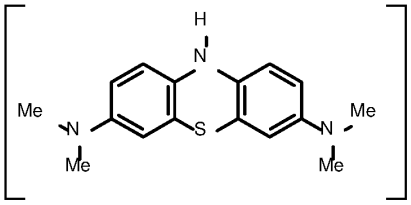
Claims

1 A method of increasing the level of synaptophysin in the brain of a mammalian subject,

which method comprises orally administering to said subject a methylthioninium (MT)-containing compound,

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,

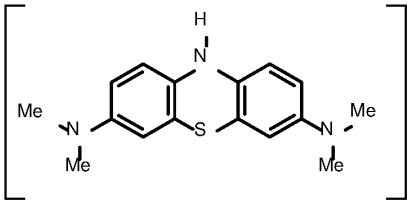
or a hydrate or solvate thereof.

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2 A method of therapeutic treatment a synaptopathy disorder in a subject which disorder is selected from the list consisting of: schizophrenia; cerebral ischemia; Multiple sclerosis (MS); depression; epilepsy; Startle syndrome; Tourette's syndrome; Autism spectrum disorders (ASD); Focal hand dystonia;; Experimental allergic encephalitis (EAE); Glaucoma; late onset Alzheimer's disease synaptic dysfunction type; a Lysozomal storage disease not associated with tau pathology

which method comprises orally administering to said subject a methylthioninium (MT)-containing compound,

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.

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3 A method as claimed in claim 1 wherein the treatment is combined with a further therapeutic agent for that disorder.

4. A method as claimed in claim 1 or claim 2 wherein the total daily dose is between 2 and 100 mg of MT, optionally 10-60 mg, to the subject per day, optionally split into 2 or more doses.

5 A method as claimed in claim 4 wherein the total daily dose is from around any of 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 mg to around any of 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60 mg.

6. A method as claimed in claim 4 wherein the total daily dose is between 20 and 40mg.

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7 A method as claimed in claim 4 wherein the total daily dose is about 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40 mg.

8 A method as claimed in any one of claims 1 to 7 wherein the total daily dose of the LMTX compound is administered as a split dose twice a day or three times a day.

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9 A method as claimed in any one of claims 1 to 8 wherein the subject has not historically received treatment with a neurotransmission modifying compound which is a modifier of the activity of acetylcholine or glutamate neurotransmitters.

10 A method as claimed in any one of claims 1 to 8 wherein the subject has historically received treatment with the neurotransmission modifying compound which is a modifier of the activity of acetylcholine or glutamate neurotransmitters, but ceased that treatment at least 1, 2, 3, 4, 5, 6, 7 days, or 2, 3, 4, 5, 6, 7, 8 weeks prior to treatment with the LMTX compound.

11 A method as claimed in any one of claims 1 to 8 wherein the subject is selected as one who is receiving treatment with the neurotransmission modifying compound which is a modifier of the activity of acetylcholine or glutamate neurotransmitters, wherein said treatment is discontinued prior to treatment with the LMTX compound.

12 A method as claimed in any one of claims 1 to 11 wherein the therapeutic treatment is not combined with a neurotransmission modifying compound which is a modifier of the activity of acetylcholine or glutamate neurotransmitters.

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13 A method as claimed in any one of claims 9 to 12, wherein the neurotransmission modifying compound is an acetylcholinesterase inhibitor.

14 A method as claimed in any one of claims 9 to 13, wherein the neurotransmission modifying compound is selected from donepezil; rivastigmine; and galantamine.

15 A method as claimed in any one of claims 9 to 12, wherein the neurotransmission modifying compound is an N-methyl-D-aspartate receptor (NMDA) receptor antagonist.

16 A method as claimed in any one of claims 9 to 12 or claim 15, wherein the neurotransmission modifying compound is memantine.

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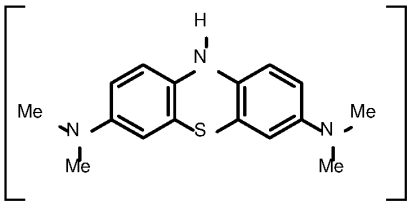
17 A method as claimed in any one of claims 1 to 16 wherein the subject is a human who has been diagnosed as having said synaptopathy disorder, or wherein said method comprises making said diagnosis.

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18 A method of prophylactic treatment of a synaptopathy disorder in a subject, which disorder is selected from the list consisting of: schizophrenia; cerebral ischemia; Multiple sclerosis (MS); depression; epilepsy; Startle syndrome; Tourette's syndrome; Autism spectrum disorders (ASD); Focal hand dystonia;; Experimental allergic encephalitis (EAE); Glaucoma; late onset Alzheimer's disease synaptic dysfunction type; a Lysozomal storage disease not associated with tau pathology,

which method comprises orally administering to said subject a methylthioninium (MT)-containing compound,

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.

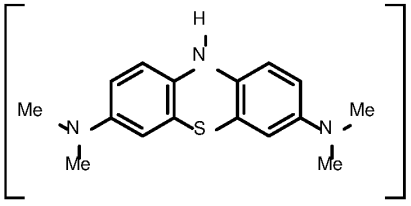
19 A method as claimed in claim 18 wherein the treatment is combined with a further prophylactic agent for that disorder.

20 A method as claimed in claim 18 wherein the dose is as defined in any one of claims 4 to 8 and/or the subject is as defined in any one of claims 9 to 11.

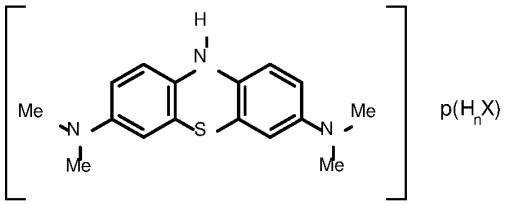
21 A method as claimed in any one of claims 18 to 20 wherein the subject is a human who has been assessed as being susceptible to, or at risk of, the disorder, optionally based on familial or genetic or other data.

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22 A method as claimed in any one of claims 1 to 21 wherein the LTMX compound has the following formula, where HA and HB are different mono-protic acids:

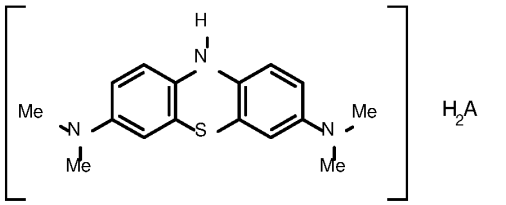


23 A method as claimed in claim 22 wherein the LTMX compound has the following formula:

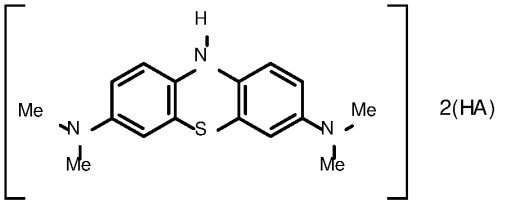


wherein each of H_nX is a protic acid.

24 A method as claimed in claim 22 wherein the LTMX compound has the following formula and H_2A is a di-protic acid:



25 A method as claimed in claim 23 wherein the LTMX compound has the following formula and is a bis-monoprotic acid:



26 A method as claimed in any one of claims 22 to 25 wherein the or each protic acid is an inorganic acid.

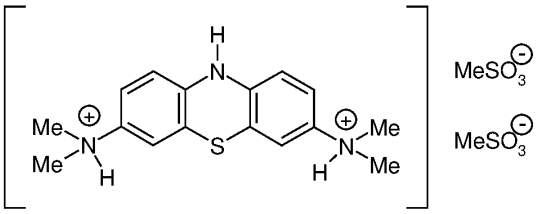
27 A method as claimed in claim 26 wherein each protic acid is a hydrohalide acid.

28 A method as claimed in claim 26 wherein the or each protic acid is selected from HCl; HBr; HNO_3; H_2SO_4.

29 A method as claimed in any one of claims 22 to 25 wherein the or each protic acid is an organic acid.

30 A method as claimed in claim 29 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.

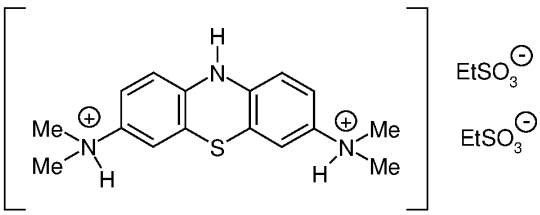
31 A method as claimed in any one of claims 1 to 30 wherein the LTMX compound is LMTM:

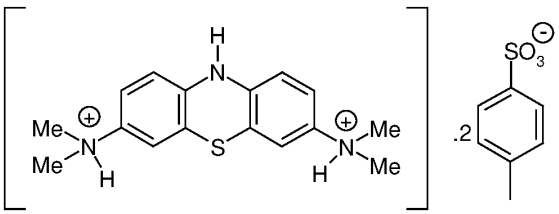


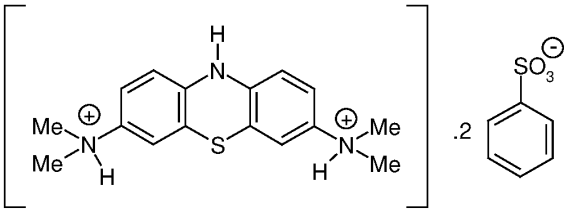
32 A method as claimed in claim 31 wherein the total daily dose of LMTM is around 34 to 67, 34 to 100, 34 to 134, or 34 to 167 mg/day.

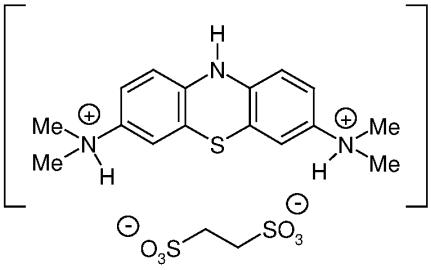
33 A method as claimed in claim 32 wherein the dose of LMTM is about 34, 38, 67, or 100 mg/once per day.

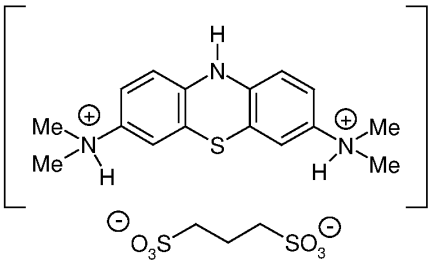
34 A method as claimed in any one of claims 1 to 21 wherein the LTMX compound is selected from the list consisting of:

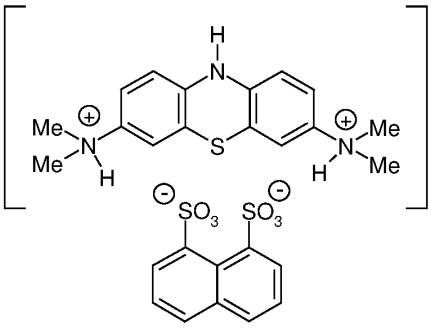












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35 A method as claimed in any one of claims 1 to 34 wherein the LTMX compound is provided as a pharmaceutical composition comprising the LMTX compound and a pharmaceutically acceptable carrier or diluent in the form of a dosage unit.

36 A method as claimed in claim 35 wherein the amount of MT in the unit is about 4, 5, 6, 7, 8, 9, 10, 20, or 30 to about 40, 50 or 60 mg.

37 A method as claimed in claim 35 wherein the dosage unit comprises about 34 to 67 mg, 34 to 100, 34 to 134, or 34 to 167 LMTM.

38 A method as claimed in any one of claims 35 to 37 wherein the composition is a tablet or capsule.

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39 A container comprising:
(i) a plurality of dosage units as defined in any one of claims 35 to 38;
(ii) a label and/or instructions for their use according to a method of treatment as defined in any one of claims 1 to 34.

40 A container as claimed in claim 39, wherein the container comprises dosage units, and the dosage units are present in a blister pack which is substantially moisture-impervious.

41 A container as claimed in claim 39 or claim 40 wherein the label or instructions provide information regarding the disorder for which the composition is intended.

42 A container as claimed in any one of claims 39 to 41 wherein the label or instructions provide information regarding the maximum permitted daily dosage of the dosage units.

43 A container as claimed in any one of claims 39 to 42 wherein the label or instructions provide information regarding the suggested duration of the treatment.

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44 An LTMX compound or composition as defined in any one of claims 1 to 34, for use in a method of treatment as defined in any one of claims 1 to 38.

45 Use of an LTMX compound or composition as defined in any one of claims 1 to 34, in the manufacture of a medicament for use in a method of treatment as defined in any one of claims 1 to 38.