



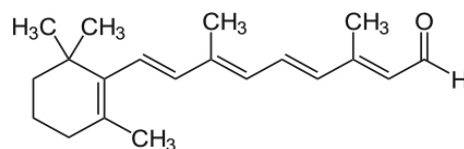
HYDROXYSOMES[®] RETINALDEHYDE

Next Generation Bioactives



LABORATORY SKIN CARE[®], INC. (LSC) has developed a novel method for co-engineering retinaldehyde (retinal) with its patented Hydroxysomes[®] Dermal Delivery Platform.

Retinaldehyde is a direct precursor to retinoic acid providing the same therapeutic benefits as retinoic acid while eliminating skin irritation. However, it is highly unstable in its pure form. Hydroxysomes[®] stabilizes retinaldehyde for use in topical formulations.



Retinoids are natural antioxidants, improving skin texture by enhancing its firmness and thickness.

Its natural metabolic pathway in the body is as follows:

Vitamin A —————> **Retinol** —————> **Retinaldehyde** —————> **Retinoic Acid (Rx)**

- Topical application of retinoic acid and retinol only delivers 2% of the retinoids into the skin¹
- The remaining retinoic acid / retinol pool remains on the skin causing irritation
- Retinaldehyde is 20x more potent than retinol, and it is not irritating

KEY ADVANTAGES OF HYDROXYSOMES[®] RETINALDEHYDE

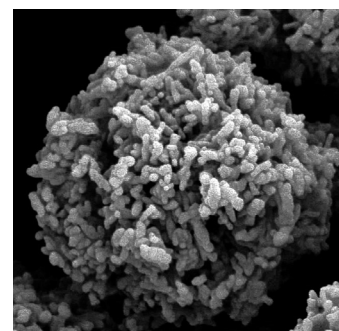
• RETINALDEHYDE AND CALCIUM DELIVERY	• HIGHLY STABLE	• SUSTAINED RELEASE
• STIMULATES COLLAGEN & ELASTIN SYNTHESIS	• NON-IRRITATING	• SKIN REJUVENATION

ADDITIONAL BENEFITS OF HYDROXYSOMES[®] RETINALDEHYDE

Hydroxysomes[®] Retinaldehyde also delivers calcium to the skin which enhances the effect of retinaldehyde. Delivering retinaldehyde and calcium simultaneously provides integrated anti-aging properties for younger looking skin.

ANTI-AGING EFFECTS OF CALCIUM

According to clinical study, calcium restores the skin's normal balance by repairing the barrier function and maintaining the barrier integrity of stratum corneum (SC). A healthy skin barrier improves firmness, cellular cohesion, and hydration, allowing skin's youthful appearance. Calcium plays a significant role in skin differentiation, which reduces the appearance of fine lines and wrinkles.



Hydroxysomes[®] Particle SEM 18,000x

References: 1. Saurat, J.H., Sorg, O., Dermatology 1999; 199(suppl 1):1-255(8):1129-41.

LABORATORY SKIN CARE[®], INC.

31019 HUNTWOOD AVE | HAYWARD, CA 94544 PHONE +1-650-373-0450 FAX +1-650-373-0455 WWW.LSCBIOACTIVES.COM

HYDROXYSOMES® RETINALDEHYDE DERMAL DELIVERY

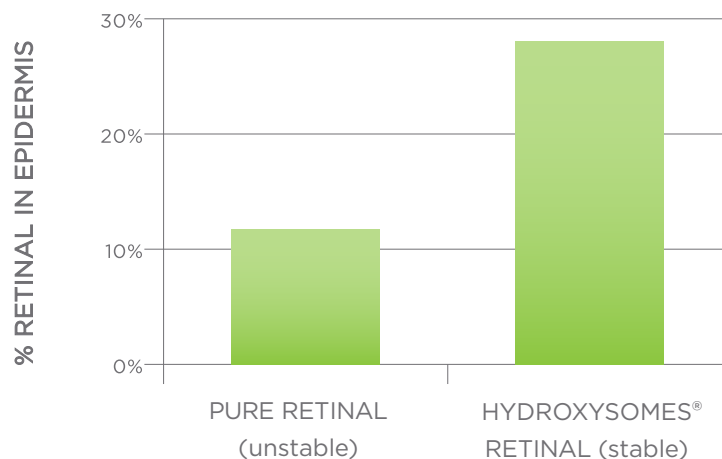
Hydroxysomes Retinaldehyde delivers stable retinaldehyde into the stratum corneum and epidermis. Notwithstanding the instability issue of retinaldehyde, more retinaldehyde penetrates the epidermis when delivered with Hydroxysomes than the standard control using retinaldehyde alone in the same formulation. The comparison was conducted with flow-through diffusion cells using human skin over a 24 hour treatment period (Figure 1). Additionally, some retinaldehyde was observed in the dermis from the Hydroxysomes Retinaldehyde formulation, but no retinaldehyde was observed in the dermis from the same formulation with retinaldehyde.

Fig. 1

Tissue: Human skin

Vehicle: Topical Formulation

Analysis: HPLC



FORMULATION STABILITY:

Several formulations with Hydroxysomes® Retinaldehyde were stable at room temperature for 24 months, and at 40° C for three months, and at 50° C for one month. No change in bioactivity, pH, color, appearance, or viscosity was observed. Retinaldehyde active assay confirmed % activity as per specifications on C of A.

PRODUCT SPECIFICATIONS

INCI NAME:	HYDROXYAPATITE, RETINAL
ACTIVE LOAD:	15 ± 3.0% RETINALDEHYDE
APPEARANCE:	POWDER
COLOR:	LIGHT YELLOW
ODOR:	ODORLESS
AVERAGE PARTICLE SIZE:	< 10 µm
STORAGE CONDITIONS:	ROOM TEMPERATURE (AVOID LIGHT AND HUMIDITY)
SHELF LIFE:	24 MONTHS
SOLUBILITY / COMPATIBILITY:	FREELY DISPERSIBLE IN ALL TYPES OF WATER AND OIL-BASED COSMETIC FORMULATIONS
RECOMMENDED USAGE:	0.07 - 0.7% HYDROXYSOMES RETINALDEHYDE (0.01 - 0.1% RETINAL)
FORMULATION GUIDELINES:	ADD BELOW 40°C AT pH ≥ 5.5
PACKAGE SIZE:	1 Kg
CATALOG NUMBER:	200130



CONFIDENTIAL: Property of
Laboratory Skin Care[®], Inc.
Do not duplicate, distribute or otherwise
use for any purpose other than review
without written permission of LSC, Inc.

Hydroxysomes[®] Retinaldehyde Stability Report

Outline:

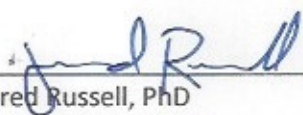
Detection Method

Extraction of Retinaldehyde from Hydroxysomes Retinaldehyde

Stability of Hydroxysomes Retinaldehyde raw material

Stability of Hydroxysomes Retinaldehyde in LSC base formulation

Signature


Jared Russell, PhD
Senior Manager, Bioanalytical Chemistry Lab

Date

29NOV22

1. HPLC Detection Method

Retinaldehyde was dissolved in 200 proof ethanol to prepare a 0.5 mg/mL solution. 2 μ L of Retinaldehyde solution was analyzed with reverse-phase HPLC.

Phenomenex Gemini™ C18 column (Cat. No. 00B-4439-E0, 4.6 \times 50 mm, 3 μ m) was used to achieve sample separation on a Shimadzu 20A system. Column temperature was kept at 40°C. The mobile phase was mixed with (A) acetonitrile and (B) methanol. The separation was conducted by 6.5 min isocratic run of solvent B at 5% at a flow rate of 0.5 mL/min. The eluent was monitored at 368 nm. Retinaldehyde was identified as a main peak eluted around 2.5 minutes. The quantification of Retinaldehyde in the sample was achieved by external standard calibration.

2. Extracting Retinaldehyde from Hydroxysomes Retinaldehyde

Retinaldehyde was co-engineered with Hydroxysomes through a proprietary procedure.

- 12 mg of Hydroxysomes Retinaldehyde was weighed in a 15 mL centrifuge tube.
- The test sample was suspended in 5 mL of 200 proof ethanol, and vortexed for 1 minute, shaken at 200 rpm for 5 minutes on the platform shaker.
- 2 mL of the mixture was centrifuged at 14,000 rpm for 5 minutes, and 2 μ L of supernatant was injected for HPLC analysis.

Results

HPLC chromatogram of Retinaldehyde extracted from Hydroxysomes Retinaldehyde matched that of the standard (Fig. 1A and 1B).

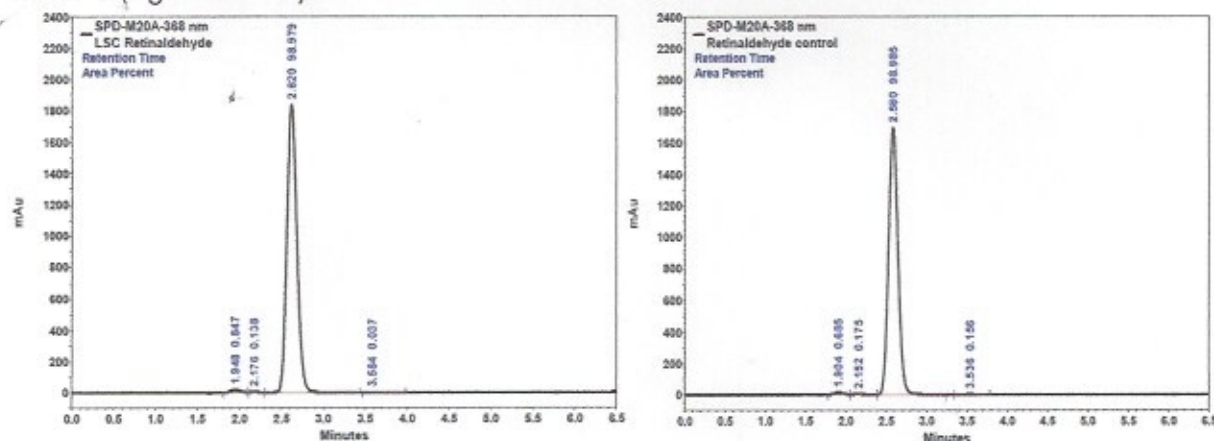


Figure 1.

(A) Retinaldehyde control*

(B) Retinaldehyde extracted from Hydroxysomes Retinaldehyde

* Retinaldehyde was purchased from Sigma (> 98% purity), to use as the control standard.

3. Product Stability of Hydroxysomes Retinaldehyde

Samples of Hydroxysomes Retinaldehyde (0.2 g each in sealed 20 mL glass vial) were stored at room temperature for 12-month stability. Accelerated stability tests were done at 40°C for 3 months and at 50°C for 1 month. After incubation, Retinaldehyde was extracted and analyzed by HPLC (See Extracting Retinaldehyde from Hydroxysomes Retinaldehyde described above).

Results

Hydroxysomes Retinaldehyde is stable at room temperature for up to 12 months, at 40°C for 3 months and at 50°C for 1 month. The results for 50°C for 1 month are displayed below; Hydroxysomes Retinaldehyde retention time and peak absorbance wavelength, matched that of the standard (Fig. 2A and 2B).

Hydroxysomes Retinaldehyde peak area was quantified by calibration curve and the amount of Retinaldehyde at 50°C for 1 month was calculated to be 96.4% of the initial concentration.

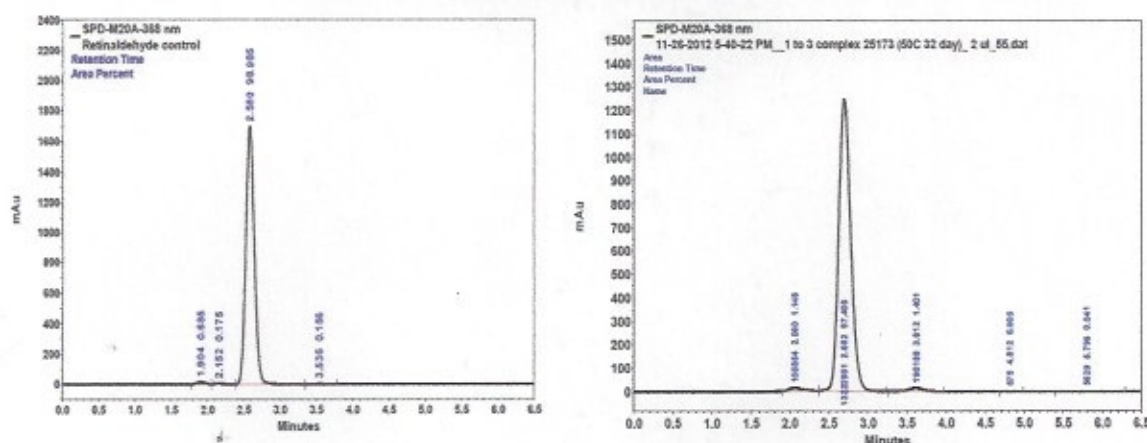


Figure 2.

(A) Retinaldehyde control*

(B) Retinaldehyde extracted from Hydroxysomes Retinaldehyde stored at 50°C for 1 month

* Retinaldehyde was purchased from Sigma (> 98% purity), to use as the control standard.

4. Stability of Hydroxysomes Retinaldehyde in Formulation

Chemical stability of the 0.5% Hydroxysomes Retinaldehyde in LSC base cream at room temperature, at 40°C for 3 months and at 50°C for 1 month was performed in the following base formulation.

Raw Material	INCI Name	% w/w
D.I Water	Water	85.187%
Vanzan NF	Xanthan Gum	0.300%
Glycerin	Glycerin	1.000%
Liponate GC	Caprylic/Capric Triglyceride	3.000%
Stearyl Alcohol	Stearyl Alcohol	2.000%
Cetyl Alcohol	Cetyl Alcohol	2.000%
Lipomulse 165	Glyceryl Stearate & PEG-100 Stearate	1.000%
Botanisil CP -33	Cyclopentasiloxane	3.000%
Sepiplus 400	Polyacrylate-13 & Polyisobutene & Polysorbate 20	1.000%
Euxyl PE 9010	Phenoxyethanol & Ethylhexylglycerin	1.000%
TEA	Triethanolamine	0.013%
Hydroxysomes Retinaldehyde	Hydroxyapatite, Retinaldehyde	0.500%
Total		100.000%

Extraction of Retinaldehyde from Base Cream

50 mg of the Hydroxysomes Retinaldehyde cream was added to 1 mL of 200 proof ethanol, vortexed for 1 minute, and shaken for 5 minutes at 200 rpm on a platform shaker. The mixture was centrifuge at 14,000 rpm for 5 minutes; 5 µL of supernatant was injected for HPLC analysis.

Results

Results are shown below (Fig. 3A and 3B).

HPLC chromatogram of Retinaldehyde extracted from Hydroxysomes Retinaldehyde in base cream stored at 50°C for 1 month matched that of the standard, and it was quantitated to be 97.87% of the initial concentration.

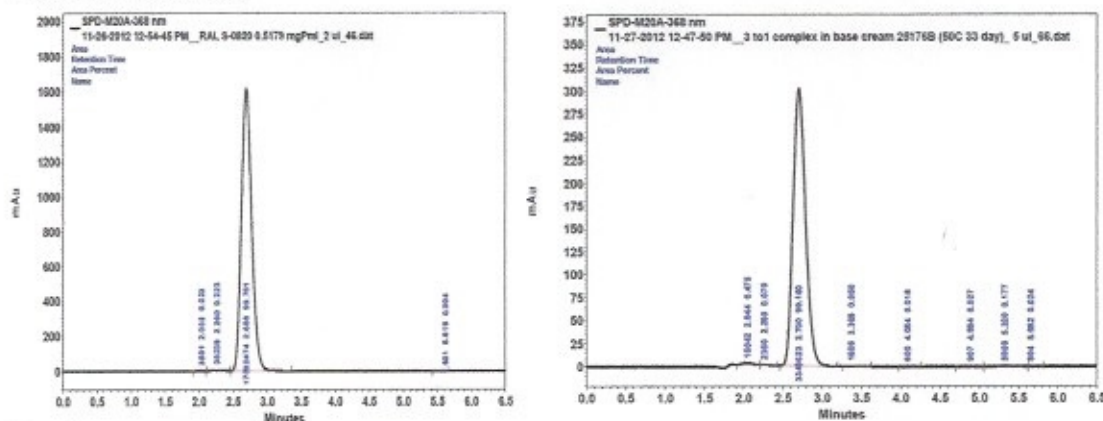


Figure 3.

(A) Retinaldehyde control*

(B) Retinaldehyde extracted from Hydroxysomes Retinaldehyde in base cream at 50°C for 1 month

* Retinaldehyde was purchased from Sigma (> 98% purity), to use as the control standard.