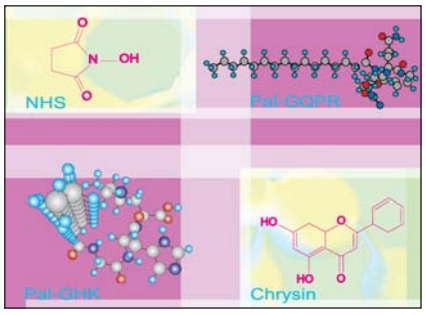
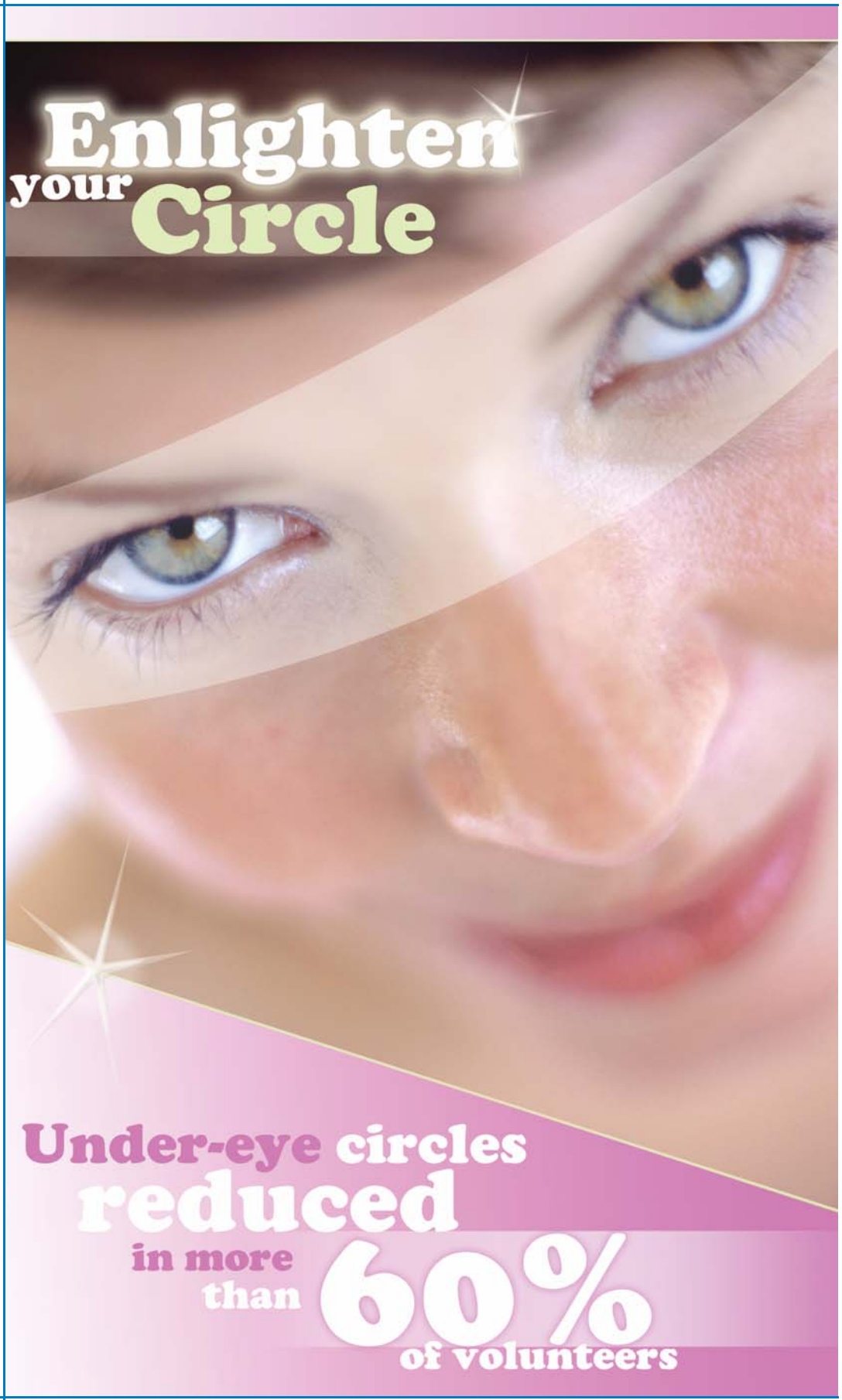
Patent N° WO 2005/102266

HALOXYL™



Composition of HALOXYL™



Function:
Lessens under eye dark circles.

Definition:
Association of 2 matrikines: Pal-GHK and Pal-GQPR with N-hydroxysuccinimide (NHS) and a flavonoid: chrysin.

Properties:
Pal-GHK and Pal-GQPR reinforce firmness and tone of the eye area. Chrysin and N-hydroxysuccinimide activate the elimination of blood originated pigments responsible for dark circle color and local inflammation.

Characteristics:
Infra-orbital shadows are due to the accumulation of hemoglobin and its colored degradation products (biliverdin, bilirubin and iron) in the dermis and epidermis. Chrysin stimulates the enzyme (UGT_1A_1) leading to the clearance of bilirubin. N-hydroxysuccinimide makes the iron soluble for elimination.

INCI name:
(Check CTFA on-line dictionary for latest INCI name)

Water (Aqua) – Glycerin – Steareth-20 – N-Hydroxysuccinimide – Chrysin – Palmitoyl Oligopeptide – Palmitoyl Tetrapeptide-7*

* former INCI name: Palmitoyl Tetrapeptide-3

Applications:
Dark-circle treatments, eye contour care, concealers.

Formulation:
Water soluble.
Incorporate at 45°C in emulsions or at room temperature in gels.

Recommended use level:
2%

In vitro tests

- **Ability of NHS to bind iron**

  The decrease of color demonstrates the iron complexation by N-hydroxysuccinimide.

- **Anti-inflammatory effect**

  Measurement of the decrease of PGE2 release by keratinocytes and fibroblasts after UVB irradiation, with HALOXYL™.

  HALOXYL™ demonstrates anti-inflammatory properties similar to those of aspirin.

- **Stimulation of expression of UGT**

  Cells in culture are incubated for 3 days with chrysin. The gene expression for UGT_1A_1 is determined by RT-PCR.

  Chrysin strongly stimulates the expression of the enzyme involved in the clearance of bilirubin (end product of hemoglobin degradation).

In vitro

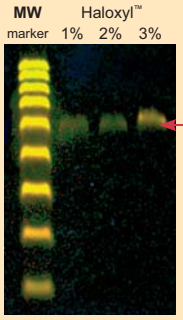
Iron complexation by NHS

N-hydroxysuccinimide binds iron to make it soluble for elimination

Increasing iron complexation by NHS

In vitro

Gene amplification



Product	Gene Amplification
Chrysin 7.8µM (eq. 2% Haloxyl™)	+247%
Chrysin 11.8 µM (eq. 3% Haloxyl™)	+600%

Clinical study: Anti-dark circle efficacy

22 female volunteers applied to the contour of one eye a gel containing 2% HALOXYL™ for 56 days against placebo on the other one. The anti-dark circle effect is assessed by image analysis and measurement of the color parameters (L,a,b system) by a specific software.

	Δa	Δb
Variation	-12.5%*	+10%**
Rate of volunteers with improvement	72%	63%
Variation for volunteers with improvement	**-19.5%**	**+19%**

*significant / T0 (p<0.01) **significant /T0 (p<0.05)

Red and blue colors of dark circles significantly decreased by 19%

Formulation

Anti-Dark Circle Gel with HALOXYL™

Tested formulation ref.: SED0308383 D1t

Part A	%
Deionized water	qs 100
Ultrez 10 *(Carbomer, Noveon)*	0.30
Part B	**%**
Glycerin	5.00
Preservatives	qs
Part C	**%**
Hydroxyethyl Cellulose	0.30
Part D	**%**
Pemulen TR2 *(Acrylates / C10-30 Alkyl Acrylate Crosspolymer, Noveon)*	0.20
Crodamol CAP *(Cetearyl Ethylhexanoate, Croda)*	6.00
Part E	**%**
Potassium sorbate	0.10
Part F	**%**
Deionized water	4.00
Sodium hydroxide 30%	0.46
Part G	**%**
Crillet 1 (Polysorbate 20, Croda)	0.50
Part H	**%**
HALOXYL™ (Sederma)	2.00

Protocol

Part A: Sprinkle Ultrez 10 in water and allow to swell for 15 minutes. Part B: heat the glycerin to 60°C, dissolve the preservatives. Cool to 40°C. Add Part C to Part B, homogenize, then add Part B+C to Part A with helix stirring. Allow to swell for 1 hour. Add Part D, then Part E to Part (A+B+C), homogenize. Neutralize with Part F. Let swell for 1 hour. Incorporate Part G, homogenize, then add Part H.

Non-warranty:
This formulation has been subjected to limited stability tests and has been shown to perform well. However formulators adopting this approach should ensure to their own satisfaction long term stability and functionality. It is good practice to conduct safety tests on all final formulations prior to marketing. Suggested uses should not be taken as an inducement to infringe any existing patents.

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