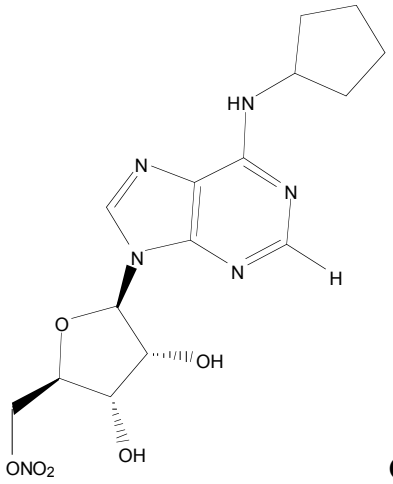
CLAIMS

1. An ophthalmic formulation comprising:

(a) an aqueous suspension of micronized Compound A from 0.1 to 5.0 % (w/v),



Compound A

(b) a surfactant,

(c) boric acid from about 0.05 to about 2.0 % (w/v), and

(d) a buffering agent that maintains the pH from about 6.0 to about 7.0.

2. An ophthalmic formulation according to Claim 1, in which the suspension of Compound A comprises fine particles of less than about 25 microns.

3. An ophthalmic formulation according to Claim 2, in which the fine particles are less than about 10 microns.

4. An ophthalmic formulation according to Claim 2 or 3, in which the fine particles are between about 3 to about 7 microns.

5. An ophthalmic formulation according to any preceding claim, in which Compound A is present in the ophthalmic formulation between about 0.5 to about 5.0 % (w/v).

6. An ophthalmic formulation according to any preceding claim, in which Compound A is present in the ophthalmic formulation between about 1.0 to about 4.0 % (w/v).

7. An ophthalmic formulation according to any preceding claim, in which Compound A is present in the ophthalmic formulation between about 2.0 to about 3.5 % (w/v).

8. An ophthalmic formulation according to any preceding claim, in which Compound A is present in the ophthalmic formulation at about 3.0 % (w/v).

9. An ophthalmic formulation according to any preceding claim, in which the surfactant is selected from polysorbate 80, polysorbate 60, polysorbate 40, polysorbate 20, polyoxyl 40 stearate, poloxamers, tyloxapol and POE 35 castor oil.

10. An ophthalmic formulation according to any preceding claim, in which the surfactant is present in the ophthalmic formulation between about 0.01 to about 0.5 %, w/v.

11. An ophthalmic formulation according to any preceding claim, in which the surfactant is present from about 0.01 to about 0.1 % (w/v).

12. An ophthalmic formulation according to any preceding claim, in which the surfactant is present from about 0.01 to about 0.005% (w/v).

13. An ophthalmic formulation according to any preceding claim, in which the surfactant is polysorbate 80.

14. An ophthalmic formulation according to any preceding claim, in which the boric acid is present from about 0.5 to about 1.0% (w/v).

15. An ophthalmic formulation according to any preceding claim, in which the boric acid is present at about 0.8% (w/v).

16. An ophthalmic formulation according to any preceding claim, in which the formulation further includes a preservative between about 0.005 and about 0.05% (w/v).

17. An ophthalmic formulation according to Claim 16, in which the preservative is benzalkonium chloride.

18. An ophthalmic formulation according to Claim 17, in which the benzalkonium chloride is present in the ophthalmic formulation between about 0.005 and about 0.02 % (w/v).

19. An ophthalmic formulation according to Claim 17, in which the benzalkonium chloride present in the ophthalmic formulation is about 0.01 % (w/v).

20. An ophthalmic formulation according to any preceding claim, in which the buffering agent is a pharmaceutically acceptable phosphate buffer.

21. An ophthalmic formulation according to Claim 20, in which the phosphate buffer is present at about 10 mM.

22. An ophthalmic formulation according to Claim 20 or 21, in which the phosphate buffer is monobasic sodium phosphate present at between about 0.1 to 0.12%.

23. An ophthalmic formulation according to any preceding claim, further including a suspending agent selected from sodium carboxymethylcellulose (NaCMC), hydroxyethylcellulose, hypromellose, polyvinyl alcohol, povidone, carbomers, hyaluronic acid and its salts, chondroitin sulfate and its salts, natural gums, and other pharmaceutically acceptable polymers.

24. An ophthalmic formulation according to Claim 23, in which the suspending agent is selected from sodium carboxymethylcellulose (NaCMC) or hypromellose.

25. An ophthalmic formulation according to any preceding claim, in which the pH is about 6.5±0.1.

26. An ophthalmic formulation according to any preceding claim, further comprising edetate disodium.

27. An ophthalmic formulation according to Claim 26, in which the edetate disodium is present between 0.01 – 0.08% (w/v).

28. An ophthalmic formulation according to Claim 26, in which the edetate disodium is present at about 0.03 % w/v.

29. An ophthalmic formulation according to Claim 1 comprising:

Ingredient	**%, w/v**
Compound A, micronized	0.4 – 5.0
A suspending agent	0.5-1.5
Boric acid	0.05 – 2.0
A preservative	0.01-0.05
A surfactant	0.01-0.1
A phosphate buffering agent	0.05-0.5

NaCl	TBD (qs to 270-330 mOsm)
NaOH/HCl (pH adjustment)	pH 6.0 – 7.0 ±0.1

30. An ophthalmic formulation according to Claim 1 comprising:

Ingredient	**%, w/v**
Compound A, micronized	0.5-3.0
Sodium CMC, low viscosity	0.7
Boric Acid	0.8
Benzalkonium Chloride	0.005-0.15
Polysorbate 80	0.05
Phosphate Buffer	0.12
edetate disodium	0.015-0.06
NaCl	0.4
NaOH/HCl (pH adjustment)	pH 6.5±0.1
Purified Water	q.s. 100.00.

31. An ophthalmic formulation according to Claim 1 comprising:

Ingredient	**%, w/v**
Compound A, micronized	0.5-3.0
Sodium CMC, low viscosity	0.70
Boric Acid	0.8
Benzalkonium Chloride	0.01
Polysorbate 80	0.05
Phosphate Buffer	0.12
edetate disodium	0.015
NaOH/HCl (pH adjustment)	pH 6.5±0.1
Purified Water	q.s. 100.00.

32. An ophthalmic formulation according to Claim 1 comprising:

Ingredient	%, w/v
Compound A, micronized	0.5-3.0
Sodium CMC, low viscosity	0.70
Boric Acid	0.8
Benzalkonium Chloride	0.005
Polysorbate 80	0.05
Phosphate Buffer	0.12
edetate disodium	0.03
NaCl	0.4
NaOH/HCl (pH adjustment)	pH 6.5±0.1
Purified Water	q.s. 100.00.

33. An ophthalmic formulation according to Claim 1 comprising:

Ingredient	**%, w/v**
Compound A, micronized	0.5-3.0
Sodium CMC, low viscosity	0.70
Boric Acid	0.8
Benzalkonium Chloride	0.01
Polysorbate 80	0.05
Phosphate Buffer	0.12
edetate disodium	0.03
NaCl	0.4
NaOH/HCl (pH adjustment)	pH 6.5±0.1
Purified Water	q.s. 100.00.

34. An ophthalmic formulation according to Claim 1 comprising:

Ingredient	**%, w/v**
Compound A, micronized	0.5-3.0

Sodium CMC, low viscosity	0.70	
Boric Acid	0.8	
Benzalkonium Chloride	0.015	
Polysorbate 80	0.05	
Phosphate Buffer	0.12	
edetate disodium	0.03	
NaCl	0.4	
NaOH/HCl (pH adjustment)	pH	6.5±0.1
Purified Water	q.s.	100.00.

35. An ophthalmic formulation according to Claim 1 comprising:

Ingredient	**%, w/v**	
Compound A, micronized	0.5-3.0	
Sodium CMC, low viscosity	0.70	
Boric Acid	0.8	
Benzalkonium Chloride	0.01	
Polysorbate 80	0.05	
Phosphate Buffer	0.12	
edetate disodium	0.06	
NaCl	0.4	
NaOH/HCl (pH adjustment)	pH	6.5±0.1
Purified Water	q.s.	100.00.

36. An ophthalmic formulation according to any preceding claim, further including a second therapeutic ophthalmic agent.

37. An ophthalmic formulation according to Claim 35, in which the second ophthalmic agent is selected from the group comprising prostaglandin analogs, β-blockers, carbonic anhydrase inhibitors, rho-kinase inhibitors, α2 adrenergic agonists, miotics, neuroprotectants,

adenosine A3 antagonists, adenosine A2A agonists, ion channel modulators and combinations thereof.

38. An ophthalmic formulation according to Claim 36, in which the second ophthalmic agent is a prostaglandin analog.

39. An ophthalmic formulation according to Claim 38, in which the prostaglandin analog is latanoprost.

40. An ophthalmic formulation according to Claim 39, in which the latanoprost is present between about 1-200 μg/ml.

41. An ophthalmic formulation according to Claim 40, in which the latanoprost is present in about 50 μg/ml.

42. An ophthalmic formulation according to any preceding claim for use in a method of reducing intraocular pressure, in which the method comprises a step of topically applying an effective amount of the ophthalmic formulation to an affected eye of a subject.

43. An ophthalmic formulation for use according to Claim 42, in which the formulation is administered to the affected eye of the subject in about 30 to about 50 μl drops.

44. An ophthalmic formulation for use according to Claim 42 or 43, in which the formulation is administered in about 1 to about 2 drops once or twice daily.

45. An ophthalmic formulation for use according to any of Claims 42 to 44, in which the subject has normal-tension glaucoma, OHT, or POAG.

46. An ophthalmic formulation according to any of Claims 1 to 41 for use in a method of treating retinal ganglion cell damage, in which the method comprises a step of applying an effective amount of the ophthalmic formulation to an affected eye of a subject.

47. An ophthalmic formulation for use according to Claim 46, in which the ophthalmic formulation is administered to the affected eye of the subject in about 30 to about 50 μl drops.

48. An ophthalmic formulation for use according to any of Claim 46 or 47, in which the ophthalmic formulation is administered in 1 to 2 drops once or twice daily.

49. An ophthalmic formulation according to any of Claims 1 to 41 for use in a method of preventing retinal ganglion cell damage, in which the method comprises the step of applying an effective amount of the ophthalmic formulation to an eye of a subject.

50. An ophthalmic formulation for use according to Claim 49, in which the ophthalmic formulation is administered to the affected eye of the subject in about 30 to about 50 µl drops.

51. An ophthalmic formulation for use according to Claim 50, in which the ophthalmic formulation is administered in 1 to 2 drops once or twice daily.

52. An ophthalmic formulation for use according to any of Claims 41 to 51, in which the method further comprises administering a second ophthalmic agent.

53. An ophthalmic formulation for use according to Claim 52, in which the second ophthalmic agent is selected from the group comprising prostaglandin analogs, β-blockers, carbonic anhydrase inhibitors, rho-kinase inhibitors, α2 agonists, miotics, neuroprotectants, A3 antagonists, A2A agonists, ion channel modulators and combinations thereof.

54. An ophthalmic formulation for use according to Claim 53, in which the second ophthalmic agent is a prostaglandin analog.

55. An ophthalmic formulation for use according to Claim 54, in which the prostaglandin analog is latanoprost.

56. A kit or packaged formulation comprising a topically applicable ophthalmic formulation according to any of Claims 1 to 41.

57. A process for preparing an ophthalmic formulation according to any of Claims 1 to 41, comprising the steps of

(a) micronizing Compound A into particle sizes of less than about 50 microns;

(b) suspending the particles of Compound A in an aqueous suspension with a surfactant and a buffering agent;

(c) curing the product from step (b) at about 40° Celsius for between about 24 to about 96 hours; and

(e) adding boric acid from about 0.05 to about 2.0 % (w/v).

58. A process according to Claim 57, in which steps (a)-(c) are performed with a volume of less than about 20% of the final volume of the ophthalmic formulation.

59. A process according to Claim 56 or 57, further comprising filtering the cured product of step (c) as a concentrated slurry.

60. A process according to any of Claims 56 to 59, in which the milled Compound A is sterilized by gamma irradiation up to a maximum of 40 kGray (kGy).

61. A process according to any of Claims 56 to 60, in which the curing step takes place at about 40° Celsius for between about 48 to about 96 hours.

62. A process according to any of Claims 56 to 61, further comprising adjusting the pH of the aqueous suspension to between about 6.0 and about 7.0 or in a further embodiment to a pH of about 6.5 ± 0.1.

63. A process according to any of Claims 56 to 62, in which the process is performed under aseptic conditions.

64. A process according to any of Claims 56 to 63, further comprising adding a second ophthalmic agent.

65. A process according to Claim 64, in which the second ophthalmic agent is selected from the group comprising prostaglandin analogs, β-blockers, carbonic anhydrase inhibitors, rho-kinase inhibitors, α2 agonists, miotics, neuroprotectants, A3 antagonists, A2A agonists, ion channel modulators and combinations thereof.

66. A process according to Claim 65, in which the second ophthalmic agent is a prostaglandin analog.

67. A process according to Claim 66, in which the prostaglandin analog is latanoprost.