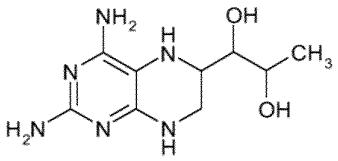
CLAIMS

What is claimed is:

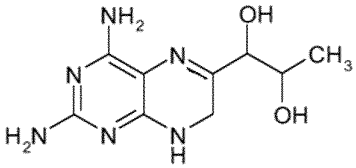
1. A solid pharmaceutical composition comprising

a) a compound having the formula (I):



(I)

and/or a compound having the formula (II):



(II)

and

b) at least one phosphate salt.

2. The pharmaceutical composition of claim 1, wherein the at least one phosphate salt is a sodium phosphate, a potassium phosphate or an ammonium phosphate.

3. The pharmaceutical composition of claim 2, wherein the phosphate salt is selected from the group consisting of Na_2HPO_4 (water free), $Na_2HPO_4 \cdot 2\,H_2O$, $Na_2HPO_4 \cdot 7\,H_2O$, $Na_2HPO_4 \cdot 12\,H_2O$, NaH_2PO_4 (water free), $NaH_2PO_4 \cdot H_2O$, $NaH_2PO_4 \cdot 2\,H_2O$, K_2HPO_4 (water free) $K_2HPO_4 \cdot 3\,H_2O$, KH_2PO_4 (water free) and mixtures thereof.

4. The pharmaceutical composition of claim 2, wherein the phosphate salt is $Na_2HPO_4 \cdot 2\,H_2O$ and wherein the quantity of the $Na_2HPO_4 \cdot 2\,H_2O$ present in the composition is chosen such that the molar ratio of the $Na_2HPO_4 \cdot 2\,H_2O$ to compound (I) or compound (II) ranges from 0.04 to 0.4.

5. The pharmaceutical composition of claim 2, wherein the sodium phosphate is $NaH_2PO_4 \cdot 2\,H_2O$, and wherein the quantity of the $NaH_2PO_4 \cdot 2\,H_2O$ present in the

composition is chosen such that the molar ratio of the $NaH_2PO_4 \cdot 2\,H_2O$ to compound (I) or compound (II) ranges from 0.01 to 0.09.

6. The pharmaceutical composition of any of claims 1-5, comprising two different sodium phosphate salts.

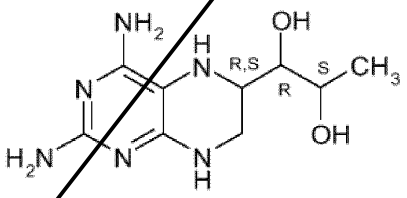
7. The pharmaceutical composition of claim 6, wherein the two different sodium phosphate salts are $NaH_2PO_4 \cdot 2\,H_2O$ and $Na_2HPO_4 \cdot 2\,H_2O$.

8. The pharmaceutical composition of claim 7, wherein the quantity of the $NaH_2PO_4 \cdot 2\,H_2O$ and $Na_2HPO_4 \cdot 2\,H_2O$ present in the composition is chosen such that the molar ratio of both $NaH_2PO_4 \cdot 2\,H_2O$ and $Na_2HPO_4 \cdot 2\,H_2O$ to compound (I) or compound (ii) ranges from 0.02 to 0.5.

9. The pharmaceutical composition of any of claims 1-8, wherein the compound (I) and/or the compound (II) are present as the free base.

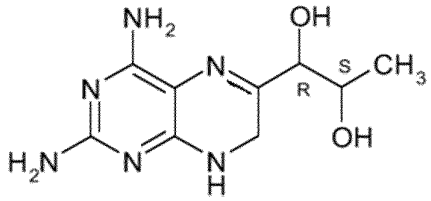
10. The pharmaceutical composition of any of claims 1-9, wherein the pharmaceutical composition is a lyophilized pharmaceutical composition.

11. The pharmaceutical composition of any of claims 1-10, wherein the compound (I) is a compound having the formula (Ia):



(Ia).

12. The pharmaceutical composition of any of claims 1-11, wherein the compound (II) is a compound having the formula (IIa):



(IIa).

13. The pharmaceutical composition of any of claims 1-12, wherein the pharmaceutical composition comprises an additional pharmaceutical excipient.

14. The pharmaceutical composition of claim 13, wherein the additional pharmaceutical excipient is an inorganic salt.

15. The pharmaceutical composition of claim 14, wherein the inorganic salt is selected from $MgCl_2$, $CaCl_2$, NH_4Cl, KCl, or NaCl.

16. The pharmaceutical composition of claim 15, wherein the inorganic salt is NaCl.

17. The pharmaceutical composition of claim 16, wherein the quantity of the NaCl present in the composition is chosen such that the molar ratio of the NaCl to compound (I) or compound (II) ranges from 1.5 to 4, preferably from 1.8 to 3.7.

18. The pharmaceutical composition of any of claims 1-17, wherein the composition further comprises crystallization water.

19. The pharmaceutical composition of any of claims 1-18, wherein the compound (I) is (6R)-4-Amino-5, 6, 7, 8-tetrahydro-L-biopterin.

20. The pharmaceutical composition of any of claims 1-19, wherein the compound (I) is (6S)-4-Amino-5, 6, 7, 8-tetrahydro-L-biopterin.

21. The pharmaceutical composition of any of claims 1-20, wherein the compound (I) is a diastereomeric mixture that comprises more (6R)-4-Amino-5, 6, 7, 8-tetrahydro-L-biopterin than (6S)-4-Amino-5, 6, 7, 8-tetrahydro-L-biopterin.

22. The pharmaceutical composition of claim 21, wherein the quantity of the (6R)-4-Amino-5, 6, 7, 8-tetrahydro-L-biopterin and the (6S)-4-Amino-5, 6, 7, 8-tetrahydro-L-biopterin is chosen such that the ratio of the amount of (6R)-4-Amino-5, 6, 7, 8-tetrahydro-L-biopterin to the (6S)-4-Amino-5, 6, 7, 8-tetrahydro-L-biopterin ranges from 0.5 to 2, preferably around 1.3.

23. The pharmaceutical composition of any of claims 1-22, wherein a unit dosage of the composition contains 650 ± 60 mg of the free base of 4-Amino-(6R,S)-5,6,7,8-tetrahydro-L-biopterin, 140 ± 30 mg of water of crystallization, 70 ± 7 mg $Na_2HPO_4 \cdot 2\ H_2O$, 16.5 ± 2 mg $NaH_2PO_4 \cdot 2\ H_2O$, and 350 ± 30 mg NaCl.

24. The pharmaceutical composition of any of claims 1-22, wherein a unit dosage of the composition contains 650 ± 60 mg of the free base of 4-Amino-(6R,S)-5,6,7,8-tetrahydro-L-biopterin, 60 ± 50 mg of water of crystallization, 70 ± 7 mg $Na_2HPO_4 \cdot 2\ H_2O$, 12 ± 2.5 mg $NaH_2PO_4 \cdot 2\ H_2O$, and 350 ± 30 mg NaCl.

25. The composition of any of claims 1-24, wherein the composition comprises 1, 2, 3, 4, 5, 6, 7, or more additional compounds, wherein the additional compounds are selected from the group consisting of one or more of the compounds selected from the group consisting of 4-Amino-L-biopterin, (6R,S)-5,6,7,8-Tetrahydro-L-biopterin, 1-[(6R,S)-2,4-Diamino-5,6,7,8-tetrahydropteridin-6-yl]propanol, 1-[(6R,S)-2,4-Diamino-5,6,7,8-tetrahydropteridin-6-yl]propane, (1R,2S)-1-[(6R,S)-2-(Acetylamino)-4-amino-5,6,7,8-tetrahydropterin-6-yl]-1,2-diacetoxy-propane, 2,4-Diamino-7,8-dihydropteridine, 2,4-Diaminopteridine.

26. Use of a lyophilized pharmaceutical composition of any of claims 1-25 for the treatment of a disease.

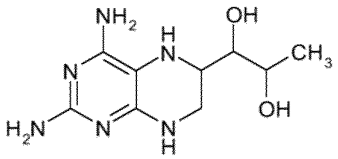
27. The use of claim 26, wherein the disease is selected from the group consisting of a traumatic brain injury, non-traumatic brain injury, preferably stoke or meningitis, elevated cranial pressure, secondary brain injury.

28. A lyophilized pharmaceutical composition of any of claims 1-25 for use in the treatment of a disease.

29. The lyophilized pharmaceutical composition for use of claim 28, wherein the disease is selected from the group consisting of a traumatic brain injury, non-traumatic brain injury, preferably stoke or meningitis, elevated cranial pressure, secondary brain injury.

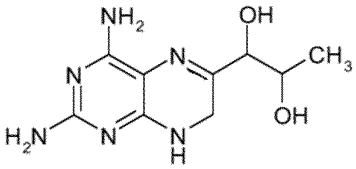
30. A method for preparing a lyophilized solid pharmaceutical composition comprising

a) a compound having the formula (I):



(I)

and/or a compound having the formula (II):



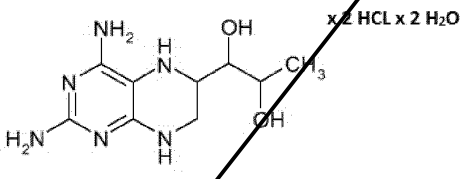
(II)

and

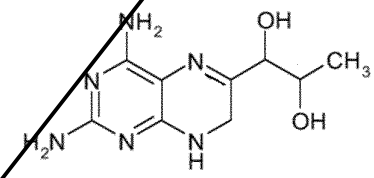
b) at least one phosphate salt and optionally NaCl;

the method comprising:

aa) dissolving the compound of the formula (III) and/or (II):



(III), or



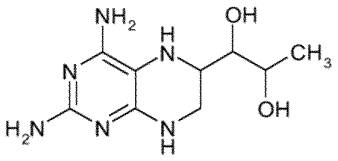
(II)

with a buffer, wherein the buffer comprises the phosphate;

bb) lyophilization of the solution obtained in aa).

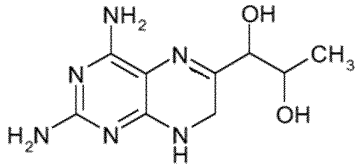
31. A method for preparing an injectable solution comprising:

a) a compound having the formula (I):



(I)

and/or a compound having the formula (II):



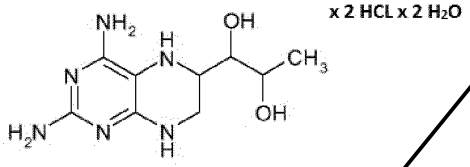
(II)

and

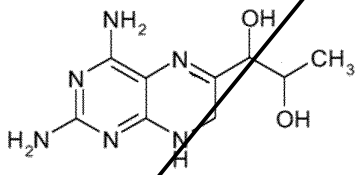
b) at least one phosphate salt and optionally NaCl;

the method comprising:

aa) dissolving the compound of the formula (III) and/or (II):



(III), or



(II)

with a buffer, wherein the buffer comprises the phosphate;

bb) lyophilization of the solution obtained in aa);

cc) reconstituting the lyophilisate obtained in bb) in a pharmaceutically acceptable fluid for the preparation of an injectable solution, wherein the lyophilisate obtained in bb) is filled into a vial.

32. The method of claim 31, wherein the lyophilisate obtained in bb) is filled into a 50 ml vial,

(i) preferably in an amount about 1-1.5 g, preferably 1.25 g solid formulation; or

(ii) preferably in an amount about 0.9-1.4 g, preferably 1.15 g solid formulation.

33. The method of any of claims 30-32, wherein the buffer in aa) is a sodium hydrogen phosphate buffer comprising at least one phosphate salt.

34. The method of any of claims 30-33, wherein the buffer in aa) comprises NaOH, sodium hydrogen phosphate buffer and water.

35. The method of claim 34, wherein the NaOH is a 5N NaOH solution.

36. The method of claim 33, wherein the sodium hydrogen phosphate buffer is prepared by separately dissolving $NaH_2PO_4 \cdot 2\,H_2O$ and $Na_2HPO_4 \cdot 2\,H_2O$.

37. The method of claim 35, wherein the sodium hydrogen phosphate buffer has a pH of 7.4 by adding the $NaH_2PO_4 \cdot 2\,H_2O$ solution to the $Na_2HPO_4 \cdot 2\,H_2O$ dissolution.

38. The method of any of claims 30-37, wherein the buffer comprises 12-16 % (w/w) NaOH 5N, 8-12 % (w/w) sodium hydrogen phosphate buffer and 74-78% (w/w) water for injection.

39. The method of any of claims 30-38, wherein the solution obtained in aa) is sterile filtered, preferably with a 0.22 μm filter.

40. The method of any of claims 30-39, wherein the buffer has a pH of about 8, 9, 10, 11, 12, 13 or 14.

41. The method of any of claims 30-40, wherein the solution in step aa) has a pH of about 4, 5, 6, 7, 8, 9, 10 or 11 preferably between 6.5-7.6, most preferably 7.4.

42. The method of any of claims 30-41, wherein buffer is prepared with degassed buffer.

43. The method of any of claims 30-42, wherein buffer is degassed with nitrogen until the oxygen content is ≤ 1.0 ppm

44. The method of any of claims 30-43, wherein after the preparation of the solution; the lyophilisation is started at most 2 hours later.

45. Use of the lyophilized pharmaceutical composition of any of claims 1-25 in the manufacture of a medicament for treating a subject having closed head injury, elevated cranial pressure and secondary brain injury.

46. A method of treating a disease in a subject, comprising the step of administering a lyophilized pharmaceutical composition of any of claims 1-25 to a subject in need thereof.

47. The method of claim 46, wherein the maximal daily dose is 20 mg/kg body weight, preferably, 17.5, 15.0 or 12.5, 10, 8.5, 7.5, 5.0, 2.5 mg/kg body weight.

48. A lyophilized pharmaceutical composition of any of claims 1 to 25 for use in treating a disease in a subject, said use comprising the step of administering a lyophilized pharmaceutical composition of any of claims 1 to 25 to a subject in need thereof.

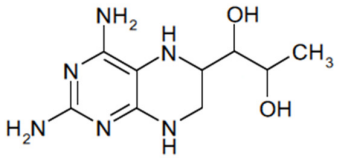
49. The lyophilized pharmaceutical composition for use of claim 48, wherein the maximal daily dose is 20 mg/kg body weight, preferably, 17.5, 15.0 or 12.5, 10, 8.5, 7.5, 5.0, 2.5 mg/kg body weight.

CLAIMS

What is claimed is:

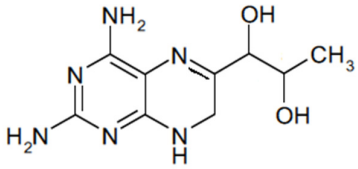
1. A solid pharmaceutical composition comprising

a) a compound having the formula (I):



(I)

and/or a compound having the formula (II):



(II)

and

b) at least one phosphate salt.

2. The pharmaceutical composition of claim 1, wherein the at least one phosphate salt is a sodium phosphate, a potassium phosphate or an ammonium phosphate.

3. The pharmaceutical composition of claim 2, wherein the phosphate salt is selected from the group consisting of Na_2HPO_4 (water free), $Na_2HPO_4 \cdot 2\,H_2O$, $Na_2HPO_4 \cdot 7\,H_2O$, $Na_2HPO_4 \cdot 12\,H_2O$, NaH_2PO_4 (water free), $NaH_2PO_4 \cdot H_2O$, $NaH_2PO_4 \cdot 2\,H_2O$, K_2HPO_4 (water free) $K_2HPO_4 \cdot 3\,H_2O$, KH_2PO_4 (water free) and mixtures thereof.

4. The pharmaceutical composition of claim 2, wherein the phosphate salt is $Na_2HPO_4 \cdot 2\,H_2O$ and wherein the quantity of the $Na_2HPO_4 \cdot 2\,H_2O$ present in the composition is chosen such that the molar ratio of the $Na_2HPO_4 \cdot 2\,H_2O$ to compound (I) or compound (II) ranges from 0.04 to 0.4.

5. The pharmaceutical composition of claim 2, wherein the sodium phosphate is $NaH_2PO_4 \cdot 2\,H_2O$, and wherein the quantity of the $NaH_2PO_4 \cdot 2\,H_2O$ present in the composition is chosen such that the molar ratio of the $NaH_2PO_4 \cdot 2\,H_2O$ to compound (I) or compound (II) ranges from 0.01 to 0.09.

6. The pharmaceutical composition of any of claims 1-5, comprising two different sodium phosphate salts.

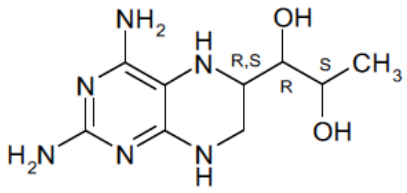
7. The pharmaceutical composition of claim 6, wherein the two different sodium phosphate salts are $NaH_2PO_4 \cdot 2\,H_2O$ and $Na_2HPO_4 \cdot 2\,H_2O$.

8. The pharmaceutical composition of claim 7, wherein the quantity of the $NaH_2PO_4 \cdot 2\,H_2O$ and $Na_2HPO_4 \cdot 2\,H_2O$ present in the composition is chosen such that the molar ratio of both $NaH_2PO_4 \cdot 2\,H_2O$ and $Na_2HPO_4 \cdot 2\,H_2O$ to compound (I) or compound (ii) ranges from 0.02 to 0.5.

9. The pharmaceutical composition of any of claims 1-8, wherein the compound (I) and/or the compound (II) are present as the free base.

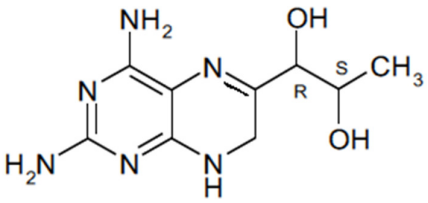
10. The pharmaceutical composition of any of claims 1-9, wherein the pharmaceutical composition is a lyophilized pharmaceutical composition.

11. The pharmaceutical composition of any of claims 1-10, wherein the compound (I) is a compound having the formula (Ia):



(Ia).

12. The pharmaceutical composition of any of claims 1-11, wherein the compound (II) is a compound having the formula (IIa):



(IIa).

13. The pharmaceutical composition of any of claims 1-12, wherein the pharmaceutical composition comprises an additional pharmaceutical excipient.

14. The pharmaceutical composition of claim 13, wherein the additional pharmaceutical excipient is an inorganic salt.

15. The pharmaceutical composition of claim 14, wherein the inorganic salt is selected from $MgCl_2$, $CaCl_2$, NH_4Cl, KCl, or NaCl.

16. The pharmaceutical composition of claim 15, wherein the inorganic salt is NaCl.

17. The pharmaceutical composition of claim 16, wherein the quantity of the NaCl present in the composition is chosen such that the molar ratio of the NaCl to compound (I) or compound (II) ranges from 1.5 to 4, preferably from 1.8 to 3.7.

18. The pharmaceutical composition of any of claims 1-17, wherein the composition further comprises crystallization water.

19. The pharmaceutical composition of any of claims 1-18, wherein the compound (I) is (6R)-4-Amino-5, 6, 7, 8-tetrahydro-L-biopterin.

20. The pharmaceutical composition of any of claims 1-19, wherein the compound (I) is (6S)-4-Amino-5, 6, 7, 8-tetrahydro-L-biopterin.

21. The pharmaceutical composition of any of claims 1-20, wherein the compound (I) is a diastereomeric mixture that comprises more (6R)-4-Amino-5, 6, 7, 8-tetrahydro-L-biopterin than (6S)-4-Amino-5, 6, 7, 8-tetrahydro-L-biopterin.

22. The pharmaceutical composition of claim 21, wherein the quantity of the (6R)-4-Amino-5, 6, 7, 8-tetrahydro-L-biopterin and the (6S)-4-Amino-5, 6, 7, 8-tetrahydro-L-biopterin is chosen such that the ratio of the amount of (6R)-4-Amino-5, 6, 7, 8-tetrahydro-L-biopterin to the (6S)-4-Amino-5, 6, 7, 8-tetrahydro-L-biopterin ranges from 0.5 to 2, preferably around 1.3.

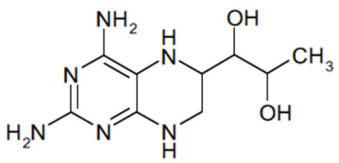
23. The pharmaceutical composition of any of claims 1-22, wherein a unit dosage of the composition contains 650 ± 60 mg of the free base of 4-Amino-(6R,S)-5,6,7,8-tetrahydro-L-biopterin, 140 ± 30 mg of water of crystallization, 70 ± 7 mg $Na_2HPO_4 \cdot 2\ H_2O$, 16.5 ± 2 mg $NaH_2PO_4 \cdot 2\ H_2O$, and 350 ± 30 mg NaCl.

24. The pharmaceutical composition of any of claims 1-22, wherein a unit dosage of the composition contains 650 ± 60 mg of the free base of 4-Amino-(6R,S)-5,6,7,8-tetrahydro-L-biopterin, 60 ± 50 mg of water of crystallization, 70 ± 7 mg $Na_2HPO_4 \cdot 2\ H_2O$, 12 ± 2.5 mg $NaH_2PO_4 \cdot 2\ H_2O$, and 350 ± 30 mg NaCl.

25. The composition of any of claims 1-24, wherein the composition comprises 1, 2, 3, 4, 5, 6, 7, or more additional compounds, wherein the additional compounds are selected from the group consisting of one or more of the compounds selected from the group consisting of 4-Amino-L-biopterin, (6R,S)-5,6,7,8-Tetrahydro-L-biopterin, 1-[(6R,S)-2,4-Diamino-5,6,7,8-tetrahydropteridin-6-yl]propanol, 1-[(6R,S)-2,4-Diamino-5,6,7,8-tetrahydropteridin-6-yl]propane, (1R,2S)-1-[(6R,S)-2-(Acetylamino)-4-amino-5,6,7,8-tetrahydropterin-6-yl]-1,2-diacetoxy-propane, 2,4-Diamino-7,8-dihydropteridine, 2,4-Diaminopteridine.

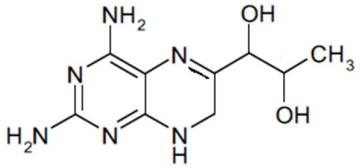
26. A method for preparing a lyophilized solid pharmaceutical composition comprising

a) a compound having the formula (I):



(I)

and/or a compound having the formula (II):



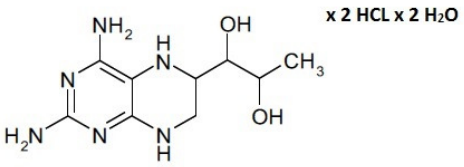
(II)

and

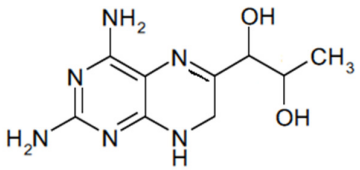
b) at least one phosphate salt and optionally NaCl;

the method comprising:

aa) dissolving the compound of the formula (III) and/or (II):



(III), or



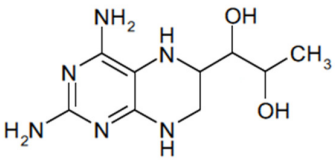
(II)

with a buffer, wherein the buffer comprises the phosphate;

bb) lyophilization of the solution obtained in aa).

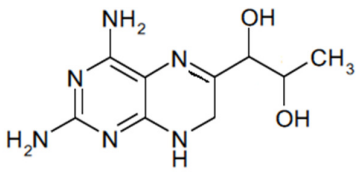
27. A method for preparing an injectable solution comprising:

a) a compound having the formula (I):



(I)

and/or a compound having the formula (II):



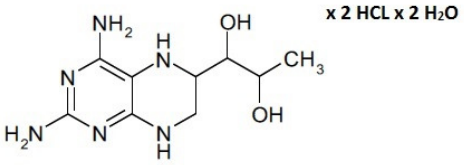
(II)

and

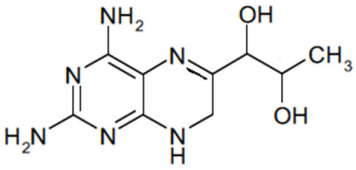
b) at least one phosphate salt and optionally NaCl;

the method comprising:

aa) dissolving the compound of the formula (III) and/or (II):



(III), or



(II)

with a buffer, wherein the buffer comprises the phosphate;

bb) lyophilization of the solution obtained in aa);

cc) reconstituting the lyophilisate obtained in bb) in a pharmaceutically acceptable fluid for the preparation of an injectable solution, wherein the lyophilisate obtained in bb) is filled into a vial.

28. The method of claim 27, wherein the lyophilisate obtained in bb) is filled into a 50 ml vial,

(i) preferably in an amount about 1-1.5 g, preferably 1.25 g solid formulation; or

(ii) preferably in an amount about 0.9-1.4 g, preferably 1.15 g solid formulation.

29. The method of any of claims 26-28, wherein the buffer in aa) is a sodium hydrogen phosphate buffer comprising at least one phosphate salt.

30. The method of any of claims 26-29, wherein the buffer in aa) comprises NaOH, sodium hydrogen phosphate buffer and water.

31. The method of claim 30, wherein the NaOH is a 5N NaOH solution.

32. The method of claim 29, wherein the sodium hydrogen phosphate buffer is prepared by separately dissolving $NaH_2PO_4 \cdot 2\,H_2O$ and $Na_2HPO_4 \cdot 2\,H_2O$.

33. The method of claim 31, wherein the sodium hydrogen phosphate buffer has a pH of 7.4 by adding the $NaH_2PO_4 \cdot 2\,H_2O$ solution to the $Na_2HPO_4 \cdot 2\,H_2O$ dissolution.

34. The method of any of claims 26-33, wherein the buffer comprises 12-16 % (w/w) NaOH 5N, 8-12 % (w/w) sodium hydrogen phosphate buffer and 74-78% (w/w) water for injection.

35. The method of any of claims 26-35, wherein the solution obtained in aa) is sterile filtered, preferably with a 0.22 µm filter.

36. The method of any of claims 26-35, wherein the buffer has a pH of about 8, 9, 10, 11, 12, 13 or 14.

37. The method of any of claims 26-6, wherein the solution in step aa) has a pH of about 4, 5, 6, 7, 8, 9, 10 or 11 preferably between 6.5-7.6, most preferably 7.4.

38. The method of any of claims 26-37, wherein buffer is prepared with degassed buffer.

39. The method of any of claims 26-38, wherein buffer is degassed with nitrogen until the oxygen content is < 1.0 ppm.

40. The method of any of claims 26-39, wherein after the preparation of the solution; the lyophilisation is started at most 2 hours later.

41. Use of the lyophilized pharmaceutical composition of any of claims 1-25 in the manufacture of a medicament for treating a subject having closed head injury, elevated cranial pressure and secondary brain injury.