CLAIMS

1. Use of haptoglobin (Hp) in the preparation of a medicament for treating or preventing an adverse secondary neurological outcome in a subject following a haemorrhagic stroke.

2. A pharmaceutical composition for use in treating or preventing an adverse secondary neurological outcome in a subject following a haemorrhagic stroke, the composition comprising haptoglobin (Hp) and a pharmaceutically acceptable carrier.

3. The use or composition of claim 1 or claim 2, wherein the Hp is present in an amount of from 2 μM to 20 mM.

4. The use or composition of any one of the preceding claims, wherein the Hp is present in an amount of from 2 μM to 300 μM, from 5 μM to 50 μM, or from 10 μM to 30 μM,

5. The use or composition of any one of the preceding claims, wherein the Hp is selected from the group consisting of an Hp1-1 homodimer, an Hp1-2 multimer, an Hp2-2 multimer and a combination of any of the foregoing.

6. The use or composition of claim 7, comprising a Hp2-2 multimer.

7. The use or composition of any one of the preceding claims, wherein the method of treating or preventing an adverse secondary neurological outcome in a subject following a haemorrhagic stroke is accompanied by extravascular erythrolysis and release of cell-free haemoglobin (Hb) into a cerebral spinal fluid (CSF), wherein the method comprising exposing the CSF of a subject in need thereof to a therapeutically effective amount of haptoglobin (Hp) and for a period of time sufficient to allow the Hp to form a complex with, and thereby neutralise, the cell-free Hb.

8. The use or composition of any one of the preceding claims, wherein the haemorrhagic stroke is a spontaneous haemorrhage or a traumatic haemorrhage.

9. The use or composition of any one of the preceding claims, wherein the haemorrhagic stroke is an intraventricular haemorrhage or a subarachnoid haemorrhage.

10. The use or composition of claim 9, wherein the subarachnoid haemorrhage is an aneurysmal subarachnoid haemorrhage.

11. The use or composition of any one of the preceding claims, wherein the adverse secondary neurological outcome is selected from the group consisting of a delayed ischaemic neurological deficit (DIND), delayed cerebral ischaemia (DCI), neurotoxicity, inflammation, nitric oxide depletion, oxidative tissue injury, cerebral vasospasm, cerebral vasoreactivity and oedema.

12. The use or composition of claim 11, wherein the adverse secondary neurological outcome is a cerebral vasospasm.

13. The use or composition of claim 11, wherein the adverse secondary neurological outcome is a delayed ischaemic neurological deficit.

14. The use or composition of claim 11, wherein the adverse secondary neurological outcome is delayed cerebral ischaemia.

15. The use or composition of any one of the preceding claims, wherein the adverse secondary neurological outcome is an adverse secondary neurological outcome within the brain parenchyma.

16. The use or composition of any one of the preceding claims9 to 15, comprising exposing the CSF to the Hp, or the functional analogue thereof, within about 21 days after onset of the haemorrhage.

17. The use or composition of claim 16, comprising exposing the CSF to the Hp from 2 days to 4 days after onset of the haemorrhage and/or from 5 days to 14 days after onset of the haemorrhage.

18. The use or composition of any one of the preceding claims, comprising the Hp to be intracranially administered to the subject.

19. The use or composition of any one of the preceding claims, wherein the Hp is to be intrathecally administered to the subject.

20. The use or composition of claim 19, wherein the Hp is to be intrathecally administered into the spinal canal.

21. The use or composition of claim 19, wherein the Hp is to be intrathecally administered into the subarachnoid space.

22. The use or composition of any one of the preceding claims, wherein the Hp is to be intracerebroventricularly administered to the subject.

23. The use or composition of any one of claims 18 to 22, wherein the period of time to which the CSF is exposed to the therapeutically effective amount of Hp is at least about 2 minutes.

24. The use or composition of claim 23, wherein the period of time to which the CSF is exposed to the therapeutically effective amount of Hp is from 2 minutes to 45 minutes.

25. The use or composition of claim 23, wherein the period of time to which the CSF is exposed to the therapeutically effective amount of Hp is from 2 minutes to 20 minutes or from 4 minutes to 10 minutes.

26. The use or composition of any one of claims 1 to 25, wherein the therapeutically effective amount of Hp is at least an equimolar amount to the concentration of cell-free Hb in the CSF of the subject following the haemorrhage.

27. The use or composition of claim 26, further comprising (i) obtaining a CSF sample from the subject following the haemorrhage and prior to exposing the CSF to the Hp; (ii) measuring the amount of cell-free Hb in the CSF sample obtained in step (i); and (iii) determining the at least equimolar amount of Hp based on the concentration of cell-free Hb from step (ii).

28. The use or composition of any one of claims 7 to 27, further comprising removing Hp:cell-free Hb complexes formed in the CSF.

29. The use or composition of any one of claims 7 to 28, comprising exposing the CSF to the therapeutically effective amount of Hp extracorporeally.

30. The use or composition of claim 29, comprising:

(i) obtaining sample of CSF from the CSF compartment of the subject following the haemorrhage;

(ii) adding to the CSF sample of step (i) Hp to obtain an Hp-enriched CSF sample;

(iii) the Hp-enriched CSF sample is to be administered to the subject, thereby exposing the CSF compartment of the subject to a therapeutically effective amount of Hp for a period of time sufficient to allow the Hp to form a complex with cell-free Hb in the CSF compartment of the subject; and

(iv) optionally repeating steps (i) to (iii).

31. The use or composition of claim 29, comprising:

(i) a volume of CSF is to be removed from the CSF compartment of the subject following the haemorrhage;

(ii) providing an artificial CSF comprising Hp;

(iii) the artificial CSF of (ii) is to be administered to the subject, thereby exposing the CSF compartment of the subject to a therapeutically effective amount of Hp for a period of time sufficient to allow the Hp to form a complex with cell-free Hb in the CSF compartment of the subject; and

(iv) optionally repeating steps (i) to (iii).

32. The use or composition of claim 29, comprising:

(i) obtaining CSF from the subject following the haemorrhage;

(ii) exposing the CSF from step (i) to the Hp under conditions to allow the Hp, or the functional analogue thereof, to form a complex with cell-free Hb in the CSF;

(iii) extracting the Hp:cell-free Hb complexes from the CSF following step (ii) to obtain an Hb-diminished CSF that has a lower amount of cell-free Hb when compared to the CSF from step (i);

(iv) optionally repeating steps (ii) and (iii) to obtain an Hb-diminished CSF that is substantially free of cell-free Hb; and

(v) the Hb-diminished CSF obtained from step (iii) or step (iv) is to be administered to the CSF compartment of the subject.

33. The use or composition of claim 32, further comprising adding to the Hb-diminished CSF prior to step (vi) a therapeutically effective amount of Hp.

34. The use or composition of claim 32 or claim 33, wherein the Hp is immobilised on a substrate.

35. The use or composition of claim 34, wherein the substrate is an affinity chromatography resin.

36. The use or composition of claim 35, wherein step (ii) comprises passing the CSF from step (i) through an affinity chromatography resin under conditions that allow the cell-free Hb in the CSF to bind to the resin; wherein step (iii) comprises eluting the CSF from the resin following step (ii); and wherein step (iv) comprising recovering the eluted CSF.

37. The use or composition of any one of claims 32 to 36, optionally comprising washing the CSF compartment following step (i) with a wash solution.

38. The use or composition of claim 37, wherein the wash solution is an artificial CSF.

39. The use or composition of claim 31 or claim 38, wherein the artificial CSF comprises NaCl, KCl, KH_2PO_4, $NaHCO_3$, $MgCl_6H_20$, $CaCl_2H_2O$ and glucose.

40. The use or composition of any one of claims 37 to 39, wherein the wash solution comprises Hp.

41. The use or composition of claim 40, wherein the wash solution comprises from 2 μM to 20 mM Hp or from 2 μM to 300 μM Hp.

42. The use or composition of any one of claims 7to 41, comprising:
    (i) the CSF is to be removed from the subject following the haemorrhage;
    (ii) the CSF compartment of the subject following step (i) is to be rinsed with a wash solution comprising a therapeutically effective amount of Hp;
    (iii) optionally repeating step (ii); and
    (iv) an artificial CSF is to be administering to the CSF compartment of the subject, following step (ii) or step (iii).

43. The use or composition of claim 42, wherein the artificial CSF comprises NaCl, KCl, KH_2PO_4, $NaHCO_3$, $MgCl_6H_20$, $CaCl_2H_2O$ and glucose.

44. The use or composition of claim 42 or claim 43, wherein the artificial CSF comprises Hp.

45. The use or composition of claim 44, wherein the artificial CSF comprises from 2 μM to 20 mM Hp or from 2 μM to 300 μM Hp.

46. The use or composition of any one of claims 1 to 45, wherein the Hp is selected from the group consisting of an Hp1-1 homodimer, an Hp1-2 multimer, an Hp2-2 multimer and a combination of any of the foregoing.

47. The use or composition of claim 46, wherein the Hp comprises an Hp2-2 multimer.

48. The use or composition of any one of claims 1 to 47, wherein the Hp is a recombinant protein.

49. The use or composition of any one of claims 1 to 47, wherein the Hp is plasma derived.

50. The use or composition of any one of claims 1 to 49, further comprising a second agent for treating or preventing an adverse secondary neurological outcome following an intraventricular haemorrhage to be administered to the subject.

51. The use or composition of claim 50, wherein the second agent is a vasodilator.

52. The use or composition of claim 50 or claim 51, wherein the second agent is selected from the group consisting of a sydnone and sodium nitroprusside.

53. An artificial cerebral spinal fluid (CSF) comprising Hp.

54. The artificial CSF of claim 53, wherein the Hp is present in an amount of from 2 μM to 20 mM, from 5 μM to 300 μM, from 5 μM to 50 μM or from 10 μM to 30 μM.

55. The artificial CSF ofany one of claims 53 to 54, wherein the Hp is selected from the group consisting of an Hp1-1 homodimer, an Hp1-2 multimer, an Hp2-2 multimer and a combination of any of the foregoing.

56. The artificial CSF of claim 55, comprising an Hp2-2 multimer.

57. The artificial CSF of any one of claims 53 to 56, wherein the Hp is a recombinant protein.

58. The artificial CSF of any one of claims 53 to 57, wherein the Hp is plasma derived.

59. A kit comprising the artificial CSF of any one of claims 53 to 58 or the composition of any one of claims 2 to 52.