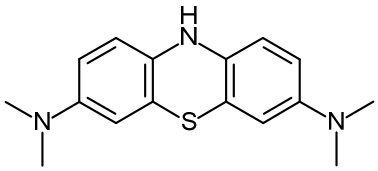
Claims

1. Use of a first compound which is a methylthioninium (MT) compound in combination with a second compound, which second compound directly modifies the activity of acetylcholine or glutamate neurotransmitters such as to modify synaptic neurotransmission in the brain of a subject, in the manufacture of a medicament for treatment of an FTLD syndrome in the subject,

wherein the MT compound is a salt of:



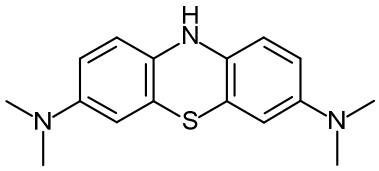
(LMT)

or a hydrate or solvate thereof, and

wherein the second compound is either an acetylcholinesterase inhibitor or an NMDA receptor antagonist.

2. Use of a methylthioninium (MT) compound in the manufacture of a medicament for use in the treatment of an FTLD syndrome in a subject, which treatment further comprises use of a second compound, which second compound directly modifies the activity of acetylcholine or glutamate neurotransmitters such as to modify synaptic neurotransmission in the brain of the subject,

wherein the MT compound is a salt of:



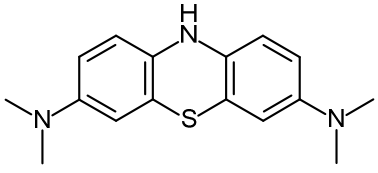
(LMT)

or a hydrate or solvate thereof, and

wherein the second compound is either an acetylcholinesterase inhibitor or an NMDA receptor antagonist.

3. Use of a compound which directly modifies the activity of acetylcholine or glutamate neurotransmitters such as to modify synaptic neurotransmission in the brain, in the manufacture of a medicament for use in the treatment of an FTLD syndrome in a subject, which treatment further comprises use of a methylthioninium (MT) compound and the compound which directly modifies synaptic neurotransmission in the brain of the subject

wherein the MT compound is a salt of:



(LMT)

or a hydrate or solvate thereof, and

wherein the second compound is either an acetylcholinesterase inhibitor or an NMDA receptor antagonist.

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4. Use as claimed in any one of claims 1 to 3, wherein:
(a) the MT compound and the neurotransmission modifying compound are administered sequentially within 12 hours of each other; or
(b) the subject is pre-treated with the neurotransmission modifying compound prior to commencement of the treatment with the MT compound; or
(c) the MT compound and the neurotransmission modifying compound are administered simultaneously, optionally within a single dosage unit.

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5. Use as claimed in any one of claims 1 to 4, wherein either:
(a) the subject is one who has been diagnosed as having said FTLD syndrome, or wherein said method comprises making said diagnosis, and the treatment is therapeutic; or
(b) the subject is one who is identified to be at risk of an FTLD syndrome based on familial or genetic analysis, and the treatment is prophylactic.

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6. Use as claimed in any one of claims 1 to 5, wherein the neurotransmission modifying compound is an acetylcholinesterase inhibitor.

7. Use as claimed in claim 6, wherein the neurotransmission modifying compound is selected from: donepezil; rivastigmine; and galantamine.

8. Use as claimed in any one of claims 1 to 5, wherein the neurotransmission modifying compound is an NMDA receptor antagonist.

9. Use as claimed in claim 8, wherein the neurotransmission modifying compound is memantine

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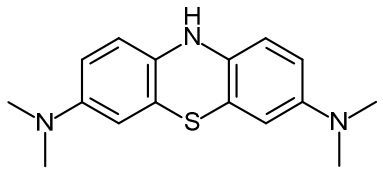
10. Use as claimed in any one of claims 1 to 9, wherein the MT compound is a salt of:



(LMT)

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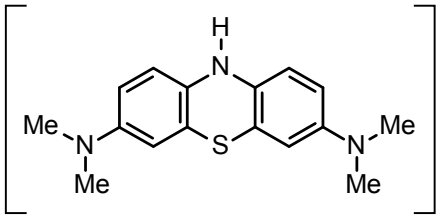
11. Use as claimed in claim 10, wherein:

(a) the MT compound has the following formula, where HA and HB are different mono-protic acids:



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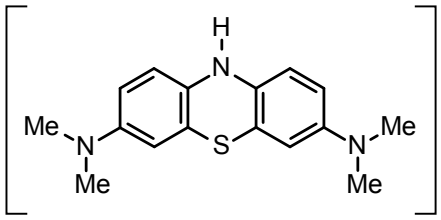
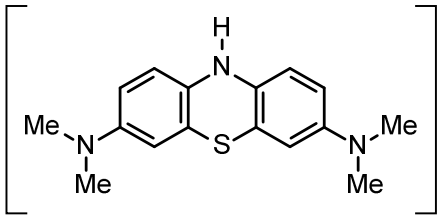
or

(b) the MT compound has the following formula:

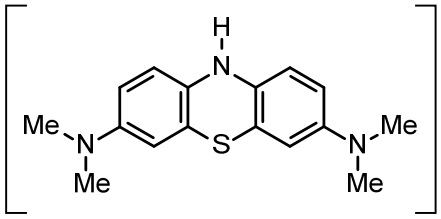


wherein each of H_nX is a protic acid, or

(c) the MT compound has the following formula and H_2A is a di-protic acid:



12. Use as claimed in claim 11, wherein the MT compound has the following formula and is a bis-monoprotic acid:

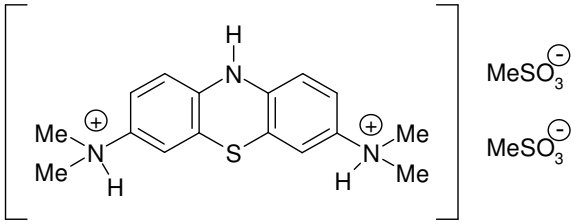


13. Use as claimed in claim 11 or claim 12, wherein the or each protic acid is an inorganic acid.

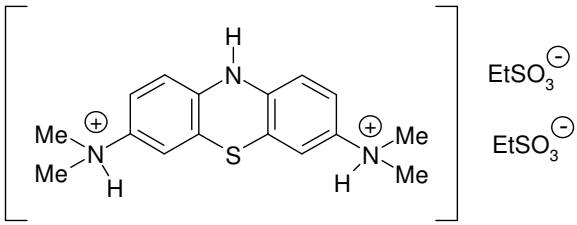
14. Use as claimed in claim 11 or claim 12, wherein the or each protic acid is an organic acid.

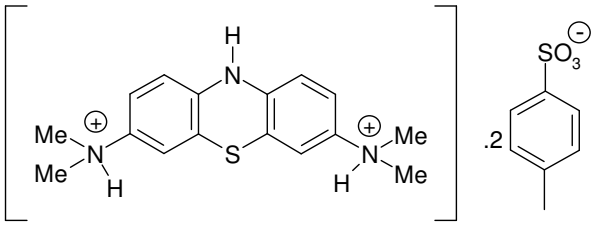
15. Use as claimed in claim 14, wherein the or each protic acid is selected from H_2CO_3; CH_3COOH; methanesulfonic acid, 1,2-ethanedisulfonic acid, ethansulfonic acid, naphthalenedisulfonic acid, p-toluenesulfonic acid.

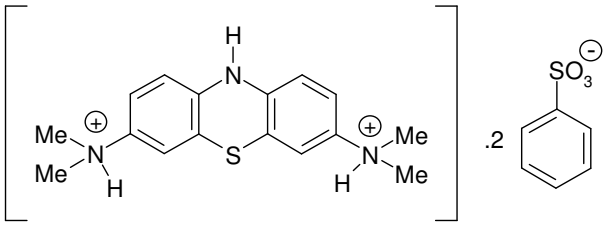
16. Use as claimed in claim 15, wherein the MT compound is LMTM:

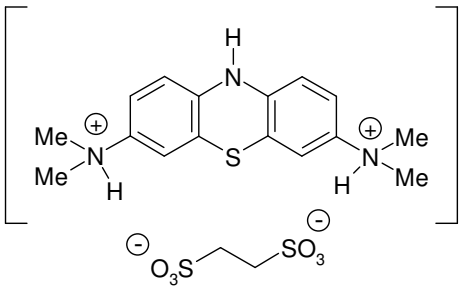


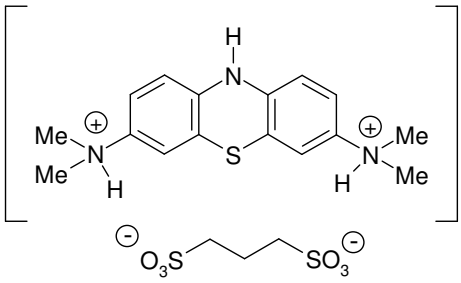
17. Use as claimed in claim 14, wherein the MT compound is selected from the list consisting of:

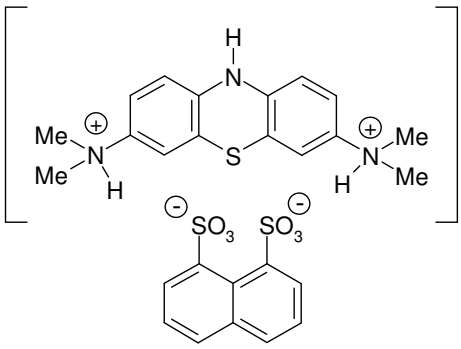












18 Use as claimed in any one of claims 1 to 17, wherein the FTLD syndrome is FTLD with tau pathology or FTLD with TAR DNA-binding protein 43 pathology.

19. Use as claimed in any one of claims 1 to 18, wherein the FTLD syndrome is selected from behavioral-variant frontotemporal dementia, primary progressive aphasia, and semantic dementia

20 Use as claimed in claim 19, wherein the FTLD syndrome is behavioral-variant frontotemporal dementia.

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21. Use as claimed in any one of claims 1 to 20 wherein the total daily dose of MT provided by the MT compound is from around any of 1 to 350 mg; 2 to 300 mg; 4 to 250 mg; 6 to 240 mg; 7 to 220 mg, 3 to 70 mg.
22. Use as claimed any one of claims 1 to 20 wherein the total daily dose of MT provided by the MT compound is from around any of 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4 mg to around any of 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 mg.

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23. Use as claimed in any one of claims 1 to 22 wherein the total daily dose of the respective neurotransmission modifying compound is as follows: Donepezil: between 5 and 23 mg; Rivastigmine: between 3 and 12 mg; Galantamine: between 4 and 24 mg; Memantine: between 5 and 20 mg.