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AN ANALYSIS OF THE NEUTRALIZATION PROCESS OF HYDROGEN PEROXIDE CARE SYSTEMS

by

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ABSTRACT

Hydrogen-peroxide based cleaning systems have been shown to be effective for contact lens disinfection as well as management of a variety of patient complaints and their use has been steadily increasing over the last decade. One step systems, the most popular, operate by submerging lenses in a 3% solution of peroxide that is decomposed with the aid of a platinum catalyst. As the number of solution brands on the market increases, questions of how different each solution is and how long is necessary for neutralization arise. In this study, the peroxide concentrations of three commonly available solutions (Alcon Clear Care, Sauflon One Step, and Bausch+Lomb Peroxiclear) were measured before any decomposition and at 13 time points during neutralization (every ten minutes for the first hour and once at every hour following). Each sample was taken from a previously unopened bottle of solution or lens case and calculations were done using average values from 3 cycles. Clear Care and One Step showed no significant difference in total peroxide exposure or decomposition rate. Peroxiclear showed significantly higher total exposure with a slower initial decomposition. All three solutions were within the "safe" threshold of 100 ppm by 4 hours of decomposition.

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INTRODUCTION

In 2014, a study by the Centers for Disease Control and Prevention (CDC) estimated that 16.7% of the United States adult population, amounting to 40.9 million people at the time of publishing, wore contact lenses[1]. A separate analysis approximated that doctor's offices and outpatient clinics in the U.S. had 230,000 visits pertaining to contact lens-related complications as well as 19,000 emergency service visits in 2010 alone[2]. Prevalence of different diagnoses varied due to the type of practice, patient population, and individual physicians, but the majority of complaints were found to be related to avoidable conditions such as lens-induced red eye, infection, or hypersensitivity. For many practitioners, the first step when dealing with a post-infection patient or surface irritation is to prescribe a hydrogen peroxide-based cleaning regimen. These consist of a sterile, buffered solution that uses hydrogen peroxide to clean and disinfect lenses (proprietary wetting agents may also be present, varying by brand). Peroxide systems have demonstrated superior disinfection compared to multipurpose solutions and are preservative free, reducing the risk of hypersensitivity complications.[3] The use of peroxide-based cleaning solutions has increased with some regularity over the past decade; the 2017 publishing of an annual survey of optometrists conducted by *Contact Lens Spectrum* has noted a 1-2% increase in the number of respondents prescribing peroxide-based treatments since 2009.[4] As could be expected, the increasing demand has led to an expanding number of choices available to practitioners and patients alike, especially in regards to private label solutions.

Peroxide-based lens treatments fall into two broad categories as either one- or

two-step regimens. Two-step methods utilize an enzyme catalyst tablet which, while effective, has not been broadly adopted by lens wearers in lieu of the more convenient one-step process. The mechanism for the one-step process has remained fairly unchanged throughout the years: lenses are submerged in a 3% hydrogen peroxide solution that is decomposed into water and oxygen gas through the use of a platinum catalyst over a minimum of 6 hours. The introduction of the Peroxiclear brand by Bausch + Lomb (B+L) in 2014 complicated the matter by changing the traditional dogma and advertising safe wear after only 4 hours of decomposition time. Furthermore, B+L claims to increase the total amount of peroxide exposure with the addition of platinum modulating compounds (PMCs), primarily carbamide, that form transient bonds with the catalyst, inhibiting early decomposition and remaining in solution to serve as wetting agents.[5]

When faced with so many choices, a few questions naturally occur: Is a 6-hour decomposition cycle really necessary? Where does that rule come from? What's the difference between all of these identical looking bottles or, even more importantly, is there a difference at all? This study attempts to address those questions in an empirical analysis that, to the experimenters' knowledge, is the first of its kind.

Note: Peroxiclear has been voluntarily removed from the market since the completion of this study.[6] Additionally, Clear Care has been reformulated to include the Hydraglyde compound; it is unknown how this new formulation would compare to the one used in this study.

METHOD

Three hydrogen peroxide care systems were chosen for investigation: Peroxiclear (B+L),

Clear Care (Alcon), and One Step (Sauflon, often packaged under various private labels). These systems were selected based on their ready availability to the average patient in the United States. Each solution was monitored over an 8-hour period using their manufacturer supplied cases.

Figure 1. Lens case packaged with Clear Care

Figure 2. Lens case packaged with Peroxiclear

Figure 3. Lens case packaged with One Step

Each case used underwent a full 8-hour cycle before testing in order to remove any possible contaminating factors from the manufacturing process (samples from this preparatory cycle were taken and showed an erratic level of variation not seen in subsequent cycles). Peroxide levels were measured before decomposition, every ten minutes for the first hour, and then every hour for 7 hours (14 samples per cycle). The sampling schedule was determined due to the rapid change in concentration over the first hour and the low rate of decomposition that follows. Unmodified samples were taken directly from freshly opened solution bottles while "in process" samples were each taken from a different unopened case. Each complete cycle was repeated three times amounting to 39 cases total per solution. An assay was prepared from each sample, acidified, and titrated using a potassium permanganate solution as described in the United States Pharmacopeia (USP)[4]. End points were determined by visual comparison to a pre-made distilled water blank and peroxide concentrations calculated from the volume of permanganate titrant using the equation supplied in the USP. Decomposition was deemed complete and safe for use at peroxide concentrations of 100 ppm or less (termed the

ocular awareness threshold); this concentration has been found to be low enough that most corneas do not register the presence of peroxide.[8]

All calculations were done using the average of all three trials to limit the effect of fluctuation between individual bottles of solution and the variance inherent to visual inspection of end points.

RESULTS

All three solutions began at slightly higher than the advertised 3% concentration, closer to 3.3% or 33,000 ppm (no explanation could be determined and no mention of this raised concentration was found in product literature). No significant variation in starting concentration was found between the different solutions. All trials reached a concentration low enough to be incapable of reliable measurement by hour 5 and had an average value of 0 ppm by hour 6. Peroxiclear did have a non-zero average at hour 6 (14.17 ppm) but it is reasonable to conclude that this was due to measurement inaccuracy.

Total peroxide exposure at 4 hours was 15,757.54 ppm for Peroxiclear, 5,563.60 ppm for One Step, and 5,973.60 ppm for Clearcare. Total exposure at 6 hours was 15,814.17 ppm, 5,600.39 ppm, and 6,011.88 ppm respectively.

All three tested solutions were below the ocular awareness threshold of 100 ppm at the hour 4 sample.

Subjective observation revealed a noticeable difference in the bubbling action between the three tested solutions. Clearcare showed rapid gas evolution within 2-3 seconds of introducing the catalyst while Peroxiclear had a much gentler appearing flow. One Step was unique in that the catalyst is located within the vial and not attached to the

top of the case (Fig. 3). Decomposition began immediately as solution was added to the vial but appeared similar to Clearcare once the top had been sealed on. Some difficulty was had in noting when the vial was properly filled the marked level but this appears to have had no effect on measurement.

CONCLUSIONS

Analysis of the data collected revealed that all three care systems were within the ocular awareness threshold after 4 hours of catalyzed decomposition, even after considering the maximum concentration noted in individual trials. Further neutralization time showed no significant effect on total peroxide exposure in any tested solution. A significant difference in total peroxide exposure was found between Peroxiclear and the other test solutions but no significant difference was noted between One Step and Clearcare (Fig. 4).

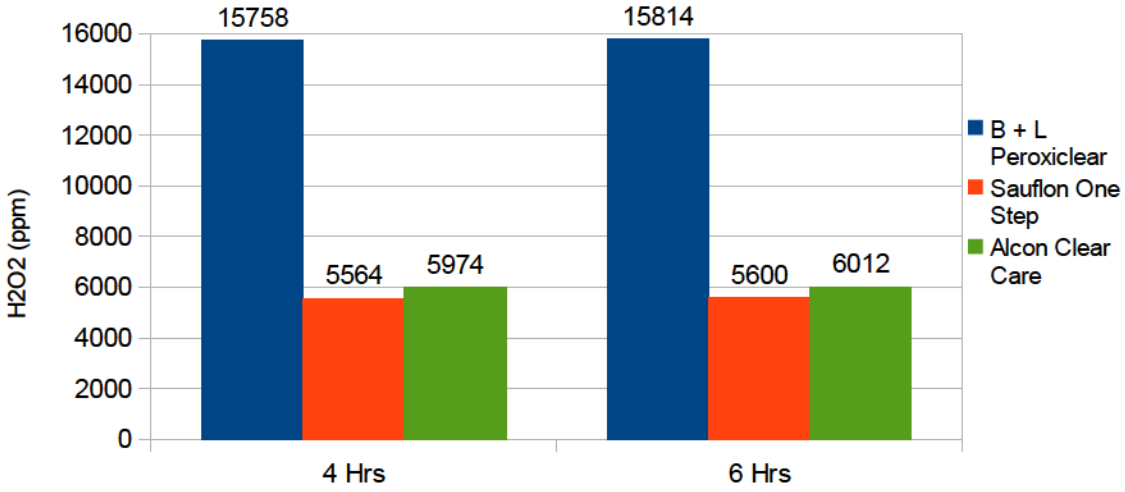

Figure 4. Total peroxide exposure. Calculated using area under the plotted average concentrations.

Over the 8-hour testing cycle, Clear Care and One Step showed very similar neutralization patterns and rates ($p > 0.05$) (Fig. 5). A rapid decrease in concentration was

measured over the first 30 minutes, plateauing around 50 minutes (Fig. 6). Approximately 70% of starting peroxide (24,000 ppm) was decomposed in both solutions within the first 10-minute interval with a further decrease of 75% and 50% of remaining peroxide over the next two intervals, respectively. Peroxiclear had a markedly slower rate of neutralization, particularly over the first hour, maintaining significantly higher peroxide concentrations ($p < 0.0001$). The first ten minute interval showed a 19% decrease in concentration followed by a 33 percent decrease in remaining peroxide in the next ten minutes. The next four intervals, up to the 1 hour mark, showed consistent decreases of around 38% every ten minutes. At the end of four hours, all three care systems showed no significant difference in remaining concentration ($p > 0.05$) or in rate of further decomposition ($p > 0.05$).

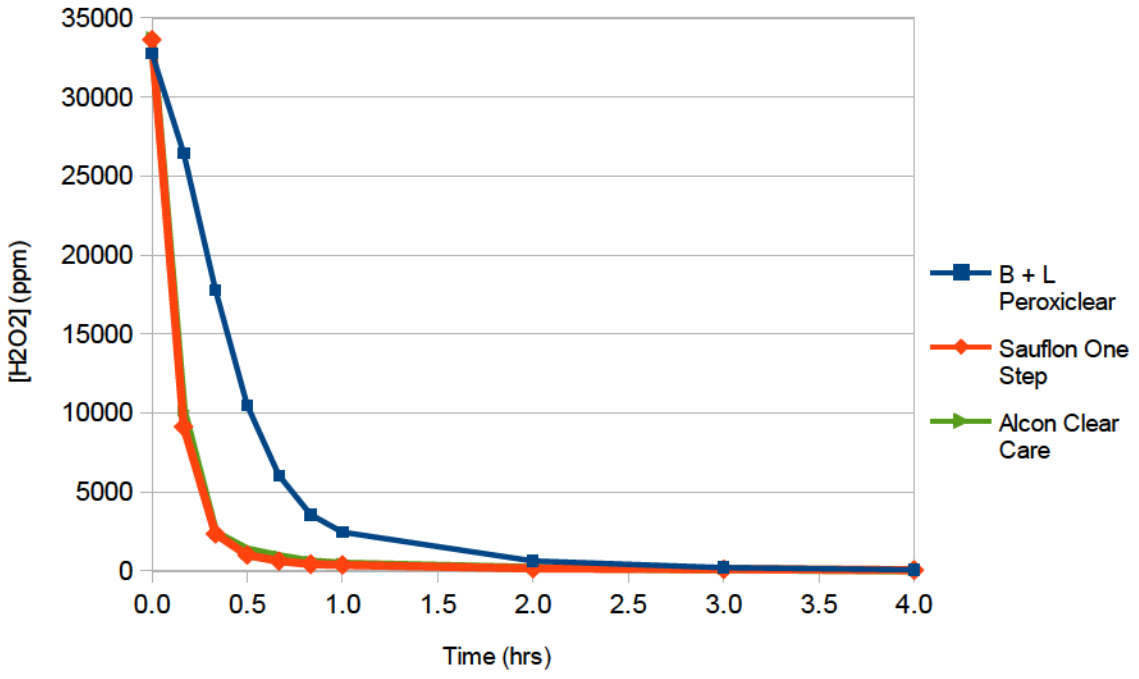

Figure 5. Average peroxide concentrations over time. Data points after 4 hours not displayed in order to better illustrate overall trends.

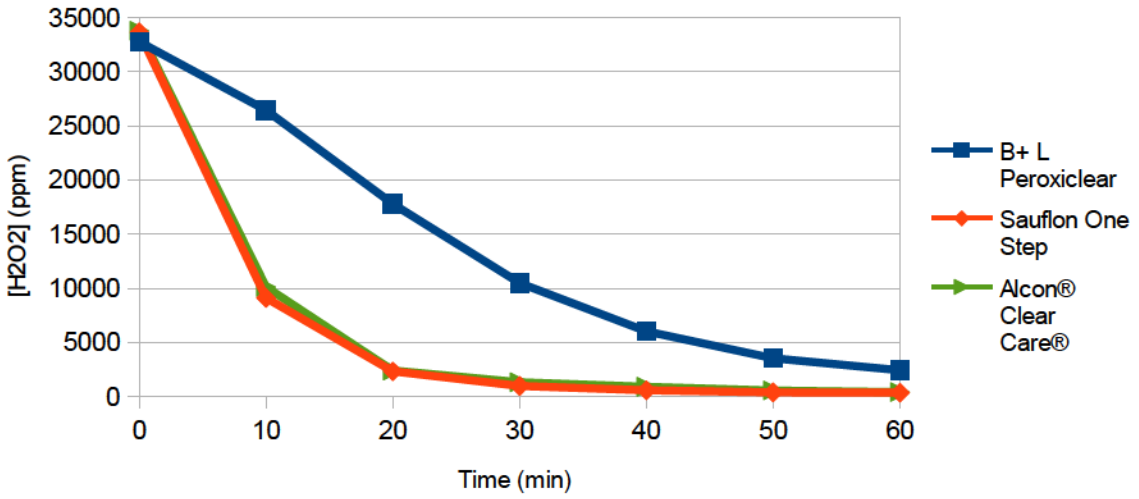

Figure 6. Average peroxide concentrations during hour 1.

DISCUSSION

Peroxide care systems have been experiencing a resurgence in recommendation and use over the past decade, especially among contact lens-focused practitioners and their patients. As lens wear becomes more common across the globe, issues such as pathogens and allergy to preservatives are brought farther into the forefront; the disinfection capability and tolerance to peroxide-based solutions make them the logical choice for patients in these instances.[8] Knowledge of individual solutions, their differences (or lack thereof), and the mechanisms behind their function are a valuable tool to the eye care professional and crucial in educating patients.

The findings of this study reveal two important facts immediately, the first being that a drastic difference exists in the total peroxide exposure of Peroxiclear compared to the other tested solutions. Combined with the slower initial decomposition of Peroxiclear, these findings indicate that the additional PMCs do in fact behave as advertised. While

this study did not assess the disinfection capability of any solution, it has been repeatedly shown that two-step peroxide solutions show the highest degree of disinfection, attributed to the high level of peroxide exposure.[9] It is not unreasonable to suppose, then, that Peroxiclear may have an edge against more resilient organisms such as A*canthamoeba* when compared to other one-step regimens. Further investigation is required to determine the specifics effects on patient health and comfort *in vivo* as that is beyond the scope of this study.

The second important outcome is the possible unimportance of a full 6 hour cycle with either Clear Care or One Step. As Clear Care was the dominant product at the time of testing and many patients have opted to not use peroxide-based solutions due to time constraints, this may be a significant factor for many lens wearers. An important caveat to this is, as above, the real-world result cannot be determined from this data alone; the threshold for discomfort in the most sensitive eyes is 40 ppm and the point in decomposition where this was reached could not be accurately identified using this procedure.[3] However, it is reasonable to predict that the peroxide levels found here would be tolerable for the majority of patients at 4 hours and all patients at 5 hours. Repetition of this study using more precise determination of titration end points would elucidate this matter and the remaining issues regarding safety and comfort for the lens wearer.

While no empirical evidence could be collected, there is also the curiosity of possible effects of case design in the care system. Some of the cleaning action in peroxide systems is thought to be from the mechanical force of passing oxygen bubbles "scrubbing" the lens. If that is indeed a significant factor, the slower degree of gas

evolution in Peroxiclear due to PMCs may result in less cleaning of the lens overall, even with higher peroxide exposure. The marked difference in catalyst surface area between the B+L supplied case (Fig. 2) and the other two manufacturers (Figs. 1,3) may also have an effect on peroxide decomposition if a patient were to use an incorrect pairing, though this is only a speculative conclusion. Finally, there is some question of early decomposition using the One Step case in instances where the lenses are not put into solution immediately after the vial has been filled. As the vast majority of peroxide exposure happens within the first few minutes of the cleaning cycle, a delay of any real length could greatly decrease effectiveness.

While the data collected in this study is useful to the practitioner as a reference in its own right, the investigators believe further study is warranted in this matter. A logical avenue for further study is the efficacy in disinfection as it relates to the different levels of peroxide exposure. Related to that would be investigation of cleaning action on the lens surface itself and whether the variance in peroxide exposure and gas evolution has an effect on protein or lipid deposits.

REFERENCES

1. Centers for Disease Control and Prevention. Contact Lens Wearer Demographics and Risk Behaviors for Contact Lens-Related Eye Infections—United States, 2014. 2015; https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6432a2.htm.
2. Centers for Disease Control and Prevention. Estimated Burden of Keratitis—United States, 2010. 2014; https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6345a3.htm.
3. Paugh JR, Brennan NA, Efron N. Ocular response to hydrogen peroxide. Am J Physiol Opt Feb 1988; 65(2): 91-98.
4. Nichols J. (2017, January) Contact Lenses 2016. *Contact Lens Spectrum*, Volume: 32, Issue: 1, pages: 22-25, 27, 29, 55.
5. Millard KA, Hook D, Hoteling A, Wygladacz K. (2014) A One-Step Hydrogen Peroxide-based Contact Lens Solution. *Contact Lens Spectrum,* Volume: 29, Issue: 13. pages: 44-48.
6. Peroxiclear 3% Hydrogen Peroxide Cleaning & Disinfecting Solution. Rochester, NY: Bausch + Lomb, 2016. Available at: http://www.bausch.com/our-products/contact-lens-care/soft-lens-multi-purpose-solutions/peroxiclear-3-hydrogen-peroxide-cleaning-disinfecting-solution. Accessed March 6, 2017.
7. Davani B. Hydrogen Peroxide Topical Solution. In: United States Pharmacopeia 32. 2005: 2587.
8. Janoff L. The effective disinfection of soft contact lenses using hydrogen peroxide. Contacto. 1979;21:1,37-40
9. Hiti K, Walochnik J, Faschinger C, Haller-Schober E-M, Aspock H. One- and two-step hydrogen peroxide contact lens disinfection solutions against *Acanthamoeba*: How effective are they? Eye 2005; 19:1301-1305.