ProliCell® BaiCare Technical Data Sheet

Exosome-Guided, Small RNA-Driven Hair Revival

Hair cycle-balancing Active

Origin

Developed from Scutellaria baicalensis (Chinese Skullcap) stem cells using ProliCell® Technology.

Effects

- Supports healthy hair growth by stimulating hair follicle activity through activation of the Wnt/β-catenin, PGE2 and Sonic Hedgehog signaling pathways.
- Helps protect against hair loss by reducing oxidative stress and inflammatory pressure in the hair follicle microenvironment.
- Contributes to enhanced follicular support by promoting mechanisms associated with angiogenesis around the hair follicle.

ProliCell® BaiCare DW (Disperses in water)
INCI Name: Glycerin, Scutellaria baicalensis callus culture, Xanthan Gum

ProliCell® BaiCare WS (Water-Soluble)
INCI Name: Glycerin, Scutellaria baicalensis callus culture, Sodium benzoate, Potassium sorbate

ProliCell® BaiCare ST (Sterile)
INCI Name: Aqua, Scutellaria baicalensis callus culture

Magic Effect with Small RNAs

DERMATOLOGICALLY TESTED

PATENT PENDING

SUSTAINABLE MATERIALS

COSMOS Approved

exosome

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ACTV BIOTECH

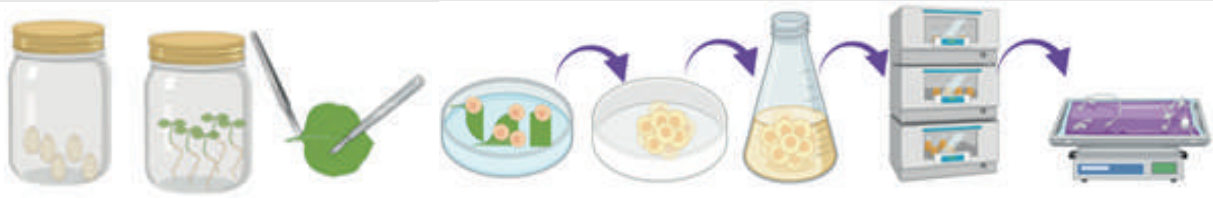
ProliCell® Technology

Prolicell® Technology has two different mechanisms of action. The first is the use of the plant stem cells and their components, and second is the use of small RNAs-enriched EVs (Extracellular vesicles), or exosomes, secreted from plant stem cells. Exosomes are small vesicles with a lipid structure that contain molecules such as peptides, lipids, secondary metabolites, mRNA, and small RNAs, and serve as important signaling molecules in intercellular communication. Small RNAs, which are found inside cells and are also encapsulated within exosomes, are short RNA molecules that play a crucial role in gene regulation. It has been shown in recent scientific studies that plant-derived small RNAs not only regulate plant cell functions but also influence gene expression in human cells.

Based on these studies, ProliCell® technology, which has a patent application, enables the synthesis of exosomes with enriched small RNA content from plant stem cells. Products developed using this technology contain plant stem cell components and exosomes enriched with small RNA secreted from stem cells. Plant stem cell-derived exosomes not only have cell renewal activity specific to stem cells, but also, due to the small RNAs they contain, exhibit regulatory effects on gene expression in human skin cells.

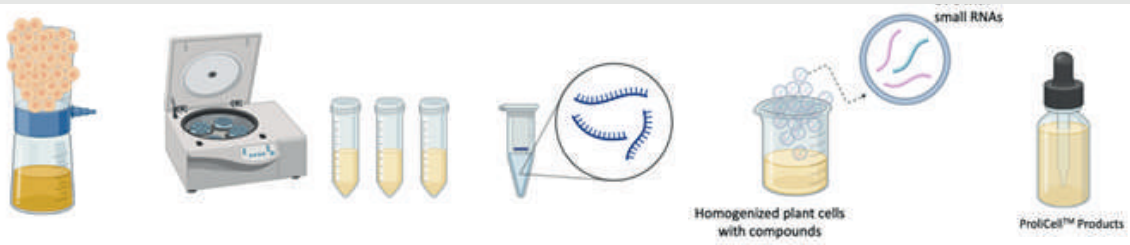
1. Actives from Plant Stem Cells

Plant stem cell technology is based on the principle of controlled propagation of dedifferentiated plant cells (plant stem cells) under sterile laboratory conditions and obtaining plant components specific to stem (dedifferentiated) cells. When plant tissues are mechanically damaged, they form cell clusters called callus to repair the damage. Callus cells have totipotent properties, meaning they have the ability to transform into all cell types and organs of the plant, and even to regenerate a whole new plant. For this reason, they are referred to as stem cells. Due to their totipotent nature, plant stem cells possess cell renewal and cell regeneration activity. Their ability to stimulate cell renewal is not limited to plants but is also observed in human skin cells. These properties make plant stem cells an effective cosmetic active ingredient.



2. . Isolation of Small RNAs from the supernatant

To obtain small RNA-enriched exosomes from plant stem cells, the cells are subjected to specific elicitor applications. Once the incubation with elicitors is complete, the cells are harvested and separated from the nutrient medium. The collected cells are kept under optimized conditions for a specific period until the next step is completed. A small sample is taken from the filtered nutrient medium, and exosomes are isolated from the medium using an ultrafiltration method.
Subsequently, small RNAs in the exosomes are isolated using RNA extraction methodologies. After the isolation step, the quantity and quality of small RNAs are measured, and the required amount of small RNA for production is optimized.
For each ProliCell product, optimization R&D studies are conducted to obtain small RNA-enriched exosomes. Once the optimization step is completed, small RNA-enriched exosomes and plant stem cells are combined to prepare ProliCell® products.



ProliCell® Technology

ProliCell® Production Process Flow:

• In vitro seedlings are obtained from seeds.
• A few leaf or stem fragments of the in vitro seedlings are mechanically injured to induce callus formation.
• The callus is transferred into a liquid culture to establish cell cultures.
• Plant stem cells are produced on a large scale in bioreactor systems under optimal growth conditions specific to each cell type.
• Through elicitor application, the synthesis yield of target small RNAs in plant cells is enhanced.
• After the incubation stage is completed, the cells are collected and separated from the culture medium.
• Exosomes are isolated from the culture medium.
• The small RNA content of the exosomes is measured.
• Exosomes (containing the target small RNAs) and plant stem cells are combined to prepare ProliCell® products.
• Finally, they are transformed into cosmetic active ingredients in both water-dispersible and water-soluble forms.

Advantages of ProliCell® Technology:

• Certified by Cosmos.
• Vegan certified.
• Halal certified.
• All production stages of ProliCell® Technology are 100% plant-based and derived from plant-origin materials. It contains no animal-derived ingredients or by-products and is not tested on animals.
• Eco-friendly. Only a few plant tissue fragments are needed to obtain plant cell cultures. This prevents excessive plant consumption, helping to conserve nature while saving labor and resources (soil and water).
• Allows the cultivation of even rare or endangered plant species.
• The plant materials used are free from environmental pollutants, herbicides, and pesticides.
• Production can be carried out independently of external factors such as soil composition, climate, and season.
• Target small RNA-containing exosomes are utilized through plant cell-specific elicitor stimulations.

ACTV BIOTECH

ProliCell® BaiCare (Chinese skullcap)

About two thousand years ago, **Scutellaria baicalensis** popularly known as Huang Qin (Chinese Skullcap) was discovered growing with its purple flowers in the foothills of ancient China. Recorded in the Shennong Bencao Jing, a classic medical text from the Han Dynasty, this plant was used to balance excess body heat and soothe inflammation. In Traditional Chinese Medicine, it was revered for supporting liver, lung, and circulatory health, as well as for its protective anti-aging properties.

Over time, Chinese Skullcap captured the attention of the scientific community with the discovery that its potent flavonoids such as baicalin and baicalein are effective in combating sensitivity, redness, and oxidative stress.

We drew inspiration from this ancient wisdom and reinterpreted it through biotechnology. Using ProliCell® technology, we developed BaiCare by utilizing exosomes enriched with small RNAs, derived from the stem cells of nature's wise plant, Scutellaria baicalensis.

ProliCell® BaiCare Production Process and Mechanism of Effect

Chinese Skullcap stem cells are incubated with elicitors during their optimum growth phases to induce the synthesis of exosomes rich in targeted small RNAs. These exosomes, containing enriched small RNAs, are combined with plant stem cells to create **ProliCell® BaiCare.**

Small RNAs, which are also carried by undifferentiated plant cells, play a role in communication with different cells, tissues, and even organisms when packaged inside exosomes. **ProliCell® BaiCare**, this intercellular communication effect of exosomes is utilized to regulate the activity of human scalp cells.

ProliCell® BaiCare, Chinese Skullcap stem cell components and enriched targeted small RNAs found in exosomes influence the expression of relevant genes in human scalp cells, thereby stimulating the expression of genes associated with hair growth and anti-hair loss activity.

ACTV Biotechnology has developed **ProliCell® BaiCare**, an active ingredient developed to fight hair loss and boost hair growth. It combines ProliCell Technology with the remarkable power of **Scutellaria baicalensis** stem cells and its exosomes enriched with small RNAs.

Proven Efficacy

ProliCell® BaiCare

- **ProliCell® BaiCare modulates cellular signaling pathways promoting hair development.**

The two most critical activator pathways for hair follicle formation, regeneration, and entry into the anagen phase are the Wnt/β-catenin and Sonic hedgehog (Shh) signaling pathways, which operate in coordination with each other. The Wnt/β-catenin signaling pathway is a regulator of hair morphogenesis, hair follicle regeneration, and specific hair cells such as hair matrix and dermal papilla cells. Activation of β-catenin, a component of the Wnt signaling pathway, promotes hair growth by prolonging the anagen phase. An increase in β-catenin expression supports proliferation and differentiation in keratinocytes, while aiding the survival of hair follicle epithelial cells.

PGE2 (prostaglandin E2) is a prostaglandin produced from arachidonic acid via cyclooxygenase enzymes. Increased PGE2 expression in keratinocytes prolongs the anagen phase by stimulating dermal papilla cells and the Wnt/β-catenin pathway in surrounding cells. PGE2 increases vascularization, balances keratinization, and contributes to maintaining a healthy follicle. As a crucial regulator of hair growth, the Wnt/β-catenin signaling pathway is stimulated by both β-catenin activation and increased PGE2 expression. The Sonic hedgehog (Shh) signaling pathway, stimulated by the Wnt/β-catenin pathway, is a critical pathway for hair follicle morphogenesis, entry into the anagen phase, and follicle regeneration. Its effect occurs directly through cell proliferation and the activation of hair epidermal stem cells. Shh signaling regulates the interaction between the dermal papilla and epidermal keratinocytes.

ProliCell BaiCare is a comprehensive and potent anagen inducer that simultaneously activates the Wnt/β-catenin, PGE2, and Shh signaling pathways.

It initiates the transition of hair stem cells into the growth phase (Wnt), maintains cell viability by extending the anagen duration (PGE2), and promotes hair thickening by increasing follicular depth (Shh).

ProliCell BaiCare ensures that hair growth signaling remains active by providing multi-targeted stimulation through these pathways.

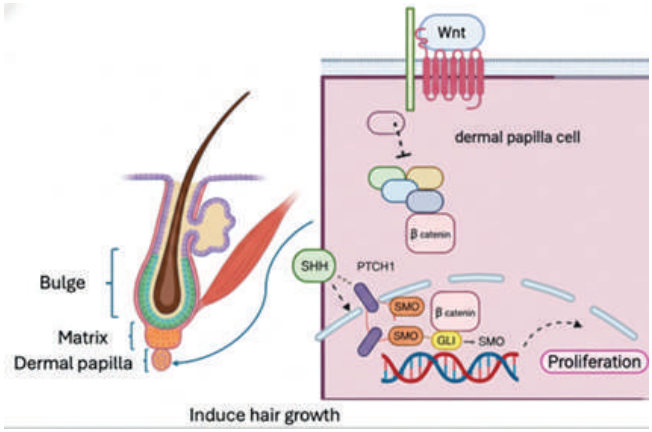


Figure 1. Wnt/β-catenin and Sonic hedgehog signaling pathways in dermal papilla cells.

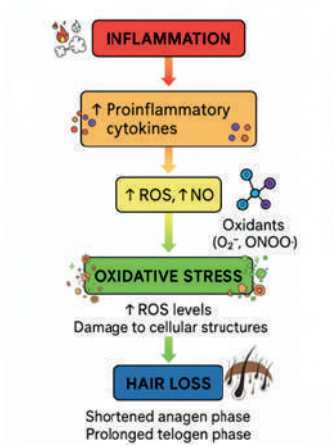


Figure 2. The process leading from inflammation to hair loss.

- **ProliCell® BaiCare prevents hair loss by suppressing scalp inflammation.**

  Environmental and physiological stressors such as UV radiation, environmental pollution, psychological stress, and microcirculation disorders activate the NF-κB signaling pathway in hair follicles, increasing the expression of pro-inflammatory cytokines like IL-8 and inflammation-associated enzymes such as iNOS. The elevation of these mediators leads to the accumulation of oxidative stress, shortening of the anagen phase, and acceleration of follicle miniaturization, thereby accelerating hair loss. TGF-β (Transforming Growth Factor-beta) is a cytokine that controls the hair growth cycle (anagen/-catagen/telogen). During inflammation, keratinocytes and fibroblasts increase TGF-β expression via secreted pro-inflammatory cytokines, while immune cells migrating to the inflammatory site both produce TGF-β and secrete cytokines that stimulate TGF-β production. Additionally, dermal papilla cells elevate TGF-β production under the influence of inflammatory cytokines and oxidative stress. Increased TGF-β causes premature termination of the anagen phase and early onset of the catagen phase, resulting in hair loss. Suppression of TGF-β expression increases keratinocyte proliferation, prevents the onset of catagen, and promotes hair growth by halting hair loss.

  ProliCell BaiCare, protects the hair structure and helps prevent hair loss by controlling oxidative stress, inflammatory pressure, and the catagen signaling pathway surrounding the hair.

- **ProliCell® BaiCare helps enhance the microcirculation surrounding the hair follicle.**

  VEGF (Vascular Endothelial Growth Factor) is the most important regulatory factor of angiogenesis (new blood vessel formation). The hair follicle requires an intense supply of nutrients and oxygen, particularly during the anagen phase. It is known that increased VEGFA expression strengthens the microvascular network surrounding the follicle, thereby supporting hair growth and maintaining follicle volume and hair shaft thickness.

  ProliCell BaiCare, supports microcirculation and hair growth by stimulating VEGFA.

- **ProliCell® BaiCare, contains exosomes enriched with small RNAs.**

  Small RNAs (sRNAs) are short, non-coding RNA molecules, typically 20–30 nucleotides in length, that regulate gene expression. Exosomes carry small RNAs such as miRNA, siRNA, and piRNA, as well as proteins, lipids, and certain metabolites.
  The small RNAs within exosomes play a role in regulating numerous biological processes, including intercellular genetic messaging, balancing oxidative stress, modulating immune response, wound healing, hair follicle regeneration, tissue regeneration, and angiogenesis.

  ProliCell BaiCare, contains exosomes derived from S. baicalensis stem cells, featuring a rich and potent content of small RNAs.

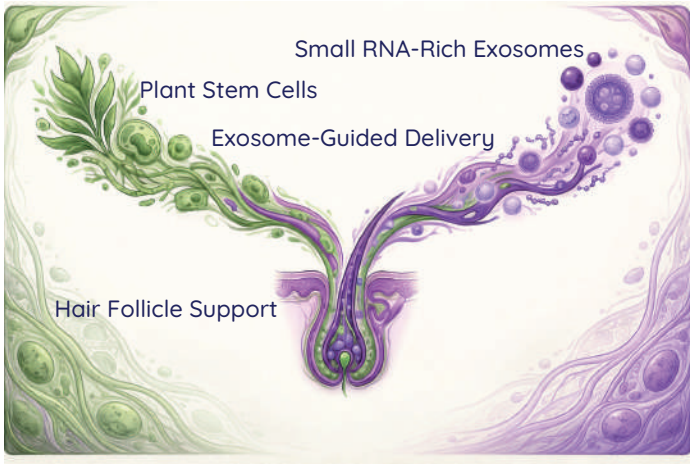
Efficacy Tests

In vitro Tests

Cell line: Keratinocyte cells and Human Umbilical Vein Endothelial Cells (HUVECs)

Test ingredient: 250 and 500 µg/mL ProliCell® BaiCare Bioactive (It is a composition of exosomes containing dissolved plant stem cells and enriched small RNAs in the cell culture medium)

Parameter: Sequence Analysis of Exosomal Small RNA, Determination of the Effect on Cell Viability by the MTT Assay, RT-qPCR Analysis of β-catenin, PGE2, SMO, GLI1, iNOS, IL-8, TGF-β and VEGFA Gene Expression. Determination of VEGF-A Protein by Western Blot Analysis, Angiogenesis Model by the Tube Formation Assay, For gene expression analysis, fibroblast cells were incubated with ProliCell BaiCare concentrations for 24 hours.



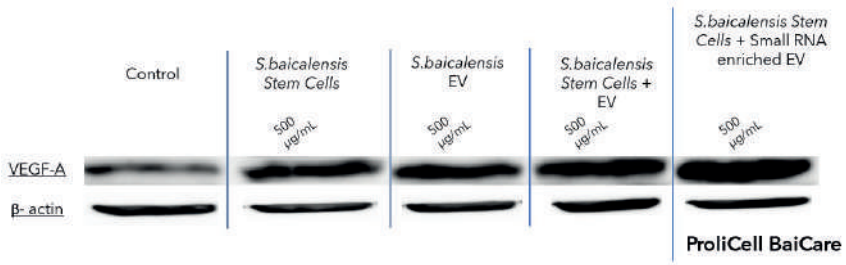
ProliCell® BaiCare
Exosome-Guided Hair Revival

Assessment of the impact of small RNA-enriched EVs

In vitro efficacy studies, comparisons were made between the group treated with S. baicalensis stem cells (Group 1), the group treated with S. baicalensis stem cells and EVs (Group 2), and the **ProliCell® BaiCare** group (Group 3, treated with S. baicalensis stem cells and small RNA-enriched EVs).
In vitro efficacy tests, while the combined application of S. baicalensis stem cells and EVs was found to be more effective than the application of S. baicalensis stem cells alone, the group treated with the combination of S. baicalensis stem cells and small RNA-enriched EVs (ProliCell® BaiCare) was determined to be the most

Expression of Angiogenesis-Related Proteins

The effect of ProliCell® BaiCare on the protein expression of **VEGF-A**, a protein associated with angiogenesis, was evaluated in HUVEC cells using Western Blot analysis.



Treatment with **ProliCell® BaiCare** resulted in a **90%** increase in **VEGF-A protein expression** relative to the control.

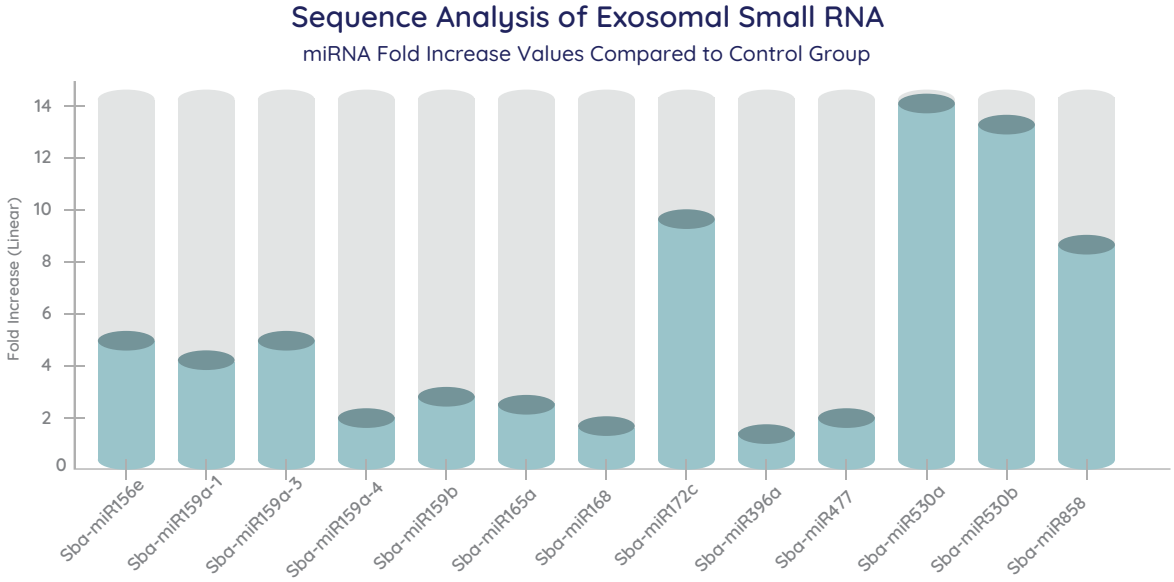
Comparative analysis of Western Blot band intensities reveals that small RNA-enriched EVs demonstrate a significantly more potent effect in upregulating VEGF-A protein expression than control EVs.

ProliCell® BaiCare contributes to the support of biological mechanisms associated with vascular formation around the hair follicle by increasing **VEGF-A protein expression.**

Efficacy Tests

Sequence Analysis of Exosomal Small RNAs Derived from Scutellaria baicalensis Stem Cells

S. baicalensis stem cells were subjected to various stress conditions to induce the synthesis of exosomes enriched with small RNAs. After isolating exosomal small RNAs from the obtained control group and the most effective treatment group, they were sequenced and analyzed on the DNBSEQ-G400 next-generation sequencing platform using a Single Primer Isothermal Amplification (SPIA)-based library preparation procedure (NuGEN, USA). High-quality exosomal small RNA NGS data were processed using comprehensive bioinformatics analysis protocols to perform the detection and characterization of miRNA profiles.
Subsequently, analyses based on quantitative abundance estimation were performed to identify differentially expressed miRNAs between the control and experimental groups. Through these analyses, significant differences in miRNA expression variations were determined, revealing the changes in the miRNA profile under experimental conditions.



ProliCell® BaiCare contains exosomes derived from Scutellaria baicalensis stem cells, carrying a rich and effective small RNA composition.

Figure 1. Differential expression of exosomal miRNAs following elicitor treatment compared to the control group.

In the most effective treatment group compared to the control, 13 different miRNAs were identified with upregulated expression: Sba-miR156e, Sba-miR159a-1, Sba-miR159a-3, Sba-miR159a-4, Sba-miR159b, Sba-miR165a, Sba-miR168, Sba-miR172c, Sba-miR396a, Sba-miR477, Sba-miR530a, Sba-miR530b, and Sba-miR858. Among these, Sba-miR156e, Sba-miR159a-1, Sba-miR159a-3, Sba-miR159a-4, and Sba-miR172c were expressed in the experimental group while being absent in the control group.Furthermore, it was determined that the expression of Sba-miR530b increased by 14-fold, Sba-miR858 by 9.5-fold, Sba-miR530a by 21-fold, and Sba-miR159b by approximately 3.2-fold.
In summary, a significant increase in the expression levels of Sba-miR530b, Sba-miR858, Sba-miR530a, and Sba-miR159b was observed in the experimental group compared to the control group.

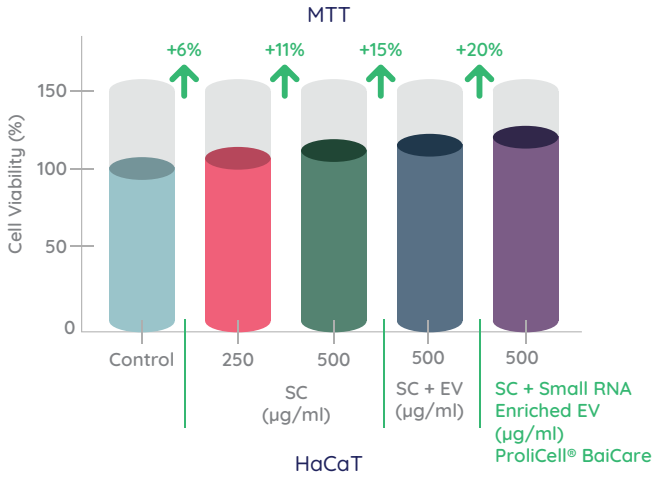
Based on findings obtained from in vitro studies, these miRNAs—known to play a role in regulating growth, tissue regeneration, and stress adaptation processes in plants—appear to offer potential for indirect contribution to supportive biological processes within the human hair follicle micro-environment (Table 1).

Table 1. Functions of exosomal small RNAs derived from Scutellaria baicalensis stem cells in plants and their potential benefits in hair follicles.

miRNA	Function in the Plant	Potential Biological Effects within the Hair Follicle Microenvironment
miR530 Family (a,b)	Regulation of plant growth, development, and maturation duration; tolerance to biotic and abiotic stresses; and organization of vascular tissues. (Li et al., 2021, Ding et al., 2022).	Regulation of the hair growth cycle, improvement of follicular stress resistance, and support of hair follicle microcirculation.
miR159 Family (a-1, a-3, a-4, b)	Regulation of cell proliferation and hormonal growth signaling (Allen et al., 2007; Alonso-Peral et. al, 2010; Millar et. al, 2019).	Promoting matrix cell proliferation and maintaining the signaling balance of the hair growth cycle.
miR156e	Initiation of early phases of growth, root and shoot development (Wu et al., 2009; Huijser & Schmid, 2011;Wang and Wang 2015)	Support of the telogen-to-anagen transition, and enhancement of hair follicle activity and hair growth.
miR172c	Initiation of flowering and developmental phase transitions, regulation of floral organ identity (Zhu & Helliwell 2011; Aukerman & Sakai, 2003)	Balancing hair follicle cycle transitions, supporting hair shaft differentiation and keratinization.
miR396a	Regulation of cell proliferation and stress response (Rodriguez 2016; Liu et al., 2009; Guo, L. et. al., 2022; Yuan, H., et al. 2024))	Promotion of follicular cell regeneration and modulation of stress-related scalp responses.
miR858	Activation of antioxidant polyphenol pathways (Sharma et al., 2016;Wang et al., 2016; Camargo-Raminez R et al., 2018)	Strengthening the defense against oxidative stress; supporting the protection of the scalp-follicle microenvironment.
miR165a	Root apical meristem, regulation of vascular activity, stress response. (Carlsbecker et al., 2010; Yan et al.,2016; Mirlohi et al., 2024).	Supporting the follicle microenvironment and hair root nutritional balance, maintaining scalp balance under stressful conditions.
Sba-miR168	Regulation of the miRNA system, developmental balance, and stress response. (Vaucheret 2008; Mllary and Vaucheret 2010; Li et al. 2012).	Helping to maintain scalp and hair follicle balance by regulating developmental balance and stress response.
Sba-miR477	Stress response (Wang et al. 2020; Hu et al. 2020).	Contributes to balancing the stress response; helps protect the scalp and hair follicles under stressful conditions.

Effects on Cellular Viability

Keratinocytes form the epidermis and the outer root sheath of the hair follicle. Cell viability of human keratinocytes **(HaCaT)** treated with ProliCell® BaiCare and other groups was assessed via the **MTT assay.**



Following 24 hours of incubation, treatment with S. baicalensis stem cells enhanced cell viability by **6%** and **11%** at concentrations of **250 µg/mL** and **500 µg/mL,** respectively. The co-administration of S. baicalensis stem cells and EVs resulted in a **15%** increase, whereas ProliCell® BaiCare (S. baicalensis stem cells + enriched EVs) achieved a **20%** increase in cell viability.

ProliCell® BaiCare, supports the regeneration of the hair follicle outer root sheath and the maintenance of scalp health by increasing keratinocyte proliferation.

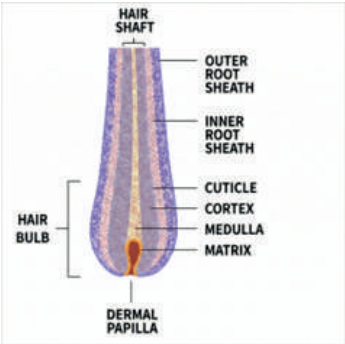
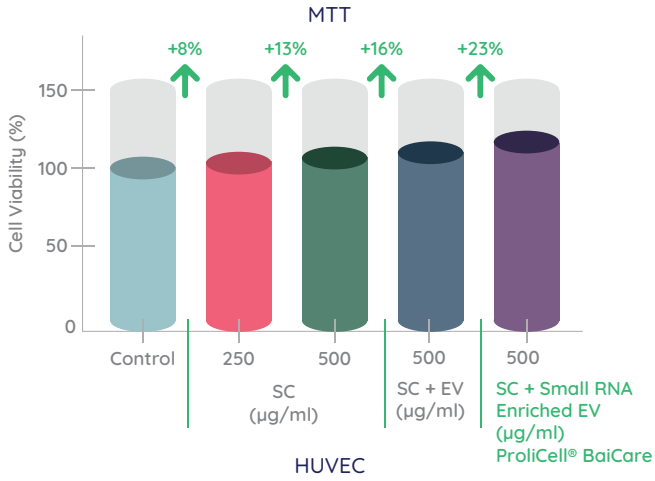


Figure 3. Hair strand structure.

Endothelial cells form the blood vessels that nourish the hair. The impact of ProliCell® BaiCare and other groups on the viability of human endothelial cells **(HUVEC)** was also assessed via the **MTT assay.**



Following 24 hours of incubation, compared to the control, treatment with S. baicalensis stem cells alone (**500 µg/mL)** increased cell viability by **13%.** This increase reached **16%** with the co-administration of S. baicalensis stem cells and EVs, and **25%** with ProliCell® BaiCare (S. baicalensis stem cells and small RNA-enriched EVs).

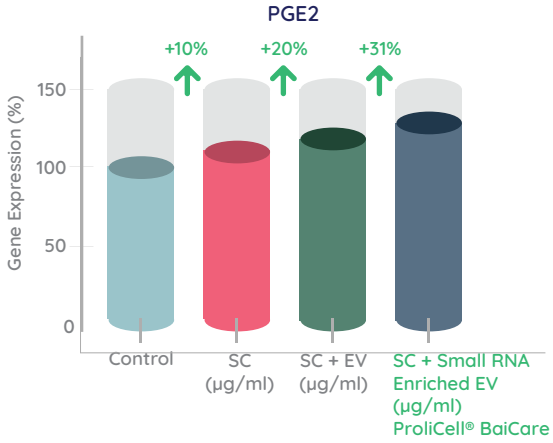
ProliCell® BaiCare, supports the maintenance of vascular integrity and the nourishment of hair follicles by promoting endothelial cell viability.

Expression Analysis of Genes Associated with Hair Growth

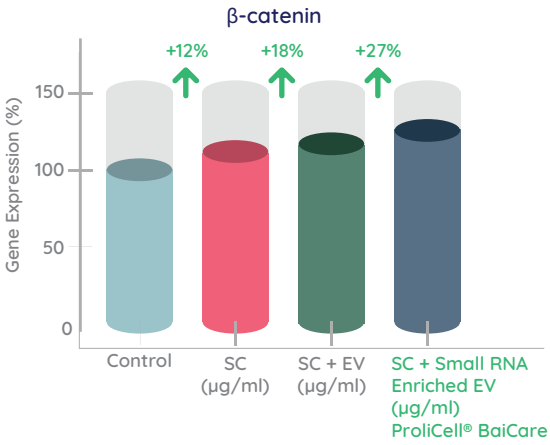
Increased PGE2 expression in keratinocytes stimulates the **Wnt/β-catenin** pathway in dermal papilla and surrounding cells, thereby prolonging the anagen phase. **PGE2** enhances vascularization, regulates keratinization, and contributes to the maintenance of follicle health.

The **SMO** receptor, activated by Sonic Hedgehog signaling, initiates the intracellular signal cascade and translocates the **GLI1** transcription factor into the nucleus, directly upregulating genes responsible for the proliferation of keratinocytes and dermal papilla cells.

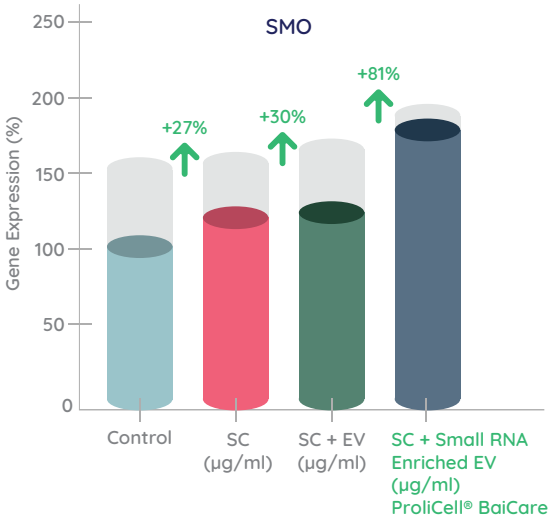
The expression levels of PGE2, β-catenin, SMO and GLI1 genes from the RT-qPCR assay performed on HaCaT cells are presented in the graphs.



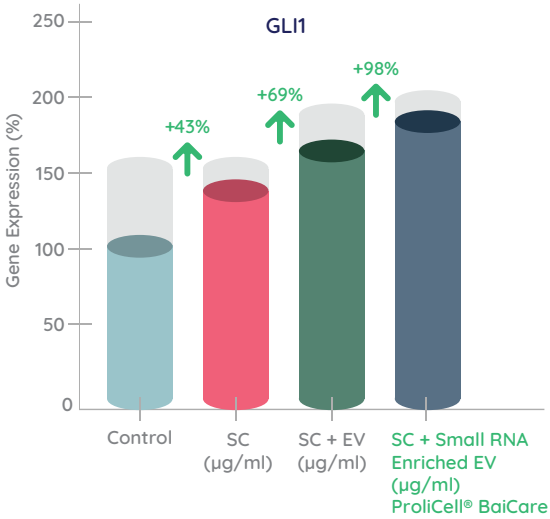
S. baicalensis 500 (µg/ml)



S. baicalensis 500 (µg/ml)



S. baicalensis 500 (µg/ml)



S. baicalensis 500 (µg/ml)

Compared to the control group, **PGE2** gene expression increased by **10%** in the group treated with S. baicalensis stem cells alone, by **20%** in the group treated with the combination of stem cells and EVs, and by **30%** in the group treated with ProliCell® BaiCare (stem cells + small RNA-enriched EVs).

Similarly, **β-catenin** gene expression increased by **12%** in the group treated with S. baicalensis stem cells alone, by **18%** in the combined stem cell and EV group, and by **27%** in the ProliCell® BaiCare group, compared to the control.

SMO gene expression increased by **27%** in the group treated only with S. baicalensis stem cells, **30%** in the group treated with a combination of stem cells and extracellular vesicles (EVs), and **81%** in the group treated with ProliCell BaiCare, compared to the control group.

GLI1 gene expression increased by **43%** in the group treated only with S. baicalensis stem cells, **69%** in the group treated with a combination of stem cells and EVs, and **98%** in the group treated with ProliCell® BaiCare, compared to the control group.

These results indicate that small RNA-enriched EVs are more effective in stimulating PGE2, β-catenin, SMO and GLI1 gene expression compared to control EVs.

ProliCell® BaiCare supports the biological activity of the hair follicle by stimulating the **Wnt/β-catenin, PGE2** and **Sonic hedgehog** signaling pathways, contributing to healthy hair growth.

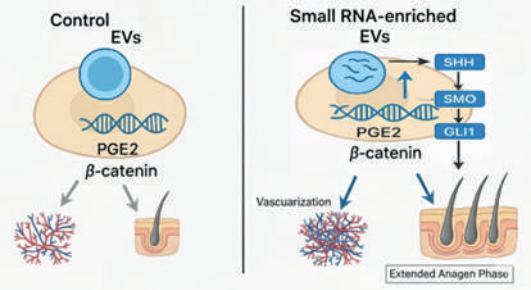
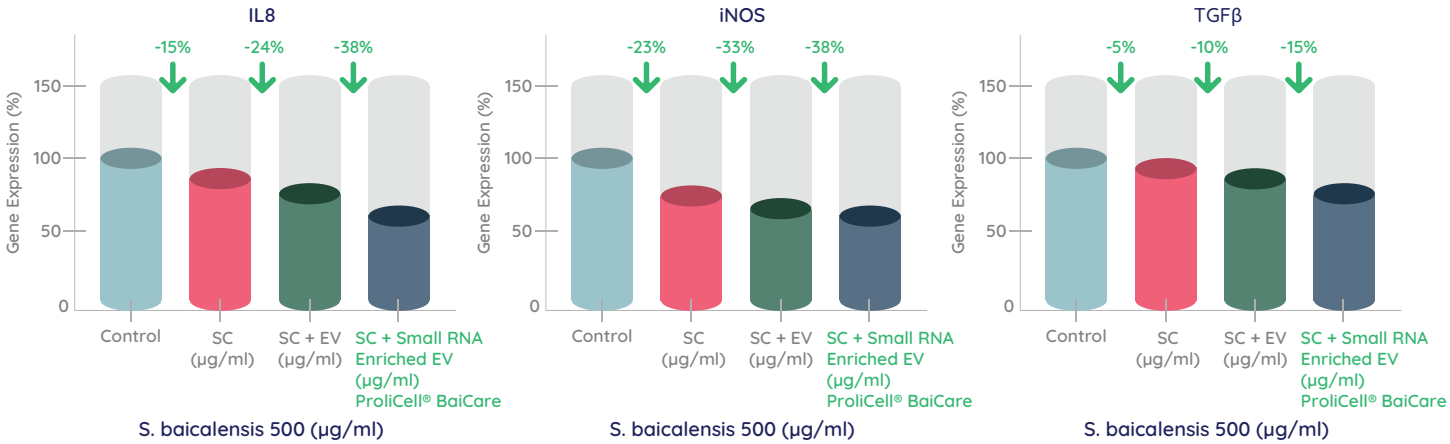


Figure 4. Effects of control and small RNA–enriched EVs on vascularization and the anagen phase.

Expression Analysis of Inflammation-Associated Genes

Suppression of the gene expression of **IL-8**, an inflammatory cytokine, protects the hair follicle against inflammation. The suppression of oxidative stress-induced **iNOS** gene expression contributes to the restoration of oxidative balance by reducing excessive NO production. Furthermore, the suppression of **TGF-β** gene expression, which initiates catagen, helps reduce hair shedding and sustain the growth phase by preventing the premature exit of the hair follicle from the anagen phase.

To induce inflammation in HaCaT cells, the cells were treated with IFN-γ (10 ng/mL) and TNF-α (10 ng/mL) cytokines for 24 hours. The inflammation-induced HaCaT cells were then incubated with ProliCell® BaiCare and the other experimental groups for 24 hours. The IL-8, iNOS, and TGF-β gene expression levels obtained from the subsequent RT-qPCR analysis are presented in the graphs.



Compared to the control group, **IL-8** gene expression decreased by **15%** in the group treated with S. baicalensis stem cells alone, by **24%** in the group treated with the combination of stem cells and EVs, and by **38%** in the group treated with ProliCell® BaiCare (stem cells + small RNA-enriched EVs).

iNOS gene expression was reduced by **23%** in the group treated with S. baicalensis stem cells, by **33%** in the combined stem cell and EV group, and by **38%** in the ProliCell® BaiCare group, compared to the control.

TGF-β gene expression decreased by **5%** in the group treated with S. baicalensis stem cells, by **10%** in the combined stem cell and EV group, and by **15%** in the ProliCell® BaiCare group relative to the control.

These results demonstrate that small RNA–enriched EVs are more effective than control EVs in suppressing the expression of IL-8, iNOS, and TGF-β genes.

ProliCell® BaiCare contributes to the regulation of the inflammatory microenvironment in the hair follicle by suppressing the expression of inflammation-associated genes **IL-8, iNOS,** and **TGF-β**.

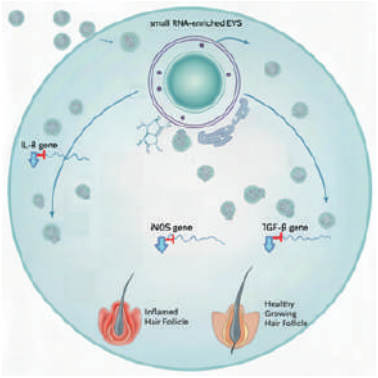
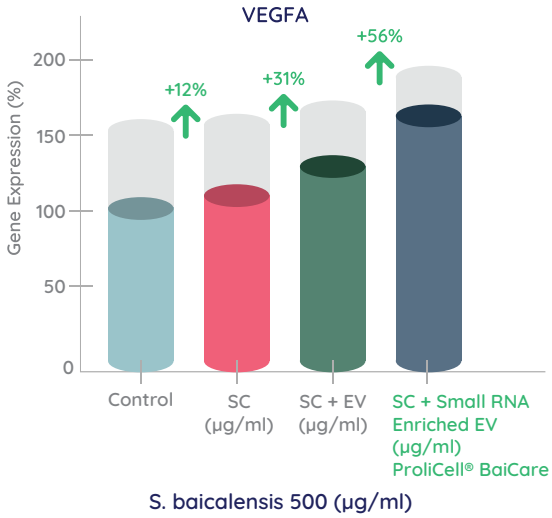


Figure 5. Effects of small RNA–enriched EVs on inflammatory gene expression.

Expression of Angiogenesis-Related Genes

Increased VEGFA expression supports angiogenesis and new capillary formation surrounding the hair follicle, thereby aiding in follicular nourishment. The results of **VEGFA** gene expression from the RT-qPCR



Compared to the control group, **VEGFA** gene expression increased by **12%** in the group treated with S. baicalensis stem cells alone, by **31%** in the group treated with the combination of stem cells and EVs, and by **56%** in the ProliCell® BaiCare group (stem cells + small RNA-enriched EVs).

These results demonstrate that small RNA-enriched EVs are more effective in stimulating VEGFA gene expression compared to control EVs.

ProliCell® BaiCare contributes to supporting the biological mechanisms associated with angiogenesis around the hair follicle by significantly increasing **VEGFA gene expression.**

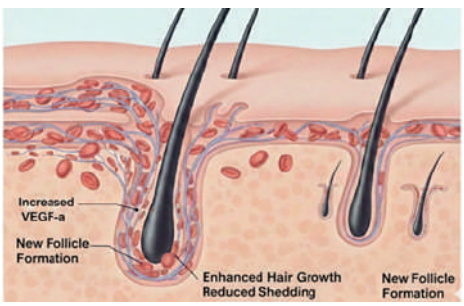
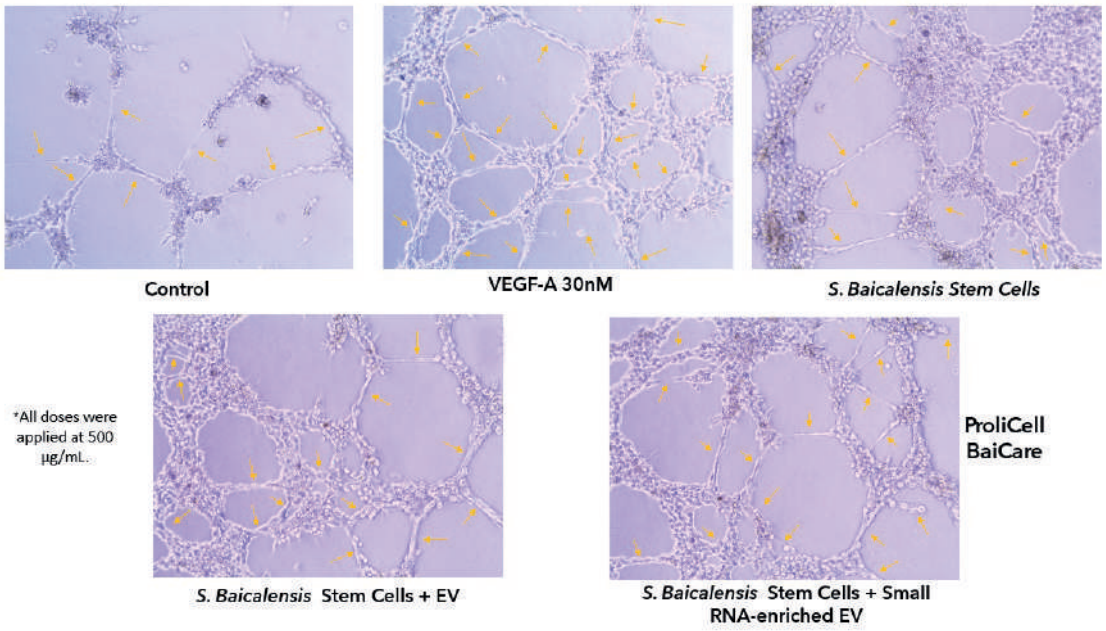


Figure 6. Vascularization in the hair follicle associated with increased VEGFA expression.

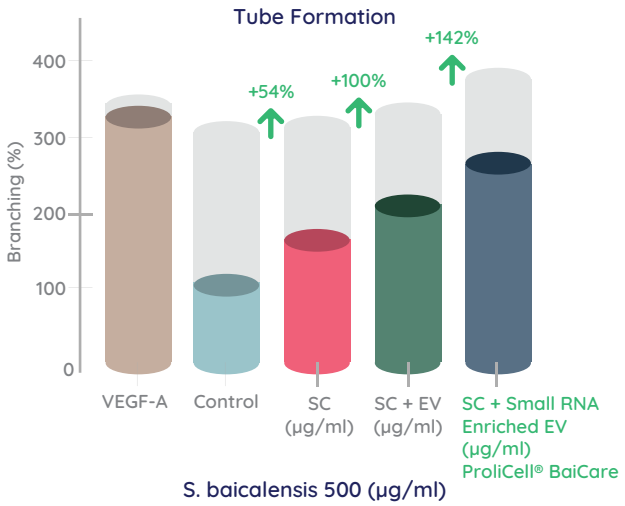
In vitro Angiogenesis Model

The effect of ProliCell® BaiCare on new blood vessel formation was evaluated using an in vitro angiogenesis model performed with HUVEC cells. VEGF-A (30 nM) was used as the positive control.



In the tube formation assay performed with **HUVEC** cells, tube branching points are indicated by yellow arrows in the images obtained via phase contrast microscopy. Limited, short, and open-ended tubular structures were observed in the control group.

In contrast, a dense and organized tube network formation was observed in the positive control group (VEGF-A 30 nM). While increased branching was observed in the groups treated with S. baicalensis stem cells, the group treated with ProliCell® BaiCare (stem cells combined with small RNA-enriched EVs) notably exhibited a denser, interconnected and organized tube network. The quantitative analysis of branching numbers is presented in the graph.



The number of branches formed by endothelial cells increased by **54%** in the group treated with S. baicalensis stem cells, by **100%** in the group treated with the combination of stem cells and EVs, and by **142%** in the group treated with ProliCell® BaiCare (stem cells + small RNA enriched EVs), compared to the control.

ProliCell® BaiCare promotes VEGF-A expression and blood vessel formation mechanisms in endothelial cells, thereby facilitating the biological processes essential for microcirculation surrounding the hair follicle.

In Vivo Efficacy Test

Anti-hair Loss Activity

Clinical evaluation with test treatment were conducted on 26 volunteers aged among 42-69.

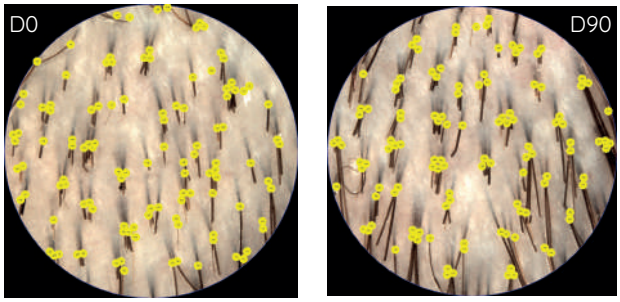
The volunteers were men and women with hair loss, varying scalp types (sensitive or non-sensitive), and different hair types (curly, straight, etc.).

The treatment involved applying shampoo containing 3% ProliCell® BaiCare to the hair three times a week and serum containing 5% ProliCell® BaiCare to the scalp daily for 90 days. Measurements were recorded before treatment (D1), during treatment (D90), and after 20 weeks of treatment (D150).

EVALUATION OF HAIR DENSITY BY TRICHOSCAN®

TrichoScan® was used as an objective and standardized method for the quantitative evaluation of hair density, providing high-resolution and reproducible measurements of hair follicles within a defined scalp area.

- Trichoscan defined as the number of hairs present in a unit of area (generally cm^2).
- Increased hair density density at the end of the study of the efficacy of regeneration treatment.
- The number of hairs present by unit of area was calculated from images of the scalp taken with the TrichoScan® microcamera.



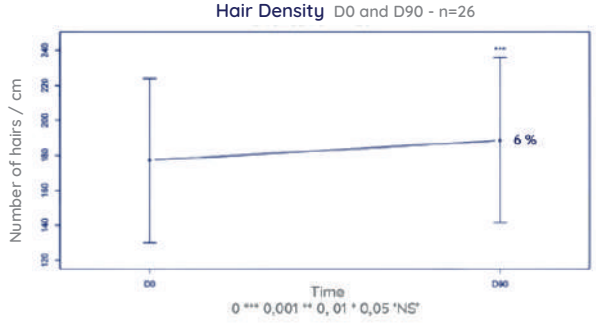
TrichoScan® microcamera photograph (D0, D90)

After 90 days of application:

- Visible reduction in miniaturized hairs,
- Enhanced scalp density and follicular productivity was observed.

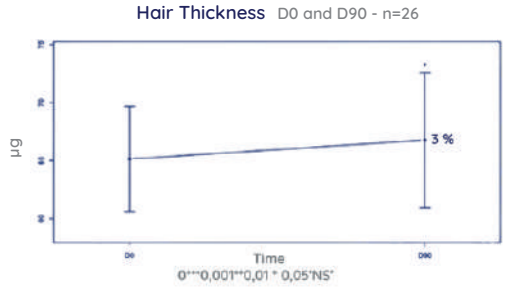
EVALUATION OF THE HAIR DENSITY

After 90 days, it showed a mean hair density improvement of 6% compared to baseline values.



EVALUATION OF THE HAIR THICKNESS

After 90 days of continuous use of the product, the hair thickness increases an average of 3% in relation to baseline.

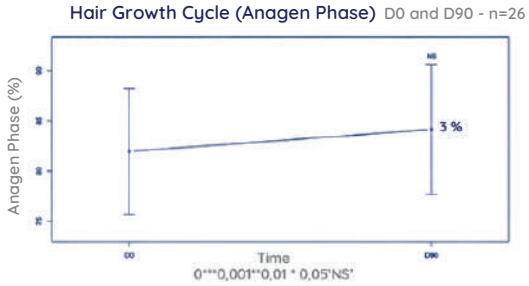


EVALUATION OF THE HAIR GROWTH CYCLE

To demonstrate the product's effect on follicular activity, hair growth cycle parameters were evaluated. The anagen phase reflects active hair growth, whereas the telogen phase represents the resting or shedding phase.
The anagen/telogen (A/T) ratio is considered a key indicator of overall hair growth dynamics and follicular health, as it reflects the balance between growing and resting hair follicles.

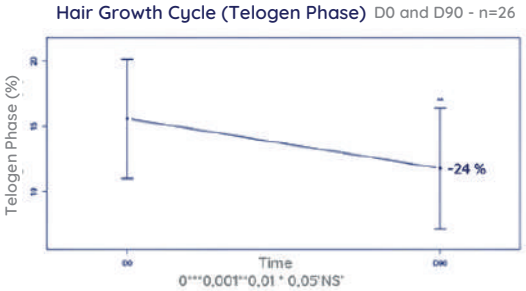
Hair Growth Cycle (Anagen Phase)

After 90 days of continuous use of the product, the number of hairs in anagen phase increases an average of 3% in relation to baseline.



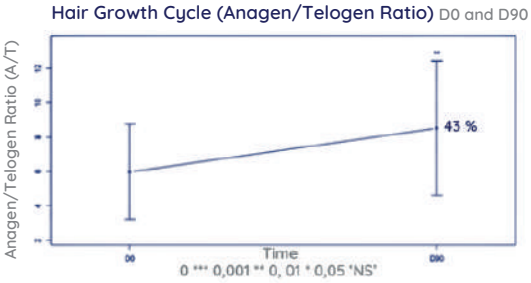
Hair Growth Cycle (Telogen Phase)

The number of hairs in telogen phase decreases an average of 24% in relation to baseline.



Hair Growth Cycle (Anagen/Telogen Ratio)

The Anagen/Telogen ratio increases an average of 43% in relation to baseline.



In Vivo Efficacy Test

COMBING AND WASH TEST:

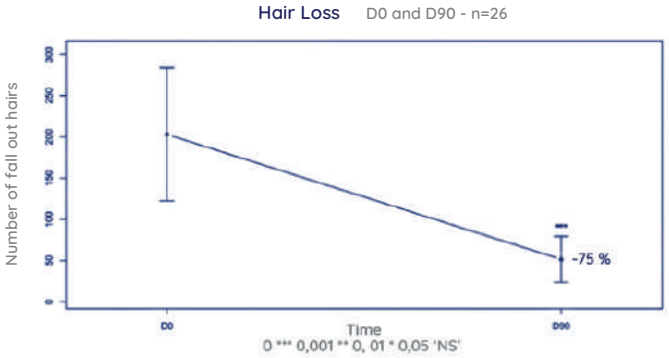
The number of hairs shed during hair combing and washing under standardized conditions was determined.

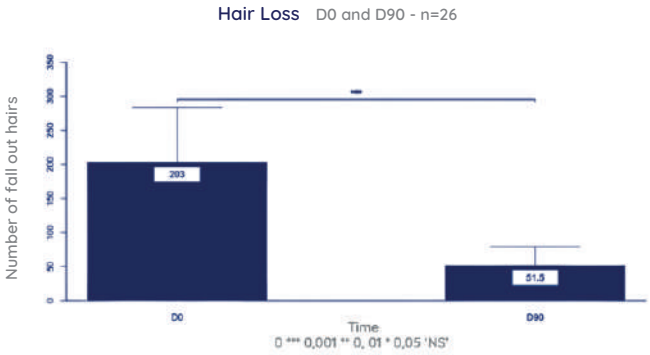
As a precondition, the volunteers came to the visit without having washed their hair at least 48 hours before and without having combed their hair at least 24 hours before, in order to maintain the hairs which are near the end of telogen phase and avoid artificial reduction in the percentage of hairs in telogen phase.

Effects of Anti-Hair Loss Shampoo and Serum on hair shedding after wash and combing (D0 and D90)

EVALUATION OF HAIR LOSS

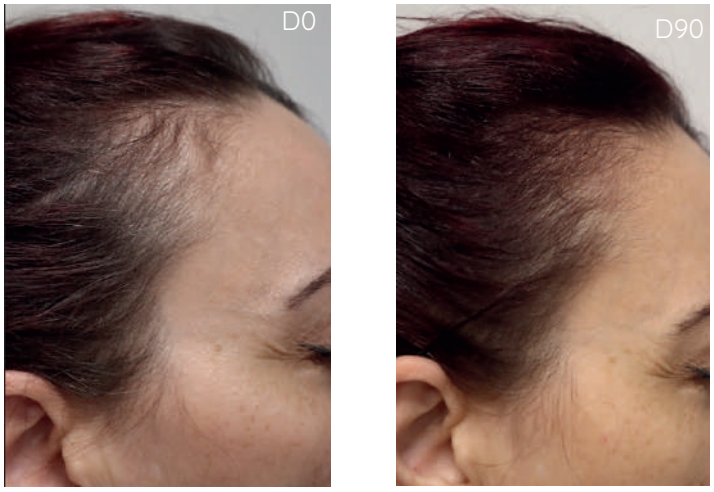
After 90 days of continuous use of the product, the number of fall out hairs decreases an average of 75% in relation to baseline.





EFFECT ON VOLUNTEERS

- ProliCell® BaiCare Shampoo was used 3 times per week at a dose of 3–4 pumps per wash.
- ProliCell® BaiCare Serum was used once daily at a dose of 4–5 pumps per application.
- Visual evaluation was performed at Day 90.



The effect of Anti-Hair Loss Shampoo and Serum on hair density (D0 vs. D90) was evaluated using a Canon EOS 250D camera

ProliCell® BaiCare Technical Data Sheet

Exosome-Guided, Small RNA-Driven Hair Revival

Hair cycle–balancing Active

Effect Mechanisms

- Supports hair follicle activity.
- Helps reduce inflammatory stress.
- Promotes vascular support and microcirculation.
- Contributes to healthier and stronger hair growth

Cosmetic Uses

- Hair Serums (leave-on / rinse-off)
- Hair Care Creams & Conditioners
- Scalp Serums & Tonics
- Anti-hair loss treatments
- Hair strengthening & growth-support products.

Features

Origin: **Herbal**
Appearance: **Viscous cell lysate suspension**
Color: **Dark Brown**
Odor: **Characteristic**
Usage: **Add below 40°C in cold-hot processes.**
Usage rate: **2-5%**
pH: **5.0-7.0**

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