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 disclosure 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 composition comprising micro particles of polyinosinic–polycytidylic acid (Poly (I:C)) and a starch carrier polymer wherein the ratio of Poly (I:C) ~~/~~ to starch carrier polymer in the microparticles is between 1/12 (w/w) and 1/9 (w/w). 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 disclosure can also be a liquid composition comprising an organic solvent, wherein the organic solvent is based on glycerol or ethanol or a combination thereof.
In another aspect, there is provided the composition as defined herein for use in medicine. The composition 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”.

A preferred way to prevent and/or treat upper respiratory infections is performed by nasal administration.

The composition of the current disclosure comprising micro particles of polyinosinic–polycytidylic acid (Poly (I:C)) and a carrier polymer selected from starch, alginate, blanose or DPPC (dipalmitoylphosphatidylcholine) can be used for the treatment and/or prevention of (viral) infections or common cold, wherein the composition is administered by nasal application at a time interval that is in the range of one day to one month, more preferably from every couple of days or even once a week.

The above mentioned composition wherein the ratio Poly (I:C) / starch 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, in combination with the micro particle size in the composition ranging 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 can be used for the treatment and/or prevention of (viral) infections or common cold, wherein said composition is administered by nasal application at a time interval that is in the range of one day to one month, more preferably from every couple of days or even once a week.

There is provided a device, in particular a nasal delivery system, comprising a composition according to the disclosure. In another aspect, there is provided a nasal delivery system comprising a composition as defined herein. ~~In another aspect, there is provided a nasal delivery system comprising a composition having micro particles of polyinosinic-polycytidylic acid (Poly (I:C)) and a starch carrier polymer.~~ In another aspect, there is provided the nasal delivery system as defined herein for use in medicine. In another aspect, there is provided the nasal delivery system as defined herein for use in treating and/or prophylacting against infections or the common cold. In another aspect, there is provided the nasal delivery system as defined herein for use in treating or prophylacting against a viral infection of the respiratory tract.

According to the disclosure, Poly (I:C) is formulated as a dry powder for nasal administration. To improve stability, Poly (I:C) is spray dried from an aqueous mixture containing drum dried waxy maize starch and Poly (I:C).

Starch is believed to have a dual function: (1) to act as a bio-adhesive in the nose, (2) the amylopectin present in high concentration in waxy maize starch is broken down by amylases in the nose to release Poly (I:C).

Nasal administration is preferably achieved using a single dose nasal powder device (Unit dose device supplied from Aptar Pharma Germany). The unit dose device is an active delivery system, meaning that the patient does not need to inhale and performance is patient independent. Dosing is performed by

Claims

1. A composition comprising micro-particles of polyinosinic-polycytidylic acid (Poly (I:C)) and a starch carrier polymer, wherein the ratio of Poly (I:C) ~~/~~ to starch carrier polymer in the microparticles is between 1/12 (w/w) and 1/9 (w/w).

2. The composition of claim 1 wherein ~~Poly (I:C) carrier polymer~~the micro-particles are produced by ~~means of~~ a particle formation spray-dry process.

3. The composition of ~~any of the~~ claim~~s~~ 1 or 2, wherein the microparticles of the composition have a D_V50 ~~of the micro particle ranges~~ from 0.1 micrometer to 200 micrometer.

4. The composition of any one of ~~the~~ claims 1-3, wherein ~~said~~ the composition is a liquid composition comprising an organic solvent.

5. The composition of claim 4, wherein the organic solvent is based on glycerol or ethanol or a combination thereof.

6. A composition according to any one of ~~the~~ claims 1-5, for use in medicine.

7. A composition according to any one of the claims 1-5, for use in treating and/or preventing infections or common cold.

8. Use of a composition according to any one of ~~the~~ claims 1-5, in the manufacture of a medicament for preventing and/or treating upper respiratory infections by nasal administration.

9. A nasal delivery system comprising a composition according to any one of claims 1-5.

~~10. Use of a composition comprising micro particles of polyinosinic-polycytidylic acid (Poly (I:C)) and a starch carrier polymer in the manufacture of a medicament for preventing and/or treating upper respiratory infections by nasal administration.~~

~~11. A nasal delivery system comprising a composition having micro particles of polyinosinic-polycytidylic acid (Poly (I:C)) and a starch carrier polymer.~~

~~12. The nasal delivery system of claim 11, wherein said micro particles are produced by means of a particle formation spray-dry process.~~

~~13. The nasal delivery system of claim 11 or 12, wherein the D_v50 of said micro particles ranges from 0.1 micrometer to 200 micrometer.~~

~~14. The nasal delivery system of claim 11, 12, or 13, wherein said composition is a liquid composition comprising an organic solvent.~~

~~15. The nasal delivery system of claim 11, 12, or 13, wherein the ratio Poly (I:C) / starch ranges from 1/200 (w/w) to 1 / 0.1 (w/w).~~

10. The composition of any one of claims 1-3, wherein the composition is a dry powder.

11. The composition of any one of claims 1-3, wherein the composition consists of the microparticles.

12. The composition of any one of claims 1-3, wherein the microparticles of the composition consist of polyinosinic–polycytidylic acid, the starch carrier polymer, and water.

13. A nasal delivery system, comprising a composition according to any one of claims 10-12.

14. The nasal delivery system of claim 13, wherein the microparticles of the composition have a Dv50 from 1 µm to 50 µm.

15. The nasal delivery system of claim 14, wherein the microparticles of the composition have a Dv50 from 2 µm to 20 µm.

16. The nasal delivery system of claim 15, wherein the microparticles of the composition have a Dv50 from 10 µm to 20 µm.

17. The nasal delivery system of any one of claims 13-16, wherein the starch carrier polymer is a partially pregelatinized starch.

18. The nasal delivery system of any one of claims 13-17, wherein the starch carrier polymer is a maize starch, potato starch, or cassava starch.

19. The nasal delivery system of claim 18, wherein the starch carrier polymer is partially pregelatinized maize starch.

20. The nasal delivery system of any one of claims 13-19, wherein the microparticles are stable during storage at room temperature for one month.

21. The nasal delivery system of any one of the claims 13-20, for use in medicine.

22. The nasal delivery system of any one of the claims 13-21, for use in treating and/or prophylacting against infections or the common cold.

23. The nasal delivery system of any one of claims 13-22, for use in treating or prophylacting against a viral infection of the respiratory tract.

24. The nasal delivery system of claim 23, wherein the viral infection is a human rhinovirus infection or an influenza virus infection.