[006] Glycosylation is the process by which sugars such as mannose form complex oligosaccharides, and bind to proteins to form glycoproteins which are important components of cell membranes. Viruses use host-cell machinery to glycosylate their own proteins including viral envelope proteins. The exposed sugars, referred to as glycans, essentially envelope cells to create a "sugar-coating" and play a vital role in viral life-cycle including immune evasion by glycan shielding and enhancement of immune cell infection.

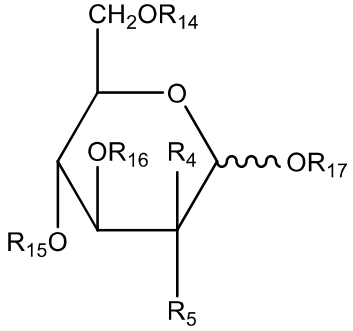
[007] A large variety of human pathogenic viruses have extensively glycosylated envelope proteins. Such viruses include HIV-1, influenza virus, Lassa virus, corona virus, SARS, Zika virus, dengue virus, and Ebola virus. By inhibiting glycolsylation and the formation of the glycan shield, one could make virus infected cells more vulnerable to attack by the immune system.

[008] 2-Deoxy-D-arabino-hexopyranose, known also as 2-deoxy-D-glucopyranose, 2-deoxy-D-mannose, and 2-deoxy-D glucose (hereinafter called "2-DG") is a so-called glucose decoy that looks like glucose but fails to perform the ultimate function of glucose. As a glucose decoy, 2-DG has been shown to inhibit glycolysis and energy production. 2-DG has also been shown to severely curtail rotovirus ("RV")and Dengue virus ("DENV") because it prevents glucose from being successfully converted into energy, so the host cell dies, and along with it, the chances for RV to replicate. Although 2-DG has been shown to posess anti-viral activity *in vitro*, is not suitable as an effective therapy *in vivo* because it lacks drug-like properties that include poor pharmacokinetics, rapid metabolism, and unsatisfactory tissue and organ distribution.

[009] Currently, the global COVID-19 pandemic shows that there is an ongoing unmet need to develop new methods of treating viral infections.

SUMMARY

[009a] In an aspect, there is provided the use of a therapeutically effective amount of a compound of Formula II



(II)

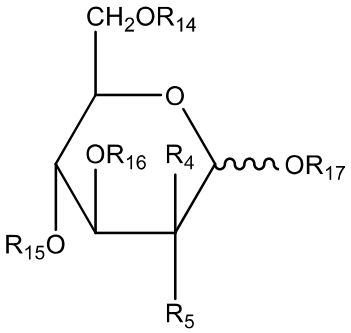
or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a viral infection caused by SARs-CoV-2 in a patient in need thereof,

wherein:

R_{14}, and R_{16}, are independently selected from the group consisting of $COCH_3$, $COCH_2CH_3$, and $COCH_2CH_2CH_3$; and

R_{15}, R_{17}, R_4 and R_5 are hydrogen.

[009b] In another aspect, there is provided Use of a therapeutically effective amount of a compound of Formula II



(II)

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a viral infection caused by HIV-1 virus, human corona virus, Lassa virus, Zika virus, Dengue virus or Ebola virus in a patient in need thereof, wherein:

R_{14}, R_{15}, R_{16}, and R_{17} are hydrogen; and

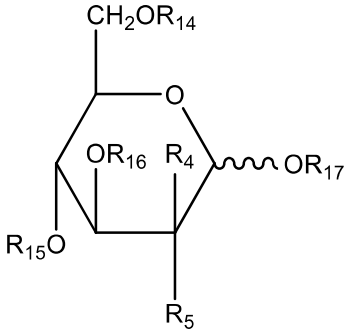
one of R_4 and R_5 is hydrogen and the other of R_4 and R_5 is selected from the group consisting of Cl, Br, I, ^{18}F, and ^{19}F.

[009c] In another aspect, there is provided the use of a therapeutically effective amount of a compound selected from the group consisting of ((2R,3S,4R)-4-acetoxy-3,6-dihydroxytetrahydro-2H-pyran-2-yl)methyl acetate, and pharmaceutically acceptable salts thereof, in the manufacture of a medicament for treating a viral infection caused by SARS-CoV-2 in a patient in need thereof.

[009d] In another aspect, there is provided the use of a therapeutically effective amount of a compound selected from the group consisting of (2-Deoxy-2-iodo-D-glucose), and (2-Deoxy-2-iodo-D-mannose), and pharmaceutically acceptable salts thereof, in the manufacture of a medicament for treating a viral infection caused by HIV-1 virus,

human corona virus, Lassa virus, Zika virus, Dengue virus or Ebola virus in a patient in need thereof.

[009e] In another aspect, there is provided the use of a therapeutically effective amount of a compound of Formula II



(II)

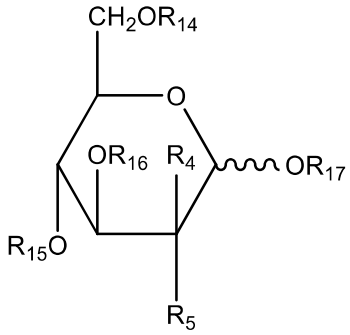
or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a viral infection caused by SARS-CoV-2, wherein:

R_{14}, and R_{16} are independently selected from the group consisting of $COCH_3$, $COCH_2CH_3$, and $COCH_2CH_2CH_3$; and

R_{15}, R_{17}, R_4 and R_5 are hydrogen,

wherein the pharmaceutical composition comprises a pharmaceutically acceptable carrier together with the compound of structural Formula II or a pharmaceutically acceptable salt thereof.

[009f] In another aspect, there is provided the use of a therapeutically effective amount of a compound of Formula II



(II)

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a viral infection caused by HIV-1 virus, human corona virus, Lassa virus, Zika virus, Dengue virus or Ebola virus, wherein:

R_{14}, R_{15}, R_{16}, and R_{17} are hydrogen; and

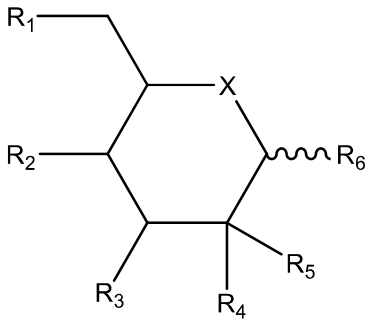
one of R_4 and R_5 is hydrogen and the other of R_4 and R_5 is selected from the group consisting of Cl, Br, I, ^{18}F, and ^{19}F,

wherein the pharmaceutical composition comprises a pharmaceutically acceptable carrier together with the compound of structural Formula II or a pharmaceutically acceptable salt thereof.

[010] In some examples, the present disclosure provides methods of treating and preventing viral infections comprising the administration of a therapeutically effective amount of a compound of Formula I, including esters of pyranose monosaccharides such as WP1122, which have surprisingly superior properties including increased levels of 2-DG in plasma, and superior distribution to critical organs such as the lung and brain which is important due to the fact that many human pathogenic viruses destroy lung function and can localize in the brain resulting in debilitating and often lethal consequences. The surprisingly superior plasma levels and tissue distribution can effectively increase the observed anti-viral properties of 2-DG *in vivo*. The present disclosure provides in some examples novel

methods of treating and preventing viral infection by administering hexose-type monosaccharides and analogs thereof to patients in need thereof. Without being limited to a particular mechanism of action, it is believed that these compounds act as mimics of D-mannose and D-glucose producing a two-pronged attack to reduce viral replication: inhibiting energy production of infected cells and altering glycosylation patterns and inhibiting desired N-glycan formation.

[011] In another examples of the disclosure, there is provided a method of treating and preventing viral infections comprising the administration of a therapeutically effective amount of a compound of Formula I:



(I)

or a pharmaceutically acceptable salt thereof, wherein:

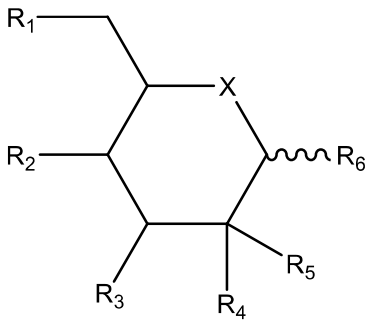
X is selected from the group consisting of O and S;

R_1, R_2, R_3, and R_6 are independently selected from the group consisting of hydrogen, hydroxyl, thiol, halogen, alkoxy, haloalkoxy, per haloalkoxy, alkoxyalkyloxy, -OC(O)alkyl, OCO_2alkyl, alkylthio, amino, alkylamino, N-sulfonamido, N-amido, and carbamate, any of which may be optionally substituted;

R_4 and R_5 are independently selected from the group consisting of hydrogen, hydroxyl, thiol, halogen, alkoxy, haloalkoxy, per haloalkoxy, alkoxyalkyloxy, -OC(O)alkyl, OCO_2alkyl, alkylthio, amino, alkylamino, N-sulfonamido, N-amido, carbamate, alkyl, haloalkyl, perhaloalkyl, $-N(R_7)OR_8$, $-ON(R_9)_2$, $-N(R_{10})N(R_{11})_2$, any of which may be optionally substituted, or R_4 and R_5, taken together, are selected from the group consisting of $=N-OR_{12}$ and $=N-N(R_{13})_2$; and

R_7, R_8, R_9, R_{10}, R_{11}, R_{12}, and R_{13} are each independently selected from the group consisting of hydrogen and alkyl, wherein said alkyl may be optionally substituted.

[012] In a further example of the disclosure, there are provided pharmaceutical compositions for use in treating viral infections comprising administration of a therapeutically effective amount of a compound of Formula I:



(I)

or a pharmaceutically acceptable salt thereof, wherein:

X is selected from the group consisting of O and S;

R_1, R_2, R_3, and R_6 are independently selected from the group consisting of hydrogen, hydroxyl, thiol, halogen, alkoxy, haloalkoxy, per haloalkoxy, alkoxyalkyloxy, -OC(O)alkyl, OCO_2alkyl, alkylthio, amino, alkylamino, N-sulfonamido, N-amido, and carbamate, any of which may be optionally substituted;

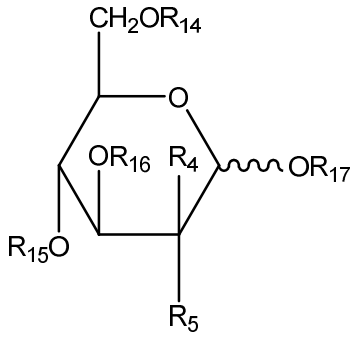
R_4 and R_5 are independently selected from the group consisting of hydrogen, hydroxyl, thiol, halogen, alkoxy, haloalkoxy, per haloalkoxy, alkoxyalkyloxy, -OC(O)alkyl, OCO_2alkyl, alkylthio, amino, alkylamino, N-sulfonamido, N-amido, carbamate, alkyl, haloalkyl, perhaloalkyl, $-N(R_7)OR_8$, $-ON(R_9)_2$, $-N(R_{10})N(R_{11})_2$, any of which may be optionally substituted, or R_4 and R_5, taken together, are selected from the group consisting of $=N-OR_{12}$ and $=N-N(R_{13})_2$; and

R_7, R_8, R_9, R_{10}, R_{11}, R_{12}, and R_{13} are each independently selected from the group consisting of hydrogen and alkyl, wherein said alkyl may be optionally substituted.

[013] In a further example, there is provided a pharmaceutical composition for use in the manufacture of a medicament for the treatment and prevention of a viral infection in a patient comprising a compound of Formula I:

CLAIMS

1. Use of a therapeutically effective amount of a compound of Formula II



(II)

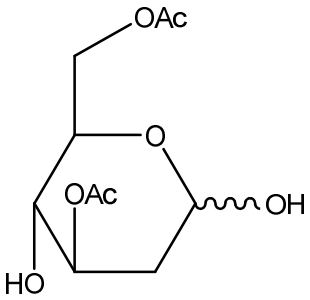
or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a viral infection caused by SARs-CoV-2 in a patient in need thereof,

wherein:

R_{14}, and R_{16}, are independently selected from the group consisting of $COCH_3$, $COCH_2CH_3$, and $COCH_2CH_2CH_3$; and

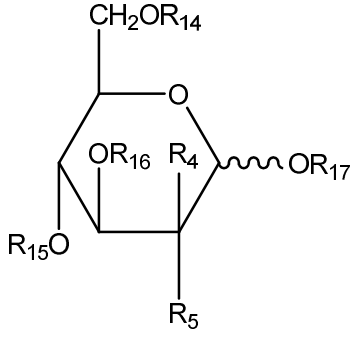
R_{15}, R_{17}, R_4 and R_5 are hydrogen.

2. The use of claim 1, wherein said compound has the structural formula:



and pharmaceutically acceptable salts thereof.

3. Use of a therapeutically effective amount of a compound of Formula II



(II)

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a viral infection caused by HIV-1 virus, human corona virus, Lassa virus, Zika virus, Dengue virus or Ebola virus in a patient in need thereof, wherein:

R_{14}, R_{15}, R_{16}, and R_{17} are hydrogen; and

one of R_4 and R_5 is hydrogen and the other of R_4 and R_5 is selected from the group consisting of Cl, Br, I, ^{18}F, and ^{19}F.

4. The use of claim 3, wherein one of R_4 and R_5 is hydrogen, and the other of R_4 and R_5 is I.

5. The use according to claim 3 or 4, wherein said viral infection is caused by SARs-CoV-2.

6. The use according to claim 3, wherein said viral infection is caused by Ebola virus.

7. The use according to claim 3, wherein said viral infection is caused by Lassa virus.

8. Use of a therapeutically effective amount of a compound selected from the group consisting of ((2R,3S,4R)-4-acetoxy-3,6-dihydroxytetrahydro-2H-pyran-2-yl)methyl acetate, and pharmaceutically acceptable salts thereof, in the manufacture of a medicament for treating a viral infection caused by SARS-CoV-2 in a patient in need thereof.

9. Use of a therapeutically effective amount of a compound selected from the group consisting of (2-Deoxy-2-iodo-D-glucose), and (2-Deoxy-2-iodo-D-mannose), and pharmaceutically acceptable salts thereof, in the manufacture of a medicament for treating a viral infection caused by HIV-1 virus, human corona virus, Lassa virus, Zika virus, Dengue virus or Ebola virus in a patient in need thereof.

10. The use according to claim 9, wherein said viral infection is caused by SARs-CoV-2.

11. The use according to claim 9, wherein the compound is selected from (2-Deoxy-2-iodo-D-glucose), and pharmaceutically acceptable salts thereof.

12. The use according to claim 9, wherein the compound is selected from (2-Deoxy-2-iodo-D-mannose), and pharmaceutically acceptable salts thereof.

13. The use according to claim 9, wherein said viral infection is caused by Ebola virus.

14. The use according to claim 9, wherein said viral infection is caused by Lassa virus.

15. The use according to any one of claims 1-14, wherein said viral infection is caused by a virus characterized by glycosylated envelope proteins on infected cells.

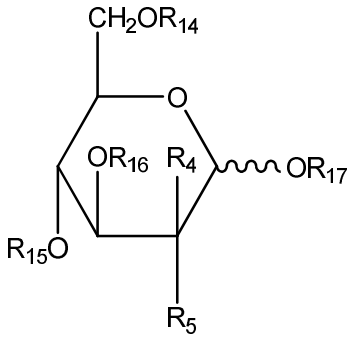
16. The use according to any one of claims 1-14, wherein the patient has COVID-19.

17. The use according to any one of claims 1-14, wherein the patient tests positive for COVID-19.

18. The use according to any one of claims 1-14, wherein the patient is asymptomatic.

19. The use of any one of claims 1-14, wherein the medicament is administered by inhalation or insufflation.

20. Use of a therapeutically effective amount of a compound of Formula II



(II)

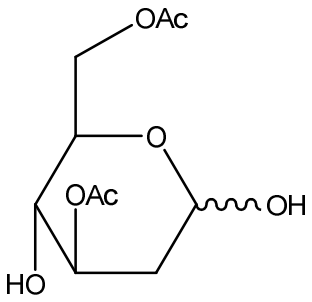
or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a viral infection caused by SARS-CoV-2, wherein:

R_{14}, and R_{16} are independently selected from the group consisting of $COCH_3$, $COCH_2CH_3$, and $COCH_2CH_2CH_3$; and

R_{15}, R_{17}, R_4 and R_5 are hydrogen,

wherein the pharmaceutical composition comprises a pharmaceutically acceptable carrier together with the compound of structural Formula II or a pharmaceutically acceptable salt thereof.

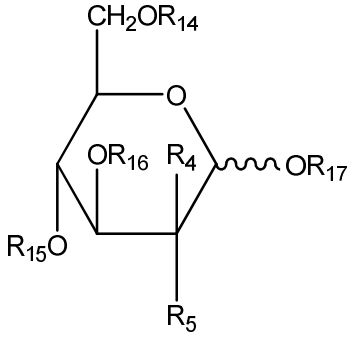
21. The use of claim 20 wherein the compound is



or pharmaceutically acceptable salt thereof.

22. Use of claim 20, wherein the compound is selected from ((2R,3S,4R)-4-acetoxy-3,6-dihydroxytetrahydro-2H-pyran-2-yl)methyl acetate, and pharmaceutically acceptable salts thereof.

23. Use of a therapeutically effective amount of a compound of Formula II



(II)

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a viral infection caused by HIV-1 virus, human corona virus, Lassa virus, Zika virus, Dengue virus or Ebola virus, wherein:

R_{14}, R_{15}, R_{16}, and R_{17} are hydrogen; and

one of R4 and R5 is hydrogen and the other of R_4 and R_5 is selected from the group consisting of Cl, Br, I, ^{18}F, and ^{19}F,

wherein the pharmaceutical composition comprises a pharmaceutically acceptable carrier together with the compound of structural Formula II or a pharmaceutically acceptable salt thereof.

24. The use of claim 23, wherein one of R_4 and R_5 is hydrogen, and the other of R_4 and R_5 is I.

25. The use of claim 23, wherein the compound is selected from the group consisting of (2-Deoxy-2-iodo-D-glucose), and (2-Deoxy-2-iodo-D-mannose), and pharmaceutically acceptable salts thereof.

26. The use according to claim 25, wherein the compound is selected from (2-Deoxy-2-iodo-D-glucose), and pharmaceutically acceptable salts thereof.

27. The use according to claim 25, wherein the compound is selected from (2-Deoxy-2-iodo-D-mannose), and pharmaceutically acceptable salts thereof.

28. The use according to claim 25, wherein said viral infection is caused by Ebola virus.

29. The use according to claim 25, wherein said viral infection is caused by Lassa virus.

30. The use according to claim 25, wherein said viral infection is caused by SARS-CoV-2.

31. The use of any one of claims 20-30, wherein the pharmaceutical composition is to be administered by inhalation or insufflation.