There is a fine line between modifying the skin microbiome’s composition to promote healthy-looking skin and disrupting its delicate balance in a potentially detrimental way. With consumer interest in microbiome-friendly skin and personal care products growing, DSM has been exploring new approaches to restoring and preserving the natural and individual balance of skin microbiota.

Thanks to an innovative data analysis technique, we have been able to go further in identifying and classifying skin microbiota composition. We have then used this information to investigate and visualise the modulatory effect two of our skin bioactives have on key microorganisms. Additionally, we have been exploring vitamin-based acne-care solutions and have also begun assessing personal care ingredients for microbiome-friendliness in line with a new, independent standard.

New potential for skin care
In the cosmetics industry, the skin microbiome is increasingly thought to play a fundamental role in maintaining a healthy skin appearance. Most microorganisms living on our skin, defined as commensals or symbiotics, have been shown to protect against pathogens and to play an important role in modulating the host’s cutaneous innate and adaptive immune system.\(^1\)\(^,\)\(^2\)

Skin-resident bacteria produce, among other molecules, acidic metabolites. Together with the lactic acid present in our sweat and the free fatty acids produced when phospholipids undergo lipase-mediated hydrolysis during cornification, these metabolites contribute to the low pH level of the surface of the skin. Resident commensal bacteria can cope with this acid mantle, but many pathogens cannot.\(^3\)\(^,\)\(^4\)

Imbalances in skin microbiota composition or dysbiosis (Figure x) are associated with several skin conditions. Some, such as eczema, acne, allergies and dandruff, are pathological, while others, including skin sensitivity, irritation and dryness, are non-pathological.\(^5\)

Additionally, the use of specific products and actions such as skin cleansing can also cause shifts in the composition of the skin microbiota. Approaches that aim to preserve or restore the natural, individual balance of the skin microbiota therefore offer potential both for dermatologists and skin care applications.

Understanding skin microbiota composition
Physiological characteristics (pH, temperature, sebum content and moisture), topography (the rough or smooth surface of corneocytes) and exogenous environmental factors (UV exposure, temperature and humidity) all influence microbial colonisation on the skin surface.\(^5\) As a result, skin microbiome composition varies considerably depending on the body site.

Facial skin is a particularly complex environment comprising sebaceous areas (the forehead, nose and chin, also known as the T-zone) and dry areas (the cheeks). The precise make-up of skin microbiota at different facial sites has not yet been described, so we...
have conducted a clinical study to assess this. We have then used this data to investigate the modulatory effect a topically applied bioactive can have on key microorganisms. We have also illustrated all our findings using 3D facial colour mapping, a technology that visualises complex and detailed data in a way end consumers can relate to and understand.

A new methodology for assessing changes in microbiota composition
Skin microbiome data are compositional, meaning that changes, or shifts, in one component affect all the others. To accurately determine which microbes are changing and to what extent, it is therefore essential to have information about the total microbial load or absolute number of microorganisms.

However, collecting such data is challenging and prone to bias, so current approaches to skin microbiome analysis tend to be based on comparing relative abundances across samples, even though these approaches are prone to high false discovery rates. To overcome this, our studies followed a new, state of the art methodology known as ‘reference frames’.

This involved a comprehensive microbiome analysis of different facial sites using 16S rRNA sequencing, the assessment of microbial changes in abundance in response to the product application, the identification and ranking of those bacteria changing most relative to each other (differential ranking) and the comparison of log-ratios of every bacterium with respect to a reference microorganism (the reference frame) to infer changes in abundance.

Reference frames provide in-depth insights into the compositional nature of microbiome data, alleviate false positives, and produce consistent results. They also help in the identification of consistent, differentially abundant microbes which are often undetected.

By using reference frames to analyse 16S–rRNA sequencing data, we were able to identify shifts in microbial composition and associate specific microbiota with the presence of specific skin bioactives. We applied our methodology to the first two studies described below.

Study 1: Shifts in skin microbiota after cleansing
Our first study focused on the effect of cleansing skin with a body wash containing saccharide isomerate (commercial name Pentavitin®). This is our well-known cosmetic ingredient, with a unique binding mechanism that delivers instant and long-lasting moisturisation to skin.

Cleansing involves the mechanical and chemical removal of dirt, pollutants, and reduction of microbial load on the skin. While cleansing can help maintain good health and protect us from infection and illness, the process also strips skin of lipids and moisture. This can lead to irritation, impair the skin barrier, and disturb the delicate cutaneous microbiome.

Our placebo-controlled clinical study investigated how cleansing impacts the body skin’s microbial composition. In this, 30 Caucasian women applied a liquid body wash on their volar forearms twice daily for one week, to mimic frequent showering.

As well as demonstrating the beneficial effects of saccharide isomerate, the study revealed cleansing-associated microbial changes. Both short- and long-term perturbation were observed because of skin cleansing, but at the same time, the skin microbiome proved to be resilient and able to adapt its composition and re-establish itself.

Additionally, the use of saccharide isomerate in our studied body wash was associated with a reduction in coryneforms, such as B. casei and R. mucilaginosus (bacteria which are increasingly implicated in skin infections) and an increase in the beneficial bacterium, P. marcusii. These shifts were observed 24 hours after showering and after seven days of frequent showering.

Study 2: Shifts in facial skin microbiota in response to a cosmetic bioactive
Some 50% of consumers have concerns about oily skin. Over the past year, such concerns have been exacerbated by mask wearing because this practice traps oil and bacteria on the skin around the chin and creates humid conditions conducive to overproduction of sebum, resulting in clogged pores and spots.

In a separate study, focusing on oily skin, we assessed the composition of the skin microbiota in five facial areas. We then analysed shifts in microbiota composition after application of a leave on formulation containing Epilobium fleischeri plant extract (commercial name Alplafor® Alp-Sebum)

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For this randomised, double-blind and placebo-controlled study, we assessed to which extent the plant extract improved the overall skin phenotype and how it interacted with the facial microbiome. The 23 subjects applied either the formulation containing the plant extract or a placebo formulation to the full face, twice daily for 28 days.

Microbiome samples were collected at the baseline and after 28 days by means of swabbing at five sites (forehead, nose, front cheek, lateral cheek and chin). By means of the reference frames method we identified differentially abundant species which led us to focus on three particularly relevant species of bacteria:

- Staphylococcus epidermidis, a commensal known for its anti-microbial activity against some pathogens and for playing a role in acne prevention and inflammation resolution
- M. yunnanensis, which plays a detoxification role and promotes skin defence; and
- S. capitis, another skin commensal suggested to play a role in acne formation.

For each of these species, we mapped median values of log ratios to a 3D image of an average face. More microbiome analysis is ongoing, but in this study, we found that the Epilobium fleischeri extract had a prebiotic effect on the skin microbiota, promoting an abundance of beneficial skin bacteria such as S. epidermidis and M. yunnanensis.

Moreover, compared to the placebo these bacteria were significantly modulated on the forehead, cheek, and chin. This is illustrated in the facial map in Figure 2, which provides a visual comparison of log ratios of S. epidermidis and S. capitis after 28 days of treatment with either the placebo or Epilobium fleischeri formulation.
Study 3: Respecting microbial balance in acne-prone skin

Acne is the most common chronic inflammation of the skin, affecting 75–95% of teenagers, but it is now prevalent in more than 50% of adults too. This can be partially explained by acne-associated bacteria developing resistance to antibiotics, meaning that conventional treatments cease to be effective after a few years of use. Additionally, typical side effects (redness, dryness, irritation) resulting from their use are worse in adult acne sufferers than in teenagers.

Cutibacterium acnes strains are one of the factors considered to play a key role in the exacerbation of acne. However, treatments that reduce C. acnes populations can also harm beneficial skin bacteria and disrupt the delicate microbiome balance. Indeed, dysbiosis between different C. acnes strains is now associated with acne development, rather than a hyperproliferation of these strains.

There is a need for effective acne care that avoids disruption of natural microbiota and minimises other unwanted side effects (such as skin redness and burning sensations) common to retinoid- and benzoyl peroxide-based conventional treatments. To address this, we have conducted a study using sodium ascorbyl phosphate (a stabilised form of vitamin C) in combination with niacinamide (vitamin B3) which is known for its skin barrier-strengthening properties, and allantoin.

In this study, we found that this combination of ingredients noticeably inhibited growth of an acne-associated C. acnes strain within two hours (Figure 3) and even outperformed 0.5% salicylic acid, which was tested in identical conditions. Our results suggest that a combination of sodium ascorbyl phosphate with niacinamide and allantoin could be an effective treatment for reducing abundance of pathogenic C. acnes strains. This would maximise the potential for improvement, while addressing a need for milder acne care treatments.

Microbiome-friendly beauty products – a precise balance

Our study findings suggest that using cosmetic bioactives to modulate specific detrimental and beneficial skin bacteria can help to promote a healthy skin microbiome and, therefore, a healthy skin appearance. However, beauty and skin care products can also contain ingredients and antimicrobial preservatives, which may negatively impact the delicate balance or diversity of the cutaneous microbiota.

In view of the growing body of scientific evidence pointing to a link between microbiota imbalances (dysbiosis) and skin and scalp concerns, such as acne, atopic dermatitis (eczema), dry skin and dandruff, it is important to make sure that any beneficial modulatory effect is not outweighed by a disruptive effect on the overall balance of skin microbiota. In other words, cosmetic ingredients and products need to respect certain microbial ratios and should not behave in the same way as anti-microbial substances.

MyMicrobiome, an independent institute that tests products and individual ingredients for their impact on the skin’s microbiome, has developed a standardised test that creates clear, digital results in vitro, referring to the latest scientific findings. By simulating product use on the human body, it also evaluates a product’s impact both on the skin’s surface and in the deeper skin layers.

Taking account of the different sets of microbes which thrive at each specific skin site, the MyMicrobiome test assesses the extent to which products influence microbiome diversity, healthy microbial balance, and microbial growth or vitality. Products and ingredients that pass these tests can be classified as microbiome-friendly and receive a ‘Microbiome-friendly’ label. This is a helpful way for personal care manufacturers to reassure end consumers who are looking for products that respect the balance, diversity, and vitality of their skin microbiome.

In parallel to the first two studies discussed above, Epilobium Flescheri and Saccharide Isomerase, have both been tested in line with the MyMicrobiome standard and both have received the ‘Microbiome-friendly’ label. To support formulators in developing products that minimise their impact on the skin microbiome’s natural balance, we have also submitted other ingredients for testing, including our 1–3 propanediol, niacinamide, and several hyaluronic acid grades. These too have been certified ‘Microbiome-friendly’.

Additionally, we have incorporated these ingredients in different Microbiome-friendly-certified, ready-to-use formulations, such as shampoos, serums and day creams. As a result, manufacturers can begin meeting the demand for more microbiome-friendly products now.

As our activities show, the skin microbiome offers real potential for innovation in skin care if we respect its balance. DSM remains committed to staying at the forefront of understanding about this topic, by leading the way with new research and developing novel solutions.

References