

# Encapsulated retinol unlocks a youthful, radiant glow with long-lasting anti-aging results, minus the irritation!

MultiSal® Retinol, developed by Salvona Technologies, revolutionizes anti-aging skincare with its cutting-edge encapsulation technology.

Unleash the skin's youthful radiance with MultiSal® Retinol! Its breakthrough double-encapsulation technology delivers gentle, long-lasting anti-aging brilliance—smoothing wrinkles, firming skin, and glowing bright, even for sensitive skin.

#### Here are the unique points that set it apart:

• Double-Layered Stability MultiSal® Retinol's dual-encapsulation locks in Retinol to protect it from degradation, leaving a fresh product for longer.

• Gentle Slow Release

The slower release of retinol minimizes side effects, making it a dream for sensitive skin while delivering long-lasting wrinkle reduction and a radiant complexion.

Superior Skin-adherent

The tiny spheres adhere to the skin for a long-lasting retinol release, unlike free Retinol, which is exposed immediately. This skin-adherent property results in a longer-lasting release that smooths lines and firms skin all day.

• Low Dose, High Impact Less is more! Just 0.1–0.2% reduces fine lines in two weeks, gently delivering potent results.

• Versatile Formulation Shine in any product! Free-flowing microspheres blend effortlessly into creams, lotions, or makeup for flawless skincare.



Figure 1: Model of MultiSal Retinol

**Hero Claim**: "Transform your skin in 4 weeks with our 1% MultiSal Retinol lotion—visibly smoother, brighter, and more even-toned."

- Anti-Aging: "Reduces the appearance of fine lines and crow's feet by up to 206% for a youthful look."
- Texture: "Delivers up to 40% smoother skin with refined texture in just 4 weeks."
- Brightness: "Boosts radiance by up to 60% for a luminous complexion."
- Dark Spots: "Fades dark spots by up to 76% for a more uniform tone."
- Time-Release: "Advanced time-release technology ensures long-lasting antiaging benefits."
- Gentle: "Gentle, non-irritating formula for daily use, powered by encapsulated retinol."





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#### **Retinol**

Retinol, a derivative of vitamin A, is a powerhouse anti-aging ingredient that promotes skin renewal, reduces wrinkles, improves skin texture, and evens skin tone. It addresses multiple concerns, including fine lines, hyperpigmentation, acne, and loss of firmness, delivering a smoother, more youthful complexion.

#### Major Challenge in Formulating Retinol

The primary challenge in formulating retinol is its instability. It is highly susceptible to degradation from light, air, heat, and pH variations, which reduces its potency and shelf life. This instability can lead to inconsistent efficacy, potential irritation from degraded byproducts, and difficulties maintaining stable formulations, especially in water-based or low-pH products.

#### How MultiSal® Retinol Addresses This:

Its double-layered encapsulation (sub-micron spheres within microspheres) protects retinol, retaining 80% potency after 50 days at 42°C (vs. 5% for free retinol), ensuring stability, gentle delivery, and compatibility with various formulations.

#### **How Retinol Works:**

Retinol penetrates the skin and accelerates cellular processes to rejuvenate and repair.

- Stimulates Cell Turnover:
  Retinol penetrates the epidermis and binds to retinoid receptors in skin cells.
  It accelerates the shedding of dead skin cells and promotes the production of new cells, resulting in smoother, brighter skin and reduced clogged pores.
- Boosts Collagen and Elastin Production: In the dermis, retinol stimulates fibroblasts to produce collagen and elastin, proteins that maintain skin's firmness and elasticity. This reduces the appearance of fine lines and wrinkles and improves skin structure over time.
- Reduces Hyperpigmentation: Retinol inhibits melanin production and promotes even cell turnover, fading dark spots, sun damage, and uneven skin tone for a radiant glow.
- Improves Acne and Pore Appearance: By unclogging pores and reducing sebum production, retinol helps clear acne and minimizes the appearance of enlarged pores.
- Antioxidant Properties: Retinol neutralizes free radicals, protecting skin from environmental damage and slowing premature aging.





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#### The color of Retinol as a marker:

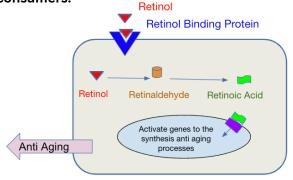
Retinol, a vitamin A derivative, exhibits a yellow-to-orange hue due to its chemical structure, specifically the conjugated double bond.

Natural Pigmentation: As a fat-soluble retinoid, retinol's molecular configuration is similar to carotenoids (e.g., beta-carotene), imparting yellow-orange hues due to similar conjugated systems.

The intensity of the yellow color can vary based on concentration, formulation, and processing, but it is an inherent property of pure retinol and its derivatives (e.g., retinal retinoic acid).

### • Color Change:

As retinol degrades, the yellow color may fade or shift to a darker, brownish hue due to oxidation and the formation of colored byproducts. This visual change signals reduced potency and can affect product aesthetics, making it less appealing to consumers.



**Figure 2:** The pathway of Retinol to the cell nucleus.

#### How MultiSal® Retinol Fights Aging:

- Speeds Cell Turnover: Boost new cell growth, smoothing fine lines and dullness.
- Boosts Collagen & Elastin: Enhances fibroblast activity and blocks collagendegrading enzymes, reducing wrinkles and sagging.
- Fades Hyperpigmentation: Inhibits melanin and accelerates turnover, evening out dark spots and tone.
- Strengthens Skin Barrier: Thickens epidermis and boosts hydration, combating dryness.
- Antioxidant Protection: Neutralizes free radicals, preventing aging damage.

### Pathway of Retinol to the Cell Nucleus

Retinol reaches the cell nucleus to modulate gene expression via these steps (figure. ):

- Penetration: Lipophilic retinol penetrates the skin's stratum corneum, reaching the epidermis and dermis.
- Cellular Uptake: Diffuses into keratinocytes and fibroblasts via the cell membrane.
- Conversion: Transforms into retinoic acid (active form) via enzymatic steps (retinol → retinal → retinoic acid).
- Transport: Retinoic acid binds to CRABPs, shuttling it to the nucleus.
- Nuclear Action: Binds to RAR/RXR receptors on DNA, activating genes for cell turnover, collagen/elastin synthesis, pigmentation reduction, and collagen protection.





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#### THE TECHNOLOGY

MultiSal® technology is a double-layered encapsulation. The retinol is first contained within sub-micron spheres and re-encapsulated within larger microspheres. The double layers are essential for the finished product's long shelf life and stability.

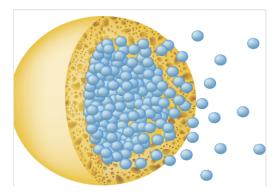


Figure 3: MultiSal® Retinol is a microsphere technology in which the Retinol is encapsulated first in submicron lipid spheres, and then the spheres are re-encapsulated into microspheres.

#### **Double-Layered Structure:**

Inner Sub-Micron Spheres (~0.1–1 µm): Retinol is encapsulated in a lipid matrix, providing the first layer of protection and controlled diffusion. Outer Microspheres (~10-50 µm): These encase multiple sub-micron spheres, forming a secondary barrier that further slows retinol release.

Figure 4: Appearance of MultiSal® Retinol as a fine powder.





Figure 5: A, Encapsulated retinol is characterized by a yellow color; B, aged and oxidinzed Retinol,

#### How MultiSal® Retinol Mitigates Degradation

- MultiSal® Retinol's double-layered encapsulation (sub-micron spheres within microspheres) addresses these issues by:
- Protecting Against Degradation: This product shields retinol from light, air, and heat.
- Minimizing Irritation: Controlled, slowrelease reduces exposure to potentially irritating byproducts.
- Maintaining Aesthetics: This prevents color shifts or formulation instability, ensuring a clear, stable product with a consistent yellow tint (if visible).

MultiSal® Retinol utilizes BHT-free Retinol, and it is available as a free-flowing powder, The powder, MultiSal® Retinol, is soft on the skin and can be formulated in most emulsions and water-based product forms.



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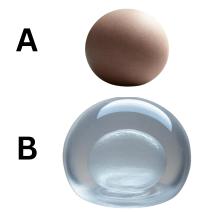
# Mechanism of MultiSal® Retinol Release and Delivery

Microspheres Swelling & Rupture: Outer microspheres (~10–50  $\mu$ m) swell in water (e.g., lotion base) and rupture when rubbed into the skin, releasing sub-micron spheres (~0.1–1  $\mu$ m) with retinol.

Sub-Micron Sphere Adhesion: These spheres adhere to the skin via hydrophobic interactions with the lipid-rich stratum corneum, ensuring prolonged contact.

Deep-Layer Release: Spheres dissolve in the skin's lipid layers, gradually releasing retinol into the epidermis and dermis, where it converts to retinoic acid, activating genes for collagen, cell turnover, and pigmentation reduction.





**Figure 6:** Illustration of MultiSal A, dry phase and B when swollen with empty core



**Figure 7:** Illustration of MultiSal® Retinol on the skin surface before penetration. The Core with infused Retinol is in red.



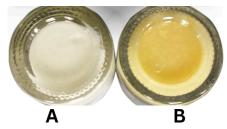
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### In-Vitro qualifications

### **Extended Shelf life, Stability**

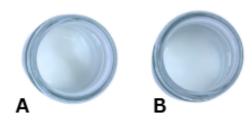
#### Stability of MultiSal® Retinol as a Raw Material

We evaluated the physical integrity and properties under controlled conditions. The aim is to ensure no changes in appearance, color, or odor.



**Figure 8:** MultiSal® Retinol containing 10% Retinol: A, fresh sample and B, 12-months aged at accelerated stability (42 C for 3 months), shows a distinctive yellow color.

# Stability of MultiSal® Retinol as a serum base at 0.1%

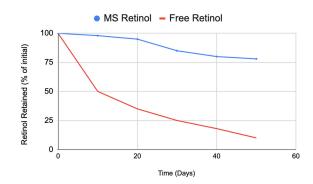


**Figure 9:** MultiSal® Retinol at 1% wt in a serum base after 1 month at 42 °C shows no color change.

#### Analytical Method, (HPLC-UV)

The gold standard for quantifying retinol content and detecting degradation products. A validated method (e.g., C18 column, methanol-acetonitrile mobile phase, UV detection at 324 nm) was used to measure retinol concentration.

The stability of MultiSal® Retinol (0.1% retinol) was compared to free retinol in lotions (Figure 3). After 50 days at 42°C, HPLC analysis revealed that the encapsulation technology facilitated retention of 80% of the retinol while the free only retained 5% of initial retinol.



**Figure 10**: Amount of retinol retained in lotions containing MultiSal® Retinol technology versus the free.

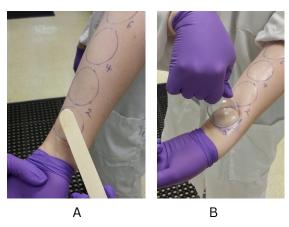


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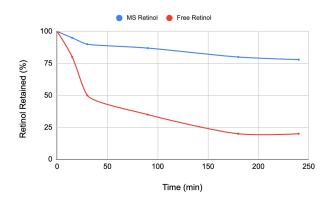
### **Controlled Release, Skin Retaintion**

We used alcohol skin extraction to quantify the amount of retinol that remains in or on the skin after topical application. This approach is commonly used to assess the penetration, deposition, and stability of retinol in skin layers.

- The test was done on the forearm of volunteers (n=4). Apply 2 mg/cm² to the skin, 4 cm² skin area, for 4 hours.
- With the glass cup, 3 ML methanol to extract the skin for 2 min.
- Sample sonicated 5 min at 32 °C, centrifuged (10K rpm, 10 min, 25°C).
- Analyze by HPLC-UV:
- Column: C18, mobile phase: methanol: acetonitrile (70:30), 0.1% trifluoroacetic acid (TFA), flow: 1 mL/min, detection: 324 nm.



**Figure 11:** A, sample loading on the skin, B, Skin extraction



**Figure 12:** Retinol Retained in the skin. Analysis of Methanol extraction and analysis.

Data highlights MultiSal Retinol's superior skin retention (80% vs. <25% for free retinol at 4 hours), strongly indicating a time-release mechanism due to encapsulation. This enhances its potential for sustained efficacy and reduced irritation in cosmetic applications.

MultiSal® Retinol maintained a stable lotion at accelerated stability conditions.

After 18 months, the emulsion shows a minimal color shift. It contained 0.1% Retinol or 1% MultiSal® Retinol.



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### Clinical Evaluation

The study compared the in vivo efficacy of 2 cosmetic products (s):

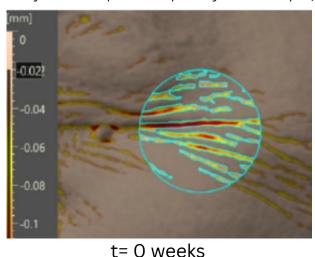
1.MultiSal® Retinol, 1% in a cream base, and 2. Cream base

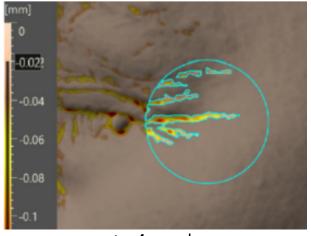
Subjects: 12 healthy Asian skin type female subjects, 57 - 65 years. Apply on LEFT or RIGHT half-face after facial cleansing, then gently massage until the product completely absorbs into the skin, twice daily in the morning and in the evening.

The evaluation is performed using an Antera 3D camera to analyze skin color (whitening effect) of normal skin, skin texture, and crow's feet wrinkles.

### **Crow's Feet Wrinkles**

Crow's feet wrinkles are commonly measured using non-invasive imaging (Antera 3D® Camera) and analysis techniques that quantify wrinkle depth, area, volume, and count.





t= 4 weeks

Figure 13: Direct images of panelist taken at initial time and after 4 weeks by a third party,

The Antera 3D data shows significant roughness reduction after 4 weeks with 1% MultiSal® Retinol lotion, confirming MultiSal's time-release mechanism enhances efficacy.





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## **Data Analysis**

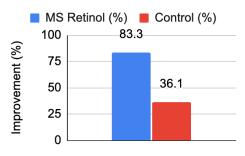


Figure 14: Effect on Wrinkels Lenght

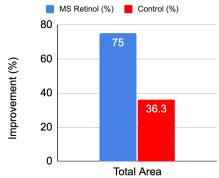


Figure 15: Effect on Total Area

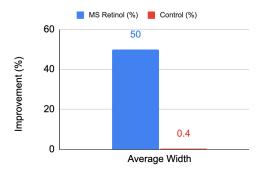


Figure 16: Effect on Average width

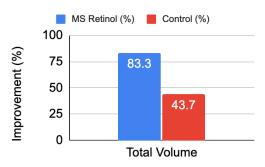


Figure 17: Effect on Total Volume

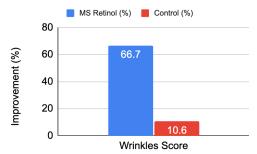


Figure 18: Effect on Wrinkles Score

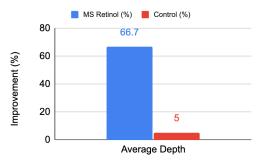


Figure 19: Effect on Average Depth



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### **Summary of Clinical Evaluation**

	MultiSal® Retinol	Control	Relative improvement (%)
Length	83.3	36.1	230.75
Total Area	75	36.3	206.61
Average Width	50	0.4	12500
Average Depth	66.7	5	1334
Total Volume	83.3	43.7	190.62
Score	66.7	10.6	629.25

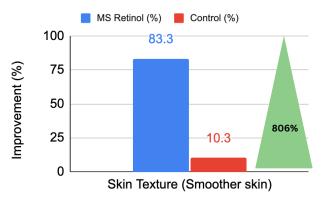
Figure 20: Summary of Crows' feet analysis

The data indicating significant improvements in crow's feet metrics—average width (12,500%), score (629%), length (230%), and total area (206%)—after 4 weeks of using a lotion with 1% MultiSal® Retinol, as measured and analyzed by Antera 3D imaging, is remarkable. Combined with previous findings on MultiSal® Retinol's high skin retention (~80% after 4 hours, indicating time-release) and reduced skin roughness, this suggests that MultiSal® Retinol effectively targets fine lines and wrinkles, likely due to its retained power and sustained delivery.

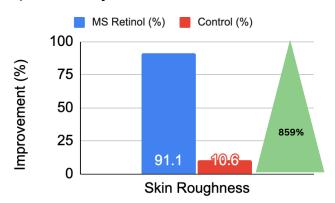


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#### **Skin Texture**



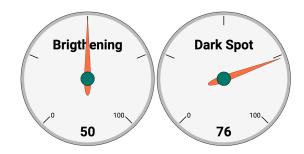
**Figure 21:** Effect on Skin Texture, relative improvement by 806%



**Figure 22:** Effect on Skin Roughness, relative improvement by 859%

Consumer Impact: Smoother, less rough skin enhances perceived youthfulness, supporting strong anti-aging claims.

### **Skin Brightening**



**Figure 23:** 50% Improvement in regular skin brightening (L\* Parameter), which is related to the skin whitening effect, and 76% showed improvement in reducing dark spots.

Practical Significance: The improvements indicate MultiSal® Retinol significantly enhances skin smoothness and reduces roughness, it aligns with crow's feet reductions (206–629% for area, length, and score). This reflects effective epidermal turnover and collagen synthesis, driven by high retention (80% at 4 hours).



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### **Skin Testing**

Another study was done with female volunteers (n=5) aged 25-35 who showed the effect of a lotion containing Retinol.



**Figure 24:** A consumer study evaluated the effect of Retinol (0.2%) from MultiSal® Retinol or Free (control) Retinol. The lotion was applied to "crow's feet," fine lines around the eye, for two weeks daily at night.

Safety: No side effects or redness irritation were observed, and RIPT backed up data. The control group used free Retinol: After seven days of application, 60% of the panelists reported slight burning and irritation.



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#### **Technical Data**

**Key INCI:** Retinol (BHT Free\*),

**Other:** Caprylic/Capric Triglyceride, PPG-3 Benzyl Ether Myristate, PEI-10, Silica, Tocopherol, Pentaerythrityl Tetra-di-t-butyl Hydroxyhydrocinnamate

\*BHT Free: Salvona offers a version without BHT, which is on California's Proposition 65 list

Dosage: Powered by 10% pure retinol, equivanlet to 330,000 IU per gram

### **Specification**

Appearance @20°C	Free flowing powder	
Applications	Lotions, creams, lip care, body powders, and make up	
Color	Off-white to light yellow	
Odor	Characteristic	
Shelf Life (months)	9.5 ± 1.5	
Usage Level (wt%)	1-2	
Storage (°C)	Closed container at 12-32° with <45% RH	

### Formulation strategies:

We saw success by formulating the MultiSal® Retinol into the oil phase and then adding the oil phase into the water phase. The alternative approach is to progress with the formula, bring it to 20 °C (room temperature), and then add the MultiSal® Retinol with the preservative of choice.

#### **Example formula**

Formulation of an accelerated recovery cream (6415-01)

Phase	INCI	(W/W%)
A1	Aqua	83.70
A2	Niacinamide	1.00
A3	Xantham gum	0.30
A3	Glycerin	2.00
A4	Sodium Carbomer	1.50
B1	Argania Spinsosa (Argan) Oil	1.00
B2	Squalane	2.00
В3	Phenoxyethanol, Ethylhexylglycerin	1.00
В3	Isododecane	2.00
B5	MS RT	1.50
C1	Sodium Acrylate/Sodum Acryloyldimethyl Taurate Copolymer & Isohexadecane & Polysorbate 80	1.50
D1	SS NAA	2.50
	Total	100

Figure: An anti-aging formula with Niacinamide and MultiSal® Retinol (1.5%) and SalSphere® Natural Antiaging (SS NAA, for skin firming).





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### **Additional References**

Claim	Source
Reduce skin hyperpigmentation, unevenness, and wrinkles. Enhance skin tone, skin elasticity, and moisture	A Clinical Anti-Ageing Comparative Study of 0.3 and 0.5% Retinol Serums: A Clinically Controlled Trial, Zasada M.a · Budzisz E.a · Erkiert-Polguj A.b", Skin Pharmacol Physiol 2020;33:102–116
Moderate skin irritation symptoms observed with 0.5% Retinol.	A Clinical Anti-Ageing Comparative Study of 0.3 and 0.5% Retinol Serums: A Clinically Controlled Trial, Zasada M.a · Budzisz E.a · Erkiert-Polguj A.b", Skin Pharmacol Physiol 2020;33:102–116
Topical retinol improves fine wrinkles associated with natural aging. Significant induction of glycosaminoglycan, which is known to retain substantial water, and increased collagen production are most likely responsible for wrinkle effacement. With greater skin matrix synthesis, retinol-treated aged skin is more likely to withstand skin injury and ulcer formation along with improved appearance.	Improvement of Naturally Aged Skin With Vitamin A (Retinol), Reza Kafi, MD; Heh Shin R. Kwak, MD; Wendy E. Schumacher, Arch Dermatol. 2007;143(5):606-612. doi:10.1001/archderm.143.5.606
Long-Lasting Anti-Aging Benefits of a Cream Containing Retinol	A Placebo-Controlled Study Demonstrates the Long-Lasting Anti-Aging Benefits of a Cream Containing Retinol, DihydroxyMethylChromone (DMC) and Hyaluronic Acid, Oddos Thierry and Romain Roure, Journal of Cosmetics, Dermatological Sciences and Applications 02(02),DOI:10.4236/jcdsa.2012.22012





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# BHT (butylated hydroxytoluene)-free (a synthetic antioxidant commonly used in cosmetics)

### It's a safer product.

#### Health Concerns

- Potential Hormonal Disruption: Some studies suggest that BHT may act as an endocrine disruptor, which could interfere with hormone function in the body. This raises concerns about its long-term effects, particularly with chronic exposure.
- Allergic Reactions: BHT may cause skin irritation or allergic reactions in some individuals, especially those with sensitive skin.
- Cancer Risks: There is ongoing debate and limited evidence regarding BHT's potential to promote cancer. While it is safe at low levels, high doses in animal studies have raised concerns.

#### **Environmental Impact**

- Persistence in the Environment: BHT is not readily biodegradable, so it can accumulate in the environment and potentially harm wildlife and ecosystems.
- Marine Pollution: BHT can enter waterways through products like sunscreens and cosmetics, contributing to marine pollution.

