CIDEX® OPA Solution Effectiveness Against Disease-Causing Microbes

MAIN POINTS

- **Five studies have evaluated the effectiveness of CIDEX® OPA Solution against:**
  - **More than 200 strains of bacteria, including antibiotic-resistant strains**
  - **Mycobacteria**
  - **Spore-forming bacteria**
  - **Viruses**
  - **Fungi[1-5]**
- **CIDEX® OPA Solution kills everything tested except spores very quickly, even under rigorous testing.[1-5]**
- **CIDEX® OPA Solution remains effective in the presence of blood and organic matter.[2, 3]**

PURPOSE

The purpose of this document is to provide a review of recent scientific findings on the killing efficacy of CIDEX® *ortho*–phthalaldehyde (OPA) Solution. Five research studies have been reviewed and summarized. Several additional sources were used to provide background information.

INTRODUCTION AND BACKGROUND

Healthcare-Associated Infections

Every year, more than 2 million healthcare-associated infections occur in the U.S.[6] These infections result in approximately 90,000 deaths each year, and are one of the most frequent "adverse medical events" in the U.S.[6, 7]

"A recent comprehensive review of the medical literature suggests that transmission of infection resulting from gastrointestinal endoscopy is an extremely rare event, and has invariably been associated with a breach in cleaning protocols or defective equipment."[8]

CIDEX® OPA SOLUTION

CIDEX® OPA Solution is a high-level disinfectant (HLD) with low odor and is highly compatible with medical materials.[1, 2, 9] It was developed by Johnson & Johnson Medical Inc. and cleared for use in the U.S. in 1999.[9] Scientists have studied the effectiveness of CIDEX® OPA Solution and have found it to be effective at killing a broad spectrum of bacteria and other disease-causing organisms.[1-5, 9-11]

STUDY METHODS

While the exact testing methods varied between studies, the same general steps were taken in all five research studies.

1. Disease-causing microorganisms (microbes) were obtained either from stock laboratory supplies or from hospitalized patients.
2. Microbes were grown.
3. Microbes on inoculated carriers or in suspension were exposed to CIDEX® OPA Solution for a set amount of time.
4. Tests were performed to measure microbe survival after exposure to CIDEX® OPA Solution.[1-5]

LOG_{10} REDUCTIONS

The effectiveness of HLDs is often measured in log_{10} reduction factors.[1, 3-5]

To illustrate the concept of log_{10} reduction factors, imagine that there are 5 million bacteria contaminating a medical instrument.

- **If disinfected with an HLD with a log_{10} reduction factor of 5.0, 50 bacteria will remain**
- **If disinfected with an HLD with a log_{10} reduction factor of 4.0, 500 bacteria will remain**
- **If disinfected with an HLD with a log_{10} reduction factor of 3.0, 5,000 bacteria will remain**

In other words, a one-unit increase on the log_{10} scale indicates an increase in killing effectiveness of 10 times.

CIDEX® OPA Solution Effectiveness Against Vegetative Bacteria

The effectiveness of CIDEX® OPA Solution has been tested against many vegetative bacteria. See Table 1.

Table 1. Vegetative Bacteria Killed by CIDEX® OPA Solution

Acinetobacter baumanii
***Acinetobacter* species unspecified**
***Enterobacter cloacae* isolated from a patient**
***Enterobacteriace* isolated from a patient**
Enterococcus faecalis
– Laboratory strain
– Isolates from patients
Escherichia coli
– 2 laboratory strains
– Isolates from patients
Helicobacter pylori
– 2 laboratory strains
Klebsiella pneumoniae
Proteus mirabilis
Pseudomonas aeruginosa
– 2 laboratory strains
– Isolates from patients
Serratia marcescens
***Staphylococcus* species unspecified**
Staphylococcus aureus
–2 laboratory strains
– Isolates from patients
Stentrophomonas maltophilia
***Streptococcus* species unspecified**
Staphylococcus epidermidis
Xanthomonas maltophilia

In three studies, CIDEX® OPA Solution was highly bactericidal against all vegetative, non-spore forming microbes.[1, 2, 4]

In two studies by Herruzo-Cabrera, both laboratory stock strains and patient-isolated strains of bacteria were utilized, and CIDEX® OPA Solution was able to reduce the bacterial load by greater than 10,000 times ($\log_{10}$ reduction factors of 4.63 and 4.7) within 10 minutes.[1, 4]

According to Akamatsu, CIDEX® OPA Solution eliminated all viable cells for 11 different strains of bacteria in 15 seconds or less.[2] In addition, CIDEX® OPA Solution remained bactericidal and fast-acting in the presence of human serum for all of the 11 organisms tested.[2]

Another study was designed to represent a "worst case scenario" by using:

- Rough-surfaced instruments.
- Inoculating the instrument with both lab and freshly isolated strains of bacteria and fungi from ICU patients.
  - Over 200 strains were tested, including 66 strains of *P. aeruginosa*, some of which were resistant or multiple drug-resistant
  - *P. aeruginosa* can cause respiratory infections in patients who have endoscopy procedures, and it can often survive high-level disinfection.[1]

CIDEX® OPA Solution easily killed all of the microbes tested with the exception of *P. aeruginosa*. While OPA was not able to kill all of the *P. aeruginosa* strains, it was still able to effectively kill 77% of 44 clinical isolates after 10 minutes of exposure.[1]

When CIDEX® OPA Solution was compared to other HLDs, CIDEX® OPA Solution was often faster and more effective.
• In one study, CIDEX® OPA Solution was twice as fast as glutaraldehyde (GTA) at eliminating 11 strains of bacteria.[2]
• In another study, CIDEX® OPA Solution killed a higher percentage of microbes than Perasafe (92% vs. 74%).[4] (see Figure 1)

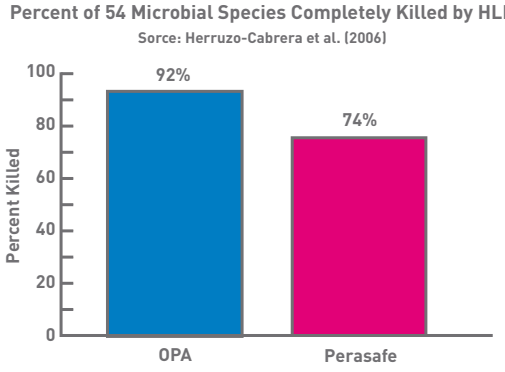

Figure 1. Percent of species killed by CIDEX® OPA Solution and Perasafe

"OPA, at a concentration of 0.55%, shows excellent mycobactericidal activity within 10 min…In comparison, 2% GTA requires at least 20 min to be effective (this time period is even longer for some mycobacteria, e.g. *M. avium intracellulare*). These findings would vindicate substitution of 2% GTA with 0.55%"[1]

CIDEX® OPA Solution Effectiveness Against Mycobacteria

Figure 2. Close-up of a *Mycobacterium tuberculosis* growth
Image Source: Public Health Image Library

Mycobacteria cause healthcare-related infections.[3] *M. tuberculosis* infections can occur from improperly disinfected endoscopes and bronchoscopes. In addition, *M. chelonae* has been implicated in hospital-acquired infections.[3]

CIDEX® OPA Solution has been shown to kill mycobacteria in multiple studies.[1, 3, 4]

- In one study:
  - CIDEX® OPA Solution reduced the number of mycobacteria by a factor greater than 10,000 (log_{10} reduction factor of 4.3) after 10 minutes of exposure.[4]
  - CIDEX® OPA Solution was more effective at killing mycobacteria than Perasafe.[4]
- In another study, CIDEX® OPA Solution was shown to be faster acting against mycobacteria than GTA.[3] (See Figure 3)

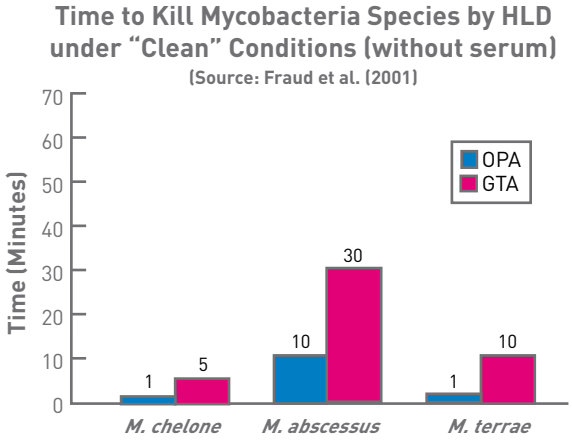

Figure 3. Killing time of Mycobacteria by CIDEX® OPA Solution and GTA in "clean" conditions

The addition of serum did not affect the efficacy of CIDEX® OPA Solution against the tested mycobacteria.[2, 3] It did, however, increase the amount of time required for GTA disinfection, doubling the required time for two of the species.[3] (See Figure 4).

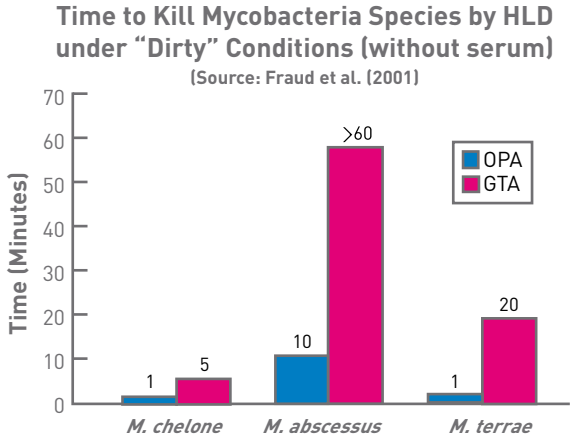

Figure 4. Killing time of Mycobacteria by CIDEX® OPA Solution and GTA in "dirty" conditions

"Results showed that 0.5% acidic and alkaline OPA were rapidly mycobactericidal, under both 'clean' and 'dirty' conditions, and more importantly were active against GTA-resistant strains."[3]

The effectiveness of CIDEX® OPA Solution has been tested against several mycobacteria.

Table 2. Mycobacteria Killed by CIDEX® OPA Solution

Mycobacterium abscessus
M. avium
– 2 laboratory strains
– a patient isolate
M. chelonae
– Laboratory strain
– a patient isolate
– 2 Laboratory strains resistant to GTA
M. fortuitum
– 2 laboratory strains
M. kansasii
M. smegmatis
M. terrae
M. tuberculosis
– 2 laboratory strains

CIDEX® OPA Solution can also kill GTA-resistant mycobacteria, such as *M. chelonae* (Epping) and *M. chelonae* (Harefield).[3] These organisms were eliminated by CIDEX® OPA Solution within two minutes or less in both clean and dirty conditions.[3]

CIDEX® OPA Solution Effectiveness Against Spores and Spore-Forming Bacteria

Figure 5. An electron micrograph of *Bacillus subtilis* cells

Because HLDs are not required to eliminate spores (only sterilization completely eliminates spores[9]),there are limited data about the efficacy of CIDEX® OPA Solution against them. The effectiveness of CIDEX® OPA Solution has been tested against the two spore-forming bacteria.

Table 3. Spores Reduced by CIDEX® OPA Solution

Bacillus subtilis
Bacillus atrophaeus

According to researchers, CIDEX® OPA Solution has shown effectiveness in reducing the number of *Bacillus atrophaeus* and *B. subtilis* spores.[4, 9]

Currently, there is great concern about hospital-acquired *Clostridium difficile* (or *"C. diff"* as it is called) infections. *C. difficile* spores are quite sensitive to standard disinfection processes and are eliminated with relatively short times of exposure to HLDs, such as CIDEX® OPA Solution.[11]

CIDEX® OPA Solution Effectiveness Against Viruses

Scientists have tested and found CIDEX® OPA Solution to be virucidal for many viruses.[10] Independent researchers have also tested the effectiveness of CIDEX® OPA on Hepatitis B and Adenovirus 8.[2, 5]

Table 4. Viruses Destroyed by CIDEX® OPA Solution

Adenovirus 2
Adenovirus 8
Coxsackie Type B-3
Cytomegalovirus
Hepatitis B (HBV)
Herpes Simplex 1 and 2
HIV-1
Human Coronavirus
Influenza Type A (Hong Kong)
Polio 1
Rhinovirus Type 42
Vaccinia (smallpox)

Hepatitis B (HBV)

In one study, scientists used radioimmunoassay to determine if the HBV remained infectious after exposure to CIDEX® OPA Solution.[2] After 30 seconds, CIDEX® OPA Solution had reduced the infectivity of HBV below the threshold value for the test.[2]

"The World Health Organization recommends hypochlorous acid and GTA as an effective disinfectant against hepatitis B virus; our results show that OPA is also an effective disinfectant against hepatitis B virus."[2]

Adenovirus 8

Adenovirus 8 is a very resilient virus and can persist in the environment on hard surfaces for more than 30 days.[5] It is a common cause of hospital-acquired eye infections and can be spread by:

- Contact with contaminated medical equipment
- Direct person-to-person contact
- Airborne droplets

CIDEX® OPA Solution was able to reduce the viral load of Adenovirus 8 to safe levels after one minute of exposure, even in the presence of serum. CIDEX® OPA Solution was also more effective on Adenovirus 8 after exposure for five minutes than all other germicides tested, including peracetic acid and 70% ethanol.[5] (See Figure 6).

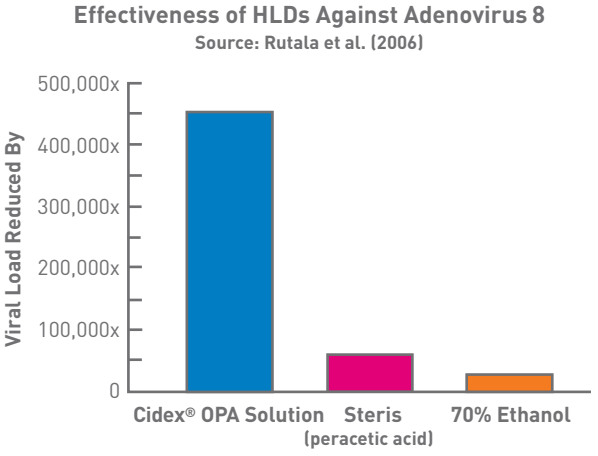

Figure 6. The number of Adenovirus 8 eliminated by three HLDs

CIDEX® OPA Solution Effectiveness Against Fungi

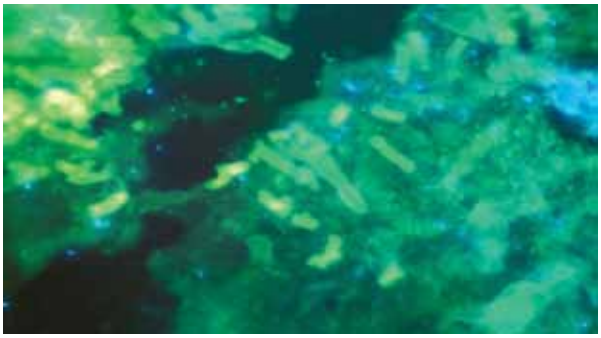

Figure 7. An electron micrograph of *Candida albicans*
Image Source: Public Health Image Library

The effectiveness of CIDEX® OPA Solution has been tested against several fungi.

Table 5. Fungi Killed by CIDEX® OPA Solution

Candida albicans
Mucor racemosus
Rhizopus nigricans
Aspergillus niger
A. terreus

The results of two studies show CIDEX® OPA Solution as an effective and fast-acting fungicide.[1, 2]

Herruzo-Cabrera et al. tested the effect of CIDEX® OPA Solution on eight different isolates of *Candida albicans*.[1] After 10 minutes of exposure, CIDEX® OPA Solution reduced the number of organisms by an average of nearly 20,000 times ($\log_{10}$ reduction factor of 4.3).[1]

Akamatsu et al. tested the fungicidal activity of CIDEX® OPA Solution and GTA against five fungi.[2] CIDEX® OPA Solution was at least twice as fast at killing the fungi tested as GTA.[2] (See Figure 8)

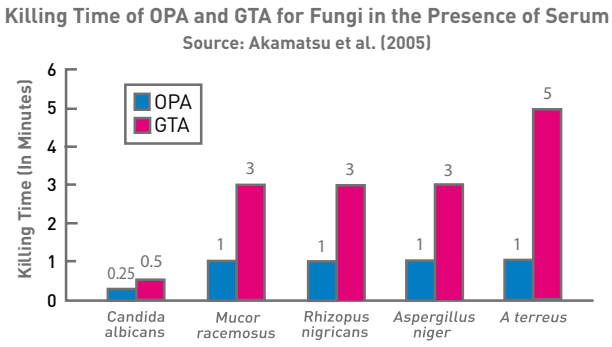

Figure 8. Fungal killing times by CIDEX® OPA and GTA in the presence of serum

Discussion and Conclusions

CIDEX® OPA Solution has demonstrated high levels of bactericidal, virucidal, and fungicidal activity in multiple studies against a wide range of organisms.[1-5, 9]

Clinically isolated bacteria should be used when determining the effectiveness of an HLD because of their increased resistance to HLDs.[1] When CIDEX® OPA Solution was used against the clinically isolated strains, it was effective against the majority of the tested organisms, even under "worst case" conditions.[1]

There have been limited published studies of the effectiveness of CIDEX® OPA Solution against viruses. In some cases, it is impossible to do direct virucidal testing because the viruses currently cannot be grown in a laboratory setting (such as human papillomavirus, and Norwalk and Norwalk-like viruses).[9] However, some of the most concerning viruses (such as hepatitis B and C and HIV) are very fragile and are easily destroyed by all HLDs.[11] CIDEX® OPA Solution was very effective at eliminating Adenovirus 8, a very hardy and persistent virus.[5]

CIDEX® OPA Solution shows fast killing action against microbes that are resistant to GTA, in addition to having other advantages over GTA.[3]

"CIDEX® OPA Solution has several potential advantages compared to Glutaraldehyde. It has excellent stability over a wide pH range (pH 3-9), is not a known irritant to the eyes and nasal passages, does not require exposure monitoring, has a barely perceptible odor, and requires no activation." [9]

Post-gastrointestinal endoscope infection occurs very rarely, and has been highly correlated with a break in disinfection procedures or faulty equipment.[8] The scientific evidence shows that CIDEX® OPA Solution is an easy to use HLD and is very effective.[1, 2, 9]

Although the data used in these papers suggest that CIDEX® OPA Solution is effective with exposure conditions different than the cleared claims, CIDEX® OPA Solution should always be used consistent with its Direction for Use.

References

1. Herruzo-Cabrera R, Vizcaino-Alcaide MJ, Fernandez-Acenero MJ. The influence of laboratory adaptation on test strains, such as Pseudomonas aeruginosa, in the evaluation of the antimicrobial efficacy of ortho-phthalaldehyde. *J Hosp Infect.* Jul 2004;57(3):217-222.
2. Akamatsu T, Minemoto M, Uyeda M. Evaluation of the antimicrobial activity and materials compatibility of orthophthalaldehyde as a high-level disinfectant. *J Int Med Res.* Mar-Apr 2005;33(2):178-187.
3. Fraud S, Maillard JY, Russell AD. Comparison of the mycobactericidal activity of ortho-phthalaldehyde, glutaraldehyde and other dialdehydes by a quantitative suspension test. *J Hosp Infect.* Jul 2001;48(3):214-221.
4. Herruzo-Cabrera R, Vizcaino-Alcaide MJ, Rodriguez J. Comparison of the microbicidal efficacy on germ carriers of several tertiary amine compounds with ortho-phthalaldehyde and Perasafe. *J Hosp Infect.* May 2006;63(1):73-78.
5. Rutala WA, Peacock JE, Gergen MF, Sobsey MD, Weber DJ. Efficacy of hospital germicides against adenovirus 8, a common cause of epidemic keratoconjunctivitis in health care facilities. *Antimicrob Agents Chemother.* Apr 2006;50(4):1419-1424.
6. Joint Commission Resources Inc., Joint Commission on Accreditation of Healthcare Organizations. *Meeting JCAHO's infection control requirements: a priority focus area.* Oakbrook Terrace, IL: Joint Commission Resources; 2004.
7. Klevens RM, Edwards JR, Richards CL, Jr., et al. Estimating health care-associated infections and deaths in U.S. hospitals, 2002. *Public Health Rep.* Mar-Apr 2007;122(2):160-166.
8. Nelson DB. Recent advances in epidemiology and prevention of gastrointestinal endoscopy related infections. *Curr Opin Infect Dis.* Aug 2005;18(4):326-330.
9. Rutala WA, Weber DJ. Disinfection and Sterilization in Healthcare Facilities. http://www.unc.edu/depts/spice/dis/DisinfectionAndSterilizationInHealthcare.pdf. Accessed August 8, 2007.
10. Advanced Sterilization Products. CIDEX® OPA High Level Disinfecting Solution Technical Information. http://sterrad.com/Products_&_Services/CIDEX/CIDEX_OPA/Files/opa_white_paper.pdf. Accessed October 3, 2007.
11. Nelson DB. Infection control during gastrointestinal endoscopy. *Can J Gastroenterol.* Jan 2007;21(1):13-15.

AD-55031-01-US_B