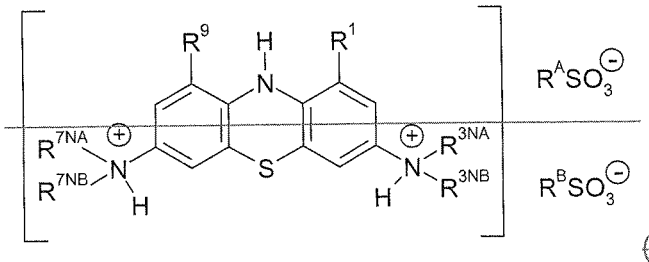
CLAIMS

1. A compound selected from compounds of general formula (I):



(I)

wherein:

each of R^1 and R^9 is independently selected from: -H, C_{1-4}alkyl, C_{2-4}alkenyl, and halogenated C_{1-4}alkyl;

each of R^{3NA} and R^{3NB} is independently selected from: -H, C_{1-4}alkyl, C_{2-4}alkenyl, and halogenated C_{1-4}alkyl;

each of R^{7NA} and R^{7NB} is independently selected from: -H, C_{1-4}alkyl, C_{2-4}alkenyl, and halogenated C_{1-4}alkyl;

and wherein:

each of R^A and R^B is independently selected from:

C_{1-4}alkyl, halogenated C_{1-4}alkyl, and C_{6-10}aryl;

or

R^A and R^B are linked to form a group selected from:

C_{1-6} alkylene and C_{6-10} arylene;

and pharmaceutically acceptable salts thereof.

2. A compound according to claim 1 wherein each of R^A and R^B is independently C_{1-4}alkyl.

3. A compound according to claim 1 wherein each of R^A and R^B is independently methyl.

4. A compound according to any one of claims 1 to 3 wherein each of R^1 and R^9 is independently -H.

5. A compound according to any one of claims 1 to 4 wherein each of R^{3NA} and R^{3NB} and is independently C_{1-4}alkyl.

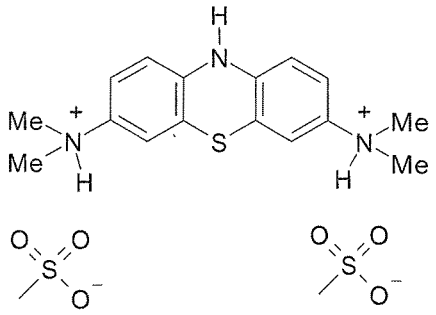
6. A compound according to claim 5 wherein each of R^{3NA} and R^{3NB} is independently methyl.

~~7. A compound according to any one of claims 1 to 6 wherein each of R^{7NA} and R^{7NB} is independently C_{1-4}alkyl.~~

~~8. A compound according to claim 7 wherein each of R^{7NA} and R^{7NB} is independently methyl.~~

CLAIMS

~~9~~1. Use of a ~~A~~ compound ~~according to claim 1~~ which is of the following formula:



or a pharmaceutically acceptable salt, solvate, or hydrate thereof~~.~~ in the manufacture of a medicament for use in the treatment or prophylaxis of a disease of protein aggregation.

~~10~~2. Use of a ~~A~~ compound according to ~~any one of~~ claim~~s~~ 1 ~~to 9~~, wherein the compound is in crystalline form.

~~11. A compound according to claim 9 in crystalline form, having a crystal structure as represented by Figures 11-16.~~

~~12~~3. Use of a ~~A~~ compound according to ~~any one of~~ claim~~s~~ 1 or claim 2 ~~to 11~~, wherein the compound is in substantially purified form.

~~13~~4. Use of a compound according to claim 1 or claim 2, wherein the medicament is a~~A~~ composition comprising the ~~a~~ compound ~~according to any one of claims 1 to 12~~ and a pharmaceutically acceptable carrier or diluent.

~~14. A process for preparing a pharmaceutical composition comprising admixing a compound according to any one of claims 1 to 12, and a pharmaceutically acceptable carrier or diluent.~~

~~15~~5. Use of a compound ~~A pharmaceutical composition~~ as claimed in claim ~~13~~ wherein said composition ~~which~~ is a pharmaceutical composition which is a solid dosage form comprising the compound ~~according to any one of claims 1 to 12~~ and at least one diluent suitable for dry compression.

~~16~~6. Use of a compound~~A composition~~ according to claim ~~15~~ wherein the solid dosage form is produced by direct compression.

~~17~~7. Use of a compound ~~A composition~~ according to claim ~~15~~ 5 wherein the solid dosage form is produced by dry granulation.

~~18~~8. Use of a compound ~~A composition~~ according to any one of claims 5 to 7~~15 to 17~~, wherein the solid dosage form dissolves to an extent of at least 80% within 30 minutes as evaluated by a standard pharmacopeial method as defined in United States Pharmacopeia (USP) General Chapter <711>.

~~19~~9. Use of a compound ~~A composition~~ according to any one of claims 5 to 8~~15 to 18~~, wherein said at least one diluent is selected from microcrystalline cellulose, lactose, mannitol, calcium salts such as, calcium phosphate dibasic, calcium sulphate, calcium carbonate, and sugars such as lactose, sucrose, dextrose and maltodextrin.

~~20~~10. Use of a compound ~~A composition~~ according to any one of claims 5 to 8~~15 to 19~~, further comprising at least one disintegrant.

~~21~~11. Use of a compound ~~A composition~~ according to claim 10~~20~~ wherein the disintegrant is selected from crosslinked polyvinylpyrrolidone (crospovidone), sodium starch glycolate, crosslinked sodium carboxymethyl cellulose (sodium croscarmellose), or pregelatinized starch.

~~22~~12. Use of a compound ~~A composition~~ according to any one of claims 5 to 11~~15 to 21~~ wherein the solid dosage form is film-coated.

~~23~~13. Use of a compound ~~A composition~~ according to any one of claims 5 to 12~~15 to 22~~ further comprising an acid having a pK1 of greater than 1.5.

~~24~~14. Use of a compound ~~A composition~~ according to claim 13~~23~~, wherein the acid is selected from maleic acid, phosphoric acid, ascorbic acid, sorbic acid, aspartic acid and sialic acid.

~~25~~15. Use of a compound ~~A composition~~ according to claim 13~~23~~ or claim 14~~24~~, further comprising a carrier selected from mannitol, a cellulosic material, a starch, or mixtures thereof.

~~26~~16. Use of a compound ~~A composition~~ according to any one of claims 5 to 15~~15 to 25~~ characterised in that said composition comprises particles of which more than 10% have a size greater than 10 microns.

~~27. A composition according to any one of claims 15 to 25 comprising a carrier having a particle shape which is averse to water, such as Elcema TM , ethylcellulose, mannitol, or Starch 1500 TM.~~

28. A free-flowing, cohesive powder comprising a compound according to any one of claims 1 to 12 and at least one diluent suitable for dry compression and optionally one or more other excipients, said powder being capable of being compressed into a solid dosage form.

29. A process as claimed in claim 14 for the manufacture of a pharmaceutical composition, which process comprises dry compression of an intimate powder mixture comprising the compound according to any one of claims 1 to 12 with at least one diluent suitable for dry compression and optionally one or more other excipients.

30. A process according to claim 29, wherein the process comprises a direct compression process wherein said compound, at least one diluent, and optional excipients are blended together in solid particulate form to create said intimate mixture and then compressed using a tablet machine.

31. A process according to claim 30, wherein said at least one diluent is selected from microcrystalline cellulose, lactose, mannitol, calcium salts such as, calcium phosphate dibasic, calcium sulphate, calcium carbonate, and sugars such as lactose, sucrose, dextrose and maltodextrin.

32. A process according to claim 30, wherein said at least one diluent is a granulated product prepared by moist granulation of one or more excipients.

33. A process according to claim 32, comprising a step of wet massing one or more excipients using a granulating fluid, and drying to form said granulated product.

34. A process according to claim 29, wherein the process comprises a dry granulation process wherein said compound, at least one diluent, and optional excipients are formed into a compressed mass, milled and then compressed using a tablet machine.

35. A process according to any one of claims 28 to 33 further comprising the step of applying a film coating to the resultant tablets.

36. A compound or composition according to any one of claims 1 to 12 or 15 to 27 for use in a method of treatment or prophylaxis of the human or animal body by therapy.

~~37. Use of a compound or composition according to any one of claims 1 to 12 or 15 to 27 in the manufacture of a medicament for use in the treatment or prophylaxis of a disease of protein aggregation.~~

3817. Use of a compound or composition according to any one of claims 1 to 1612 ~~or 15 to 27 in the manufacture of a medicament for use in the treatment or prophylaxis of a~~ wherein the disease of protein aggregation is aTDP-43 proteinopathy.

3918. Use of a compound ~~or composition~~ according to any one of claims 1 to 1612 ~~or 15 to 27 in the manufacture of a medicament for use in the treatment or prophylaxis of~~ wherein the disease of protein aggregation is a tauopathy.

4019. Use of a compound ~~or composition~~ according to any one of claims 1 to 1612 ~~or 15 to 27 in the manufacture of a medicament for use in the treatment or prophylaxis of~~ wherein the disease of protein aggregation is Alzheimer's disease ~~(AD)~~, Pick's disease, progressive supranuclear palsy (PSP), frontotemporal dementia (FTD), FTD with parkinsonism linked to chromosome 17, frontotemporal lobar degeneration (FTLD) 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, dementia with Lewy bodies, subacute sclerosing panencephalitis, mild cognitive impairment, Niemann-Pick disease, type C, Sanfilippo syndrome type B, myotonic dystrophies DM, DM1 or DM2 or amyotrophic lateral sclerosis (ALS).

4120. Use of a compound ~~or composition~~ according to claim 19 ~~any one of claims 1 to 12 or 15 to 27 in the manufacture of a medicament for use in the treatment or prophylaxis of~~ wherein the disease of protein aggregation is Alzheimer's disease.

4221 Use of a compound ~~or composition~~ according to any one of claims 1 to 1612 ~~or 15 to 27 in the manufacture of a medicament for use in the treatment or prophylaxis of~~ wherein the disease of protein aggregation is Parkinson's disease.

4322 Use of a compound or composition according to claim 19~~any one of claims 1 to 12 or 15 to 27 in the manufacture of a medicament for use in the treatment or prophylaxis of~~ wherein the disease of protein aggregation is PSP, ALS or FTLD.

4423. Use of a compound ~~or composition~~ according to any one of claims 1 to 1612 ~~or 15 to 27 in the manufacture of a medicament for use in the treatment or prophylaxis of~~ wherein the disease of protein aggregation is a polyglutamine disorder.

~~45~~24. Use of a compound ~~or composition~~ according to claim 2~~3~~44 ~~in the manufacture of a medicament for use in the treatment or prophylaxis of~~ wherein the disease of protein aggregation is Huntington's disease, spinal bulbar muscular atrophy, dentatorubropallidoluysian atrophy or spinocerebellar ataxias.

~~46. Use of a compound or composition according to any one of claims 1 to 12 or 15 to 27 in the manufacture of a medicament for use in the treatment or prophylaxis of skin cancer or melanoma; or a viral, bacterial or protozoal disease condition.~~

~~47. Use according to claim 46, wherein the viral, bacterial or protozoal disease is selected from Hepatitis C, HIV, West Nile Virus and malaria.~~

48. A method of reversing and/or inhibiting the aggregation of a protein comprising contacting the protein with an effective amount of a compound or composition according to any one of claims 1 to 12 or 15 to 27.

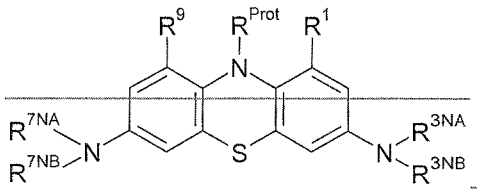
49. A method of inactivating a pathogen in a sample, comprising the steps of introducing a compound according to any one of claims 1 to 12 into the sample, and then exposing the sample to light.

50. A process for the preparation of a compound according to any one of claims 1 to 12 from a *N*-protected 3,7-diamino-10H-phenothiazine, comprising the steps of:

ring amino deprotection (DP); and

salt formation (SF).

51. A process according to claim 50, wherein the *N*-protected 3,7-diamino-10H-phenothiazine is a compound of formula (II):



(II)

wherein R^{Prot} is an amine protecting group and R^1, R^9, R^{3NA}, R^{3NB}, R^{7NA}, R^{7NB}, R^A and R^B are as previously defined.

52. A process according to claim 51, wherein R^{Prot} is acyl.

53. A process according to any one of claims 50 to 52, wherein ring amino deprotection (DP) and salt formation (SF) are performed simultaneously.

54. A process according to claim 53, wherein ring amino deprotection (DP) and salt formation (SF) comprise treatment of the *N*-protected 3,7-diamino-10H-phenothiazine with at least one sulfonic acid.

55. A process according to claim 54, wherein ring amino deprotection (DP) and salt formation (SF) comprise treatment of the *N*-protected 3,7-diamino-10H-phenothiazine with methanesulfonic acid and water, in an organic solvent, to produce the *bis*(methanesulfonate) salt.