



Clearing Age-Promoting Cells for Youthful Skin

Alpine Rose Active is a natural active ingredient based on an organic Swiss alpine rose leaf extract. It is the first cosmetic ingredient to act as a so-called senolytic. That means it specifically eliminates senescent cells to rejuvenate the tissue. Clinical studies demonstrate a decrease in skin redness, increased elasticity and photoprotection, rejuvenating the skin from the inside-out.

Alpine Rose Active is based on the leaves of *Rhododendron ferrugineum*, which is also known as alpine rose. This is one of the most typical and iconic plants of the Swiss Alps. This evergreen plant, which grows at high altitudes (up to 2,800 m) in the Alps but also in the Jura, Pyrenees, and Apennines, in acidic and nutrient-poor soils, can live for more than 100 years. Like other alpine plants, the alpine rose has developed diverse strategies in order to cope with extreme environmental conditions, such as large variations in temperature, UV and dryness, and a nutrient-poor soil.

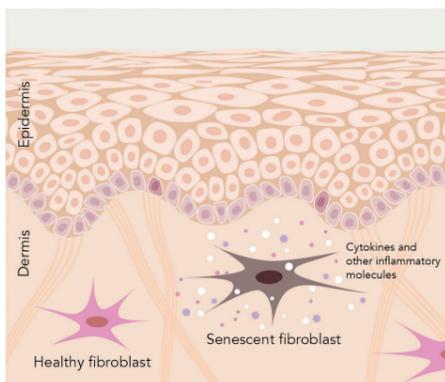
Due to the difficulty of cultivating the alpine rose, Mibelle Biochemistry collaborates with organic farmers in the Swiss Alps who harvest the precious leaves of the alpine rose using a simple harvesting technique. This method involves the leaves being carefully handpicked. The practice is completely sustainable as the leaves are regenerated the following year. This approved controlled wildcrafting makes it possible to extract leaves from plants that are stressed by natural environmental factors with steep temperature gradients and extremely high UV irradiation. The resulting extract from the leaves is COSMOS approved and Ecocert certified.

SENOLYTICS – A NOVEL ANTI-AGEING CONCEPT

Fibroblasts in the dermis are responsible for the production of collagen to form the connective tissue, as well as for assisting in the healing of skin wounds. When these fibroblasts either age or encounter too many harmful oxidative stresses, such as UV light and pollution,

they become senescent. The formation and accumulation of senescent cells is one of the hallmarks of ageing. In ageing skin, senescent cells secrete signalling molecules that promote inflammation and can influence surrounding cells into also becoming senescent. Therefore, eliminating senescent cells has emerged as a promising anti-ageing therapy in the medical field in the past few years.

This novel concept, known as "senolytics," helps to clear tissues of senescent cells without affecting healthy cells in order to reduce inflammation and rejuvenate the tissue. For the first time, this concept has been adapted for cosmetics. In vitro testing demonstrated a clear senolytic activity of the Alpine Rose Active on senescent fibroblasts. That means it helps to eliminate senescent fibroblasts without negatively affecting healthy fibroblasts to rejuvenate the deep layers of the skin.



CLINICAL STUDIES OF PHOTOAGEING PROTECTION AND SKIN REJUVENATION

Oxidative stress protection was evaluated *in vivo* by measuring the carbonyl protein content in human skin after exposure to UVA radiation. Environmental stress factors, such as UV light, infrared radiation, tobacco smoke, and pollution, generate reactive oxygen species (ROS). ROS oxidize proteins and lipids, which are the main components of cell membranes. This leads to carbonylation, which is one of the most harmful irreversible modifications of protein structure. Accumulation of carbonylated proteins can lead to cellular senescence. Therefore, preventing protein carbonylation is an important step in preventing skin ageing.

To demonstrate that Alpine Rose Active can protect against protein carbonylation *in vivo*, 12 female and male volunteers, aged 40 to 54 years, applied a cream with 2% alpine rose extract and a placebo cream twice daily for 14 days on the inner side of the forearms. After the final product application, the test sites were irradiated with UVA-light. Subsequently, suction blisters were induced, the suction blister fluids were collected, and their content of protein carbonyls was analysed as a marker of oxidative stress. The carbonyl protein content was significantly reduced in the suction blister fluid of the test site that was previously treated with Alpine Rose Active compared to the placebo-treated skin area. This indicated a protective effect *in vivo* against the damage caused by oxidative stress induced by UVA, indicating a prevention of photoageing by Alpine Rose Active.



This means that the formation of senescent cells in the skin caused by oxidative stress can be reduced.

However, for the senescent cells that are already present in the skin, a different approach is needed. As mentioned previously, an accumulation of senescent cells in the skin leads to latent inflammation through the secreted pro-inflammatory molecules of these cells. Therefore, a senolytic activity should reduce the pro-inflammatory signals and thus decrease skin redness. To test this in a double-blind, placebo-controlled clinical study, 44 female volunteers aged 40 to 65 years with redness on the cheeks were selected and split in two groups for 2% Alpine Rose Active or placebo application on the whole face. Twice daily application of 2% Alpine Rose Active for 14 days resulted a reduction of the redness parameter *a** by 8.4%, which was significant compared to initial conditions as well as the placebo. The effect was also visible in macrophotographs taken of the volunteers. Furthermore, an increase in skin lightness by 2.1% was measured in volunteers who applied 2% alpine rose extract, which was significant compared to initial conditions and the placebo. After 28 days of treatment, skin elasticity increased by 16.1%, also significant compared to initial conditions and the placebo. After senescent cells are cleared from the tissue, collagen can be

produced to improve the extracellular matrix of the dermis and increase the elasticity of the skin.

CONCLUSION

An extract from organic alpine rose leaves inhibits the carbonylation of cutaneous proteins and therefore protect skin proteins against oxidative damage, a known cause of cellular senescence. When senescence has already occurred, the alpine rose extract eliminates senescent cells while not affecting healthy cells through its senolytic activity. In this way, skin redness is reduced, and skin elasticity is increased for a youthful appearance.

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Mibelle Biochemistry, Stand H40

