/5 (w/w).

7. The microparticle of any preceding claim, wherein the ratio of the combination of polyinosinic acid and polycytidylic acid to carrier polymer is between 1/12 (w/w) and 1/9 (w/w).

8. The microparticle of any preceding claim, wherein the polyinosinic acid and polycytidylic acid are each present as a sodium salt.

9. The microparticle of claim 1, wherein the carrier polymer is pea starch or potato starch.

10. The microparticle of claim 1, wherein the carrier polymer is a pregelatinized pea starch or a pregelatinized potato starch.

11. The microparticle of claim 10, wherein the pea starch is hydroxypropylated pregelatinized pea starch.

12. A microparticle, wherein the microparticle consists essentially of polyinosinic acid, polycytidylic acid, water, and one or more carrier polymers selected from pea starch, potato starch, microcrystalline cellulose, and hyaluronate.

13. The microparticle of any preceding claim, wherein the size of the microparticle ranges from 0.1 μm to 200 μm.

14. The microparticle of any preceding claim, wherein the size of the microparticle ranges from 0.1 μm to 100 μm.

15. The microparticle of any preceding claim, wherein the size of the microparticle ranges from 1 μm to 50 μm.

16. The microparticle of any preceding claim, wherein the size of the microparticle ranges from 2 μm to 40 μm.

17. The microparticle of any preceding claim, wherein the size of the microparticle ranges from 2 μm to 20 μm.

18. The microparticle of any preceding claim, wherein the size of the microparticle ranges from 10 μm to 20 μm.

19. The microparticle of any preceding claim, wherein the polyinosinic acid, polycytidylic acid and carrier polymer are admixed in the microparticle.

20. A composition comprising a plurality of microparticles according to any preceding claim.

21. The composition of claim 20, wherein the composition consists essentially of the plurality of the microparticles.

22. The composition of claim 21, wherein:
the polyinosinic acid, polycytidylic acid and carrier polymer are admixed in the microparticles;
the ratio of the combination of polyinosinic acid and polycytidylic acid to carrier polymer in the microparticles is 1/100 (w/w) to 1/1 (w/w); and
the composition is a dry powder.

23. The composition of any one of claims 20-22, wherein the microparticles of the plurality have a D_v50 from 0.1 μm to 200 μm.

24. The composition of claim 23, wherein the microparticles of the plurality have a D_v50 from 1 μm to 50 μm.

25. The composition of claim 24, wherein the microparticles of the plurality have a D_v50 from 2 μm to 20 μm.

26. The composition of claim 25, wherein the microparticles of the plurality have a D_v50 from 10 μm to 20 μm.

27. The composition of claim 20, wherein the composition is a liquid.

28. The composition of claim 27, wherein the composition comprises an organic solvent.

29. The composition of claim 28, wherein the organic solvent is glycerol, ethanol, or a combination thereof.

30. The composition of claim 27, wherein the composition comprises phosphate-buffered saline.

31. The composition of claim 20, wherein the composition is a dry powder.

32. The composition of claim 31, wherein the composition is prepared using a spray dry process.

33. The composition of claim 31, wherein the microparticles are stable during storage at room temperature for one month.

34. The composition of any one of claims 20-33, wherein the composition is suitable for nasal administration.

35. A composition of any one of claims 20-34, for use in medicine.

36. Use of a composition according to claim 35, for the manufacture of a medicament for activating an innate immune response.

37. Use of a composition according to claim 35, for the manufacture of a medicament for treating or inhibiting a respiratory viral infection, or prophylaxing against a respiratory virus .

38. The use of claim 37, wherein the respiratory viral infection is an infection of the upper respiratory tract.

39. The use of claim 37 or 38, wherein the viral infection is a human rhinovirus infection or an influenza virus infection.

40. The use of any one of claims 36-39, wherein the medicament is for nasal administration.

41. A nasal delivery device, comprising the composition of any one of claims 20-35.