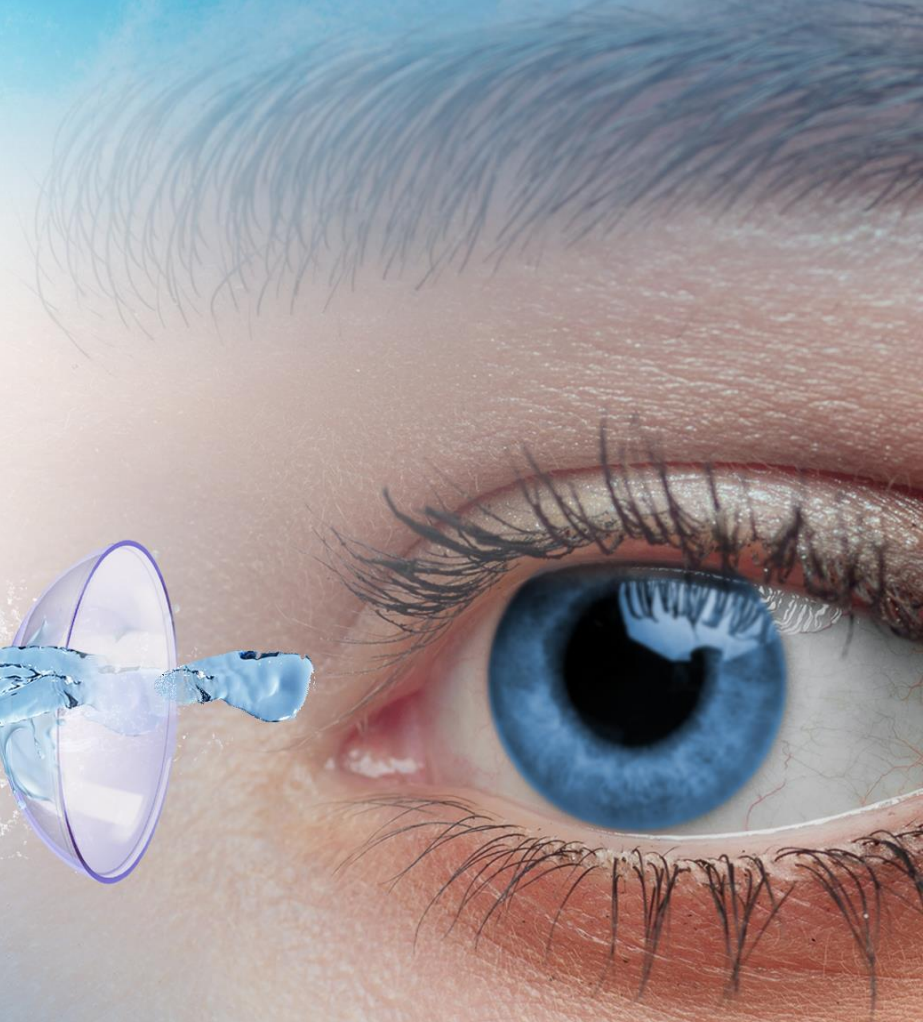
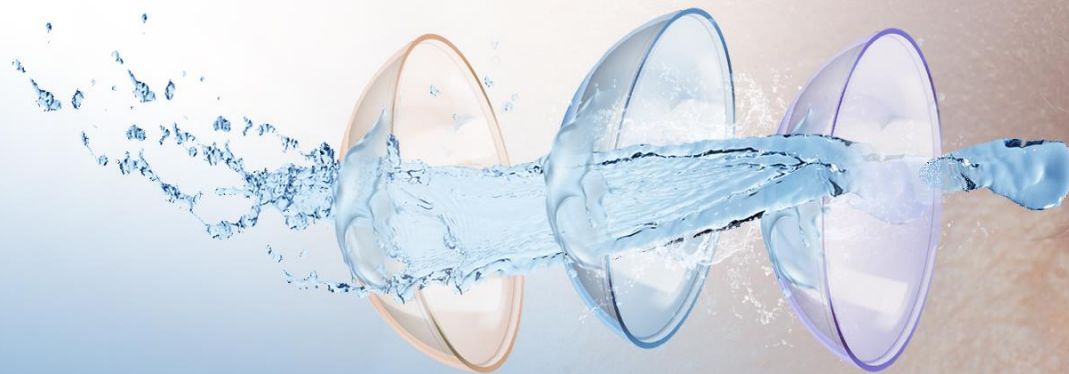



LUMIXA[®]
ADVANCED



A COMPLETE TEAR SUBSTITUTE

FOR THE TREATMENT OF DRY EYE

Triple Layer Action for Triple Targeted Protection

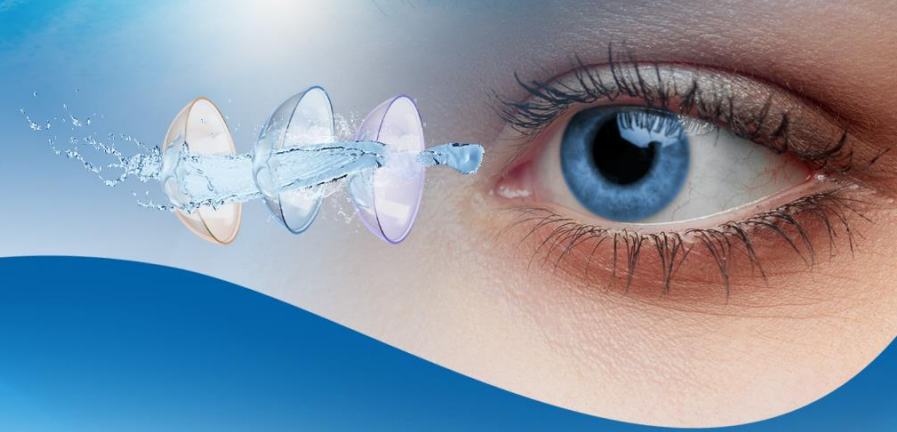
**ADVANCED
PROTECTION**

**ADVANCED
RETENTION**

**ADVANCED
ANTI-INFLAMMATION**



**Triple Layer
Action for Triple
Targeted
Protection**



LUMIXA[®] ADVANCED CONTENT

- ◆ DRY EYE DISEASE

- ◆ A NEW ERA OF DRY EYE DISEASE MANAGEMENT

- ◆ TRIPLE LAYER ACTION FOR TRIPLE TARGETED PROTECTION

- ◆ ACTIVE INGREDIENTS- CROSS LINKED HYALURONIC ACID, CROCIN, LIPOSOMES

- ◆ LUMIXA[®] ADVANCED TRIPLE TARGETED ACTION
 - MUCO-ADHESIVE AND TEAR FILM STABILIZING ACTION
 - ANTI-OXIDANT AND PROTECTION AGAINST BLUE LIGHT DAMAGE
 - ANTI-INFLAMMATORY ACTION

- ◆ INTERNATIONALLY PUBLISHED CLINICAL STUDIES

- ◆ NEW ADVANCED NOVELIA BOTTLE

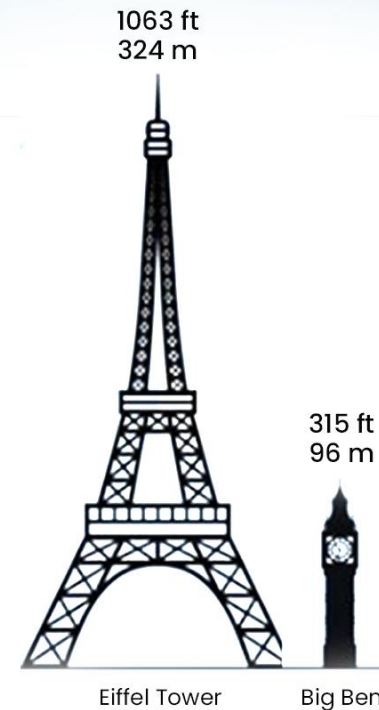
- ◆ LUMIXA[®] ADVANCED - A COMPLETE TEAR SUBSTITUTE FOR THE TREATMENT OF DRY EYE



Triple Layer Action for Triple Targeted Protection



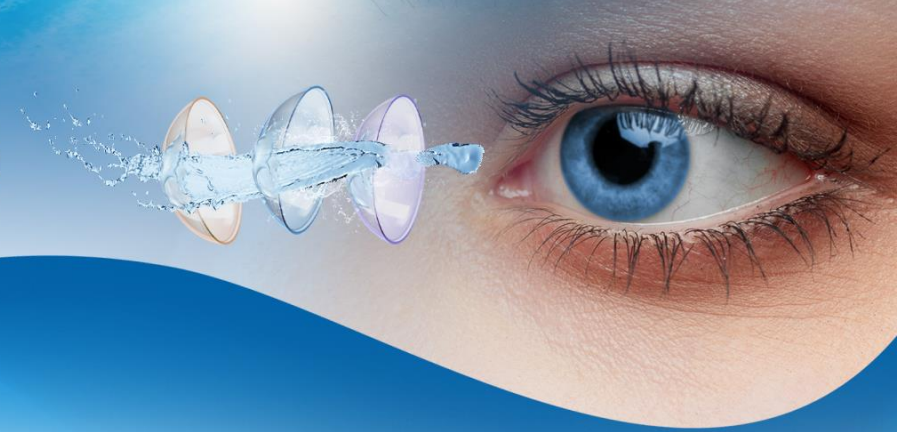
- ◆ The prevalence of Dry Eye Disease Management, with and without symptoms, ranges from 5 to 50%.
- ◆ Signs and symptoms of dry eye disease increase with age
- ◆ 86% of patients with dry eye disease are effected by MGD. Meibomian gland dysfunction (MGD) is the most frequent cause of dry eye disease (DED) and is associated with multiple pathological mechanisms including inflammation, microbial factors, and lipid deficiencies.



EVAPORATIVE
DRY EYE DISEASE
FORM IS 3
TIMES HIGHER
THAN
AQUEOUS TEAR
DEFICIENT ONE



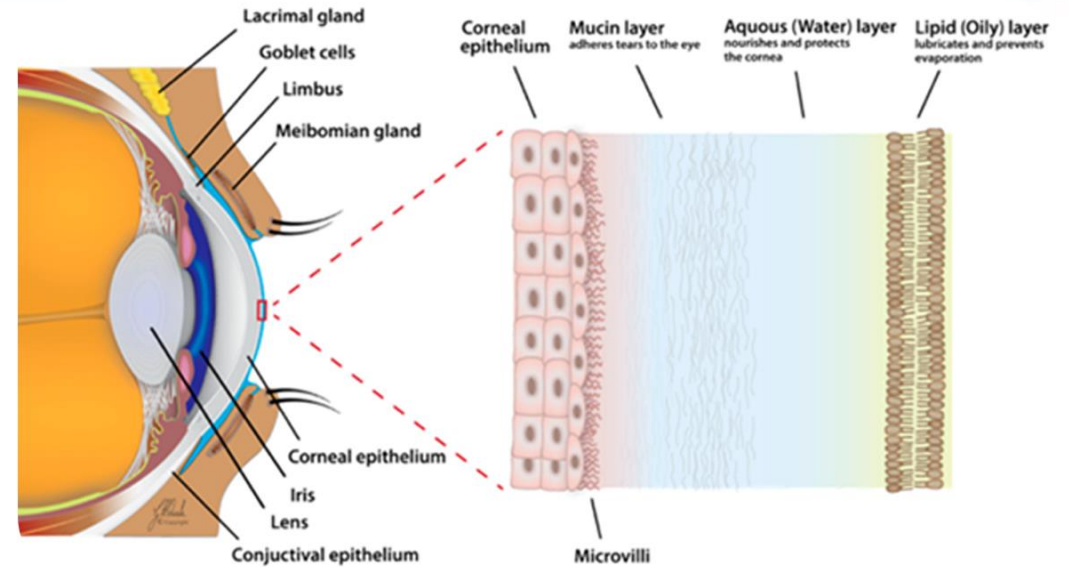
**Triple Layer
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DRY EYE DISEASE'S EFFECTIVE MANAGEMENT STILL REMAINS AN ISSUE

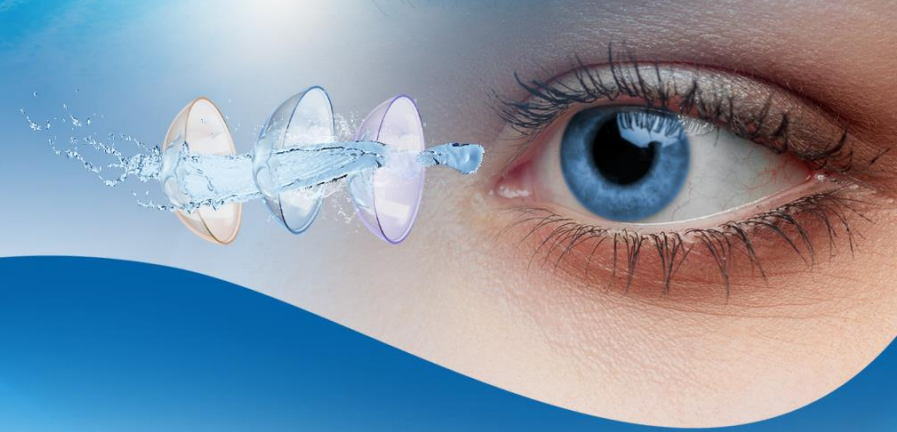
Effective dry eye disease management includes not only symptomatic treatment but therapeutic care to **restore homeostasis** within the tear film – this includes active intervention within the **lipid layer**, **mucin layer** and **aqueous layer**.

UNTIL NOW





**Triple Layer
Action for Triple
Targeted
Protection**



ENTERING A NEW ERA WITH LUMIXA[®] ADVANCED

**PAKISTAN'S FIRST DRY EYE CARE DROP THAT PROVIDES
SYNERGISTIC ACTION OF 3 COMPONENTS FOR ALL 3
LAYERS OF THE TEAR FILM**

- ◆ MUCO-ADHESIVE AND TEAR FILM STABILIZING ACTION
- ◆ ANTI- OXIDANT AND PROTECTIVE ACTION AGAINST
BLUE LIGHT (EMITTED FROM DIGITAL SCREENS)
DAMAGES
- ◆ ANTI-INFLAMMATORY AND CORNEAL SURFACE
REPAIRING ACTION





**Triple Layer
Action for Triple
Targeted
Protection**



LUMIXA'S TRIPLE TARGETED AND SYNERGISTIC ACTION ON ALL 3 LAYERS OF THE TEAR FILM

ENABLES:

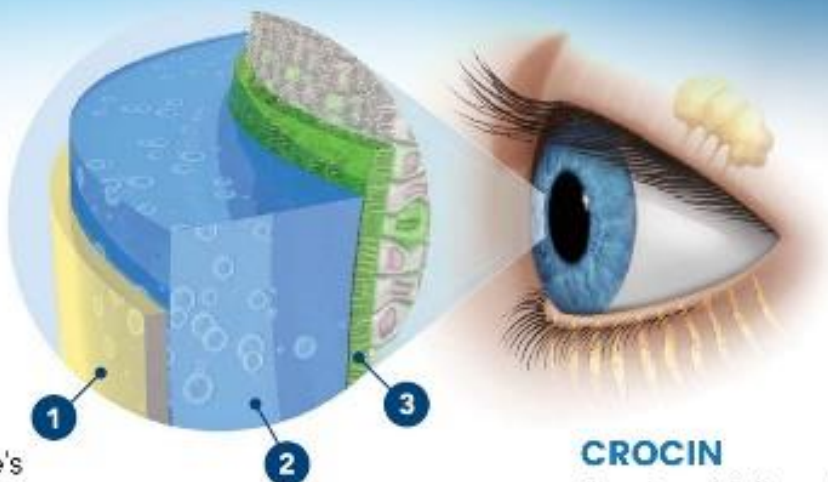
ADVANCED PROTECTION,

ADVANCED RETENTION,

AND ADVANCED ANTI-INFLAMMATION

LIPOSOMES 0.6%

Liposomes repairs the eye's protective lipid layer and reduces moisture evaporation. Liposomes facilitates the passage of crocin in aqueous layer and then in mucin, through the bond with phospholipid polar heads.



CROSSLINKED HA 0.15%

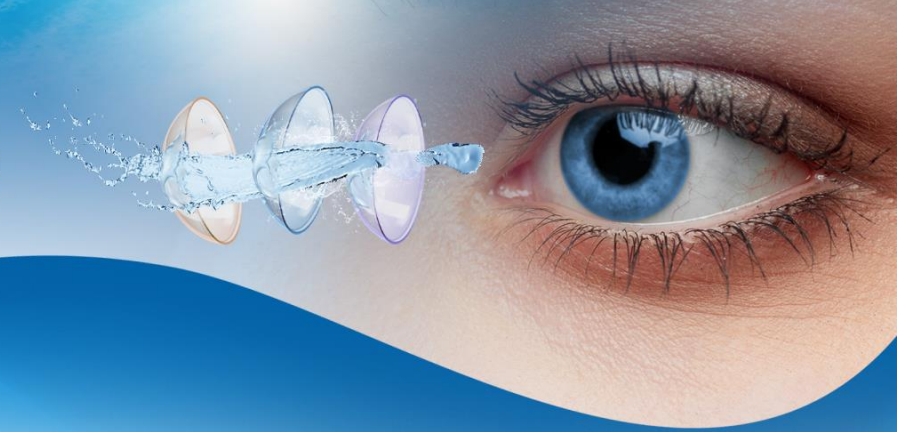
CXL-HA in combination with crocin further increases the anti-inflammatory and anti-oxidant activity of crocin. Hyaluronic acid is a highly stable viscous ocular lubricant.

CROCIN

Crocin exhibits a strong anti-inflammatory and anti-oxidant effect on ocular surface. Crocin interacts through non-covalent bonds with mucin and CXL-HA, thus increasing the cross-linkage level and mucoadhesiveness on the ocular surface.

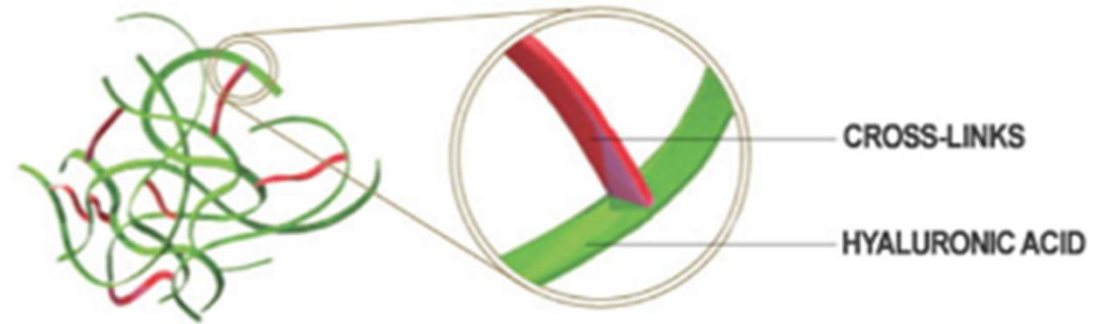


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Protection**



CROSS LINKED HYALURONIC ACID (CXL-HA)

- ◆ Hyaluronic Acid hydrates and lubricates the ocular surface and possesses water retention properties and viscoelasticity, helping in the healing of the corneal and conjunctival epithelium.
- ◆ **Cross-Linked Hyaluronic Acid (CXL-HA)**, is a complex molecule obtained from several linear HA molecules joined together by bridge bonds formed by a compound, called crosslinker (e.g. EDC) that interposes between two chains.
- ◆ **Cross-Linked Hyaluronic Acid (CXL-HA)** is a more viscoelastic material, with higher stability, and greater resistance to enzymatic degradation by hyaluronidase.





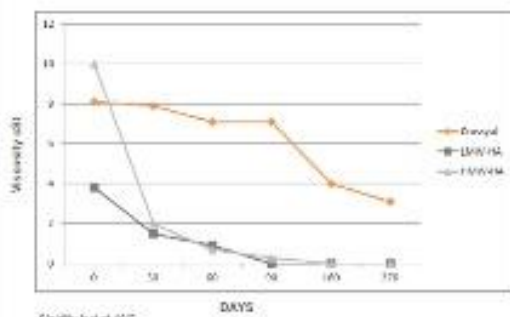
**Triple Layer
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Targeted
Protection**



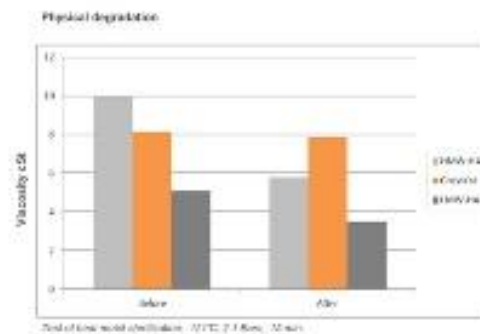
CROSS-LINKED HYALURONIC ACID – PROVIDES GREATER STABILITY AND MAINTENANCE OF VISCOELASTIC COMPONENT OVERTIME COMPARED TO LINEAR HYALURONIC ACID

- ◆ Normal HA, after 30 days at 40° C, has a viscosity reduction comprised between 60% and 80%
- ◆ CXL-HA at a concentration of 0.15%, showed a viscosity loss of 10-12% after 90 days at 40° C.
- ◆ Osmolarity and pH remained stable in the CXL-HA group

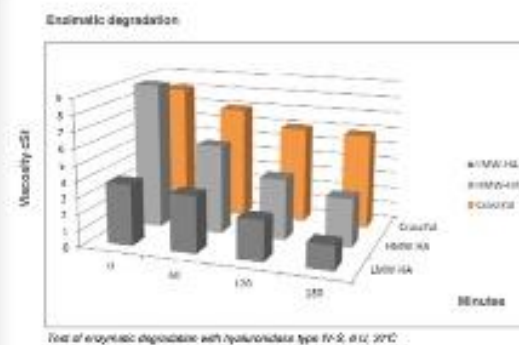
1. CXL-HA MANTAINS ITS PROPERTIES OVERTIME



2. HIGH STABILITY AT ELEVATED TEMPERATURES



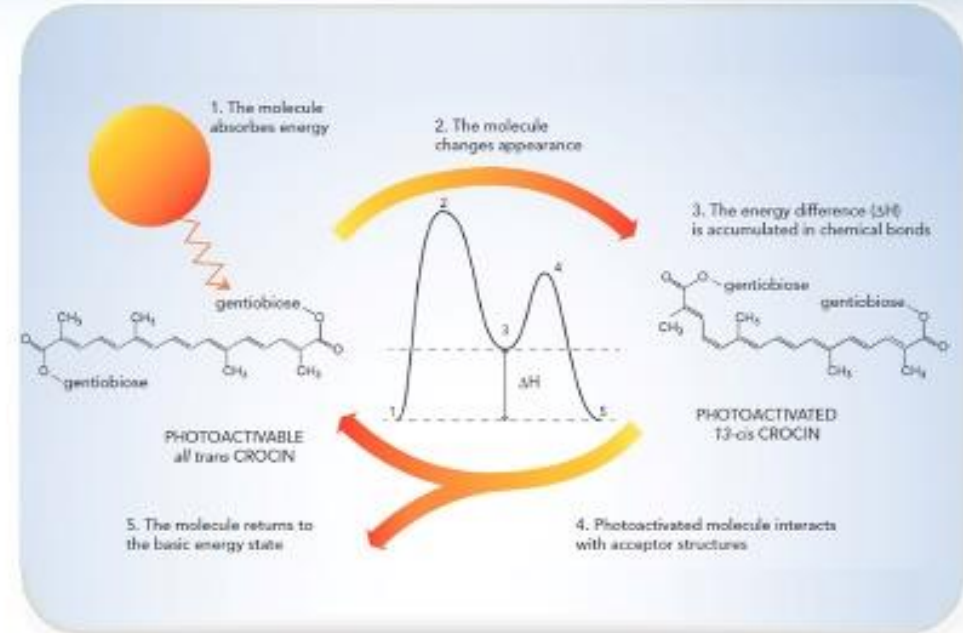
3. HIGH RESISTANCE TO HYALURONIASIS





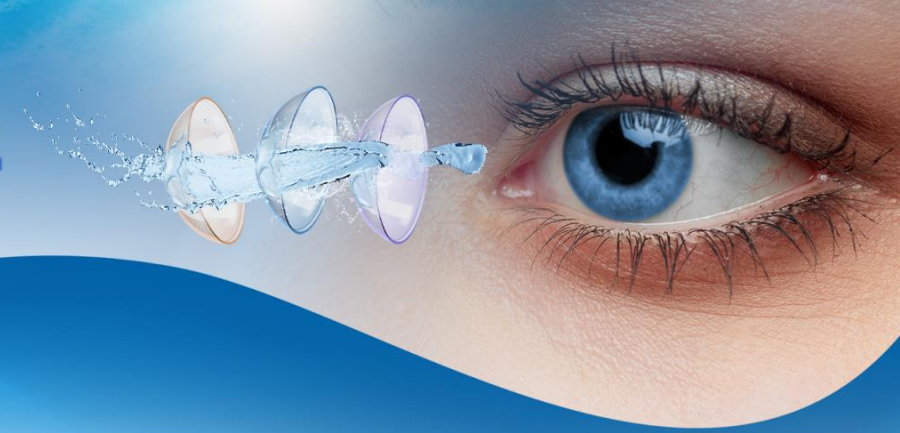
LUMIXA® ADVANCED is the first eye drop made with the Biophotonic Technology that exploits the interaction between light energy and photoactivable molecule (the chromophore crocin) for an effective treatment of Dry Eye.

- ◆ Crocin is a water-soluble photoactivable carotenoid.
- ◆ Crocin can interact with light in the wavelength range of 80–510 nm (violet-blue and green spectral colors) and undergoes a reversible photochemical reaction.
- ◆ Photo activation of Crocin increases the degree of cross-linkage and consequently, viscosity and muco-adhesive properties.





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Action for Triple
Targeted
Protection**



CROCIN PROVIDES ANTI-OXIDANT PROPERTIES AND IMPROVES CROSS LINKED HYALURONIC ACID PERFORMANCE

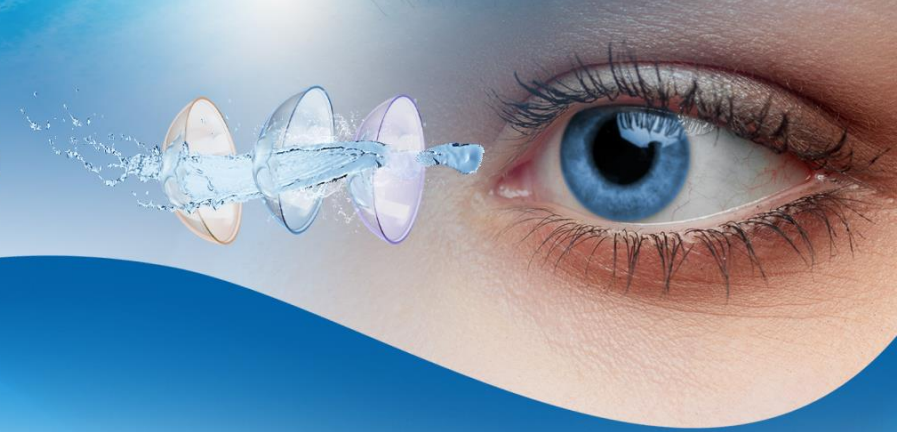
- ◆ **Crocin is a potent antioxidant with a double-action of:**
 - ✓ Quenching inhibits the formation of free radicals,
 - ✓ Scavenging reduces the levels of reactive oxygen species.
- ◆ Crocin interacts with CXL HA and improves its **viscoelastic characteristics and mucus-adhesiveness**

**PROTECTION
OF OCULAR
SURFACE FROM
OXIDATIVE
STRESS**

**IMPROVED PER-
SISTENCE OF THE
EYE DROPS FOR
A DURABLE
COMFORT**

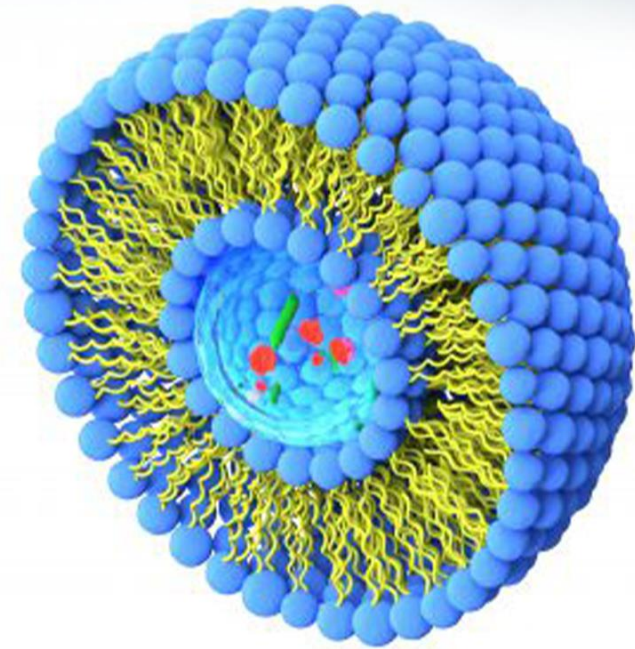


**Triple Layer
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Targeted
Protection**



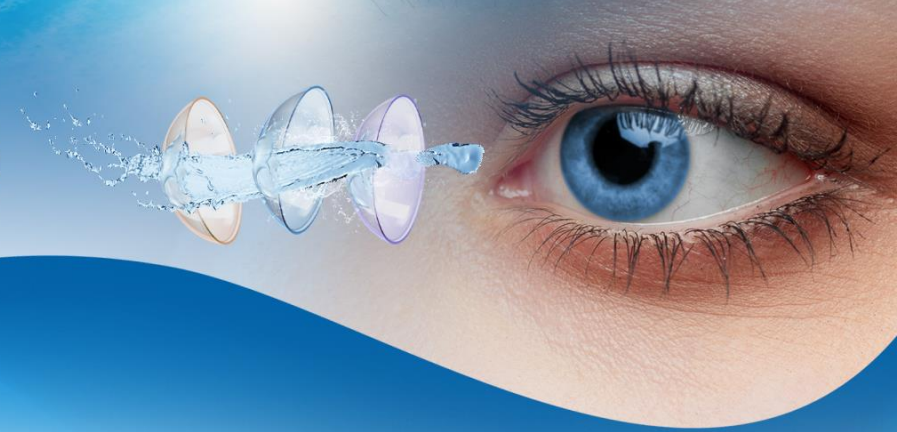
LIPOSOMES

- ◆ The constituents of the liposomes (phospholipids) are biocompatible and devoid of toxic or allergic effects.
- ◆ High concentration LIPOSOMES (0.6%) regenerates the lipid layer of the tear film by integrating the phospholipids of the inner polar portion that connects the non-polar outer portion to the aqueous layer.





**Triple Layer
Action for Triple
Targeted
Protection**



LUMIXA® ADVANCED

- 1 **MUCO-ADHESIVE AND TEAR FILM STABILIZING ACTION**
(Cross Linked Hyaluronic Acid, Liposomes)
- 2 **ANTIOXIDANT AND PROTECTIVE ACTION AGAINST
BLUE LIGHT DAMAGES**
(Crocin)
- 3 **ANTI-INFLAMMATORY AND CORNEAL SURFACE
REPAIRING ACTION**
(Crocin, Cross Linked Hyaluronic Acid)





**Triple Layer
Action for Triple
Targeted
Protection**



1

MUCO-ADHESIVE AND TEAR FILM STABILIZING ACTION

LUMIXA[®] ADVANCED eye drops allows to maintain an effective and extended hydration of the corneal surface, without fogging. ^{2,5}

MUCOADHESION: One of the main challenges associated with conventional artificial tears is the short retention time on the ocular surface.

CROCIN: Lumixa's Advanced photo activated Crocin exhibits a high mucoadhesiveness under illuminated conditions, as its interaction with mucin is **seven-fold higher** than Crocin alone.

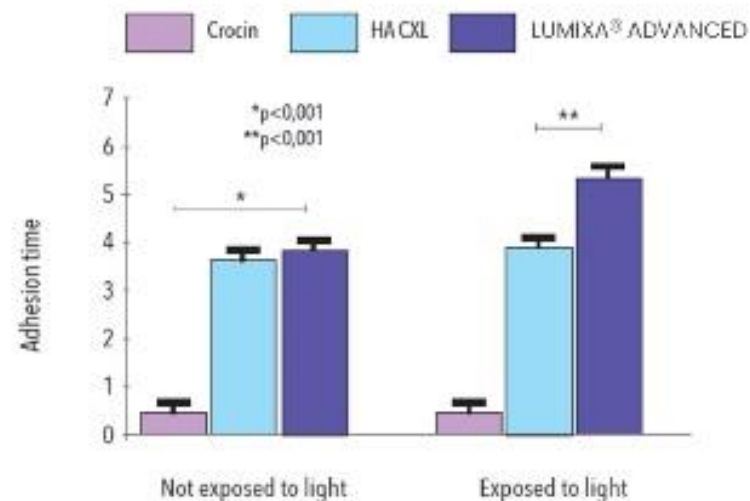


Fig.1 - increase of muco-adhesiveness of a formulation based on crocin + cross-linked hyaluronic acid + liposomes (LUMIXA[®]) before and after light exposure in comparison to stand alone crocin and CXL hyaluronic acid.²



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Protection

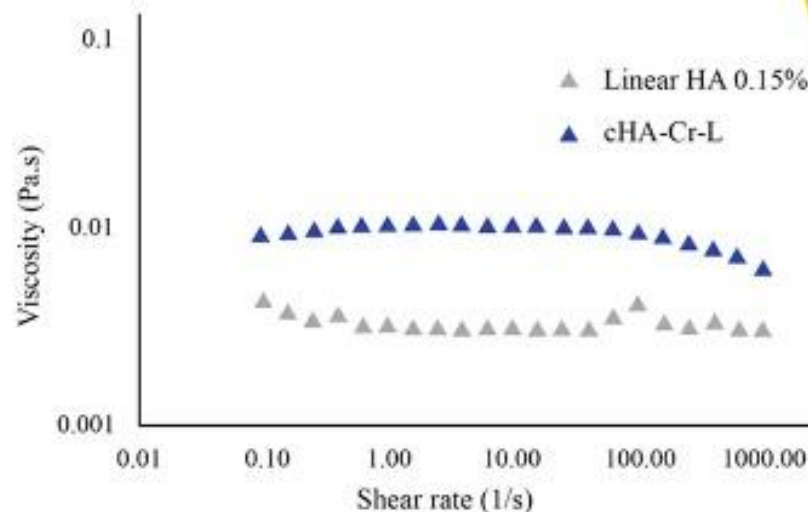


1

MUCO-ADHESIVE AND TEAR FILM STABILIZING ACTION

◆ VISCOSITY:

Artificial tears that display low viscosity at low shear rates are more likely to drain or evaporate. LUMIXA ADVANCED exhibits a higher shear viscosity compared to linear HA 0.15%.



Viscosity
over 4 times
higher than a
linear HA with same
concentration

Figure 2 Shear viscosity of cHA-Cr-L compared to linear hyaluronic acid (HA) 0.15%. Molecules. 2021; 26(4):849.



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Protection**

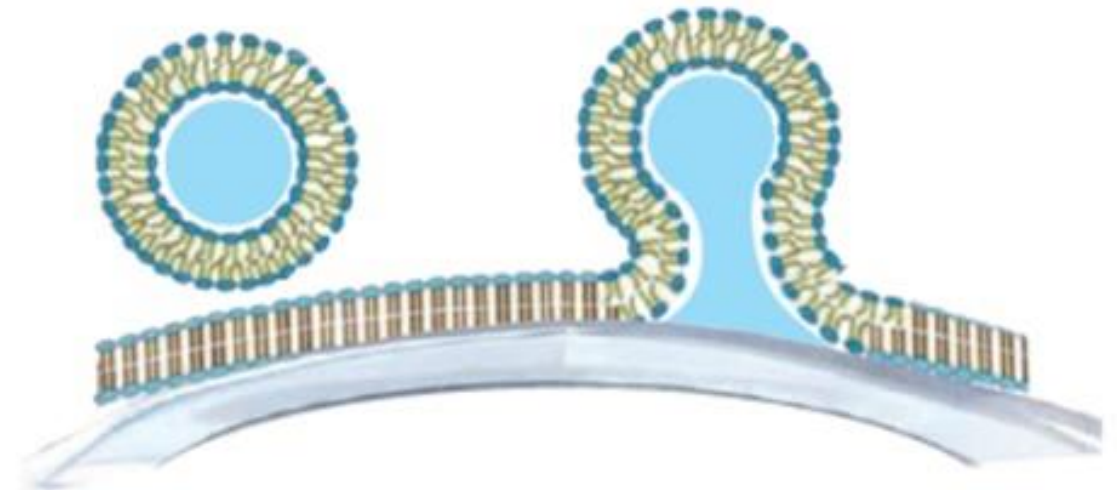


1

MUCO-ADHESIVE AND TEAR FILM STABILIZING ACTION

◆ LIPOSOMES (0.6%):

- Help to regenerate the lipid layer of the tear film integrating the phospholipids of the polar portion.
- They stabilize the tear film by lowering the surface tension and preventing excessive evaporation.
- They convey the passage of crocin in the aqueous layer and then in the mucin, through the bond with "phospholipids polar heads"





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Targeted
Protection



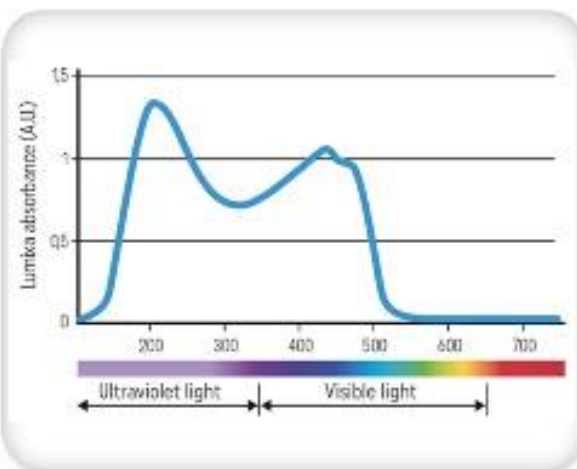
2

ANTIOXIDANT AND PROTECTIVE ACTION AGAINST BLUE LIGHT DAMAGES

LUMIXA® ADVANCED performs a corneal surface protection action due to the high antioxidant activity of the crocin with dual mechanism: ^{2,6,7}

CROCIN PROTECTION AGAINST UV RAYS AND BLUELIGHT:

Due to the presence of photo-activated carotenoid crocin, Lumixa's Advanced absorbs both blue light (380-500 nm) and ultraviolet light (200-300 nm), acting as a shield against light radiation.



Formulation based on crocin + CXL HA+ liposomes (LUMIXA®ADVANCED) significantly reduced free radical production in human corneal epithelial cells.

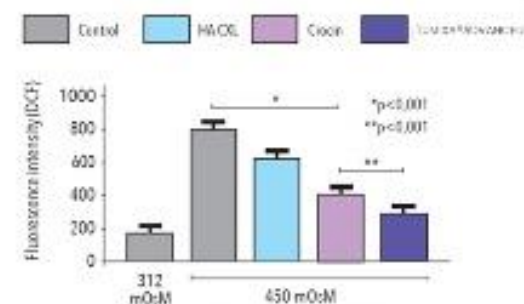
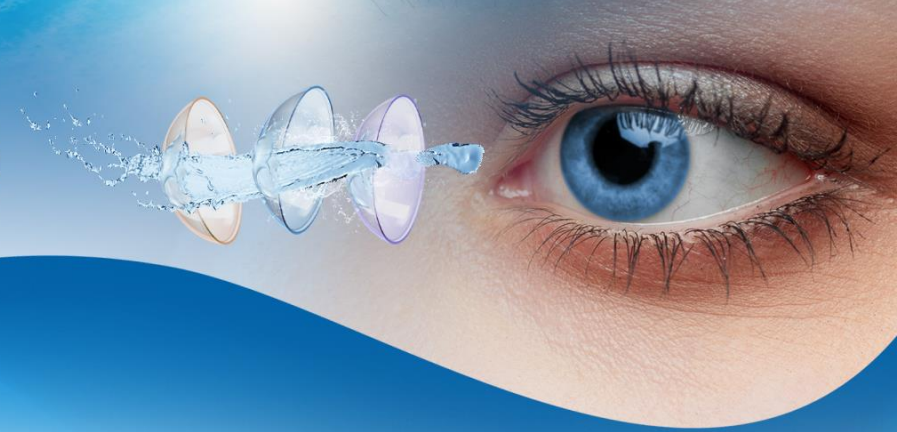


Figure 3 ROS overproduction in hyperosmolarity-stimulated HCECs was effectively diminished by cHA-Cr-L, as determined by DCF fluorescent intensity.



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Protection**

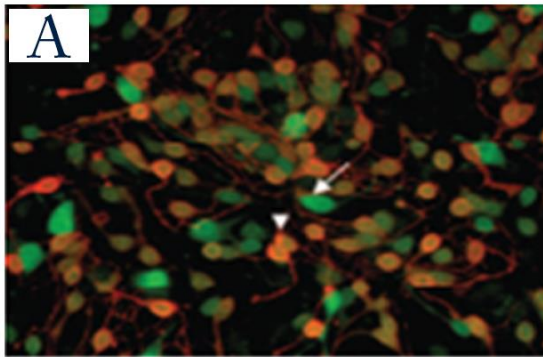


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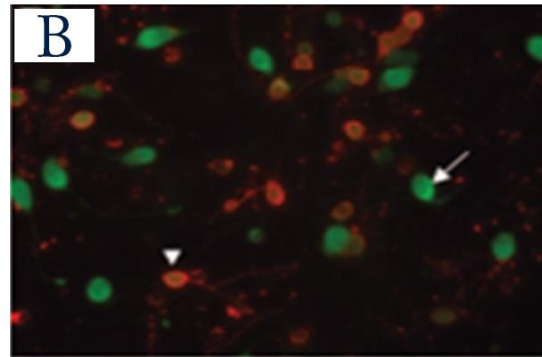
ANTI-OXIDANT AND PROTECTION AGAINST BLUE LIGHT DAMAGES

PROTECTION AGAINST CELL DEATH: Blue and white light selectively induce death of photoreceptors in retina. Crocin protects retinal photoreceptors against light-induced cell death.⁴

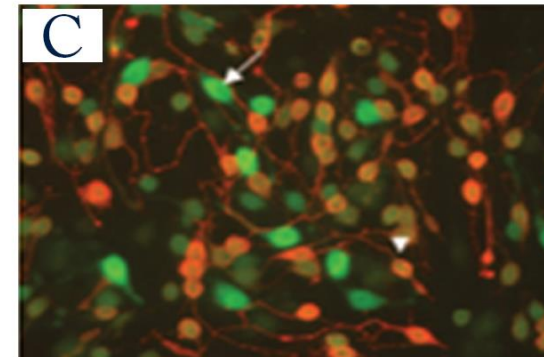
No significant differences observed between control and Crocin treated group



A: control cell culture was kept in the dark.



B: cell culture exposed to blue actinic light for 24 hours.



C: Cell were pretreated with 80 micrograms of crocin.



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3

ANTI-INFLAMMATORY AND CORNEAL SURFACE REPAIRING ACTION

LUMIXA® Advanced help to prevent contrast the damages of the typical inflammatory process of dry eye and facilitate the healing process of the corneal surface:^{2,4,8,9}

CROCIN multiple anti-inflammatory action:

The combination of CROCIN and HA CXL, present in LUMIXA Advanced®, results in a significant increase of anti-inflammatory properties of the individual.

CROSS-LINKED HYALURONIC ACID: promotes corneal repair processes, stimulates migration and proliferation of keratinocytes.⁴

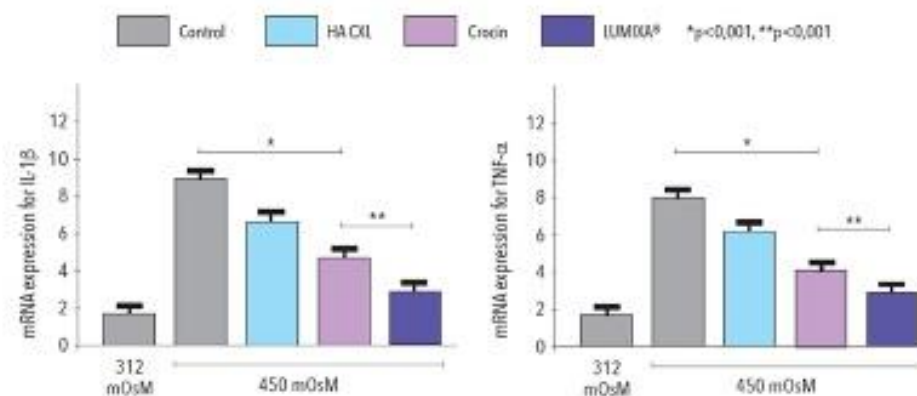


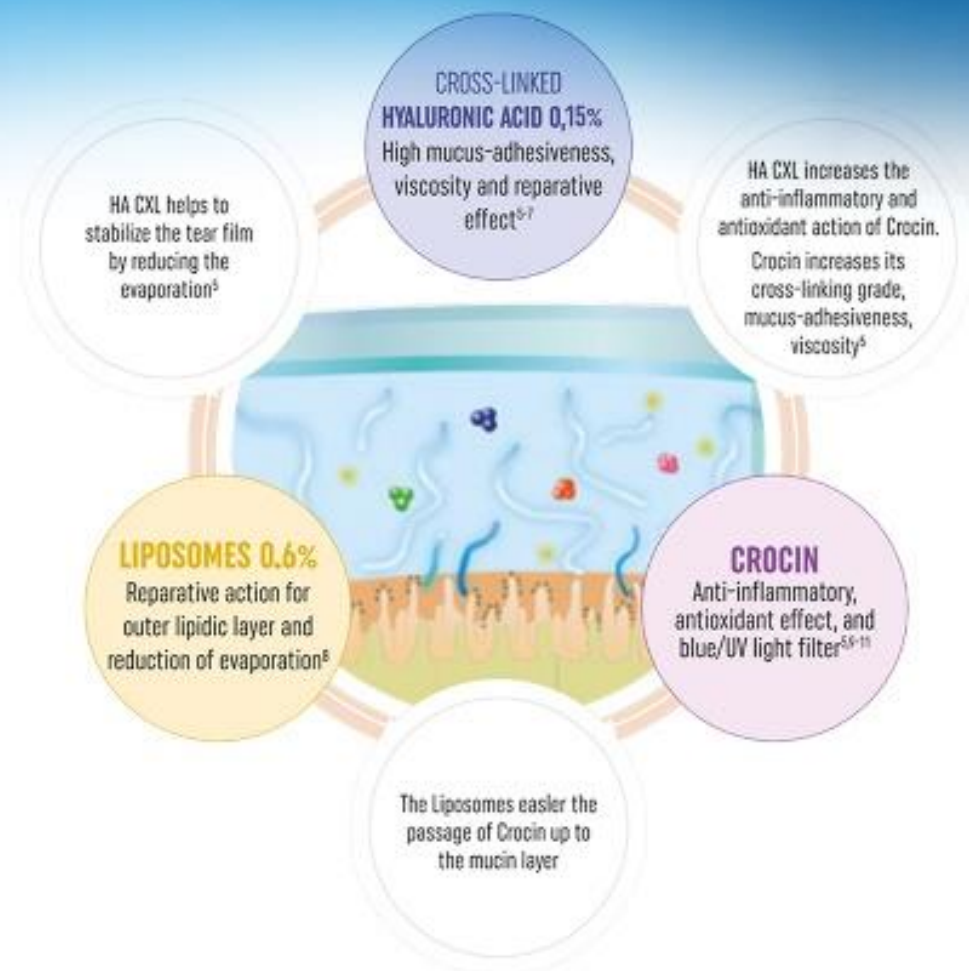
Fig.5- anti-inflammatory effect evaluated on a culture of human corneal epithelial cells placed in hyperosmotic solution, of a formulation of crocin + CXL HA + liposomes (LUMIXA), compared to the two components alone and an untreated control group.⁵



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3 COMPONENTS FOR 3 LAYERS OF THE TEAR FILM





**Triple Layer
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Targeted
Protection**



CLINICAL TRIALS

STUDY 1



**Triple Layer
Action for Triple
Targeted
Protection**



LUMIXA® ADVANCED FORMULATION IS SUPERIOR TO HYALURONIC ACID 0.2% IN STABILIZATION OF TEAR FILM AND IMPROVEMENT OF DRY EYE SYMPTOMS AFTER ONE MONTH OF THERAPY

In a study conducted on 50 patients with dry eye, the STABILITY of the tear film was evaluated, by NBUT Avg and the EFFECTIVENESS in reducing the symptoms of the disease by OSDI, after instillation of Lumixa® Advanced in comparison to a solution of HA 0.2% linear, 4 times a day, for 30 days.¹³

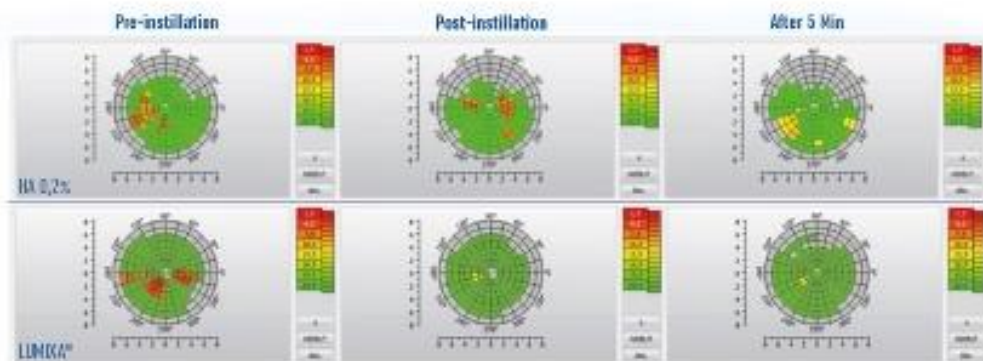


Fig. 3 Examples of NBUT Avg and NBUT first (Keratograph 5M) at the different times from the instillation of HA 0.2% (A) and Lumixa® (B)

NIH U.S. National Library of Medicine
ClinicalTrials.gov

OSDI scores categorization:

- Normal ocular surface (0-32 points)
- Mild dry eye (13-32 points)
- Moderate dry eye (23-32 points)
- Severe dry eye (above 31)

fig.3 Examples of NBUT Avg and NBUT first (Keratograph 5M) at the different times from the instillation of HA 0.2% (A) and lumixa (B)

RESULTS:

1. OSDI QUESTIONNAIRE SCORE

OSDI score after 30 days treatment

Linear HA 0.2%: 20.5

LUMIXA (CHA-Cr-L): 12.1

2. TEAR BREAKUP TIME (TBUT)

	TBUT before instillation	TBUT after instillation	TBUT after 5 minutes
HA 0.2%	8.12s	9.5s	9.9s
LUMIXA (CHA-Cr-L)	5.78s	12.36s	12.31s

OSDI scores categorization:

- Normal ocular surface (0-32 points)
- Mild dry eye (13-32 points)
- Moderate dry eye (23-32 points)
- Severe dry eye (above 31)



**Triple Layer
Action for Triple
Targeted
Protection**



CLINICAL TRIALS

STUDY 2



Triple Layer
Action for Triple
Targeted
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LUMIXA® ADVANCED SHOWN TO SIGNIFICANTLY INCREASE VOLUME AND STABILITY OF TEAR FILM, WITH HIGHER EFFECTIVENESS COMPARED TO LINEAR HA 0.15%

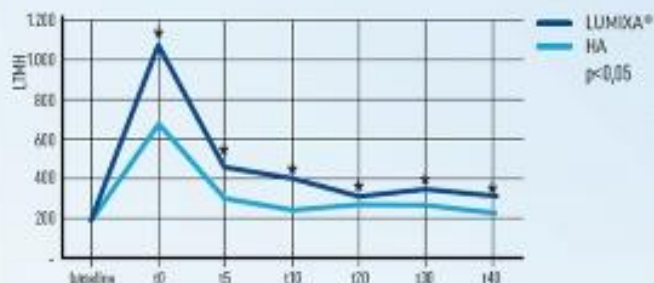


Fig. 1 Height of the lower tear meniscus (LTMH) at different times from the instillation for the two preparations in patients with dry eye.

LUMIXA® Advanced results in a rapid and persistent increase in tear VOLUME of 70% compared to HA 0.15%, maintaining the difference for up to 40 minutes.¹⁶



Fig. 2 f-TFBUT at different times from the instillation of the two eye drops in patients with dry eye.

LUMIXA® Advanced results in a marked and lasting increase in tear film STABILITY, demonstrated by a 100% increase in tear film break-up, compared to 0.15% HA, up to 20 minutes.¹⁷



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Targeted
Protection**



CLINICAL TRIALS

STUDY 3



THE TRIPLE ACTIVE COMPONENT OF LUMIXA® ADVANCED SHOWED THE SAME EFFICACY AS A HIGH-DOSE LINEAR HA IN THE TREATMENT OF DRY EYE.

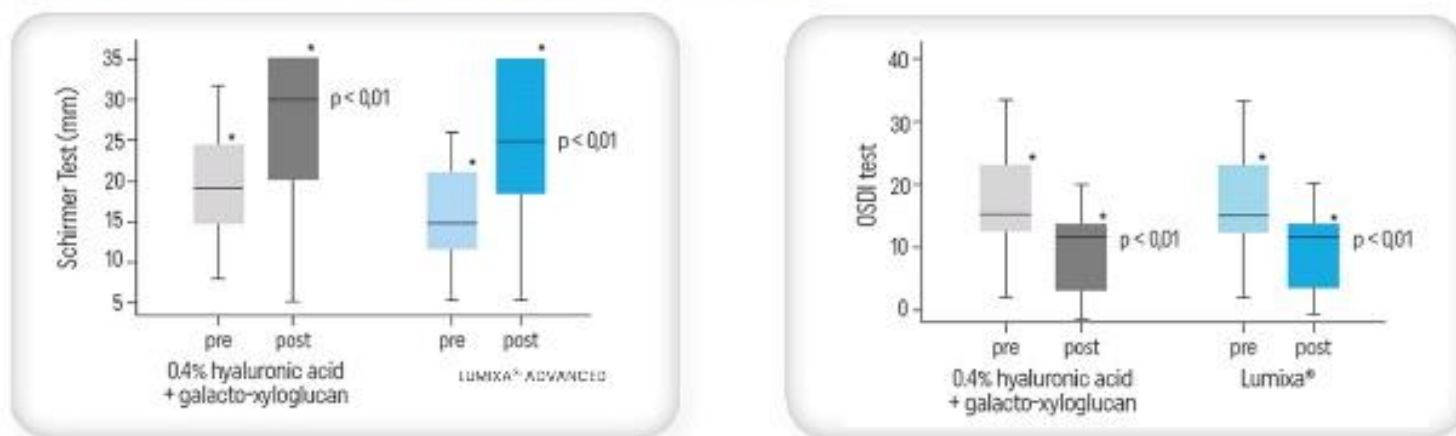


Fig.5 Comparison of the results of the Schirmer test (A) and of the OSDI (B) between a group treated with a 0.4% linear HA solution + galactoxyloglucan and a group treated with Lumixa for 45 days. The test results improve significantly after both treatments, without significant differences (* $p < 0.01$).

A: the Schirmer test, TBUT, and OSDI score before treatment; B: The Schirmer test, TBUT, and OSDI score after treatment. Wilcoxon test was used for related nonparametric variables.



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Targeted
Protection



NOW EQUIPPED WITH A STATE OF THE ART BOTTLE, THE FIRST OF IT'S KIND IN PAKISTAN

NEW NOVELIA® BOTTLE

MULTIDOSE, PRESERVATIVES FREE,
SOFTER AND WITH A TIP FOR EASY
ADMINISTRATION

FORMULATION WITH **MORE**
PHOTOACTIVE CROCIN, 0.15%
HIGH-MW **HA CXL** AND **LIPOSOMES**

LUMIXA® ADVANCED'S NOVELIA®
BOTTLE **REMAINS STERILE FOR UP TO**
60 DAYS AFTER FIRST USE



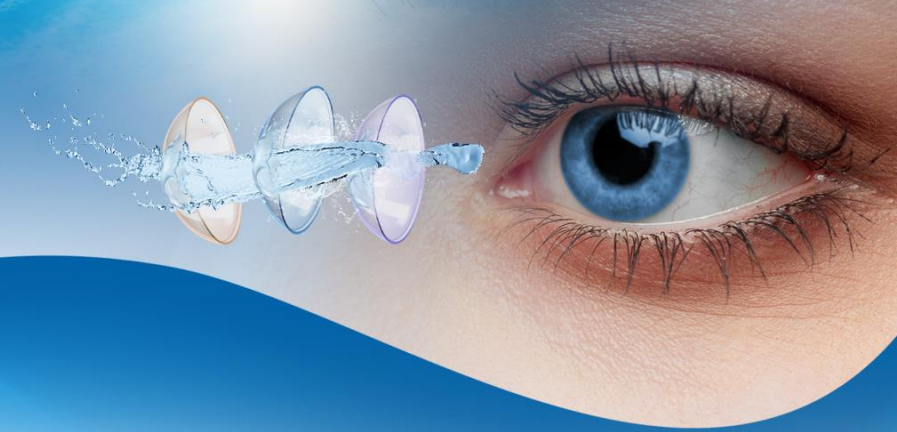
**EASIER
INSTILLATION**
NEW NOVELIA® BOTTLE MULTIDOSE
SOFTER AND WITH A TIP
FOR EASY ADMINISTRATION



Lumixa® can be administered also
while contact lenses are being worn.



**Triple Layer
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Targeted
Protection**



PHOTOACTIVE LACRIMAL INTEGRATION WITH SYNERGISTIC ACTION OF 3 COMPONENTS FOR 3 LAYERS OF TEAR FILM

- ◆ SUITABLE FOR ALL TYPES OF DRY EYE CAUSED BY AQUEOUS TEAR-DEFICIENCY AND EXCESSIVE TEAR EVAPORATION
- ◆ MULTIDOSE PRESERVATIVE FREE FORMULATION (10 ML)
- ◆ LONG LASTING COMFORT FOR PATIENTS
- ◆ RAPID RESOLUTION FOR DRY EYE SYMPTOMS





**Triple Layer
Action for Triple
Targeted
Protection**



INDICATIONS

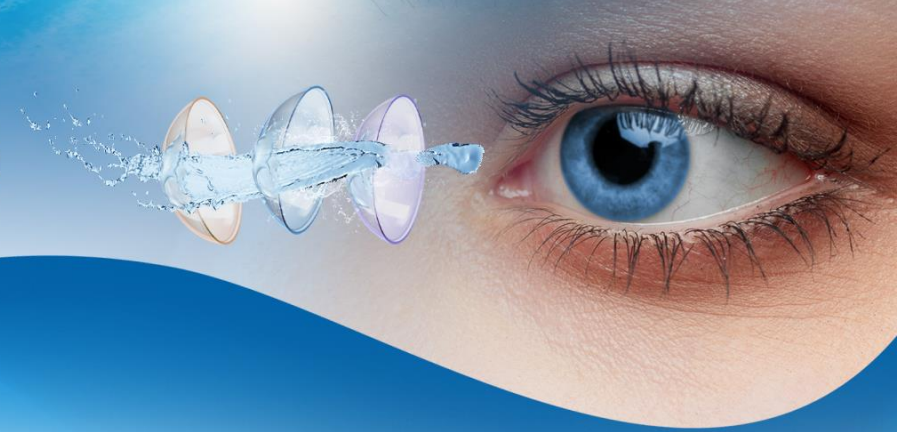
Symptomatic treatment for dry eye syndrome. Also suitable for corneal protection as a tear substitute after surgery, ocular trauma, or in case of environmental or visual stress.

HOW TO USE:

Instill one or two drops in each eye more times a day or according to medical advice.



Triple Layer Action for Triple Targeted Protection



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Targeted
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SUPPLEMENTARY



**Triple Layer
Action for Triple
Targeted
Protection**



**Crocin stabilizes the
ophthalmic solution**

Less blurring and fogging

**Liposomes-based eye
drop**



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