the anterior segment, while providing availability of an effective concentration of the active at the posterior segment.

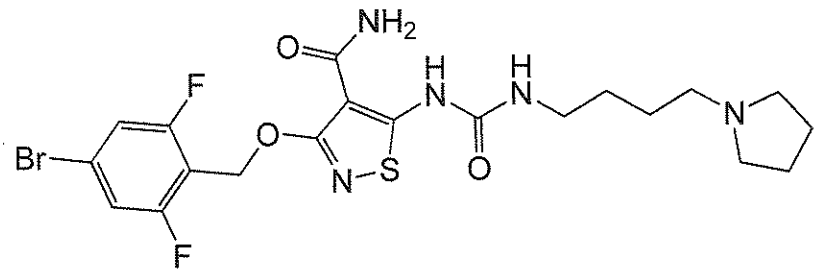
[0007] The current embodiments provide novel formulations which circumvent the problems encountered in ocular delivery of existing topical therapeutic agents. The current invention accomplishes the combined effects of decreasing corneal and anterior segment drug exposure, while increasing posterior segment bioavailability. By lowering corneal exposure and increasing posterior segment bioavailability, the formulation of the current invention improves ocular tolerability and increases therapeutic index of the active agent.

SUMMARY

[0008] The present disclosure relates to pharmaceutical formulations in form of a solution and/or a suspension, which lower exposure to the active agent in the anterior segment of the eye, for example the cornea, while increasing the bioavailability of the agent at the posterior segment of the eye, for example at the central choroid and/or the central retina.

[0008a] In one aspect of the present disclosure, there is provided a topical ocular formulation, the formulation comprising:

an active agent of Formula II:



(II),

or a pharmaceutically acceptable salt thereof,

wherein the active agent or the pharmaceutically acceptable salt is present in about 0.1% to about 2.0% w/v,

about 0.2% to about 1% tromethamine,

about 1% to about 2% glycerin, and

hydroxy ethyl cellulose (HEC) or hydroxy propyl methyl cellulose (HPMC), such that the formulation forms a suspension.

[0009] The embodiments provide two distinct forms of formulation comprising the active agent, a solution and a suspension, with superior characteristics compared to another composition formed as a gel. The embodiments provide that the active agent formulated as a solution and/or a suspension are superior compared to when the same active ingredient is formulated as a gel form in delivering the active at the posterior segment of eye, while lowering the exposure in the front of the eye. Increased levels of the active agent in the front of the eye limit ocular tolerability of topical drops containing the active. Therefore, reduced bioavailability of the active agent at the corneal or conjunctival surface, while maintaining adequate concentrations necessary to bind the relevant receptors at the target tissues and confer a therapeutic effect in the posterior segment of the eye, such as the choroid and the retina, are highly desirable and are the outcomes achieved from the specific embodiments described here.

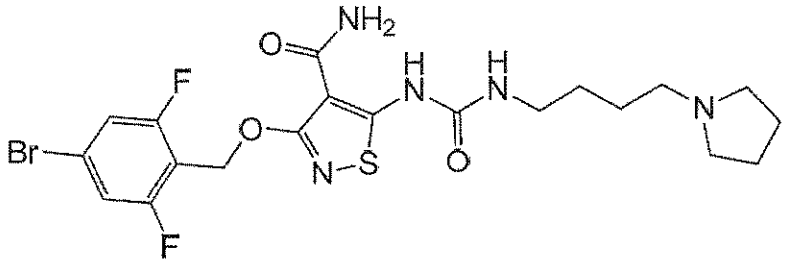
[0010] The present disclosure relates to formulations and methods useful for treating pathological states that arise or are exacerbated by ocular angiogenesis and vascular leakage, for example, in diabetic retinopathy (including background diabetic retinopathy, proliferative diabetic retinopathy and diabetic macular edema); age-related macular degeneration (AMD) (including neovascular (wet/exudative) AMD, dry AMD, and Geographic Atrophy); pathologic choroidal neovascularization (CNV) from any mechanism (*i.e.* high myopia, trauma, sickle cell disease; ocular histoplasmosis, angioid

CLAIMS

What is claimed is:

1. A topical ocular formulation, comprising:

an active agent of Formula II:



(II),

or a pharmaceutically acceptable salt thereof,

wherein the active agent or the pharmaceutically acceptable salt is present in about 0.1% to about 2.0% w/v,

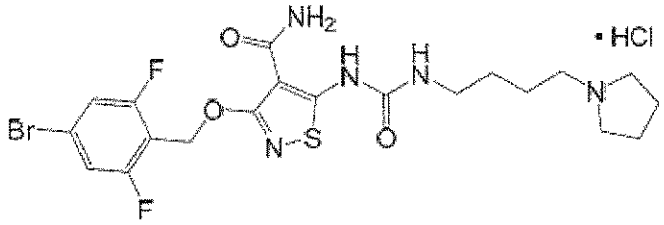
about 0.2% to about 1% tromethamine,

about 1% to about 2% glycerin, and

hydroxy ethyl cellulose (HEC) or hydroxy propyl methyl cellulose (HPMC), such that the formulation forms a suspension.

2. The formulation of claim 1, further comprising a solubilizing agent.

3. The formulation of claim 1, wherein the pharmaceutically acceptable salt is a hydrochloride salt of the formula:



4. The formulation of claim 1, comprising about 0.1% to about 1.0% w/v of the active agent or a pharmaceutically acceptable salt thereof.

5. The formulation of claim 1, comprising one or more of benzalkonium chloride (BAK), sodium chloride, and a pH adjusting agent.

6. The formulation of claim 1, comprising about 0.1%, 0.2%, 0.3%, 0.4%, 0.5%, 0.6%, 0.7%, 0.8%, 0.9%, 1.0%, or 2.0% w/v of the active agent or a pharmaceutically acceptable salt thereof, and about 0.6% w/v tromethamine.

7. The formulation of claim 1, comprising about 0.1%, 0.2%, 0.3%, 0.4%, 0.5%, 0.6%, 0.7%, 0.8%, 0.9%, 1.0%, or 2.0% w/v of the active agent or a pharmaceutically acceptable salt thereof, about 0.6% w/v tromethamine, and about 2% glycerin.

8. The formulation of claim 1, having a pH value of about 4.5 to 7.5 at or under about 40° C.

9. The formulation of claim 1, having a pH value of about 6.0 at or under about 40° C.

10. The formulation of claim 1, having a pH value of about 5.0 to 7.0 at or under about 40° C.

11. The formulation of claim 1, wherein the formulation is suitable for treating ocular neovascularization.