pressurized metered-dose inhalers (pMDIs). Ultrasonic wave nebulizers use an electronic oscillator that at high frequency causes vibration of a piezoelectric element for generating ultrasonic waves in the liquid reservoir with the active principle.

The most promising technology are vibrating mesh nebulizers. They use a mesh, respectively a polymer membrane having a very large number of laser-drilled holes. This membrane is placed between the liquid reservoir and the aerosol chamber. A piezoelectric element placed on the membrane induces high frequency vibrations of the membrane, leading to droplet formation in the aqueous solution and pressuring these droplets through the holes of the membrane into the aerosol chamber. With this technique very small droplet sizes can be generated. Moreover, a significantly shorter inhalation time for the patient can thus be achieved, a feature which drastically increases patient compliance. Only these mesh nebulizers are regarded to be able to generate liquid droplets with the active principle in the desired size range and bring them in a therapeutically effective amount into the patient's alveoli in a reasonable time.

However, not all agents that might be effective in the pharmaceutic treatment of inflammatory pulmonary diseases are suitable for the mesh nebulization technology. For example, some agents are nearly insoluble in water, or their intrinsic physicochemical molecule properties do not allow for the generation of an aerosol in the desired particle size range. Therefore, many nebulized anti-inflammatory agents met only mixed success in the treatment of inflammatory pulmonary diseases.

Thus, there is a medical need to find a pharmaceutical agent that shows a high efficacy in the treatment of inflammatory pulmonary diseases and at the same time allows for the generation of an aerosol in the desired liquid droplet or solid particle size range in order to be able to reach the alveoli of a patient in need thereof.

Surprisingly, this task could be solved by the nebulization (preferred) or alternatively in the case of solid particles their suspension with a dry-powder inhaler in a gas (especially an oxygen comprising gas, such as air) of selected human anti-inflammatory peptides.

Summary

In one aspect, the present disclosure refers to a use of a human anti-inflammatory peptide in the manufacture of a medicament for prophylaxis or treatment of inflammatory pulmonary diseases, wherein an aerosol comprising solid particles or liquid droplets containing said anti-inflammatory peptide is to be administered through inhalation by a metered-dose inhaler to a patient of the inflammatory pulmonary disease, especially ARDS, especially in a patients suffering or having suffered from an infection by a Coronavirus, especially SARS-CoV-2, where said human anti-inflammatory peptide is selected from a group consisting of vasoactive

intestinal peptide, C-type natriuretic peptide, B-type natriuretic peptide, pituitary adenylate cyclase-activating peptide, adrenomedullin, alpha-melanocyte stimulating hormone, relaxin and interferon gamma.

In another aspect, the present disclosure provides a use of a human anti-inflammatory peptide as described herein in the manufacture of a medicament for the prophylaxis or treatment of inflammatory pulmonary diseases, wherein the medicament is to be administered through inhalation using an aerosol, wherein said aerosol is characterized in that the fine particle mass is at least 60 % of the liquid droplets of the aerosol, and in that the median mass aerodynamic diameter of the liquid droplets of the aerosol is between 3.0 µm and 3.5 µm.

In yet another aspect, the present disclosure refers to an aerosol produced by a mesh nebulizer, containing a human anti-inflammatory peptide as described herein in the range of 0.01 % per weight to 10 % per weight, an aqueous solution in the range of 70 % per weight to 99.99 % per weight, and optionally at least one pharmaceutically acceptable excipient in the range of 0 % per weight to 20 % per weight, wherein said percentages add up to 100 %.

In one aspect, the present disclosure provides a use of a pharmaceutically active amount of a human anti-inflammatory peptide as defined herein, especially aviptadil, in the manufacture of a medicament for treating an inflammatory pulmonary disease, wherein the medicament is to be administered in the form of an aerosol to a patient suffering or expected to suffer from an inflammatory pulmonary disease in need of such treatment, especially a human suffering from a Coronavirus, especially SARS-CoV-2, infection, in particular suffering or having suffered from CoViD-19, where especially the aerosol is in the form of liquid droplets and is produced using a mesh nebulizer.

In another aspect, the present disclosure refers to a method for producing an aerosol as defined herein, comprising the following steps:

a) filling 0.1 ml to 10 ml of an aqueous solution containing at least one of the human anti-inflammatory peptides as defined herein and optionally at least one pharmaceutically acceptable excipient into the nebulization chamber of a mesh nebulizer,

b) starting vibration of the mesh of the mesh nebulizer at a frequency of 80 kHz to 200 kHz, and

c) discharging the generated aerosol at the side of the mesh of the mesh nebulizer opposite to the nebulization chamber.

In yet another aspect, the present disclosure refers to a kit comprising a mesh nebulizer and a pharmaceutically acceptable container with an aqueous solution containing at least one of the human anti-inflammatory peptides and optionally at least one pharmaceutically acceptable excipient, especially for use in inhalation treatment of a patient suffering or having suffered from an inflammatory pulmonary disease, especially a Coronavirus infection, in particular CoViD-19.

In one aspect, the present disclosure refers to a kit comprising a mesh nebulizer, a first pharmaceutically acceptable container with water for injection or physiological saline solution and a second pharmaceutically acceptable container with a solid form of a human anti-inflammatory peptide as defined herein, wherein optionally at least one pharmaceutically acceptable excipient is contained in the first pharmaceutically acceptable container and/or the second pharmaceutically acceptable container.

In another aspect, the present disclosure refers to a kit as described herein, additionally comprising a mouthpiece for inhalation fitting to said mesh nebulizer.

In yet another aspect, the present disclosure provides a use of an aerosol in the manufacture of a medicament for treating inflammatory pulmonary diseases, wherein the medicament is to be administered by

a) providing an aerosol as defined herein by nebulization with a mesh nebulizer, and

b) wherein a therapeutically effective amount of said aerosol is to be administered to a patient in need thereof via a mouthpiece for inhalation fitting to said mesh nebulizer via self-inhalation by the patient.

DETAILED DESCRIPTION OF THE INVENTION

The following human peptides were found to be outstandingly suitable for inhalatory application to a human suffering from a pulmonary disease:

Vasoactive Intestinal Peptide (VIP)

Claims

1. Use of a human anti-inflammatory peptide in the manufacture of a medicament for prophylaxis or treatment of inflammatory pulmonary diseases, wherein an aerosol comprising solid particles or liquid droplets containing said anti-inflammatory peptide is to be administered through inhalation by a metered-dose inhaler to a patient of the inflammatory pulmonary disease, especially ARDS, especially in a patients suffering or having suffered from an infection by a Coronavirus, especially SARS-CoV-2, where said human anti-inflammatory peptide is selected from a group consisting of vasoactive intestinal peptide, C-type natriuretic peptide, B-type natriuretic peptide, pituitary adenylate cyclase-activating peptide, adrenomedullin, alpha-melanocyte stimulating hormone, relaxin and interferon gamma.

2. The use according to claim 1, wherein the anti-inflammatory peptide is aviptadil.

3. The use according to claim 1 or claim 2, wherein a mesh nebulizer releases an aerosol to be administered through inhalation containing liquid droplets of said human anti-inflammatory peptide according to the invention, and said aerosol is characterized in that the fine particle mass is at least 60% of the liquid droplets of the aerosol, and in that the median mass aerodynamic diameter of the liquid droplets of the aerosol is between 3.0 µm and 3.5 µm.

4. The use according to claim 3, wherein said mesh nebulizer is a vibrating mesh nebulizer, especially wherein said vibrating mesh nebulizer is trigger-activated; in particular wherein the vibration frequency of the vibrating mesh nebulizer is in the range of 80 kHz to 200 kHz.

5. The use according to any one of claims 1 to 4, wherein the inflammatory pulmonary disease is selected from a group comprising inflammations of the lower airways due to a bacterial, viral, fungal or parasitic infection, chronic lower respiratory diseases, lung diseases due to an external agent, respiratory diseases principally affecting the interstitium, suppurative and/or necrotic conditions of lower respiratory tract, pleura diseases, postprocedural or related lower respiratory diseases, pulmonary diseases specific to the perinatal period, trauma and injuries of the lower respiratory tract and/or the thorax, malignant neoplasms of the lower respiratory tract and inflammatory diseases of the pulmonary circulation.

6. The use according to any one of claims 1 to 5, wherein the inflammatory pulmonary disease is selected from a group comprising chronic obstructive pulmonary disease, asthma, sarcoidosis of the lung, cystic fibrosis, bronchiectasis, adult respiratory distress syndrome (preferred), pulmonary fibrosis, berylliosis, chronic lung allograft dysfunction, pulmonary edema, lung ischemia reperfusion injury and primary graft dysfunction after lung transplantation.

7. Use of a human anti-inflammatory peptide as defined in claim 1 or claim 2 in the manufacture of a medicament for the prophylaxis or treatment of inflammatory pulmonary diseases, wherein the medicament is to be administered through inhalation using an aerosol, wherein said aerosol is characterized in that the fine particle mass is at least 60 % of the liquid droplets of the aerosol, and in that the median mass aerodynamic diameter of the liquid droplets of the aerosol is between 3.0 µm and 3.5 µm.

8. An aerosol produced by a mesh nebulizer, containing
a human anti-inflammatory peptide as defined in Claim 1 in the range of 0.01% per weight to 10 % per weight,
an aqueous solution in the range of 70 % per weight to 99.99 % per weight, and
optionally at least one pharmaceutically acceptable excipient in the range of 0 % per weight to 20 % per weight,
wherein said percentages add up to 100 %.

9. Use of a pharmaceutically active amount of a human anti-inflammatory peptide as defined in claim 1, especially aviptadil, in the manufacture of a medicament for treating an inflammatory pulmonary disease, wherein the medicament is to be administered in the form of an aerosol to a patient suffering or expected to suffer from an inflammatory pulmonary disease in need of such treatment, especially a human suffering from a Coronavirus, especially SARS-CoV-2, infection, in particular suffering or having suffered from CoViD-19, where especially the aerosol is in the form of liquid droplets and is produced using a mesh nebulizer.

10. A method for producing an aerosol as defined in claim 8, comprising the following steps:
    a) filling 0.1 ml to 10 ml of an aqueous solution containing at least one of the human anti-inflammatory peptides as defined in Claim 1 and optionally at least one pharmaceutically acceptable excipient into the nebulization chamber of a mesh nebulizer,
    b) starting vibration of the mesh of the mesh nebulizer at a frequency of 80 kHz to 200 kHz, and

c) discharging the generated aerosol at the side of the mesh of the mesh nebulizer opposite to the nebulization chamber.

11. The method according to claim 10,
characterized in that at least 50 % in weight of said at least one of the human anti-inflammatory peptides contained in said aqueous solution are nebulized in the generated aerosol.

12. The method according to any one of claims 10 or 11,
characterized in that at least 80 % of the generated aerosol are produced during three minutes after starting nebulization in the mesh nebulizer.

13. A kit, comprising a mesh nebulizer and a pharmaceutically acceptable container with an aqueous solution containing at least one of the human anti-inflammatory peptides and optionally at least one pharmaceutically acceptable excipient, especially for use in inhalation treatment of a patient suffering or having suffered from an inflammatory pulmonary disease, especially a Coronavirus infection, in particular CoViD-19.

14. A kit, comprising a mesh nebulizer, a first pharmaceutically acceptable container with water for injection or physiological saline solution and a second pharmaceutically acceptable container with a solid form of a human anti-inflammatory peptide as defined in Claim 1,
wherein optionally at least one pharmaceutically acceptable excipient is contained in the first pharmaceutically acceptable container and/or the second pharmaceutically acceptable container.

15. A kit as defined in any one of claims 13 or 14, additionally comprising a mouthpiece for inhalation fitting to said mesh nebulizer.

16. Use of an aerosol in the manufacture of a medicament for treating inflammatory pulmonary diseases, wherein the medicament is to be administered by
a) providing an aerosol as defined in claim 8 by nebulization with a mesh nebulizer, and
b) wherein a therapeutically effective amount of said aerosol is to be administered to a patient in need thereof via a mouthpiece for inhalation fitting to said mesh nebulizer via self-inhalation by the patient.