solubility, poor absorption and low oral bioavailability would limit its clinical development as an antiviral agent.

[0007] Cabitra et al., JCI Insight. 2019; 4(15):e128414 discloses the treatment of mice using niclosamide dissolved in corn oil and administered by I.P. injection showed that niclosamide reduced mucus production and secretion, as well as bronchoconstriction, and showed additional anti-inflammatory effects in asthmatic mice.

[0008] Niclosamide (tradenames are for instance Yomesan®, Tredemine®) is currently approved and marketed for the oral treatment of tapeworm infections with administration of a single 2 g regimen or 2 g daily for 7 days in adults and children (> 2 years of age). The PK analysis revealed that after oral administration, between 2-25% of the administered dose was detected in the urine, which can be considered as the minimum level of absorption. When treating human volunteers each with a single oral dose of 2,000 mg niclosamide, maximal serum concentration of niclosamide was equivalent to 0.25-6.0 μ g/mL (0.76 – 18.3 μM). The wide concentration range was caused by the intraindividual absorption differences. Niclosamide is only partially absorbed from intestinal tract, and the absorbed part is rapidly eliminated by the kidneys. Niclosamide has several other weaknesses such as low absorption and oral bioavailability (F = 10%) which may hamper its extensive clinical development as a systemic agent.

[0009] WO 2017/157997 discloses certain compositions comprising niclosamide for the topical treatment of conditions such as atopic dermatitis.

[0010] There remains a need to identify effective treatments for viral infections.

~~BRIEF~~ SUMMARY ~~OF THE DISCLOSURE~~

[0010a] In a first aspect, the present disclosure refers to a use of an inhalable pharmaceutical composition comprising niclosamide, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the prevention or treatment of a viral infection in a subject, wherein the niclosamide, or a pharmaceutically acceptable salt thereof, is to be administered to the subject by inhalation.

[0010b] In another aspect, the present disclosure refers to an aerosol of a solution comprising niclosamide, or a pharmaceutically acceptable salt thereof.

[0010c] In yet another aspect, the present disclosure refers to a use of an aerosol as disclosed herein, in the manufacture of a medicament for the prevention or treatment of a viral infection in a subject, wherein the aerosol is to be administered to the subject by inhalation.

[0010d] In a further aspect, the present disclosure refers to a use of an aerosol as disclosed herein, in the manufacture of a medicament for the prevention or treatment of a

viral infection in a subject, wherein the aerosol is to be administered to the subject intranasally.

[0010e] In another aspect, the present disclosure refers to an inhalable unit dosage comprising a solution of niclosamide, or a pharmaceutically acceptable salt thereof, and PEG, wherein niclosamide is present in an amount of from 1 mg to 600 mg based on the weight of niclosamide, for example from about 150 mg to about 500 mg, based on the weight of niclosamide.

[0010f] In yet another aspect, the present disclosure refers to an inhalable unit dosage comprising a solution of niclosamide ethanolamine and PEG, wherein niclosamide ethanolamine is present in an amount of from 2 mg to 600 mg, for example from about 150 mg to about 500 mg.

[0010g] In a further aspect, the present disclosure refers to a system comprising a container comprising a solution of niclosamide, or a pharmaceutically acceptable salt thereof, and polyethylene glycol (PEG); and an inhaler device and/or an intranasal delivery device.

[0010h] In another aspect, the present disclosure refers to a kit comprising a container comprising a solution of niclosamide, or a pharmaceutically acceptable salt thereof, and polyethylene glycol (PEG); and an inhaler device and/or an intranasal delivery device.

[0010i] In yet another aspect, the present disclosure refers to an inhalable solution comprising from about 1 % to 10 % by weight niclosamide ethanolamine and PEG, wherein the PEG has an average molecular weight of less than 600; and optionally a taste-masking agent.

[0010j] In a further aspect, the present disclosure refers to an inhalable pharmaceutical composition comprising niclosamide, or a pharmaceutically acceptable salt, or an aerosol as disclosed herein, for use in therapy.

[0011] In accordance with the present ~~invention~~disclosures there is provided an inhalable pharmaceutical composition comprising niclosamide, or a pharmaceutically acceptable salt thereof, for use in the prevention or treatment of a viral infection in a subject, wherein the niclosamide, or a pharmaceutically acceptable salt thereof, is administered to the subject by inhalation.

[0012] Also provided is a pharmaceutical composition comprising niclosamide, or a pharmaceutically acceptable salt thereof, for use in the prevention or treatment of a viral infection in a subject, wherein the niclosamide, or a pharmaceutically acceptable salt thereof, is administered to the subject intranasally.

[0013] The pharmaceutical composition comprising niclosamide or a pharmaceutically acceptable salt thereof is in a form suitable for pulmonary administration. For example, it may be that the pharmaceutical composition comprising niclosamide or a pharmaceutically

acceptable salt thereof is in the form of a powder, a suspension, an aerosol of the suspension, a solution or an aerosol of the solution.

[0014] It may be that the pharmaceutical composition is in the form of a suspension or solution comprising niclosamide or a pharmaceutically acceptable salt thereof, wherein the composition is administered to a subject as an aerosol of the solution or suspension. Preferably the niclosamide or a pharmaceutically acceptable salt thereof is administered to the subject in the form of an aerosol of a solution comprising niclosamide, or a pharmaceutically acceptable salt thereof. Solutions and suspensions comprising niclosamide, or a pharmaceutically acceptable salt thereof may be any of the solutions described herein.

[0015] In certain ~~embodiment~~example~~s~~ the pharmaceutical composition is a solution or suspension comprising niclosamide, or a pharmaceutically acceptable salt thereof. Thus it may be that the pharmaceutical composition is a suspension comprising niclosamide, or a pharmaceutically acceptable salt thereof. Preferably the pharmaceutical composition is a solution comprising niclosamide, or a pharmaceutically acceptable salt thereof.

[0016] It may be that the solution or suspension comprises niclosamide, or a pharmaceutically acceptable salt thereof, and polyethylene glycol (PEG), wherein the solution or suspension is administered to the subject by inhalation (e.g. wherein the composition is administered as an aerosol of the solution or suspension). It may be that the PEG has an average molecular weight of less than about 600. It may be that the PEG has an average molecular weight of from about 150 to about 600, for example an average molecular weight of about 200 or about 400. In preferred ~~embodiment~~example~~s~~ the PEG has a molecular weight of about 400.

[0017] It may be that the PEG is present in the solution or suspension comprising niclosamide, or a pharmaceutically acceptable salt thereof, in an amount of at least 25% by weight of the solution or suspension, for example, wherein the PEG is present in an amount of at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95% or at least 98% by weight of the solution or suspension. For example it may be that the PEG is present in an amount of from about 40% to about 99% by weight of the solution or suspension. It may be that the PEG is present in an amount of from about 50% to about 98% by weight of the solution or suspension. It may be that the PEG is present in an amount of from about 55% to about 98%, by weight of the solution or suspension. It may be that the PEG is present in an amount of from about 60% to about 98% by weight of the solution or suspension. It may be that the PEG is present in an amount of from about 65% to about 98% by weight of the solution or suspension. It may be that the PEG is present in an amount of from about 70% to about 98% by weight of the

solution or suspension. It may be that the PEG is present in an amount of from about 75% to about 98% by weight of the solution or suspension. It may be that the PEG is present in an amount of from about 80% to about 98% by weight of the solution or suspension. It may be that the PEG is present in an amount of from about 85% to about 98% by weight of the solution or suspension. It may be that the PEG is present in an amount of from about 75% to about 96% by weight of the solution or suspension. It may be that the PEG is present in an amount of from about 80% to about 96% by weight of the solution or suspension. It may be that the PEG is present in an amount of from about 85% to about 96% by weight of the solution or suspension. It may be that the PEG is present in an amount of from about 90% to about 96% by weight of the solution or suspension. It may be that the PEG is present in an amount of from about 93% to about 96% by weight of the solution or suspension. It may be that the PEG is present in an amount of about 90%, about 91% about 92%, about 93%, about 94%, about 95%, about 96% about 97%, or about 98% by weight of the solution or suspension.

[0018] In preferred ~~embodiment~~example**s** the solution comprises a solution of niclosamide ethanolamine in PEG. For example, a solution comprising niclosamide ethanolamine in PEG, wherein the PEG has an average molecular weight of from about 150 to about 600, more preferably the PEG has an average molecular weight of from about 200 to about 400. In certain preferred ~~embodiment~~example**s** the solution comprises niclosamide ethanolamine in PEG 200. In certain preferred ~~embodiment~~example**s** the solution comprises niclosamide ethanolamine in PEG 400.

[0019] Preferably the solutions and suspensions comprising comprises niclosamide, or a pharmaceutically acceptable salt thereof, are liquid solutions or liquid suspensions.

[0020] Suitably when the inhalable pharmaceutical composition is a solution or suspension comprising niclosamide or a pharmaceutically acceptable salt thereof, the composition is administered to the subject by inhalation as an aerosol of the solution or suspension.

[0021] Accordingly in another ~~aspect~~example there is provided an aerosol of a solution comprising niclosamide, or a pharmaceutically acceptable salt thereof, for use in the prevention or treatment of a viral infection in a subject, wherein the aerosol is administered to the subject by inhalation.

[0022] In another ~~aspect~~example there is provided an aerosol of a solution comprising niclosamide, or a pharmaceutically acceptable salt thereof, for use in the prevention or treatment of a viral infection in a subject, wherein the aerosol is administered to the subject intranasally.

[0023] In another ~~aspect~~example there is provided an aerosol of a suspension comprising niclosamide, or a pharmaceutically acceptable salt thereof, for use in the prevention or

treatment of a viral infection in a subject, wherein the aerosol is administered to the subject by inhalation.

[0024] In another ~~aspect~~example there is provided an aerosol of a suspension comprising niclosamide, or a pharmaceutically acceptable salt thereof, for use in the prevention or treatment of a viral infection in a subject, wherein the aerosol is administered to the subject intranasally.

[0025] The solution or suspension in the above ~~aspect~~examples may be any of the solutions or suspensions disclosed herein. Preferably wherein the solution or suspension comprises niclosamide, or a pharmaceutically acceptable salt thereof and PEG.

[0026] In certain ~~embodiment~~examples the inhalable pharmaceutical composition (e.g. solution, the suspension, an aerosol of the solution or suspension, or powder) comprises niclosamide in the free acid form.

[0027] In certain ~~embodiment~~examples the inhalable pharmaceutical composition (e.g. solution, the suspension, an aerosol of the solution or suspension, or powder) comprises a pharmaceutically acceptable salt of niclosamide, for example niclosamide ethanolamine.

[0028] In certain ~~embodiment~~examples the niclosamide, or a pharmaceutically acceptable salt thereof, is present in an amount of about 0.01 % to about 10 % by weight of the inhalable pharmaceutical composition. For example, the niclosamide or a pharmaceutically acceptable salt thereof is present in an amount of 0.05 % to 10, 0.1 % to 9 %, 0.2 % to 8.5 %, 0.05 % to 8 %, 0.5 % to 8 %, 1 % to 8 %, 1.5 % to 8 %, 2 % to 8 %, 2.5 % to 8 %, 3 % to 8 %, 3.5 % to 8 %, 4 % to 8 %, 4.5 % to 8 %, 5 % to 8 %, 5.5 % to 8 %, 6 % to 8 %, 3 % to 7 %, 3.5 % to 7.5 %, 3.5 % to 7 %, 3.5 % to 6.5 %, 3.5 % to 6 %, 3.5 % to 5.5 %, 4 % to 7 %, 4 % to 7 %, 4 % to 6.5 %, 4 % to 6 %, 4 % to 5.5 %, 4.5 % to 7 %, 4.5 % to 6.5 %, 4.5 % to 6.5 % or 4.5 % to 5.5 % by weight of the inhalable pharmaceutical composition. In a preferred ~~embodiment~~example the niclosamide or a pharmaceutically acceptable salt thereof is present in the inhalable pharmaceutical composition in an amount of about 4.5 % to 5.5 % by weight of the composition. Thus it may be that the niclosamide or a pharmaceutically acceptable salt is present in the inhalable pharmaceutical composition in an amount of about 3.5% about 4%, about 4.5 %, about 5 %, about 5.5 %, about 6 %, about 6.5 %, about 7 %, about 7.5 %, or about, 8 % by weight of the inhalable pharmaceutical composition. In a preferred ~~embodiment~~example the inhalable composition comprises about 5 % by weight of niclosamide or a pharmaceutically acceptable salt thereof. The amounts of niclosamide present in the inhalable composition is applicable to any of the compositions comprising niclosamide described herein, for example a solution comprising niclosamide or a pharmaceutically acceptable salt thereof; a suspension comprising niclosamide or a pharmaceutically acceptable salt thereof; an aerosol of a solution comprising niclosamide or a pharmaceutically acceptable salt thereof; an aerosol of a suspension comprising

niclosamide or a pharmaceutically acceptable salt thereof; or a powder comprising niclosamide or a pharmaceutically acceptable salt thereof.

[0029] In certain ~~embodiment~~examples the inhalable composition is a solution or suspension (preferably a solution) comprising from about 1% to about 10 % by weight niclosamide ethanolamine and PEG, wherein the PEG has an average molecular weight of less than 600.

[0030] In certain ~~embodiment~~examples the inhalable composition is a solution comprising from about 4.5 % to about 6.5 % by weight niclosamide ethanolamine and about 93.5 % to about 95.5 % by weight PEG 400

[0031] Niclosamide has a very low solubility in water and may be prone to precipitation when formulated in compositions that contain water. Accordingly, in certain ~~embodiment~~examples the composition administered to the subject is a non-aqueous inhalable composition) comprising niclosamide or a pharmaceutically acceptable salt thereof. In certain ~~embodiment~~examples it may be that the composition administered to the subject is a non-aqueous inhalable solution or suspension comprising niclosamide or a pharmaceutically acceptable salt thereof. In certain ~~embodiment~~examples the niclosamide administered to the subject is in the form of an inhalable non-aqueous solution comprising niclosamide, or a pharmaceutically acceptable salt thereof. In certain ~~embodiment~~examples the niclosamide administered to the subject is in the form of a non-aqueous inhalable solution comprising niclosamide. In certain ~~embodiment~~examples the niclosamide administered to the subject is in the form of a non-aqueous inhalable solution comprising a pharmaceutically acceptable salt of niclosamide. In certain ~~embodiment~~examples the niclosamide administered to the subject is in the form of a non-aqueous inhalable solution comprising niclosamide ethanolamine. Preferably the niclosamide administered to the subject is a non-aqueous solution comprising niclosamide, or a pharmaceutically acceptable salt thereof and PEG. Suitably the non-aqueous solution or dispersion comprising niclosamide or a pharmaceutically acceptable salt thereof described herein comprise less than 2% by weight water, preferably less than 0.1 % more preferably less that 0.01 % by weight water. In particular ~~embodiment~~examples the solution or dispersion comprising niclosamide or a pharmaceutically acceptable salt thereof is anhydrous.

[0032] Accordingly, it may be that the ~~embodiment~~examples it may be that the composition administered to the subject is a non-aqueous solution comprising from about 2 % to about 8 % by weight niclosamide or a pharmaceutically acceptable salt thereof and from about 92 % to about 98 % by weight PEG, wherein the PEG has an average molecular weight of from 150 to 600. It may be that the solution is a non-aqueous solution comprising from about 4% to about 8 % by weight niclosamide or a pharmaceutically acceptable salt thereof and from about 92 % to about 96 % by weight PEG, wherein the PEG has an

average molecular weight of about 400. It may be that the solution is a non-aqueous solution comprising from about 4 % to 8 % by weight niclosamide or a pharmaceutically acceptable salt thereof and from about 92 % to about 96 % by weight PEG, wherein the PEG has an average molecular weight of about 200. It may be that the solution is a non-aqueous solution comprising from about 4% to about 8 % by weight niclosamide ethanolamine and from about 92 % to about 96 % by weight PEG, wherein the PEG has an average molecular weight of about 400. It may be that the solution is a non-aqueous solution comprising from about 4 % to 8 % by weight niclosamide ethanolamine and from about 92 % to about 96 % by weight PEG, wherein the PEG has an average molecular weight of about 200.

[0033] In certain preferred ~~embodiment~~examples the inhalable pharmaceutical composition is a solution or dispersion comprising niclosamide, or a pharmaceutically acceptable salt thereof and is administered to the subject in the form of an aerosol of the solution or dispersion. The solution or suspension comprising niclosamide or a pharmaceutically acceptable salt thereof may be administered to the subject using a suitable nebulizer, inhalation device or intranasal delivery device. For example, it may be that the nebulizer or inhalation device is selected from a vibrating mesh nebulizer, a piezoelectric nebulizer a jet nebulizer and a pressurised metered dose inhaler (pMDI).

[0034] In certain ~~embodiment~~examples when the inhalable pharmaceutical composition is a liquid (e.g. a liquid solution or suspension comprising niclosamide or a pharmaceutically acceptable salt thereof) the composition is administered as an aerosol of the composition, the aerosol has a mass median diameter of less than about 5 µm. It may be that the MMD of less than about 2 µm. It may be that the MMD of the aerosol is from about 0.5 µm to about 5.5 µm. Preferably the MMD of the aerosol is from about 1 µm to about 5 µm.

[0035] Suitably the aerosol of the composition (e.g. aerosol of a solution or suspension comprising niclosamide or a pharmaceutically acceptable salt thereof), has a narrow particle-size distribution, for example a geometric standard deviation (GSD) of less than about 2.2, for example less than 2.0, or less than 1.8. Preferably the GSD of the aerosol is less than 1.6.

[0036] In certain ~~embodiment~~examples the inhalable pharmaceutical composition is a powder comprising niclosamide, or a pharmaceutically acceptable salt thereof. It may be that the powder comprising niclosamide, or a pharmaceutically acceptable salt thereof is administered to the subject using a dry-powder inhaler. In certain ~~embodiment~~examples powder administered to the subject (e.g. particles of niclosamide or a pharmaceutically acceptable salt thereof) have a MMD of less than about 5 µm. For example, the MMD of the powder particles is from about 1 µm to about 5 µm. Suitably the particles administered to the

subject (e.g. as an aerosol of the powder) have a GSD of less than about 2.2, for example less than 2.0, or less than 1.8.

[0037] Also provided is a method for preventing or treating a viral infection in a subject, the method comprising administering to the subject by inhalation an effective amount of an inhalable pharmaceutical composition comprising niclosamide, or a pharmaceutically acceptable salt thereof. It may be that the inhalable pharmaceutical composition is any of the inhalable compositions disclosed herein. For example, in certain ~~embodiment~~examples the inhalable pharmaceutical composition is in the form of a solution comprising niclosamide, or a pharmaceutically acceptable salt thereof; a suspension comprising niclosamide, or a pharmaceutically acceptable salt thereof; an aerosol of a solution comprising niclosamide, or a pharmaceutically acceptable salt thereof; an aerosol of a suspension comprising niclosamide, or a pharmaceutically acceptable salt thereof; or a powder comprising niclosamide or a pharmaceutically acceptable salt thereof.

[0038] Also provided is a method for preventing or treating a viral infection is a subject, the method comprising administering to the subject by inhalation an effective amount of a solution comprising niclosamide.

[0039] Also provided is a method for preventing or treating a viral infection is a subject, the method comprising administering to the subject by inhalation an effective amount of an aerosol of a solution comprising niclosamide.

[0040] Also provided is a method for preventing or treating a viral infection in a subject, the method comprising administering to the subject intranasally an effective amount of a pharmaceutical composition comprising niclosamide, or a pharmaceutically acceptable salt thereof.

[0041] Also provided is a method for preventing or treating a viral infection is a subject, the method comprising administering to the subject intranasally an effective amount of a solution comprising niclosamide.

[0042] Also provided is a method for preventing or treating a viral infection is a subject, the method comprising administering to the subject intranasally an effective amount of an aerosol of a solution comprising niclosamide.

[0043] The solution, suspension, aerosols and powders comprising niclosamide or pharmaceutically acceptable salt thereof used in the methods of treatment may be any of those described herein. For example in certain ~~embodiment~~examples the method of treatment administers a solution comprising niclosamide or a pharmaceutically acceptable salt thereof and PEG. Preferably the method of treatment administers an aerosol of a solution comprising niclosamide or a pharmaceutically acceptable salt thereof and PEG. The solution, or aerosol of a solution, comprising niclosamide or a pharmaceutically acceptable salt thereof may be any of the PEG based solutions described herein. For example an

aerosol of any of the solutions comprising niclosamide ethanolamine and PEG disclosed herein.

[0044] In certain ~~embodiment~~example~~s~~ the niclosamide, or a pharmaceutically acceptable salt thereof, is administered to the subject in a daily dose of from about 1 mg to about 3000 mg based on the weight of niclosamide, for example from about 10 mg to about 3000 mg, based on the weight of niclosamide. Thus it may be that the niclosamide, or a pharmaceutically acceptable salt thereof, is administered to the subject in a daily dose of from about 400 mg to about 2000 mg based on the weight of the niclosamide. Thus it may be that the daily dose is 5 mg, 10 mg, 25 mg, 50 mg, 75 mg, 100 mg, 150 mg, 250 mg, 500 mg, 750 mg, 1000 mg, 1500 mg or 2000 mg, based on the weight of niclosamide. It may be that the total daily dose is administered as a single dose. It may be that the total daily dose is administered as one or more divided doses, for example 2, 3, 4 or 5 divided doses. The total daily dose may be divided evenly or unevenly. Preferably, when the total daily dose is administered as a divided dose the total daily dose is divided into equal doses.

[0045] In certain ~~embodiment~~example~~s~~ the niclosamide, or a pharmaceutically acceptable salt thereof, is administered to the subject in a unit dosage of from about 1 mg to about 1000 mg based on the weight of niclosamide, for example from about 10 mg to about 1000 mg based on the weight of niclosamide. Thus it may be that the niclosamide, or a pharmaceutically acceptable salt thereof, is administered to the subject in a unit dosage of from about 100 mg to about 600 mg based on the weight of niclosamide. Preferably the niclosamide, or a pharmaceutically acceptable salt thereof, is administered to the subject in a unit dosage of from about 150 mg to about 500 mg.

[0046] In certain ~~embodiment~~example~~s~~ the inhalable pharmaceutical composition comprising niclosamide, or a pharmaceutically acceptable salt thereof, is administered to the subject by inhalation intraorally or intranasally. Preferably the composition is administered to the subject by inhalation intraorally. Thus it may be that the composition, is administered to the subject by inhalation intraorally or intranasally in a form as described herein, for example as a powder, a solution, a suspension, an aerosol of a solution or an aerosol of a suspension comprising the niclosamide or a pharmaceutically acceptable salt thereof as described herein.

[0047] In some ~~embodiment~~example~~s~~ the pharmaceutical composition comprising niclosamide, or a pharmaceutically acceptable salt thereof, is administered intranasally. It will be understood that “intranasal” administration means administration into the nasal cavity, i.e. through the nose. Intranasal administration encompasses both administration of the composition to the nasal mucosa and the upper respiratory tract, and administration of the composition to the lower respiratory tract (e.g. via inhalation).

[0048] In certain ~~embodiment~~examples the inhalable pharmaceutical composition comprising niclosamide, or a pharmaceutically acceptable salt thereof, is administered to the subject by inhalation and/or intranasally at least once per day, for example 1 ,2, 3, 4, or 5 times per day. Thus it may be that the composition, is administered to the subject by inhalation and/or intranasally 1 to 4 times per day. It may be that the composition comprising niclosamide, or a pharmaceutically acceptable salt thereof, is administered to the subject by inhalation and/or intranasally once per day. It may be that the composition comprising niclosamide, or a pharmaceutically acceptable salt thereof, is administered to the subject by inhalation and/or intranasally twice per day. It may be that the composition comprising niclosamide, or a pharmaceutically acceptable salt thereof, is administered to the subject by inhalation and/or intranasally three times per day. It may be that the composition comprising niclosamide, or a pharmaceutically acceptable salt thereof, is administered to the subject by inhalation and/or intranasally four times per day.

[0049] In certain ~~embodiment~~examples the viral infection may be a pulmonary viral infection.

[0050] In certain ~~embodiment~~examples the viral infection may be caused by or associated with a virus selected from respiratory syncytial virus, influenza virus, parainfluenza virus, human metapneumovirus, severe acute respiratory syndrome coronavirus (SARS-CoV), severe acute respiratory syndrome coronavirus (SARS-CoV-2), Middle East respiratory syndrome coronavirus (MERS-CoV), human coronavirus OC43, Semliki Forest Virus, a human rhinovirus (HRVs) and human adenovirus (HAdV).

[0051] In certain ~~embodiment~~examples the viral infection is caused by or associated with a Pneumoviridae virus, for example a Human respiratory syncytial virus (HRSV) (e.g. HRSV-A2, HRSV-B1 or HRSV-S2).

[0052] In certain ~~embodiment~~examples the viral infection is caused by or associated with a Coronaviridae virus. In certain ~~embodiment~~examples the viral infection is caused by or associated with a virus is selected from Alphacoronavirus, Betacoronavirus, Gammacoronavirus and Deltacoronavirus. Preferably the viral infection is caused by or associated with a Betacoronavirus. Thus is certain ~~embodiment~~examples the viral infection is caused by or associated with a virus is selected from severe acute respiratory syndrome coronavirus (SARS-CoV), severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), Middle East respiratory syndrome coronavirus (MERS-CoV), HCoV-229E, HCoV-NL63, HCoV-OC43 and HCoV-HKU1.

[0053] In a particular ~~embodiment~~example the viral infection is caused by or associated with SARS-CoV-2. This it may be that the viral infection is COVID-19.

[0054] In some ~~embodiment~~examples the viral infection is caused by or associated with an influenza virus.

[0055] The viral infection may be caused by or associated with a virus selected from Flaviviridae (e.g. Zika virus (ZIKV), dengue (e.g. DENV 1−4), West Nile virus (WNV), yellow fever virus (YFV, e.g. yellow fever 17D virus), Japanese encephalitis virus (JEV), Hepatitis C virus (HCV), Filoviridae (e.g. Ebolavirus)), Togaviridae (e.g. Alphaviruses such as Chikungunya virus (CHIKV), Sindbis virus and Ross River virus), Herpes (e.g. γ-herpesvirus, Human herpesvirus 8, herpesvirus 1 and herpesvirus 2) and Adenoviridae (e.g. Human adenoviruses (HAdVs)).

[0056] Recent research has identified a gradient of expression levels of the human angiotensin-converting enzyme (ACE)-2, which is targeted by SARS-CoV-2, from the nasal tissues (high expression) and the distal intrapulmonary regions (low expression). This expression pattern was found to be mirrored by a gradient of SARS-CoV-2 infectivity which was high in the nasal epithelium and markedly reduced in the distal lung (bronchioles, alveoli). In light of these findings, it has been suggested that the nasal surfaces may be the dominant initial site of SARS-CoV-2 infection (Hou et al., “SARS-CoV-2 Reverse Genetics Reveals a Variable Infection Gradient in the Respiratory Tract”, Cell, 2020). Intranasal administration may therefore be beneficial to subjects suffering from mild COVID-19, or those in the early stages of disease, prior to progression to the later stages of the disease which are characterised by pulmonary inflammation. In some ~~embodiment~~examples, subjects whose symptoms include a loss of taste and/or smell, and/or ocular symptoms (e.g. one or more of conjunctival hyperemia, chemosis, epiphora, or increased secretions) may be treated via intranasal administration of the composition of the present ~~invention~~disclosure. Intranasal administration may also be beneficial for treating asymptomatic subjects, for prophylactic treatment of high risk populations as identified herein (e.g. healthcare professionals, or those with underlying conditions), for treating subjects suspected of having contracted SARS-CoV-2, and/or for treating close contacts of a person with COVID-19.

[0057] In some ~~embodiment~~examples, the inhalable pharmaceutical composition is administered both intranasally and intraorally. Thus it may be that a first pharmaceutical composition of the present ~~invention~~disclosure is administered by inhalation intraorally (e.g. as an aerosol) separately, sequentially or simultaneously with a second pharmaceutical composition, wherein the second pharmaceutical composition is administered intranasally (e.g. as spray). It may be that the first and second pharmaceutical compositions are different. It may be that the first and second compositions are the same.

[0058] Subjects with pulmonary viral infections may be prone to coughing when drugs are administered by inhalation. This can make administration of the drug difficult and/or may reduce the dose of drug delivered to the airway and lungs. In certain ~~embodiment~~examples the subject is administered an antitussive agent prior to or concurrently with the inhaled

niclosamide, or a pharmaceutically acceptable salt thereof. Thus it may be that the subject is treated with antitussive agent is selected from codeine, dextromethorphan, hydrocodone, methadone, butorphanol, benzonatate, ethylmorphine, oxeladin, pipazethate, pholcodine, noscapine, butamirate and a local anaesthetic (e.g. lidocaine) prior to or concurrently with the inhaled administration of the niclosamide or a pharmaceutically acceptable salt thereof. Preferably the subject is treated with the antitussive agent prior to administration of the niclosamide or pharmaceutically acceptable salt thereof to reduce or eliminate coughing associated with the inhaled administration of the niclosamide. Thus it may be that the subject is treated with a local anaesthetic prior to or concurrently with the inhaled administration of the niclosamide or a pharmaceutically acceptable salt thereof. Suitably the local anaesthetic is administered so as to provide a local anaesthetic effect in the oral cavity and/or airways. Thus it maybe that the local anaesthetic is administered by inhalation or as a gel or liquid to the oral and/or nasal cavity. Suitably the local anaesthetic is lidocaine.

[0059] In some ~~embodiment~~example**s**, the subject is treated with a bronchodilator prior to or concurrently with the composition comprising niclosamide, or pharmaceutically acceptable salt thereof. Advantageously, this may help to reduce side effects, such as coughing. Suitable bronchodilators include short-acting β2-adrenergic agonists (e.g. salbutamol, levosalbutamol, pirbuterol, epinephrine, terbutaline or ephedrine), long-acting β2-adrenergic agonists (e.g. salmeterol, clenbuterol, bambuterol, indacaterol or formoterol), anticholinergics (e.g. tiotropium or ipratropium bromide), and theophylline.

[0060] Another ~~aspect~~example provides an aerosol of a solution comprising niclosamide, or a pharmaceutically acceptable salt thereof. Thus it may be that the aerosol is an aerosol of a solution comprising niclosamide, or a pharmaceutically acceptable salt thereof and PEG. The aerosol of a solution, comprising niclosamide or a pharmaceutically acceptable salt thereof may be any of the PEG based solutions of niclosamide described herein. For example, an aerosol of any of the solutions comprising niclosamide ethanolamine and PEG disclosed herein. Suitably the solution is a non-aqueous solution.

[0061] Also provided is an inhalable unit dosage comprising a solution of niclosamide, or a pharmaceutically acceptable salt thereof, and PEG, wherein niclosamide is present in an amount of from 1 mg to 600 mg based on the weight of niclosamide, for example from 100 mg to 600 mg based on the weight of niclosamide, for example from about 150 mg to about 500 mg, based on the weight of niclosamide. The solution, comprising niclosamide or a pharmaceutically acceptable salt thereof may be any of the PEG based solutions of niclosamide described herein. For example any of the solutions comprising niclosamide ethanolamine and PEG disclosed herein. Suitably the solution is a non-aqueous solution. The unit dosage is suitably present in a container, for example a vial, blister pack, bottle

(e.g. a nasal spray), syringe (e.g. as part of an intranasal delivery device) or reservoir within an inhaler device (e.g. a nebulizer). The unit dosage volume of the solution administered to the subject may be from 1 to 10 ml, from 2 to 9 ml, from 3 to 8 ml or from 4 to 6 ml. In some ~~embodiment~~examples, the unit dosage volume administered to the subject is from 10 µl to 10 ml, from 20 µl to 8 ml, from 30 µl to 6 ml, from 40 µl to 5 ml, from 50 µl to 2 ml, from 100 µl to 1 ml, from 120 µl to 0.8 ml, from 130 µl to 0.7 ml, from 140 µl to 0.6 ml, from 150 µl to 0.5 ml or from 200 µl to 400 µl. In some ~~embodiment~~examples, the unit dosage volume administered to the subject is from 100 to 200 µl, from 110 to 190 µl, from 120 to 180 µl, from 130 to 170 µl, from 140 to 160 µl or from 150 to 155 µl. It will be appreciated that the mass of the niclosamide, or a pharmaceutically acceptable salt thereof, administered for a given volume will depend on the concentration of the solution. In some ~~embodiment~~examples, the niclosamide, or a pharmaceutically acceptable salt thereof, is present in the solution in an amount of from about 0.01 % to about 10 % by weight. Preferably the solution comprises about 5 % by weight of niclosamide ethanolamine. The volume may be administered one or more times per day, for example once per day, twice per day, three times per day or four times per day. It may be that the volume is administered once or twice per day. It may be that the volume is administered once per day. It may be that the volume is administered twice per day.

[0062] In some ~~embodiment~~examples wherein the solution is administered intranasally, the volume administered to the subject may be from 50 to 500 µl, from 100 to 400 µl, from 150 to 300 µl or from 200 to 250 µl. It will be appreciated that approximately half of the volume should be administered to each nostril. In some ~~embodiment~~examples, from about 50 to about 150 µl is administered to each nostril (i.e. about 100 to about 300 µl in total). In some ~~embodiment~~examples, a volume of about 130 µl-150 µl (e.g. 140 µl) is administered to each nostril (i.e. about 260-300 µl, e.g. 280 µl, in total). Preferably the solution administered intranasally comprises about 5 % by weight of niclosamide ethanolamine. The volume may be administered intranasally one or more times per day, for example once per day, twice per day, three times per day or four times per day. It may be that the volume is administered intranasally once or twice per day. It may be that the volume is administered intranasally once per day. It may be that the volume is administered intranasally twice per day. It will further be appreciated that in some ~~embodiment~~examples wherein the solution is administered both intraorally and intranasally, the total volume administered to the subject will be the sum of the volume administered intraorally and the volume administered intranasally. The total volume may be from 10 µl to 10 ml, from 20 µl to 8 ml, from 30 µl to 6 ml, from 40 µl to 5 ml, from 50 µl to 2 ml, from 100 µl to 1 ml, from 150 µl to 0.5 ml or from 200 µl to 400 µl. Preferably the solution administered intranasally comprises about 5 % by weight of niclosamide ethanolamine. As will be appreciated, when the solution is administered both

intraorally and intranasally the volume administered intranasally may be the same or different to the volume administered intranasally. Similarly the frequency of the intraoral and intranasal administration may be the same or different. For example, the intraoral and intranasal doses may be administered sequentially (e.g. the intraoral administration followed shortly (e.g. within 10 minutes) by the intranasal administration, or vice versa. In certain ~~embodiment~~examples the intraoral and intranasal doses may be administered separately (e.g. where the intraoral dosing is separated from the intranasal dosing by more than 10 minutes (e.g. by more than one hour). Also contemplated is substantially simultaneous intraoral and intranasal administration. It may be that the volume administered intranasally is administered once or twice per day. It may be that the volume administered intraorally is administered once or twice per day.

[0063] Also provided is a system comprising a container comprising an inhalable pharmaceutical composition comprising niclosamide, or a pharmaceutically acceptable salt thereof; and an inhaler device.

[0064] Also provided is a kit comprising a container comprising an inhalable pharmaceutical composition comprising niclosamide, or a pharmaceutically acceptable salt thereof; and an inhaler device.

[0065] Also provided is a system comprising a container comprising: a pharmaceutical composition comprising niclosamide, or a pharmaceutically acceptable salt thereof; and an intranasal delivery device.

[0066] Also provided is a kit comprising a container comprising a pharmaceutical composition comprising niclosamide, or a pharmaceutically acceptable salt thereof; and an intranasal delivery device.

[0067] In certain ~~embodiment~~examples the inhalable pharmaceutical composition comprising niclosamide, or a pharmaceutically acceptable salt thereof present in the system or kit is in the form of a powder, a solution, a suspension, for example any of the niclosamide compositions described herein. Suitably the inhalable pharmaceutical composition is a non-aqueous composition.

[0068] In certain ~~embodiment~~examples the inhalable pharmaceutical composition comprising niclosamide, or a pharmaceutically acceptable salt thereof present in the system or kit is a solution comprising niclosamide, or a pharmaceutically acceptable salt thereof and PEG. For example any of the PEG-based niclosamide solutions described herein. For example, any of the solutions comprising niclosamide ethanolamine and PEG disclosed herein.

[0069] In certain ~~embodiment~~examples the inhaler device of the system or kit is adapted to aerosolize a solution or suspension comprising niclosamide or a pharmaceutically acceptable salt thereof. Suitably the inhaler device is adapted to deliver the aerosolized solution or suspension intranasally or intraorally to a subject.

[0070] In certain ~~embodiment~~examples the inhaler device of the system or kit is a nebulizer selected from a jet nebulizer, a vibrating mesh nebulizer, an ultrasonic nebulizer or a pressurised metered dose inhaler (pMDI).

[0071] Also provided is an inhalable solution comprising from about 1% to 10 % by weight niclosamide ethanolamine and PEG, wherein the PEG has an average molecular weight of less than 600; and optionally a taste-masking agent. Thus it may be the inhalable solution is any of the solutions described herein comprising niclosamide or a pharmaceutically acceptable salt thereof and PEG, for example any of the solutions disclosed herein comprising niclosamide ethanolamine and PEG. Thus it may be the inhalable solution comprises from about 1% to 10 % by weight niclosamide ethanolamine and PEG with an average molecular weight of 400. Thus it may be the inhalable solution comprising from about 1% to 10 % by weight niclosamide ethanolamine and PEG with an average molecular weight of 200. In certain ~~embodiment~~examples the inhalable solution is a solution comprising from about 4.5 % to about 6.5 % by weight niclosamide ethanolamine and about 93.5 % to about 95.5 % by weight PEG 400. In certain ~~embodiment~~examples the inhalable solution comprises from about 4.5 % to about 6 % by weight niclosamide ethanolamine; about 90 % to 95.5 % by weight PEG 400 and optionally a taste-masking agent. In certain ~~embodiment~~examples the inhalable solution comprises from about 4.5 % to about 6 % by weight niclosamide ethanolamine; about 90 % to 95.5 % by weight PEG 200 and optionally a taste-masking agent.

[0072] ~~Embodiment~~Examples of the present ~~invention~~disclosure will now be described by way of example and with reference to the accompanying Figures, in which:

Figure 1 shows graphs showing the epithelial lining fluid (ELF) concentration of niclosamide free base following pulmonary administration in sheep compared to systemic exposure of highest human oral dose, relative to IC90 against SARS-CoV-2. (A) Mean ELF concentration of niclosamide over time following pulmonary administration of a composition of the present ~~invention~~disclosure (± SEM); (B) Comparison of mean Cmax levels of niclosamide following administration of a composition of the present ~~invention~~disclosure in ELF to systemic Cmax following a 2 g/day oral dose in humans (Data of Andrews et al. 1983, Pharmacology & therapeutics, 19(2), 245–295 (healthy volunteers) and Burock et al. 2018, BMC Cancer, 18(1): 297 (colorectal cancer patients) combined in “2000 mg single/qd” column);

Figure 2 shows plots showing the pharmacokinetic profile of niclosamide ethanolamine per cohort in the phase 1 clinical trial described in Example 8;

Figure 3 is a comparison of systemic exposure (Cmax; mean ± SEM) of niclosamide administered orally (as reported in the literature) versus inhalation of a composition according to the present ~~invention~~disclosure in humans. No mean for “2000 mg, single” column generated as only range of Cmax reported in literature. Data for 500-1000 mg obtained from Schweizer et al., 2018, PLoS ONE.;13(6): e0198389. Data for 2000 mg obtained from Andrews et al. 1983 and Burock et al. 2018 (as above);

Figure 4 shows a correlation plot of systemic exposure (Cmax-, mean ±) of human versus sheep study;

Figure 5 shows the Inhibition of SARS-CoV-2 replication in VeroE6 cells (Fig. 5A) and Caco-2 cells (Fig. 5B) by niclosamide ethanolamine salt;

Figure 6 is a graph showing that niclosamide ethanolamine salt inhibits replication of several variants of SARS-CoV-2;

Figure 7 shows the effect of niclosamide ethanolamine salt on apical viral infectious titer TCID50 (Fig. 7A) and intracellular RNA levels (Fig. 7B) of SARS-CoV-2 in a trans-well system of infection. N= 2. Mean with 95% levels shown for Fig. 7A, and Mean ± SD for Fig. 7B. * $p < 0.05$, Ordinary one-way ANOVA with Dunetts’ multiple comparison test; and

Figure 8 shows the clinical score of SARS-COV-2 infected K18-hACE2 transgenic mice on Day 6 post infection with a composition according to the present ~~invention~~disclosure compared to saline. N=5 for composition and N=6 for saline. ** = $p < 0.01$ (Mann Whitney Test).

DETAILED DESCRIPTION

Definitions

[0073] Unless otherwise stated, the following terms used in the specification and claims have the following meanings set out below.

[0074] References to “composition of the invention”, “compositions of the invention” “solution of the invention” refer to any of the compositions described herein comprising niclosamide, or a pharmaceutically acceptable salt thereof. A “solution of the invention” refers to a composition of the invention wherein the niclosamide or pharmaceutically acceptable salt thereof is dissolved in the composition. The terms “composition” and “formulation” may be used interchangeably.

[0075] The terms “treating” or “treatment” refers to any indicia of success in the treatment or amelioration of a disease, pathology or condition, including any objective or subjective parameter such as abatement; remission; diminishing of symptoms or making the pathology or condition more tolerable to the subject; slowing in the rate of degeneration or decline; making the final point of degeneration less debilitating; improving the physical or mental well-being of the subject. For example, in relation to the treatment of viral infections disclosed herein the treatment may include one or more of the following: Reduce or eliminate

Claims

1. Use of anAn inhalable pharmaceutical composition comprising niclosamide, or a pharmaceutically acceptable salt thereof, for usein the manufacture of a medicament for in the prevention or treatment of a viral infection in a subject, wherein the niclosamide, or a pharmaceutically acceptable salt thereof, is to be administered to the subject by inhalation.

2. The composition for the use of claim 1, wherein the pharmaceutical composition is in the form of a powder, a suspension or a solution comprising niclosamide, or a pharmaceutically acceptable salt thereof.

3. The composition for the use of claim 1, wherein the pharmaceutical composition is in the form of a solution or suspension comprising niclosamide, or a pharmaceutically acceptable salt thereof, preferably a liquid solution or liquid suspension.

4. The composition for the use of claim 3, wherein the solution or suspension comprises niclosamide, or a pharmaceutically acceptable salt thereof, and polyethylene glycol (PEG).

5. The composition for the use of claim 4, wherein the PEG has an average molecular weight of less than about 600.

6. The composition for the use of claim 4 or claim 5, wherein the PEG has an average molecular weight of from about 150 to about 600, for example an average molecular weight of about -200 or about 400.

7. The composition for the use of any one of claims 4 to 6, wherein the PEG is present in an amount of at least 25% by weight of the composition, for example, wherein the PEG is present in an amount of at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95% or at least 98% by weight of the composition.

8. The composition for the use of any one of claims 4 to 6, wherein the PEG is present in an amount of from about 40% to about 98% by weight of the composition, for example from about 70% to about 96% by weight of the composition.

9. The composition for the use of any one of claims 3 to 8, wherein the solution or suspension further comprises a solvent (e.g. a glycol such as propylene glycol).

10. The composition use of any one of claims 3 to 9, wherein the composition is in the form of a suspension comprising niclosamide, or a pharmaceutically acceptable salt thereof.

11. The composition for the use of any one of claims 3 to 9, wherein the composition is in the form of a solution comprising niclosamide, or a pharmaceutically acceptable salt thereof.

12. The ~~composition for the~~ use of any one of claims 3 to 11, wherein the composition is to be administered to the subject in the form of an aerosol of the solution or suspension comprising niclosamide, or a pharmaceutically acceptable salt thereof.

13. The ~~composition for the~~ use of any one of claims 1 to 12, wherein the composition comprises niclosamide in the free-acid form.

14. The ~~composition for the~~ use of any one of claims 1 to 12, wherein the composition comprises a pharmaceutically acceptable salt of niclosamide.

15. The ~~composition for the~~ use of any one of claims 1 to 12, wherein the composition comprises niclosamide ethanolamine.

16. The ~~composition for the~~ use of any one of claims 1 to 15, wherein the niclosamide or a pharmaceutically acceptable salt thereof is present in the composition in an amount of from about 0.1 % to about 10 % by weight of the composition, for example about 5 % by weight of the composition.

17. The ~~composition for the~~ use of claim 1, wherein the composition is a solution comprising from about 1% to about 10 % by weight niclosamide ethanolamine and PEG, wherein the PEG has an average molecular weight of less than 600.

18. The ~~composition for the~~ use of claim 1, wherein the composition is a solution comprising from about 4.5 % to about 6.5 % by weight niclosamide ethanolamine and about 93.5 % to about 95.5 % by weight PEG 400.

19. The ~~composition for the~~ use of claim 17 or claim 18, wherein the solution is to be administered to the subject in the form of an aerosol of the solution.

20. The ~~composition for the~~ use of any one of claims 1 to 19, wherein the composition further comprises a taste-masking agent.

21. The ~~composition for the~~ use of claim 20, wherein the taste-masking agent is selected from a sugar (e.g. sucrose, dextrose, or lactose), an amino acid or amino acid derivative (e.g. arginine, lysine, or monosodium glutamate), an oil (e.g. a natural oil, or plant extract), a sweetener (e.g. sucrose, dextrose, aspartame, acesulfame-K, sucralose or saccharin), an organic acid (e.g. citric acid or aspartic acid), and maltodextrin.

22. The ~~composition for the~~ use of any one of claims 1 to 21, wherein the composition is a non-aqueous composition, for example a composition containing less than 2% by weight water, preferably less than 0.1 % by weight water, more preferably wherein the composition is anhydrous.

~~23. A method for preventing or treating a viral infection is a subject, the method comprising administering to the subject by inhalation an effective amount of an inhalable pharmaceutical composition comprising niclosamide, or a pharmaceutically acceptable salt thereof.~~

~~24. The method of any claim 23, wherein the composition is as defined in any one of claims 2 to 22.~~

~~25.~~23. The ~~composition for~~ use~~, or method~~ of any one of claims 1 to 2~~24~~, wherein the niclosamide, or a pharmaceutically acceptable salt thereof, is to be administered to the subject in a daily dose of from about 1 mg to about 3000 mg based on the weight of niclosamide (for example, from about 400 mg to about 2000 mg based on the weight of the niclosamide).

~~26.~~24. The ~~composition for~~ use~~, or method~~ of any one of claims 1 to 2~~35~~, wherein the niclosamide, or a pharmaceutically acceptable salt thereof, is to be administered to the subject in a unit dosage of from about 10 mg to about 1000 mg based on the weight of niclosamide (for example from about 100 mg to about 600 mg, preferably about 150 mg to about 500 mg, based on the weight of niclosamide).

~~27.~~25. The ~~composition for~~ use~~, or method~~ of any one of claims 1 to 2~~46~~, wherein the composition is to be administered by inhalation intraorally and/or intranasally, preferably wherein the niclosamide or solution is to be administered by inhalation intraorally.

~~28.~~26. The ~~composition for~~ use~~, or method~~ of any one of claims 1 to 2~~46~~, wherein the composition is to be administered intranasally.

~~29.~~27. The ~~composition for~~ use~~, or method~~ of any one of claims 1 to 2~~68~~, wherein the composition is to be administered to the subject one to five times per day, for example from 1 to 4 times per day.

~~30.~~28. The ~~composition for~~ use~~, or method~~ of any one of claims 1 to 2~~79~~, wherein the subject is to be treated with an antitussive agent prior to or concurrently with the inhaled niclosamide, or a pharmaceutically acceptable salt thereof.

~~31.~~29. The ~~composition for~~ use~~, or method~~ of claim 28~~30~~, wherein the antitussive agent is selected from codeine, dextromethorphan, hydrocodone, methadone, butorphanol, benzonatate, ethylmorphine, oxeladin, pipazethate, ~~-~~pholcodine, noscapine, butamirate and a local anaesthetic.

~~32.~~30. The ~~composition for~~ use~~, or method~~ of claim 28~~30~~, wherein the antitussive agent is a local anaesthetic, preferably lidocaine.

~~33.~~31. The ~~composition for~~ use~~, or method~~ of any one of claims 28~~30~~ to 30~~32~~, wherein antitussive agent is to be administered to the subject prior to the inhaled niclosamide.

~~34.~~32. The ~~composition for~~ use~~, or method~~ of any one of claims 1 to 31~~33~~, wherein the viral infection is a pulmonary viral infection.

~~35.~~33. The ~~composition for~~ use~~, or method~~ of any one of claims 1 to 32~~34~~, wherein the viral infection is caused by or associated with a virus selected from respiratory syncytial virus, influenza virus, parainfluenza virus, human metapneumovirus, severe acute respiratory syndrome coronavirus (SARS-CoV), severe acute respiratory syndrome

coronavirus (SARS-CoV-2), Middle East respiratory syndrome coronavirus (MERS-CoV), a human rhinovirus (HRVs) and human adenovirus (HAdV).

~~36.~~34. The ~~composition for~~ use~~, or method~~ of any one of claims 1 to 32~~34~~, wherein the viral infection is caused by or associated with a Pneumoviridae virus, for example a Human respiratory syncytial virus (HRSV) (e.g. HRSV-A2, HRSV-B1 or HRSV-S2).

~~37.~~35. The ~~composition for~~ use~~, or method~~ of any one of claims 1 to 32~~34~~, wherein the viral infection is caused by or associated with a Coronaviridae virus.

~~38.~~36. The ~~composition for~~ use~~, or method~~ of claim 33~~35~~, wherein the virus is selected from Alphacoronavirus, Betacoronavirus, Gammacoronavirus and Deltacoronavirus.

~~39.~~37. The ~~composition for~~ use~~, or method~~ of claim 34~~36~~, wherein the virus is a Betacoronavirus.

~~40.~~38. The ~~composition for~~ use~~, or method~~ of claim 35~~37~~, wherein the virus is selected from severe acute respiratory syndrome coronavirus (SARS-CoV), severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), Middle East respiratory syndrome coronavirus (MERS-CoV), HCoV-229E, HCoV-NL63, HCoV-OC43 and HKU1.

~~41.~~39. The ~~composition for~~ use~~, or method~~ of any one of claims 1 to 31~~33~~, wherein the viral infection is caused by or associated with SARS-CoV-2.

~~42.~~40. The ~~composition for~~ use~~, or method~~ of any one of claims 1 to 31~~33~~, wherein the viral infection is COVID-19, optionally wherein the viral infection is moderate or mild COVID-19.

~~43.~~41. The ~~composition for~~ use~~, or method~~ of any one of claims 1 to 31~~33~~, wherein the viral infection is caused by or associated with influenza virus.

~~44.~~42. An aerosol of a solution comprising niclosamide, or a pharmaceutically acceptable salt thereof.

~~45.~~43. The aerosol of claim 42~~44~~, wherein the solution comprises niclosamide, or a pharmaceutically acceptable salt thereof, and polyethylene glycol (PEG).

~~46.~~44. The aerosol according to claim 42~~44~~ or claim 43~~45~~, wherein the PEG has an average molecular weight of less than about 600.

~~47.~~45. The aerosol of any one of claims 43~~45~~ or claim 44~~46~~, wherein the PEG has an average molecular weight of from about 150 to about 600, for example an average molecular weight of about ~~-~~200 or about 400.

~~48.~~46. The aerosol of any one of claims 43~~45~~ to 45~~47~~, wherein the PEG is present in an amount of at least 25% by weight of the solution, for example, wherein the PEG is present in an amount of at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95% or at least 98% by weight of the solution.

~~49.~~47. The aerosol of any one of claims 4~~35~~ to 4~~68~~, wherein the PEG is present in an amount of from about 40% to about 98% by weight of the solution.

~~50.~~48. The aerosol of any one of claims 4~~24~~ to 4~~79~~, wherein the solution comprises a solution of niclosamide in the free-acid form.

~~51.~~49. The aerosol of any one of claims 4~~24~~ to 4~~79~~, wherein the solution comprises a solution of a pharmaceutically acceptable salt of niclosamide.

~~52.~~50. The aerosol of any one of claims 4~~24~~ to 4~~79~~, wherein the solution comprises a solution of niclosamide ethanolamine.

~~53.~~51. The aerosol of any one of claims 4~~24~~ to 5~~02~~, wherein the niclosamide or a pharmaceutically acceptable salt thereof is present in the solution in an amount of from 0.1 % to 10 % by weight of the solution, for example about 5 % by weight of the solution.

~~54.~~52. The aerosol of claim 4~~24~~, wherein the composition is a solution comprising from about 4.5 % to about 6.5 % by weight niclosamide ethanolamine and about 93.5 % to about 95.5 % by weight PEG 400.

~~55.~~53. The aerosol of any one of claims 4~~24~~ to 5~~24~~, wherein the solution further comprises a taste-masking agent.

~~56.~~54. The aerosol of claim 5~~35~~, wherein the taste-masking agent is selected from a sugar (e.g. sucrose, dextrose, or lactose), a amino acid or amino acid derivative (e.g. arginine, lysine, or monosodium glutamate), an oil ~~-~~(e.g. a natural oil, or plant extract), a sweetener (e.g. aspartame, acesulfame-K, sucralose or saccharin), an organic acid (e.g. citric acid or aspartic acid), and maltodextrin.

~~57.~~55. The aerosol of any one of claims 4~~24~~ to 5~~46~~, wherein the solution further comprises a solvent (e.g. e.g. a glycol such as propylene glycol).

~~58.~~56. The aerosol of any one of claims 4~~24~~ to 5~~46~~, wherein the solution is a non-aqueous solution, for example a solution containing less than 2% by weight water, preferably less than 0.1 % by weight water, more preferably wherein the solution is anhydrous.

~~59.~~57. The aerosol of any one of claims 4~~24~~ to 5~~68~~, wherein the mass median diameter (MMD) of the aerosol is less than about 5 µm.

~~60.~~58. The aerosol of any one of claims 4~~24~~ to 5~~68~~, wherein the mass median diameter (MMD) of the aerosol is less than about 2 µm.

~~61.~~59. The aerosol of any one of claims 4~~24~~ to 5~~68~~, wherein the mass median diameter (MMD) of the aerosol is from about 0.5 µm to about 5.5 µm, preferably from about 1 µm to about 5 µm.

~~62.~~60. The aerosol of any one of claims 4~~24~~ to 5~~68~~, wherein the mass median diameter (MMD) of the aerosol is less than about 500 µm, preferably less than about 200 µm.

~~63.~~61. The aerosol of any one of claims 4~~24~~ to 5~~68~~, wherein the mass median diameter (MMD) of the aerosol is from about 5 to about 150 µm, preferably from about 20 to about 100 µm.

~~64.~~62. Use of an~~An~~ aerosol according to any one of claims 4~~24~~ to 6~~13~~, in the manufacture of a medicament for ~~use in~~ the prevention or ~~-~~treatment of a viral infection in a subject, wherein the aerosol is to be administered to the subject by inhalation.

~~65.~~63. Use of an~~An~~ aerosol according to any one of claims 4~~24~~ to 6~~13~~, in the manufacture of a medicament for ~~use in~~ the prevention or ~~-~~treatment of a viral infection in a subject, wherein the aerosol is to be administered to the subject intranasally.

~~66.~~64. An inhalable unit dosage comprising a solution of niclosamide, or a pharmaceutically acceptable salt thereof, and PEG, wherein niclosamide is present in an amount of from 1 mg to 600 mg based on the weight of niclosamide, for example from about 150 mg to about 500 mg, based on the weight of niclosamide.

~~67.~~65. An inhalable unit dosage comprising a solution of niclosamide ethanolamine and PEG, wherein niclosamide ethanolamine is present in an amount of from 2 mg to 600 mg, for example from about 150 mg to about 500 mg.

~~68.~~66. The inhalable unit dosage according to claim 6~~46~~ or 6~~57~~, wherein the unit dosage form is present in a container, for example a vial, blister pack, bottle, syringe or drug reservoir within an inhaler device (e.g. a nebulizer).

~~69.~~67. The inhalable unit dosage according to any one of claims 6~~46~~ to 6~~68~~, wherein the solution is a non-aqueous solution, for example a solution containing less than 2% by weight water, preferably less than 0.1 % by weight water, more preferably wherein the solution is anhydrous.

~~70.~~68. A system comprising a container comprising a solution of niclosamide, or a pharmaceutically acceptable salt thereof, and polyethylene glycol (PEG); and an inhaler device and/or an intranasal delivery device.

~~71.~~69. A kit comprising a container comprising a solution of niclosamide, or a pharmaceutically acceptable salt thereof, and polyethylene glycol (PEG); and an inhaler device and/or an intranasal delivery device.

~~72.~~70. The system or kit according to claim 68~~70~~ or claim 69~~71~~, wherein the inhaler device or the intranasal delivery device is adapted to aerosolize the solution.

~~73.~~71. The system or kit according to claim 7~~02~~, wherein the inhaler device or the ~~or an~~ intranasal delivery device is adapted to deliver the aerosolized solution intranasally or intraorally to a subject.

~~74.~~72. The system or kit according to any one of claims 68~~70~~ to 7~~13~~, wherein the inhaler device is selected from a jet nebulizer, a vibrating mesh nebulizer, an ultrasonic nebulizer or a pressurised metered dose inhaler (pMDI).

~~75.~~73. An inhalable solution comprising from about 1 % to 10 % by weight niclosamide ethanolamine and PEG, wherein the PEG has an average molecular weight of less than 600; and optionally a taste-masking agent.

~~76.~~74. An inhalable solution according to claim 7~~35~~, comprising from about 4.5 % to about 6 % by weight niclosamide ethanolamine; about 90 % to 95.5 % PEG 400 and optionally a taste-masking agent.

~~77.~~75. An inhalable solution according to claim 7~~35~~, comprising from about 4.5 % to about 6 % by weight niclosamide ethanolamine; about 90 % to 95.5 % PEG 200 and optionally a taste-masking agent.

~~78.~~76. The inhalable solution according to any one of claims 7~~35~~ to 7~~57~~, wherein the solution is a non-aqueous solution, for example a solution containing less than 2% by weight water, preferably less than 0.1 % by weight water, more preferably wherein the solution is anhydrous.

~~79.~~77. The ~~composition for~~ use ~~or method~~ according to any one of claims 1 to 41~~78~~ and 62 to 63, wherein the subject is hospitalized.

~~80.~~78. The ~~composition for~~ use ~~or method~~ according to any one of claims 1 to 41~~79~~, 62 to 63, and 77, wherein the composition or the aerosol is for preventing, or reducing the likelihood of, progression of the disease, e.g. from mild to moderate or from moderate to severe COVID-19.

~~81.~~79. The ~~composition for~~ use ~~or method~~ according to any one of claims 1 to 41, 62 to 63 and 77-78~~80~~, wherein the composition or the aerosol is to be administered prophylactically.

~~82.~~80. The ~~composition for~~ use ~~or method~~ according to claim 79~~81~~, wherein the composition or the aerosol is to be prophylactically administered to a subject who has been, or is suspected as having been, exposed to a person who is diagnosed as being infected with a viral infection.

~~83.~~81. The ~~composition for~~ use ~~or method~~ according to claim 80~~2~~, wherein the viral infection is SARS-CoV-2.

~~84.~~82. The ~~composition for~~ use ~~or method~~ according to claim 79~~81~~, wherein the composition or the aerosol is to be prophylactically administered to a non-infected subject who is at a higher risk from COVID-19.

~~85.~~83. The ~~composition for~~ use ~~or method~~ according to any one of claims 79~~81~~ to 82~~4~~, wherein the composition or the aerosol is to be prophylactically administered ~~the prophylactic administration is~~ for:

- reducing the risk of the subject contracting symptomatic or non-symptomatic COVID-19 infection;
- reducing the risk of mortality from COVID-19;

- reducing the severity of symptoms of COVID-19; and/or
- reducing the risk of the subject contracting moderate or severe COVID-19.

~~86.~~84. The ~~composition for~~ use ~~or method~~ according to any one of claims 79~~81~~ to 8~~24~~, wherein the composition or the aerosol is to be prophylactically administered ~~the prophylactic administration is~~ for:

- reducing the risk of the subject contracting a secondary infection (e.g. a secondary bacterial infection
- reducing the risk of mortality from a secondary infection; and/or
- reducing the severity of a secondary infection.

~~87.~~85. The ~~composition for~~ use ~~or method~~ according to claim 8~~24~~, wherein the subject has an existing condition or disease, such as: such as diabetes, cancer, heart disease, hypertension, cerebrovascular disease, SCID, sickle cell disease, thalassemia, pulmonary fibrosis, interstitial lung disease, chronic lung disease such as COPD, asthma and cystic fibrosis, emphysema, bronchitis, chronic kidney disease, chronic liver disease, hepatitis, autoimmune disease, a condition affecting the brain or nerves, a muscle wasting condition, or a severe or profound learning disability.

~~88.~~86. The ~~composition for~~ use ~~or method~~ according to claim 8~~24~~, wherein the subject is selected from: subjects who have had a body tissue (e.g. an organ) transplant; subjects who have had an organ (e.g. spleen) removed; subjects receiving (or who have received) chemotherapy, immunotherapy, antibody therapy or radiotherapy; subjects receiving (or who have received) cancer treatment; subjects receiving (or who have received) protein kinase inhibitors or PARP inhibitors; subjects who have had a blood, bone marrow or stem cell transplant; subjects taking immunosuppressants; subjects with HIV or AIDS; and subjects on haemodialysis.

~~89.~~87. The ~~composition for~~ use ~~or method~~ according to any preceding claim, wherein the composition or the aerosol is for use in the treatment of a viral infection in an asymptomatic subject, optionally wherein the viral infection is SARS-CoV-2.

~~90.~~88. The ~~composition for~~ use ~~or method~~ according to any preceding claim, wherein the treatment is for:

- reducing or eliminating the viral load in the subject;
- accelerating seroconversion in the subject;
- reducing inter-subject transmission of the viral;
- reducing viral shedding;
- preventing or reducing the risk of the subject developing symptoms; and/or
- preventing or reducing the risk of progression of disease.

~~91.~~89. The ~~composition for~~ use ~~or method~~ according to any preceding claim, wherein the composition or the aerosol is to be administered intranasally.

90. An inhalable pharmaceutical composition comprising niclosamide, or a pharmaceutically acceptable salt, or an aerosol according to any of claims 42-61, for use in therapy.