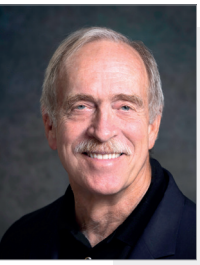
Panel Discussion on

Commentary article



PHIL GEIS, PHD
Geis Microbiological Quality

A native Texan, Dr. Geis is consultant and Principal for Geis Microbiological Quality with expertise in preservation and manufacturing hygiene for consumer and industrial product microbiology. A former US Army medical microbiologist, Phil is an industry veteran having led for decades global microbiology for The Procter & Gamble Company's cosmetic and household products businesses. He has lectured and written extensively about preservation and hygienic manufacturing, most recently as the 3rd edition of Cosmetic Microbiology - A Practical Approach. Former instructor and current consultant for the Microbiology and Cell Science Department of the University of Florida, Dr. Geis is currently editor for International Biodeterioration and Biodegradation and an editorial board member for Food Safety and Applied Biotechnology.

In satisfying the regulatory and ethical demands for effective preservation through consumer use, formulators and marketers face a dilemma. Application of historically-effective, traditional preservative systems are discouraged by consumer and retail demands for alternative systems driven by perceived safety concerns and claims of green/natural/sustainable products. However, these alternatives are generally less effective and have driven in some applications significantly increased reports of microbial adulteration. This summarizes and discusses perspectives of a panel of preservative suppliers and service providers regarding efforts to serve this growing consumer segment. The article addresses and compares traditional preservatives and alternative systems, identifying risks that must be managed in their continued development and application.

Preservatives are an essential element of cosmetic microbiological quality. Necessary but not sufficient to control contamination, they must be accompanied by appropriate good manufacturing practices (GMPs), manufacturing hygiene and protective packaging to achieve the primary goal – consumer microbiological safety. In the manufacturing context, GMPs and manufacturing hygiene are the primary tools for microbiological quality with preservatives as necessary agents to mitigate contamination risks due to inadvertent and limited microbial exposure during production. Failure in these can result in product contamination, significant not only to brand and regulatory compliance but also establishing significant consumer risks. At greatest risk are those with compromised immunity who can suffer serious infection possibly leading to death (1).
However and as observed by Francesco Tursi of Complife Italia, the primary role of preservation is to control contamination introduced during and through consumer use. This objective is regulatory policy and confirmed in practical impact as consumers have suffered blindness and even death following infection traced to cosmetics contaminated in use (2, 3).

In that role, preservatives are the only cosmetic ingredients used exclusively to satisfy a safety objective. Despite this essential role, preservatives are perhaps the least understood and most reviled of cosmetic ingredients. Traditional preservatives including parabens, formaldehyde-releasers, isothiazolinones and organic alcohols used in combinations from mid-20th century until now have experienced the greatest negative attention. As observed by Tom Fricke of Clariant, the rise of marketing claims such as natural, green, sustainable and "free-from" have impacted the use of these core ingredients as consumer preference for products bearing such claims has grown substantially. The traditional preservatives as these are synthetic and some petroleum based, making them ready marketing targets. As observed by Rosanna Stokes of Emerald Kamala Chemical, some mass retailers have discouraged and even banned marketing of products including some of these preservative ingredients.

Dr. Ibarra of Evident Ingredients recalls the mythical silver bullet - the ideal preservative based on perfection of antimicrobial efficacy, cost, safety, environmental fate, etc. This has clearly not been satisfied. Of these, efficacy is the focus on this discussion. Preservatives as formulated in combination, must effectively mitigate risk for Gram positive bacteria such as Staphyloccoccus aureus, Gram negative bacteria such as Escherichia coli and Pseudomonas aeruginosa, yeast and mold. This efficacy is specifically evaluated in a compendial preservative challenge test such as the relevant PCPC, USP, ASTM or ISO protocol. As consumer protection through the entire product use is their primary preservative objective, many use ad hoc, in house tests validated to consumer use (e.g., 4).

Traditional Preservatives

Considered here are the primary preservatives parabens, formaldehyde releasers, isothiazolinones and organic alcohols with organic acids typically used as secondary preservatives in combination. Although paraben have been used since early in the 20th century, the above group of materials was largely developed and applied in the latter half of the 20th century.

PRESERVATIVES IN COSMETICS

Used in combinations with synthetic chelator, developed manufacturing hygiene and appropriate packaging, these established a substantial record of microbiological quality. Many major marketers continue to use these traditional preservative systems presumably based on their internal risks assessments and perspective of consumer safety. Additional considerations driving continued use of traditional preservatives include their established safety-in-use profiles, consistent efficacy across and between formulas variations and regulatory compliance in those regions that specifically list allowable preservatives. Although parabens and formaldehyde releasers current garner the greatest negative attention, all these primary preservatives are at risk again despite their generally-accepted safety in use. It is noteworthy that traditional preservatives with developed manufacturing controls established a record of excellent microbiological quality recognized by the US FDA.

Alternative Preservative Systems

Certainly, many preservatives and preservatives combinations are offered as alternatives to the traditional systems. One group of alternative preservatives is composed of "natural" preservatives. Preservation using materials obtained unchanged in chemical composition from nature is a very problematic effort. In the cosmetic context, this involves expensive, niche ingredients of limited efficacy, many of undefined and potentially inconsistent composition and purity. At least one preservative considered to be natural has been exposed as adulterated with synthetic biocides. As composition of preservatives obtained directly from nature is typically complex and specific chemical responsible for efficacy is not defined, batch-to-batch compositional differences bring concern for inconsistent efficacy. For botanical ingredients such as essential oils, contamination with pesticides can be a concern and scale up of supply to meet the needs of a global marketer must address concerns for expanded cultivation of invasive plants and social concerns. Sylvai Nefkens of Celanese notes single antimicrobial compounds such as the traditional preservatives Benzoic and Sorbic acids and Benzyl alcohol can be purified from natural sources. However, sourcing on an industrial scale is simply not practical. In fact, magnitude of supply for preservatives obtained unchanged from nature is unlikely to satisfy the demands of any major global brand.

However, the definition of "natural" finds variable consideration. Ms. Nefkens notes the effective definition of "natural" in some considerations such as those of COSMOS and ISO 16128 addresses the use of synthetic production of materials found in nature. Termed by some as "naturally compliant", the preservative status of "natural" has been effectively established via credentialing organizations. For example, synthetic petroleum based preservatives such as Benzoic and Sorbic acids and Benzyl alcohol are established as effectively "natural" in claims by the organization based on their parallel presence in nature. In some marketing efforts, the concept is extended to materials obtained from nature and subsequently modified in chemical composition such as Sorbitan and Glyceryl caprylates and Capryl hydroxamic acid. Whether natural or naturally compliant, these preservatives with preservative boosters are less effective than traditional preservatives and so are used typically at higher concentrations and in more extended combinations.

Ms. Stokes emphasized application of the "Hurdle concept" in preservation. Here, a product is preserved by extended combinations of antimicrobial factors including but not limited to recognized preservatives. Whereas traditional preservatives typically use two or three recognized primary preservatives, products preserved by the Hurdle concept may use a few chemicals of materials of limited preservative capacity combined with formulation factors such pH, water activity, surfactant concentration, chelators, increased manufacturing controls, protective packaging and other factors that mitigate risk of microbiological contamination. The concept of multifunctional materials, ingredients serving cosmetic functions that also possess antimicrobial efficacy. Dr. Ibara referred to this process in context of an established "toolbox" with alternatives and antimicrobials specific to formulation needs.

A final alternative concept is expressed in the claim "preservative-free." Virtually all aqueous (water containing) cosmetics require preservation. Whereas some products bearing this claim are indeed at substantial risk for contamination, others use antimicrobial ingredients not listed and established as "preservatives" in official regulatory documents.

A unique aspect of preservation and product quality was identified by Shaheen Majeed of Sabinsa– direct and indirect impact of preservatives on the microbiome. Arianna Filippini of ROELMI HPC extended this concern to preservative effect of efficacy of microbiome directed, pre and probiotic products. Whereas the impact of long term cosmetic use on skin microbiome is a subject of ongoing research, Ms. Filipinni presented data addressing the immediate impact of preservatives on the efficacy of prebiotic cosmetics. Even more problematic is preservation and product quality of probiotic products – those formulated to offer effective populations of living microorganism to skin. Microbial contamination of probiotic nutritional products has been reported, in some cases resulting in serious and even fatal infections (5, 6). Such risk will certainly require management in probiotic cosmetic products. However, even if intensified GMP and manufacturing hygiene controls adequately mitigate potential contamination in cosmetic production, the question of contamination in use must also be addressed and without compromising viability of the probiotic active microorganism.

This risk mitigation effort does not lend itself to traditional methods. Dr. Sylvie Cupferman on behalf of Cosmetics Europe observed the challenge documented by EU Scientific Committee for Consumer Safety notes of guidance from 2021 "Total germ count and challenge tests are not directly applicable for the case of probiotic cosmetic formulations to which live or viable microorganisms have been intentionally added."

The Conundrum

Traditional preservatives face strong consumer preference and marketing heads winds against which industry's preservative defense efforts have shown little success. However, alternatives currently available bring diminished efficacy, substantial complexity, and an increasing record of microbiological quality failures. So, what has the cosmetic industry done in response? Many major marketers have maintained the use of traditional preservatives. Despite of growing consumer interest in alternative, especially natural, preservatives, apparent interpretation of responsibility for consumer safety in context of corporate risk assessment fails to find alternatives of sufficient efficacy in their products. As judged by records of enforcement for cosmetics, traditional preservation was associated with a substantial record of microbiological safety from the latter decades of the 20th century to now.

Whereas some maintain traditional preservatives, there are clearly forces from consumer-perceived safety concerns that drive to alternative systems. These are available and apparently can successfully establish microbiological quality despite comprise in efficacy. However, application of such alternatives has not maintained the record of microbiological safety established by traditional preservatives. Contamination of such systems continues to dominate cosmetic enforcement reports (7) with numbers in one pre-covid year the greatest this 40 year veteran of the industry can recall. Dr. Ibarra also noted an additional challenge - the extremely limited supply of preservation technologists with expertise to effectively establish alternative systems. Unlike the academic programs of food microbiology and the extended professional literature base and training of pharmaceutical microbiology, cosmetic microbiology is an arcane practice that can only be learned in practice and application. Clearly, the industry faces challenges in defending the appropriate and safety in use of traditional preservations and the appropriate application of alternatives systems, especially in the broad concept of natural/natural identical ingredients (8).

REFERENCES AND NOTES

1. Geis, Philip A., ed. Cosmetic microbiology: A Practical Approach. CRC Press, 2020.
2. Wilson, L.A. and Ahearn, D.G., 1977. Pseudomonas-induced corneal ulcers associated with contaminated eye mascaras. Am J Ophthalmology, 84:112..
3. Fainstein, V. et al., 1988. Hair clipping: another hazard for granulocytopenic patients?. J Infect Dis 158:655.
4. Brannan, et al., 1987. Correlation of in vitro challenge testing with consumer use testing for cosmetic products. Appl Env Microbiol 53:1827.
5. Benedict, K., et al. 2016. Invasive fungal infections acquired from contaminated food or nutritional supplements: a review of the literature. Foodborne Path Dis 13:343.
6. Vallabhaneni, et al. Fatal gastrointestinal mucormycosis in a premature infant associated with a contaminated dietary supplement—Connecticut, 2014. Morbidity and mortality weekly report, 64:155.
7. Periz, G., et al. 2018. FDA 2014 survey of eye area cosmetics for microbiological safety. Lett Appl Microbiol 67:32.
8. Lundov, M.D. and Zachariae, C., 2008. Recalls of microbiologically contaminated cosmetics in EU from 2005 to May 2008. Int J Cosm Sci 30:471.

Panelists

SYLVIE CUPFERMA
on behalf of Cosmetics Europe Expert Team
in Product Preservation

SYLVIA NEFKENS
Technical market specialist Home and Personal Care
Celanese

TOM FRICKE
Manager Technical Application Cosmetics EMEA
Clariant

PETRA SCHAAL
Application Development Manager Preservatives
Clariant

FRANCESCO TURSI
Laboratory director
CompLife Italia

ROSANNA STOKES
Business Development Manager,
Emerald Kalama Chemical

FERNANDO IBARRA
Managing Director
Evident Ingredients

ARIANNA FILIPPINI
Product Manager Formula Protection
ROELMI HPC

SHAHEEN MAJEED
President
Sabinsa

ASSOCIATION

ANTIMICROBIAL PROTECTION OF COSMETIC PRODUCTS KEY FOR CONSUMER SAFETY

Ensuring consumer safety is a priority for the cosmetic industry, but it is also a legal requirement. The European Cosmetic Products Regulation (CPR) requires i) that cosmetic products are protected from microbial contamination to avoid consumer health issues, and ii) that preservatives used in cosmetics are safe. The CPR provides a limited list of permitted preservatives, however, if a potential safety concern is identified, the preservative, like any other cosmetic ingredient, may undergo a safety evaluation by the European Commission's Scientific Committee for Consumer Safety (SCCS). The CPR requires that the Cosmetic Product Safety Report – Part A includes the results of a preservation challenge test report, which confirms the microbial stability of the cosmetic products. Cosmetics do not need to be sterile. However, they must not be contaminated with microorganisms considered as potentially harmful to the consumer, and the density of other microorganisms should remain low. Preservatives are incorporated into cosmetic products to prevent the growth of microorganisms that could adversely affect the health of the consumers. Without preservation, bacteria, yeast and mould could develop, leading to product deterioration, spoilage as well as potential consumer health and safety issues. The safety of the individual cosmetic ingredients is important, but equally important is the safety of the finished cosmetic products. Preservation is key to deliver a finished cosmetic product, which is both safe for the consumer to use and brings the benefits that the consumer expects.

Microorganisms that are always present on our skin and in the air around us can get into products during normal use. Therefore, most cosmetics products require some form of preservation to protect them from contamination. The antimicrobial protection of a cosmetic product can be ensured by various means: chemical preservation, inherent characteristics of the formulation, package design, manufacturing process (cf. ISO 29621-2017) or a combination of these. Adding preservatives to cosmetic formulations is a common way to achieve this objective.

Water-based cosmetic products in particular provide favourable conditions for growth of a wide range of microorganisms. This is especially the case with multiple use products. Therefore, reducing water in the formula may be an option, also for sustainability reasons. However, even though ISO 29621 states that, *"a low water activity level alone is more than sufficient to keep a product adequately preserved*", depending on the composition and the conditions of use, addition of a preservative may be needed. For example, the development of formulations marketed as concentrates or solids, which have to be diluted by the consumer to refill a standard pack for multiple use, requires additional preservation considerations to be taken into account. The challenge is to find a preservative system that is effective in the final formulation, but does not exceed the allowed concentration limits in the non-diluted form.

Similarly, a case-by-case approach should be considered for natural and/or organic products. These can be more prone to support microbial growth compared to other products. Usually, raw materials included in them contain a higher bioburden and additionally can be considered as 'food' for microorganisms. Appropriate product preservation is therefore equally important for natural and/or organic products as it is for other types of products. Natural and/or organic products need to undergo the same safety assessment by manufacturers to ensure that they are adequately preserved. However, the number of acceptable preservatives that can be used in such products is even more limited due to the requirements of the organic labels.

Preservation is also key in case of microbiome friendly, but also probiotic products. The latter are products to which microorganisms can be intentionally added. However, even these types of products need to be properly protected from the microbiological contamination such as unwanted pathogenic microorganisms. The challenge with the preservation of such products was acknowledged in the latest revision of the SCCS Notes of Guidance issued in April 2021 (11th revision) that states: *"Total germ counts and challenge test are not directly applicable for the case of probiotic cosmetic formulations to which live or viable microorganisms have been deliberately added."*

There is a rising trend of re-filling cosmetic product packaging, which is an option desired by many consumers and contributing to sustainability goals by reducing the quantity of packaging waste. This presents another interesting case from the product preservation perspective. Regardless of where the refilling takes place, in a retail setting or at home, it could pose additional preservation challenges, given an enhanced potential for contamination. Consequently, the formula of a refillable product needs to be specifically designed to respond to this concern.

The science of preserving cosmetic products is complex and an individual approach needs to be taken for each product. Numerous aspects such as the ingredients to be used, manufacturing process, packaging, product delivery and consumer use and storage need to be considered each time. Given this complexity, a wide palette of preservative ingredients helps to ensure that cosmetics are adequately preserved across the whole spectrum of products and they deliver the benefits that the consumers expect.

SYLVIE CUPFERMAN
on behalf of Cosmetics Europe
Expert Team in Product Preservation

COMPANIES

HOW DOES THE CONSUMER NEED FOR NATURAL AND SUSTAINABLE PRODUCTS IMPACT PRESERVATION?

Celanese is a global chemical and specialty materials company that manufactures and engineers a variety of raw materials and products essential to everyday living. Among those are sorbic acid and potassium sorbate, which have a long history of safe use as preservatives in food, feed, pharmaceutical and personal care products. Celanese is the only Western producer of sorbic acid and potassium sorbate and has been manufacturing these for over 50 years.

Sorbic acid and potassium sorbate are currently manufactured from petrochemical resources. Sorbic acid has been isolated from natural resources, such as the mountain ash berry; however, sourcing from these berries on an industrial scale is not practical.

For several decades, the personal care industry has focused on natural (derived) ingredients. Natural ingredients are attractive to consumers – even though they are not necessarily better, safer or more sustainable than synthetic ingredients. There is no objective definition of the term "natural," although within the COSMOS and the ISO 16128 standards, definitions exist for "natural" and "natural-derived" raw materials. These definitions encompass the origin of the raw material, as well as the processes used to obtain and/or derivatize the raw material.

Consumer demand for natural products has a big impact on preservation, given that according to Annex V of the Regulation (EC) No 1223/2009 on Cosmetic Products, the options for natural preservatives allowed in cosmetic products are very limited. Therefore, formulators must often resort to the use of 'multifunctional' ingredients that boost preservative efficacy, or to plant extracts having some antimicrobial efficacy, but which are not officially listed on the Annex V list of allowed preservatives. Consequently, formulators often struggle with finding an effective preservative system that is completely natural, compliant with the COSMOS or ISO 16128 definitions, and which is also attractive from a cost standpoint.

Organic acid derivatives, such as sodium benzoate and potassium sorbate, are recognized as nature-identical by European labels such as COSMOS and NATRUE. The use of these preservatives is compliant with these certifications, but they are still considered synthetic.

It is possible to manufacture sorbic acid and potassium sorbate using bio-based and renewable feedstocks, and Celanese is currently investigating the options to produce these from non-petrochemical - hence naturally derived and renewable – sources. Using bio-based raw materials can be considered a major step towards reducing the dependence on petrochemical feedstocks and it responds to the increasing consumer demand for more sustainable products. The utilization of bio-based feedstocks is, however, not covered in the current COSMOS standard as option to achieve a naturally derived ingredient.

In addition, in a continuous production process, the best way to start switching production towards a more sustainable bio-based product is by using a mass-balance approach - however, this approach is also not recognized within the COSMOS and ISO 16128 standards.

With the increased focus on sustainability, and the positive policy context created by the new European Chemical Strategy for Sustainability which encourages innovation in safe and sustainable chemicals, we believe that nature-identical ingredients manufactured from renewable resources, using a mass balance approach should either have their own definition, classifying them as more sustainable options to the same petrochemically derived product – or alternatively, they should be considered to qualify for a Natural Origin Index according to ISO 16128 or COSMOS certification.

Having their own definition would allow the alignment of claims on cosmetics products on a clear and harmonized legal basis, enabling consumers to make informed consumption choices; while having them qualify as natural derived would broaden the portfolio of preservatives available to formulators of natural and sustainable products that conform with Annex V of the Cosmetic Regulation.

SYLVIA NEFKENS
Technical market specialist Home and Personal Care
Celanese

THE GREEN CHALLENGE – BOOSTING PRESERVATION WITH NATURALLY DERIVED INGREDIENTS

The offer of Personal Care products following the natural and sustainable trend continues to grow quickly. Green claims are rising, and this market trend is also affecting preservatives as core ingredients of a cosmetic formulation. Traditional preservatives are typically petro-based and some of them are under either regulatory or public scrutiny. As a result, the number of broadly accepted preservatives for cosmetics continues to shrink. Therefore, it is highly desired to either reduce the amount of the synthetic preservatives or move to natural alternatives which generally show weaker performance. For natural certifications like COSMOS or Natrue especially, only a few selected preservatives are allowed (1, 2).

Nevertheless, cosmetic formulations must be safe against the growth of microorganisms to avoid product spoilage and to protect consumers. Although certain ingredients gain higher attention or are under public scrutiny. Therefore, the efficient preservation is a key requirement in formulation design, and solutions need to meet the high-quality standards as well as consumer demands.

A promising reasonable way to achieve this goal is to use multifunctional preservative boosters. Their use decreases the preservative levels to the minimum quantity needed for preservation without compromising on performance.

RENEWABLE PRESERVATION BOOSTERS AS SOLUTION FOR NATURAL AND SUSTAINABLE COSMETICS

Preservation boosters are not a new topic but established solutions like Ethylhexylglycerin and Caprylyl Glycol are typically fully synthetic and consequently formulators face a challenge to use these solutions in highly natural formulations.

To overcome these limitations most of the recent innovations in the field of preservative boosters follow the powerful market trend for renewable and natural solutions. For example, Clariant offers three different naturally derived solutions, addressing the needs of various kinds of cosmetic formulations from rinse-off to leave-on covering also a broad pH range. Cosmetic products containing these boosters need considerably less preservative to ensure safe protection. Their efficiency with various preservatives has been proven in extensive testing according to high standards like Ph. Eur., usually enabling the amount of listed preservative to be cut by half.

SORBITAN CAPRYLATE - THE ESTABLISHED NATURALLY DERIVED PRESERVATION BOOSTER

Sorbitan Caprylate is in the meantime a well-established COSMOS and Natrue conform multifunctional ingredient with a renewable carbon index (RCI) of 100%. Due to its boosting properties, it has been the base for numerous broad spectrum efficient blends for many years. These blends with Benzoic Acid, Benzyl Alcohol or Potassium Sorbate are based on powerful synergistic effects (3, 4). Therefore, *Sorbitan Caprylate* is used in various market formulations in the segment of leave-on, rinse-off and even wet wipes, which are known to be difficult to preserve. As multifunctional ingredient it acts in leave-on formulations as co-emulsifier and in rinse-off systems it can support the build-up of viscosity as thickening agent (5).

CAPRYLOYL/CAPROYL ANHYDRO METHYL GLUCAMIDE - THE FLEXIBLE BOOSTER OPTION FOR VARIOUS APPLICATIONS

Capryloyl/Caproyl Anhydro Methyl Glucamide is a biodegradable, naturally derived (ISO 16128), COSMOS approved, multifunctional ingredient based on glucose sirup and palm kernel oil. As preservation booster it synergistically supports the antimicrobial protection of a formulation and allows to reduce the amount of actual preservative needed up to 50%. Its unique property compared to other preservation boosters is its very high water solubility. Therefore, it can be used as preservation support in almost all cosmetic formulations, including transparent natural formats, without any additional need for a solubilizer. In addition, *Capryloyl/Caproyl Anhydro Methyl Glucamide* also acts as a PEG-free solubiliser (6-8).

CAPRYLYL GLYCERYL ETHER - THE EFFICIENT NATURAL DERIVED BOOSTER SOLUTION

Caprylyl Glyceryl Ether is an effective preservative booster over a wide pH range and offers a powerful solution for natural, COSMOS approved leave-on formulations with a RCI target of 100%. As it outperforms the chemically similar, fully synthetic Ethylhexylglycerin it is applicable at low levels also beyond just natural formulations. Beside this, it acts as a pure colourless oil as it is a medium spreading emollient which provides a light skin feel (9).

SUMMARY

In future, preservation of cosmetic formulations remains a challenge due to a shrinking toolbox of traditional preservatives. The strong trend towards more natural formulations will continuously increase the need for multifunctional ingredients and versatile preservative boosters. Now, several biodegradable and naturally derived boosters with high RCI like *Sorbitan Caprylate*(5), *Capryloyl/Caproyl Anhydro Methyl Glucamide*(6, 7, 8) and *Caprylyl Glyceryl Ether*(9) are available for various applications in Personal Care. This enables formulators to overcome the green challenge and to ensure a safe protection of their products including those for the fast-growing natural cosmetic market.

REFERENCES AND NOTES

1. COSMOS Standard available online at https://www.cosmos-standard.org/about-the-cosmos-standard
2. Natrue standard available online at https://www.natrue.org/our-standard/natrue-criteria-2/
3. Gauczinski J., Pilz F., Desikan A., Neuhoff H. (2014). New preservation alternatives to meet latest market requirements for safer and greener preservation. *SOFW-Journal*, *4*, 42-47.
4. Gauczinski J., Vielkanowitz C., Lasbistes N. (2017). Next generation preservation options. *Personal Care Magazine*, *11*, 69-72.
5. Pilz F., P. Klug P. (2010). A welcome side effect. *Houshold and Personal Care Today*, *3*, 22-24.
6. Schaal P. (2020). A derived natural option supporting less preservative use & more formulation flexibility. *Speciality Chemicals*, *4*, 28-30.
7. Schaal P., Starkulla G., Breffa C. (2021). Clean and simple. *Cosmetics & Toiletries*, 136, 45.
8. Ilao C., Breffa C. (2021). Lightening the load of preservation challenges. *Personal Care Magazine*, *2*, 1-3.
9. Fricke T., Back U., Grohmann J., (2021). New 100% natural booster. *Pharmacos*, *3*, 32-33.

TOM FRICKE
Manager Technical Application Cosmetics EMEA
Clariant

PETRA SCHAAL
Application Development Manager Preservatives
Clariant

PRESERVED AND ANTIMICROBIAL COSMETIC PRODUCTS, BIOCIDES AND PMCs, SOME CLARITY NEEDED!

Preservatives are added to cosmetic products in order to avoid the microbial contamination that could occur from utilization by consumers.

Such approach is necessary for water-based cosmetic products formulated without applying measures for making them self-preserved, i.e. using structural ingredients aimed at reducing the water activity of the formulation (e.g. glycols) or including functional actives endowed with a secondary antimicrobial activity (e.g. essential oils, conditioners, betaine).

Preservatives allowed in cosmetics are listed in the Annex V of the Regulation (EC) 1223/2009, where concentration limits are defined for the different cosmetic categories as a result of a correct balance between their antimicrobial effect and the assessed exposure risk to biocidal ingredients. Efficacy of preservative systems in cosmetic products is evaluated according to standardized/published methods (ISO 11930/PCPC Microbiology Guidelines) that also define acceptance criteria to be compliant with. Cosmetic products may also claim antimicrobial properties, in terms of reducing global cutaneous microbial load, to be attained mainly through the mechanical removal of dirt from the skin and contextually the removal of the microorganisms contained/associated to it. Such antimicrobial activity, or better hygienizing/sanitizing effect, claimed in cosmetics as detergent activity, fulfils the regulatory requirements set out for cleansing products, when it is visibly presented as a secondary activity with respect to the primary cosmetic functions, according to the following scope of application: "with a view exclusively or mainly to cleaning external parts of the human body or with the teeth and the mucous membranes of the oral cavity, perfuming them, changing their appearance, protecting them, keeping them in good condition or correcting body odours".

Even cosmetics formulated with specific antimicrobial ingredients fulfills the above requirements: activity achieved – for example - by the presence of Climbazole (an antifungal agent that is effective in preventing the growth of the dandruff-causing fungus) in shampoos, or Chlorexidine in mouthwashes, has to be considered secondary to the cosmetic function of a shampoo or a mouthwash in cleaning and keeping in good condition, as long as a correct presentation of the products is used.

Therefore, a proper handwashing with a cosmetic liquid detergent or bar/powder soaps on a regular basis, especially when responding to general WHO procedures, represents one of the most effective measure to prevent current infection from Covid-19, since it helps mechanically and physically hinder microorganisms from hands without appealing any disinfectant activity, which in fact falls under the biocides scope of application: "to protect humans, animals, materials or articles against harmful organisms like pests or bacteria, by the action of the active substances contained in the biocidal product".

The Biocides Product Regulation (BPR) 528/2012 concerns the placing on the EU market and the use of biocidal products, through a process that foresees the approval of active substances and the authorization of biocidal products containing them. Biocidal products are divided into 22 different product types (PT), based on their intended use, and are grouped into four main groups, namely disinfectants, preservatives, pest control, and other biocidal products. The main group "disinfectants" contains products to be used for human hygiene (PT1), and can explicitly revendicate such claim, together with a peculiar category of finished products which contain active biocidal substances that have not yet been approved according to the BPR; such products have different denominations and rules in EU states. In Italy they are named Presidi Medico-Chirurgici (PMC).

However, Biocides Products or PMCs are characterized by a strong and fast antimicrobial activity, evaluated according to International Standards (ISO) that define the potency and the time – generally in the order of minutes - by which the effect has to be reached. A comparison - even if not fully appropriate - with the acceptance criteria of the cosmetic Antimicrobial Efficacy Tests may be indicative of the differences between the two classes of aforementioned products and their intended objectives.

One last question still remains regarding the Covid-19 pandemic management and the large demand of leave-on hydroalcoholic hand gels: their correct classification depends on the way these products are presented with the cosmetic primary function (cleaning, emollient, etc.) clearly relevant with respect to specific functional ingredients; nevertheless, it also needs to be remarked that without any rinsing the mechanical and physical removal of microorganisms cannot be achieved, leaving the sanitizing effect, i.e. the reduction of the microbial load to the high alcoholic content.

FRANCESCO TURSI
Laboratory director
Complife Italia

PROTECT CONSUMERS & BRANDS WITH ROBUST PRESERVATION

Imagine driving in a car many decades ago. What safety features are present? Maybe you are wearing a seatbelt, but does the vehicle have airbags? ABS brakes? A back-up camera? Or perhaps the child safety seat is flimsy. Today's automobiles incorporate decades of layered safety features built on an evolving understanding of safety requirements. No single safety feature is enough on its own, but together, they create a robust framework to protect the consumer from dangerous accidents.

The approach to preserving personal care products has evolved in a similar fashion. As we understand what is required for long-term product safety, preservation has become more challenging. With this understanding, new methods to enhance preservative efficacy and make formulations more robust are developing. Preservation is an essential element of a consumer product. Just like a car's integrated safety system, protecting products against microbial contamination requires consideration of every aspect of the formulation's multilayered safety system.

EVOLVING CONSUMER SENTIMENTS DRIVE GREENER CHOICES

Since the beginning of the pandemic, consumers are very aware of the importance of safety for themselves and their families. In their time at home, many consumers are intently scanning labels and reading articles on the safety of products. Even retailers such as Target and Amazon are pursuing this effort by banning products containing certain ingredients.

Preservatives are one of those required safety features, which provide products with a long shelf life and protect consumers from contamination by bacteria, yeasts, and molds and the safety hazards posed by these microbes. This critical safety component also protects the brand from product recalls that are detrimental to future sales. Nothing could be worse for a brand's reputation than a consumer opening a container, discovering mold growing in the product, and then sharing a photo on social media.

Additionally, the pandemic has increased consumers' exposure to products such as hand soaps, wipes, surface cleaners, and laundry care. Several traditional chemistries have been scrutinized for safety, irritation, and sustainability concerns, including preservatives that are not readily biodegradable.

Just like the car's safety system, it is important to design a well-constructed preservative safety system within your product formulation. It is no longer feasible to add a single preservative as an after-thought at the end of formulation.

CREATING A ROBUST, INTEGRATED SAFETY NETWORK

Emerald's recent innovations have focused on how to tailor a safety formula creating robust products that resist microbial growth and provide long shelf life. Similar to a car's safety network, the formulator must create layers of protection to safeguard consumers from contamination of their personal care products.

By carefully selecting ingredients, prioritizing plant hygiene, and utilizing hurdle technologies, formulators can tailor products for robust microbial protection. In addition to selecting an effective, green, skin-friendly preservative, incorporate the following:

- Use high purity ingredients and quality water.
- Consider the appropriate pH and water activity for the product.
- Leverage ingredient synergies by including beneficial levels of multifunctional boosters or chelating agents in the formula.
- Ensure the manufacturing process and final product packaging minimize potential for microbial contamination.

It's also important to consider the full product lifespan, from manufacturing, to how the consumer will use the product, to how long it will be used before disposal.

All of these considerations should influence the overall approach to microbial control and must be determined at the beginning of formulating. In addition to protecting the consumer, this can help to prevent a potential recall, as well as the associated costs and damage to brand reputation.

ROSANNA STOKES
Business Development Manager, Emerald Kalama Chemical

THE FUTURE OF COSMETIC PRESERVATION

I have a dream:
The unprecedented situation caused by a worldwide pandemic has a few good side-effects. Primarily of course it has caused a disruption in social life, economies, supply chains and careers. Not to mention the millions who fell sick and even lost their lives.

So what could a positive side of all this be in the scope of this discussion?
People are starting to care about science.

All of a sudden we are surrounded by friends and family, who are interested in science, learning how to read statistics and follow research that a little over a year ago was only interesting for science nerds.

In the cosmetic industry we are often dealing with fabricated opinions and unscientific chemophobia. Unfortunately, some companies gladly use this as a marketing tool to sell their products, but for most of us this represents an additional hurdle that needs to be overcome. Usually these opinions do not come from within our community but are pushed by popular magazines, influencers and the like. Sure, the cosmetic brands are selling dreams, but to fill them with life you need solid studies, cosmetic science and chemistry rather than unsubstantiated marketing stories.

My dream is that we now start to talk about chemistry and preservation in a more relaxed way. I am sure that among this panel there are experts with different opinions, different strategies for preservation, some using "chemical" preservatives, others "green" alternatives. In the end there are many ways to create a safe preservation that is designed to protect the product and health of its users, and all of them are fine and should be respected as long as they have a solid database to prove their performance and toxicological safety.

There is no need to trash-talk competitive products if you have the ability to convince with know-how and quality. Recently I witnessed a case of a Paraben-critical post on social media. To my surprise, the overwhelming reaction of industry experts was very angry with comments about missing facts and poor scientific background.

The take away from this should be that opinions about preservation are diverse and your ideas should always be built on a sound scientific architecture.

If consumers continue to learn eagerly not only about virology but also about chemistry and cosmetic science then it will be more difficult to lure them with misleading claims. It is our responsibility to educate them rather than finding new loopholes to sell products with unscientific claims.

The future of preservation will be followed up by more educated and critical consumers. Since the silver bullet in preservation chemistry is still not found - and most certainly never will be - we at Evident Ingredients continue to build the protection of products on a variety of chemicals (vegetal and petrochemical based) with complementing activities. If you are dealing with microorganisms for years, these little fellows teach you a good lesson or two. There are millions of different microbes and not all react to the same preservative.

The one fits all, simple-to-use, natural and cheap preservative does not exist (unfortunately). We need to combine different ones in smart ways and make them work against different types of microbes and in different environments (cosmetic formulations).

A toolbox filled with many effective antimicrobials is necessary to meet the needs of every formulation.

Experts for preservation will be needed, too. They are the ones who can advise the formulator on how to improve the protection when the preservative performance is not sufficient.

While the life cycle of some preservatives seems to come to an end, the industry will require new, effective materials to replace them. Maybe not everything needs to be natural, but obviously there is a continuing trend pointing at sustainable raw materials. Research will be necessary and is under way in many R&D labs, but regulations are making it more difficult to launch new chemistries. Even if there was a totally new substance found – it would be anything but easy to make it available to the market. It is more likely that existing raw materials need to be studied in more detail and used in a broader way. The "hurdle approach" and new packaging technologies are already helping to reduce the preservative load. Effective antimicrobials will do the rest.

FERNANDO IBARRA
Managing Director
Evident Ingredients

PERSONAL CARE PRESERVATIVES AND SKIN MICROBIOTA: ANY CORRELATION?

As many of you might know, our body is full (inside and outside) of microorganisms. The ones covering our skin are what is called the Skin Microbiota, a topic that in the past few years aroused a growing interest in the Personal Care field thanks to its extreme importance for skin ecosystem so, it is essential to guarantee its own vitality and activity. The way to achieve this balance is to keep a state of health in which all the different species composing the microbiota are in equilibrium. That's something we can do by selecting what we apply on our skin, which is a hard job! Not to consider all the factors that sometimes we cannot control, like pollution and UV-rays. Luckily, we can choose which products to use. Cosmetics are a complex and well-studied formulation that gives benefit to our skin but at the same time need to be protected themselves. In fact, they can be easily contaminated by the surrounding environment, including consumer's behaviour. That's basically why all cosmetic products need a preservative system that avoids contamination by potentially pathogenic microorganisms.

Knowing this, let's take a step back to skin microbiota. One big question mark is addressed to preservatives, since they have an intrinsic antimicrobial activity. It is then logic and interesting to ask, do they affect skin microbiota? And if they do, to what extent? Or do they act selectively on pathogens? These are really difficult questions to answer to. Some researchers in a few articles tried to evaluate this interaction with tests, unfortunately without coming to a concrete common answer, so far. The difficulty lies in the experimental approach. *In-vitro* methods have some limitations, like the possibility to analyse only a limited part of all the microorganisms inhabiting the skin area taken in consideration. An *in-vivo* approach would imply to use the preservative in a finished formulation, where other ingredients could interfere with the experiment. Moreover, factors like lifestyle, geographical location and diet would affect results with no universal answer. We see now that it's not that easy to test this interaction, right? Well, we can start with studies and trials that partially answer this topic and that's what here at ROELMI HPC started to do a few years ago.

One of our R&D project is focused on answering the following questions: Microbiota-friendly ingredients may interfere with Preservatives efficacy? Preservatives may impact on Skin microbiota? As said before, there would be many more, but let's start from the basics. We considered two emulsions with the same formula and introduced prebiotics in one of them and tyndallized microorganisms in the other one, in order to strengthen the skin barrier, to balance the skin microbiota composition and to make it stronger against external factors and potential pathogens aggression. The two formulations were compared to a blank emulsion (without the addition of microbiota-friendly ingredients). All of them were protected by one of our preservative system.

The Challenge tests we performed highlighted that the presence of "good for microorganisms" ingredients did not affect the antimicrobial activity of the preservative system against bacteria and the yeast. Speaking about mould (*Aspergillus brasiliensis*), it would seem that when the prebiotic is in the formula, there is a slightly lower decrease of the count but still respecting the criteria, while with tyndallized microorganisms the efficacy of the preservative system seems to be even boostered. This is of course a preliminary study, but let's collect what we can: ingredients used in the formulas did not affect considerably the preservation system, which is in contrast with the reasonable expectation that these Microbiota-friends would affect the preservatives efficacy. We could suppose that the vice versa is true as well, meaning that also preservatives do not affect that much the skin microbiota *eubiosis*, but at the same time we can't be sure about it. That's why this topic needs to be deepened, for example with *in-vivo* treatments and metagenomic analysis, which are the next steps in our research project. So as you can see, when we talk about cosmetics, it's not only a decorative benefit, rather it is something that contributes to our wellness. And who are we not to care about our skin's health?

ARIANNA FILIPPINI
Product Manager Formula Protection
ROELMI HPC

COSMETIC PRESERVATIVES IN TODAY'S MICROBIOME WORLD

Preservatives are natural or synthetic ingredients that are used to prevent microbial growth, spoilage, and contamination of personal care products. Microbial contamination can lead to significant health problems, from skin irritation to infections. A preservative may also be added to protect against oxidative damage, and in this instance, these ingredients are also called antioxidants. Developing a robust system of preservation is critical to maintain long term stability and safety of a cosmetic formulation. An ideal preservative should be stable and effective at the target pH of the product, easy to use, compatible with raw materials and formulations, non-irritating and globally approved by regulatory agencies.

DO ALL PRODUCTS NEED PRESERVATIVES?

All water-based formulations including creams, lotions, shampoos require preservatives. Preservatives are normally added to eye care agents, even if they are water free. Anhydrous products such as balms and oil-based products, do not necessarily require preservatives.

THE INTRIGUING CASE OF PARABENS IN COSMETICS

Parabens, organic acids, alcohols, formaldehyde releasers, and inorganic compounds are some commonly used preservatives (1). Parabens are a group of *p*-hydroxybenzoic acid esters that are used widely as antimicrobial agents. The methyl, ethyl, propyl and butyl derivatives

are effective at low dose, easy to use, have no smell or color of their own and are well tolerated by the skin. Today, parabens are one of the vilified ingredients in the cosmetic industry. They are thought to be estrogen mimetics and an endocrine disruptor. These concerns are based on a study that detected traces of parabens in the breast tumors of 19 out of 20 women studied. Although this was a small study and does not prove a causal relationship between parabens and breast cancer, it is important because it detected the presence of intact parabens in tumors (2). The toxic effects, endocrine disruption, carcinogenicity or genotoxicity of parabens have not been confirmed in humans, as repeated dose toxicity studies were found to be safe (3, 4). Few studies have correlated urinary paraben levels with decreased fertility, disruptions in regular menstrual cycle (5, 6). Further, parabens are linked to ecological harm, as low levels of butylparaben can kill corals, they are detected in the surface waters and fish, and thus have been a cause of concern (7, 8).

THE REGULATION OF PARABEN-BASED COSMETICS

The European Union and Southeast Asian countries have banned isopropyl- and isobutylparaben in all personal care products. The use of propyl- and butylparaben is restricted in these countries and Japan. Major retailers in the U.S. have planned active bans or restrictions and are planning to slowly phase out the use of parabens in the coming years. However, cosmetic products and ingredients, do not need FDA approval before they go on the market (9) and parabens are not banned by the USFDA.

PRESERVATIVES AND SKIN MICROBIOME

The consortium of microorganisms that reside on human skin is called skin microbiota. These microbes prevent the pathogenic organisms from colonizing the skin surface, by secreting antimicrobial chemicals, competing for nutrients, and also by stimulating the skin's immune system(10). Preservatives can potently inhibit skin-resident microbiota along with the pathogens. Based on a recent study the application of phenoxyethanol-containing cosmetics (PEC) to the skin caused the disturbance of skin microbiota (11). Microbiome friendly ingredients can preserve the skin microbiota, without compromising the cosmetic safety. This is an emerging concept, and the choice of preservative should be also based on its interference with skin microbiota. Among the natural preservatives, essential oils, and various herbs such as rosemary, clove, thyme, cinnamon, tea tree and lavender, neem, and grape seed to name a few, are most effective. The gel from the plant, Aloe vera acts as a natural protective coating for beauty products. It protects the cosmetics from moisture and oxygen and can be incorporated in a wide range of sustainable cosmetics. The advantage of natural preservatives is their organism specific activity. They may be effective against one organism but not another, and thus the chances of disrupting the microbiome are minimal. They must be carefully blended to create a synergistic effect against a range of organisms. Addition of antioxidants along with natural preservatives can protect a variety of formulations against microbial contamination without disturbing the natural flora of the skin.

The use of probiotics, prebiotics and postbiotics are another emerging category of natural and biotech ingredients, which can have a positive effect on the skin microbiome. These ingredients protect, optimize, and restore skin microbial balance for better skin health: antimicrobial short chain peptides extracted from Lactobacillus acidophilus were able to destroy pathogenic bacteria whilst maintaining the skin microbiome (12).

PRESERVATIVE FREE CLAIMS – IS IT ETHICAL?

While preservative-free or "all-natural" skin care products are on the rise, almost all skin care products need preservatives because of the water content. The presence of water makes it possible for waterborne bacteria to contaminate the whole product. Without preservatives, it would soon become a breeding ground for various microbes.

CONCLUSION

The antimicrobial efficacy is considered the main function of a cosmetic preservative. The unavoidable use of preservatives in water-based formulations and their inherent toxicity is a problem that the cosmetic industry should be concerned about. Therefore, it is necessary to continue the search for non-toxic or least toxic and effective preservatives. Also, they could be paired with natural and safe ingredients that can minimize their toxic effects. Thus, improving the safety and effectiveness of the formulation in general.

REFERENCES AND NOTES

1. Halla, N., et al., Cosmetics Preservation: A Review on Present Strategies. Molecules, 2018. 23(7): p. 1571.
2. Darbre, P.D., et al., Concentrations of parabens in human breast tumours. J Appl Toxicol, 2004. 24(1): p. 5-13.
3. E. V. S Hessel, P.E.B., S.P. den Braver-Sewradj, J. A. J. Meesters, M. Weda and W. Brand, , Review on butylparaben: exposure, toxicity and risk assessment – With a focus on endocrine disrupting properties and cumulative risk assessment, T. 2018, The Netherlands Food and Consumer Product Safety Authority (NVWA), National Institute for Public Health and the Environment,: Bilthoven (The Netherlands)
4. Petric, Z., J. Ružić, and I. Žuntar, The controversies of parabens - an overview nowadays. Acta Pharm, 2021. 71(1): p. 17-32.
5. Harley, K.G., et al., Reducing Phthalate, Paraben, and Phenol Exposure from Personal Care Products in Adolescent Girls: Findings from the HERMOSA Intervention Study. Environ Health Perspect, 2016. 124(10): p. 1600-1607.
6. Nishihama, Y., et al., Association between paraben exposure and menstrual cycle in female university students in Japan. Reprod Toxicol, 2016. 63: p. 107-13.
7. Danovaro, R., et al., Sunscreens cause coral bleaching by promoting viral infections. Environmental health perspectives, 2008. 116(4): p. 441-447.
8. Haman, C., et al., Occurrence, fate and behavior of parabens in aquatic environments: a review. Water Res, 2015. 68: p. 1-11.
9. FDA: U.S. Food and Drug Administration. Parabens in Cosmetics. 2016.
10. Cogen, A.L., V. Nizet, and R.L. Gallo, Skin microbiota: a source of disease or defence? British Journal of Dermatology, 2008. 158(3): p. 442-455.
11. Jeong, J.-J. and D.-H. Kim, Effects of Cosmetics and Their Preservatives on the Growth and Composition of Human Skin Microbiota. Journal of the Society of Cosmetic Scientists of Korea, 2015. 41: p. 127-134.
12. Lebeer, S., et al., Topical cream with live lactobacilli modulates the skin microbiome and reduce acne symptoms. bioRxiv, 2018: p. 463307.

SHAHEEN MAJEED
President
Sabinsa