Title: ANTIBiotic COMPOSITIONS FOR treatment of the EYE, EAR AND NOSE

Abstract:
Ophthalmic, otic and nasal compositions containing a new class of antibiotics (e.g., moxifloxacin) are disclosed. The compositions preferably also contain one or more anti-inflammatory agents. The compositions may be utilized to treat ophthalmic, otic and nasal conditions by topically applying the compositions to the affected tissues.
ANTIBIOTIC COMPOSITIONS FOR TREATMENT OF THE EYE, EAR AND NOSE

Ophthalmic, otic and nasal compositions containing a new class of antibiotics (e.g., moxifloxacin) are disclosed. The compositions preferably also contain one or more anti-inflammatory agents. The compositions may be utilized to treat ophthalmic, otic and nasal conditions by topically applying the compositions to the affected tissues.
ANTIBIOTIC COMPOSITIONS FOR
TREATMENT OF THE EYE, EAR AND NOSE

Background of the Invention

The present invention is directed to the provision of topical antibiotic pharmaceutical compositions for the treatment of ophthalmic, otic and nasal infections, particularly bacterial infections, and to methods of treating ophthalmic, otic and nasal infections by applying those compositions to the affected tissues. The compositions and methods of the invention are based on the use of a new class of antibiotics. The compositions of the present invention may also contain one or more anti-inflammatory agents.

The use of quinolone antibiotics to treat infections represents the current state of the art in the field of ophthalmic pharmaceutical compositions and methods of treatment. For example, a topical ophthalmic composition containing the quinolone ciprofloxacin is marketed by Alcon Laboratories, Inc. under the name CILOXAN™ (Ciprofloxacin 0.3%) Ophthalmic Solution. The following quinolones have also been utilized in ophthalmic antibiotic compositions:

<table>
<thead>
<tr>
<th>Quinolone</th>
<th>Product</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ofloxacin</td>
<td>OCUFLOX™</td>
<td>Allergan</td>
</tr>
<tr>
<td>Norfloxacin</td>
<td>CHIBROXIN™</td>
<td>Merck</td>
</tr>
<tr>
<td>Lomefloxacin</td>
<td>LOMEFLOX™</td>
<td>Senju</td>
</tr>
</tbody>
</table>

The foregoing quinolone antibiotic compositions are generally effective in treating ophthalmic infections, and have distinct advantages over prior ophthalmic antibiotic compositions, particularly those having relatively limited spectrums of antimicrobial activity, such as: neomycin, polymyxin B, gentamicin and tobramycin,
which are primarily useful against gram negative pathogens; and bacitracin, gramicidin, and erythromycin, which are primarily active against gram positive pathogens. However, despite the general efficacy of the ophthalmic quinolone therapies currently available, there is a need for improved compositions and methods of treatment based on the use of antibiotics that are more effective than existing antibiotics against key ophthalmic pathogens, and less prone to the development of resistance by those pathogens.

There is an even greater need for effective topical compositions and methods for treating otic and nasal infections, particularly bacterial infections. The use of oral antibiotics to treat otic infections in children has limited efficacy, and creates a serious risk of pathogen resistance to the orally administered antibiotics.

Ophthalmic, otic and nasal infections are frequently accompanied by inflammation of the infected ophthalmic, otic and nasal tissues and perhaps even surrounding tissues. Similarly, ophthalmic, otic and nasal surgical procedures that create a risk of microbial infections frequently also cause inflammation of the affected tissues. Thus, there is also a need for ophthalmic, otic and nasal pharmaceutical compositions that combine the anti-infective activity of one or more antibiotics with the anti-inflammatory activity of one or more steroid or non-steroid agents in a single composition.

**Summary of the Invention**

The invention is based on the use of a potent new class of antibiotics to treat ophthalmic, otic and nasal infections, as well as the prophylactic use of these antibiotics following surgery or other trauma to ophthalmic, otic or nasal tissues. The compositions of the present invention may also be administered to the affected tissues during ophthalmic, otic or nasal surgical procedures to prevent or alleviate post-surgical infection.

The compositions preferably also contain one or more anti-inflammatory agents to treat inflammation associated with infections of ophthalmic, otic or nasal tissues. The
anti-inflammatory component of the compositions is also useful in treating inflammation associated with physical trauma to ophthalmic, otic or nasal tissues, including inflammation resulting from surgical procedures. The compositions of the present invention are therefore particularly useful in treating inflammation associated with trauma to ophthalmic, otic or nasal tissues wherein there is either an infection or a risk of an infection resulting from the trauma.

Examples of ophthalmic conditions that may be treated with the compositions of the present invention include conjunctivitis, keratitis, blepharitis, dacryocystitis, hordeolum and corneal ulcers. The compositions of the invention may also be used prophylactically in connection with various ophthalmic surgical procedures that create a risk of infection.

Examples of otic conditions that may be treated with the compositions of the present invention include otitis externa and otitis media. With respect to the treatment of otitis media, the compositions of the present invention are primarily useful in cases where the tympanic membrane has ruptured or tympanostomy tubes have been implanted. The compositions may also be used to treat infections associated with otic surgical procedures, such as tympanostomy, or to prevent such infections.

The compositions of the present invention are specially formulated for topical application to ophthalmic, otic and nasal tissues. The compositions are preferably sterile, and have physical properties (e.g., osmolality and pH) that are specially suited for application to ophthalmic, otic and nasal tissues, including tissues that have been compromised as the result of preexisting disease, trauma, surgery or other physical conditions.
According to one aspect of the present invention, there is provided a use of moxifloxacin, or a pharmaceutically useful hydrate or salt thereof in preparation of a pharmaceutical composition for topically treating or preventing an ophthalmic, otic or nasal infection, wherein the moxifloxacin or the hydrate or salt thereof is at a concentration of 0.1 to 1.0 wt. %.
Detailed Description of the Invention

The antibiotics used in the compositions and methods of the present invention have the following formula:

\[
\text{(I)}
\]

wherein:

- A is CH, CF, CCl, C-OCH₃, or N;
- \( X^1 \) is H, halogen, NH₂, or CH₃;
- \( R^1 \) is C₁ to C₃ alkyl, FCH₂CH₂, cyclopropyl or phenyl, optionally mono-, di- or tri-substituted by halogen, or A and \( R^1 \) together can form a bridge of formula C-O-CH₂-CH(CH₃);
- \( R^2 \) is H, C₁ to C₃ alkyl (optionally substituted by OH, halogen or NH₂), or 5-methyl-2-oxo-1,3-dioxol-4-yl-methyl; and
- B is a selected from the group consisting of:

\[
\text{R}^3 \quad \text{R}^4
\]

and
wherein:

Y is O or CH₂;

R³ is C₂-C₅ alkoxyl, CH₂-CO-C₆H₅, CH₂CH₂CO₂R', R'O₂C-CH=C-CO₂R',
CH=CH-CO₂R' or CH₂CH₂-CN,

wherein:

R₁ is H or C₁ to C₃ alkyl;

R⁴ is H, C₁ to C₃ alkyl, C₂-C₅ alkoxyl, CH₂-CO-C₆H₅, CH₂CH₂CO₂R',
R'O₂C-CH=C-CO₂R', CH=CH-CO₂R', CH₂CH₂-CN or 5-methyl-2-oxo-
1,3-dioxol-4-yl-methyl,

wherein:

R' is as defined above; and

their pharmaceutically useful hydrates and salts.

The compound Moxifloxacin is most preferred. Moxifloxacin has the following structure:

Further details regarding the structure, preparation, and physical properties of Moxifloxacin and other compounds of formula (I) are provided in United States Patent No. 5,607,942.

The concentrations of the antibiotics of formula (I) in the compositions of the present invention will vary depending on the intended use of the compositions (e.g., treatment of existing infections or prevention of post-surgical infections), and the relative
antimicrobial activity of the specific antibiotic selected. The antimicrobial activity of antibiotics is generally expressed as the minimum concentration required to inhibit the growth of a specified pathogen. This concentration is also referred to as the “minimum inhibitory concentration” or “MIC”. The term “MIC90” refers to the minimum concentration of antibiotic required to inhibit the growth of ninety percent (90%) of the strains of a species. The concentration of an antibiotic required to totally kill a specified bacteria is referred to as the “minimum bactericidal concentration” or “MBC”. The minimum inhibitory concentration of Moxifloxacin for several bacteria commonly associated with ophthalmic, otic and nasal infections are provided in the following table:

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>MIC&lt;sub&gt;90&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. aureus/methicillin sensitive</td>
<td>0.13</td>
</tr>
<tr>
<td>S. aureus/methicillin resistant</td>
<td>4.0</td>
</tr>
<tr>
<td>S. aureus/quinolone resistant</td>
<td>4.0</td>
</tr>
<tr>
<td>S. epidermidis/methicillin sensitive</td>
<td>0.25</td>
</tr>
<tr>
<td>S. epidermidis/methicillin resistant</td>
<td>4.0</td>
</tr>
<tr>
<td>S. pneumoniae/penicillin sensitive</td>
<td>0.25</td>
</tr>
<tr>
<td>S. pneumoniae/penicillin resistant</td>
<td>0.25</td>
</tr>
<tr>
<td>P. aeruginosa</td>
<td>8.0</td>
</tr>
<tr>
<td>H. influenzae/β-lactamase positive</td>
<td>0.06</td>
</tr>
<tr>
<td>H influenzae/β-lactamase negative</td>
<td>0.06</td>
</tr>
</tbody>
</table>

All of the foregoing concentrations are expressed as micrograms per milliliter (“mcg/ml”).
The appropriate antibiotic concentration for ophthalmic compositions will generally be an amount of one or more antibiotics of formula (I) sufficient to provide a concentration in the aqueous humor and lacrimal fluid of the eye equal to or greater than the MIC$_{90}$ level for the selected antibiotic(s), relative to gram-negative and gram-positive organisms commonly associated with ophthalmic infections. The appropriate concentration for otic and nasal compositions will generally be an amount of one or more antibiotics of formula (I) sufficient to provide a concentration in the infected tissues equal to or greater than the MIC$_{90}$ level for the selected antibiotic(s), relative to gram-negative and gram-positive organisms commonly associated with otic or nasal infections. Such amounts are referred to herein as “an antimicrobial effective amount”. The compositions of the present invention will typically contain one or more compounds of formula (I) in a concentration of from about 0.1 to about 1.0 percent by weight ("wt. %") of the compositions.

The compositions of the present invention may also contain one or more anti-inflammatory agents. The anti-inflammatory agents utilized in the present invention are broadly classified as steroidal or non-steroidal. The preferred steroidal anti-inflammatory agents are glucocorticoids.

The preferred glucocorticoids for ophthalmic and otic use include dexamethasone, loteprednol, rimexolone, prednisolone, fluorometholone, and hydrocortisone. The preferred glucocorticoids for nasal use include mometasone, fluticasone, beclomethasone, flunisolide, triamcinolone and budesonide.

The dexamethasone derivatives described in U.S. Patent No. 5,223,493 (Boltralik) are also preferred steroidal anti-inflammatory agents, particularly with respect to compositions for treating ophthalmic inflammation. The following compounds are especially preferred:
These compounds are referred to herein as "21-ether derivatives of dexamethasone". The 21-benzyl ether derivative (i.e., compound AL-2512) is particularly preferred.

The preferred non-steroidal anti-inflammatory agents are: prostaglandin H synthetase inhibitors (Cox I or Cox II), also referred to as cyclooxygenase type I and type II inhibitors, such as diclofenac, flurbiprofen, ketorolac, suprofen, nepafenac, amfenac, indomethacin, naproxen, ibuprofen, bromfenac, ketoprofen, meclofenamate, piroxicam, sulindac, mefanamic acid, diflunisal, oxaprozin, tolmetin, fenoprofen, benoxaprofen, nabumetone, etodolac, phenylbutazone, aspirin, oxyphenbutazone, NCX-4016, HCT-1026, NCX-284, NCX-456, tenoxicam and carprofen: cyclooxygenase type II selective inhibitors, such as NS-398, vioxx, celecoxib, P54, etodolac, L-804600 and S-33516; PAF antagonists, such as SR-27417, A-137491, ABT-299, apafant, bepafant, minopafant, E-6123, BN-50727, nupafant and modipafant; PDE IV inhibitors, such as ariflo, torbayline, rolipram, filaminast, piclamilast, cipamfylline, CG-1088, V-11294A, CT-2820, PD-168787, CP-293121, DWP-205297, CP-220629, SH-636, BAY-19-8004, and roflumilast; inhibitors of cytokine production, such as inhibitors of the NFκB transcription factor; or other anti-inflammatory agents known to those skilled in the art.
The concentrations of the anti-inflammatory agents contained in the compositions of the present invention will vary based on the agent or agents selected and the type of inflammation being treated. The concentrations will be sufficient to reduce inflammation in the targeted ophthalmic, otic or nasal tissues following topical application of the compositions to those tissues. Such an amount is referred to herein as "an anti-inflammatory effective amount". The compositions of the present invention will typically contain one or more anti-inflammatory agents in an amount of from about 0.01 to about 1.0 wt.%.

The compositions are typically administered to the affected ophthalmic, otic or nasal tissues by topically applying one to four drops of a sterile solution or suspension, or a comparable amount of an ointment, gel or other solid or semisolid composition, one to four times per day. However, the compositions may also be formulated as irrigating solutions that are applied to the affected ophthalmic, otic or nasal tissues during surgical procedures.

The ophthalmic, otic and nasal compositions of the present invention will contain one or more compounds of formula (I) and preferably one or more anti-inflammatory agents, in pharmaceutically acceptable vehicles. The compositions will typically have a pH in the range of 4.5 to 8.0. The ophthalmic compositions must also be formulated to have osmotic values that are compatible with the aqueous humor of the eye and ophthalmic tissues. Such osmotic values will generally be in the range of from about 200 to about 400 milliosmoles per kilogram of water ("mOsm/kg"), but will preferably be about 300 mOsm/kg.

Ophthalmic, otic and nasal pharmaceutical products are typically packaged in multidose form. Preservatives are thus required to prevent microbial contamination during use. Suitable preservatives include: polyquaternium-1, benzalkonium chloride, thimerosal, chlorobutanol, methyl paraben, propyl paraben, phenylethyl alcohol, edetate disodium, sorbic acid, or other agents known to those skilled in the art. The use of polyquaternium-1 as the antimicrobial preservative is preferred. Typically such preservatives are employed at a level of from 0.001% to 1.0% by weight.
The solubility of the components of the present compositions may be enhanced by a surfactant or other appropriate co-solvent in the composition. Such co-solvents include polysorbate 20, 60, and 80, polyoxyethylene/polyoxypropylene surfactants (e.g., Pluronic F-68, F-84 and P-103), cyclodextrin, or other agents known to those skilled in the art. Typically such co-solvents are employed at a level of from 0.01% to 2% by weight.

The use of viscosity enhancing agents to provide the compositions of the invention with viscosities greater than the viscosity of simple aqueous solutions may be desirable to increase ocular absorption of the active compounds by the target tissues or increase the retention time in the eye, ear or nose. Such viscosity building agents include, for example, polyvinyl alcohol, polyvinyl pyrrolidone, methyl cellulose, hydroxy propyl methylcellulose, hydroxyethyl cellulose, carboxymethyl cellulose, hydroxy propyl cellulose or other agents known to those skilled in the art. Such agents are typically employed at a level of from 0.01% to 2% by weight.

The following examples are provided to further illustrate the ophthalmic, otic and nasal compositions of the present invention.

**Example 1**

**Ophthalmic/Otic/Nasal Solution**

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Amount (wt. %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moxifloxacin</td>
<td>0.35</td>
</tr>
<tr>
<td>Sodium Acetate</td>
<td>0.03</td>
</tr>
<tr>
<td>Acetic Acid</td>
<td>0.04</td>
</tr>
<tr>
<td>Mannitol</td>
<td>4.60</td>
</tr>
<tr>
<td>EDTA</td>
<td>0.05</td>
</tr>
<tr>
<td>Benzalkonium Chloride</td>
<td>0.006</td>
</tr>
<tr>
<td>Water</td>
<td>q.s. 100</td>
</tr>
</tbody>
</table>
**Example 2**

**Ophthalmic/Otic/Nasal Suspension**

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Amount (wt. %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moxifloxacin</td>
<td>0.3</td>
</tr>
<tr>
<td>Dexamethasone, Micronized USP</td>
<td>0.10</td>
</tr>
<tr>
<td>Benzalkonium Chloride</td>
<td>0.01</td>
</tr>
<tr>
<td>Edetate Disodium, USP</td>
<td>0.01</td>
</tr>
<tr>
<td>Sodium Chloride, USP</td>
<td>0.3</td>
</tr>
<tr>
<td>Sodium Sulfate, USP</td>
<td>1.2</td>
</tr>
<tr>
<td>Tyloxapol, USP</td>
<td>0.05</td>
</tr>
<tr>
<td>Hydroxyethylcellulose</td>
<td>0.25</td>
</tr>
<tr>
<td>Sulfuric Acid and/or Sodium Hydroxide, NF</td>
<td>q.s. for pH adjustment to 5.5</td>
</tr>
<tr>
<td>Purified Water, USP</td>
<td>q.s. to 100</td>
</tr>
</tbody>
</table>

**Example 3**

**Ophthalmic Ointment**

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Amount (wt. %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moxifloxacin</td>
<td>0.35</td>
</tr>
<tr>
<td>Mineral Oil, USP</td>
<td>2.0</td>
</tr>
<tr>
<td>White petrolatum, USP</td>
<td>q.s 100</td>
</tr>
</tbody>
</table>
**Example 4**

**Ophthalmic Ointment**

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Amount (wt.%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moxifloxacin</td>
<td>0.3</td>
</tr>
<tr>
<td>Fluorometholone Acetate, USP</td>
<td>0.1</td>
</tr>
<tr>
<td>Chlorobutanol, Anhydrous, NF</td>
<td>0.5</td>
</tr>
<tr>
<td>Mineral Oil, USP</td>
<td>5</td>
</tr>
<tr>
<td>White Petrolatum, USP</td>
<td>q.s. 100</td>
</tr>
</tbody>
</table>

The invention has been described herein by reference to certain preferred embodiments. However, as obvious variations thereon will become apparent to those skilled in the art, the invention is not to be considered as limited thereto.
CLAIMS:

1. A use of moxifloxacin, or a pharmaceutically useful hydrate or salt thereof in preparation of a pharmaceutical composition for topically treating or preventing an ophthalmic infection, wherein the moxifloxacin or the hydrate or salt thereof is at a concentration of 0.1 to 1.0 wt. %.

2. A use according to claim 1, wherein the composition further comprises a steroidal or non-steroidal anti-inflammatory agent.

3. A use according to claim 2, wherein the anti-inflammatory agent comprises the steroidal agent.

4. A use according to claim 3, wherein the steroidal agent comprises a glucocorticoid.

5. A use according to claim 4, wherein the glucocorticoid is selected from the group consisting of dexamethasone, rimexolone, prednisolone, fluorometholone, hydrocortisone, mometasone, fluticasone, beclomethasone, flunisolide, triamcinolone, budesonide and combinations thereof.

6. A use according to claim 4, wherein the glucocorticoid comprises dexamethasone.

7. A use according to claim 4, wherein the glucocorticoid comprises a 21-ether derivative of dexamethasone.

8. A use according to claim 4, wherein the glucocorticoid comprises a 21-benzyl ether derivative of dexamethasone.
9. A use according to claim 2, wherein the anti-inflammatory agent comprises the non-steroidal agent.

10. A use according to claim 9, wherein the non-steroidal agent is selected from the group consisting of prostaglandin H synthetase inhibitors, cyclooxygenase type II selective inhibitors, PAF antagonists, PDE IV inhibitors, and combinations thereof.

11. A use according to claim 9, wherein the non-steroidal agent comprises a prostaglandin H synthetase inhibitor.

12. A use according to claim 11, wherein the prostaglandin H synthetase inhibitor comprises nepafenac.

13. A use according to claim 11, wherein the prostaglandin H synthetase inhibitor comprises ketorolac.

14. A use according to claim 11, wherein the prostaglandin H synthetase inhibitor comprises diclofenac.

15. A use according to claim 9, wherein the non-steroidal agent comprises a cyclooxygenase type II selective inhibitor.

16. A use according to any one of claims 1 to 15, wherein the moxifloxacin or the pharmaceutically useful hydrate or salt thereof is at a concentration of 0.35 wt. % to 1.0 wt. %.

17. A use according to any one of claims 1 to 16, wherein the composition is a liquid further comprising sodium chloride.
18. A use according to claim 17, wherein the composition further comprises a viscosity enhancing agent and a surfactant.

19. A use according to any one of claims 1 to 18, wherein the composition has a pH in the range of from 4.5 to 8.0.

20. A use according to any one of claims 1 to 18, wherein the composition has a pH in the range of from 5.5 to 8.0.

21. A use according to any one of claims 1 to 20, wherein the composition has an osmotic value from about 200 to about 400 milliosmoles per kilogram of water.

22. A use according to any one of claims 1 to 20, wherein the composition has an osmotic value of about 300 milliosmoles per kilogram of water.

23. A use according to any one of claims 1 to 22, wherein the composition further comprises an antimicrobial preservative at a concentration of 0.001 to 1.0 wt. %.

24. A use according to any one of claims 1 to 23, wherein the composition is a sterile solution in a multi-dose form.

25. A use according to any one of claims 1 to 24, wherein the composition is for application in connection with an ophthalmic surgical procedure.

26. A use according to any one of claims 1 to 25, wherein the ophthalmic infection is selected from the group consisting of conjunctivitis, keratitis, blepharitis,
dacytrocystitis, hordeolum, corneal ulceration, and combinations thereof.

27. A use according to any one of claims 1 to 25, wherein the ophthalmic infection is conjunctivitis.

28. A use according to any one of claims 1 to 25, wherein the ophthalmic infection is keratitis.

29. A use according to any one of claims 25 to 28, wherein the composition is for inhibiting growth of at least one pathogen selected from the group consisting of S. aureus, S. epidermidis, S. pneumoniae, and H. influenzae.

30. A use according to any one of claims 25 to 28, wherein the composition inhibits growth of S. aureus.

31. A use according to any one of claims 25 to 28, wherein the composition inhibits growth of S. epidermidis.

32. A use according to any one of claims 25 to 28, wherein the composition inhibits growth of S. pneumoniae.

33. A use according to any one of claims 25 to 28, wherein the composition inhibits growth of H. influenzae.

34. A use according to any one of claims 25 to 28, wherein the composition inhibits growth of P. aeruginosa.

35. A use of moxifloxacin, or a pharmaceutically useful hydrate or salt thereof for topically treating or preventing an ophthalmic infection for topical administration in a composition comprising the moxifloxacin or the hydrate or salt thereof and a pharmaceutically acceptable vehicle, wherein the moxifloxacin or the hydrate or salt thereof is at a concentration of 0.1 to 1.0 wt. %.
36. A use according to claim 35, wherein the moxifloxacin is for co-administration with a steroidal or non-steroidal anti-inflammatory agent.

37. A use according to claim 36, wherein the anti-inflammatory agent comprises the steroidal agent.

38. A use according to claim 37, wherein the steroidal agent comprises a glucocorticoid.

39. A use according to claim 38, wherein the glucocorticoid is selected from the group consisting of dexamethasone, rimexolone, prednisolone, fluorometholone, hydrocortisone, mometasone, fluticasone, beclomethasone, flunisolide, triamcinolone, budesonide and combinations thereof.

40. A use according to claim 38, wherein the glucocorticoid comprises dexamethasone.

41. A use according to claim 38, wherein the glucocorticoid comprises a 21-ether derivative of dexamethasone.

42. A use according to claim 38, wherein the glucocorticoid comprises a 21-benzyl ether derivative of dexamethasone.

43. A use according to claim 36, wherein the anti-inflammatory agent comprises the non-steroidal agent.

44. A use according to claim 43, wherein the non-steroidal agent is selected from the group consisting of prostaglandin H synthetase inhibitors, cyclooxygenase type II selective inhibitors, PAF antagonists, PDE IV inhibitors, and combinations thereof.
45. A use according to claim 43, wherein the non-steroidal agent comprises a prostaglandin H synthetase inhibitor.

46. A use according to claim 44, wherein the prostaglandin H synthetase inhibitor comprises nepafenac.

47. A use according to claim 44, wherein the prostaglandin H synthetase inhibitor comprises ketorolac.

48. A use according to claim 44, wherein the prostaglandin H synthetase inhibitor comprises diclofenac.

49. A use according to claim 44, wherein the non-steroidal agent comprises a cyclooxygenase type II selective inhibitor.

50. A use according to any one of claims 35 to 49, wherein the moxifloxacin or the pharmaceutically useful hydrate or salt thereof is at a concentration of 0.35 wt. % to 1.0 wt. %.

51. A use according to any one of claims 35 to 50, wherein the composition is for application in connection with an ophthalmic surgical procedure.

52. A use according to any one of claims 35 to 51, wherein the ophthalmic infection is selected from the group consisting of conjunctivitis, keratitis, blepharitis, dacyrocystitis, hordeolum, corneal ulceration, and combinations thereof.

53. A use according to any one of claims 35 to 51, wherein the ophthalmic infection is conjunctivitis.

54. A use according to any one of claims 35 to 51, wherein the ophthalmic infection is keratitis.
55. A use according to any one of claims 51 to 54, wherein the ophthalmic infection is associated with at least one pathogen selected from the group consisting of *S. aureus*, *S. epidermidis*, *S. pneumoniae*, and *H. influenzae*.

56. A use according to any one of claims 51 to 54, wherein the ophthalmic infection is associated with *S. aureus*.

57. A use according to any one of claims 51 to 54, wherein the ophthalmic infection is associated with *S. epidermidis*.

58. A use according to any one of claims 51 to 54, wherein the ophthalmic infection is associated with *S. pneumoniae*.

59. A use according to any one of claims 51 to 54, wherein the ophthalmic infection is associated with *H. influenzae*.

60. A use according to any one of claims 51 to 54, wherein the ophthalmic infection is associated with *P. aeruginosa*.

61. A pharmaceutical composition comprising moxifloxacin or a pharmaceutically useful hydate or salt thereof and a pharmaceutically acceptable vehicle therefor for topically treating or preventing an ophthalmic infection, wherein the moxifloxacin or the hydate or salt thereof is at a concentration of 0.1 to 1.0 wt. %.

62. A pharmaceutical composition according to claim 61, further comprising a steroidal or non-steroidal anti-inflammatory agent.
63. A pharmaceutical composition according to claim 62, wherein the anti-inflammatory agent comprises the steroidal agent.

64. A pharmaceutical composition according to claim 63, wherein the steroidal agent comprises a glucocorticoid.

65. A pharmaceutical composition according to claim 64, wherein the glucocorticoid is selected from the group consisting of dexamethasone, rimexolone, prednisolone, fluorometholone, hydrocortisone, mometasone, fluticasone, beclomethasone, flunisolide, triamcinolone, budesonide and combinations thereof.

66. A pharmaceutical composition according to claim 64, wherein the glucocorticoid comprises dexamethasone.

67. A pharmaceutical composition according to claim 64, wherein the glucocorticoid comprises a 21-ether derivative of dexamethasone.

68. A pharmaceutical composition according to claim 64, wherein the glucocorticoid comprises a 21-benzyl ether derivative of dexamethasone.

69. A pharmaceutical composition according to claim 62, wherein the anti-inflammatory agent comprises the non-steroidal agent.

70. A pharmaceutical composition according to claim 69, wherein the non-steroidal agent is selected from the group consisting of prostaglandin H synthetase inhibitors, cyclooxygenase type II selective inhibitors, PAF antagonists, PDE IV inhibitors, and combinations thereof.
71. A pharmaceutical composition according to claim 69, wherein the non-steroidal agent comprises a prostaglandin H synthetase inhibitor.

72. A pharmaceutical composition according to claim 71, wherein the prostaglandin H synthetase inhibitor comprises nepadenc.

73. A pharmaceutical composition according to claim 71, wherein the prostaglandin H synthetase inhibitor comprises ketorolac.

74. A pharmaceutical composition according to claim 71, wherein the prostaglandin H synthetase inhibitor comprises diclofenac.

75. A pharmaceutical composition according to claim 69, wherein the non-steroidal agent comprises a cyclooxygenase type II selective inhibitor.

76. A pharmaceutical composition according to any one of claims 61 to 75, wherein the moxifloxacin or the pharmaceutically useful hydrate or salt thereof is at a concentration of 0.35 wt. % to 1.0 wt. %.

77. A pharmaceutical composition according to any one of claims 61 to 76, wherein the composition is a liquid further comprising sodium chloride.

78. A pharmaceutical composition according to claim 77, further comprising a viscosity enhancing agent and a surfactant.

79. A pharmaceutical composition according to any one of claims 61 to 78, wherein the composition has a pH in the range of from 4.5 to 8.0.
80. A pharmaceutical composition according to any one of claims 61 to 78, wherein the composition has a pH in the range of from 5.5 to 8.0.

81. A pharmaceutical composition according to any one of claims 61 to 80, wherein the composition has an osmotic value from about 200 to about 400 milliosmoles per kilogram of water.

82. A pharmaceutical composition according to any one of claims 61 to 80, wherein the composition has an osmotic value of about 300 milliosmoles per kilogram of water.

83. A pharmaceutical composition according to any one of claims 61 to 82, further comprising an antimicrobial preservative at a concentration of 0.001 to 1.0 wt. %.

84. A pharmaceutical composition according to any one of claims 61 to 82, wherein the composition is a sterile solution in a multi-dose form.

85. A pharmaceutical composition according to any one of claims 61 to 84, wherein the composition is for application in connection with an ophthalmic surgical procedure.

86. A pharmaceutical composition according to any one of claims 61 to 85, wherein the ophthalmic infection is selected from the group consisting of conjunctivitis, keratitis, blepharitis, dacyrocystitis, hordeolum, corneal ulceration, and combinations thereof.

87. A pharmaceutical composition according to any one of claims 61 to 85, wherein the ophthalmic infection is conjunctivitis.
88. A pharmaceutical composition according to any one of claims 61 to 85, wherein the ophthalmic infection is keratitis.

89. A pharmaceutical composition according to any one of claims 85 to 88, wherein the composition is for inhibiting growth of at least one pathogen selected from the group consisting of *S. aureus*, *S. epidermidis*, *S. pneumoniae*, and *H. influenzae*.

90. A pharmaceutical composition according to any one of claims 85 to 88, wherein the composition inhibits growth of *S. aureus*.

91. A pharmaceutical composition according to any one of claims 85 to 88, wherein the composition inhibits growth of *S. epidermidis*.

92. A pharmaceutical composition according to any one of claims 85 to 88, wherein the composition inhibits growth of *S. pneumoniae*.

93. A pharmaceutical composition according to any one of claims 85 to 88, wherein the composition inhibits growth of *H. influenzae*.

94. A pharmaceutical composition according to any one of claims 85 to 88, wherein the composition inhibits growth of *P. aeruginosa*.

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