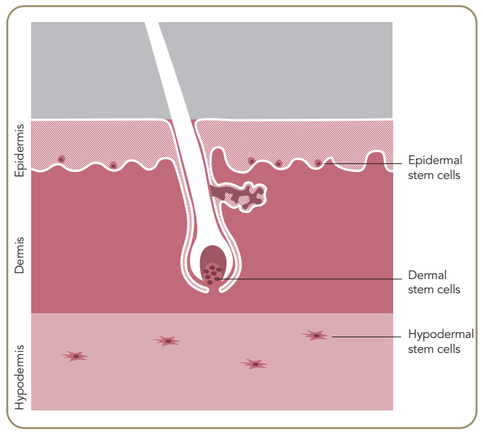
Redensified skin through stem cell activation

Deep-seated rejuvenation of the skin
In order to maintain the skin in a healthy condition, cutaneous tissue is being continuously regenerated. This regenerative capacity relies on adult stem cells in the skin. While considerable research has been carried out on epidermal stem cells, dermal stem cells were identified only a few years ago. The dermis is the middle layer of the skin and gives it tensile strength and elasticity, therefore it is also the site where wrinkles originate. Furthermore, a pool of adult stem cells is present in an even deeper layer of the skin, the hypodermis. These stem cells are precursors of different cell types including adipocytes, which proliferate to replenish the hypodermis and fill furrows from the inside.



Skin stem cells are needed to maintain youthful skin
While the epidermis acts as a barrier for the skin against the environment, the function of the dermis is to provide mechanical support and elasticity. Even deeper in the skin, the hypodermis predominantly consists of connective tissue and adipocytes. Its function is to anchor the skin to the underlying layers, to provide thermal insulation and to protect the skin from impacts. A healthy tissue is required to maintain these important functions. Therefore, the skin undergoes a constant cell turnover in order to maintain, renew and repair the skin tissue. New cells are produced to replace damaged or dead ones. Responsible for these regenerative processes are adult stem cells residing in special niches in different layers of the skin. However, the regenerative potential of skin stem cells does not last forever.

Old skin stem cells – old skin
Skin stem cells have a limited life expectancy. As one ages, these cells become less active and decrease in number. As a consequence, elastin and collagen production drops in the dermis, and the skin loses its elasticity and firmness – wrinkles appear. In the hypodermis, the loss of adipocytes that cushion and anchor the skin results in deep wrinkles, folds and sagging of the skin. Therefore, the protection of dermal and hypodermal stem cells is of great importance if one wishes to maintain a firm and youthful appearance.

Stem cells in the lower skin layers need protection and activation

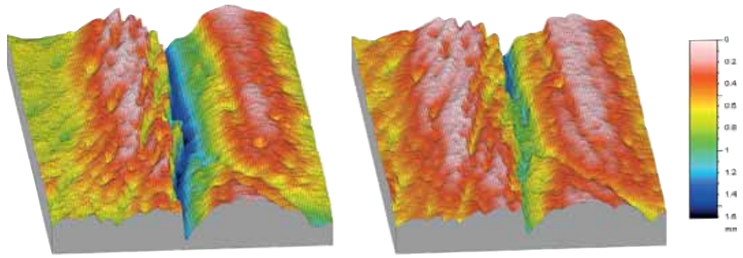
Reinforcement of the regenerative capacity of skin stem cells
The activity of stem cells is regulated by certain epigenetic factors. Such epigenetic factors are present in all stem cells of plants, animals and humans alike. Their function is to maintain the self-renewal capacity of stem cells. Therefore, epigenetic factors of stem cells from the argan tree *(Argania spinosa)* are used to help to preserve the vitality of stem cells in the human skin. Experiments with stem cells isolated from the dermis and hypodermis clearly showed that PhytoCellTec™ Argan helps these cells to maintain their stem cell characteristics.

Argania Spinosa, one of the oldest tree species in the world
The argan tree *(Argania spinosa)* is indigenous to the arid southwest region of Morocco. The tree has perfectly adapted to intense droughts and extremely high temperatures, which are typical in this region. Roots of the argan tree can extend 30m deep into the sandy soil to bring the water from the depth to the surface. This also benefits smaller plants that grow in its shade. Therefore, the tree helps to prevent soil erosion and holds back desertification.

Unfortunately, the argan tree population has shrunk due to extensive cultivation of the land. Consequently, nowadays the Moroccan argan tree forests cover an area of just 8000 km^2. In order to protect the remaining trees the *arganeraie* forests in Morocco were designated as a UNESCO International Biosphere Reserve in 1998.

Advanced biotechnology to cultivate plant stem cells from the rare argan tree
Mibelle Biochemistry has developed a plant cell culture technology that enables the large-scale cultivation of callus cells from rare plant species such as *Argania spinosa*.

Our PhytoCellTec™ technology relies on the wound healing mechanism of a plant: after an injury, the healing of the cut surface begins with the formation of callus cells. This healing tissue consists of dedifferentiated cells, which are stem cells. For this purpose argan shoots were injured to induce callus formation. Argan callus cells were then cultivated in an appropriate medium and large-scale production was achieved in a specialized WAVE bioreactor system. In order to obtain PhytoCellTec™ Argan (INCI (EU / PCPC) Declaration: *Argania Spinosa* Callus Culture Extract, Isomalt, Lecithin, Sodium Benzoate and Aqua/Water), the stem cells are harvested and homogenized at 1200 bar together with phospholipids to encapsulate and stabilize oil-soluble and water-soluble components into liposomes. The resulting extract is carefully sprayed onto a powder based on isomalt.



Before After 84 days

Activation of lower skin stem cells to plump and smooth the skin

Anti-wrinkle effect on the nasolabial fold

A filling effect of PhytoCellTec™ Argan on the nasolabial fold was evaluated in a half-face study with 30 women aged from 35 to 65 (mean age: 48.8 years) with visible nasolabial folds. Volunteers applied a 1 % PhytoCellTec™ Argan emulsion on one side of the face and the corresponding placebo on the other side. The test products were applied twice a day for 84 days. Silicon imprints were taken of the nasolabial fold at different time points. The surface structure of the imprint was captured and the wrinkle depth was measured using PRIMOS.

Results showed that PhytoCellTec™ Argan significantly reduces nasolabial fold depth by 7.9 % after 56 days of treatment and by 13.1 % after 84 days of treatment.

Visualisation of the imprint surface structure shows the filling effect of PhytoCellTec™ Argan.

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PhytoCellTec™ Argan improves skin density
The capacity of PhytoCellTec™ Argan to improve dermal tissue density was evaluated by visualising the structure of the dermis using ultrasonography. The ultrasonic wave generates echoes when it is partially reflected at the boundaries between different tissue structures. The intensity of the reflected echoes can be evaluated and visualised in a colour image. The collagen and elastic fibre structure of an intact dermis yields many reflections that are visible as bright colours in the ultrasonographic image. However, disruption of this regular architecture leads to weaker reflections and dark patches as shown in the left image below. These so-called subepidermal low-echogenic bands (SLEB) are commonly found in aged and photo-damaged skin.

In a study performed with 21 women aged from 39 to 61 years (mean age: 49.2 years), PhytoCellTec™ Argan was shown to improve the density of the dermis. Volunteers applied a 0.4 % PhytoCellTec™ Argan emulsion and a corresponding placebo on the inner side of their forearms twice daily for 56 days. Changes in SLEB were monitored by analysing the ultrasonographic images.

Results clearly showed that PhytoCellTec™ Argan stimulates the regenerative capacity of the upper dermis tissue compared to the placebo. The SLEB is reduced due to an improved dermal tissue density by 5.5 % after 28 days of treatment and by 12.7 % after 56 days of treatment.

PhytoCellTec™ Argan is the very first active ingredient that is capable of protecting and vitalising both human dermal and hypodermal stem cells. This will not only help to accelerate the skin's natural repair process but also fights skin ageing right at the root by filling wrinkles from within.

Mibelle Biochemistry, Stand L30