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FILING RECEIPT

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ALCON
IP LEGAL, TB4-8
6201 SOUTH FREEWAY
FORT WORTH, TX 76134

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If Required, Foreign Filing License Granted: 11/02/2011
The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 61/548,957**
Projected Publication Date: None, application is not eligible for pre-grant publication
Non-Publication Request: No
Early Publication Request: No
Title

High Concentration Olopatadine Ophthalmic Compositions

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HIGH CONCENTRATION OLOPATADINE OPHTHALMIC COMPOSITION

Technical Field of the Invention

The present invention relates to an ophthalmic composition containing a relatively high concentration of olopatadine. More particularly, the present invention relates to an ophthalmic aqueous solution containing a relatively high concentration of solubilized olopatadine wherein the solution is capable of providing enhanced relief from symptoms of ocular allergic conjunctivitis in the early phase, the late phase or preferably both phases.

Background of the Invention

Individuals suffering from ocular allergic conjunctivitis experience symptoms such as ocular irritation, itchiness, redness and the like. It has been found that these symptoms are significantly reduced using topical ophthalmic solutions containing olopatadine. Such solutions are sold under the tradenames PATANOL® and PATADAY®, which are both commercially available from Alcon Research Ltd., Fort Worth, TX.

Recently, and as discussed further below, it has been discovered that relatively high concentration solutions of olopatadine provide significantly improved reduction of late phase ocular allergic conjunctivitis symptoms in addition to relief from early phase symptoms. Such discovery is significant since relief from such late phase symptoms is particularly desirable for individual suffering from ocular allergic conjunctivitis. Further, it has been discovered that relief from these late phase symptoms can be achieved through once a day dosing of relatively high concentration olopatadine solution as opposed to greater dosing frequencies. Avoiding more frequent dosing is more convenient for patients and helps assure better compliance with a simpler dosing regimen.

The discovery that relatively high concentration solutions of olopatadine can relieve late phase ocular allergic conjunctivitis symptoms provides hope to sufferers of ocular allergic conjunctivitis that a single dose of olopatadine per day could provide a substantial degree of full day relief from their symptoms. However, the development of a multi-dose ophthalmic solution that includes high

concentrations of olopatadine necessary to achieve desired levels of efficacy is extremely difficult and complex.

Solubilizing high concentrations of olopatadine in a stable manner has proven difficult by itself. Olopatadine, by itself, is only soluble up to a concentration of about 0.18 w/v% in water at a pH of about 7.0 and at about room temperature. However, it is desirable to achieve solubilization of much higher concentrations of olopatadine in an effort to treat late phase ocular allergic conjunctivitis.

Solubilizing such higher concentrations of olopatadine has proven difficult. As one example, excipients such as polyethylene glycol (PEG) 400 and polyvinylpyrrolidone (PVP), when used at reasonably desirable concentrations, have proven to be insufficient, alone or in combination, to solubilize sufficient concentrations of olopatadine. Thus, innovation is required to solubilize a sufficient concentration of olopatadine.

In the process of such innovation, is has been discovered that higher molecular weight PEGs such as PEG 6000 can significantly enhance solubility of olopatadine. However, such PEGs cause risk of discomfort when administered to humans. It has also been discovered that cyclodextrins such as hydroxypropyl-γ-cyclodextrin, hydroxypropyl-β-cyclodextrin and sulfoalkyl ether-β-cyclodextrin have the ability to solubilize significantly higher concentrations of olopatadine, however, use of undesirably high concentrations of these cyclodextrins has been found to reduce olopatadine efficacy and/or preservation efficacy of solutions including the undesirably high concentrations of cyclodextrin. As such, still further innovation was needed to create a desirable olopatadine formulation that not only solubilized sufficient amounts of olopatadine, but also allowed the formulation to achieve other desired characteristics.

Thus, the present invention is directed at an ophthalmic composition that can provide high concentrations of olopatadine topically to the eye. Further, the present invention is directed to such a composition wherein the olopatadine is solubilized in solution in a stable manner, the composition exhibits consistent efficacy against late phase symptoms of ocular allergic conjunctivitis, the composition exhibits sufficient antimicrobial activity to provide desired levels of preservation efficacy or any combination thereof.

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