neovascularization, radiation treatment, transpupillary thermotherapy of subfoveal occult choroidal neovascularization, submacular surgery, limited macular translocation, adjuncts in surgery, argon laser to drusen, infrared diode laser photocoagulation for treatment of wet AMD. Recently, compositions for treating the non-neovascular or dry AMD comprising hypotensive agents, such as hydralazine, were described in U.S. Patent No. 8,088,773 to Chiou, which is incorporated by reference herein.

[0005] The foregoing examples of the related art and limitations related therewith are intended to be illustrative and not exclusive. Other limitations of the related art will become apparent to those of skill in the art upon a reading of the specification and a study of the drawings.

~~BRIEF~~ SUMMARY

[0006] The following aspects and embodiments thereof described and illustrated below are meant to be exemplary and illustrative, not limiting in scope.

[0007] ~~In one aspect, an o~~Ophthalmic compositions are~~is~~ described. In one embodiment, the ophthalmic composition comprises a pharmaceutically active drug comprising hydralazine in an amount between about 0.02-2 wt%, and one or more of: one or more buffer solutions having a pH of between 3.5-4.5; one or more chelating agents; one or more isotonicity agents; one or more preservatives; one or more viscosity enhancers, and one or more diluents. In an embodiment, the composition has a pH of between 4.0-4.4.

[0007a] In one aspect, there is provided an ophthalmic composition, comprising:

a pharmaceutically active drug comprising hydralazine in an amount between about 0.02-2 wt%;

an acetate buffer solution having pH of between 3.9-4.5 in an amount between 8-12 wt%;

propylene glycol in an amount between 0.5-2 wt%;

sodium chloride in an amount between 0.25-1 wt%;

methylparaben in an amount between 0.015-0.06 wt%;

benzalkonium chloride in the form of a 50% solution, present in an amount between 0.01-0.04 wt%; and

edetate disodium in an amount between 0.008-0.030 wt%;

wherein said composition has a pH of between 4.0-4.4.

In another embodiment, the ophthalmic composition comprises a pharmaceutically active drug comprising hydralazine in an amount between about 0.02-

2 wt%; an acetate buffer solution having pH of between 3.9-4.5 in an amount between 8-12 wt%; propylene glycol in an amount between 0.5-2 wt%; sodium chloride in an amount between 0.25-1 wt%; methylparaben in an amount between 0.015-0.06 wt%; benzalkonium chloride in the form of a 50% solution, present in an amount between 0.01-0.04 wt%; and edetate disodium in an amount between 0.008-0.030 wt%. In an embodiment, the composition has a pH of between 4.0-4.4.

[0008] The pharmaceutically active drug may comprise hydralazine hydrochloride. In another embodiment, the drug is present in an amount between 0.5-2 wt%.

[0009] In another embodiment, the acetate buffer solution has a pH of about 4.2 and is present in an amount of about 10 wt%. The acetate buffer solution may be comprised of sodium acetate and 2N acetic acid.

[0010] In an embodiment, propylene glycol is present is an amount of about 1 wt%. In another embodiment, methylparaben is present in an amount of about 0.03 wt%. In

yet another embodiment, benzalkonium chloride is present in the form of a 50% solution and is present in an amount of about 0.02 wt%. In an additional embodiment, edetate disodium is present in an amount of about 0.015 wt%.

[0011] In another ~~aspect~~embodiment, a method for preparing an ophthalmic formulation is contemplated. In one embodiment, the method comprises mixing a diluent and one or more buffer solutions having a pH between about 3.5 to 4.5 to form a first interim mixture, adding one or more chelating agents to the first interim mixture to form a second interim mixture, adding one or more lubricants to the second interim mixture to form a third interim mixture, adding one or more isotonicity agents to the third interim mixture to form a fourth interim mixture, adding one or more preservatives to the fourth interim mixture to form a fifth interim mixture, adding a pharmaceutically active drug comprising hydralazine to the fifth interim mixture to form the ophthalmic formulation.

[0011a] In one aspect, there is provided a method for preparing an ophthalmic formulation, comprising:

mixing water and an acetate buffer solution having a pH 3.9-4.5 to form a first interim mixture, the acetate buffer solution added in an amount to provide between about 8-12 wt% of acetate buffer solution in the formulation;

adding to the first interim mixture edetate disodium, to form a second interim mixture, the edetate disodium added in an amount to provide between about 0.008-0.030 wt% of edetate disodium in the formulation;

adding to the second interim mixture propylene glycol to form a third interim mixture, the propylene glycol added in an amount to provide between about 0.5-2 wt% of propylene glycol in the formulation;

adding to the third interim mixture sodium chloride to form a fourth interim mixture, the sodium chloride added in an amount to provide between about 0.25-1 wt% of sodium chloride in the formulation;

adding to the fourth interim mixture benzalkonium chloride to form a fifth interim mixture, the benzalkonium chloride added in an amount to provide between about 0.01-0.04 wt% of benzalkonium chloride in the formulation; and

adding to the fifth interim mixture methylparaben to form a sixth interim mixture, the methylparaben added in an amount to provide between about 0.015-0.06 wt% of methylparaben in the formulation;

adding to the sixth interim mixture to form said formulation, a pharmaceutically active drug comprising hydralazine.

[0012] In an embodiment, the buffer is an acetate buffer solution having a pH of about 3.9-4.5 which is added in an amount to provide between about 8-12 wt% of the

acetate buffer solution in the formulation. In another embodiment, acetate buffer solution is added in an amount to provide about 10 wt% acetate buffer in the formulation. In a further embodiment, the acetate buffer solution is comprised of sodium acetate and 2N acetic acid.

[0013] In an embodiment, the chelating agent is edetate disodium, which is added in an amount to provide between about 0.008-0.030 wt% of edetate disodium in the formulation. In a further embodiment, edetate disodium is added in an amount to provide about 0.015 wt% edetate disodium in the formulation.

[0014] In an embodiment, the lubricant is propylene glycol added in an amount to provide between about 0.5-2 wt% of propylene glycol in the formulation. In a further embodiment, propylene glycol is added in an amount to provide about 15 wt% propylene glycol in the formulation.

[0015] In a further embodiment, the isotonicity agent is sodium chloride added in an amount to provide between about 0.25-1 wt% of sodium chloride in the formulation. In an embodiment, sodium chloride is added in an amount to provide about 0.5 wt% sodium chloride in the formulation.

[0016] In yet another embodiment, a preservative is benzalkonium chloride added in an amount to provide between about 0.01-0.04 wt% of benzalkonium chloride in the formulation. In another embodiment, benzalkonium chloride is added in an amount to provide about 0.02 wt% benzalkonium chloride in the formulation. In a further embodiment, a second preservative is added, where the second preservative is methylparaben added in an amount to provide between about 0.015-0.06 wt% of

methylparaben in the formulation. In yet another embodiment, methylparaben is added in an amount to provide about 0.03 wt% methylparaben in the formulation.

[0017] In embodiments, the pharmaceutically active drug is hydralazine present in the formulation at between about 0.5-2 wt%. In further embodiments, the pharmaceutically active drug is hydralazine hydrochloride. In a particular embodiment, the pharmaceutically active drug is hydralazine hydrochloride present in the formulation at about 1 wt%.

[0018] In embodiments, one or more of the steps of adding further comprise mixing while adding.

[0019] ~~In a further aspect, a m~~Methods for treating a macular degeneration are~~is~~ contemplated.

[0019a] In one aspect, there is provided the ophthalmic composition as described herein for use in treating macular degeneration.

[0019b] In one aspect, there is provided use of the ophthalmic composition as described herein or the formulation prepared according to the method as described herein in the manufacture of a medicament for treating macular degeneration, wherein said medicament is to be administered to an eye of a subject at risk of or diagnosed with macular degeneration.

In embodiments, the method comprises administering to an eye of a subject at risk of or diagnosed with macular degeneration, an ophthalmic composition described herein or prepared by methods described herein. In an embodiment, the macular degeneration is age-related macular degeneration. In a particular embodiment, the age-related macular degeneration is dry age-related macular degeneration.

[0020] It will be appreciated that the above embodiments may be combined with one or more, or all, of the additional embodiments described. In addition to the exemplary aspects and embodiments described above, further aspects and embodiments will become apparent by reference to the drawings and by study of the following descriptions.

[0021] Additional embodiments of the present methods and compositions, and the like, will be apparent from the following description, drawings, examples, and claims. As can be appreciated from the foregoing and following description, each and every feature described herein, and each and every combination of two or more of such features, is included within the scope of the present disclosure provided that the features included in such a combination are not mutually inconsistent. In addition, any feature or combination of features may be specifically excluded from any embodiment of the present ~~invention~~disclosure. Additional aspects and advantages of the present ~~invention~~ disclosure

are set forth in the following description and claims, particularly when considered in conjunction with the accompanying examples and drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

[0022] **Figure 1** is a graph of choroidal blood flow in µl/min/mg at 0, 30, 60, and 120 minutes after instillation of a 1% hydralazine hydrochloride formulation.

15. The method of any one of claims 10-14, wherein propylene glycol is added in an amount to provide 15 wt% propylene glycol in the formulation.

16. The method of any one of claims 10-15, wherein sodium chloride is added in an amount to provide 0.5 wt% sodium chloride in the formulation.

17. The method of any one of claims 10-16, wherein benzalkonium chloride is added in an amount to provide 0.02 wt% benzalkonium chloride in the formulation.

18. The method of any one of claims 10-17 wherein methylparaben is added in an amount to provide 0.03 wt% methylparaben in the formulation.

19. The method of any one of claims 10-18, wherein the pharmaceutically active drug is hydralazine present in the formulation at between 0.5-2 wt%.

20. The ophthalmic composition of any one of claims 1-9 for use in treating macular degeneration.

21. The composition of claim 20, wherein said macular degeneration is dry age-related macular degeneration.

22. ~~A method for treating macular degeneration, comprising:~~

~~administering to an eye of a subject at risk of or diagnosed with macular degeneration,~~ Use of the ophthalmic composition of any one of claims 1-9 or the formulation prepared according to the method of any one of claims 10-19 in the manufacture of a medicament for treating macular degeneration, wherein said medicament is to be administered to an eye of a subject at risk of or diagnosed with macular degeneration.

23. The ~~method~~ use of claim 22, wherein said macular degeneration is age-related dry macular degeneration.