

Regard: a multipurpose solution

Nick Atkins introduces Regard, a new preservative-free multipurpose contact lens solution

THIS YEAR MARKS the 10th anniversary of the availability of multipurpose contact lens solutions in the UK. During this period practitioners have almost performed a complete turnaround in their prescribing habits, from a market dominated by one and two-step hydrogen peroxide systems.

According to the annual review of UK practitioner prescribing trends by Eurolens Research,¹ 90 per cent of care products recommended by practitioners in the 2004 survey period were multipurpose solutions (MPS).

Over the past six years, there have been significant new formulations and reformulations, with the introduction of advanced cleaning and comfort-enhancing agents to further improve product performance. However, the basic chemicals involved in the preservation and disinfection process have remained unchanged.

CONTINUING DEVELOPMENT

Since the historic launch of the first multipurpose solutions – Complete and ReNu – in the summer of 1994 and the switch from the Medicine Control Agency control to the Medical Devices Agency with the introduction of CE marking from January 1995, there has been a plethora of product introductions.

AOSept is another solution that benefited from the change in regulatory control from 1995 and for the following 10 years there were two basic types of 'simpler' systems that dominated in varying proportions, the one-step hydrogen peroxide solutions (HPS) and the multipurpose solutions.

The relative pros and cons of these

products are shown in Table 1. Within the multipurpose category there are two principal active ingredients for chemical disinfection; Polyhexanide and Polyquad. Polyhexanide is used more extensively, with Polyquad only available in Alcon Laboratories' products such as Optifree Express.

Table 2 shows examples of the basic formulation of a sample of these solutions.

SEARCH FOR THE IDEAL SOLUTION

All the products ever developed and commercialised have been trying to get closer the 'Holy Grail' of contact lens care.

The ideal solution can be said to require the following key features:

- ◆ Kills all ocular pathogens
- ◆ Is non-toxic to the ocular surface
- ◆ Simple to use
- ◆ Effectively removes deposits
- ◆ Affordable.

While other benefits may be desirable, particularly as we get closer to perfection, these are the core attributes required. As some manufacturers turn their attention to other attributes such as improving the lens comfort and hydration characteristics, one manufacturer has gone back to the drawing board and developed a new method of disinfection for a multipurpose solution, which uses a 'preservative-free' approach for the first time in multipurpose solutions.

A novel multipurpose solution, Regard was presented, via a poster at the BCLA meeting in May 2003² and is marketed through Advanced Eyecare Research. It came to the attention, interest and use of



FIGURE 1. Regard is marketed through Advanced Eyecare Research

the author due to its method of disinfection that claimed a complete absence of conventional preservatives in its mode of action. The key components of Regard can be seen in Table 3.

MECHANISM OF ACTION

From Table 3 it can be seen that the disinfecting action of Regard is the result of the synergy between the chlorite ion and hydrogen peroxide, which provides an active disinfection and then releases oxygen to the corneal surface.

Sodium chlorite generates chlorine dioxide which is very effective in killing Gram +ve and Gram -ve bacteria, yeasts and fungi, subsequently breaking down into the components of natural tears:

- ◆ Salt
- ◆ Water
- ◆ Oxygen.

Sodium chlorite is activated by acidic cellular components and has been used safely for many years as a treatment for municipal drinking water. The chlorite/peroxide formulation is based on the synergistic microbial activities both chemicals. Chlorine dioxide (ClO₂) generated at the surface of and inside the micro-organism is mainly responsible for the antimicrobial activities of chlorite:

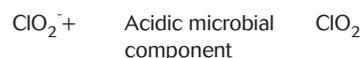
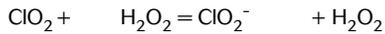


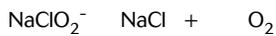
TABLE 1. MPS VERSUS H2O2

	Pros	Cons
Multipurpose Solutions	Selective antimicrobial action Continuous disinfection activity Simple to use Convenient single bottle	Corneal staining with some lens/Px combinations Poor disinfection efficacy against fungi and <i>Acanthamoeba</i>
Hydrogen Peroxide Systems	Potent, non-specific, rapid disinfection Preservative-free following neutralisation	Highly toxic without neutralisation Relatively impotent for long-term storage Complex, particularly in two-step format

To stabilise the ClO_2 , a trace amount of H_2O_2 is employed. Due to its neutrality and small size, H_2O_2 can easily penetrate the micro-organisms' membranes and its subsequent oxidativative interaction with the micro-organism components produces altered membrane components as well as chlorite to generate ClO_2 . Since H_2O_2 can easily reduce ClO_2 to ClO_2^- via a single electron transfer, H_2O_2 can maintain the stability of the notoriously unstable chlorite ions, creating a self-stabilising formula:



Once the contact lenses are removed from the solution (which maintains stability) sodium chlorite breaks down into sodium chloride and oxygen:



The overall reaction mechanism is presented in Figure 2.

Role of hydrogen peroxide

By now the question that will occur to many practitioners concerns the use of H_2O_2 and why this does not cause toxicity problems.

In a hydrogen peroxide-based care system the concentration typically used is 3 per cent or 30,000 parts per million (ppm), which requires neutralisation before instilling into the eye.

H_2O_2 is used at 100ppm in the Regard chlorite/peroxide complex, not for its stand-alone oxidativative activity (which would require 300 times the concentration) but for the synergistic effect to enhance the chlorine dioxide production and always revert back into chlorite in a closed system.

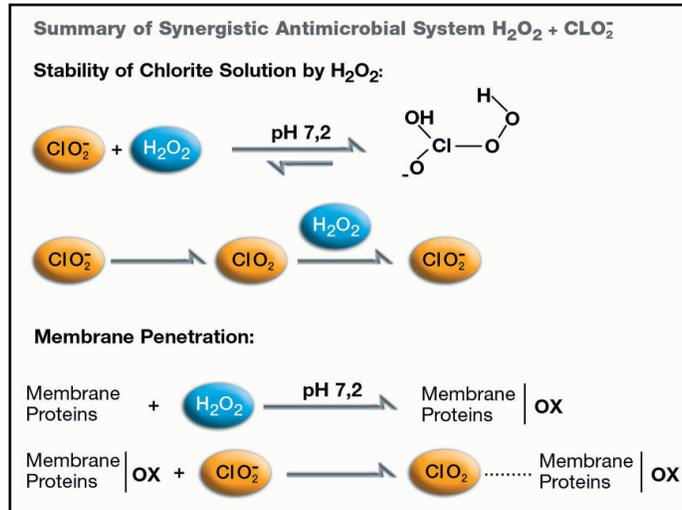


FIGURE 2 Summary of the synergistic antimicrobial system $\text{H}_2\text{O}_2 + \text{ClO}_2^-$

At this concentration, H_2O_2 is broken down by enzymes in the tear film, such as catalase and superoxide desmutase, into oxygen and water. Literature studies clearly show that 100ppm is below the ocular sensitivity threshold and non-toxic in the ocular environment.^{3,4,5}

Efficacy

As a result of the chlorite/peroxide complex, Regard is a very effective broad spectrum antimicrobial agent.²

Tables 4 and 5 show that in antimicrobial testing Regard completes a 6 log reduction of the regulatory panel of challenge bacteria in three hours, as well as a 6.34 log reduction of human resistant strain *Pseudomonas aeruginosa* in two hours. In addition, the formulation shows a 5.54

log reduction of the yeast *Candida albicans* in seven days and a 2.32 log reduction of the mould *Aspergillus niger* in seven days.

Safety

A potential concern with use of sodium chlorite and chlorine dioxide could be the oxidative stress that they may induce on the body.

Both have been the subject of numerous animal and human studies^{6,7} and are rapidly reduced following ingestion. Chronic human studies have shown no negative effects at ingesting 500ml at 500ppm daily.⁷

Even if the content of the lens case wells (say 5ml for both) entered the ocular/nasal pathways the estimated daily intake would be 1/100th of a typical ingestion of chlorite in drinking water.

DISCUSSION

Regard is non-toxic² and can be instilled directly into the eyes making it ideal for other functions such as rinsing and storage.

The addition of Pluronic F-68 and hydroxypropylmethylcellulose (HPMC) provides a completely multifunctional solution by providing surfactant cleaning and lubricating properties.

It is somewhat ironic that practitioners now find themselves with a

TABLE 3. Regard composition

Components	Action
NaClO_2	Disinfection
H_2O_2	Stabilisation/re-activation of disinfection
Hydroxypropylmethylcellulose	Lubrication
Pluronic F-68	Cleaning/lubrication

TABLE 2. Examples of multipurpose solutions formulations

Product	Manufacturer	Disinfectant	Conc'n	Surfactant (ppm)	Additional lubricant/conditioners
ReNu	B&L	PHMB	.5	Poloxamine	None
Focus Aqua	Ciba Vision	PHMB	1.0	Pluronic F127	Dexpathenol
Complete	AMO	PHMB	1.0	Poloxamer 237	HPMC 0.15% Propylene Glycol 0.5%
All in One	Sauflon	PHMB	5.0	Poloxamine	None
Opti-Free Express	Alcon ALDOX*	Polyquad 5.0	11.0	Poloxamine	Aminomethyl-propanol
ReNu with Moisture-Loc	B&L	Alexidine	4.5	Poloxamine	Poloxamer 407 Polyquaternium 10

*Myrisamidopropyl dimethylamine

TABLE 4. Log reduction of micro-organisms

ATCC Bacteria	<i>S Aureus</i>	<i>P Aeruginosa</i>	<i>E Coli</i>	<i>S Marcescens</i>	<i>C Albicans</i>	<i>A Niger</i>
Log Initial inoculum	6.09	5.65	5.96	6.40	5.54	5.48
Log reduction 2 hours	3.60	4.67	5.12	4.83	—	—
Log reduction 3 hours	6.09	5.65	5.96	5.90	—	—
Log reduction 4 hours	6.09	5.65	5.96	6.40	—	—
Log reduction 7 days	—	—	—	—	5.54	2.32
Log reduction 14 days	—	—	—	—	—	5.48

TABLE 5. Log reduction of human resistant strains

Human Resistant Bacteria	<i>S Haemolyticus</i>	<i>P Aeruginosa</i>
Log initial inoculum	7.03	6.35
Log reduction 2 hours	2.43	6.35
Log reduction 4 hours	7.03	6.35

better than ever choice of care systems when parts of the contact lens industry have been tracking a parallel path towards the abolition of lens care with the development of single use lenses, for either daily or 30-day continuous wear. So is this technology a case of 'too little, too late'?

In the opinion of this author the answer is a definite 'No'. A further review of UK prescribing trends¹ reveals that the majority of patients (60 per cent of new fits and 70 per cent of refits) are still fitted with reusable lenses, without considering the large population of existing wearers still not wearing single-use lenses.

Additionally, the more lens care alternatives a practitioner has in his or her armoury the better, in order to ensure the optimal selection of a lens-care combination for every patient. Thus the development of a 'preservative-free' multipurpose solution must be seen as a useful addition to the contact lens practitioners' armoury of lens care options.

The growth of daily disposable lenses has dramatically changed the contact lens market, making lens wear easily accessible to many patients who do not wish to wear lenses on a full time basis. However, being conventional hydrogel materials they can suffer from the same performance limitations as other 'disposables'.

With silicone hydrogel lenses offering patients improved ocular health with the elimination of hypoxia and many patients finding that they prolong their comfort

during the day, it is reasonable to assume that the future for many wearers is to continue with daily lens care.

While 30-day continuous wear will work counter to this – many patients are not desperate to wear lenses overnight and many practitioners are still reluctant to regularly prescribe this modality. It is, therefore, likely that the short to medium-term future for solutions and their manufacturers is looking brighter than predicted at the turn of the millennium.

Additionally, perhaps the introduction of less toxic modes of action combined with claimed comfort enhancing additives included in some of the newer multipurpose solutions, will offer performance benefits that could see some patients more comfortable in a monthly or two-weekly replacement lens than a daily disposable?

CONCLUSION

The chlorite/peroxide complex in Regard is an active anti-microbial agent and is safe and non-irritating to the corneal epithelium.²

The complexed molecule is self-stabilised in the bottle or lens case and rapidly degrades into salt, water and oxygen in the ocular environment. Data available so far has shown the formulation to be both safe and efficacious.

It provides improved choice and its unique mode of action offers practitioners something of a 'best-of-both-worlds' option by combining the convenience of a

multipurpose solution with the preservative free benefits previously only available from hydrogen peroxide-based systems. Additionally, the addition of HPMC and Pluronic F-68 can improve lens surface characteristics.

Practitioners who have become blasé about contact lens solutions, believing that all solutions are the same or similar are advised to take another look at new products such as Regard and ensure that they are familiar with the differences in their mode of action and formulations. The correct selection of lens care product has the potential to significantly improve the comfort and wearing times of many patients. Along with the appropriate selection of contact lens material and modality, this will have an important role to play in the long-term success of the patient and with it the ultimate success of individual contact lens practices.

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