Claims

1 A pharmaceutical composition which is a film-coated solid tablet, the table comprising a diaminophenothiazine (DAPTZ) compound as active ingredient in a gastro-retentive platform,

wherein the DAPTZ compound is selected from an oxidized methylthioninium (MT^+) compound or a leucomethylthioninium (LMT) compound or a combination thereof,

wherein the composition comprises a rapid release matrix including a hydrophilic macromolecule and is adapted to float in the stomach,

where in the composition further comprises one or more other accompanying active ingredients, additives, excipients, diluents, binders, lubricants, disintegrators, fillers, stabilizers, surfactants, antioxidants, or combinations thereof,

wherein the amount of MT^+ or LMT in the composition is equal to or between 1 and 30mg, more preferably about 1 to 20, about 1 to 10, about 2 to 6 mg, about 2 to 5 mg, more preferably about or equal to 4 mg.

2 A composition as claimed in claim 1, wherein the composition:
(i) has a floating time of at least 120 seconds, more preferably at least 3, 4 or 5 minutes when placed on potable water, and/or
(ii) has a disintegration time of less than 5 minutes, preferably less than 4 minutes, or less than 3 minutes, and/or
(iii) has a disintegration time in 50 to 200% of the floating time.

3 A composition as claimed in any one of claims 1 to 2, wherein the composition:
(i) is generally circular with a diameter of about 4 to 6 mm, optionally about 5 mm, and a thickness of 2 to 3mm, optionally 2.2 to 2.6 mm, and/or
(ii) has a hardness of 3 to 9 kp, preferably about 6 to 7 kp, and/or
(iii) has a total weight of equal to or between 30 and 60mg, optionally 40 and 60 mg, 50 and 60 mg, optionally about 53 mg, 54 mg, 55 mg, 56 mg, 56 mg, 58 mg, 59 mg, 60 mg, and/or
(iv) has a bulk density of less than 1.5 g/cm^3, optionally about 0.8 to 1.5 g/cm^3, optionally about 1.0, 1.1, 1.2, 1.3 or 1.4. e.g. about 1.2, 1.3 or 1.4 g/cm^3.

4 A composition as claimed in any one of claims 1 to 3, wherein the composition: (i) comprises a diluent which is optionally mannitol and/or microcrystalline cellulose, and/or
(ii) comprises a disintegrant which is optionally crospovidone, and/or
(iii) comprises a lubricant which is optionally magnesium stearate, and/or
(iv) has a friability of less 1%.

5 A composition as claimed in any one of claims 1 to 4, wherein:
(i) the hydrophilic macromolecule is a hydrophilic polymer which is Poly(vinyl alcohol) part-hydrolysed (PVA) which is present in the film coating on the tablet,

wherein optionally the coating further comprises one or more of: talc, titanium dioxide, macrogel 3350, lecithin, colouring, which is optionally FD&C blue #2/indigo carmine aluminium lake (dialuminum;2-(3-hydroxy-5-sulfonato-1*H*-indol-2-yl)-3-oxoindole-5-sulfonate), and

wherein optionally the film coating is an Opadry ® II coating, and/or

(ii) the coating is 5 to 8% of the total tablet weight.

6 A process for the manufacture of the pharmaceutical composition according to any one of claims 1 to 5, which process comprises:

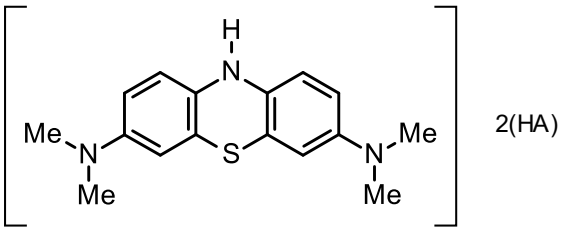
(i) compression or granulation of the DAPTZ compound with the one or more other accompanying active ingredients, additives, excipients, diluents, binders, lubricants, disintegrants, fillers, stabilizers, surfactants, antioxidants, if present;

(ii) applying the film coating to the tablets,

optionally wherein the step of applying a film coating is carried out by spray-coating the tablet core in a coating machine, wherein the coating machine and cores are optionally pre-heated to 42-52°C, and adjusting temperature of inlet air so the exhaust temperature is maintained between 42-52°C.

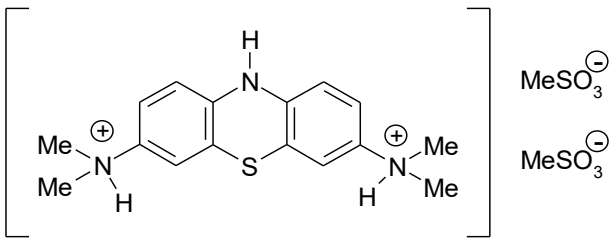
7 A pharmaceutical composition obtainable by the process of claim 6.

8 A composition or process as claimed in any one of claims 1 to 7 wherein the DAPTZ compound has the following formula wherein HA is a monoprotic acid:



2(HA)

9 A composition or process as claimed in claim 8 wherein the DAPTZ compound is LMTM:



10 A composition or process as claimed in any one of claims 1 to 7 wherein the DAPTZ compound is methylthioninium chloride, which is optionally polymorph A pentahydrate.

11 Use of a composition as claimed in any one of claims 1 to 6 or 8 to 10 in the manufacture of medicament for the treatment of a disease in a subject.

12 Use as claimed in claim 11 wherein the disease is a neurodegenerative disorder of protein aggregation.

13 Use as claimed in any one of claims 11 to 12 wherein the disorder is a tauopathy, wherein the disorder is optionally selected from the list consisting of: Pick's disease, progressive supranuclear palsy, frontotemporal dementia, FTD with parkinsonism linked to chromosome 17, frontotemporal lobar degeneration syndromes; disinhibition-dementia-parkinsonism-amyotrophy complex, pallido-ponto-nigral degeneration, Guam-ALS syndrome, pallido nigro luysian degeneration, cortico-basal degeneration, dementia with argyrophilic grains, dementia pugilistica or chronic traumatic encephalopathy, Down's syndrome, subacute sclerosing panencephalitis, mild cognitive impairment, Niemann-Pick disease, type C, Sanfilippo syndrome type B, or a myotonic dystrophy DM1 or DM2.

14 Use as claimed in claim 13 wherein the disorder is Alzheimer's disease or mild cognitive impairment.

15 Use as claimed in any one of claims 11 to 12 wherein the disorder is a polyglutamine disorder, such as Huntington's disease, spinal bulbar muscular atrophy, dentatorubropallidoluysian atrophy or spinocerebellar ataxias; wherein the disorder is a TDP-43 proteinopathy, such as FTLD-TDP; wherein the disorder is a synucleinopathy, such as Parkinson's disease, dementia with Lewy bodies or multiple system atrophy; wherein the disorder is hereditary cerebral angiopathy; wherein the disorder is amyotrophic lateral sclerosis; or wherein the disorder is familial encephalopathy with neuronal inclusion bodies.