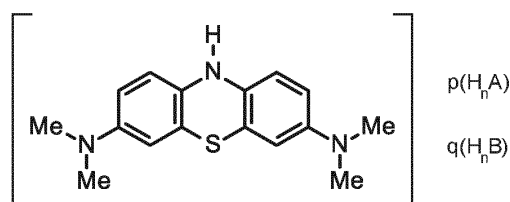


Claims

1. A method of therapeutic treatment of COVID-19 in a subject,
 5 which method comprises administering to said subject a methylthioninium (MT)-
 containing compound,
 wherein said administration provides a total daily oral dose of between more than
 30 to 250 mg of MT to the subject per day, optionally split into 2 or more doses,
 or wherein said administration provides a total daily intravenous (IV) dose of
 10 between 10 and 200 mg of MT to the subject per day,
 wherein the MT-containing compound is an LMTX compound of the following
 formula:



15 wherein each of H_nA and H_nB (where present) are protic acids which may be the same or
 different,
 and wherein $p = 1$ or 2 ; $q = 0$ or 1 ; $n = 1$ or 2 ; $(p + q) \times n = 2$,
 or a hydrate or solvate thereof.

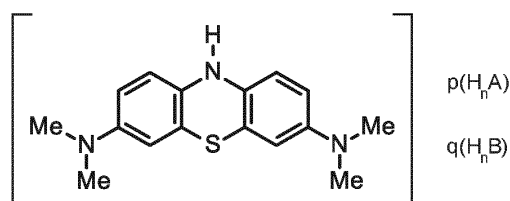
20 2. A method as claimed in claim 1 wherein the subject is a human who has been
 diagnosed with COVID-19, or wherein said method comprises making said diagnosis.

25 3. A method as claimed in claim 2 wherein the subject is characterised by having
 definite evidence of SARS-CoV-2 infection plus one, two or all of:
 (1) requiring medical care for COVID-19;
 (2) having an SpO_2 less than 95% on room air;
 (3) having radiographic evidence of pulmonary infiltrates.

30 ***

35 4. A method of prophylactic treatment of COVID-19 in a subject,
 which method comprises administering to said subject a methylthioninium (MT)-
 containing compound,
 wherein said administration provides a total daily oral dose of between more than
 30 to 250mg of MT to the subject per day, optionally split into 2 or more doses,
 or wherein said administration provides a total daily intravenous (IV) dose of
 40 between 10 and 200 mg of MT to the subject per day,
 wherein the MT-containing compound is an LMTX compound of the following
 formula:

- 33 -



wherein each of H_nA and H_nB (where present) are protic acids which may be the same or different,

and wherein $p = 1$ or 2 ; $q = 0$ or 1 ; $n = 1$ or 2 ; $(p + q) \times n = 2$,
or a hydrate or solvate thereof.

5. A method as claimed in claim 4 wherein the subject is a human who has been assessed as having suspected or probable COVID-19, and is optionally selected from: a subject who has been in close contact with one or more COVID-19 cases; a subject who is at least 65 years old; a subject living in a nursing home, care home, or long-term care facility; a subject with an underlying medical condition which increases the likelihood of adverse effects from COVID-19.

6. A method as claimed in any one of claims 1 to 5 wherein the total daily oral dose is:
(i) greater than 35, 40, 50, or 60 mg and less than or equal to 250 mg of MT to the subject per day; and/or
(ii) greater than or equal to about 30.5, 30.6, 31, 35, 37.5, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 120, 125, 130, 140, 150, 160, 170, 180, 190 or 200 mg MT.

7. A method as claimed in any one of claims 1 to 6 wherein the total daily oral dose is about 60, 75, 120, or 150 mg MT, which is optionally split twice a day or three times a day.

8. A method as claimed in any one of claims 1 to 5 wherein the total daily IV dose is between 26 and 200 mg of MT to the subject per day.

9. A method as claimed in any one of claims 1 to 5 wherein the total daily IV dose is:
(i) about 10, 11, 12, 13, 14, 15, 20, 25, 30, 35, 40, 45, 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190 or 200 mg/day by continuous dosing.
(ii) about, 20, 25, 30, 35, 40, 45, 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, 150 mg/day by bolus dosing.

- 34 -

10 A method as claimed in any one of claims 1 to 9 wherein the treatment is combined with a second agent.

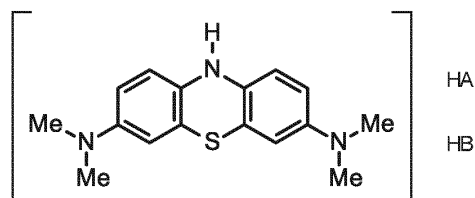
11 A method as claimed in claim 10 wherein the second agent is selected from:
5 chloroquine or hydroxychloroquine; lopinavir-ritonavir; arbidol; azithromycin, remdesivir, favipiravir, actemra; dexamethasone; convalescent plasma; a SARS-CoV-2-neutralizing antibody.

12 A method as claimed in claim 10 or claim 11 wherein the MT-containing
10 compound and the second agent are administered sequentially within 12 hours of each other.

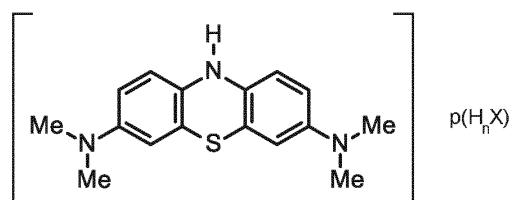
13 A method as claimed in any one of claims 10 to 12 wherein the subject is pre-
15 treated with the second agent prior to commencement of the treatment with the MT-containing compound.

14 A method as claimed in claim 10 or claim 11 wherein the MT-containing
20 compound and the second agent are administered simultaneously, optionally within a single dosage unit.

15. A method as claimed in any one of claims 1 to 14 wherein the MT-containing
25 compound has the following formula, where HA and HB are different mono-protic acids:



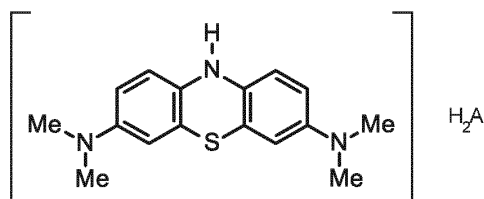
16. A method as claimed in any one of claims 1 to 14 wherein the MT-containing
30 compound has the following formula:



wherein each of H_nX is a protic acid.

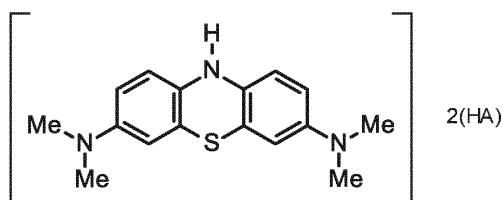
- 35 -

17. A method as claimed in any one of claims 1 to 14 wherein the MT-containing compound has the following formula and H₂A is a di-protic acid:



5

18. A method as claimed in claim 16 wherein the MT-containing compound has the following formula and is a bis-monoprotic acid:



10

19. A method as claimed in any one of claims 1 to 18 wherein the or each protic acid is an inorganic acid.

20. A method as claimed in claim 19 wherein each protic acid is a hydrohalide acid.

15

21. A method as claimed in claim 19 wherein the or each protic acid is selected from HCl; HBr; HNO₃; H₂SO₄.

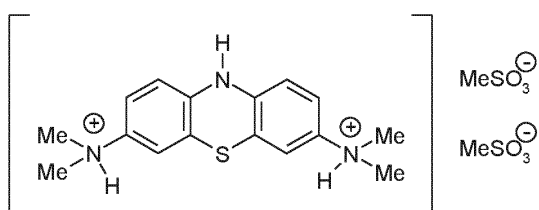
22. A method as claimed in any one of claims 1 to 18 wherein the or each protic acid is an organic acid.

20

23. A method as claimed in claim 22 wherein the or each protic acid is selected from H₂CO₃; CH₃COOH; methanesulfonic acid, 1,2-ethanedisulfonic acid, ethansulfonic acid, naphthalenedisulfonic acid, p-toluenesulfonic acid.

25

24. A method as claimed in any one of claims 1 to 18, or claim 23 wherein the MT-containing compound is LMTM:

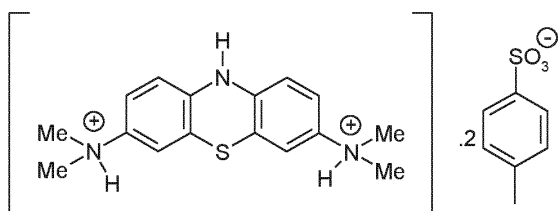
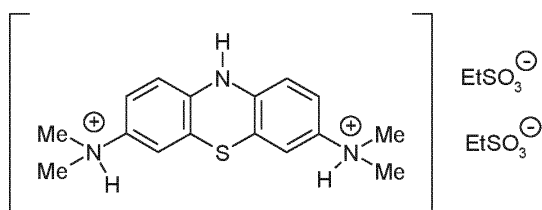


25. A method as claimed in claim 24 wherein the total daily dose of LMTM is at least 52 mg/day.

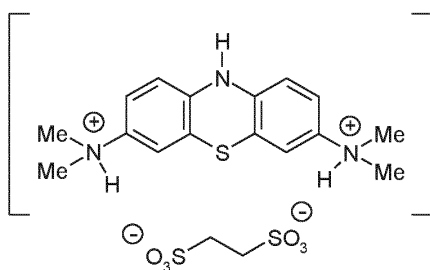
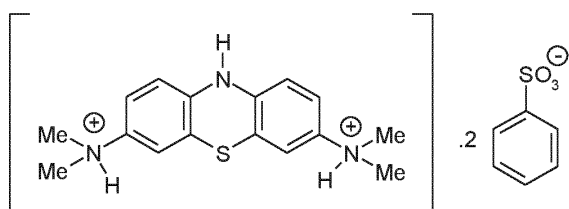
5 26. A method as claimed in claim 25 wherein the dose of LMTM is about 125 mg/once per day.

27. A method as claimed in any one of claims 1 to 18 wherein the MT-containing compound is selected from the list consisting of:

10

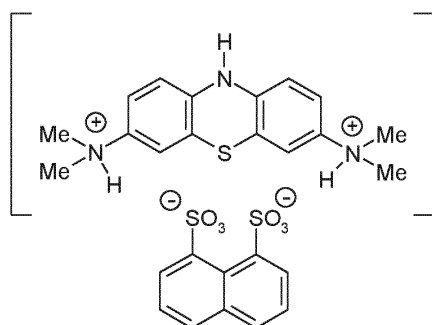
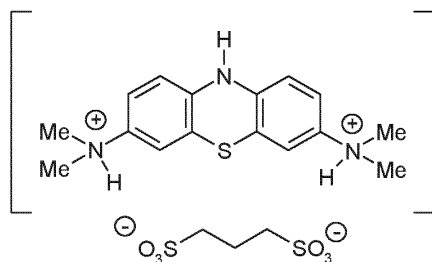


15



20

- 37 -



5

28. A method as claimed in any one of claims 1 to 27 wherein the treatment with the MT compound is such as to achieve one or more of the following in the subject:

- (i) enhanced mitochondrial function;
 (ii) enhanced blood oxygen capacity;
 (iii) improved CNS sequelae arising from COVID-19.

15

29. An MT-containing compound as defined in any one of claims 1 to 28, for use in a method of treatment as defined in any one of claims 1 to 28.

20

30. Use of an MT-containing compound as defined in any one of claims 1 to 28, in the manufacture of a medicament for use in a method of treatment as defined in any one of claims 1 to 28.