



Reinforcing the skin barrier

As microorganisms' role in skin health and beauty has become clearer, innovative active ingredients are hitting the market. In this issue, **Sabrina Leoty-Okombi, Valérie André Frei, Philippe Moussou and Torsten Clarius** explain how two of those, Relipidium and Phytosoothe, help to protect the skin

According to recent research, almost 60% of cells on and inside our bodies are not human, but belong to microbiota such as bacteria, viruses, fungi and archaea. Over the last decade, our understanding of this microbiome – as microorganisms in their entirety are called – has improved significantly, which is in large part thanks to the Human Microbiome Project (HMP), launched in 2008.

One of the project's key discoveries is that, while the human genome contains around 22,000 protein-coding genes, estimates now place the number of bacterial protein-coding

Consumers who have embraced the role of microorganisms in gut health are turning their attention to the skin microbiome

genes in the millions. And many of these proteins are essential to our bodies: bacteria residing in the gastro-intestinal tract, for example, allow us to digest foods and absorb nutrients that would otherwise be unavailable to us.

Consumers have embraced the role of bacteria in digestive health and have increasingly turned to ingestible probiotics and prebiotics. However, consumer interest in the role of microbiomes on skin health and beauty is still in its early stages.

A BALANCING ACT

The skin and its microbiota – which live on the surface of the epidermis, as well as deep within the epidermis and dermis – form an ecosystem containing both commensal (good) bacteria and opportunistic pathogens.

The composition of the microbiota is unique to each individual and continues to evolve throughout our lives, depending on skin condition (water, pH, lipid, proteins) and the environment to which it is exposed (temperature, UV rays).

Up to one million microorganisms live on each square centimetre of skin, subsisting on nutrients provided by skin cells. A healthy commensal flora actively prevents the skin from being colonised by opportunistic pathogens through the secretion of antimicrobial peptides (direct defence) and stimulation of the skin cells' natural defences (indirect defence).

A good balance of commensal and pathogenic bacteria keeps the skin healthy, enabling it to act as an efficient barrier that keeps dirt and bacteria out while keeping moisture locked in.

When there are fewer commensal bacteria present, pathogenic bacteria thrive and cause the skin to go into a state of microbial imbalance, or dysbiosis – often leading to conditions such as inflammation, dry skin, redness and acne.

Maintaining this fragile balance is essential to skin health and beauty.

To further explore the microbiome's role in skin health and to help manufacturers meet the growing demand for solutions acting on or through microbiota, BASF established a dedicated innovation platform in 2016, bringing together internal and external researchers at its research facilities in Lyon.

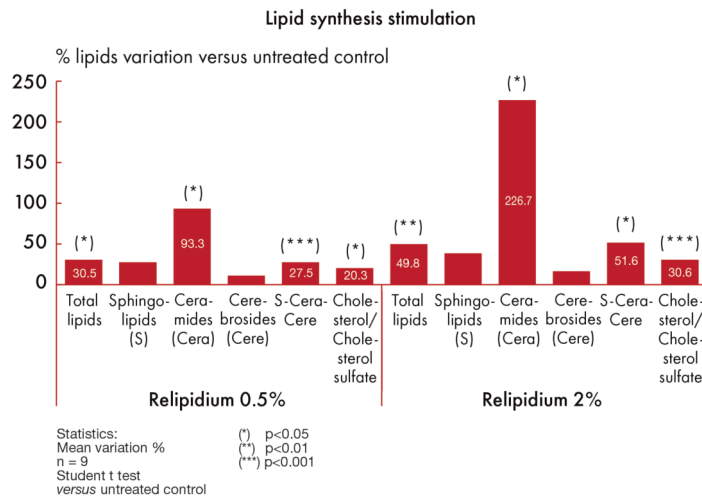
The research team's first achievements included creating new engineered skin models embedded with bacteria to study the interactions between active ingredients and skin microflora, as well as the development of several new active ingredients. These include Relipidium and Phytosoothe, which both reinforce the skin and protect it against external aggression.

SKIN UNDER ATTACK

Every day, our skin is exposed to external

Figure 1

Epidermal lipid synthesis in presence of Relipidium at 0.5% and 2%



aggression from the sun, air conditioning, cold and heat, water from repeated showers and harsh detergents.

These factors can impair lipids, which are crucial for maintaining the physical skin barrier and throw the microbiome off balance; beneficial commensal bacteria such as *Staphylococcus epidermidis* are weakened and become harmful, while inflammatory bacteria such as *S. aureus* colonise or grow excessively on the skin.

This results in a vicious cycle. The skin's weakened physical and microbiotic barriers create the perfect conditions for water evaporation from the skin, and for irritants and other harmful substances to penetrate the skin from outside. In turn, dry skin reinforces microbiota dysbiosis, further aggravating the problem.

RELIPIDIUM REINFORCES

To reverse this cycle and rebalance the skin's lipid barrier, BASF has developed Relipidium (INCI: Hydrolyzed yeast protein, butylene glycol, pentylene glycol), a stabilised yeast hydrolysate biofermented by the probiotic *Lactobacillus plantarum*.

It reinforces the skin's lipid barrier and defences by creating a favourable environment for a balanced skin microflora, which in turn helps to preserve moisture.

In vitro, Relipidium has proven to stimulate lipid synthesis on reconstructed epidermis, restoring the skin barrier function. Applied at 0.5%, it increases total lipids by 30.5% and ceramides by 93.3% after a ten-day incubation period; used at 2%, it increases total lipids by 50% and ceramides by 227% (figure 1).

Moreover, Relipidium applied at 0.5% speeds up skin barrier recovery after chemical disruption with acetone.

This was tested *ex vivo* on abdominal skin

biopsies from a 27-year-old male donor. After one day, the skin biopsies were less permeable compared with the disrupted and untreated control, which was reflected in a significantly better retention of a fluorescent Lucifer yellow solution (figures 2 and 3).

In vivo, Relipidium at 1% improved the skin barrier function after 14 days of daily application.

In a second clinical test, performed on 20 healthy females with dry skin aged 18-45, Relipidium applied twice daily at 2% for two weeks improved skin hydration by 12% and increased the abundance of the beneficial commensal *S. epidermidis* bacteria in relation to total bacteria by a factor of 2.1.

In the ten participants who had displayed the skin transient pathogenic *S. aureus* on their cheek at day zero, the *S. epidermidis* population relative to *S. aureus* increased by a factor of 2.3 after 14 days (figures 4 and 5).

The preservative-free, water-soluble hydrolysate can be used at a concentration of 0.5-2% and can be incorporated at room temperature for *in vitro* testing.

Figure 2

Visualisation of skin barrier recovery after disruption using permeation assay with Lucifer yellow. Green: Lucifer yellow; red: filaggrin; blue: DAPI nuclear staining

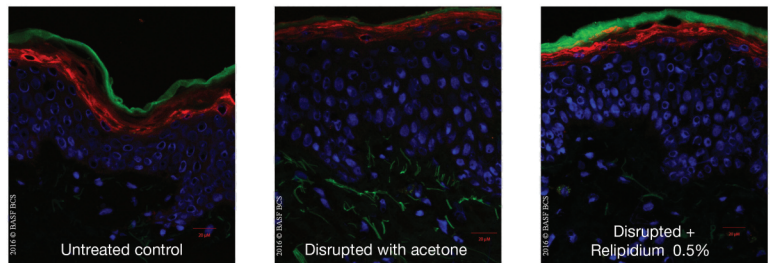


Figure 3

Quantification of Lucifer yellow dye after skin barrier disruption and treatment with Relipidium

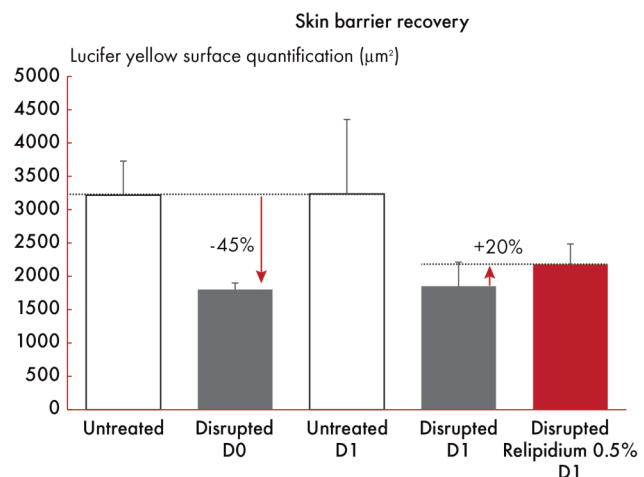
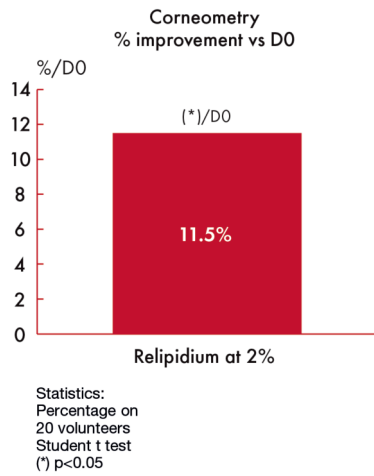


Figure 4

Evolution of skin hydration after 14 days of Relipidium application, measured by corneometry



For clinical testing, the entire Relipidium formula is used at 1% and 2%.

PHYTOSOOTHE REPAIRS

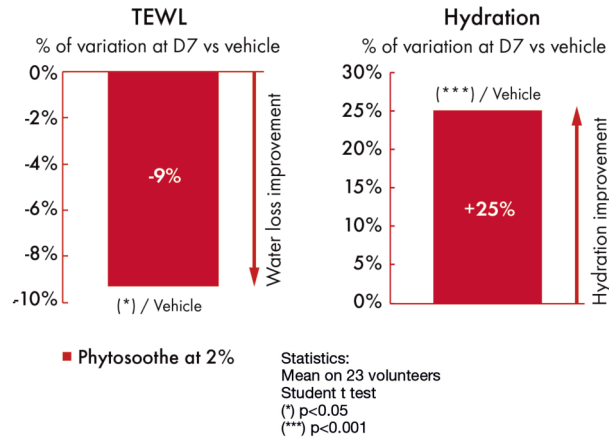
Phytosoothe (INCI: Brassica campestris (rapeseed) sterols, cetearyl alcohol), a blend of phytosterols from rapeseed and cetearyl alcohol, protects the skin's physical and microbiotic barrier, and restores it after impairment.

In a study featuring 23 fair-skinned female volunteers aged 20-64, Phytosoothe was proved to strengthen the skin barrier function, and help repair and rehydrate impaired skin.

An occlusive patch containing 1% of sodium lauryl sulfate (SLS) was applied for 24 hours on both inner sides of the forearms.

Figure 6

Repairing effect of Phytosoothe at 2% vs vehicle. Measurement of TEWL by Tewameter and hydration by Corneometer



Phytosoothe was proved to strengthen the skin barrier function, and help repair and rehydrate impaired skin

After application of 2% Phytosoothe in an oily vehicle for seven days, transepidermal water loss (TEWL) by evaporation was reduced by 9% and hydration increased by 25% compared with the vehicle alone (figure 6).

A study with 29 female volunteers aged 18-45, who declared having reactive skin without a specific skin condition demonstrated microbiotic barrier restoration after the application of a 0.5% SLS occlusive patch.

After seven days of a single-daily Phytosoothe application at 2% in an oily vehicle, the relative abundance of the commensal bacteria *Corynebacterium* genus, for example, was significantly improved by 88% compared with D0. The same effect was seen with *Paracoccus* and *Micrococcus* genus.

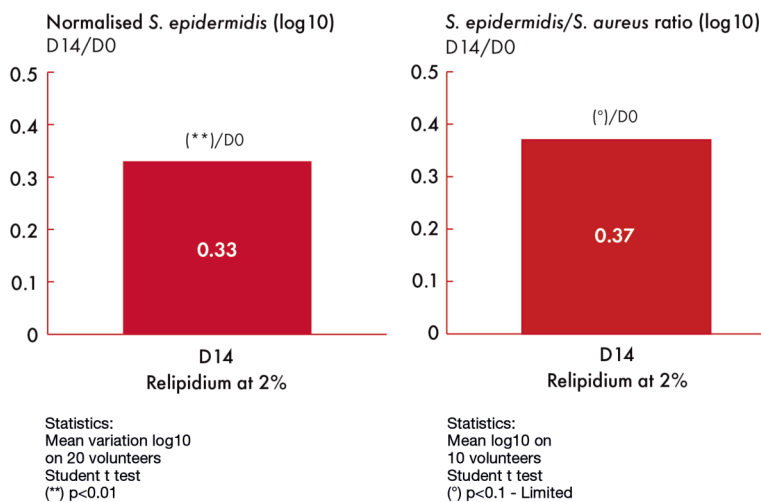
Phytosoothe is 100% natural-origin and preservative-free. The powder is soluble in oils and fats, and can be used at a concentration of 0.5-3%.

It is suitable for a wide range of applications including face, body and scalp care applications; cleansers, conditioners and shampoos; and intimate care products.

Besides Relipidium and Phytosoothe, BASF offers a range of other active ingredients that act on or through microbiota. These include Betapur, a boldo extract that stimulates the skin's natural antibacterial systems; the *Bixa orellana* seed extract Bix'Activ, which helps to decrease sebum production; and Patch2O technology, which provides immediate and long term moisturisation while protecting the skin barrier and microbiota against pollution and the virulence of harmful bacteria ●

Figure 5

(A) Evolution of normalised *S. epidermidis* quantity. (B) Evolution of ratio *S. epidermidis*/*S. aureus* after 14 days of Relipidium application (expressed as log10)



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