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"All inclusive" microbiome-friendly cosmetic ingredient portfolio – galenic ingredients that allow the development of formulations that do not harm the healthy skin microbiome

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1. Introduction

The human microbiome comprises a complex ecosystem of microorganisms residing in and on the human body. It is estimated that these microorganisms outnumber the human cells by at least a factor of 1.3 [1]. It is now recognized that microorganisms play a crucial role in maintaining our health and overall well-being. Over the past decade, the awareness has grown that even the microorganisms inhabiting our skin play a beneficial role in skin and health. There is an intricate interaction between microorganisms and the skin as well as with other microorganisms on the skin. Yet, it is also clear that the healthy balance of microbial inhabitants is essential and a disbalance can lead to or exacerbate skin conditions, e.g. acne. Currently, the effects of cosmetics are primarily being explored in terms of how actives (e.g. pre/pro/postbiotics) can modulate the microbial composition of the skin with the goal to promote growth of beneficial microorganisms. Yet, personal care formulations are primarily comprised of other ingredients, sometimes termed "galenics".

Galenics cover a wide range of ingredients including various emollients, emulsifiers, surfactants and polymers. These are essential for other properties of the product, e.g. to provide certain sensorial, moisturizing or cleansing properties. They also serve as a means of incorporating actives into a formulation that consumers will accept as well as to generate their mode of use (e.g. shampoo, skin cream). As they represent a major part of a formulation and are applied to the skin, they could interact with skin's microflora. As such, they could, but should not, affect the healthy skin microbiome. As the effects of these components have been far less explored than that of some actives, they were therefore the focus of this study.

2. Materials and Methods

A large range of cosmetic ingredients were screened and tested as depicted in Figure 1. Water-soluble ingredients were screened using minimal inhibitory concentration tests (MICs), and emollients were subjected to use tests followed by microbial analyses of skin swabs taken from human volunteers with healthy skin (n=20; in vivo; Figure 1). Limit of use concentrations were then defined and used to develop both leave-on and rinse-off proof of principal formulations (Table 2 A, B). These formulations passed both challenge and stability testing. These were then subjected to clinical testing with volunteers having healthy skin, having given their informed consent and using the volar forearm as the site of application. Rinse-off formulations were tested twice daily for two weeks on Caucasian volunteers (30s application time, followed by 10s rinse, tap dry; swabbing area 4 x4 cm for 16S analyses). Leave-on products twice daily for four weeks on Asian volunteers (followed by 10s rinse, tap dry; swabbing area 4 x4 cm for 16S analyses). Microbial 16S rDNA sequencing was used to assess possible changes to the skin microbial communities (before vs. after treatment). Alpha-diversity analyses via Shannon diversity indices were used to assess changes in the skin's microbial communities. Selected formulations were subjected to additional clinical testing, e.g. skin hydration (leave-on) or suitability for sensitive scalps (shampoo). Evaluation of perceived properties and acceptance by the volunteers was based on questionnaires.

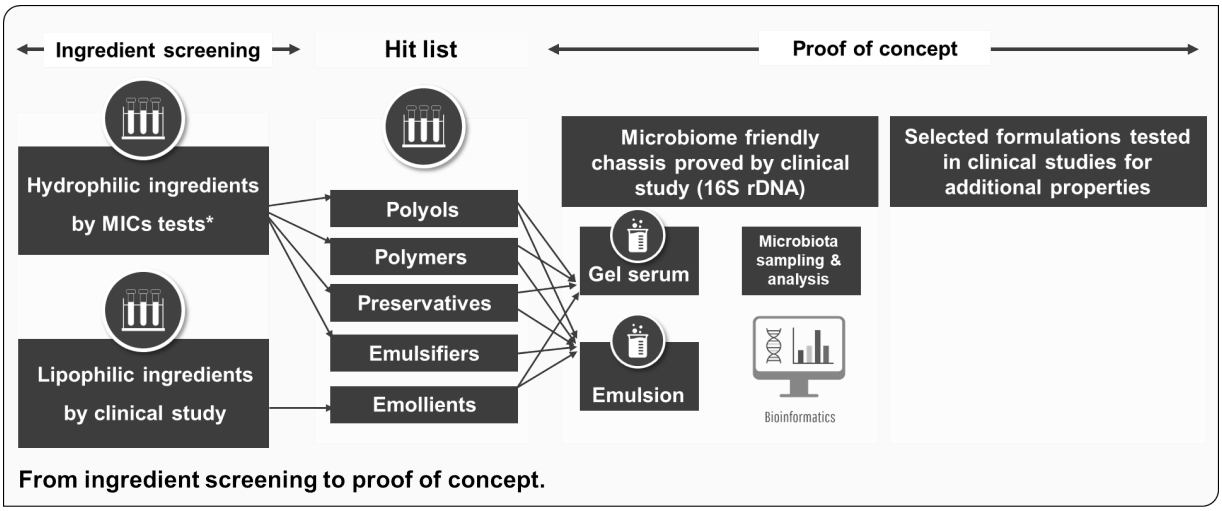


Figure 1. Schematic of the screening and testing procedure

3. Results

The number of ingredients not leading to significant changes in the skin's microbial communities of healthy individuals at the tested concentrations are found in Table 1 at concentrations tested. As the volar forearm exhibits a higher diversity of microorganisms than the face, products were applied there. This also allowed for testing of 3 products versus the untreated control.

Table 1. Galenic ingredient classes, number of different ingredients tested and exhibiting no significant change to the microbial communities on healthy human skin.

Class	Number of ingredients tested
Emollients	25
Emulsifiers	11
Rheology modifier	7
Surfactants	5
Other (e.g. preservatives, conditioning agents, pearlizer)	17

Formulations were developed (examples: Table 2 A, B) and then subjected to clinical studies and 16S rDNA analyses. Shannon diversity indices are used as a measure of alpha diversity and take species and differences in abundance into account.

Table 2. Examples of tested formulations A) rinse-off (HB-DE-22-MW-2988704-40); B) leave-on (SC-DE-22-JM-3049647-136)

A) Rinse-off

INCI	% by weight
Aqua	To 100
Sodium Benzoate	0.10
Guar Hydroxypropyltrimonium Chloride	0.20
Lactic Acid	0.31
Lauryl Glucoside	5.50
Cocamidopropyl Betaine	6.10
Coco-Glucoside, Glyceryl Oleate	1.00
Dicaprylyl Ether, Decyl Glucoside, Glyceryl Oleate	3.00
Coco-Glucoside, Hydrogenated Castor Oil	5.00
Glycerin	10.00
Xanthan Gum	1.20

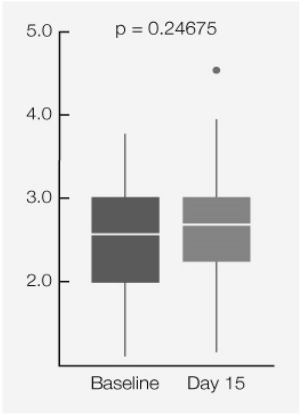
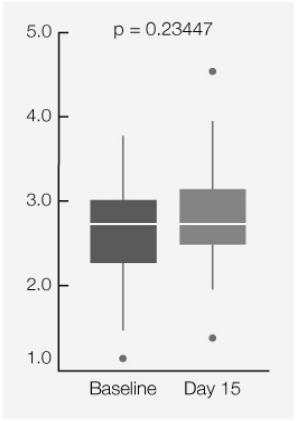
B) Leave-on

INCI	% by weight
Aqua	To 100
Glycerin	5.00
Algin	0.60
Caesalpinia Spinosa Gum	0.20
Glucomannan	0.20
Lauryl Glucoside, Polyglyceryl-2 Dipolyhydroxystearate, Glycerin	2.00
Propylheptyl Caprylate	5.00
Dicaprylyl Carbonate	5.00
Calcium Chloride	0.06
Water, Sodium Benzoate, Potassium Sorbate	1.00
Citric acid	q.s.

Results of studies with the rinse-off formulation

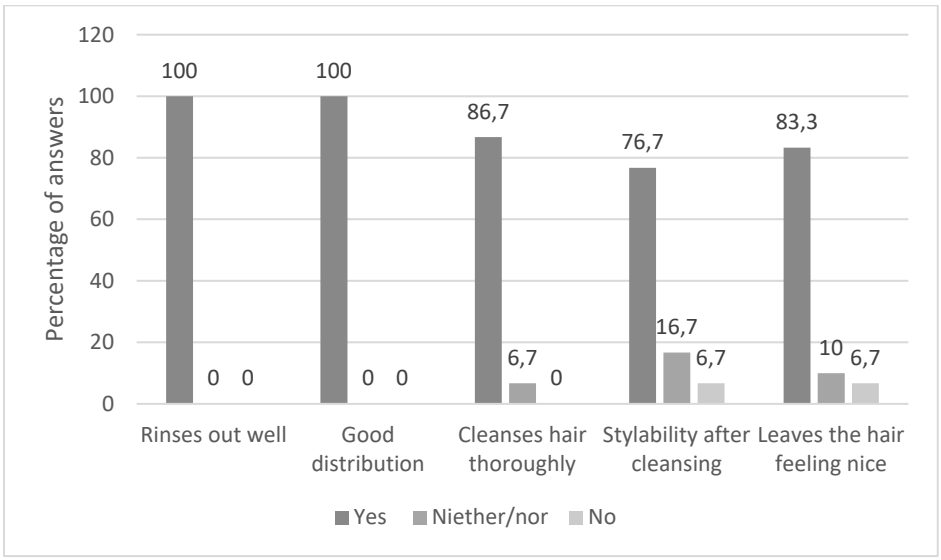
After a twice daily application of the rinse-off product over a time-period of two weeks 16S rDNA analyses revealed no significant differences ($p<0.5$ being significant) between before treatment and after treatment (Figure 2).

Figure 2. Alpha diversity (Shannon diversity) following two weeks of use (forearm; no significant changes were observed; $p<0.05$)

Untreated (tap water, before and after)	Treated (before and after)
	

As consumer acceptance is a key attribute for use of a product, a clinical study was conducted with the rinse-off formulation to assess its acceptance by the volunteers and its suitability for sensitive scalp applications. After a one-week preconditioning phase, the formulation was used once daily for 28 days by Caucasian volunteers with sensitive scalps. No further hair care products were permitted over the study period. Based on the results of this study (before vs. after treatment), the formulation can claim to be suitable for sensitive scalps and to reduce tautness, itching and flaking. In addition, the majority of the volunteers found the formulation to have positive attributes, e.g. cleansing properties and rinseability (Figure 3).

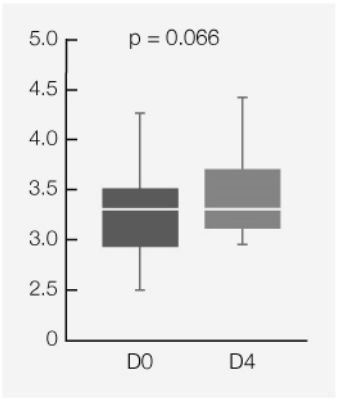
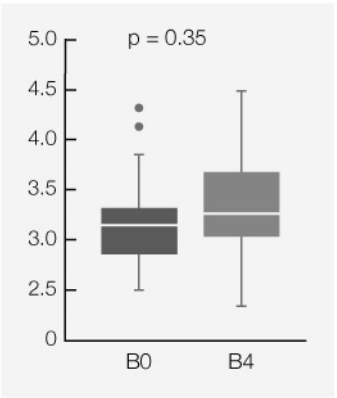
Figure 3. Product properties as assessed by volunteers with sensitive scalps



Results of studies with the leave-on formulation

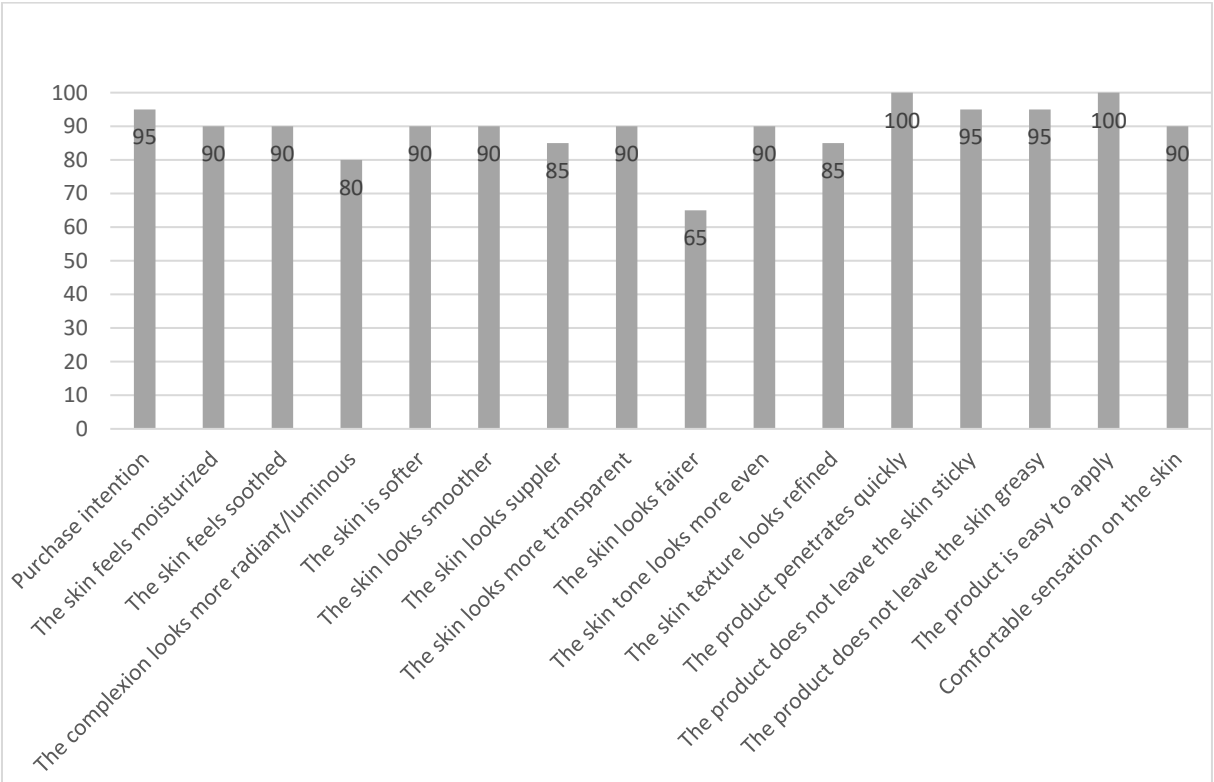
Following four weeks of twice daily application to the volar forearm of Asian volunteers, the alpha diversity indices indicated no significant change ($p<0.05$ being significant) to the healthy skin microflora (Figure 4).

Figure 4. Alpha diversity (Shannon diversity) before (D0/B0) and after four weeks (D4/B4) of use twice daily (no significant changes observed; $p<0.05$)

Untreated (before and after)	Treated (before and after)
	

During this study, consumer-perceived effects were also monitored via a questionnaire after four weeks of use. The results indicated favorable profiles and acceptance of the formulation (Figure 5).

Figure 5. Volunteer acceptance (strongly agree + agree in %)



4. Discussion

The skin microbiome plays a crucial role in maintaining skin health and homeostasis. It acts as a biological barrier against pathogenic microorganisms by competing for nutrients and space, producing antimicrobial substances and modulating the host's immune responses [2] [3]. Hygiene practices, such as the use of soaps and shampoos, can alter the skin's microbial community by removing both pathogenic and beneficial microorganisms. Frequent washing with antimicrobial products may lead to dysbiosis, a disrupted microbial balance, which has been associated with skin conditions like eczema and acne [4]. Use of skin care products have also been reported to alter the composition of microbial communities on the skin [5]. In 2022, the International Cooperation on Cosmetic Regulations (ICCR) published working definitions on the terminology associated with the skin "microbiome" [6]. The ICCR also noted in the working definitions that "The composition of the skin microbiome is dynamic, site-specific but also differs from individual to individual" – indeed, it has even been compared to a fingerprint. The aging process can also have effects on the composition of the microbial communities on skin [7]. As a healthy skin microbiome is essential for skin health, the composition should not be significantly changed by topical or other treatments.

Based on the results of this study, a large portfolio of cosmetic ingredients is now available that can be used up to the concentrations tested to develop formulations that do not significantly change the composition of the healthy skin. As the proof-of-concept (PoC) formulations (both leave-on and rinse-off) did not significantly alter the microbial compositions found on healthy skin of human volunteers, the results indicate that they were "microbiome-friendly". Actives were incorporated into model formulations and the formulations remained stable (data not shown). Therefore, these formulations can also be used as chassis for the incorporation of actives (e.g. pre/pro/postbiotics) should conditions prevail that could benefit from modulated growth of e.g. beneficial microorganisms. The PoC formulations highlighted here are not only gentle to the skin's microbiota, they also exhibit properties essential for consumer use. The rinse-off formulation was found to be suitable for sensitive scalps while also providing attributes needed such as cleansing and rinse-out performance. The leave-on formulation left the skin feeling more comfortable, supple and moisturized. The comprehensive range of galenic ingredients and formulations tested now allow "all-in" holistic approaches to be developed for microbiome-friendly and consumer-friendly formulations.

5. Conclusion

Formulations are primarily composed of galenic ingredients – they can form the chassis for the delivery of actives. As they are therefore also applied topically, the main intent of this study was to identify galenic ingredients which do not disrupt the complex microbial communities found on healthy skin. Substantially adding to a small-scale study (leave-on only) [8], the results demonstrate that by careful screening of ingredients combined with formulation expertise, science-backed personal care products for both rinse-off and leave-on applications can be developed that can truly be claimed to be microbiome-friendly. These can also fulfil other consumer expectations linked to personal care products (e.g. moisturization, mildness, cleansing and sensorial properties). Formulations can also be used as a chassis to incorporate active ingredients if needed. The comprehensive range of galenic ingredients and formulations tested now allow "all-in" holistic approaches to be developed for microbiome-friendly formulations.

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