CLAIMS

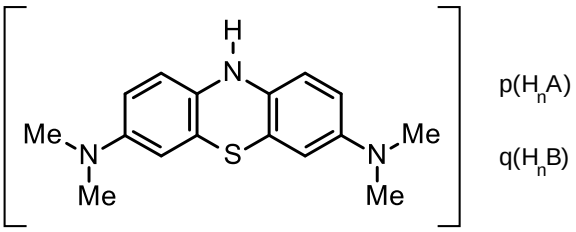
1. Use of an MT-containing compound in the manufacture of a medicament for use in a~~A~~ method of therapeutic or prophylactic treatment of COVID-19 in a subject,

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 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 between 10 and 200 mg of MT to the subject per day,

wherein the MT-containing compound ~~is an LMTX compound of~~ has the following formula:



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) × n = 2,
or a hydrate or solvate thereof.

2. ~~A method~~The use 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.

3 ~~A method~~The use 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 SpO2 less than 95% on room air;
(3) having radiographic evidence of pulmonary infiltrates.

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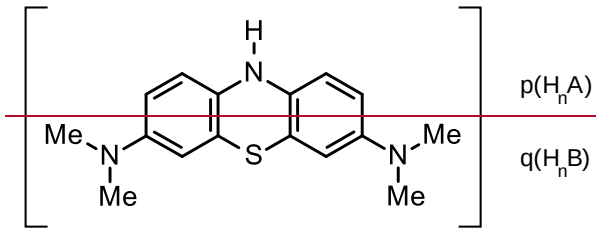
~~4. A method of prophylactic treatment of COVID-19 in a subject,~~

~~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 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:~~



~~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) × 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.~~
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4~~6~~. ~~A method~~The use as claimed in any one of claims 1 to 3~~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.

5~~7~~ ~~A method~~The use as claimed in any one of claims 1 to 4~~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.

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6~~8~~. ~~A method~~The use as claimed in any one of claims 1 to 3~~5~~ wherein the total daily IV dose is between 26 and 200 mg of MT to the subject per day.

7~~9~~. ~~A method~~The use as claimed in any one of claims 1 to 3~~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.

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8~~10~~ ~~A method~~The use as claimed in any one of claims 1 to 7~~9~~ wherein the treatment is combined with a second agent.

9~~11~~ ~~A method~~The use as claimed in claim 8~~10~~ wherein the second agent is selected from: chloroquine or hydroxychloroquine; lopinavir-ritonavir; arbidol; azithromycin, remdesivir, favipiravir, actemra; dexamethasone; convalescent plasma; a SARS-CoV-2-neutralizing antibody.

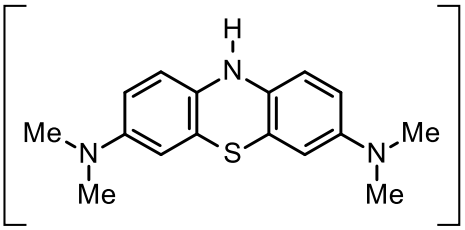
10~~12~~ ~~A method~~The use as claimed in claim 8~~10~~ or claim 9~~11~~ wherein the MT-containing compound and the second agent are administered sequentially within 12 hours of each other.

11~~13~~ ~~A method~~The use as claimed in any one of claims 8~~10~~ to 10~~12~~ wherein the subject is pre-treated with the second agent prior to commencement of the treatment with the MT-containing compound.

12~~14~~ ~~A method~~The use as claimed in claim 8~~10~~ or claim 9~~11~~ wherein the MT-containing compound and the second agent are administered simultaneously, optionally within a single dosage unit.

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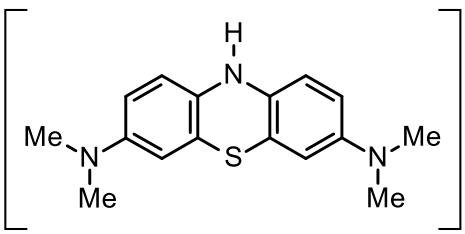
13~~15~~. ~~A method~~The use as claimed in any one of claims 1 to 12~~14~~ wherein the MT-containing compound has the following formula, where HA and HB are different mono-protic acids:



HA

HB

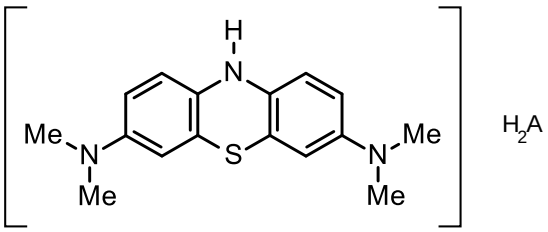
14~~16~~. ~~A method~~The use as claimed in any one of claims 1 to 12~~14~~ wherein the MT-containing compound has the following formula:



$p(H_nX)$

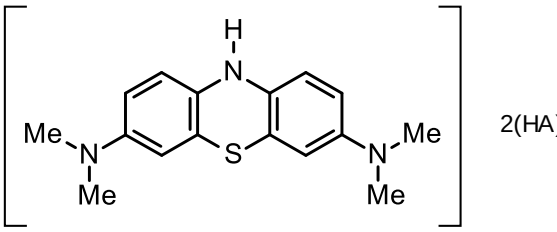
wherein each of H_nX is a protic acid.

1517. ~~A method~~The use as claimed in any one of claims 1 to 1214 ~~4~~ wherein the MT-containing compound has the following formula and H_2A is a di-protic acid:



H_2A

1618. ~~A method~~The use as claimed in claim 1416 ~~6~~ wherein the MT-containing compound has the following formula and is a bis-monoprotic acid:



2(HA)

1719. ~~A method~~The use as claimed in any one of claims 1 to 1618 ~~8~~ wherein the or each protic acid is an inorganic acid.

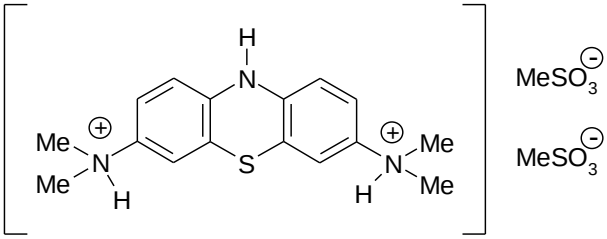
1820. ~~A method~~The use as claimed in claim 1719 ~~9~~ wherein each protic acid is a hydrohalide acid.

1921. ~~A method~~The use as claimed in claim 1719 ~~9~~ wherein the or each protic acid is selected from HCl; HBr; HNO_3; H_2SO_4.

2022. ~~A method~~The use as claimed in any one of claims 1 to 1618 ~~8~~ wherein the or each protic acid is an organic acid.

2123. ~~A method~~The use as claimed in claim 2022 ~~2~~ wherein the or each protic acid is selected from H_2CO_3; CH_3COOH; methanesulfonic acid, 1,2-ethanedisulfonic acid, ethansulfonic acid, naphthalenedisulfonic acid, p-toluenesulfonic acid.

2224. ~~A method~~The use as claimed in any one of claims 1 to 1618 ~~8~~, or claim 2123 ~~3~~ wherein the MT-containing compound is LMTM:



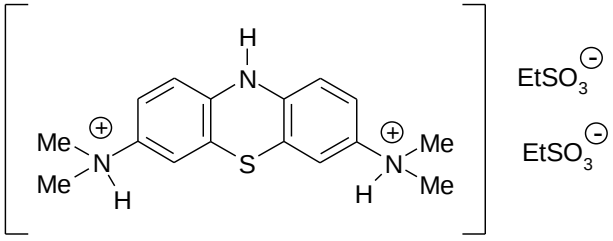
$MeSO_3^{\ominus}$

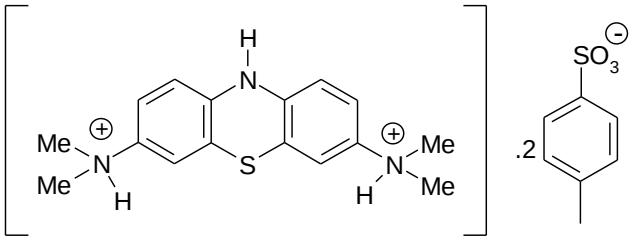
$MeSO_3^{\ominus}$

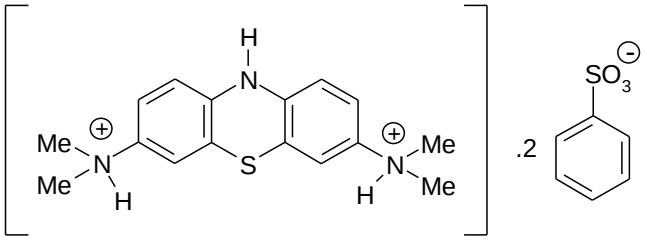
2325. ~~A method~~The use as claimed in claim 2224 wherein the total daily dose of LMTM is at least 52 mg/day.

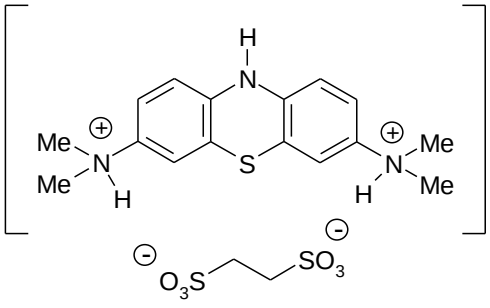
2426. ~~A method~~The use as claimed in claim 2325 wherein the dose of LMTM is about 125 mg/once per day.

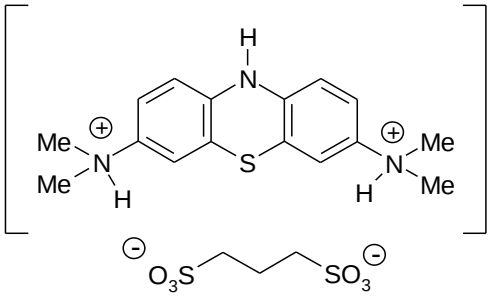
2527. ~~A method~~The use as claimed in any one of claims 1 to 1218 wherein the MT-containing compound is selected from the list consisting of:

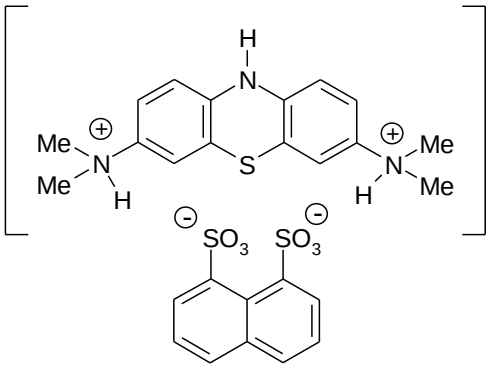












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26~~28~~. ~~A method~~The use as claimed in any one of claims 1 to ~~27~~ 25, wherein the treatment with the MT compound is such as to achieve one or more of the following in the subject:
(i) enhanced mitochondrial function;
(ii) enhanced blood oxygen capacity;
(iii) improved CNS sequelae arising from COVID-19.

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~~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.~~

~~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.~~