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OcuHeal-UV400+ Eyedrops Protect HCEC from UV-Induced Damage by Scavenging of Reactive Oxidative Species

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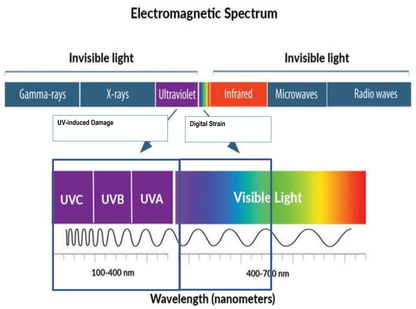
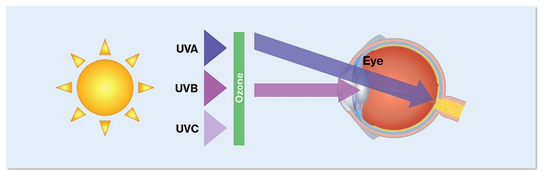
The Problem : UV Light is Absorbed by Ocular Tissues and is Correlated with a Multitude of Ocular Disorders

Clinical Need: UV exposure leads to ocular disorders, such as corneal pterygia, cataracts, keratoconus, glaucoma, CNV and AMD. UVR is categorized as: UVA (315-400 nm), UVB (280-315 nm) and UVC (100-280 nm**).** >90% of UVB, 60% of UVA are absorbed by the cornea, whereas the retina absorbed UV light (UVA) and blue light in the range 300-800 nm. UVA and UVB cause damage to cellular DNA due to the production of reactive oxygen species (ROS), triggering tissue-damaging inflammatory cytokines





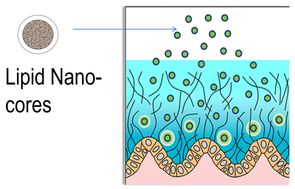
The Solution: We present data on **OcuHeal-UV400+**, a lipid nanoparticulate (LNP) eye-drop containing IB0108, a GRAS antioxidant, with decades of history of safe use as an oral supplement. IB0108 is biocompatible and blocks portions of UVA and UVB. *Encapsulated into LNP, the entire UV light wavelength range from 200-600 nm is blocked, thus enhancing the UV-blocking characteristics of IB0108*. It's anti-oxidant and anti-inflammatory properties renders a healing / protective effect to ocular tissues. The data demonstrate UV-blocking properties of the product, distribution of IB0108 throughout the eye and preclinical safety and tolerability.

Intellectual Property: OcuHeal LNP are fully patented in 14 global jurisdictions.

Materials and Methods (Characterization and *In-Vivo*)

OcuHeal-UV400+ was prepared as a nano-dispersion using a proprietary process; IB0108 Analysis: was measured by a HPLC method, using a Shimadzu Prominence HPLC; Particle Size Distribution (PSD): Particle sizing was carried out using a laser diffraction method (Horiba 950V2). UV-light blocking studies were conducted using a Shimadzu UV-Vis Spectrometer. IB0108 incubation studies with HCEC in the presence of UV light (254 nm, UVB). Bioanalysis: Analysis was performed by LC/MS/MS, Thermo Scientific TSQ Quantum Ultra Mass Spectrometer, paired with Shimadzu Nexera-i LC-2040C 3D Plus and using a C-18 column. Ocular tissues (tears, sclera, conjunctiva, eyelids, conjunctiva, AH, VH, retina, lens, choroid/RPE, optic nerve, cornea); Blood was analyzed for systemic extraction. Safety and Tolerability: in NZW rabbits (PARF, MA) of the prototypes were measured by assessment of ocular tissue at predetermined timepoints.. Tolerability of the wafers were assessed by a SPOTS scoring system.

OcuHeal™: The Platform Sustained Release Lipid Nano-Depots



- Lipid Nanoparticles
- Enhanced Bioavailability
- Nano-core size (<200 nm) penetrates the ocular mucosal meshwork pores (500 nm)

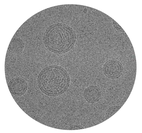
Target Product Profile of OcuHeal-UV400+

IB0108

- FDA GRAS compound for daily oral consumption as a supplement
- Decades of safe use in humans and animals
- ROS quencher/anti-oxidant
- UV-protective
- **Anti-oxidant, anti-inflammatory, immunoprotective, anti-aging**

IB0108-in-lipid nanoparticles

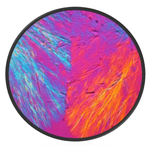
Aqueous Continuous phase



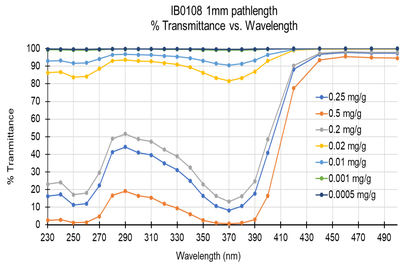
Cryo-Transmission Electron Microscopy of OcuHeal™ Dispersion

Liquid-Crystalline Lipid Depots Enable Interaction with Cell Membranes and Enhanced Residence Time on Tissues

- Lipid depots demonstrate a liquid crystalline order, enabling sustained presence in tissues, due to lipid-membrane interaction.

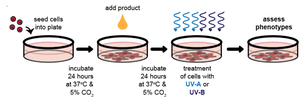


IB0108 Blocks UV-R in a Dose Responsive Fashion: Lower % Transmittance is Higher "UV-Blocking"

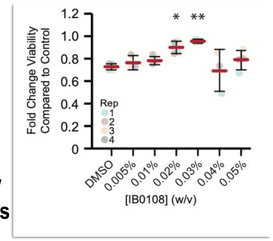


- Assuming a 40 microliter eye-drop of 1 mg/mL IB0108 and a 10 microliter tear volume, the concentration of IB0108 on the eye will be 0.8 mg/mL.

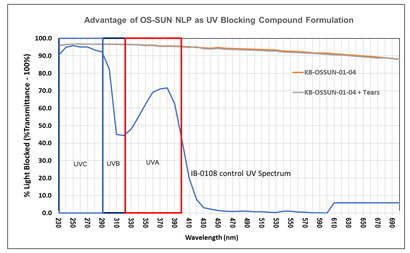
IB0108 Protects Human Corneal Epithelial Cells from UV-Damage by ROS Scavenging as an Antioxidant



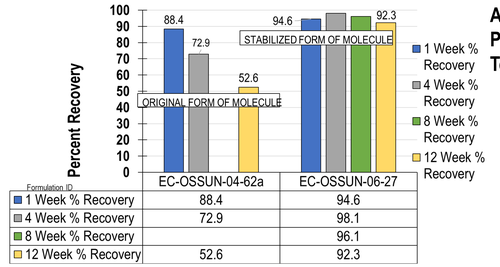
- IB0108-in-DMSO was used for initial study
- **DPPH scavenging studies show rapid scavenging of free radicals**



Novel IP: Encapsulation of IB-0108 in OcuHeal LNP Blocks Entire UVA, UVB, UVC Wavelengths



Formulation has Stabilized IB0108 from Spontaneous Self-Oxidation: Enables 6 month Storage at 25°C and Long Term Storage at 2-5°C

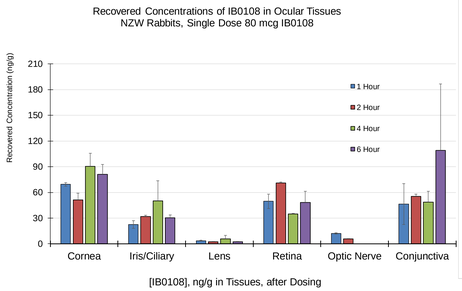


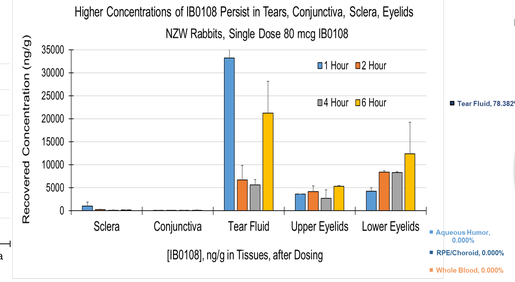
Formulation ID	EC-OSSUN-04-62a	EC-OSSUN-06-27
1 Week % Recovery	88.4	94.6
4 Week % Recovery	72.9	98.1
8 Week % Recovery		96.1
12 Week % Recovery	52.6	92.3

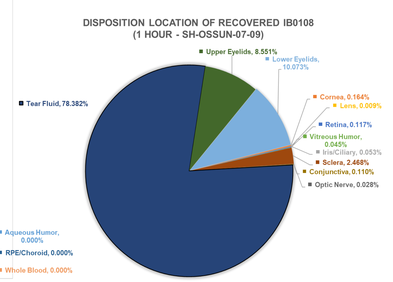
Arrhenius Rate Modeling of Stability Predicts Acceptable Storage Temperatures

	5°C	25°C	40°C
-6/R	-5132.5	-5132.5	-5132.5
-Ea/RT	-18.462	-17.223	-16.398
Y-Int.= Ln(A)	14.623	14.623	14.623
Ln(k) = Ln(A)-Ea/RT	-3.839	-2.600	-1.775
k =	0.02151	0.07426	0.16952
	5°C	25°C	40°C
Shelf Life (months)	27.9	8.1	3.5
Shelf Life (years)	2.32	0.67	0.29

PK of IB0108-in-OcuHeal Eyedrops Demonstrate Enhanced Residence Time on the Ocular Surface







Attributes of OcuHeal-UV400+

Assay (UV-Block)	0.1±10% LC
Viscosity (cP at 50°C)	120-130 cP
Size Distribution	D90<160 nm; span < 0.6 microns
Surface Tension	39
Non-Settling	Yes
Terminally Sterilized	Yes (Sterile Filtered)
Preservative-Free	Yes

OcuHeal-UV400+ is Tolerated *In-Vivo*

OcuHeal-UV400+ lipid nanoparticles were assessed for signs of non-biocompatibility on the ocular surface at all timepoints, including IOP testing, redness, eyelid swelling, discharge, hyperemia, corneal opacity, etc. using SPOTS scoring system. All scores were 0, at all timepoints.

Conclusions

OcuHeal-UV400+ is a well-tolerated UV-blocking anti-oxidant, with ocular surface residence time of 6 hours.

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Contact PI

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