

# Clear—Fill—Revive: A Three-Step Approach for Age-Defying Skin

By Julia Baumann • Mibelle Biochemistry

For decades, traditional anti-aging treatments have focused on surface-level symptoms such as wrinkles and age spots. However, recent advances in cellular biology have revealed that aging is not merely a cosmetic concern, but a complex biological process rooted in cellular dysfunction. Among the most critical contributors to skin aging are cellular senescence and stem cell depletion. These mechanisms compromise skin renewal, structure, and resilience. As such, there has recently been a shift towards more integrative approaches that target these root causes of skin aging. By simultaneously addressing multiple molecular mechanisms, this strategy ensures more effective and lasting skin rejuvenation.

## THE NEXT-GENERATION SENOLYTIC ACTIVE

In response to this challenge, Mibelle Biochemistry introduced the novel stem cell senolytic active, a next-generation cosmetic active that targets the root causes of aging at the cellular level. Its unique Clear—Fill—Revive strategy supports the skin's natural regenerative processes at multiple levels, helping to visibly boost overall skin vitality and create an even more youthful appearance. The stem cell senolytic combines three potent extracts that will clear, fill, and revive the skin (INCI: Malus Domestica Fruit Cell Culture Extract (and) Vitis Vinifera (Grape) Fruit Cell Extract (and) Rhododendron Ferrugineum Extract (and) Glycerin (and) Pentylene Glycol (and) Aqua/Water). Firstly, alpine rose extract provides senolytic activity, which helps to eliminate senescent cells. Meanwhile, apple stem cell extract activates dermal stem cells, which helps to boost collagen production and improve skin density. Finally, grape stem cell extract enhances keratinocyte stem cell function, refining the epidermis and strengthening the skin barrier. Combined, the stem cell senolytic

active addresses aging at multiple levels, which results in smoother, firmer, and more youthful-looking skin.

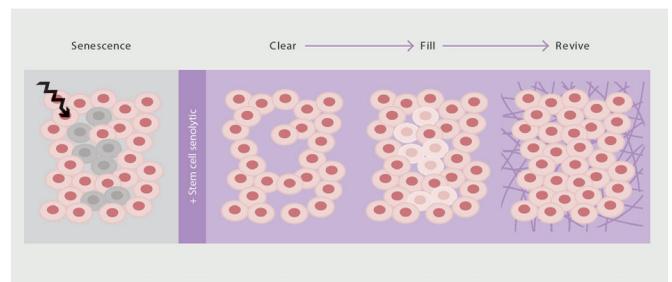


Figure 1: Clear-Fill-Revive: A Targeted Approach for Skin Rejuvenation

## CELLULAR SENESCENCE, “ZOMBIE CELLS” AND SKIN AGING

Cellular senescence is a state of irreversible cell cycle arrest and can significantly contribute to the aging process throughout the entire body. Senescent cells no longer divide but remain metabolically active, secreting a mix of inflammatory molecules known as the senescence-associated secretory phenotype (SASP). Senescent cells have earned the nickname “zombie cells” because much like zombies, they are not fully alive (as they no longer divide), but they are also not dead (as they continue to function and release harmful substances). Zombie cells accumulate in tissues over time and disrupt normal cellular function.

In the skin, zombie cells contribute to collagen degradation, elastin breakdown, and impaired fibroblast function. This will ultimately result in wrinkles, sagging, and a loss of skin elasticity. The SASP factors secreted by the zombie cells can also negatively impact neighboring cells, including skin stem cells, which will further worsen tissue dysfunction, reduce the skin's ability to regenerate, and accelerate aging.

**SENOLYTICS: CLEARING THE PATH FOR RENEWAL**

Senolytics are compounds that selectively induce programmed cell death (apoptosis) in senescent cells, thereby reducing their harmful impact. By clearing senescent cells, senolytic interventions can help to rejuvenate tissues and promote healthy aging. The novel active incorporates alpine rose extract, a natural senolytic agent that has demonstrated potent activity in clearing zombie cells.

In a study using human dermal fibroblasts exposed to oxidative stress, treatment with 1% alpine rose extract reduced the proportion of senescent cells from 28.1% to 10.1%, outperforming the well-known senolytic drug Navitoclax (12.3%). Importantly, healthy cells remained unaffected, confirming the selective nature of the extract.

**STEM CELL ACTIVATION: FILLING THE GAPS FROM WITHIN**

Stem cells in the skin play a vital role in maintaining firmness, resilience, and a youthful appearance. Epidermal stem cells re-

generate keratinocytes, while dermal stem cells produce fibroblasts essential for collagen synthesis and structural integrity. However, with age, both populations decline in number and function, leading to reduced collagen production, diminished elasticity, and visible signs of aging. Stimulating these stem cells can restore skin density, reinforce the barrier, and support long-term rejuvenation.

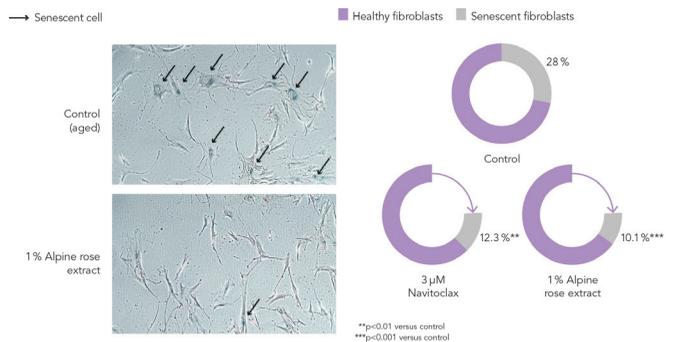


Figure 2: Senolytic Activity: Selective Clearance of Senescent Cells

**happi**

**2026 CORPORATE PROFILES**

A year-round reference guide published in February and sent to more than 16,000 Happi subscribers worldwide and distributed at industry events throughout the year.

Tom Frangis | 201-787-8240  
tfrangis@rodmanmedia.com

Andrew Downey | 973-487-0567  
adowney@rodmanmedia.com

**Reserve your space by January 6!**

Once senescent cells are cleared, the skin is primed for renewal. The stem cell senolytic activates both dermal and epidermal stem cells, replenishing the skin with fresh, functional cells. Treatment with 0.1% apple stem cell extract, an individual component of the active, increased secondary sphere formation by 43% in dermal stem cells, indicating improved regenerative potential. Furthermore, grape stem cell extract boosts keratinocyte stem cell activity in a dose-dependent manner, with colony formation rising up to 77.5% at 1.25%. In summary, the individual components of the stem cell senolytic boost dermal and epidermal stem cell function.

**REVIVING SKIN STRUCTURE AND VITALITY**

The final phase of the Clear-Fill-Revive approach focuses on revitalizing the skin by integrating newly generated cells into the dermal and epidermal architecture. This step is essential for restoring the skin’s structural integrity and enhancing its functional capacity.

In a 3D dermis model, aged dermal stem cells treated with 0.4% of the stem cell senolytic formed stratified dermal structures with a thickness of 66.7 μm, comparable the dermal architecture produced by young stem cells (66.4 μm). In contrast, untreated aged cells produced significantly thinner and less organized structures (53.0 μm), highlighting the rejuvenating effect of the active. Using Herovici staining, the active was further shown to increase collagen III (young collagen) levels by 19% in human skin explants. This collagen type is essential for elasticity and resilience, and its stimulation helps combat sagging and wrinkles. Together, these findings demonstrate that the active not only promotes cellular renewal but also restores the skin’s foundational matrix, completing the rejuvenation process from within.

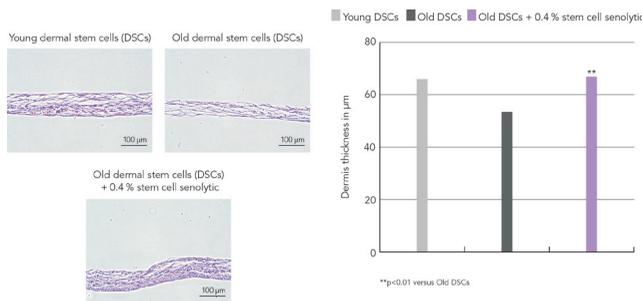


Figure 3: Strengthened Dermal Structure Despite Aging

**CLINICAL EFFICACY**

To confirm the cellular and mechanistic effects observed in vitro and ex vivo, a placebo-controlled clinical study was conducted involving 22 female volunteers between the ages of 40

and 70. Each participant applied a cream containing 2% of the active ingredient to one side of the face and a placebo to the other, twice daily for a duration of 28 days. Instrumental measurements revealed significant improvements in key skin parameters: hydration increased by 14.8%, elasticity improved by 16.0%, density was enhanced by 5.0%, and firmness showed the most pronounced change with a 20.5% increase. These results demonstrate that the active delivers visible anti-aging benefits under real-world conditions.

The study also evaluated the impact of gravitational strain on facial skin, comparing wrinkle depth in both sitting and lying positions. Before treatment, wrinkles appeared deeper in the sitting position due to the effects of gravity. After 28 days of treatment, wrinkle depth was significantly reduced by 10.4% in the sitting position and by 8.5% in the lying position, suggesting that the active not only improves skin structure but also helps counteract gravity-induced signs of aging.

These quantitative findings were supported by high-resolution photographs taken before and after the treatment period. The images revealed a noticeable reduction in crow’s feet, softening of fine lines, and less pronounced nasolabial folds. The skin appeared smoother, firmer, and more lifted, reinforcing the efficacy of the Clear-Fill-Revive strategy not only at the cellular level but also in terms of visible, real-world results.

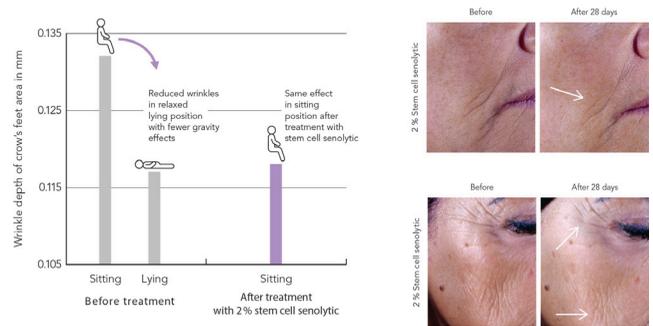


Figure 4: Anti-Gravity Effects and Visible Rejuvenation after 28 Days

**CONCLUSION: REDEFINING SKIN REJUVENATION**

The novel stem cell senolytic active represents a significant advancement in cosmetic science, moving beyond symptom-focused anti-aging to address the root causes of skin aging. Certified by COSMOS and NATRUE, and free from preservatives and alcohol, it meets modern standards for clean and ethical formulation. By combining senolytic clearance, stem cell activation, and structural reorganization, the Clear-Fill-Revive mechanism offers a holistic and effective solution for long-lasting skin rejuvenation. ■

[www.mibellebiochemistry.com](http://www.mibellebiochemistry.com)