Novel Contact Lens Disinfection Solution

with Broad Antimicrobial Activity and Low Cytotoxicity

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I, along with Dr. Chad Roy and Dr. Robert Reimers, am an inventor on a patent application covering the compounds and methods described in this talk. The patent application is assigned to Tulane University.

I have NO financial disclosures!
Contact Lens Disinfection Solution (CLDS)

40 million U.S. contact lens wearers

≈ 80,000 infections annually

Variety of OTC contact lens disinfecting solutions (CLDS)

Major source of eye infections & common among CLDS users (1:500)

Major recent eye infection outbreaks (2006, 2007)

Painful/debilitating corneal infection, eye loss; permanent loss of vision

1 FDA. Looking good: safe use and care of contact lenses (May 2010). 2010
Medical Disinfection

Contact Lens Disinfecting Solution

Standard Of Care

‘Active’ ingredient
  • (bis)biguanide class (>95%)
    • polyaminopropylbiguanide (PAPB)

(SoC) disinfection marginal against vegetative bacteria
  • poorly against
    • biofilms [Bispo et al., 2015]
    • fungi, yeasts, viruses, & infectious protozoa

Promotes a ‘single stressor’ environment
Medical Disinfection
Contact Lens Disinfecting Solution

New formulation with novel active ingredients

- **Multiple** active components chemically distinct from organic biguanide salts
- **Broad spectrum antimicrobial** effective killing/disinfection across microbial kingdoms
- Minimally cytotoxic
- ‘Multiple stressor’ environment
**Multiple Stressors:** The importance of broad spectrum effectiveness across multiple microbial kingdoms

<table>
<thead>
<tr>
<th>Protista</th>
<th>Fungi</th>
<th>Monera</th>
<th>Viruses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single-celled eukaryotes</td>
<td>Fungi, yeast</td>
<td>Eubacteria, archeobacteria</td>
<td>herpes virus adenovirus</td>
</tr>
<tr>
<td>acanthamoeba</td>
<td>Fusarium solani</td>
<td>Pseudomonas aeruginosa</td>
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<tr>
<td></td>
<td>Candida albicans</td>
<td>Staphylococcus aureus</td>
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Disruptive technology application in CL disinfection

Current Disinfection Technology

- Single ‘stressor’ environment
- Limited effectiveness across microbial spectrum
- Limited cytotoxicity
Disruptive technology application in CL disinfection

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Novel Component Solution

- Multiple stressor environment
- Broad spectrum antimicrobial effectiveness
- Limited cytotoxicity

Chem oxidizer (1)
Chem (1)
Chem oxidizer (2)
Disruptive technology application in CL disinfection

**Novel Component Solution**

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- Broad spectrum antimicrobial effectiveness
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**Chem oxidizer (1)**

**Chem (1)**

**Chem oxidizer (2)**
Preliminary Testing – Novel Solutions v. (over the counter) Comparator Commercially Available CLDS

**sl-1 & sl-2**

Novel component CLDS formulations

**OTC - SOL03**
- Opti-Free
  (Novartis/Alcon)

**OTC - SOL04**
- ReNu
  (Valeant/B+L)

**OTC - SOL05**
- Biotrue
  (Valeant/B+L)
Antimicrobial Assay (ISO14729)

Microbiological requirements and test methods for products and regimens for hygienic management of contact lenses

The stand-alone test

Standard inoculum of a representative range of microorganisms; establishes the extent of their viability loss at predetermined time intervals comparable with those during which the product may be used.

The size of the microbial challenge chosen in this test is not intended to be representative of the likely challenge in practice but to provide countable numbers from which estimation of the rate and extent of viability loss can be determined.
# Challenge Organisms + Timing

## Pathogens

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>Fungi</th>
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<tbody>
<tr>
<td>Pseudomonas aeruginosa,</td>
<td>Candida albicans,</td>
</tr>
<tr>
<td>Staphylococcus aureus,</td>
<td>Fusarium solani</td>
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<tr>
<td>Serratia marcescens</td>
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## Challenge

- **100 µl** of solution to **9.9 ml** of **microbial challenge inocula**
- **Challenge** (1, 4 hours contact time)
- **Washed completely** - 0.45 µm filter prior to plating (TSA, PDA)
- **48 hr** growth at 33 d C
**Staphylococcus aureus**

*Staphylococcus aureus* (GM+) is a coccal bacterium that is a member of the Firmicutes, and is frequently found in the human respiratory tract and on the skin. It is positive for catalase and nitrate reduction. Although S. aureus is not always pathogenic, it is a common cause of skin infections (e.g. boils), respiratory disease (e.g. sinusitis), and food poisoning. Disease-associated strains often promote infections by producing potent protein toxins, and expressing cell-surface proteins that bind and inactivate antibodies. The emergence of antibiotic-resistant forms of pathogenic S. aureus (e.g. MRSA) is a worldwide problem in clinical medicine.
### Staphylococcus aureus

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<tr>
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<th>sl-1</th>
<th>sl-2</th>
<th>OTC-03</th>
<th>OTC-04</th>
<th>OTC-05</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1 Hour Contact</strong></td>
<td><img src="sl-1.png" alt="Image" /></td>
<td><img src="sl-2.png" alt="Image" /></td>
<td><img src="OTC-03.png" alt="Image" /></td>
<td><img src="OTC-04.png" alt="Image" /></td>
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<td><strong>4 Hour Contact</strong></td>
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Pseudomonas aeruginosa (GM-) is a common bacterium that can cause disease in animals, including humans. It is citrate, catalase, and oxidase positive. It is found in soil, water, skin flora, and most man-made environments throughout the world. It thrives not only in normal atmospheres, but also in hypoxic atmospheres, and has, thus, colonized many natural and artificial environments. It uses a wide range of organic material for food; in animals, its versatility enables the organism to infect damaged tissues or those with reduced immunity. The symptoms of such infections are generalized inflammation and sepsis. If such colonization occurs in critical body organs, such as the lungs, the urinary tract, and kidneys, the results can be fatal. Because it thrives on moist surfaces, this bacterium is also found on and in medical equipment, including catheters, causing cross-infections in hospitals and clinics.
Pseudomonas aeruginosa

1 Hour Contact

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4 Hour Contact

| sl-1 | sl-2 | OTC-03 | OTC-04 | OTC-05 |
Serratia marcescens is a species of rod-shaped Gram-negative bacteria in the family Enterobacteriaceae. A human pathogen, S. marcescens is involved in hospital-acquired infections (HAIs), particularly catheter-associated bacteremia, urinary tract infections and wound infections, and is responsible for 1.4% of HAI cases in the United States. It is commonly found in the respiratory and urinary tracts of hospitalized adults and in the gastrointestinal system of children. Due to its abundant presence in the environment, and its preference for damp conditions, S. marcescens is commonly found growing in bathrooms (especially on tile grout, shower corners, toilet water line, and basin), where it manifests as a pink, pink-orange, or orange discoloration and slimy film feeding off phosphorus-containing materials or fatty substances such as soap and shampoo residues.
Serratia marcescens

1 Hour Contact

sl-1

sl-2

OTC-03

OTC-04

OTC-05

4 Hour Contact
Candida Albicans is a diploid fungus that grows both as yeast and filamentous cells and a causal agent of opportunistic oral and genital infections in humans, and candidal onychomycosis, an infection of the nail plate. Systemic fungal infections (fungemias) including those by C. albicans have emerged as important causes of morbidity and mortality in immunocompromised patients (e.g., AIDS, cancer chemotherapy, organ or bone marrow transplantation). C. albicans biofilms may form on the surface of implantable medical devices. In addition, hospital-acquired infections by C. albicans have become a cause of major health concerns.
Candida Albicans

**sl-1**

**sl-2**

**OTC-03**

**OTC-04**

**OTC-05**

↑ 1hr  
↑ 1hr  
↑ 1hr  
↑ 1hr  
↑ 1hr
Fusarium solani is a filamentous fungus in the genus Fusarium, and the anamorph of Haematonectria haematococca. It is commonly isolated from soil and plant debris.

The fungus has a worldwide distribution, but its frequency as a medically important pathogen is not fully known. Aside from keratitis, it is an infrequent cause of fungal infections but remains the most common disease-causing fungus in its genus.
Fusarium solani

1 Hour Contact

sl-1  sl-2  OTC-03  OTC-04  OTC-05

4 Hour Contact
Cytotoxicity Assay (ISO10993)

Vero76 cells (C. atheiops kidney)

Application of dilution of solution(s) on adherent cells

XTT proliferation assay for measurement of cell death

Colorimetric reading
  • convert to relative % of absorbance for untreated cells
Cytotoxicity
Cytotoxicity

Optimal Viability
Conclusions

Multi-stressor approach is completely novel

In comparison to currently available OTC multipurpose CLDS, our novel solution was found superior for antimicrobial killing over multiple kingdoms
  • STERILIZING, not simply disinfecting!

Cytotoxicity is equivalent to current OTC multipurpose CLDS

Future testing is to be done against Acanthamoeba and in live animal infection models
Acknowledgements

Laboratories involved

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Dr. Chad Roy, Professor Tulane School of Medicine, Department of Microbiology and Immunology

Dr. Delmar Caldwell, Chairman of Ophthalmology Tulane University School of Medicine

Stephanie Killeen, lab technician

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Thank you for your attention!