mibelle GROUP biochemistry

BSB Innovation Award® NATURAL Products 2024
3. Prize Category Most Innovative Raw Material

Approved by ECOCERT RAW MATERIAL
COSMOS APPROVED

PhytoSpherix™

Plant-based glycogen to energize the skin

SWISS QUALITY PRODUCT

PhytoSpherix™
Plant-based glycogen to energize the skin

Naturally Energize the Skin with PhytoSpherix™ for a Youthful Appearance
Skin cells are continuously exposed to environmental stresses, and, therefore, greatly rely on large amounts of energy to combat cellular – and consequently skin – damage. As we age, cellular energy levels decline and the deficiencies in skin energy can result in premature skin aging.

By providing glycogen, the cells are given energy to use whenever it is needed and wherever it is needed. This can then result in many beneficial effects for the skin. There is, however, one problem: Glycogen is the glucose storage unit found in mammalian cells and it is usually isolated from animal sources. Nevertheless, Mibelle Biochemistry can provide an alternative: the plant-based phytoglycogen PhytoSpherix™.

PhytoSpherix™ is a phytoglycogen that is isolated from a special non-GMO sweet corn. It is chemically identical to the glycogen stored in animal cells but is produced and stored in plants.

In vitro and *in vivo* studies have shown that PhytoSpherix™
- stimulates ATP production and increases cell proliferation and metabolic activity
- increases hyaluronic acid and collagen production
- provides fast and long-lasting hydrating effects
- effectively reduces visible wrinkles
- boosts the effects of hyaluronic acid in a formulation
- reduces skin hyperpigmentation.

PhytoSpherix™ is naturally produced by a special variety of sweet corn and it is extracted through a mild water-based process. It is a safe and natural botanical extract.

These qualities, combined with the chemical properties and the known beneficial effects of glycogen for the skin, make PhytoSpherix™ an excellent and multi-purpose cosmetic active.

PhytoSpherix™ is COSMOS approved*

PhytoSpherix™
- Energizes skin cells
- Promotes collagen and hyaluronic acid production
- Reduces wrinkles and fine lines
- Improves skin hydration
- Reduces pigment spots

Applications
- Anti-aging formulas
- Hydration creams
- Skin-energizing essences
- Pigment correction and brightening fluids

Formulating with PhytoSpherix™
- Recommended use level: 0.1–0.3 %
- Incorporation: For cold processes, dissolve PhytoSpherix™ into the aqueous phase. In hot/cold processes, add during the cooling phase below 40 °C
- Thermostability: Temperatures of up to 70 °C for a short time will not affect the stability of PhytoSpherix™

INCI (EU/PCPC) Declaration
PhytoSpherix™ (standard version, COSMOS approved*): Glycogen

PhytoSpherix™ L105 (10 % liquid version, COSMOS approved*): Aqua (and) Pentylene Glycol (and) Glycogen

Adveen™ (powder, vaginal treatments, feminine hygiene, COSMOS approved*): Glycogen

Additional Information
- Vegan
- Pure substance
- Produced from non-GMO sweet corn

** Raw material approved by ECOCERT GREENLIFE in accordance with the COSMOS Standard*

Cell and Energy Metabolism
Energize the skin at the cellular level

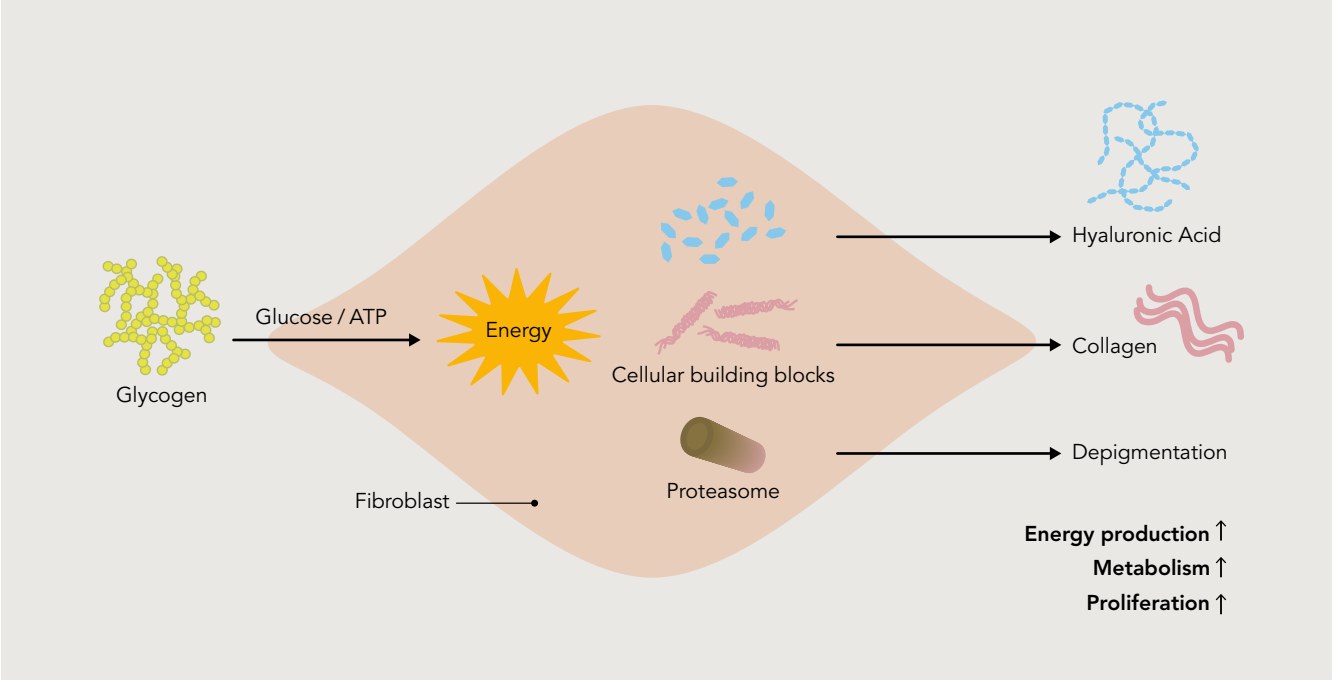
Energy Needs for Cell Metabolism
Living organisms require energy to perform the tasks of everyday life. At the cellular level, the energy is used for overall cell maintenance, protection, and the production of molecules that are essential for cell and organ function. Skin cells, which are continuously exposed to environmental factors such as sunlight or pollution, greatly rely on large amounts of energy to combat cellular – and consequently skin – damage. As we age, cellular energy levels decline and the deficiencies in skin energy can manifest in age-related changes in the skin (1). One consequence of this includes the formation of wrinkles or skin hyperpigmentation due to photodamage. Therefore, increasing cell energy levels can be a good approach with which to target skin aging.

Healthy Skin Maintenance Requires Energy
To maintain a healthy and youthful skin, the skin produces various essential molecules including hyaluronic acid (HA) and collagen. To produce these molecules, the skin cells require energy. However, energy levels are unfortunately reduced during the aging process. The reduced energy levels can lead to impaired production of skin essential molecules and, indeed, decreased levels of HA and collagen are observed in the aging skin (2). Evidently, boosting the production of these molecules by increasing the available energy that is needed can benefit the skin.

Energy Stores: Glycogen
A preferred energy substrate for cell metabolism is glucose. When energy is needed, glucose is broken down into a series of biochemical reactions that release energy in the form of ATP (adenosine triphosphate). The ATP derived from these processes is used to fuel virtually every energy-requiring process in the body. Glucose can be packed and stored for later use. This ensures enough energy is available, even in times of stress. Efficient and dense packaging is required to store as much glucose as possible while using minimal space. One of the densest storage units of glucose in the cell is glycogen.

(1) Blatt et al. (2008) BioFactors 25: 179–185.
(2) Calleja-Agius J. (2007) Menopause Int. 13(2): 60–4.

Skin Cells, Energy, and Metabolism



Glycogen
Energy stores for anti-aging

Glycogen: Densely Packed Energy
Glycogen is an energy-storage unit found in animal cells. It is a highly branched structure of repeating glucose units that are linked together by specific bonds, termed α(1-4) and α(1-6) glycosidic bonds. The structure of glycogen itself is very dense, making this molecule an ideal storage unit of energy inside the cell.

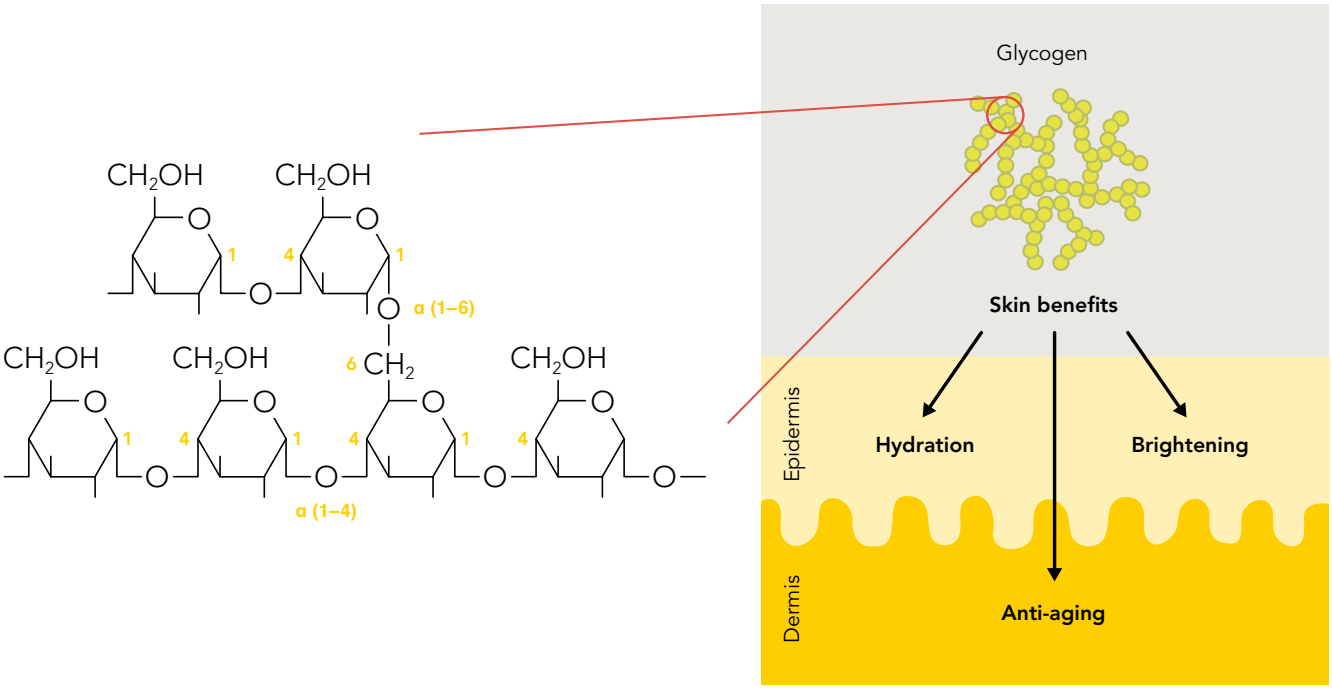
Glycogen and the Skin
The largest stores of glycogen are usually found in the muscles and liver, which are very metabolically active and require a lot of energy. However, a small amount of glycogen is also present in the skin, where it is an important skin energy source (3). It can be used for various metabolic processes, such as the generation of essential molecules. Importantly, glycogen content in the skin also declines with aging, which suggests that glycogen loss may also play a role in skin aging.

Glycogen: Energy to Reduce Hyperpigmentation
By providing glycogen, the cells can be given more glucose – and therefore more energy – to use not only in building new molecules, but also in cleaning the skin from damaged molecules (4). Delivering energy to improve the skin damage response, such as the degradation of damaged molecules by the proteosome, can also help prevent skin hyperpigmentation (5).

Sources of Glycogen for Cosmetics
Evidently, glycogen may have many benefits for the (aging) skin and is, therefore, a popular ingredient for cosmetic formulations. There is, however, one problem: Glycogen is the glucose storage unit found in mammalian cells and it is usually isolated from animal sources. Nevertheless, Mibelle Biochemistry has managed to provide an alternative vegan solution: the plant-based phytoglycogen known as PhytoSpherix™.

(3) Halprin K. M. and Ohkawara A. J. (1966). Invest. Dermatol 46 (1): 43–50.
(4) Ando H. et al. (2009) Int. J. Mol. Sci. 10: 4428–4434.
(5) Shi. J. et al. (2022) J. Cosmet. Dermatol. 21: 6661–6668.

Glycogen: Structure and Skin Benefits



PhytoSpherix™
A plant-based glycogen

PhytoSpherix™: a Plant-based Glycogen
PhytoSpherix™ is a plant-based glycogen that is isolated from a special non-GMO sweet corn. It is chemically identical to the glycogen stored in animal cells but is naturally produced and stored in these plants.

The structure of PhytoSpherix™ clearly differentiates it from other polysaccharides found in plants, such as amylopectin. PhytoSpherix™ is made up of α-1,4-linked glucose units, which form linear chains that branch after every 10 units of glucose (via α-1,6 glycosidic bonds). This number of branches is almost double that of normal maize amylopectin, which branches out after every 20 units of glucose (6). Various physical characterization techniques have further investigated and confirmed the structure of PhytoSpherix™ to indeed be chemically identical to that of mammalian glycogen. Therefore, this special molecule can be used for cosmetic formulations as a natural plant-based alternative to animal-derived glycogen (7).

Properties of PhytoSpherix™
PhytoSpherix™ is a compact, spherical, and water-soluble molecule. The highly branched dendrimer structure of PhytoSpherix™ further yields some interesting properties, including high water-binding, low viscosity, and high stability in water. The efficient water-binding capacity, for example, can enhance the moisturizing properties of skincare formulations.

A Natural and Safe Extract
PhytoSpherix™ is naturally produced by a special variety of sweet corn and is extracted through a mild water-based process. It is therefore a safe and natural botanical extract. These qualities, combined with the chemical properties and the known beneficial effects of glycogen for the skin, make PhytoSpherix™ an excellent and multi-purpose cosmetic active.

(6) Roman et al. (2022). Carbohydrate Polymers 298: 120080.
(7) Dutcher et al. (2017). La Physique au Canada. 73(2): 91–94.

Plant-based Phytoglycogen

	Glycogen	PhytoSpherix™
Source	Animal	Plant (special sweet corn variety, non-GMO)
Function	Energy storage	Energy storage
Subunit	α-glucose	α-glucose
Bonds	1–4 and 1–6	1–4 and 1–6
Branches	Yes (~per 10 subunits)	Yes (~per 10 subunits)

PhytoSpherix™
Study results

Stimulation of ATP Production

As one of the main energy-carrying molecules found in the cell, ATP drives many essential processes. To determine the effects of PhytoSpherix™ on intracellular ATP production, human keratinocytes were cultured in the presence or absence (control) of 1 % PhytoSpherix™ for periods of 2 hours and 24 hours. After the treatment, the intracellular ATP content was quantified using a specialized luminescence-based assay.

After just 2 hours, treatment with 1 % PhytoSpherix™ resulted in a significant stimulation of ATP production. Meanwhile, after 24 hours, PhytoSpherix™ further increased ATP levels by almost 50 % compared to control.

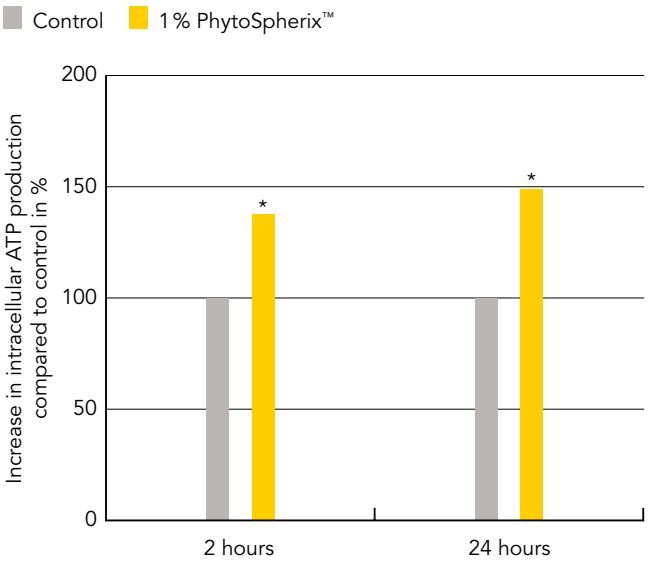
Therefore, PhytoSpherix™ has a stimulating effect on cellular ATP production, which can benefit the cell in metabolic processes.

Increased Proliferation and Metabolic Activity

Stimulated ATP levels can boost cell proliferation and metabolism. Therefore, we further investigated the cellular response of human fibroblasts to PhytoSpherix™. The cells were cultured in the presence or absence of 0.025 % PhytoSpherix™ for 36 hours. Following this, the cells were counted (proliferation assay) or treated with a special dye, AlamarBlue™ (metabolism assay). AlamarBlue™ is only taken up by viable and metabolically active cells, thereby turning fluorescent. The fluorescence, thus, corresponds to cell metabolic activity.

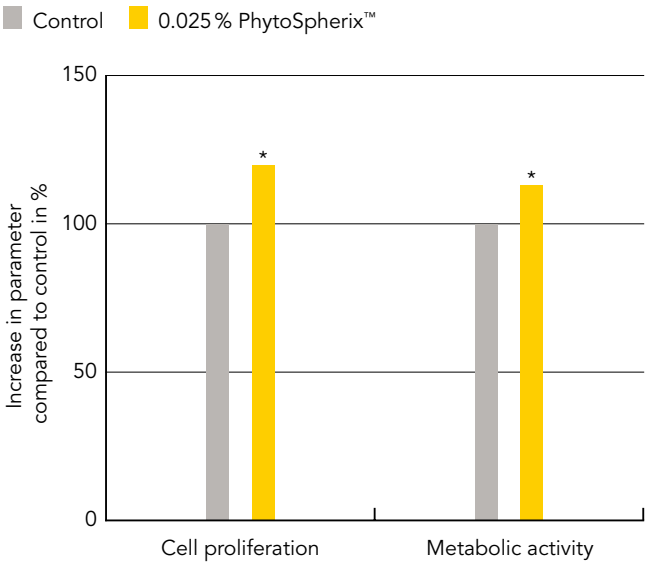
After treatment with 0.025 % PhytoSpherix™ for 36 hours, cell proliferation was significantly increased by 20 %. In line with this, cell metabolic activity was also significantly increased by 12 % compared to untreated control.

Stimulation of ATP Production



*p<0.01 versus control

Increased Proliferation and Metabolic Activity



*p<0.01 versus control

PhytoSpherix™
Study results

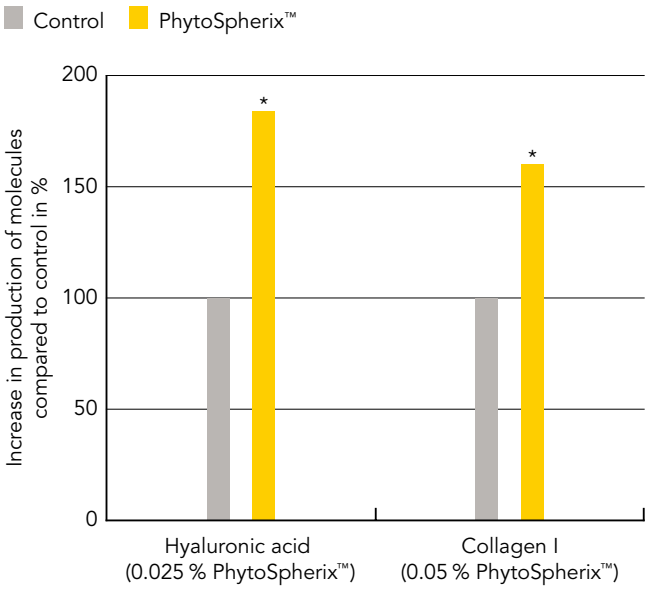
Increase in Hyaluronic Acid (HA) and Collagen
The stimulation of cell metabolic activity could lead to increased synthesis of essential components of the skin, such as HA and collagen. During aging, a reduction of these compounds is observed, and stimulation of HA and collagen synthesis could, therefore, be considered beneficial anti-aging strategies for the skin.

To measure HA production, human fibroblasts were either treated or not (control) with 0.025 % PhytoSpherix™ for 36 hours. Following this, the amount of HA synthesized was measured using ELISA. To determine collagen production, cells were either treated or not (control) with 0.05 % PhytoSpherix™ for 36 hours. The cells were then fixed and processed for immunohistochemistry. Collagen content outside the cell (extracellular collagen I deposition) was fluorescently labeled and visualized using antibodies specific for human type I collagen. Cell nuclei were stained with the nuclear dye DAPI.

Treatment with 0.025 % PhytoSpherix™ led to a significant increase in HA secretion from the fibroblasts. Compared to control, HA present in the media was increased by 83 %. Stimulating effects of PhytoSpherix™ were also observed when evaluating collagen I production: Treatment with 0.05 % PhytoSpherix™ led to a significant increase of collagen I, as measured and quantified by immunofluorescent staining. This was also evident in the images obtained.

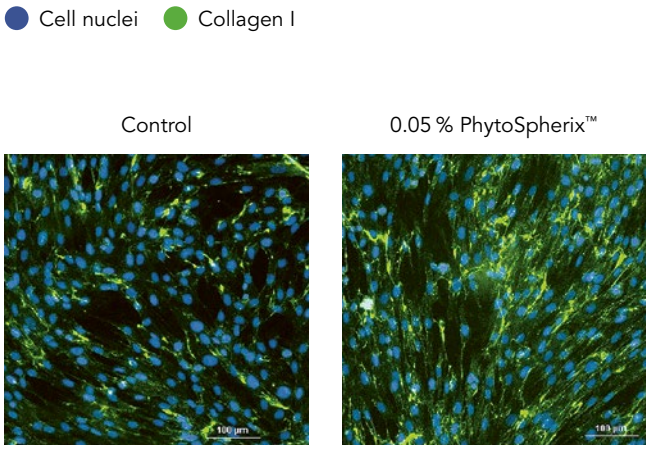
In conclusion, PhytoSpherix™ stimulates cell metabolic activity, which results in the increased production of beneficial molecules such as HA and collagen.

Increase of HA and Collagen I Production



*p<0.01 versus control

Visible Increase of Extracellular Collagen Deposition



S-1179 / © Mibelle Biochemistry

Fast Effects on Skin Hydration

Increased HA levels, as observed in the *in vitro* assays, can have beneficial effects, such as better skin hydration. To investigate this, a placebo-controlled study was performed on 63 female volunteers, aged between 51 and 65 years (mean 58.8 years) with self-perceived dry skin. The volunteers were divided into two groups. The first group applied a cream containing 0.1 % PhytoSpherix™ while the placebo group applied a placebo cream without the active. The test products were applied to the entire face, twice daily, for 6 weeks.

Just 1 hour after the first application, treatment with 0.1 % PhytoSpherix™ significantly increased skin hydration by 53.3 % compared to baseline. This hydration increase remained significantly enhanced after 2 weeks of treatment and after 6 weeks of treatment.

As evidenced by this study, PhytoSpherix™ has fast and continuous hydrating effects on the skin.

Visible Anti-Aging Effects

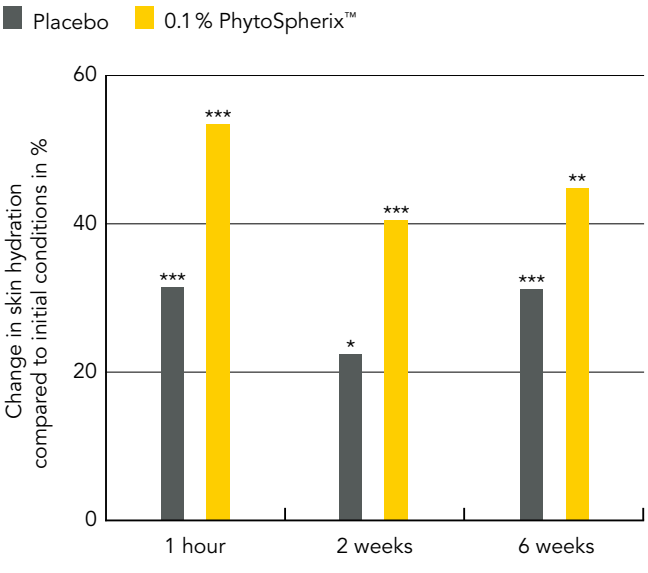
In the same study, the anti-aging benefits of PhytoSpherix™ were evaluated after 6 weeks of treatment. Images taken from select volunteers (n = 4 – 5) were analyzed by Newtone Inc. using their proprietary imaging technology.

6 weeks of treatment with 0.1 % PhytoSpherix™ led to:
- decreased crow's feet wrinkle area by 42 %
- reduced crow's feet volume by 49.6 %
- reduced crow's feet length by 29.6 %.

Similar effects were obtained when analyzing forehead wrinkles. Compared to initial conditions, PhytoSpherix™:
- decreased the wrinkle area by 54.9 %
- reduced the wrinkle volume by 45.6 %
- decreased forehead wrinkle length by 53.2 %.

The anti-aging effects were clearly visible in the images taken.

PhytoSpherix™ Increases Skin Hydration



*p<0.5 versus initial conditions
**p<0.01 versus initial conditions
***p<0.001 versus initial conditions

S-1180 / © Mibelle Biochemistry

Visible Improvement of Wrinkles

S-1181 / © Mibelle Biochemistry

PhytoSpherix™
Study results

Hyaluronic Acid Boosting Effects

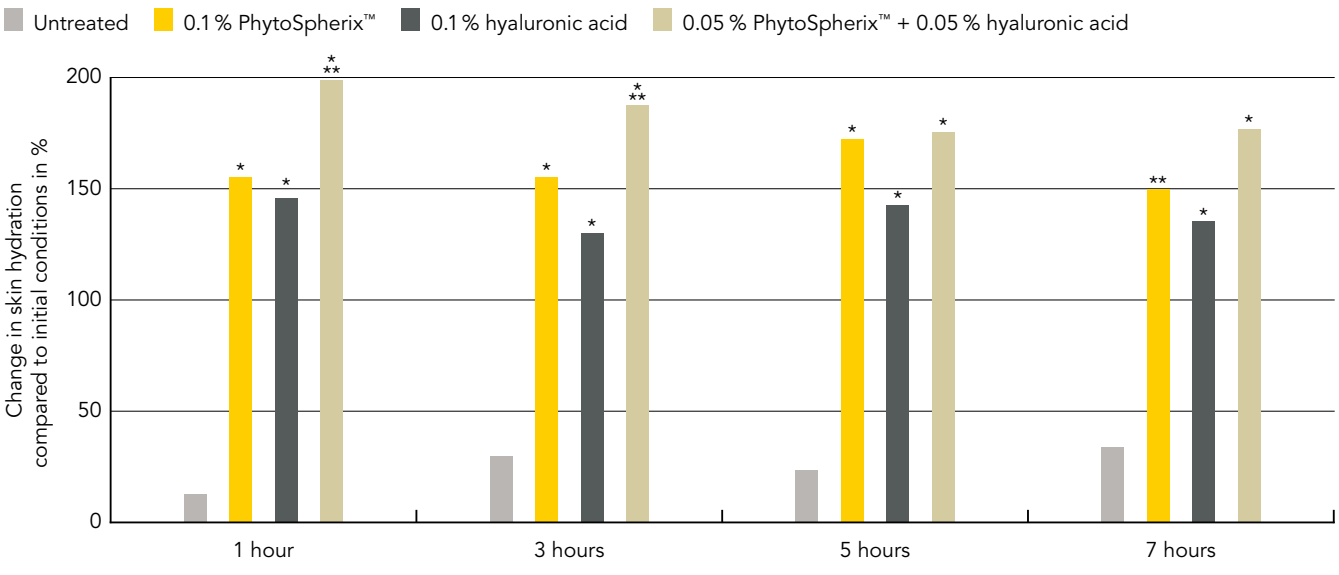
As previously shown, treatment with PhytoSpherix™ leads to improved skin hydration. A known benchmark for skin hydration includes the use of hyaluronic acid (HA) in formulations. However, this can encounter certain difficulties including viscosity issues of the formulation. Therefore, exploring effective alternatives to HA are attracting increasing interest. To compare the moisturizing effects of PhytoSpherix™ with HA, a randomized clinical study was performed on 13 male and female volunteers, aged between 25 and 60 years. Tested formulations included PhytoSpherix™ and hyaluronic acid (HA) with a combined total of 0.1% were either used alone at 0.1% each or blended with 0.05% each. After a single application, skin hydration measurements were taken over the time course of 7 hours and compared to baseline and untreated (no formulation) controls.

After just 1 hour, a single treatment with 0.1% PhytoSpherix™ led to a significant skin hydrating effect compared to untreated controls. In comparison to initial conditions, skin hydration was boosted by 155.3%. This effect was still present after 7 hours, demonstrating its long-lasting effect on skin hydration. Furthermore, these effects were comparable to the treatments with 0.1% HA.

Intriguingly, the combination blend with lower concentrations (0.05% each) of PhytoSpherix™ and hyaluronic acid led to a superior hydrating effect (+199% after just 1 hour). This indicates a synergistic effect of the two actives, leading to superior effects compared to the treatments featuring the single actives alone.

In conclusion, PhytoSpherix™ demonstrates a significant hydrating effect, which is comparable to HA. Moreover, a blend of HA and PhytoSpherix™, at half the concentrations each, even yields superior moisturizing effects to comparable higher concentrations of either ingredient. This demonstrates that formulating with PhytoSpherix™ can boost the skin moisturizing effects of HA. Therefore, less material is required to achieve the same hydration levels as either ingredient would produce on its own, and hyaluronic acid formulations can reach higher hydration levels without sacrificing texture or skin feel.

Synergistic Hydration Effect with Hyaluronic Acid



*p<0.01 versus untreated control
**p<0.05 versus hyaluronic acid

Reduction of Skin Hyperpigmentation

Glycogen can deliver energy, which can help the skin damage response and possibly help prevent skin hyperpigmentation. Application of this molecule could therefore lead to brightening effects. *In vitro*, we indeed observed a minor but significant inhibition of melanin synthesis with 0.5 % PhytoSpherix™ after 72 hours. Therefore, we investigated whether PhytoSpherix™ can also have a clinical effect on skin hyperpigmentation.

The effects on skin hyperpigmentation were analyzed in the placebo-controlled study that was previously described on 63 volunteers with global facial photodamage. The volunteers applied either a placebo cream or a cream containing 0.1% PhytoSpherix™ for 6 weeks. Following this, the effects on skin hyperpigmentation were analyzed by expert clinical grading.

After the application of a cream containing 0.1% PhytoSpherix™ for 6 weeks, skin hyperpigmentation and skin tone evenness was significantly improved, compared to placebo, by 30 % and 37 %, respectively.

Visible Reduction of Pigment Spots

Furthermore, select images taken from the PhytoSpherix™ treated group (n = 4 – 5) were analyzed by Newtone Inc. to determine changes in the pigment spots, using their proprietary imaging technology. For this analysis, the lightness (L*) and redness (a*) and yellow pigment (b*) factors of the skin inside the pigment spot and the skin surrounding the spot were measured an, which yields a difference in contrast (visibility) of the pigment spot.

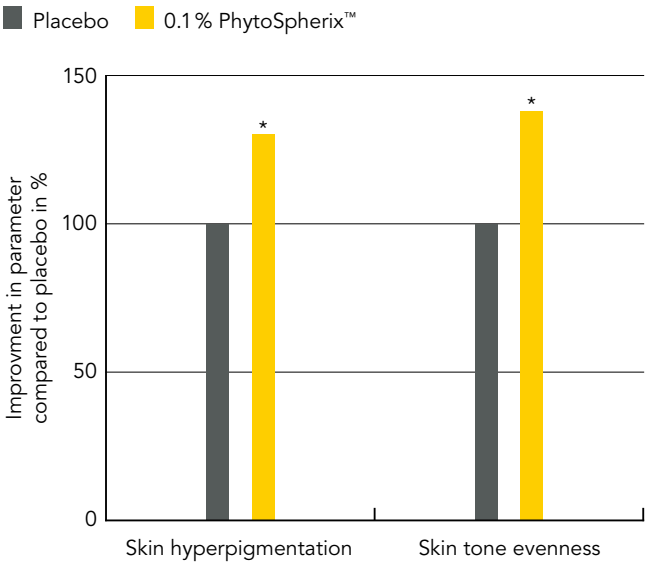
The reduction of skin hyperpigmentation was also evident in the analysis of the pigment spots. The contrast differences improved by

- 22.1 % for L*
- 24.1 % for a*
- 15.2 % for b*

which indicates that the age spots became less visible. This was also clearly evident in the images taken.

To summarize, the skin-energizing effects of PhytoSpherix™ can also improve skin hyperpigmentation, leading to a more even complexion.

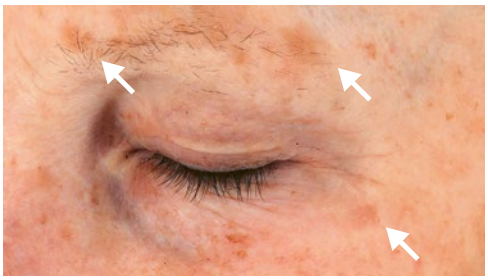
Reduction of Skin Pigmentation



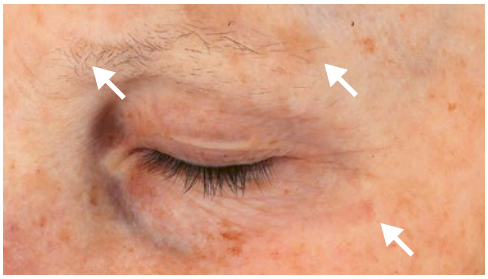
*p<0.05 versus placebo

Visible Reduction of Pigment Spots

Before



After 6 weeks



PhytoSpherix™
Plant-based glycogen to energize the skin

PhytoSpherix™
- Energizes skin cells
- Promotes collagen and hyaluronic acid production
- Reduces wrinkles and fine lines
- Improves skin hydration
- Reduces pigment spots

Applications
- Anti-aging formulas
- Hydration creams
- Skin-energizing essences
- Pigment correction and brightening fluids

Marketing Benefits
- Unique phytoglycogen based on non-GMO sweet corn
- Synergistic effect with hyaluronic acid
- Patented production process (EP 2 989 156 B1)
- 3rd Prize at the BSB Innovation Award in the category Natural Products – Raw Materials
- 100 % natural origin
- COSMOS approved

COSMOS APPROVED

Innovating for your success
Mibelle Biochemistry designs and develops innovative, high-quality actives based on naturally derived compounds and profound scientific know-how. Inspired by nature – Realized by science.

myclimate neutral Operations
myclimate.org/01-22-602304

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