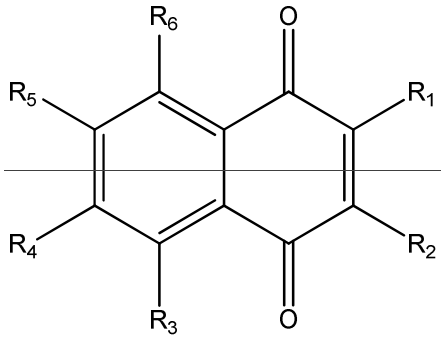
WHAT IS CLAIMED IS:

1. A compound for use in the treatment of a coronavirus infection, the compound being represented by Formula I:



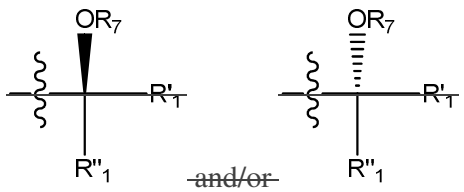
Formula I

wherein R_1-R_6 are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, heteroalicyclic, halo, hydroxy, alkoxy, aryloxy, thiohydroxy, thioalkoxy, thioaryloxy, sulfinyl, sulfonyl, sulfonate, sulfate, cyano, nitro, azide, phosphonyl, phosphinyl, carbonyl, thiocarbonyl, a urea group, a thiourea group, O-carbamyl, N-carbamyl, O-thiocarbamyl, N-thiocarbamyl, S-thiocarbamyl, C-amido, N-amido, C-carboxy, O-carboxy, sulfonamido, guanyl, guanidinyl, hydrazine, hydrazide, thiohydrazide, and amino, or alternatively, R_1 and R_2 together form a five- or six-membered aromatic or aliphatic ring.

2. The compound for use according to claim 1, wherein at least one of R_3 and R_6 is OH.

3. The compound for use according to claim 1, wherein R_3 and R_6 are each OH.

4. The compound for use according to any one of claims 1 to 3, wherein R_1 is represented by:



~~wherein R'$_1$, R"$_1$, and R_7 are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heteroalicyclic, and carbonyl.~~

~~5. The compound for use according to claim 4, wherein R'$_1$ is alkenyl.~~

~~6. The compound for use according to claim 5, wherein R'$_1$ is $-CH_2-CH=C(CH_3)_2$.~~

~~7. The compound for use according to any one of claims 4 to 6, wherein R_7 is a saccharide moiety or a peptide moiety.~~

~~8. The compound for use according to any one of claims 4 to 7, wherein R_7 is hydrogen or carbonyl.~~

~~9. The compound for use according to any one of claims 1 to 8, wherein R_2, R_4 and R_5 are hydrogen.~~

~~10. The compound for use according to claim 1, wherein the compound is shikonin or a glycoside of shikonin, or an ester thereof.~~

~~11. The compound for use according to any one of claims 1 to 10, wherein said treatment is of a subject in which inhibiting inflammation would be beneficial.~~

~~12. The compound for use according to any one of claims 1 to 11, wherein said treatment comprises intravenous administration of the compound.~~

~~13. The compound for use according to claim 12, wherein said treatment comprises administering the compound at a dose in a range of from 0.04 mg to 400 mg.~~

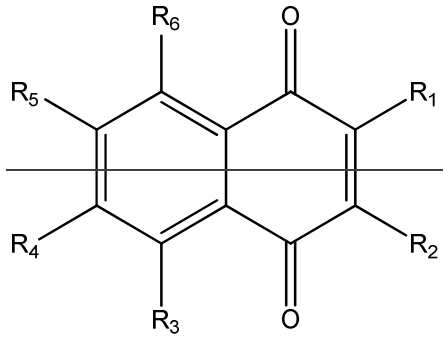
~~14. The compound for use according to any one of claims 1 to 11, wherein said treatment comprises oral administration of the compound.~~

~~15. The compound for use according to claim 14, wherein said treatment comprises administering the compound at a dose in a range of from 10 mg to 5 grams.~~

16. The compound for use according to any one of claims 14 to 15, wherein said treatment comprises administering the compound at a dosage in a range of from 2 mg per kg per day to 200 mg per kg per day.

17. A pharmaceutical composition comprising:

a compound represented by Formula I:



Formula I

wherein R_1-R_6 are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, heteroalicyclic, halo, hydroxy, alkoxy, aryloxy, thiohydroxy, thioalkoxy, thioaryloxy, sulfinyl, sulfonyl, sulfonate, sulfate, cyano, nitro, azide, phosphonyl, phosphinyl, carbonyl, thiocarbonyl, a urea group, a thiourea group, O-carbamyl, N-carbamyl, O-thiocarbamyl, N-thiocarbamyl, S-thiocarbamyl, C-amido, N-amido, C-carboxy, O-carboxy, sulfonamido, guanyl, guanidinyl, hydrazine, hydrazide, thiohydrazide, and amino, or alternatively, R_1 and R_2 together form a five- or six-membered aromatic or aliphatic ring; and

at least one phospholipid,

wherein a weight ratio of said at least one phospholipid to said compound in the composition is in a range of from 10:1 to 1:10.

18. The composition of claim 17, further comprising liposomes.

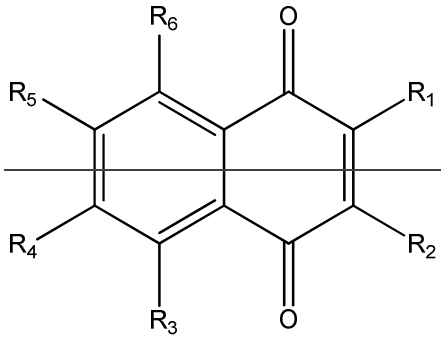
19. The composition of any one of claims 17 to 18, further comprising at least one additional active agent selected from the group consisting of a vitamin, N-acetyl cysteine, an anticoagulant, an anti-inflammatory agent, an antipyretic agent, an antiviral agent, and a protease inhibitor.

20. The composition of claim 19, wherein said protease inhibitor is capable of inhibiting 3C protease and/or a 3CL protease.

21. The composition of any one of claims 17 to 20, being for use in the treatment of a coronavirus infection.

22. The compound for use according to any one of claims 1 to 16, or the composition for use according to claim 21, wherein said treatment further comprises administering at least one additional active agent selected from the group consisting of a vitamin, N-acetyl cysteine, an anticoagulant, an anti-inflammatory agent, an antipyretic agent, an antiviral agent, and a protease inhibitor.

23. A method of inhibiting a coronavirus 3CL protease, the method comprising contacting the 3CL protease with a compound represented by Formula I:



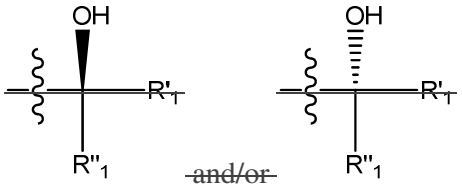
Formula I

wherein R_1-R_6 are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, heteroalicyclic, halo, hydroxy, alkoxy, aryloxy, thiohydroxy, thioalkoxy, thioaryloxy, sulfinyl, sulfonyl, sulfonate, sulfate, cyano, nitro, azide, phosphonyl, phosphinyl, carbonyl, thiocarbonyl, a urea group, a thiourea group, O-carbamyl, N-carbamyl, O-thiocarbamyl, N-thiocarbamyl, S-thiocarbamyl, C-amido, N-amido, C-carboxy, O-carboxy, sulfonamido, guanyl, guanidinyl, hydrazine, hydrazide, thiohydrazide, and amino, or alternatively, R_1 and R_2 together form a five- or six-membered aromatic or aliphatic ring.

24. The method of claim 23, wherein at least one of R_3 and R_6 is OH.

25. The method of claim 23, wherein R_3 and R_6 are each OH.

26. The method of any one of claims 23 to 25, wherein R_1 is represented by the formula:



and/or

wherein R'$_1$ and R''$_1$ are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, and heteroalicyclic.

27. The method of claim 26, wherein R'$_1$ is alkenyl.

28. The method of claim 27, wherein R'$_1$ is CH_2-CH=C(CH_3)$_2$.

29. The method of any one of claims 26 to 28, wherein R_7 is a saccharide moiety or a peptide moiety.

30. The method of any one of claims 26 to 29, wherein R_7 is hydrogen or carbonyl.

31. The method of any one of claims 23 to 30, wherein R_2, R_4 and R_5 are hydrogen.

32. The method of claim 23, wherein the compound is shikonin or a glycoside of shikonin, or an ester thereof.

33. The method of any one of claims 23 to 32, comprising administering said compound to a subject in need thereof.

34. The method of claim 33, further comprising inhibiting inflammation and/or autophagy in said subject.

35. The method of claim 33 or 34, wherein said administering comprises intravenous administration.

36. The method of claim 35, comprising administering said compound at a dose in a range of from 0.04 mg to 400 mg.

~~37. The method of claim 33 or 34, wherein said administering comprises oral administration.~~

~~38. The method of claim 37, comprising administering the compound at a dose in a range of from 10 mg to 5 grams.~~

~~39. The method of any one of claims 37 to 38, comprising administering the compound at a dosage in a range of from 2 mg per kg per day to 200 mg per kg per day.~~

~~40. The method of any one of claims 33 to 39, wherein the compound is part of a composition which further comprises phospholipids, and a weight ratio of said phospholipids to the compound in said composition is in a range of from 10:1 to 1:10.~~

~~41. The method of any one of claims 33 to 40, wherein the compound is part of a composition which further comprises liposomes.~~

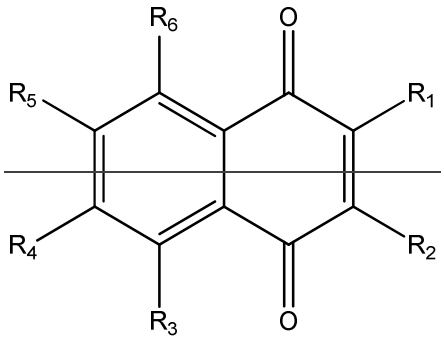
~~42. The method of any one of claims 33 to 41, further comprising administering to said subject at least one additional active agent selected from the group consisting of a vitamin, N-acetyl cysteine, an anticoagulant, an anti inflammatory agent, an antipyretic agent, an antiviral agent, and a protease inhibitor.~~

~~43. A method of treating a coronavirus infection in a subject in need thereof, the method comprising administering to the subject at least one compound that exhibits at least two of:~~
~~(i) inhibition of an activity of a 3CL protease of said coronavirus;~~
~~(ii) inhibition of inflammation in said subject; and~~
~~(iii) inhibition of autophagy in said subject,~~
~~thereby treating the coronavirus infection.~~

~~44. The method of claim 43, comprising administering to the subject a compound capable of at least two of said inhibition of an activity of a 3CL protease, said inhibition of inflammation, and said inhibition of autophagy.~~

~~45. The method of claim 44, wherein said compound is capable of each of said inhibition of an activity of a 3CL protease, said inhibition of inflammation, and said inhibition of autophagy.~~

~~46. The method of claim 45, wherein said compound is represented by Formula I:~~



~~Formula I~~

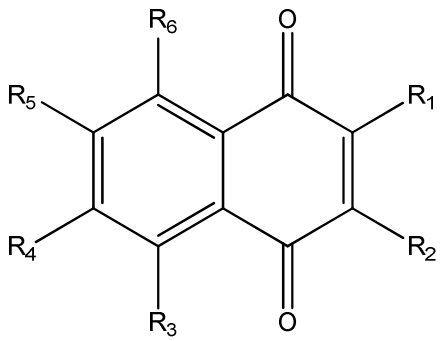
~~wherein R_1-R_6 are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, heteroalicyclic, halo, hydroxy, alkoxy, aryloxy, thiohydroxy, thioalkoxy, thioaryloxy, sulfinyl, sulfonyl, sulfonate, sulfate, cyano, nitro, azide, phosphonyl, phosphinyl, carbonyl, thiocarbonyl, a urea group, a thiourea group, O carbamyl, N carbamyl, O thiocarbamyl, N thiocarbamyl, S thiocarbamyl, C amido, N amido, C carboxy, O carboxy, sulfonamido, guanyl, guanidinyl, hydrazine, hydrazide, thiohydrazide, and amino, or alternatively, R_1 and R_2 together form a five- or six-membered aromatic or aliphatic ring.~~

~~47. The method of claim 46, comprising administering to the subject said compound of Formula I and at least one additional agent that exhibits said inhibition of an activity of a 3CL protease, said inhibition of inflammation, and/or said inhibition of autophagy.~~

~~48. The compound for use according to any one of claims 1 to 16 and 22, the composition for use according to any one of claims 21 to 22, or the method of any one of claims 23 to 47, wherein said coronavirus is a betacoronavirus.~~

~~49. The compound for use, composition for use, or method according to claim 48, wherein said coronavirus is a SARS-related coronavirus.~~

1. A compound for use in the treatment of a coronavirus infection, the compound being represented by Formula I:



Formula I

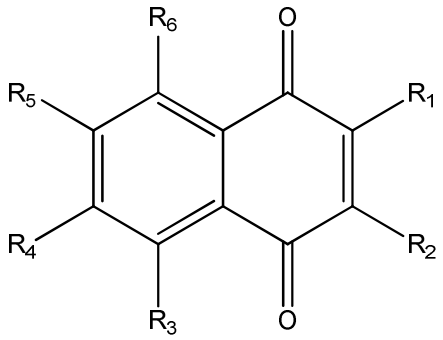
wherein R_1-R_6 are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, heteroalicyclic, halo, hydroxy, alkoxy, aryloxy, thiohydroxy, thioalkoxy, thioaryloxy, sulfinyl, sulfonyl, sulfonate, sulfate, cyano, nitro, azide, phosphonyl, phosphinyl, carbonyl, thiocarbonyl, a urea group, a thiourea group, O-carbamyl, N-carbamyl, O-thiocarbamyl, N-thiocarbamyl, S-thiocarbamyl, C-amido, N-amido, C-carboxy, O-carboxy, sulfonamido, guanyl, guanidinyl, hydrazine, hydrazide, thiohydrazide, and amino, or alternatively, R_1 and R_2 together form a five- or six-membered aromatic or aliphatic ring.

2. The compound for use according to claim 1, wherein the compound is shikonin or a glycoside of shikonin, or an ester thereof.

3. The compound for use according to any one of claims 1 to 2, wherein said treatment is of a subject in which inhibiting inflammation would be beneficial.

4. A pharmaceutical composition comprising:

a compound represented by Formula I:



Formula I

wherein R_1-R_6 are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, heteroalicyclic, halo, hydroxy, alkoxy, aryloxy, thiohydroxy, thioalkoxy, thioaryloxy, sulfinyl, sulfonyl, sulfonate, sulfate, cyano, nitro, azide, phosphonyl, phosphinyl, carbonyl, thiocarbonyl, a urea group, a thiourea group, O-carbamyl, N-carbamyl, O-thiocarbamyl, N-thiocarbamyl, S-thiocarbamyl, C-amido, N-amido, C-carboxy, O-carboxy, sulfonamido, guanyl, guanidinyl, hydrazine, hydrazide, thiohydrazide, and amino, or alternatively, R_1 and R_2 together form a five- or six-membered aromatic or aliphatic ring; and

at least one phospholipid,

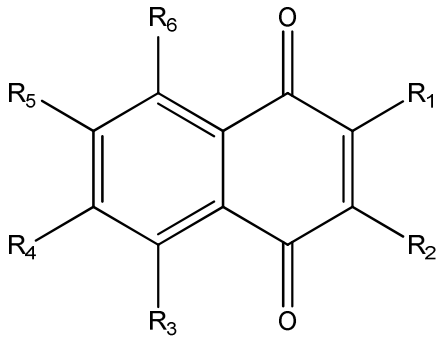
wherein a weight ratio of said at least one phospholipid to said compound in the composition is in a range of from 10:1 to 1:10.

5. The composition of claim 4, further comprising liposomes.

6. The composition of any one of claims 4 to 5, further comprising at least one additional active agent selected from the group consisting of a vitamin, N-acetyl cysteine, an anticoagulant, an anti-inflammatory agent, an antipyretic agent, an antiviral agent, and a protease inhibitor.

7. The composition of any one of claims 4 to 6, being for use in the treatment of a coronavirus infection.

8. A compound represented by Formula I:



Formula I

wherein R_1-R_6 are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, heteroalicyclic, halo, hydroxy, alkoxy, aryloxy, thiohydroxy, thioalkoxy, thioaryloxy, sulfinyl, sulfonyl, sulfonate, sulfate, cyano, nitro, azide, phosphonyl, phosphinyl, carbonyl, thiocarbonyl, a urea group, a thiourea group, O-carbamyl, N-

carbamyl, O-thiocarbamyl, N-thiocarbamyl, S-thiocarbamyl, C-amido, N-amido, C-carboxy, O-carboxy, sulfonamido, guanyl, guanidinyl, hydrazine, hydrazide, thiohydrazide, and amino, or alternatively, R_1 and R_2 together form a five- or six-membered aromatic or aliphatic ring, for use in inhibiting a coronavirus 3CL protease.

9. The compound for use of claim 8, wherein the compound is shikonin or a glycoside of shikonin, or an ester thereof.

10. The compound for use of any one of claims 8 to 9, wherein said inhibiting is by administering the compound to a subject in need thereof.

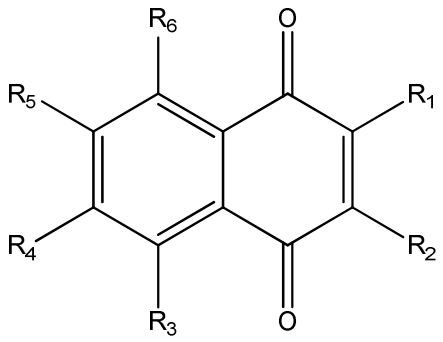
11. The compound for use of claim 10, further comprising inhibiting inflammation and/or autophagy in said subject.

12. The compound for use of claim 10 or 11, wherein the compound is part of a composition which further comprises phospholipids, and a weight ratio of said phospholipids to the compound in said composition is in a range of from 10:1 to 1:10.

13. The compound for use of any one of claims 10 to 12, wherein the compound is part of a composition which further comprises liposomes.

14. A compound that exhibits at least two of:
(i) inhibition of an activity of a 3CL protease of said coronavirus;
(ii) inhibition of inflammation in said subject; and
(iii) inhibition of autophagy in said subject,
for use in treating a coronavirus infection in a subject in need thereof.

15. The compound for use of claim 14, being represented by Formula I:



Formula I

wherein R_1-R_6 are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, heteroalicyclic, halo, hydroxy, alkoxy, aryloxy, thiohydroxy, thioalkoxy, thioaryloxy, sulfinyl, sulfonyl, sulfonate, sulfate, cyano, nitro, azide, phosphonyl, phosphinyl, carbonyl, thiocarbonyl, a urea group, a thiourea group, O-carbamyl, N-carbamyl, O-thiocarbamyl, N-thiocarbamyl, S-thiocarbamyl, C-amido, N-amido, C-carboxy, O-carboxy, sulfonamido, guanyl, guanidinyl, hydrazine, hydrazide, thiohydrazide, and amino, or alternatively, R_1 and R_2 together form a five- or six-membered aromatic or aliphatic ring.