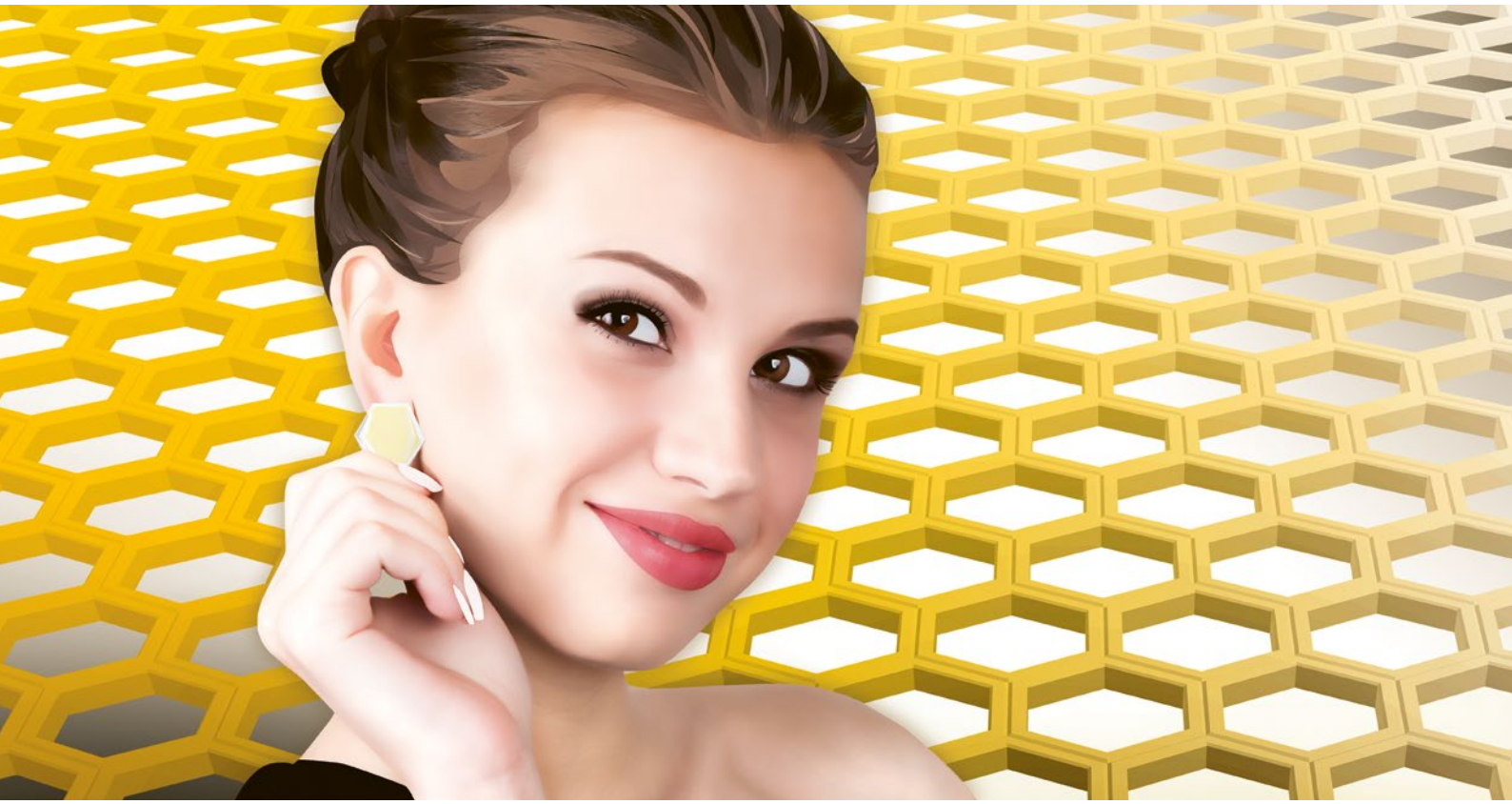
mibelle GROUP biochemistry



BSB Innovation Award® NATURAL Products 2019
1. Prize Category Most Innovative Raw Material

Black BeeOme™

Black bee honey ferment to restore the skin's natural microflora

SWISS QUALITY PRODUCT

Black BeeOme™

Black bee honey ferment to restore the skin's natural microflora

Expert in Managing the Skin Ecosystem
Black BeeOme™ is an elixir that results from the fermentation of the rare wild dark bee *Apis mellifera mellifera* honey with the bacteria *Zymomonas mobilis*. Black BeeOme™ has been designed to harmonize the skin microflora after stress to ensure a healthy and pure skin.

Billions of microorganisms colonize the human skin at various sites and constitute the skin microbiota. They form complex communities that function together with the host immune system in order to defend against pathogens and to maintain skin health. Since having a well-balanced cutaneous microflora is important for a healthy and beautiful skin, protecting its balance and its recovery represents a winning strategy for skin care products.

Honey has always been highly valued both as food and in cosmetics. In the case of Black BeeOme™ the honey from the rare bee *Apis mellifera mellifera*, adapted to live in the harsh conditions of the valleys of Switzerland, has been fermented with *Zymomonas mobilis*. The fermentation eliminates the basic sugars glucose, fructose and sucrose in the honey. The remaining long-chain sugars stabilise and promote the individual microflora of the skin and form an ideal basis for its growth.

In vitro and clinical studies have shown that Black BeeOme™ promotes a faster skin flora recovery after washing as well as skin barrier recovery. In addition, the fermented black bee honey diminished the sebum production and improved the uniformity of oily and uneven face skin. When applied on a sheet mask, Black BeeOme™ showed a clear improvement of impure skin of volunteers living in urban, polluted areas after only 15 minutes of a single application.

Black BeeOme™
- Reduces sebum production for a matte and pure skin
- Regenerates the skin microflora after washing
- Protects and strengthens the skin barrier

Applications
- Sheet masks
- Mattifying skin care
- Anti-blemish formulations
- Sensitive skin care

Formulating with Black BeeOme™
- Recommended use level: 1–2%
- Incorporation: For cold processes, dissolve Black BeeOme™ into the aqueous phase. In hot/cold processes, add during the cooling phase below 40°C.
- Thermostability: Temperatures of up to 40°C for a short time will not affect the stability of Black BeeOme™.

For further information, please refer to our formulation guidelines.

INCI (EU/PCPC) Declaration
Black BeeOme™ (standard version):
(Honey + Zymomonas Ferment) Extract (and) Alcohol (and) Aqua/Water

Black BeeOme™ pwd (powder version without preservatives, 2-fold concentrated):
(Honey + Zymomonas Ferment) Extract (and) Maltodextrin (and) Aqua/Water

The Microorganism Universe

The skin is an ecosystem

The human microbiota comprises all microorganisms – the commensal bacteria, viruses, yeasts and fungi, – that consider human bodies to be home. Each of us hosts 10 to 100 trillion microbes in a symbiotic relationship which, in the normal healthy state, suits both them and us. The human body microbiota are mostly found in the gut, the nasal and oral cavity, and on the skin surface (1). Most of these microorganisms can vary throughout life, based on lifestyle, diet, the environment and also – in the case of the skin – by the local ecosystem (2). While estimates vary, there could be over 1,000 different species of microorganism making up the human microbiota. All of the genes of these microbial cells in their environment are what constitute the microbiome (3).

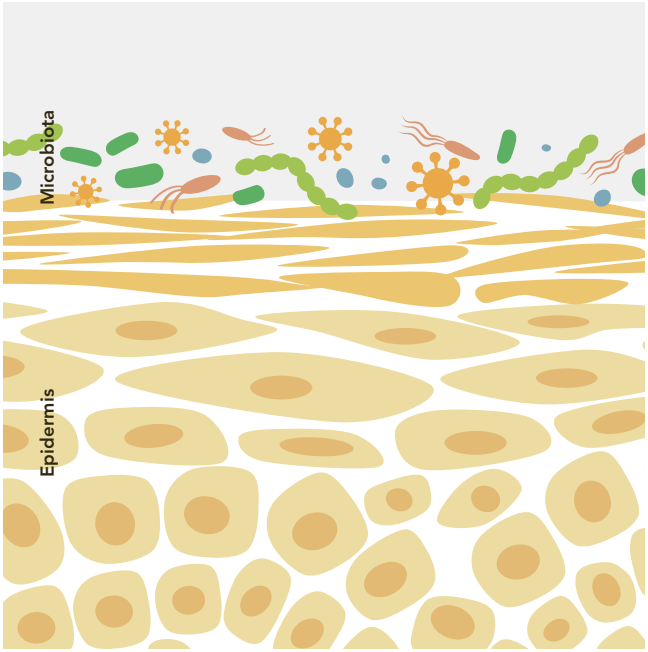
Shifting Paradigm

The microorganisms hosted on the human skin had been previously acknowledged for their role in various skin diseases and therefore the emphasis in medical implication involved how to eradicate the pathogenic organisms. However, research in recent years through microbiome studies has revealed that the microbes on the skin are an indispensable part of the host–microbiota symbiotic system, which suggests that skin commensals play important roles in terms of maintaining skin health and proper function (4). This new view appeals for paradigm-shifting acknowledgment of the functions of the skin microorganisms in skin health and new treatment strategies for microorganism-associated skin diseases.

The Cutaneous Microbiota

The most recent research has revealed the complexity of this field as the amount and type of microbes varies significantly between different subjects and also between different skin areas within one person. In general, it is believed that the broader the variety of microbes at a specific skin site, the better it is for the health of the skin (5). A disruption of this skin ecosystem may not only influence diseases such as psoriasis or acne, but also skin aging, barrier function and wellbeing.

The Skin Microbiota Ecosystem



Skin Microflora Friendly

The fermentation of black bee honey with *Zymomonas mobilis*

The Black Bee Honey

Honey has been used since ancient times as food and later on in cosmetics. However, the production of honey has been endangered lately as bee population is significantly decreasing as a result of diseases. In tune with the valleys of Switzerland, the wild dark bee *Apis mellifera mellifera* has adapted to live in such harsh conditions. It is only this very special breed that is resistant to varroa (the mite that attacks bees), which is one of the attributed reasons for the worldwide bee population decline. The honey made by these special wild dark bees has been used by Mibelle Biochemistry as a fermentation substrate in the new active Black BeeOme™.

Drink of the Gods-like Fermentation

For more than 1,000 years *Zymomonas mobilis* was used by the Aztecs to make the Mexican drink pulque. This ancient drink, which is known as the Aztec drink of the Gods, is the ancestor of mezcal and tequila. All three drinks come from the same family of plants, but pulque is made by fermenting – as opposed to distilling – the sap of the agave with *Zymomonas mobilis* (among other things). These bacteria are able to only ferment sucrose, glucose and fructose, and leaves the complex sugars intact. Therefore, the black bee honey has been fermented with *Zymomonas mobilis* to eliminate the basic sugars (glucose, fructose and sucrose) in the honey which may act, for example, as a carbon source for unwanted bacterial growth on the skin. On the other hand, the ferment of *Zymomonas mobilis* contains factors that may help to control the growth of bacteria, yeast and fungi on the skin (6).

The Prebiotic Action of Black BeeOme™

Under normal conditions, the microbiotic film protects the skin against other harmful bacteria or pathogens. As it is the first barrier, this film is constantly stressed not only by factors such as UV light, pollution, domestic chemicals, but also by cosmetic products or treatments. This dynamic creates an imbalance in the skin microflora and their niches may be later colonized by transient, harmful bacteria. Frequent washing of the skin, for example, can reduce and unbalance the skin's ecosystem. Therefore, the skin microbiota has to recover from these threats on a daily basis. A healthy barrier should not require extensive treatment and support an innate ability to bounce back to normal homeostasis after being challenged. Black BeeOme™ has been shown to efficiently exert its prebiotic effect: incorporating nutrients and generating conditions to restore the healthy skin's natural microbiota following daily stress.

(1) "The Human Microbiome Project Consortium, Structure, function and diversity of the healthy human microbiome." Nature 486(7402): 207–214.

(2) Costello, E. K., C. L. Lauber, et al. (2009). "Bacterial community variation in human body habitats across space and time." Science 326(5960): 1694–1697

(3) Kong, H. H. and J. A. Segre, The Molecular Revolution in Cutaneous Biology: Investigating the Skin Microbiome. J Invest Dermatol, 2017. 137(5): p. e119–e122.

(4) Sanford, J. A. and R. L. Gallo (2013). "Functions of the skin microbiota in health and disease." Semin Immunol 25(5): 370–377.

(5) Jo, J. H., E. A. Kennedy, et al. (2016). "Research Techniques Made Simple: Bacterial 16S Ribosomal RNA Gene Sequencing in Cutaneous Research." J Invest Dermatol 136(3): e23–27.

(6) Escalante, A., D. R. Lopez Soto, et al. (2016). "Pulque, a Traditional Mexican Alcoholic Fermented Beverage: Historical, Microbiological, and Technical Aspects." Front Microbiol 7: 1026.

Black BeeOme™
Study results

Skin Integrity Recovery after Washing Stress

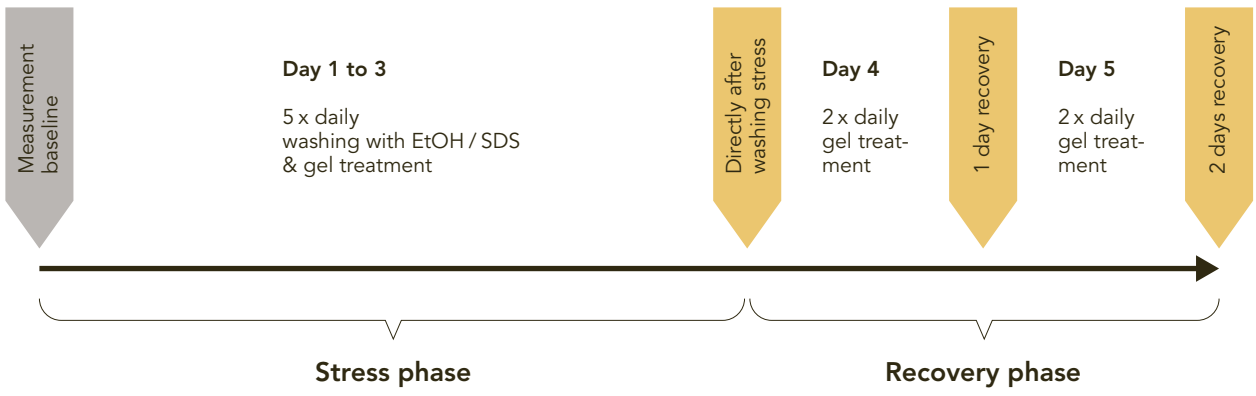
The skin barrier enhancing effect of Black BeeOme™ was evaluated on 22 volunteers (16 females, 6 males) aged between 29 and 69 years, in a double-blind placebo-controlled clinical study.

During the first 3 days of the study, the skin area on the elbow fold was washed 5 times daily with a 50% ethanol/4% SDS mixture in order to strip the skin of its microflora (stress phase). The test products, a gel containing 1% Black BeeOme™ pwd and the corresponding placebo were applied to the skin after each wash.

For the following 2 days (recovery phase), only the test products were applied onto the elbow fold (twice daily – morning and night). The test parameters TEWL and erythema were determined:

- at the beginning of the study
- after the stress phase
- after 1 day recovery
- after 2 days recovery

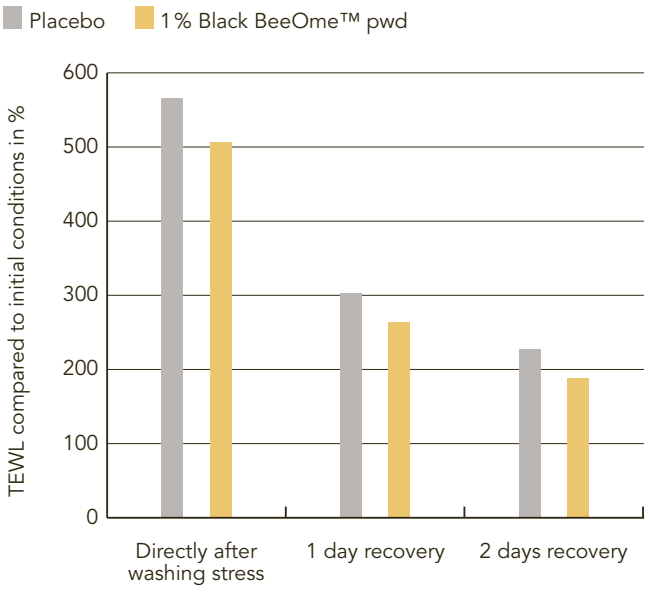
Study Design – Washing and Treatment Procedure

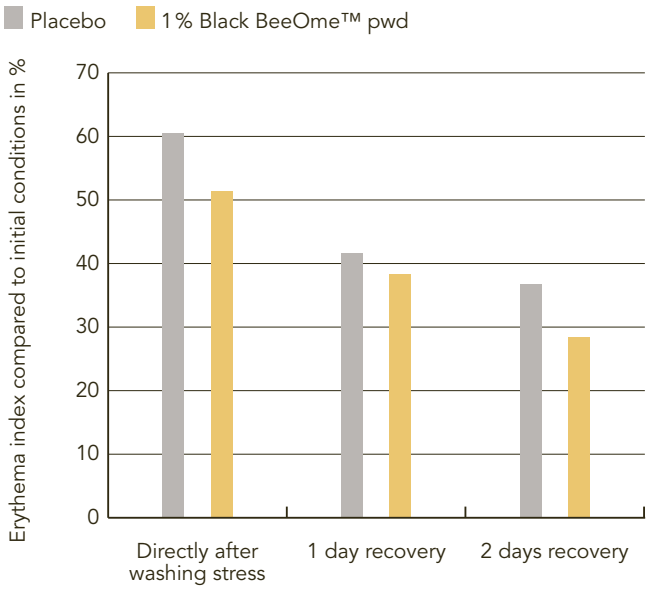


The harsh wash disrupted skin microflora resulted in damage to the skin function. The results revealed that the application of 1% Black BeeOme™ pwd protected and reinforced the recovery of the skin barrier. The faster recovery of the skin ecosystem had a positive influence on the skin barrier regeneration as seen by the reduction of TEWL compared to the placebo.

After the stress phase, the decrease of redness on the skin areas treated with the product containing 1% Black BeeOme™ pwd was faster than that on the placebo-treated skin.

Improvement of TEWL and Redness of the Skin after Harsh Washing





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Black BeeOme™
Study results

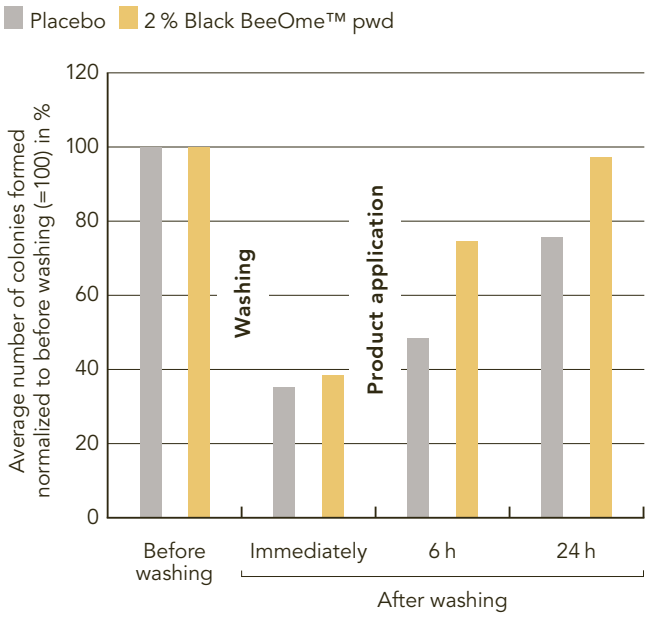
Support of the Skin Flora Recovery after Washing

In a placebo-controlled clinical study with 7 volunteers (3 males, 4 females) aged between 17 and 38 years, the skin microflora recolonization efficacy of Black BeeOme™ pwd was determined.

The volunteers (who had normal skin conditions) applied a standardized single application of water spray containing 2% Black BeeOme™ pwd after washing the skin with an 4% SDS/50% ethanol mixture to strip the skin of the microflora. In order to determine the number of microorganisms, skin surface samples were taken from volunteers with contact plates before and immediately after the washing, and then after 6 hours and after 24 hours.

Results showed that harsh washing had a detrimental impact on the skin microflora layer. However, the skin treated with 2% Black BeeOme™ pwd was able to recover faster from the washing than the placebo. The reestablishment of the skin's natural microflora was realized sooner following the use of Black BeeOme™ pwd.

Recolonization of the Skin Microflora after Washing



Skin Barrier and Overall Improvement of Impure Skin

In a randomized, placebo-controlled clinical study the efficacy of Black BeeOme™ pwd was investigated. The volunteers, 23 Caucasian women aged between 19 and 57 years, presented oily and uneven skin.

The tested products, a gel containing 1 % Black BeeOme™ pwd or the placebo, were applied twice daily to the face (one side) and to the inner side of the forearm. In addition, a daily washing stress was induced on the forearms by washing daily with a non-hydrating shower gel.

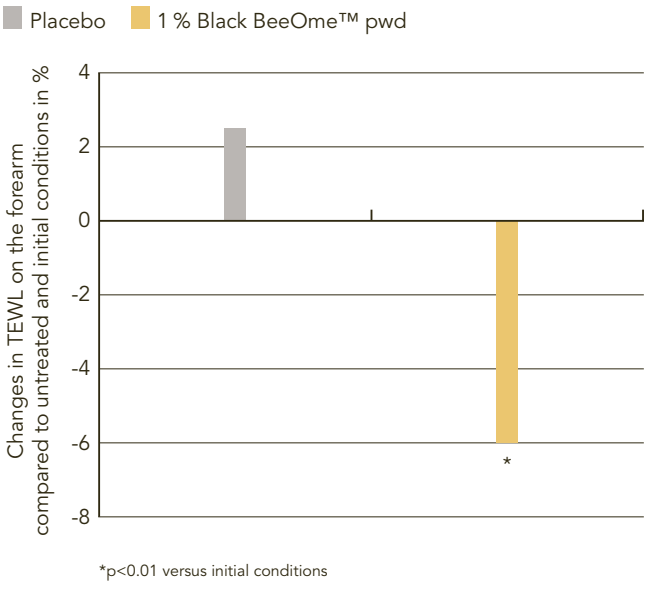
The parameters determined at the beginning of the study and after 14 days were:

- TEWL on the inner side of the forearms (Tewameter)
- sebum level and skin evenness on the face (by Sebumeter® SM 815 and clinical grading of color face pictures respectively)

After 14 days of treatment with 1 % Black BeeOme™ pwd, an improvement of TEWL compared to the placebo was observed on the inner forearms, despite the daily washing stress. In comparison to initial conditions, the improvement in TEWL was significant.

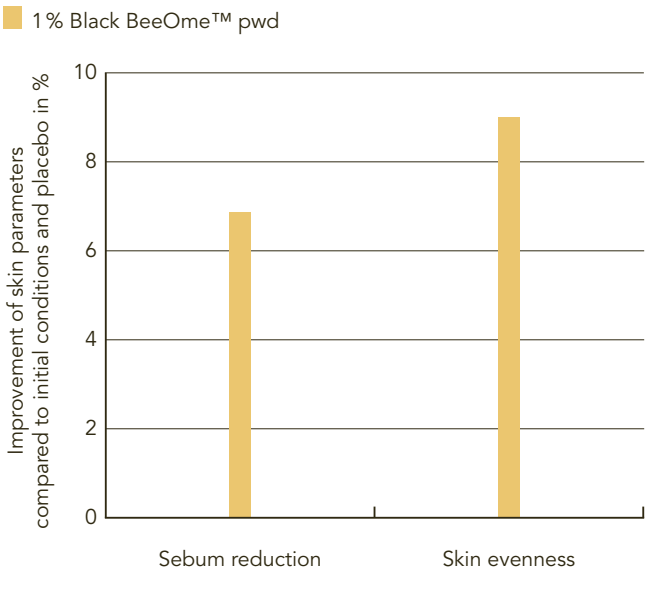
Furthermore, it was achieved a 6.8 % reduction in sebum production and a 9 % increase in skin evenness compared to the placebo and to initial conditions. The positive effect was also visible in the ColorFace® photographs (data is available separately).

Reduction of Transepidermal Water Loss (TEWL)



*p<0.01 versus initial conditions

Improvement of Skin Parameters after 14 Days



S-816 / © Mibelle Biochemistry

Black BeeOme™
Study results

Improvement of Impure Skin in Urban Areas

Air pollution has been recognized as a key factor for impure, oily and irritated skin. This can be as a result of, among other things, the negative impact of the pollution on the skin microbiota. In order to investigate the efficacy of Black BeeOme™ on the improvement of various skin parameters in urban areas, a clinical study was conducted in Bangkok on 22 female volunteers (aged between 19 and 41 years) with impure and oily skin. The volunteers applied a sheet mask containing 2 % Black BeeOme™ for 20 minutes, once daily over a period of 3 days.

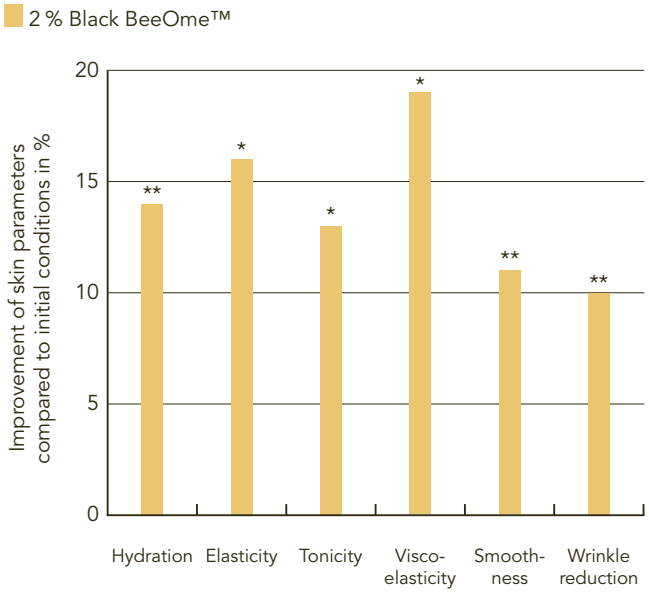
The measured parameters were:
- skin hydration (on the cheek)
- tonicity and elasticity (on the temple)
- skin relief parameters (roughness, wrinkle depth) on the cheek

at the beginning of the study and 15 minutes after the first application.
Clinical grading of skin texture, mattified skin, unified complexion and the number of lesions were determined at the beginning of the study and after 3 days of treatment.

Results showed that 15 minutes after a single treatment with 2 % Black BeeOme™, a significant improvement was achieved in all parameters compared to initial conditions:
+14 % improvement in skin hydration
+16 % improvement in elasticity
+13 % improvement in tonicity
+19 % improvement in visco-elasticity
+11 % improvement in smoothness
+10 % improvement in wrinkle reduction

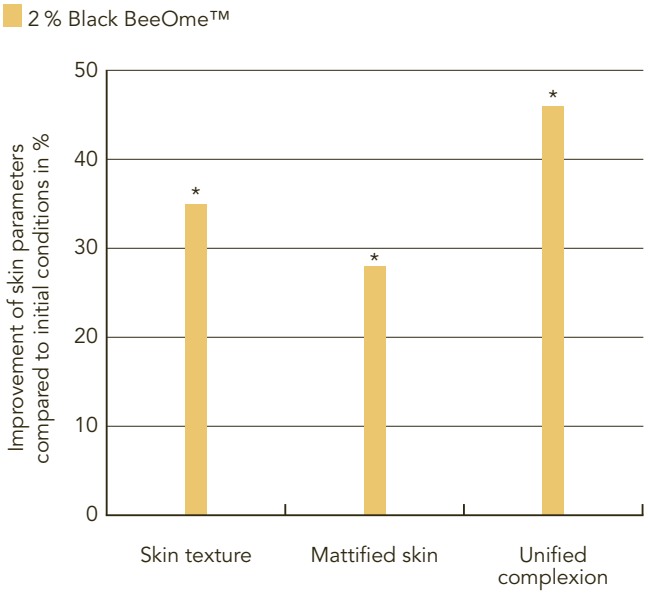
After 3 days of applying the mask containing 2 % Black BeeOme™, a significant improvement was observed in the clinical grading:
+35 % improvement in skin texture
+28 % improvement in mattified skin aspect
+46 % improvement in unified complexion

Skin Improvement after 15 Minutes of a Single Application



*p<0.05 versus initial conditions
**p<0.001 versus initial conditions

Skin Complexion Upgrading after 3 Days



*p<0.001 versus initial conditions

The parameters that characterize impure and oily skin associated with urban and polluted living areas were reduced after 3 days using the sheet mask:
12 % reduction in inflammatory lesions
9 % reduction in retentional lesions

Meanwhile, a reduction of skin redness was also achieved:
2 % reduction after 15 minutes
5 % reduction after 3 days

Therefore, Black BeeOme used in a sheet mask at 2 % contributed to ameliorate the skin impurities and skin redness of the volunteers living in urban areas.

Perception of the Efficacy by Self-Evaluation

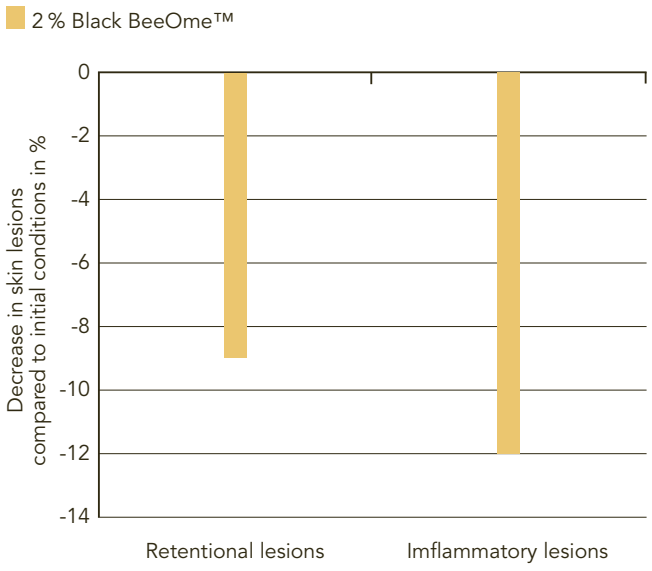
The volunteers were asked via a questionnaire to confirm whether they perceived improvements of specific criteria. The analysis of the self-assessment questionnaires showed statistically significant statements:

100 % of volunteers either agreed or somewhat agreed with the statement:
"Leaves the skin soft and comfortable"

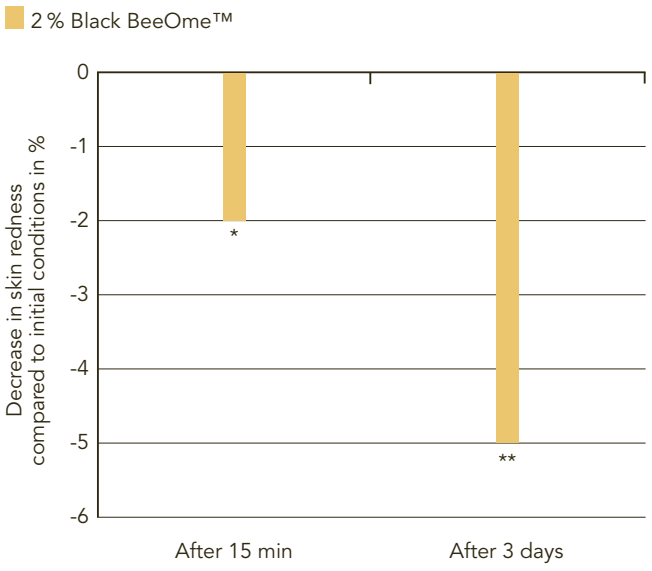
95 % of volunteers either agreed or somewhat agreed with the statements:
"Skin is less shiny"
"The skin seems rebalanced"
"The skin seems purified"

91% of volunteers either agreed or somewhat agreed with the statements:
"Excess sebum is eliminated"
"The product leaves the skin clear and fresh"
"The skin is mattified over a long time"

Reduction of Skin Impurities after 3 days



Reduction of Skin Redness



*p<0.001 versus initial conditions
**p<0.0001 versus initial conditions

Black BeeOme™

Black bee honey ferment to restore the skin's natural microflora

Black BeeOme™
- Reduces sebum production for a matte and pure skin
- Regenerates the skin microflora after washing
- Protects and strengthens the skin barrier

Applications
- Sheet masks
- Mattifying skin care
- Anti-blemish formulations
- Sensitive skin care

Marketing benefits
- Gold Award at BSB Innovation Prize in the category "Natural Product"
- Honey of a rare and extremely resistant Swiss bee
- Honey is a precious ingredient for skin care with a long tradition
- Assists general skin microbiota recovery
- Sheet mask formulation with proven efficacy

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.

Mibelle AG Biochemistry, 5033 Buchs / Switzerland, Phone +41 62 836 17 31, info@mibellebiochemistry.com, www.mibellebiochemistry.com