

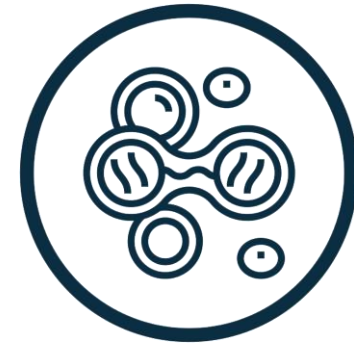


# AC ExoCalm

BioAuthentic Exosome

INCI: Water & Glycyrrhiza Glabra (Licorice) Root Extract & Phospholipids

# Evolving Modern Incarnations Of Cosmetic Delivery



Delivery systems offer a vesicle for active delivery, allowing formulators to customize their products, and ensure an increased uptake of benefits.

In the realm of cosmetic delivery systems, formulators in the personal care industry have traditionally used *liposomes* as a vesicle for active delivery.

While Active Concepts already capitalizes on the benefits of delivery systems, is there a way to *revolutionize* traditional methods?

If there was a way to do so, **why do we care?**



# From Pharma to Cosmetics



In our pursuit of innovation, Active Concepts set our sights on the pharmaceutical industry, drawing inspiration from **precision and efficacy-driven results**.

Recognizing the sophisticated methods employed in pharmaceuticals to **enhance the absorption and targeted delivery** of active ingredients, we sought to adapt similar principles into our ingredients.

We aimed to adopt exosomes into our skincare portfolio, aspiring to **elevate the performance** of our cosmetic products with the same commitment to excellence the pharmaceutical industry is so well-known for.

Our upcoming launch combines a harmonious blend of **cosmetic allure and pharmaceutical precision**, displaying our dedication to pushing the boundaries of beauty and skincare through scientific innovation.

# Breaking Conventional Practices

Our research led to *exosomes* which are extracellular vesicles that are shed by most cells in response to intracellular and extracellular stimuli and have been **proven to serve as therapeutic and diagnostic applications.**

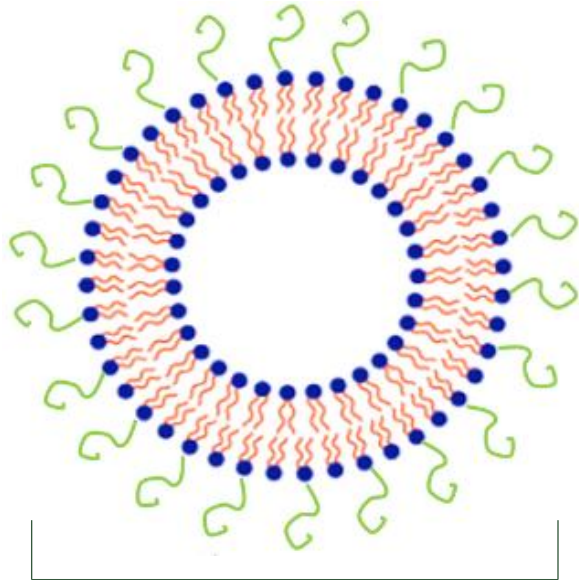
Exosomes are capable of **increasing cell-to-cell contact** and intracellular communication, therefore **increasing the efficiency** of which actives and ingredients can be delivered to intended cells.

Currently, exosomes are mainly being used in modern medical treatments for the repair and regeneration of skin tissue and are **derived from human or animal stem cells.**



# Liposomes vs. Exosomes: What Sets These Delivery Systems Apart?

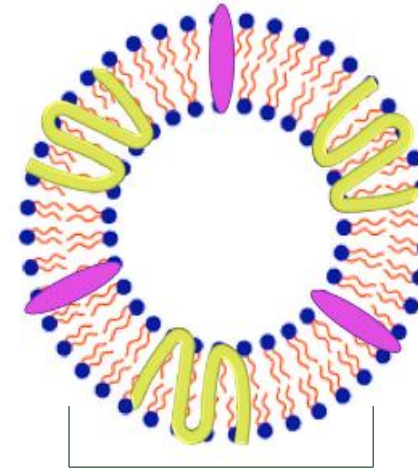
## Liposomes



50 - 450 nm

- ✓ Phospholipid bilayer
- ✓ Can be loaded with lipophilic & hydrophilic actives
- ✓ Traditionally artificial

## Exosomes



40 - 100 nm

- ✓ Phospholipid bilayer
- ✓ Can be loaded with lipophilic & hydrophilic actives
- ✓ Natural
- ✓ Membrane Proteins
- ✓ Smaller Particle Size

# Green Chemistry Practices



## Active Concepts' Renowned Commitment

As a company, we pride ourselves on **sustainable and eco-friendly practices**, so when our research led us to exosomes, we did not want to derive them from animal or human stem cells.

Additionally, exosomes on the market are only being **targeted one way**: skin tissue regeneration.

## *What if...*

We created all natural vesicles that are biomimetic to exosomes, but  
derived from botanicals

*and*

targeted each vesicle for a **specific benefit?**

# Introducing BioAuthentic Exosomes

We are experts in green chemistry, and, therefore, have added to our **Delivery System** technology platform by looking at how **nature does delivery**. Active Concepts releases **BioAuthentic Exosomes** – all-natural vesicles that are functionally identical to exosomes, extracted from **natural sources**, and target **specific benefits**.

By encapsulating actives held together with protein boats for **increased stabilization**, these natural delivery systems ensure increased activity of personal care benefits.

*Evolving Technology • Sustainable Practices • Brand Differentiation • Targeted & Enhanced Benefits*



# Leading the Future of Skincare Innovation

Since the initial release of our BioAuthentic Exosomes in 2023, market interest in exosome delivery systems has continued to increase. As the **trailblazers who introduced exosomes** to the cosmetic space, we continue to stay ahead of the curve, **constantly evolving** our products to align with the latest consumer trends and innovations.

According to Market Watch, the **global skincare exosomes** market size was valued at US \$256 million in 2023 and is expected to grow at a CAGR of 9.6% from 2024 to 2030.



# AC ExoCalm

INCI: Water & Glycyrrhiza Glabra (Licorice)  
Root Extract & Phospholipids



## Inhibit Inflammation

Skin inflammation is a common issue for a wide range of consumers that can cause red spots, blotchiness, and a reduction in confidence. Introducing AC ExoCalm: a BioAuthentic Exosomal delivery system that is specifically designed to provide potent anti-inflammatory benefits.

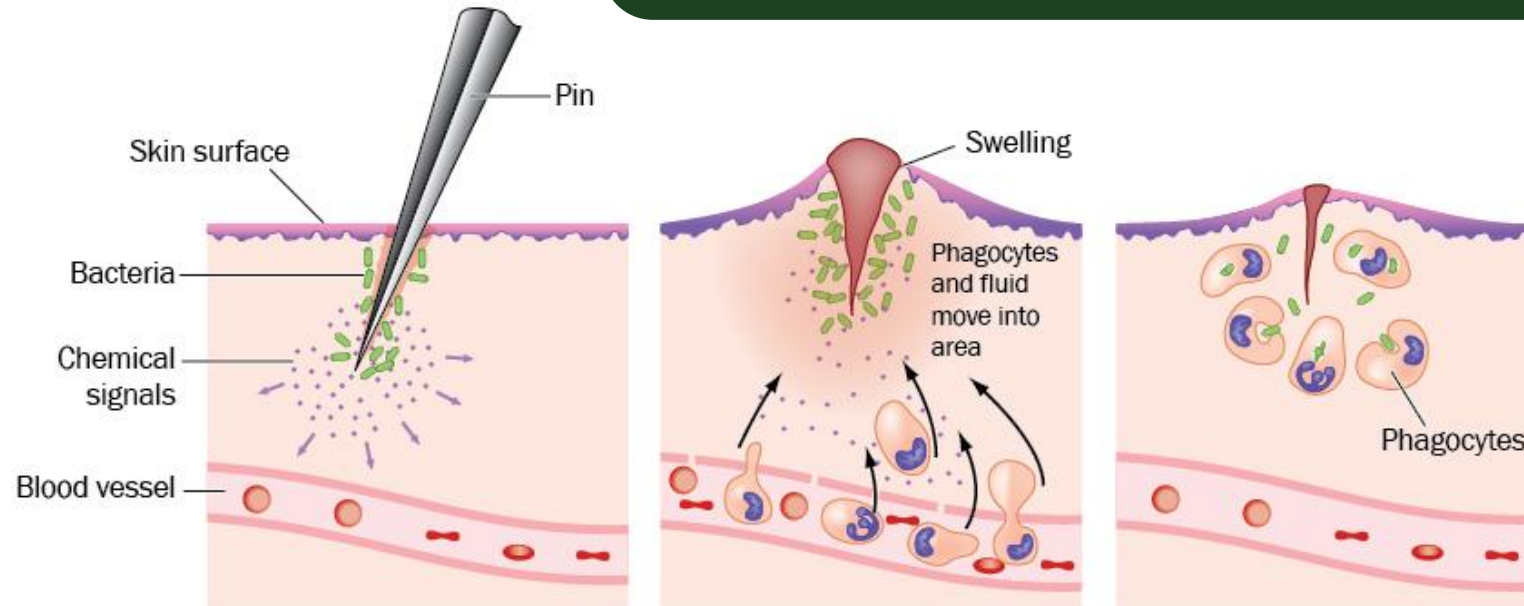
AC ExoCalm utilizes upcycled licorice root extract, grown on a farm in Italy, to capitalize on licorice's ability to decrease inflammation and provide antioxidant benefits.

This ingredient delivers soothing properties that can calm the skin more effectively by making the actives more bioavailable.

*anti-inflammation | upcycled licorice | calm the skin*

# Skin Inflammation

*Skin inflammation* occurs when the body's immune response is triggered by various factors such as injury, infection, or irritation. This process involves the release of inflammatory mediators like cytokines, which attract immune cells to the affected area to begin the healing process.



Tissue injury, infection, or irritation; release of chemical signals such as cytokines.

Migration of immune cells, like phagocytes, to the area of injury, infection, or irritation.

Phagocytes, like macrophages and neutrophils, consume the bacteria and cell debris. This allows for the tissue to heal.

As a result, the skin may become red, swollen, warm, and painful. This response is essential for healing, as it helps fight off pathogens and facilitates tissue repair, but excessive or prolonged inflammation can lead to chronic skin conditions. Topical application of cosmetics formulated with anti-inflammatory ingredients can soothe irritated skin and reduce redness, promoting a healthier complexion.

# Farm Level Sourcing



Experience the world's finest licorice, sourced straight from the heart of Southern Italy! Active Concepts is excited to partner with a renowned licorice producer in Calabria, where the unique microclimate of the Sibari plain and nutrient-rich clay soils create the ideal environment for this exceptional root to flourish. Their dedicated team hand-harvests each batch to ensure the highest quality and authenticity.



When licorice root goes through its extraction process, it leaves behind a solid residue, also known as pomace. Active Concepts unlocks the potential of licorice pomace, effectively transforming a would-be waste by-product into a valuable resource for cosmetic formulations. Our innovative approach utilizes licorice pomace, characterized by glycyrrhetic acid, for its known antioxidant, lenitive, and antimicrobial activities.

# Available Efficacy Studies

## In Vivo

- VISIA: Reduction in Red Areas
- Anti-Erythema Study
- 24-hour Hydration Study
- 24-hour TEWL Study
- Brightness Study
- Scalp Care Study
- Scalp Sebum Reduction Study
- UV Dye Penetration Study

NEW!

## In Vitro

- IL-6 ELISA
- ROS Assay
- ORAC Assay
- Airborne Pollutants Assay

## Tox & Safety

- OECD 201 Fresh Water Algae Growth Inhibition
- OECD 301B Ready Biodegradability Assay
- OECD TG 442C – Direct Peptide Reactivity Assay
- OECD TG 442D – In Vitro Skin Sensitization Report
- AMES
- Cellular Viability
- Dermal & Ocular Irritation
- Phototoxicity Assay



# IL-6 ELISA

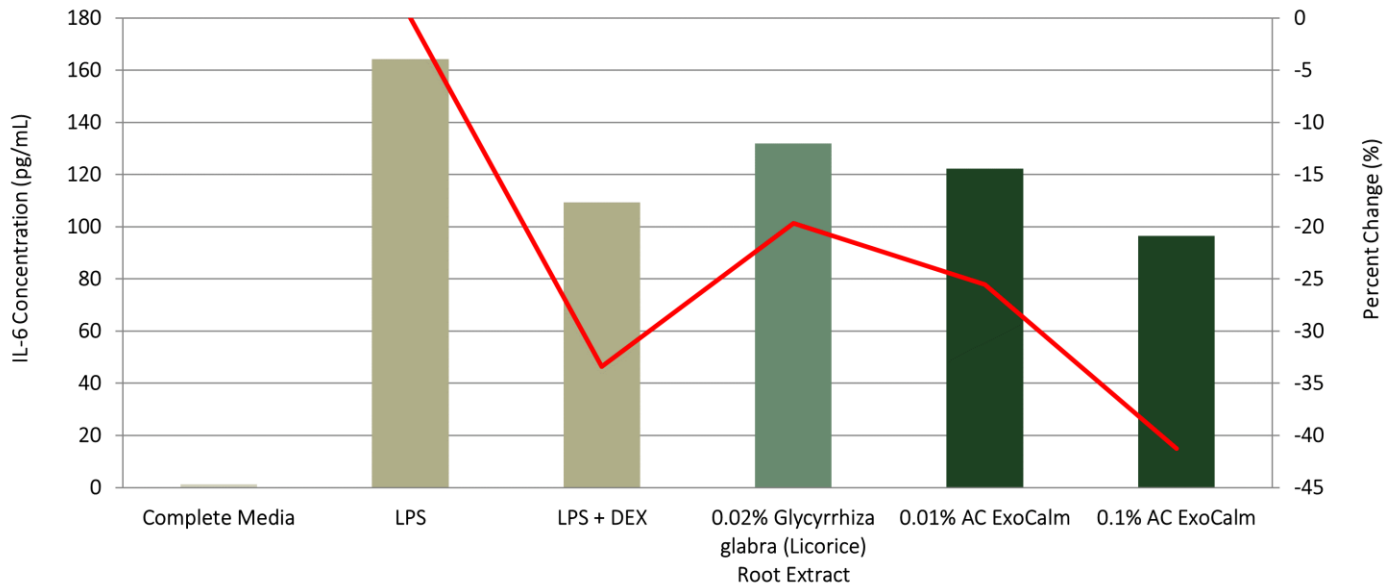


Figure 1. The Effect of AC ExoCalm treated Keratinocytes on IL-6 Concentrations.

IL-6 is a pro-inflammatory cytokine that is crucial for skin inflammation, activating immune cells and enhancing inflammatory responses and tissue repair. It activates the NF- $\kappa$ B pathway, leading to the production of inflammatory mediators like MMP-1, which degrades the extracellular matrix and collagen, contributing to skin aging, including wrinkles and loss of elasticity. Lowering IL-6 levels may help reduce skin matrix breakdown and promote renewal. An IL-6 ELISA was conducted to assess the effect of AC ExoCalm on IL-6 production in keratinocytes under pro-inflammatory conditions.

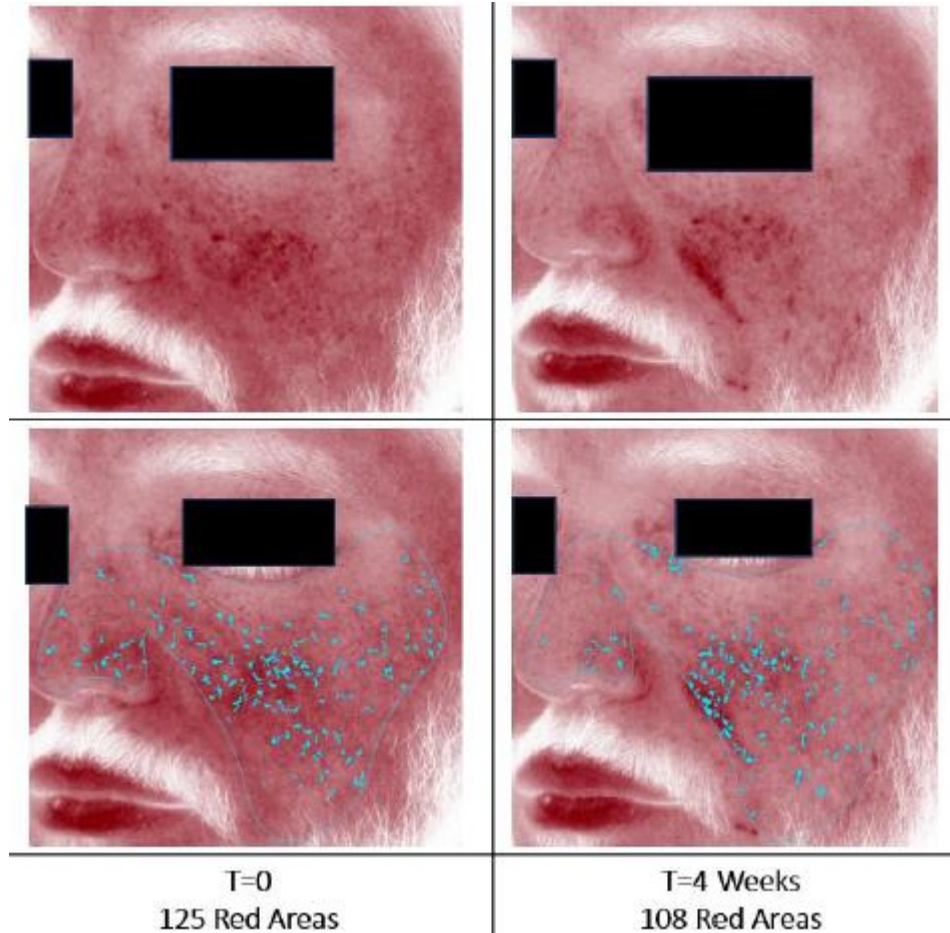
Keratinocytes treated with AC ExoCalm at 0.1% outperformed the licorice root extract and demonstrated a reduction in IL-6 levels by

-41%

# Benefits

AC ExoCalm provides calming and anti-inflammatory properties that help diminish skin inflammation and visibly address the signs of cellular aging, promoting a more youthful look.

# VISIA: Reduction in Red Areas



Photographic assessments were performed using the VISIA Complexion Analysis System. 10 M/F participants applied 3.0% AC ExoCalm twice a day over a four-week period. Images were taken once a week for 4 weeks and analyzed for Red Area Feature Counts. The Red Area Feature Counts indicate the number of discrete instances of red areas within the analyzed region.

Figure 2. Images of Participants treated with 3.0% AC ExoCalm. Natural photos (top) and VISIA Image Enhancement (bottom) Before and After Four weeks.

At 3.0%, AC ExoCalm demonstrated a decreased red area count compared to the baseline by

-16%

# Benefits

AC ExoCalm improves skin health by reducing the number of red areas on the skin. Additionally, it can decrease simulated skin age, providing a more youthful appearance!

# Anti-Erythema Study

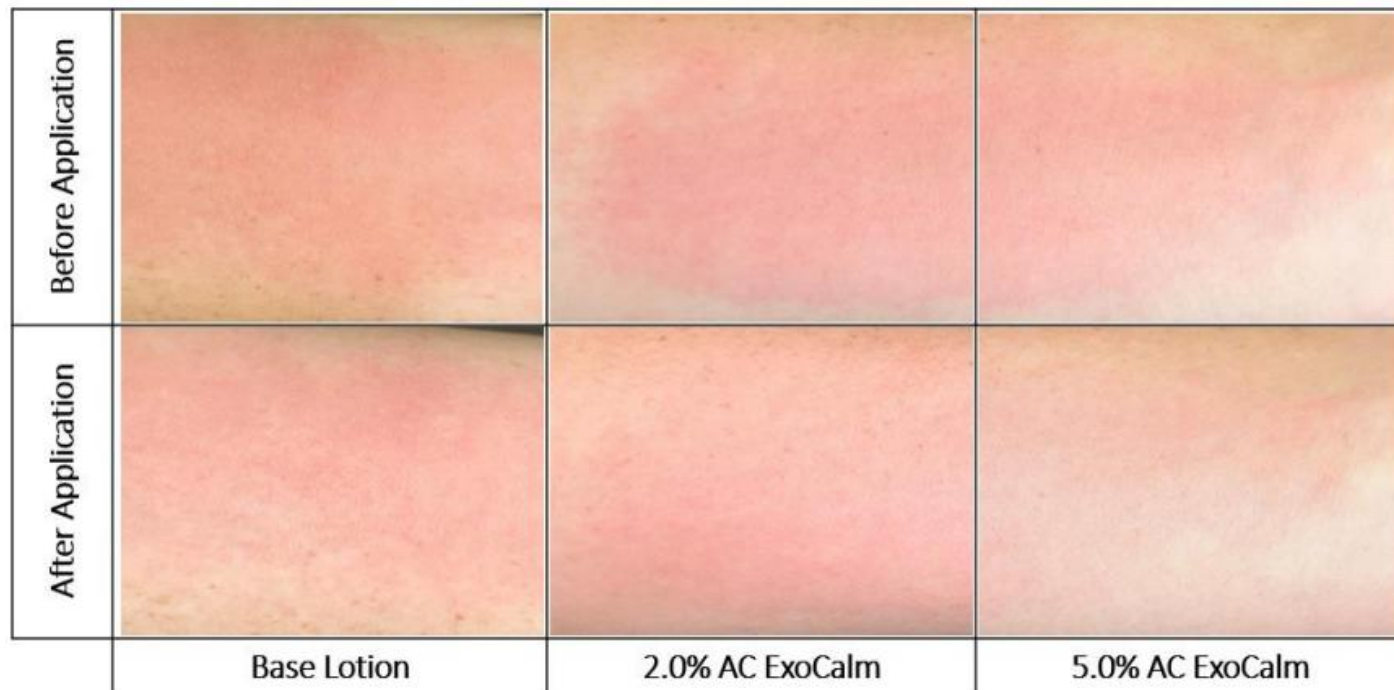


Figure 3. Participant Image Before (Top) and After (Bottom) Application of Base Lotion and AC ExoCalm.

Skin erythema is the redness of the skin caused by the dilation and irritation of superficial capillaries, resulting in increased blood flow. This condition can be visually similar to a rash and is often undesirable. An Anti-Erythema Study was conducted to assess the redness-reducing effects of AC ExoCalm. To induce irritation, surgical tape was applied to the skin, and erythema measurements were taken after removal. Test sites were treated with either a base lotion, 2.0% AC ExoCalm, or 5.0% AC ExoCalm. After 15 minutes, erythema was measured again, and participants rated the visual reduction in redness on a scale from 1 (no change) to 10 (no redness).

At 2.0%, AC ExoCalm significantly reduced skin redness 15 minutes after application by

-3.1%

# Benefits

AC ExoCalm dramatically reduces both visible and perceived redness while enhancing your skin's protective barrier, showcasing its powerful anti-redness and anti-irritation properties for a healthier, more radiant complexion!

# ROS Assay

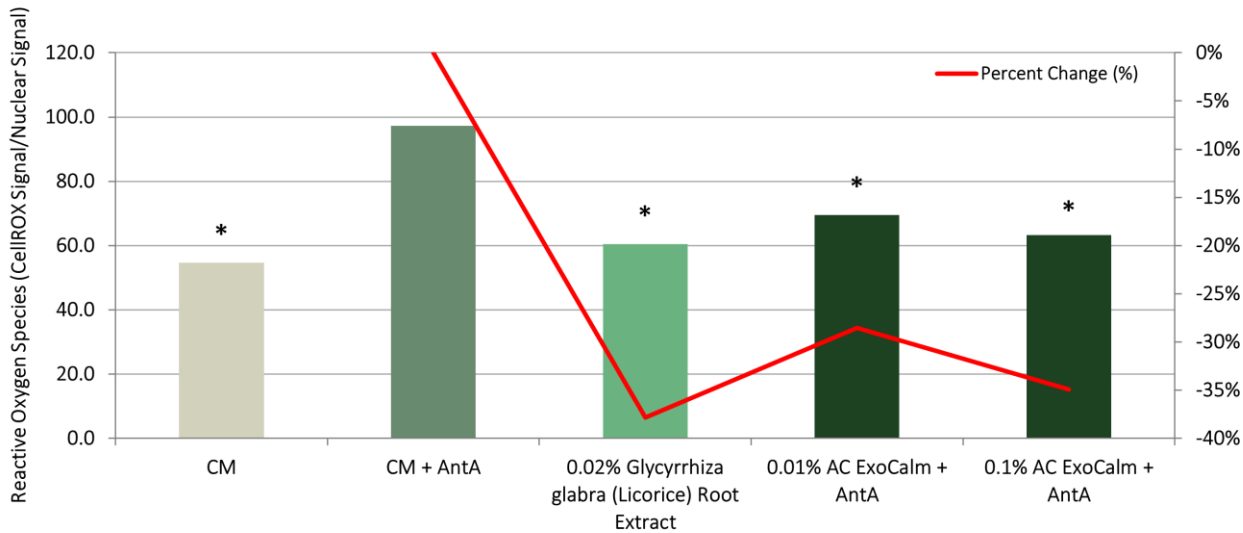
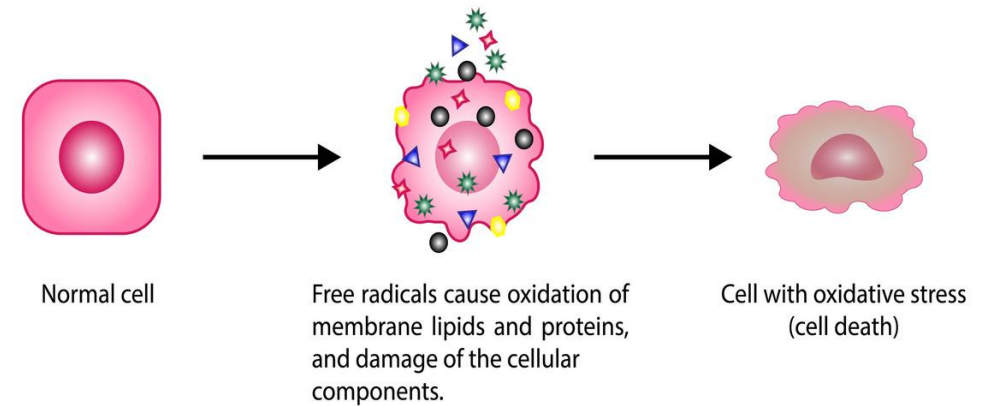


Fig 4. Effect of AC ExoCalm on ROS scavenging.

## Oxidative Stress



UV irradiation, pollutants, foreign substances, and aging elicit unrestricted increases in reactive oxygen species (ROS). These deregulated augmentations in oxidative stress lead to an acceleration of DNA mutation, cellular senescence, protein oxidation, and collagen degradation.

AC ExoCalm at 0.1%  
outperformed the licorice  
root extract and decreased  
ROS levels by

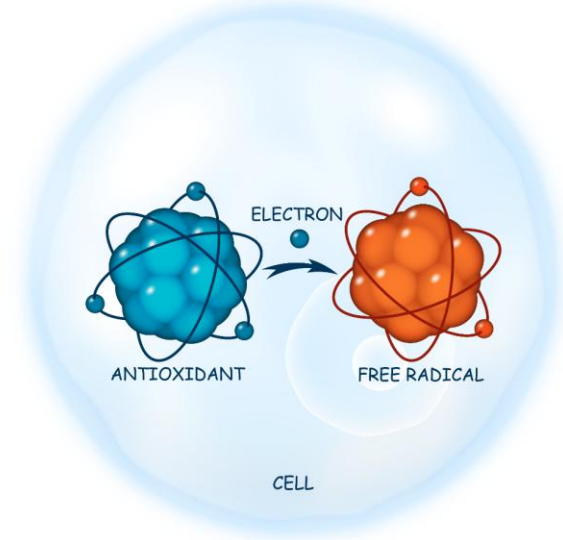
-35%

*Benefits*

These data indicate AC ExoCalm scavenges unnecessary ROS, which may help to attenuate characteristics of cellular aging.

# ORAC Assay

## Free Radical



Maximizing the antioxidant capacity on a cellular level allows for free radicals to be dealt with at a rate that provides protection from cellular damage. This cellular damage can be seen as physical signs of aging, such as wrinkles, loss of elasticity, unwanted pigmentation and skin unevenness with slow regeneration.

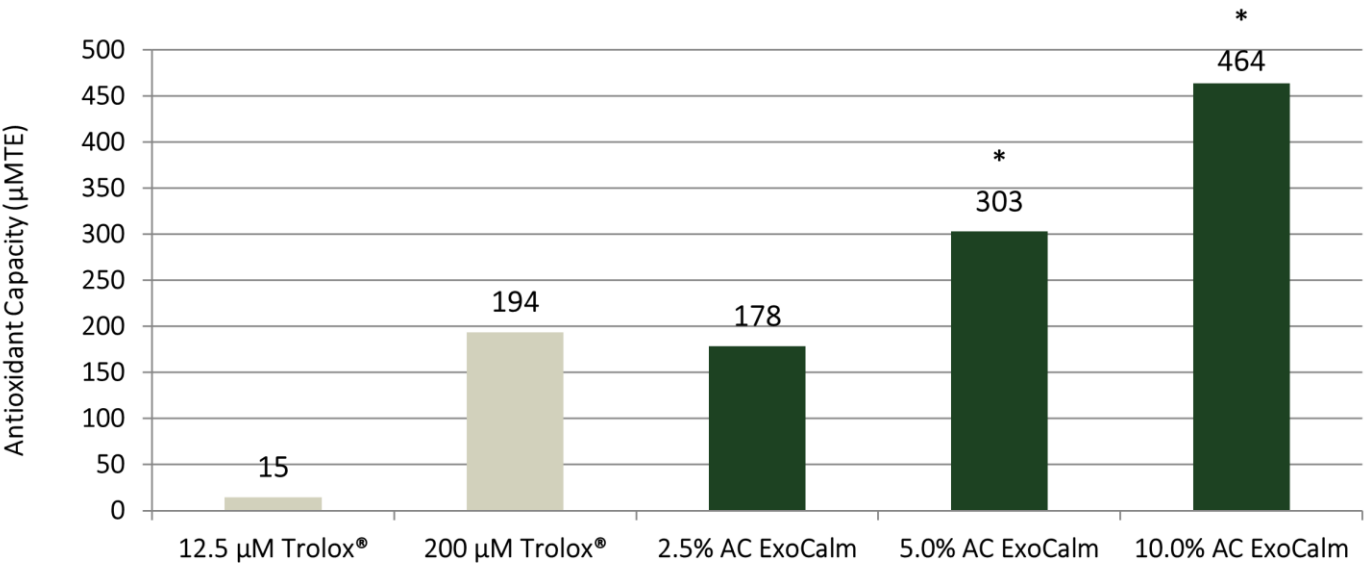


Figure 5. Antioxidant capacity of ExoCalm.

AC ExoCalm at 5.0%  
exhibited greater  
antioxidant activity than  
200  $\mu\text{M}$  Trolox® with a  
value of

# Benefits

303  
 $\mu\text{MTE}$

AC ExoCalm exhibits antioxidant properties and promotes the anti-aging process through its protective action at the cellular level.

# Airborne Pollutants Study

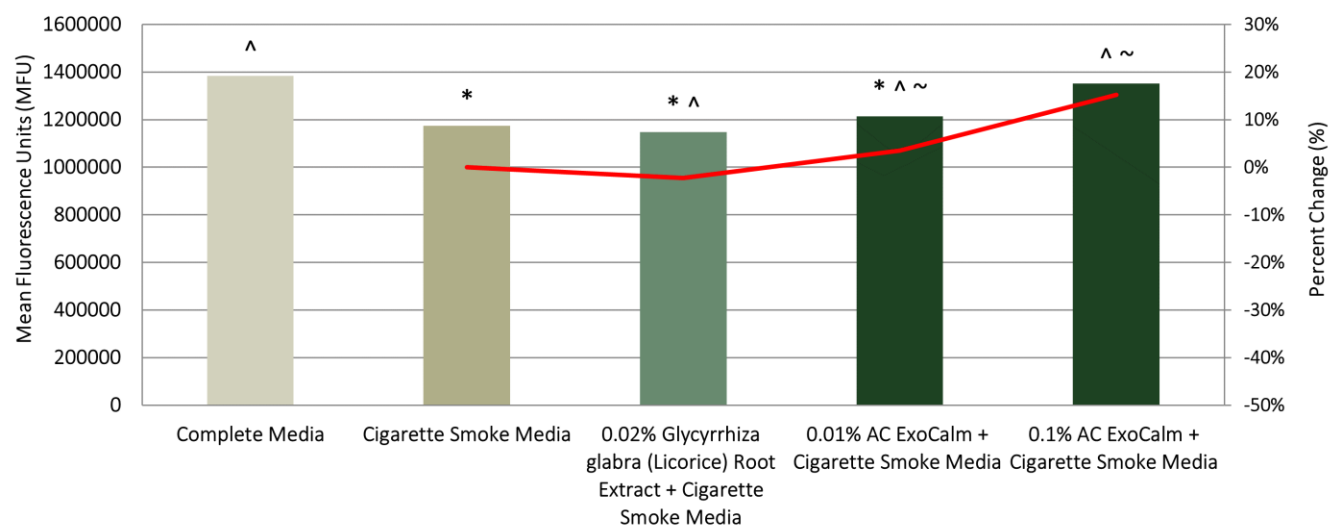


Figure 6. Cellular Viability of Fibroblasts.

Airborne pollutants, such as cigarette smoke and secondhand smoke, **disrupt natural biological processes and can cause inflammation, physical damage, and accelerate symptoms of aging.** An Airborne Pollutants Study was conducted to assess the ability of AC ExoCalm to **protect cellular homeostasis** against exposure to soluble cigarette smoke pollutants. **Cigarette smoke** contains various airborne pollutants (carbon monoxide, particulate matter, nitrogen dioxide, etc.) and is not heavily influenced by environmental factors. Exposure of cigarette smoke can also be standardized, making it easier to quantify the effects of airborne pollutants on human dermal fibroblast cell viability.

Fibroblasts treated with 0.1% AC ExoCalm prior to pollution exposure demonstrated significant increases in cellular viability by

# Benefits

+15%

This data indicates that AC ExoCalm attenuates the negative impacts of airborne pollution on cellular viability. Collectively, AC ExoCalm offers protection against airborne pollutants at a cellular level.

# Brightness Study



Figure 7. VISIA Images of a Participant Over Time (Right Side (R) = 2.0% AC ExoCalm, Left Side (L) = Base Lotion)

Skin luminosity is referred to as the intensity of light reflected from the skin's surface. Increasing skin luminosity brightens the appearance of skin and enhances natural radiance. By enhancing skin brightness, the appearance of dark and dull skin is lessened, which is highly desired by consumers. Accordingly, a Brightness Study was conducted to evaluate the ability of AC ExoCalm to increase skin luminosity. The key active ingredient in AC ExoCalm, Glycyrrhiza glabra (Licorice) Root Extract, was tested to demonstrate the superior nature of Bioauthentic Exosomes as a delivery system.

2.0% AC ExoCalm significantly increased overall face brightness compared to base lotion by

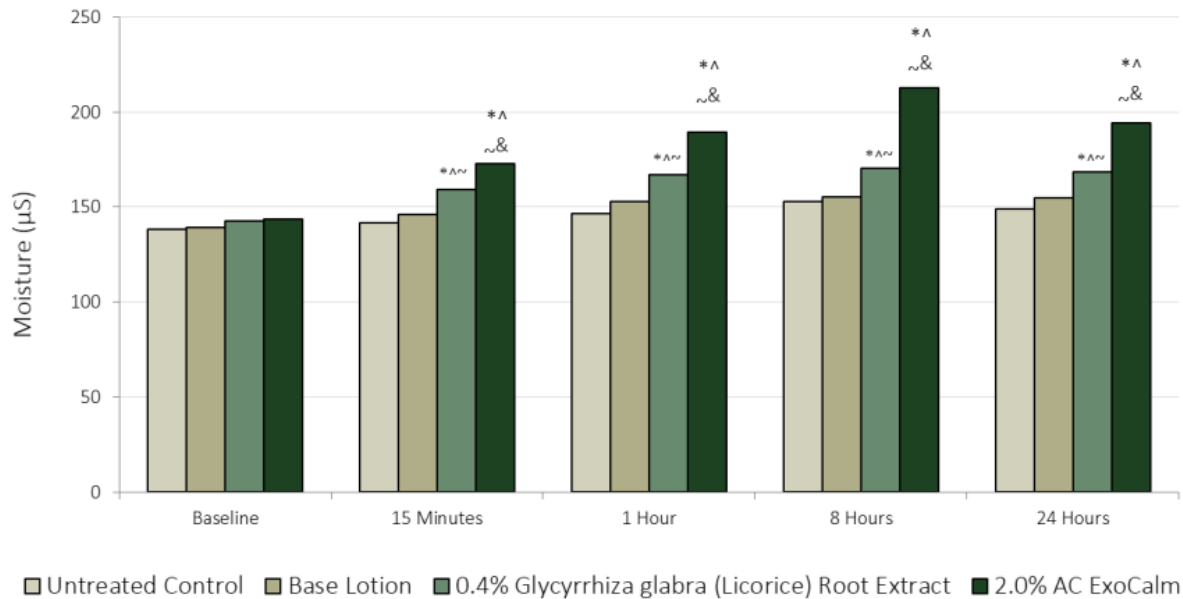
# Benefits

+1.6%

AC ExoCalm demonstrates immediate and short-term skin brightening properties, transforming dullness into a radiant glow!

# 24 Hour Moisturization Study

## Skin Hydration AC ExoCalm



A Moisturization Study was conducted to evaluate the immediate and short-term skin hydrating properties of AC ExoCalm. The key active ingredient in AC ExoCalm, *Glycyrrhiza glabra* (Licorice) Root Extract, was tested to demonstrate the superior nature of Bioauthentic Exosomes as a delivery system. Hydration measurements are made by placing a probe on the skin of preidentified test sites. The hydration probe evaluates conductance properties by alternating voltages in the upper layers of skin and provides a measurement of local hydration. The controls and test materials are applied to the skin test site once and hydration is measured at four time increments within a 24-hour period.

Figure 8. Skin Hydration Overtime. \* indicates significance ( $p \leq 0.05$ ) compared to Baseline values. ^ indicates significance ( $p \leq 0.05$ ) compared to Untreated Control within the same timepoint. ~ indicates significance ( $p \leq 0.05$ ) compared to Base Lotion within the same timepoint. & indicates significance ( $p \leq 0.05$ ) compared to *Glycyrrhiza glabra* (Licorice) Root Extract within the same timepoint.

2.0% AC ExoCalm increased skin moisturization after 8 hours of application by

+48%

# Benefits

AC ExoCalm showcases both immediate and long-term skin hydration benefits, enhancing the skin's protective barrier function and promoting a visibly healthier complexion.

# 24 Hour Transepidermal Water Loss Study

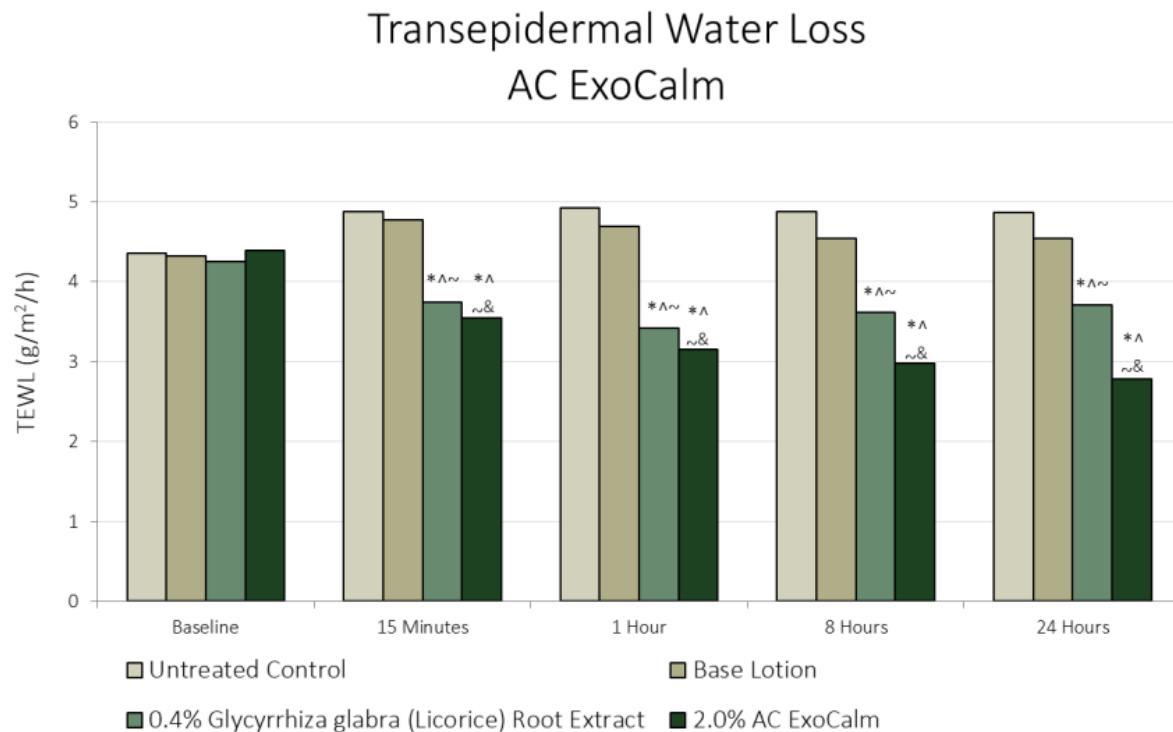


Figure 9. TEWL Measurements Overtime. \* indicates significance ( $p \leq 0.05$ ) compared to Baseline values. ^ indicates significance ( $p \leq 0.05$ ) compared to Untreated Control within the same timepoint. ~ indicates significance ( $p \leq 0.05$ ) compared to Base Lotion within the same timepoint. & indicates significance ( $p \leq 0.05$ ) compared to Glycyrrhiza glabra (Licorice) Root Extract within the same timepoint.

A Transepidermal Water Loss Study was conducted to evaluate the immediate and short-term moisture retention properties of AC ExoCalm. The key active ingredient in AC ExoCalm, Glycyrrhiza glabra (Licorice) Root Extract, was tested to demonstrate the superior nature of Bioauthentic Exosomes as a delivery system. Moisture retention is essential for maintaining the skin's protective barrier. Transepidermal water loss (TEWL) occurs when water evaporates from the skin's surface, with higher TEWL indicating lower hydration levels. Compromised skin barriers lead to increased TEWL, resulting in dryness and roughness.

Applying 2.0% AC ExoCalm  
once in a 24-hour period  
significantly reduced TEWL by

-36%

# Benefits

AC ExoCalm showcases immediate and short-term moisture retention properties, effectively strengthening the skin's protective barrier and promoting a healthier, more hydrated appearance.

# Scalp Care Study

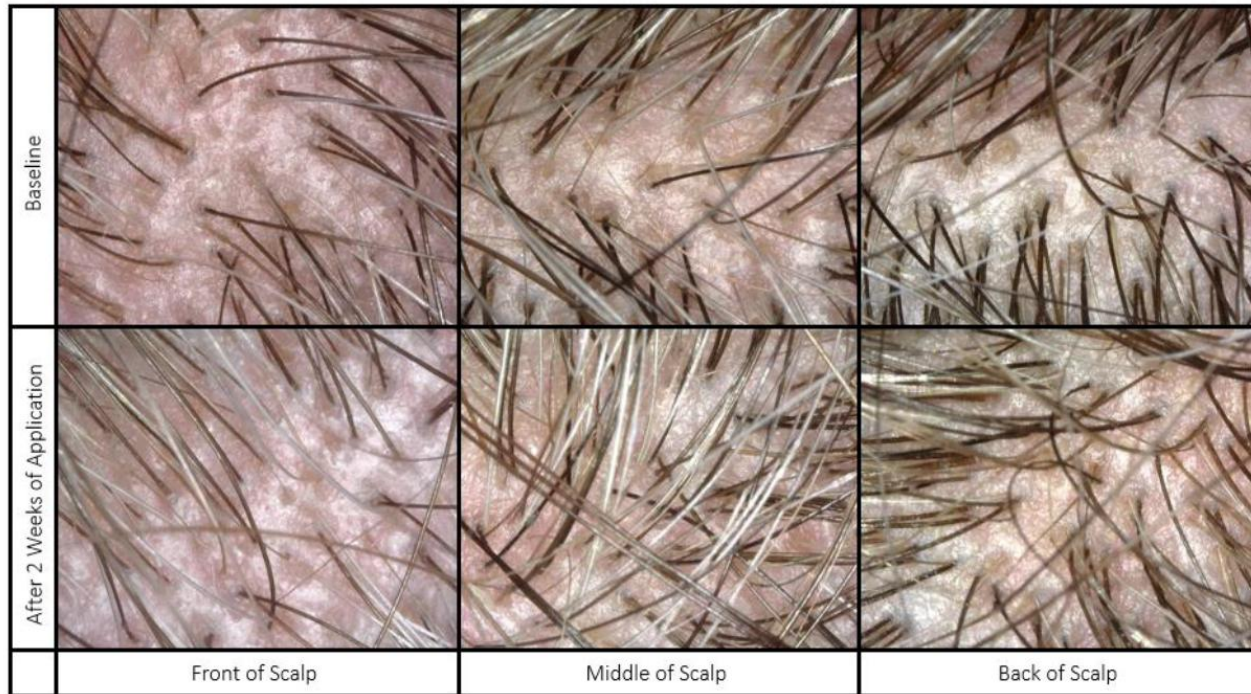


Figure 10. Representative Scalp Images of a Participant at Baseline and After Two Weeks of Base Shampoo and Base Conditioner Application.

Erythema is abnormal redness of the skin or scalp which occurs when blood capillaries are congested and dilated. Irritation of the skin and scalp are often associated with increased erythema levels. As a result of erythema on the scalp, consumers may experience a tightening sensation, scalp flakiness, and poor scalp hydration. Therefore, reducing scalp erythema while also improving scalp hydration can alleviate the unwanted symptoms of irritation. Accordingly, a Scalp Care Study was conducted to assess the ability of AC ExoCalm to reduce scalp erythema overtime while maintaining moisturization.

2.0% AC ExoCalm significantly reduced erythema levels on the scalp by

-19%

# Benefits

AC ExoCalm demonstrates erythema reducing properties while maintaining scalp hydration which improves overall scalp feel, visual appearance, and alleviates unwanted symptoms of irritation.

# Scalp Sebum Reduction Study

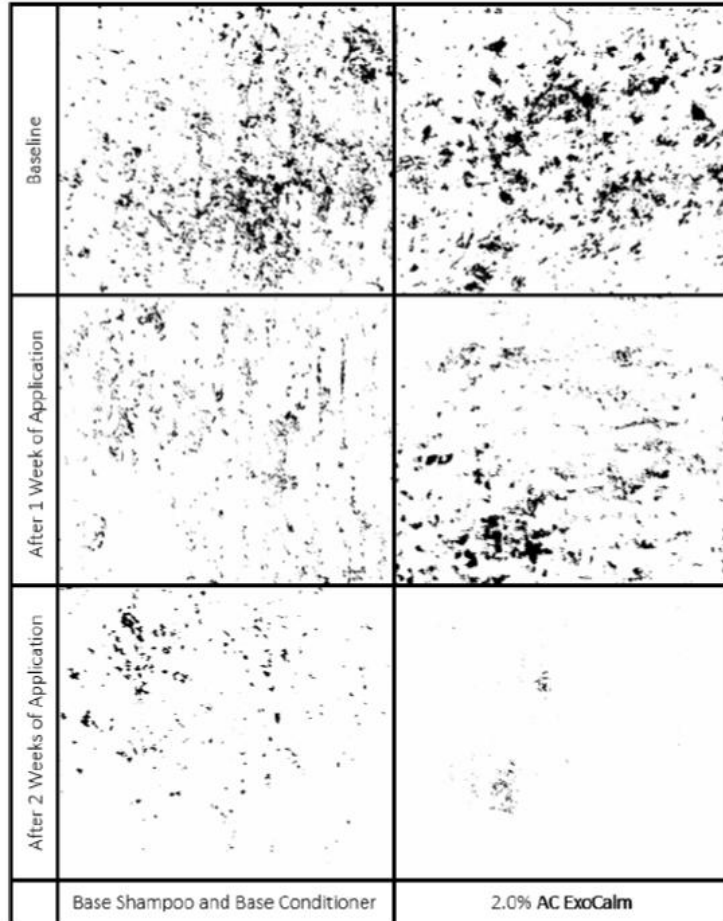


Figure 11. Representative Images of Sebufix® SF16 Foils Indicating Sebum Present on Participant's Scalps Overtime. Dark spots represent sebum content. Skin with lower sebum content shows few small spots, whereas oily skin is displayed by a great number of large spots.

Sebum is the oily, waxy secretion of sebaceous glands helping to moisturize and protect the skin from bacterial and fungal pathogens. An insufficient amount of sebum can trigger dry, red, and itchy skin on the scalp whereas an overproduction of sebum leads to an oily scalp, increased presence of dandruff, and leaves a visible shine. The shiny and greasy appearance associated with excess sebum and oily skin is undesirable and reducing these attributes through cosmetic applications is highly sought after. Accordingly, a scalp sebum reduction study was conducted to evaluate the ability of AC ExoCalm to decrease sebum on the scalp while maintaining moisturization.

2.0% AC ExoCalm decreased scalp sebum content after two weeks of application by

-61%

*Benefits*

AC ExoCalm elicits hydrating properties on the scalp, preventing dryness and irritation, while simultaneously providing sebum reducing benefits.

# Polydispersity Index

Polydispersity index (PDI) is a value assigned to describe how uniform/homogenous the distribution of particle size is. All BioAuthentic Exosomes are now standardized for PDI.

## → Stability and Efficacy

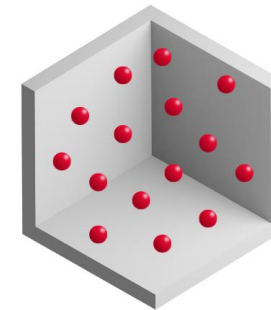
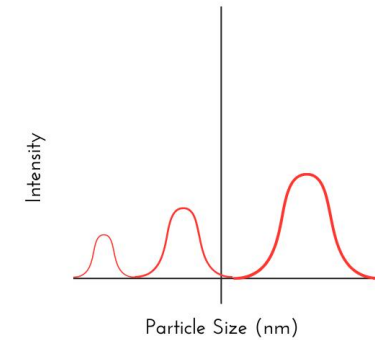
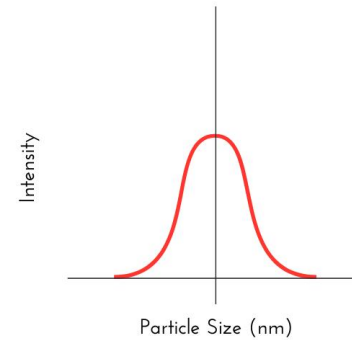
A low PDI (close to 0) indicates a narrow size distribution, which often correlates with better stability and uniformity in the formulation.

## → Cell Interaction

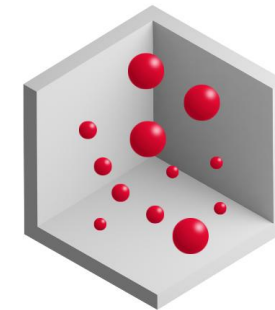
The size and uniformity of exosomes can influence their interaction with skin cells. A smaller particle size can enhance penetration and cellular uptake, optimizing the benefits of the active compounds they carry.

## → Quality Control

Monitoring the PDI during production helps ensure that the exosomes maintain consistent quality. Variations in size distribution can affect product performance and safety.



PDI: <0.5



PDI: >0.5

# UV Dye Penetration

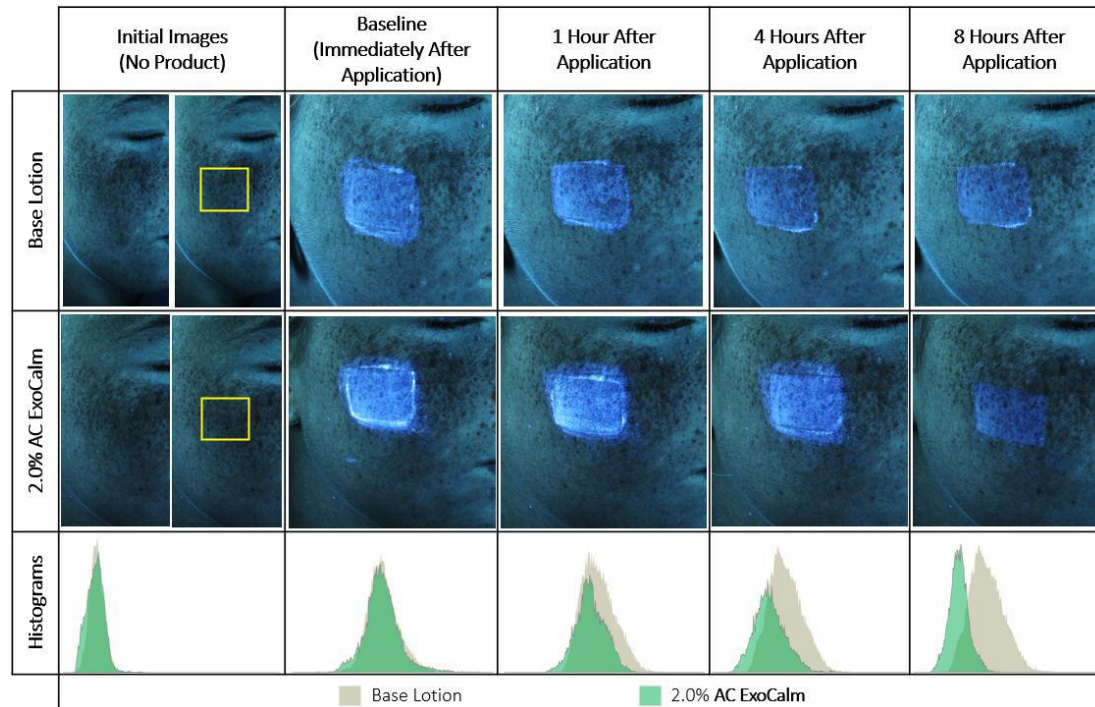


Figure 12. VISIA UV Dye Participant Images and Intensity Histograms at All Timepoints.

A fluorescent dye was attached to the lipid bilayer in AC ExoCalm, allowing us to visually track exosome-associated fluorescence. 2.0% AC ExoCalm and a base lotion were applied to predetermined test sites on participants' cheeks and photographed under UV light at various time points after application. The brightness visible in these photos indicates how much product remains on the skin's surface. **As the brightness diminishes, it shows that the exosomes have been absorbed into the skin.**

2.0% AC ExoCalm decreased  
UV dye intensity after eight  
hours of application by

-50%

*Benefits*

AC ExoCalm exhibits robust skin penetration  
properties with just one application!

# Summary

## WHAT.

AC ExoCalm is a natural BioAuthentic Exosomal delivery system that **inhibits inflammation** in both the skin and scalp.

## WHY.

AC ExoCalm effectively **reduces pro-inflammatory cytokines** to provide soothing relief to irritated skin.

## MADE OF.

AC ExoCalm upcycles **licorice pomace** from a farm in Italy for its natural anti-inflammatory benefits.

## ACTION.

AC ExoCalm revolutionizes delivery systems in cosmetics, targeting the specific benefit of **reducing the inflammatory response**. Allow this innovative ingredient to calm the skin!



# AC ExoCalm

Code: 60192

INCI: Water & Glycyrrhiza Glabra (Licorice) Root Extract & Phospholipids

Appearance: Liquid Exosomal Dispersion, Light Beige to Orange

Suggested Use Level: 1 - 10%

Suggested Applications: Anti-Inflammation, Anti-Pollution, Antioxidant

Standardized for: Reduction in IL-6, Protein, Particle Size, Polydispersity Index



In Vitro



In Vivo



ISO 16128  
NI & NOI



Vegan  
Compliant



COSMOS  
Compliant



China  
Compliant

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