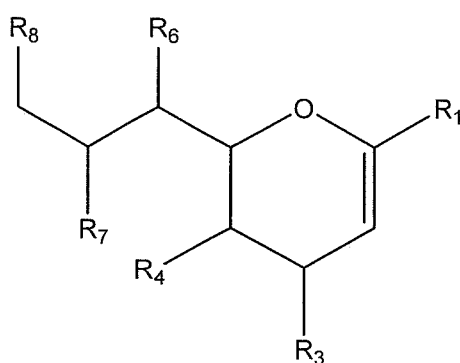


[0006] An initial interaction of the parainfluenza virus with the host cell is through its surface glycoprotein, haemagglutinin-neuraminidase (HN) and involves recognition of *N*-acetylneuraminic acid-containing glycoconjugates. The parainfluenza virus HN is a multifunctional protein that encompasses the functions of receptor binding (for cell adhesion) and receptor destruction (facilitating virus release), not only within the one protein, but apparently in a single binding site. In addition, the HN is involved in activation of the viral surface fusion (F) protein necessary to initiate infection of the target host cell. Inhibition of haemagglutinin and/or neuraminidase enzymes may therefore provide a target for antivirals.

SUMMARY

[0007] According to a first aspect of the invention, there is provided a compound of formula (I), or a pharmaceutically acceptable salt thereof:



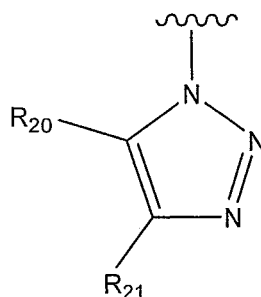
Formula (I)

wherein,

R₁ is selected from the group consisting of COOH, or a salt thereof, C(O)NR₉R₁₀, C(O)OR₁₁ wherein R₉, R₁₀ and R₁₁ are independently selected from the group consisting of hydrogen and optionally substituted C₁-C₆ alkyl;

R₃ is selected from the group consisting of optionally substituted N-linked tetrazole, optionally substituted N-linked indole, optionally substituted N-linked isoindole, optionally substituted N-linked benzotriazole, and N-linked triazole substituted at one or both ring carbon atoms having the below structure:

2a



wherein, R₂₀ and R₂₁ are selected from the group consisting of hydrogen, hydroxyl, cyano, halo, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ alkylether, optionally substituted pyridyl and optionally substituted phenyl, with the proviso that when R₂₀ is hydrogen and R₄ is AcHN then R₂₁ is selected from the group consisting of hydroxyl, cyano, halo, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ alkylether, substituted pyridyl and substituted phenyl wherein substitution of pyridyl and phenyl is independently with a moiety selected from the group consisting of methyl, propyl, isopropyl, *n*-butyl, *sec*-butyl, isobutyl, *tert*-butyl, pentyl, isoamyl, 2-methylbutyl, 3-methylbutyl, hexyl, C₁-C₆ haloalkyl, C₁-C₆ alkylhydroxy, C₁-C₂ alkoxy, carboxy and salts thereof, C₄-C₆ alkoxy, Cl, Br, I, and -CH₂OCH₃;

and wherein at least one of R₂₀ and R₂₁ is not hydrogen;

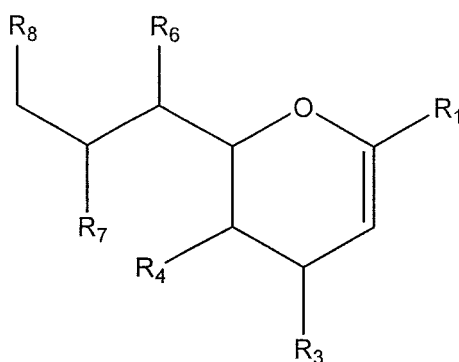
R₄ is NHC(O)R₁₇ wherein R₁₇ is selected from the group consisting of optionally substituted C₁-C₆ alkyl, optionally substituted C₁-C₆ haloalkyl and optionally substituted C₃-C₆ cycloalkyl;

R₆, R₇ and R₈ are independently selected from the group consisting of OH, NH₂, C₁-C₆ alkyl, NR₁₈R_{18'}, C₁-C₆ alkoxy, -OC(O)R₁₈, -NH(C=O)R₁₈, and S(O)_nR₁₈, wherein n = 0 – 2 and each R₁₈ and R_{18'} are independently hydrogen or optionally substituted C₁-C₆ alkyl;

and with the proviso that when R₄ is NHAc and R₃ is a triazole substituted only at the R₂₁ position then the triazole is not substituted with propyl, substituted propyl, substituted *tert*-butyl or diethoxyalkyl.

[0007a] In one example, there is disclosed a compound of formula (I), or a pharmaceutically acceptable salt thereof:

2b



Formula (I)

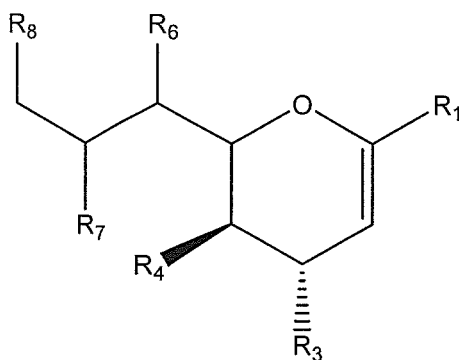
wherein, R_1 is selected from the group consisting of COOH , or a salt thereof, $\text{C}(\text{O})\text{NR}_9\text{R}_{10}$, $\text{C}(\text{O})\text{OR}_{11}$ wherein R_9 , R_{10} and R_{11} are independently selected from the group consisting of hydrogen and optionally substituted $\text{C}_1\text{-C}_6$ alkyl;

R_3 is selected from the group consisting of N-linked triazole substituted at one or both ring carbon atoms, optionally substituted N-linked tetrazole, optionally substituted N-linked indole, optionally substituted N-linked isoindole, and optionally substituted N-linked benzotriazole;

R_4 is $\text{NHC(O)}R_{17}$ wherein R_{17} is selected from the group consisting of $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_1\text{-C}_6$ haloalkyl and $\text{C}_3\text{-C}_6$ cycloalkyl ;

R_6 , R_7 and R_8 are independently selected from the group consisting of OH , NH_2 , $\text{C}_1\text{-C}_6$ alkyl, $\text{NR}_{18}\text{R}_{18}'$, $\text{C}_1\text{-C}_6$ alkoxy, $-\text{OC(O)}R_{18}$, $-\text{NH(C=O)}R_{18}$, and $\text{S(O)}_n\text{R}_{18}$, wherein $n = 0 - 2$ and each R_{18} and R_{18}' are independently hydrogen or optionally substituted $\text{C}_1\text{-C}_6$ alkyl.

[0008] In one example of the first aspect, the compound of formula (I) is a compound of formula (II):



Formula (II)

wherein, R_1 , R_3 , R_4 , R_6 , R_7 and R_8 are as described above.

[0009] According to a second aspect of the invention there is provided a pharmaceutical composition comprising an effective amount of a compound of the first aspect, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, diluent and/or excipient.

[0010] Suitably, the pharmaceutical composition is for the treatment or prophylaxis of a disease, disorder or condition caused by viral infection.

[0011] In one example, there is disclosed a method of treating a disease, disorder or condition caused by viral infection in a patient including the step of administering an effective amount of a compound of the first aspect, or a pharmaceutically effective salt thereof, or the pharmaceutical composition of the second aspect to the patient.

[0012] In another example, there is disclosed a compound as disclosed herein, or a pharmaceutically effective salt thereof, or the pharmaceutical composition of the second aspect for use in the treatment of a disease, disorder or condition caused by viral infection in a patient.

[0013] In one aspect, the present invention refers to the use of a compound as disclosed herein, or a pharmaceutically effective salt thereof, or the pharmaceutical composition as disclosed herein, in the manufacture of a medicament for treating a disease, disorder or condition, in a patient, caused by parainfluenza virus. In one example, there is disclosed the use of a compound as described herein, or a pharmaceutically effective salt thereof, in the manufacture of a medicament for the treatment of a disease, disorder or condition caused by viral infection.

[0014] In one example, the disease, disorder or condition is influenza.

[0015] The influenza may be influenza A, B or C or parainfluenza.

[0016] In one example, the parainfluenza is an hPIV-1, -2 or -3 virus.

[0017] Preferably, the patient is a domestic or livestock animal or a human.

[0018] In one example, there is disclosed a method of modulating the activity of a viral haemagglutinin and/or neuraminidase enzyme including the step of contacting the enzyme with a compound as disclosed herein. In another aspect, the present invention refers to use of a compound as described herein, or a pharmaceutically effective salt thereof in the manufacture of a medicament for modulating the activity of a parainfluenza hemagglutinin and/or parainfluenza neuraminidase enzyme.

[0019] The various features and embodiments of the present invention, referred to in individual sections above apply, as appropriate, to other sections, *mutatis mutandis*. Consequently features specified in one section may be combined with features specified in other sections as appropriate.

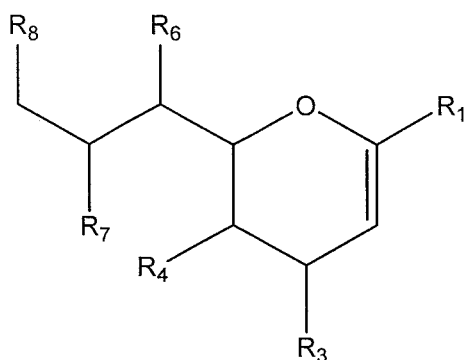
[0020] Further features and advantages of the present invention will become apparent from the following detailed description.

BRIEF DESCRIPTION OF THE DRAWINGS

[0021] In order that the invention may be readily understood and put into practical effect, preferred embodiments will now be described by way of example with reference to the accompanying figures wherein:

CLAIMS

1. A compound of formula (I), or a pharmaceutically acceptable salt thereof:

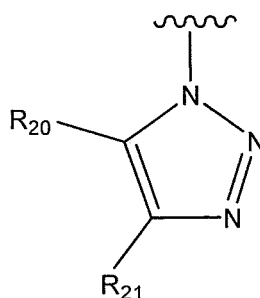


Formula (I)

wherein,

R₁ is selected from the group consisting of COOH, or a salt thereof, C(O)NR₉R₁₀, C(O)OR₁₁ wherein R₉, R₁₀ and R₁₁ are independently selected from the group consisting of hydrogen and optionally substituted C₁-C₆ alkyl;

R₃ is selected from the group consisting of optionally substituted N-linked tetrazole, optionally substituted N-linked indole, optionally substituted N-linked isoindole, optionally substituted N-linked benzotriazole, and N-linked triazole substituted at one or both ring carbon atoms having the below structure:

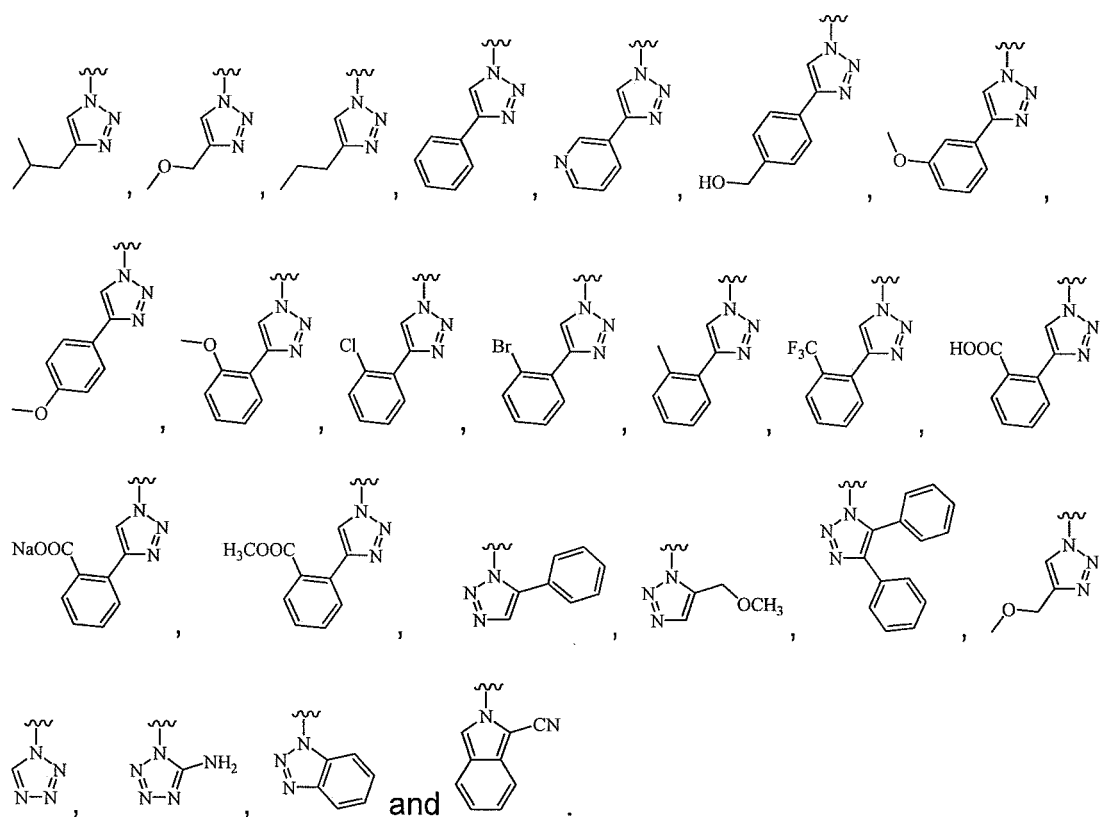


wherein, R₂₀ and R₂₁ are selected from the group consisting of hydrogen, hydroxyl, cyano, halo, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ alkylether, optionally substituted pyridyl and optionally substituted phenyl, with the proviso that when R₂₀ is hydrogen and R₄ is AcHN then R₂₁ is selected from the group consisting of hydroxyl, cyano, halo, C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ alkylether, substituted pyridyl and substituted

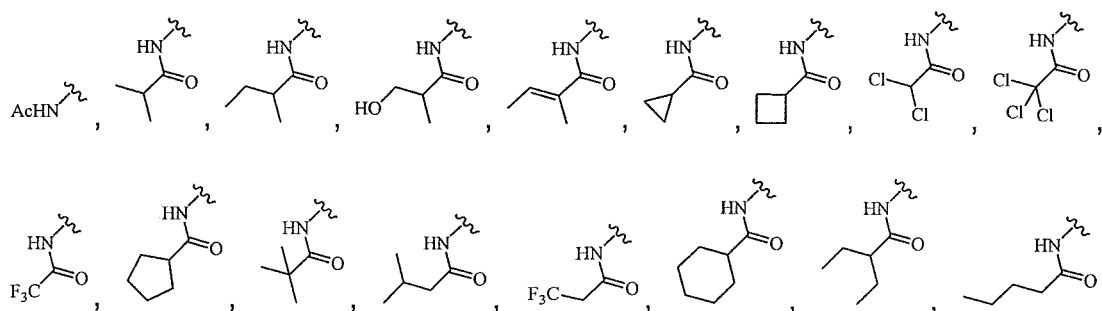
R₂₃ and R₂₄ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halo, C₁-C₆ alkyl and C₁-C₆ haloalkyl.

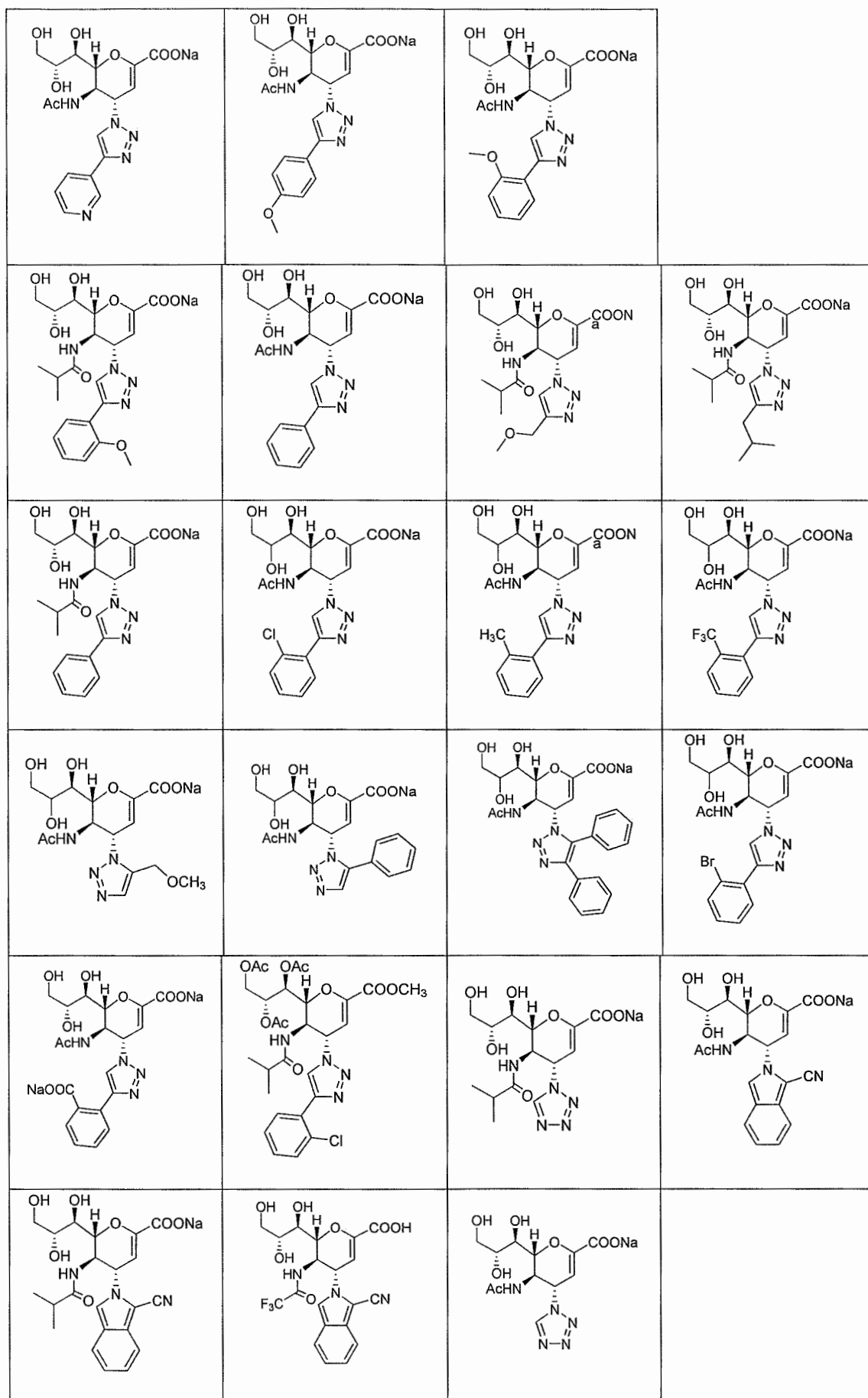
4. The compound of claim 3 wherein when R₂₂ is optionally substituted phenyl then the substitution is with a moiety selected from the group consisting of C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₁-C₆ alkylhydroxy, C₁-C₆ alkoxy, halo, -C(O)OMe and -CH₂OCH₃.

5. The compound of any one of the preceding claims wherein R_3 is selected from the group consisting of:



6. The compound of any one of the preceding claims wherein R₄ is selected from the group consisting of:





and analogues thereof wherein the C-2 carboxy group is in the protonated form, sodium salt form or C₁-C₃ ester prodrug form and wherein the R₄ position is substituted with any –NHC(O)R group wherein R is C₁-C₄ alkyl or haloalkyl.

11. A pharmaceutical composition comprising an effective amount of a compound of any one of claim 1 to claim 10, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, diluent and/or excipient.
12. Use of a compound of any one of claim 1 to claim 10, or a pharmaceutically effective salt thereof, or the pharmaceutical composition of claim 11, in the manufacture of a medicament for treating a disease, disorder or condition, in a patient, caused by parainfluenza virus.
13. The use of claim 12 wherein the parainfluenza virus is selected from the group consisting of the hPIV-1, 2 and 3 virus.
14. The use of claim 12 or claim 13 wherein the patient is a domestic or livestock animal or a human.
15. Use of a compound of any one of claim 1 to claim 10, or a pharmaceutically effective salt thereof in the manufacture of a medicament for inhibiting the activity of a parainfluenza hemagglutinin and/or a parainfluenza neuraminidase enzyme.