The Science Behind Stable, Super-Oxidized Water

Exploring the various applications of super-oxidized solutions

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Electrolysis is a process in which an electric current is passed through water or a solution, generating various reactive chemical species that depend on the solute and the electrode material used for producing electrolysis. Most super-oxidized solutions (or waters) are electrochemically processed aqueous solutions manufactured from pure water and sodium chloride. In general, the concept of electrolysis is relatively simple: tap water is purified through reverse-osmosis and USP-grade sodium chloride is added before being submitted to an electric field. During this electrolysis process, molecules are pulled apart in a chamber with positive and negative poles, and hypochlorite/ous species and free radicals are formed. The final result is a blend of reactive species of chlorine and oxygen with numerous applications in medicine and disinfection. This article will review some of these applications as they apply to wound care.

The Dawn of a New Solution

Researchers from the United States, United Kingdom, and Japan have investigated super-oxidized solutions as disinfectants for instruments and hard, inanimate surfaces in hospitals.\textsuperscript{1-3} For example, super-oxidized solutions have decreased the time, toxicity, and costs of material disinfection in endoscopes.\textsuperscript{4} The literature also describes the use of super-oxidized solutions on humans for various indications including the treatment of infectious skin defects or ulcers, mediastinal irrigation after open-heart surgery, and treatment of peritonitis and intraperitoneal abscesses.\textsuperscript{5-8} Super-oxidized solutions have also been recommended for hand washing in medical personnel.\textsuperscript{9}

Unfortunately, the instability and corrosion potential of the first solutions completely destroyed the market at the end of the 1990s. At that time, Oculus Innovative Sciences generated Microcyn\textsuperscript{®} Technology (a super-oxidized, non-toxic, non-irritating, no-rinse dermal wound irrigant) that could be used for wound care treatment. The electrolysis cells used to produce this super-oxidized solution are significantly different from those previously designed by other companies. This solu-

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In-Vitro Antimicrobial Activity

The first results of the antimicrobial activity of Microcyn Technology have recently been published by independent researchers.\textsuperscript{11} In addition, many other tests have been conducted by third-party laboratories in accordance with Good
Laboratory Practices (GLP), as specified in 21CFR Part 58. Some examples are described.

**Bactericidal and fungicidal activity (suspension tests).** An in-vitro time kill evaluation was performed using Microcyn Technology versus challenge suspensions of 50 different microorganism strains (25 American Type Culture Collection [ATCC] strains and 25 clinical isolates of those same species) as described in the Tentative Final Monograph. After exposure for 30 seconds, there was a reduction of the bacterial load >5 log_{10} in the following samples: *Pseudomonas aeruginosa*, *Escherichia coli*, *Enterococcus hirae*, *Acinetobacter baumannii*, *Acinetobacter species*, *Bacteroides fragilis*, *Enterobacter aerogenes*, *Enterococcus faecalis*, vancomycin-resistant enterococcus (VRE), *Haemophilus influenzae*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, *Micrococcus luteus*, *Proteus mirabilis*, *Serratia marcescens*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Staphylococcus pyogene*, and *Candida albicans* (BioScience Labs, Bozeman, Mont.).

**Bactericidal and fungicidal activity (carrier tests).** In various tests, the bactericidal and fungicidal properties of Microcyn Technology have been tested in accordance to EPA DIS/TSS guidelines. Under these conditions, Microcyn Technology has totally inhibited the growth of the following microorganisms: *Mycobacterium bovis* (OT #105401) in 5 minutes; *P. aeruginosa* (ATCC #15442), *S. aureus* (ATCC #6538), *Salmonella choleraesuis* (ATCC #10708), methicillin-resistant *S. aureus* (MRSA, ATCC #33592); and *Trichophyton mentagrophytes* (ATCC #9533) in 10 minutes; and vancomycin-resistant *Enterococcus faecalis* (VRE, ATCC #51299) in 15 minutes (ATS Labs, Eagan, Minn.).

**Virucidal activity.** Microcyn Technology was tested to determine the virucidal characteristics against the human immunodeficiency virus type 1 (HIV-1) strain HTLV-IIB in accordance with the United States EPA DIS/TSS-07 guidelines. In an independent study, the reduction in viral titer was >3 log_{10} after a 5-minute exposure to Microcyn Technology.11

**Sporicidal activity.** Microcyn Technology was tested to determine sporicidal characteristics against spores of *Bacillus atrophaeus* (ATCC #6633). The test was conducted in accordance with the BS En 14347:2002 “draft” standard. After 15 minutes of exposure, the reduction in spores was >6.5 log_{10} on average, thus completing the requirements of the applied test method (MicroMed Laboratories, Petaluma, Calif.).

**Toxicology Studies**

Safety has also been a major issue in formulating Microcyn Technology. A series of testing have been conducted to show that the use of Microcyn Technology does not cause toxicity, irritation, or sensitivity (Table 1). All of these tests have been conducted according to FDA standards or

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<th>Type of Study</th>
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<td>Acute Skin Irritation</td>
<td>ISO 10993-01:2002</td>
<td>Rabbit</td>
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<tr>
<td>Acute Dermal Toxicity</td>
<td>US EPA OPPTS 870.1200</td>
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<td>Genotoxicity Micronucleus Test</td>
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International Organization for Standardization (ISO) standards at GLP facilities.

A major concern when using super-oxidized solutions is the potential induction of genotoxicity. In accordance, a micronucleus testing conducted as per ISO standards has shown that Microcyn Technology is not genotoxic.

The effects of Microcyn Technology on fibroblast viability and wound healing have also been addressed in 2 unpublished, third-party lab studies at North American Science Associates, Inc. (NAMSA), Northwood, Ohio, and Comparative Biosciences, Inc., Sunnyvale, Calif., in 2004. In the first study, the cytotoxicity test on fibroblasts was executed in accordance with ISO 10993-5:1999 standards. A filter disc with 0.1 ml of Microcyn Technology was placed onto an agarose surface, directly overlaying a monolayer of mouse fibroblast cells (L-292). The prepared samples were observed for cytotoxic damage after 24 hours. Under these conditions, Microcyn Technology-containing samples did not reveal any evidence of cell lysis or toxicity (NAMSA).

The second study was conducted with 16 rats to evaluate the local tolerability of Microcyn Technology and its effects on the histopathology of wound beds in a model of full-thickness dermal wound healing. It had already been shown that neutral pH super-oxidized solutions were not only nontoxic to wounds, but that they could even induce wound healing. In this study, Masson’s trichrome-stained sections and collagen type II-stained sections of the Microcyn Technology and saline-treated surgical wound sites were evaluated by a board-certified veterinary pathologist. As expected, there were no relevant histopathologic differences between the treatment groups, indicating that the Microcyn Technology treatment was well-tolerated. There were no significant differences between groups in collagen type II expression. As expected, Microcyn Technology did not have an adverse effect on fibroblasts or on collagen elaboration under the conditions of this study (Comparative Biosciences).

Worldwide Approvals

In 2004, a European approval was obtained (CE KEMA Medical Device Class IIb). Dermacyn Wound Care (formulated with Microcyn Technology) is a super-oxidized solution intended for use in the moistening, irrigation, debridement, and microbial load reduction of acute and chronic wounds, ulcers, cuts, abrasions, and burns. In the United States, 2 510(k)s from the FDA were approved in May 2005:

1. Dermacyn™ Wound Dressing is indicated for use in moistening and lubricating absorbent wound dressings for traumatic wounds, cuts, abrasions, and minor burns

2. Dermacyn Wound Care is intended for cleansing, debriding, and removing foreign material from acute and chronic dermal lesions such as stage IV pressure ulcers, diabetic ulcers, postsurgical wounds, first- and second-degree burns, abrasions, and minor irritations of the skin.

Clinical Studies

Microcyn Technology has been effective and safe when applied in different ways (eg, spray, immersion, irrigation), as well as in combination with other technologies such as vacuum-assisted closure (VAC Therapy, KCI, San Antonio, Texas) and the Versajet Hydrosurgery system (Smith & Nephew, Largo, Fla.). According to the type and stage of the lesion, it can be applied once, twice, or 3 times daily.

Pilot clinical evaluations—mainly in Latin America and Europe—have already been conducted by independent physicians to test for efficacy and safety in diabetic foot and venous stasis ulcers, burns, and postoperative wounds. Good results have been reported in these cases. For example, one study has shown better results with Dermacyn Wound Care over povidone iodine in the treatment of 208 patients with diabetic foot ulcers in Italy.

Oculus is also currently involved in the planning and execution of numerous clinical studies and postapproval human-use evaluations throughout the United States, Mexico, and Europe.

Conclusion

The use of super-oxidized solutions as wound care products is a cutting-edge concept. The first stable and commercially available super-oxidized solution, Dermacyn Wound Care (Europe) and Oculus Microcyn60 (Mexico), has been shown to be an efficient antimicrobial agent in in-vitro experiments. The moistening effect and the minimum toxicity found with the
use of this super-oxidized solution makes it a good choice for wound care management. However, new controlled trials must be conducted to fully characterize the antimicrobial, anti-inflammatory, and positive effects in wound healing. Nevertheless, preliminary results suggest that this non-antibiotic technology appears to offer a broad new paradigm for the prevention and treatment of acute and chronic wounds. The potential application of this technology warrants further research, and specialized formulations are now being developed for various indications.

References

The provided information contains a discussion of off-label use or uses that have not been evaluated by the Food and Drug Administration. Oculus Innovative Sciences is not aware of any significant risks or safety concerns that are not discussed in the publication. This study was funded in part or fully funded by Oculus Innovative Sciences.
Indications for Use

510(k) Number (if known):

Device Name: Dermacyn™ Wound Cleanser

Indications for Use: Dermacyn Wound Cleanser is intended for moistening and debriding acute and chronic dermal lesions, such as Stage I-IV pressure ulcers, statis ulcers, diabetic ulcers, post-surgical wounds, first and second degree burns, abrasions and minor irritations of the skin.

Prescription Use X AND/OR Over-The-Counter Use
(21 CFR 801 Subpart D)

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Concurrence of CDRH, Office of Device Evaluation (ODE)