

An innovative extract of the microalga *Haematococcus salinus* Dunal. to fight Glyc-Aging™ and protect the skin from intense solar irradiation.

Poster #33

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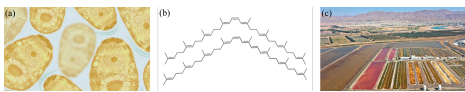
INTRODUCTION

Advanced Glycation End product (AGE) accumulation is a key driver of skin aging^[1-3]. Among other lifestyle factors, solar irradiation likely accelerates this process. Targets of glycation in the skin include key proteins with slow turnover rates such as collagens I/IV, fibronectin).

Glycated biomolecules' functions are hampered, e.g. due to modifications of conformation and solubility^[4]. Glycation and cross-linking of ECM proteins leads to tissue stiffness and hinders enzymatic removal^[5]. AGE receptor (RAGE) signaling induces inflammation, further driving skin aging. Natural detoxification of AGEs (glyoxalase pathway) is insufficient to manage glycation over a lifetime^[6-7].

Haematococcus salinus Dunal. is a halophile microalga, adapted to intense solar radiation through carotenoid production^[8].

We present a supercritical CO₂ *Haematococcus* extract standardized in the colorless carotenoids phytoene and phytofluene^[9], effective for protection of skin against some effects of solar exposure, mitigating glycation and its associated effects on skin, through multiple anti-glycative strategies: inhibiting AGE formation; minimizing existing AGEs; and reducing RAGE signaling.



(a); *Haematococcus salinus* Dunal., illustrative microscopy image; (b); phytoene (top) and phytofluene (bottom); *Haematococcus salinus* Dunal. cultivation ponds (southern Israel) showing a range of colors produced by the alga under various conditions.

MATERIALS & METHODS

EXTRACT

Hydrophobic SCCO₂ *Haematococcus salinus* Dunal. extract in jojoba oil (IBR-Solage[®], IFF - Lucas Meyer Cosmetics), purified to remove colored components and standardized for phytoene and phytofluene content.

ANTI-GLYCATION EFFECT EX VIVO

Normal human skin explants were treated topically with 0.5% extract in jojoba oil for 7 days (vs. untreated control); glycation was induced in half of the explants with 500 μM methylglyoxal. At D10, samples were immunostained for glycation marker N-epsilon-(carboxymethyl)lysine (CML); RAGE; and Glo-1, using specific antibodies. Staining was quantified by image analysis.

ANTI-INFLAMMATORY EFFECT EX VIVO

Normal human skin explants were treated topically with 0.5% extract in jojoba oil or jojoba oil alone (control) over 24h. IL6 and IL8 were quantified in supernatants by ELISA. NRF2 was labeled in frozen tissue with a specific antibody, and the labeling was quantified by image analysis.

CLINICAL EVALUATION UNDER INTENSE SOLAR EXPOSURE

1% extract in formulation was used in a 56-day double-blind, randomized split-face placebo-controlled trial carried out during the peak summer months on 25 female volunteers, aged 35-60, selected for expected daily intense solar exposure (beachgoing).

Measurements: Glycation status (AGE Reader[®]); Anti-inflammatory effect (Periflux[®] Doppler laser flowmetry with histamine stimulation, recording onset times and maxima of reaction); Red spots (VISIA-CA[®] cross-polarized image analysis); Wrinkling (AEVA-HE[®] 3D image analysis).

STATISTICS

Wilcoxon or two-way paired Student t-test (*p<0.05, **p<0.01, ***p<0.001). (Some SD bars were scaled for readability).

CONCLUSIONS

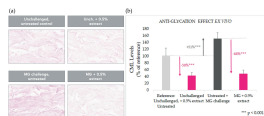
The *Haematococcus* extract was shown to strongly reduce glycation and inflammation in skin explants, inhibiting AGE formation; removing / detoxifying formed AGEs; and reducing RAGE signaling. In a clinical trial under intense solar exposure, the extract reduced glycation, strengthened skin resilience to irritation, and reduced skin redness and wrinkles. These results demonstrate the value of this extract as an active ingredient in cosmetic applications aimed at protecting the skin from damage and premature aging, including under intense solar exposure conditions.

REFERENCES

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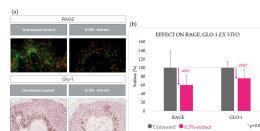
RESULTS

EX VIVO STUDY RESULTS

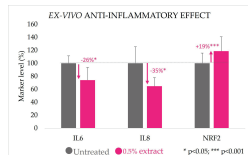


Clear anti-glycation effect, both in unchallenged and MG-challenged explants (most strongly in the latter).

Reduction of RAGE and Glo-1, corroborating a reduced glycation state.

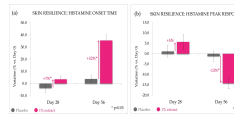
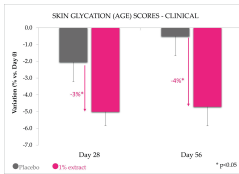


Anti-inflammatory effect: reduced IL6 and IL8, increased NRF2.

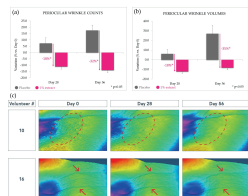
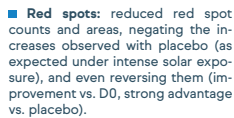


CLINICAL STUDY RESULTS (1% in formulation)

Anti-glycation effect: reduced glycation scores at D28 and D56 (*p < 0.05 vs. D0 and vs. placebo).



Resilience to histamine insult: strongly improved reaction onset time and peak response intensity at D56.



Anti-aging effect: strong reduction in wrinkle counts and volume. Here also, this negates the worsening in wrinkling observed with placebo (as expected under intense solar exposure), and reverses it (improvement vs. D0, strong advantage vs. placebo).