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.
In addition the formulation enhances the efficacy of Poly (I:C) and permits much less frequent dosing with even greater TLR3 stimulating activity.

The disclosure therefore relates to a composition comprising micro particles of polyinosinic–polycytidylic acid (Poly (I:C)) and a carrier polymer selected from starch, alginate, blanose or DPPC (dipalmitoylphosphatidylcholine).

In one aspect, there is provided a microparticle consisting of polyinosinic acid and polycytidylic acid mixed with one or more carrier polymers and water; wherein each carrier polymer is selected from starch, alginate, sodium carboxymethyl cellulose, and dipalmitoylphosphatidylcholine.

In another aspect, there is provided a composition comprising a plurality of microparticles as defined herein.

In another aspect, there is provided a composition as defined herein, for use in a method of activating innate immune response.

In another aspect, there is provided a composition as defined herein, for use in medicine.

In another aspect, there is provided a composition for use in preventing, inhibiting and/or treating upper respiratory infections by nasal administration of the composition, wherein the composition comprises a plurality of microparticles; the microparticles consist of polyinosinic acid and polycytidylic acid mixed with one or more carrier polymers and water; and wherein each carrier polymer is selected from starch, alginate, carboxymethyl cellulose, and dipalmitoylphosphatidylcholine.

In another aspect, there is provided a nasal delivery system, comprising the composition as defined herein.

In another aspect, there is provided use of a composition as defined herein, for the manufacture of a medicament for activating an innate immune response.

In another aspect, there is provided use of a composition as defined herein, for the manufacture of a medicament for preventing, inhibiting and/or treating upper respiratory infections by nasal administration of the composition.

In another aspect, there is provided use of a composition for the manufacture of a medicament for preventing, inhibiting and/or treating upper respiratory infections by nasal administration of the composition, wherein the composition comprises a plurality of microparticles; the microparticles consist of polyinosinic acid and polycytidylic acid mixed with one or more carrier polymers and water; and wherein each carrier polymer is selected from starch, alginate, carboxymethyl cellulose, and dipalmitoylphosphatidylcholine.

In another aspect, there is provided a nasal delivery device comprising a composition, wherein the composition comprises a plurality of microparticles; the microparticles comprise polyinosinic acid and polycytidylic acid mixed with one or more carrier polymers and water; and wherein each carrier polymer is selected from starch, alginate, carboxymethyl cellulose, and dipalmitoylphosphatidylcholine.

Micro particles are particles with an average particle size between 0.1 µm and 100 µm. Preferably the carrier polymer is starch obtained from maize, potato or cassava.

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) / 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) / starch between 1/12 and 1/9 (w/w) is most preferred.

The D_v50 (= volume based 50% cumulative undersize of the particle) of the micro particle in the composition according to the invention ranges from 0.1 micrometer to 200 micrometer, preferably from 1 micrometer to 50 micrometer, more preferably from 2 micrometer to 40 micrometer, even more preferably from 2 micrometer to 20 micrometer, and most preferred from 10 micrometer to 20 micrometer.

The composition of the invention can also be a liquid composition comprising an organic solvent, wherein the organic solvent is based on glycerol or ethanol or a combination thereof.

The composition of the invention can be used in medicine preferably for use in preventing and/or treating viral infections of the upper respiratory tract such as what are referred to as “common colds”.

The current composition can be used by patients suffering from asthma and/or COPD (Chronic Obstructive Pulmonary Disease) in order to potentially prevent and/or treat upcoming common cold symptoms.

Claims

1. A microparticle consisting of polyinosinic acid and polycytidylic acid mixed with one or more carrier polymers and water; wherein each carrier polymer is selected from starch, alginate, sodium carboxymethyl cellulose, and dipalmitoylphosphatidylcholine.

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

3. The microparticle of claim 1 or 2, wherein the average chain length of each of the polyinosinic acid and polycytidylic acid is 300 bases to 6,000 bases.

4. The microparticle of any one of claims 1 to 3, wherein the polyinosinic acid and polycytidylic acid are each present as a sodium salt.

5. The microparticle of any one of claims 1 to 4, wherein the microparticle consists of one carrier polymer, water, polyinosinic acid and polycytidylic acid.

6. The microparticle of any one of claims 1 to 5, wherein at least one carrier polymer is starch.

7. The microparticle of claim 6, wherein the starch carrier polymer is a maize starch, potato starch, or cassava starch.

8. The microparticle of claim 6, wherein the starch is partially pregelatinized maize starch.

9. The microparticle of any of the claims 6 to 8, wherein the ratio of the combination of polyinosinic acid and polycytidylic acid to starch ranges from 1/200 (w/w) to 1/0.1 (w/w).

10. The microparticle of any one of claims 6 to 9, wherein the ratio of the combination of polyinosinic acid and polycytidylic acid to starch is between 1/12 (w/w) and 1/9 (w/w).

11. The microparticle of any one of claims 1 to 5, wherein at least one carrier polymer is alginate, and the alginate is sodium alginate.

12. The microparticle of any one of claims 1 to 5, wherein at least one carrier polymer is dipalmitoylphosphatidylcholine.

13. A composition comprising a plurality of microparticles according to any one of claims 1 to 12.

14. The composition of claim 13, wherein the D_V50 of the composition ranges from 0.1 µm to 200 µm.

15. The composition of claim 13 or 4, wherein the Dv50 of the composition ranges from 0.1 µm and 100 µm.

16. The composition of any one of claims 13 to 15, wherein the Dv50 of the composition ranges from 1 µm to 50 µm.

17. The composition of any one of claims 13 to 6, wherein the Dv50 of the composition ranges from 2 µm to 40 µm.

18. The composition of any one of claims 13 to 17, wherein the Dv50 of the composition ranges from 2 µm to 20 µm.

19. The composition of any one of claims 13 to 8, wherein the Dv50 of the composition ranges from 10 µm to 20 µm.

20. The composition of any one of claims 13 to 19, wherein the composition is a liquid.

21. The composition of any of the claims 13 to 19, wherein the composition comprises an organic solvent.

22. The composition of claim 21 wherein the organic solvent is glycerol, ethanol or a combination thereof.

23. The composition of any one of claims 13 to 19, wherein the composition is a dry powder.

24. The composition of any one of claims 13 to 3, wherein the composition is suitable for nasal administration.

25. A composition of any one of claims 13 to 24, for use in a method of activating innate immune response.

26. A composition of any one of claims 13 to 24, for use in medicine.

27. The composition of claim 26, for use in preventing, inhibiting and/or treating upper respiratory infections by nasal administration of the composition.

28. The composition of claim 25 or 6, for use in treating or inhibiting a viral infection of the upper respiratory tract, or prophylaxing against a respiratory virus.

29. The composition of claim 28, wherein the viral infection is a human rhinovirus infection or an influenza virus infection.

30. A composition for use in preventing, inhibiting and/or treating upper respiratory infections by nasal administration of the composition, wherein

the composition comprises a plurality of microparticles;

the microparticles consist of polyinosinic acid and polycytidylic acid mixed with one or more carrier polymers and water; and

wherein each carrier polymer is selected from starch, alginate, carboxymethyl cellulose, and dipalmitoylphosphatidylcholine.

31. The composition of claim 29, wherein the composition consists of a plurality of microparticles.

32. A nasal delivery system, comprising the composition according to any one of claims 13 to 24.

33. Use of a composition according to any one of claims 13 to 24, for the manufacture of a medicament for activating an innate immune response.

34. Use of a composition according to claim 26, for the manufacture of a medicament for preventing, inhibiting and/or treating upper respiratory infections by nasal administration of the composition.

35. Use of a composition according to claim 34, for the manufacture of a medicament for treating or inhibiting a viral infection of the upper respiratory tract, or prophylaxing against a respiratory virus.

36. Use of a composition according to claim 35, wherein the viral infection is a human rhinovirus infection or an influenza virus infection.

37. Use of a composition for the manufacture of a medicament for preventing, inhibiting and/or treating upper respiratory infections by nasal administration of the composition, wherein

the composition comprises a plurality of microparticles;

the microparticles consist of polyinosinic acid and polycytidylic acid mixed with one or more carrier polymers and water; and

wherein each carrier polymer is selected from starch, alginate, carboxymethyl cellulose, and dipalmitoylphosphatidylcholine.

38. Use of a composition of claim 37, wherein the composition consists of a plurality of microparticles.

39. A nasal delivery device comprising a composition, wherein

the composition comprises a plurality of microparticles;
the microparticles comprise polyinosinic acid and polycytidylic acid mixed with one or more carrier polymers and water; and

wherein each carrier polymer is selected from starch, alginate, carboxymethyl cellulose, and dipalmitoylphosphatidylcholine.