

AC Melatonin Liposome SF



inflammaging defense
antioxidant
grape derived melatonin
visible wrinkle reduction
natural
encapsulation technology

BACKGROUND

Sleep is nature's most powerful beauty treatment. Our skin switches from 'protect' to 'repair' during the night to recover from daily exposure of stresses. Melatonin, a naturally-occurring hormone, controls the sleep-wake cycle and plays a vital role in skin regeneration and antioxidant production. This natural restorative powerhouse can be used to recharge skin's radiance and reinforce the skin's capacity for repair, renewal, and revitalization. **AC Melatonin Liposome SF** is an innovative ingredient that features grape-derived melatonin in a liposomal solution for enhanced activity. The efficacy of melatonin as a topical agent offers a promising avenue to enhance the skin's nightly repair cycle. Incorporate **AC Melatonin Liposome SF** to minimize inflammation, visibly reduce wrinkles, and defend against oxidative stress for a refreshed complexion.

Our bodies naturally increase melatonin production in anticipation of darkness to prepare for sleep. Synthesis and release of melatonin from the pineal gland, a small endocrine gland found in the brain, occurs daily to help regulate biological rhythms. However, over the past twenty years, research has revealed a multitude of benefits associated with melatonin, including anti-inflammatory, both direct and indirect antioxidant activity, tissue regenerative benefits, and preservation of mitochondrial function.¹ Additionally, melatonin synthesis is not restricted to the pineal gland, but extends to various organs, including the skin. Scientists have recently revealed that the skin contains melatonin receptors, which suggests that melatonin also plays an important role in regulating skin function and structure.¹ Melatonin's anti-inflammatory and antioxidant support make it an appealing target for use to support skin health.

Melatonin is a natural hormone present in both animal and plant sources, including bananas, beets, tomatoes, and grapes.² Melatonin has many roles in plant physiology, such as acting as a growth promoter, rooting agent, and being a key component of plant stress defense. Melatonin present in grape (*Vitis vinifera*) has been shown to boost the plant's tolerance against environmental stressors, including extreme temperature, through a direct scavenging of reactive oxygen species (ROS) by enhancing antioxidant enzymes activity, non-enzymatic antioxidants, and enzymes related to oxidized protein repair.² Active Concepts' specialization in natural product

Code Number: 61012

INCI Name: Water & Phospholipids & Melatonin

INCI Status: Conforms

REACH Status: Compliant

CAS Number: 7732-18-5 & 123465-35-0 & 73-31-4

EINECS Number: 231-791-2 & N/A & 200-797-7

Origin: Botanical

Processing:

GMO Free

No Ethoxylation

No Irradiation

No Sulphonation

Additives:

Preservatives: None

Antioxidants: None

Other additives: None

Solvents Used: Water

Appearance: Yellow to Amber, Liquid Liposomal Dispersion

Soluble/ Miscible: Water Dispersible

Microbial Count:

< 100CFU/g, No Pathogens

Suggested Use Levels: 1.0 – 10.0%

Suggested Applications:

Antioxidant, Wrinkle Reduction, Anti-Inflammatory

Benefits of **AC Melatonin Liposome SF**:

- Antioxidant Protection
- 'Inflammaging' Defense
- Visible Wrinkle Reduction



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chemistry, along with our eco-conscious ethos, has harnessed the natural melatonin present in grapes exposed to cold stress for cosmetic benefit. Grape biomass from ice wineries in Canada achieves new life as the source for melatonin isolation in the production of **AC Melatonin Liposome SF**.

SCIENCE

Chemically speaking, melatonin is N-acetyl-5-methoxytryptamine, a derivative of serotonin, which is another neurotransmitter derived from the amino acid tryptophan. Mammalian skin possesses a melatonergic system where the synthesis involves the sequential transformation of tryptophan to melatonin in a cascade of enzymatic reactions.^{1,3} The cutaneous melatonergic system has several critical roles, including preventing the proliferation of cancer cells, ameliorating inflammation, and promoting wound healing. With aging comes a decrease in the skin's melatonin production, as does the density of melatonin receptors present within the skin.³ This decrease in the amount of melatonin produced, as well as the melatonin receptors lessens ability of the skin to effectively utilize this restorative powerhouse. The topical application of melatonin is a novel way to reverse many of the aging related declines in the skin melatonergic system.

The properties of melatonin suggest it is an important effector of stress responses in the skin and may counteract both environmental and intrinsic stressors to maintain skin integrity. Melatonin itself can behave as a scavenger of free-radicals, or as activator of pathways protective against oxidative stress.⁴ Additionally, topically applied melatonin has been shown to offer strong protection against ultraviolet light-induced erythema through the suppression of oxidative damage.⁴

Melatonin also plays a key role in revitalizing skin through its interactions with keratinocytes and fibroblasts.⁵ Melatonin protects keratinocytes against cell death, and stimulates the growth of fibroblasts.⁵ Fibroblasts are responsible for the production of collagen and elastin, which are essential proteins that provide the skin with structural support. With age, fibroblast cells encounter significant mitochondrial dysfunction and are less able to produce enough energy to fulfill their role in supporting the skin. Melatonin is capable of increasing mitochondrial membrane potential and ATP production, enhancing the activity of electron transport chain complexes and, consequently, helps to maintain mitochondrial efficiency.⁵ Therefore, melatonin exhibits a number of properties that could benefit a stress-response system of the skin.

LIPOSOMES

The liposomal incorporation of melatonin serves to enhance its stability and bioavailability in cosmetic applications. Liposomes can be used in the delivery of various cosmetic materials, vitamins, and minerals throughout the body, typically to the skin, for an array of advantages. The liposomes may attach and fuse to the cellular membranes, releasing their contents into the target cells. Liposomes are microscopic vesicles that consist of an aqueous center with a phospholipid membrane. Phospholipids contain a glycerol bonded to two fatty acids and a phosphate group with a polar head. The fatty acid portion of this biomolecule is hydrophobic and is located toward the outside of the lipid bilayer whereas the phosphate group is hydrophilic and faces the aqueous interior. These phospholipid walls are identical to those that comprise other human cell membranes. Liposomes act as vehicles to transport nutrients to the cells through layers of skin and enhance delivery of active ingredients.

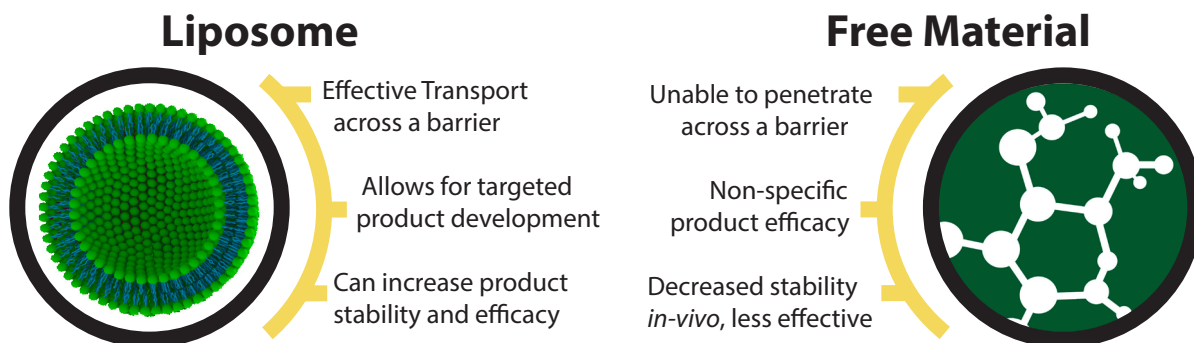


Figure 1. Comparison of liposomal encapsulation vs. free material.

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When non-encapsulated materials are placed on the skin a range of factors determine the fate of the material. Stability, solubility, lipophilicity, and size are all obstacles the active must overcome to penetrate the epidermal barrier. Liposomes, which resemble the basic structures of cellular membranes, create a more beneficial interaction with skin cells. The structure and amphiphilic nature allows the liposomes to penetrate the epidermal barrier and travel deeper than free materials to deliver the anticipated results.

Liposomes are readily compatible with epidermal surface lipids, the skin's primary moisture barrier, as these epidermal lipids exist as lamellar bilayers. Lamellar bilayers require less moisture to maintain their structure. When a liposome fuses with the epidermal lipids, the epidermal lipid structure becomes overloaded with water and out of equilibrium. To restore equilibrium, the water and phospholipid, as well as the loaded active, are rapidly churned through the top cell layers of the stratum corneum. Enhanced delivery of the active occurs as it is rapidly carried down through the stratum corneum. Liposomes' proven delivery system yields a multitude of benefits; enhancing the penetration of actives yielding increased efficacy, offering time release mechanisms, protecting and delivering otherwise unstable ingredients, and the ability to target specific cells.

BENEFITS

Enjoy the benefits of beauty sleep with the anti-inflammatory and antioxidant protection of melatonin. This natural restorative powerhouse can be used to recharge skin's radiance and reinforce the skin's capacity for repair, renewal, and revitalization. **AC Melatonin Liposome SF** is an innovative ingredient that features natural, grape-derived melatonin in a liposomal solution for enhanced activity. Incorporate **AC Melatonin Liposome SF** into finished formulas to minimize inflammation, visibly reduce wrinkles, and defend against oxidative stress for a refreshed complexion.

EFFICACY

The anti-inflammatory effect of **AC Melatonin Liposome SF** was evaluated and compared to a 4.0% non-encapsulated melatonin solution in an *in-vitro* Interleukin-6 Enzyme-Linked Immunosorbent Assay (IL-6 ELISA) on cultured human dermal fibroblasts. IL-6 is a pro-inflammatory cytokine known to play an active role in inflammation, immunology, and aging. IL-6 signals through the nuclear factor-kappa B (NF-κB) pathway that results in the transcription of inflammatory mediators, including matrix metalloproteinase-1 (MMP-1). MMP's are responsible for breaking down the extracellular matrix and collagen in the skin leading to wrinkles and loss of skin elasticity. Reducing the level of IL-6 and other inflammatory mediators is believed to slow down degradation of the skin matrix and stimulate its replenishment.

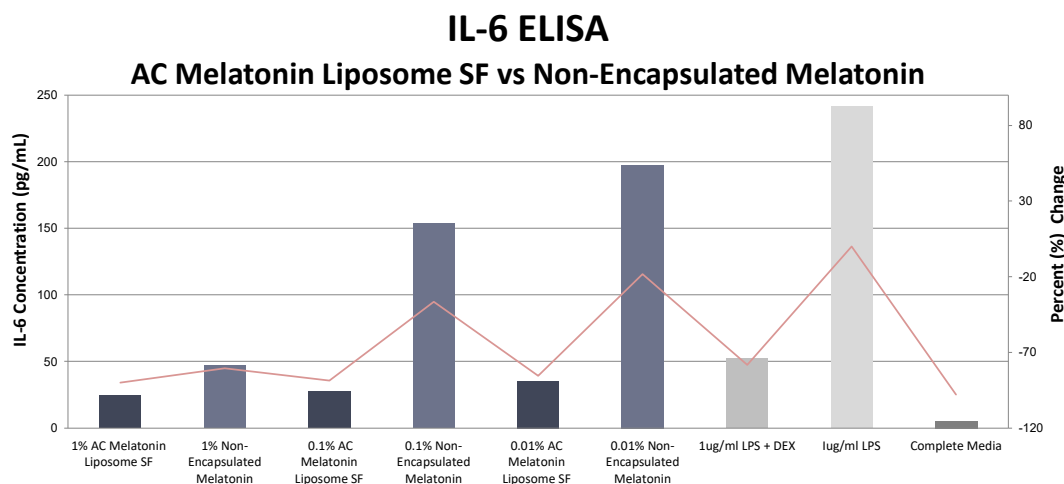


Figure 2. Comparative anti-inflammatory benefits.

As shown in Figure 2, **AC Melatonin Liposome SF** was able to decrease IL-6 production when compared to the LPS Positive Control and all concentrations of Non-Encapsulated Melatonin. This decrease in IL-6 production indicates a reduced inflammatory environment which could decrease the signs of aging and reduce the formation of fine lines and wrinkles. This direct comparison of 4.0% encapsulated melatonin in **AC Melatonin Liposome SF** to the 4.0% non-encapsulation solution supports the use of the liposomal delivery system to enhance product activity and performance. This data suggests that **AC Melatonin Liposome SF** enhances soothing and anti-inflammatory properties at normal use concentrations.

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An Oxygen Radical Absorbance Capacity (ORAC) assay was conducted to assess the antioxidant capacity of **AC Melatonin Liposome SF**. The oxygen radical absorbance capacity (ORAC) assay is a standard method used to assess antioxidant capacity of physiological fluids, foods, beverages, and natural products. The assay quantitatively measures a sample's ability to quench free radicals that have the potential to react with and damage cellular components. As shown in Figure 3, AC Melatonin Liposome SF exhibited antioxidant activity comparable to 200µM Trolox®. The antioxidant capacity of AC Melatonin Liposome SF increased as the concentration increased. As a result, we can assure that its ability to minimize oxidative stress is dose dependent and that **AC Melatonin Liposome SF** is capable of providing antioxidant properties and aids in the anti-aging process through protection at the cellular level.

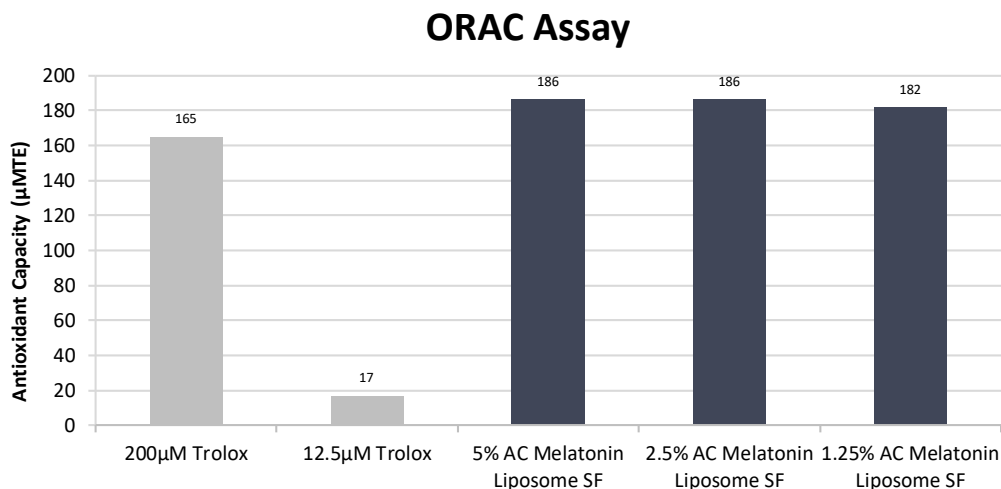


Figure 3. Antioxidant capacities.

An *in-vivo* study was conducted over a period of four weeks to evaluate the effects of 2.0% **AC Melatonin Liposome SF** in a base lotion on wrinkle parameters compared to the base lotion alone. Digital photographs and facial surface analysis were conducted as objective computer assessments by VISIA Complexion Analysis. Improvements in wrinkles were evaluated by comparing feature counts throughout the course of treatment. 2.0% **AC Melatonin Liposome SF** in base lotion demonstrated the ability to reduce the average feature count of wrinkles after one week by 9.30%, compared to the baseline. After four weeks of treatment, 2.0% **AC Melatonin Liposome SF** in base lotion demonstrated the ability to reduce the average feature count of wrinkles by 12.58%. **AC Melatonin Liposome SF** in base lotion demonstrated a statistically significant difference in feature counts for wrinkles over the course of the study, when comparing the percent change of experimental and control groups.

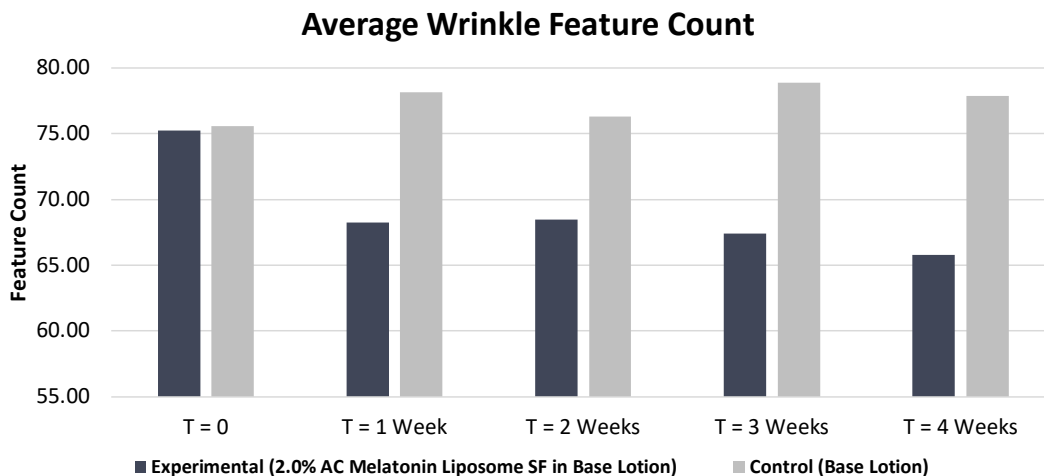


Figure 4. Average feature counts comparing experimental and control values at each time point.

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Figure 5. Panelist #3 treated with 2.0% AC Melatonin Liposome SF in Base Lotion displays a reduction (40.0%) in feature counts for wrinkles from beginning of treatment (T=0) to T=4 Weeks via VISIA Image Analysis. Images on the left are panelist #3 with image enhancement, through VISIA, which provides higher visualization of feature changes. Images on the right are natural photos of panelist #3.



Figure 6. Panelist #4 treated with 2.0% AC Melatonin Liposome SF in Base Lotion displays a reduction (9.18%) in feature counts for wrinkles from beginning of treatment (T=0) to T=4 Weeks via VISIA Image Analysis. Images on the left are panelist #4 with image enhancement, through VISIA, which provides higher visualization of feature changes. Images on the right are natural photos of panelist #4.

References:

1. Slominski A, Fischer TW, Zmijewski MA, Wortsman J, Semak I, Zbytek B, Slominski RM, Tobin DJ. On the role of melatonin in skin physiology and pathology. *Endocrine*. 2005 Jul;27(2):137-48.
2. Vitalini S, Gardana C, Zanzotto A, et al. The presence of melatonin in grapevine (*Vitis vinifera* L.) berry tissues. *J Pineal Res*. 2011;51(3):31-337.
3. Kleszczynski K, Fischer TW. Melatonin and human skin aging. *Dermatoendocrinol*. 2012;4(3):245-252.
4. Day D, Burgess CM, Kircik LH. Assessing the Potential Role for Topical Melatonin in an Antiaging Skin Regimen. *J Drugs Dermatol*. 2018;17(9):966-969.
5. Rusanova I, Martinez-Ruiz L, Florido J, et al. Protective Effects of Melatonin on the Skin: Future Perspectives. *Int J Mol Sci*. 2019;20(19):4948.



Active Concepts, LLC
 Lincolnton, NC. USA
www.activeconceptsllc.com
 Office: +1 (704) 276 7100
info@activeconceptsllc.com

Active Concepts S.r.l.
 Milano ITALY
www.activeconcepts.it
 Tel +39 02 90360719
info@activeconcepts.it

Active Concepts LLC, Asia
 Kaohsiung, Taiwan
www.activeconceptsllc.com
 Tel + 886 73599900
info@activeconceptsllc.com.tw

Active Concepts Japan
 Tokyo, Japan
www.activeconceptsllc.com
 Tel + 813 62311022
info-tokyo@activeconceptsllc.com