

Aqua Balance®

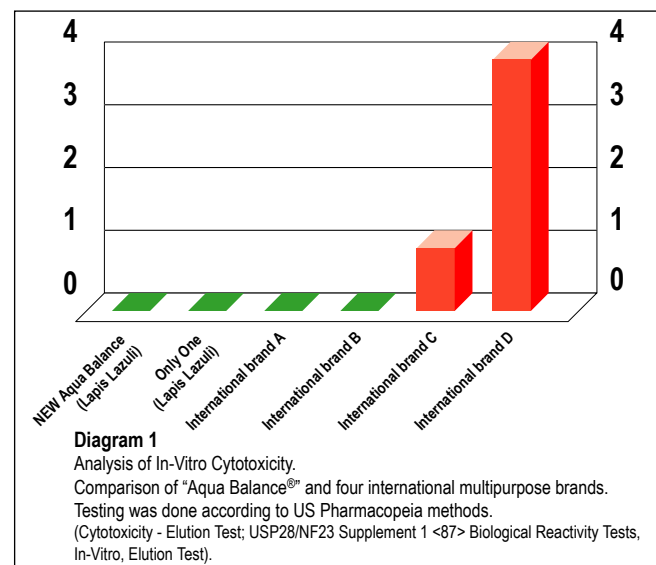
Multipurpose Contact Lens Care Solution
with natural Hyaluronate and Allantoin
for all soft contact lenses, also for silicone hydrogels

Lens Care goes Natural!

Lapis Lazuli's "Aqua Balance®" multipurpose solution with Hyaluronate and Allantoin has been developed on the basis of recent progress in biomedicine and biotechnology. One of the most important issues for a successful contact lens care product is the wearing comfort experienced by the contact lens wearer, after the lenses have properly been disinfected, cleaned, rewetted and inserted onto the eye. During contact lens wear, lens awareness should be negligible or at least as limited as possible. This is the case when the lens material has an optimal oxygen transmissibility and is completely free from irritating depositions (biofilm) such as proteins coming from tear fluid or micro-organisms. Unfortunately, a significant proportion of contact lens wearers reports lens awareness, irritation and symptoms of dryness and, as a result, the number of those who discontinue wearing contact lenses is considerable. Therefore, thorough cleaning, disinfection and rewetting of contact lenses and the prevention of the building up of biofilm deposits is key to the wearing comfort. The "Aqua Balance®" multipurpose solution has been developed to exactly address these issues.

Safety First!

The safety profile of "Aqua Balance®", including efficient disinfecting and cleaning capacity, meets the most stringent European and US criteria. The safety characteristics in terms of in-vitro cytotoxicity have been tested according to US Pharmacopeia methods and compared with four commercially available international brands. For in-vitro cytotoxicity testing, lenses were soaked in a given multipurpose solution and subsequently brought in contact with the prescribed cell cultures. The classification of the cytotoxicity was done according to that of the US Pharmacopeia, which runs from "Zero Grade" (no cytotoxicity) to "Grade 4" ("severe").



As can be seen in Diagram 1, Lapis Lazuli's "Aqua Balance®" scores an optimal safe "Zero Grade", as does Lapis Lazuli's standard multipurpose solution "Only One". Out of the four international brands tested, two also score a safe "Zero Grade", whereas one scores a "Grade 1" and the last one scores a "Grade 4".

Fighting Corneal Acidosis

When it comes to contact lens wearing comfort in relation to contact lens care, an issue which deserves special attention, is what happens in the area between lens and corneal surface during prolonged wearing of contact lenses.

A key role is played by the lens polymers which should be adequately oxygen permeable, so that across this space the corneal cells are supplied with sufficient oxygen. It has been extensively documented that inadequate oxygen supply causes signs of hyperaemia, neovascularisation and compromised ability of the cornea (epithelium, stroma, aqueous humor) to adapt to hypoxic conditions, leading to morphological and functional changes (1-3). Under hypoxic conditions, the corneal cells produce and also deliver increased amounts of (mostly acidic) metabolic products, such as lactic acid and carbon dioxide (4,5). Due to the presence of the contact lens, the disposal of these acidic substances is -at least to a certain degree- hampered. As a result, and in combination with hypoxia, there is a continuous risk of acidification which occurs in the space between contact lens and cornea ("corneal acidosis"). It is known, that such a local acidosis may lead to a decreased lens wearing comfort and to a feeling of eye fatigue, irritation and even to eye dryness. Eventually, inflammatory processes may come into play and worsen this undesired condition (6).

The "Aqua Balance® Complex"

Counteracting complications caused by corneal acidosis is important when it comes to comfortable prolonged contact lens wear. Lapis Lazuli's "Aqua Balance®" multipurpose solution has been developed to specifically address this item, in addition to a state-of-the-art disinfecting, cleaning and rewetting performance.

This goal has been achieved with the development of the proprietary "Aqua Balance® Complex". An important component of this complex is the biological substance Hyaluronate, which is naturally present in many body fluids, including healthy tears (7), where it seems to be involved in the maintenance of corneal integrity (8).

In the case of "Aqua Balance®", Hyaluronate contributes to the formation of a "cushion" between the contact lens and the ocular surface (cornea). This cushion functions as a sponge: the viscosity-enhancing Hyaluronate has a high water-binding capacity: it is able to bind a multiple of its own weight of water. Under mechanical pressure (e.g. blinking), water is squeezed

out of the Hyaluronate molecules and, just like in the case of a sponge, is taken up again when the pressure decreases. For this reason, Hyaluronate is being referred to as a "visco-elastic" substance. As a substance which naturally occurs in the body, Hyaluronate can bind to cells by means of specific physiological receptors (9) and this mechanism prolongs the effective staying time (e.g. on the cornea) as compared to non-biological rewetting substances. It has been shown, that Hyaluronate has anti-oxidative and cytoprotective activity (10). As a biological rewetting substance, Hyaluronate has been shown to be effective in the treatment of dry eye symptoms (10,11) and it enhances tear film stability (12). The Hyaluronate used in "Aqua Balance®" is manufactured on the basis of an exclusive, safe recombinant DNA fermentation technology. The advantage of this patented technology is that no potentially harmful micro-organisms (e.g. Streptococcus) need to be used as vehicles to produce the Hyaluronate. Moreover, the isolation procedures involved are more gentle and, as a consequence, this material has a higher stability than conventional fermentation-based Hyaluronate. Characteristics of the main technologies used for obtaining Hyaluronate (animal-derived; fermentation-based) are summarised in Table 1.

Table 1: Current Production Methods for Hyaluronate

Rooster combs	Streptococcal fermentation
Advantages: - Typical higher molecular weight	Advantages: - Non-animal source
Disadvantages: - Animal source - Contamination with proteins and sulfated GAGs (immunogenicity) - Stability	Disadvantages: - Pathogenic - Fastidious - Potential antigenicity - Stability
Bacillus fermentation*	
Advantages: - Water based recovery - Non-pathogenic - Biosynthetic - Non-animal source - Stability	
*Hyaluronate used in "Aqua Balance®"	

The moisturising and rewetting properties of Hyaluronate in the "Aqua Balance® Complex" are supported by several other viscosity enhancing substances. These include hypromellose and glycerine.

The naturally occurring biomolecule Allantoin (applications in ophthalmic preparations patented) is a cell protector against toxic substances. For instance, it has been shown, that the cell damaging effects of high concentrations of preserving agents like Polyhexanide and/or similar biguanide derivatives can be reversed by Allantoin. In addition, Allantoin was shown to have a marked fungicidal activity, thus contributing to the antimicrobial safety of "Aqua Balance®" (De Bruijn et al., unpublished data on file).

Allantoin is a metabolite of uric acid, which, in turn, is a product of DNA metabolism in plants and animals, including mammals; it is abundantly present in certain plants, of which Comfrey (*Symphytum officinale*) is the most widely known. Extracts of such plants, but also purified Allantoin, are a valuable constituent of skin creams and ointments for supporting the function of epithelial cells (especially the enhancement of wound healing and skin regeneration) (13-15).

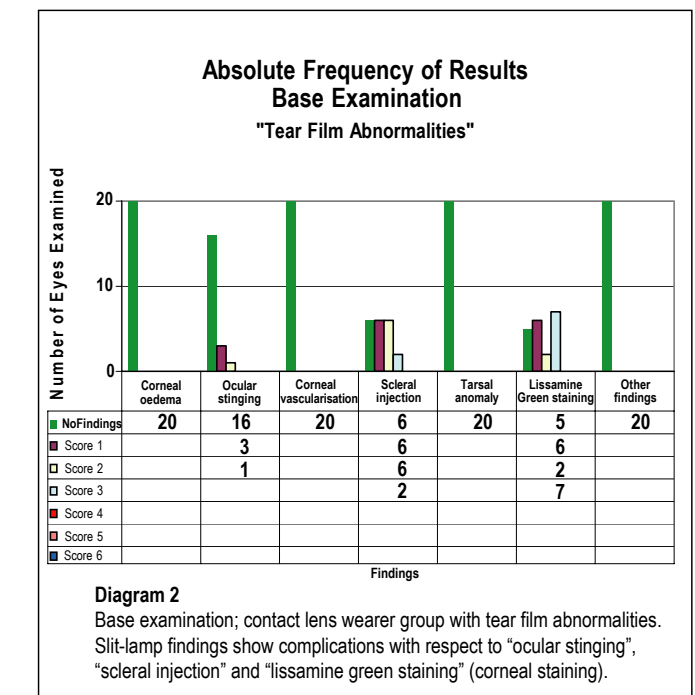
The Evidence

Lapis Lazuli's "Aqua Balance®" multipurpose solution not only fulfils the most stringent criteria with respect to disinfection and cleaning, but also significantly contributes to improved eye compatibility and enhanced wearing comfort of soft contact lenses, including silicone hydrogels.

This „natural" approach is highly appreciated by contact lens wearers, as has become evident from a clinical ophthalmic study with 30 volunteers, who tested the "Aqua Balance®" multipurpose solution during a period of 30 days.

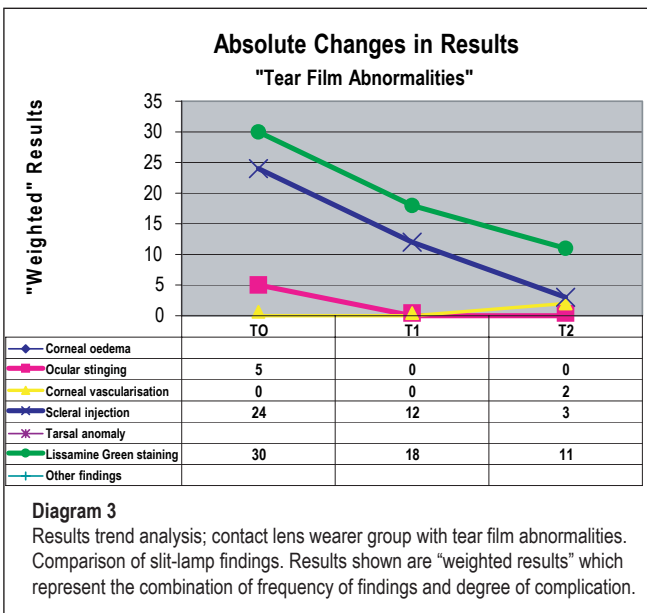
The study included three groups of contact lens wearers: "first-time" wearers, "existing" wearers and lens wearers with "tear film abnormalities". For each of the three groups of contact lens wearers, the changes in the findings at two weeks and four weeks were compared with the findings at base examination. Since both the trend in the number of findings and the degree of complications is decisive for analysis of the changes compared with the initial situation, the results have been expressed in the form of "weighted results". These "weighted results", therefore, take account of both criteria and are defined as the number of findings multiplied by the respective degree of complications observed.

As an example of the effects of the "Aqua Balance®" multipurpose solution, the observations in the (most problematic) group of lens wearers with "tear film abnormalities" are shown in Diagram 2 (base examination) and Diagram 3 (trend analysis after 2 and 4 weeks).



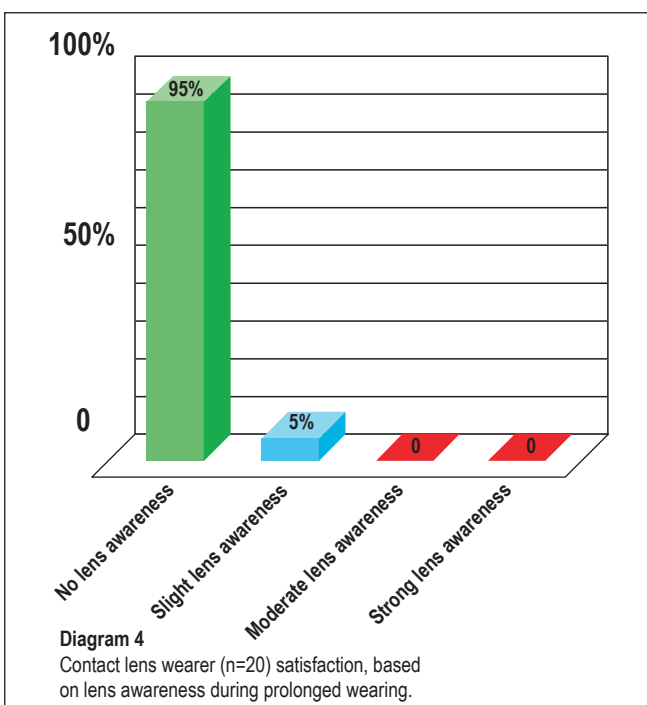
The objective slit-lamp findings revealed that the action of the "Aqua Balance®" solution can be described as "eye-health and comfort enhancing": the occurrence of parameters such as "corneal staining", "scleral injection" and "ocular stinging" decreased during the course of the study. These findings were most pronounced in the case of the contact lens wearers with "tear film abnormalities", who, not surprisingly, at base examination typically displayed a range of complications (Diagram 2 and 3).

From this, it is evident that "Aqua Balance®" has a protective effect on the basis of the slit-lamp findings.



With respect to the contact lens care product that had been used thus far, the outcome of the study confirmed the excellent properties of the "Aqua Balance®" multipurpose solution. Especially, the long lasting "clean" and "fresh" feeling after putting the lenses in was regarded as a highly attractive feature of the "Aqua Balance®" multipurpose solution.

The subjective evaluation by the lens wearers showed a level of satisfaction of over 95%, both with respect to the situation when inserting the lenses and during prolonged wearing. The data on "lens awareness" is summarised in Diagram 4.



Lens compatibility

The physical compatibility of "Aqua Balance®" according to the ISO 11981 test method has been evaluated with the following five soft contact lenses:

- Vistakon Acuvue 2 (FDA classification Group 4)
- Vistakon Acuvue Advance (Group 1)
- Vistakon Acuvue Oasys (Group 1)
- CIBA Vision O₂Optix (Group 1)
- CooperVision Proclear Compatibles (Group 2)

Twelve lenses of each type were put through 30 cleaning and disinfection cycles using the "Aqua Balance®" solution and a further 12 lenses of each type were used as active controls and soaked in ISO saline. None of the lenses showed significant changes in back vertex power (BVP) or total diameter (TD). Furthermore, none of the lenses sustained damage or showed discoloration.

It was therefore concluded that the "Aqua Balance®" multipurpose solution is physically compatible with a representative range of silicone hydrogel and conventional hydrogel lenses (Etafilcon A, Galyfilcon A, Lotrafilcon B, Omafilcon A, Senofilcon A).

Lenscare goes natural!

The incorporation of non-toxic biological, eye supporting substances in "Aqua Balance®" opens a new era for contact lens care: „Lenscare goes Natural!“

On the basis of the evidence presented it can be concluded that this new solution, focusing on the use of natural, eye protecting and contact lens compatible substances such as hyaluronate and allantoin, significantly reduces the risk for symptoms such as lens awareness, irritation, dryness and corneal staining. Its use will significantly contribute to contact lens wearer satisfaction and may lead to lower numbers of consumers who discontinue contact lens wear.

References

1. Liesegang TJ. Physiologic changes of the cornea with contact lens wear. CLAO J. 2002;28:12-27.
2. Rivera RK, Polse KA. Effects of hypoxia and hypercapnia on contact lens-induced corneal acidosis. Optom Vis Sci. 1996;73:178-83.
3. Jalbert I, Stapleton F. The corneal stroma during contact lens wear. Cont Lens Anterior Eye. 2005;28:3-12.
4. Bonanno JA. Contact lens induced corneal acidosis. CLAO J. 1996;22:70-4.
5. Nguyen T, Soni PS, Brizendine E, Bonanno JA. Variability in hypoxia-induced corneal swelling is associated with variability in corneal metabolism and endothelial function. Eye Contact Lens. 2003;29:117-25.
6. Nilsson SE. Bacterial keratitis and inflammatory corneal reactions: possible relations to contact lens oxygen transmissibility: the Harold A. Stein Lectureship 2001. CLAO J. 2002;28:62-5.
7. Frescura M, Berry M, Corfield A, Carrington S, Easty DL. Evidence of hyaluronan in human tears and secretions of conjunctival cultures. Biochem Soc Trans. 1994;22:228S.
8. Gomes JA, Amankwah R, Powell-Richards A, Dua HS. Sodium hyaluronate (hyaluronic acid) promotes migration of human corneal epithelial cells in vitro. Br J Ophthalmol. 2004;88:821-5.
9. Forsberg N, Von Malmberg A, Madsen K, Rolfsen W, Gustafson S. Receptors for hyaluronan on corneal endothelial cells. Exp Eye Res. 1994;59:689-96.
10. Debbasch C, De La Salle SB, Brignole F, Rat P, Warnet JM, Baudouin C. Cytoprotective effects of hyaluronic acid and Carbomer 934P in ocular surface epithelial cells. Invest Ophthalmol Vis Sci. 2002;43:3409-15.
11. Aragona P, Papa V, Micali A, Santocono M, Milazzo G. Long term treatment with sodium hyaluronate-containing artificial tears reduces ocular surface damage in patients with dry eye. Br J Ophthalmol. 2002;86:181-4.
12. Hamano T, Horimoto K, Lee M, Komemushi S. Sodium hyaluronate eyedrops enhance tear film stability. Jpn J Ophthalmol. 1996;40:62-5.
13. Kucera M, Barma M, Horacek O, Kovarikova J, Kucera A. Efficacy and safety of topically applied Symphytum herb extract cream in the treatment of ankle distortion: results of a randomized controlled clinical double blind study. Wien Med Wochenschr. 2004;154:498-507.
14. Koll R, Klingenburg S. [Therapeutic characteristic and tolerance of topical comfrey preparations. Results of an observational study of patients] Fortschr Med Orig. 2002;120(1):1-9. German.
15. Wadhams PS, Griffith J, Nikraves P, Chodosh D. Efficacy of a surfactant, allantoin, and benzalkonium chloride solution for onychomycosis. Preliminary results of treatment with periodic debridement. J Am Podiatr Med Assoc. 1999;89:124-30.



Lenscare goes Natural!

Aqua Balance®

**Moisturising Multi Purpose Solution
for Prolonged Wearing Comfort
of all Soft Contact Lenses**

LAPIS LAZULI
EYE CARE