The formulator's guide to safe cosmetic preservation

For a long time now, questions regarding the right preservative system in cosmetics have been neglected by most formulators. European legislators created a list of approved preservatives, called Annex V (former Annex VI) of the EU Cosmetic Regulation. This list is filled with a wide range of substances that have been raised with respect to antimicrobial efficacy and beyond that had little influence on the physical parameters of the cosmetic product. This comfortable situation has fundamentally changed in recent years. Today, the application of a growing number of listed preservatives has been restricted, due to their skin irritating or sensitising potentials. In some cases preservatives were first restricted and then finally even banned and deleted from the list. Because of an animal testing ban anchored in the Cosmetic Regulation, the development and listing of new preservatives has become extremely difficult. These circumstances are limiting the selection of approved preservatives and are complicating the development of new cosmetic products. This article tries to provide an overview of the present situation and to offer formulators a guidance for future decisions.

Cosmetic products in general, especially oil and water emulsions, offer microorganisms ideal growth conditions and therefore need to be preserved. Preservation is achieved by antimicrobial ingredients, whose properties also bear a potential for undesired skin side effects. This is why, years ago, legislators in Europe started to regulate the application of preservatives in cosmetic products. Preservatives, whose safety was evaluated in toxicological tests, have been listed since 1982 in the respective current version of the Cosmetic Directive/ Regulation, together with restrictions regarding the application, if necessary.[1] The actual version of the positive list is Annex V of the 1223/2009/EG Cosmetic Regulation. Many Asian countries, like China, Korea, New Zealand and the ten ASEAN countries have adopted the Cosmetic Regulation together with Annex V for the establishment of their own regulatory system. Moreover, for many cosmetic companies in countries, e.g. Australia, the European Annex V serves as a regulatory guideline.[2]

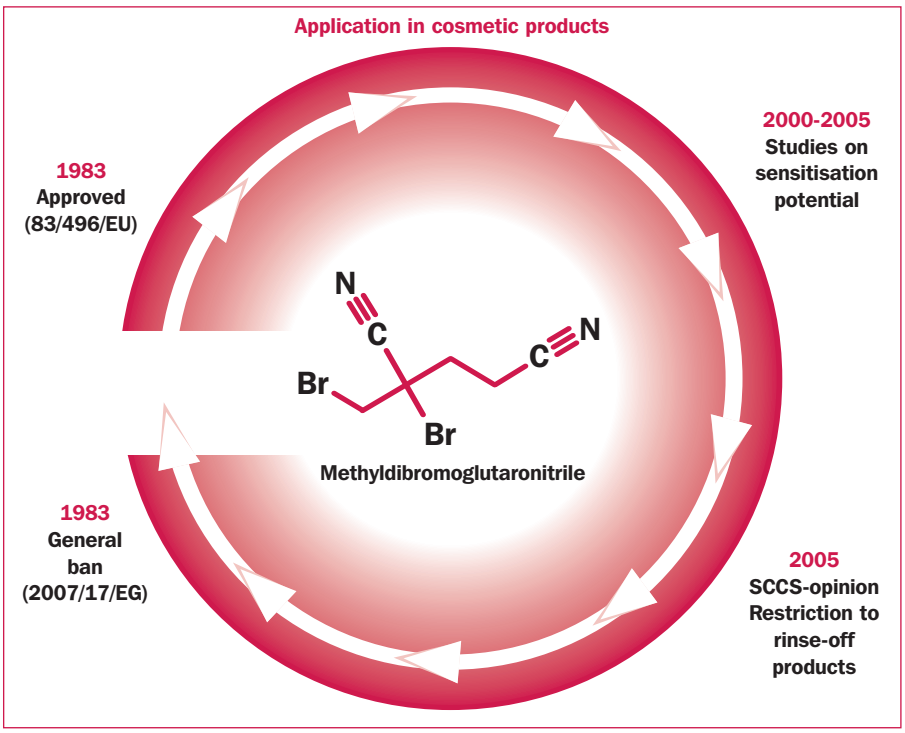

Figure 1: *Life-cycle of MFBG – from its admission to its ban.*

The approval of new preservatives in Annex V is a complex procedure, including extensive toxicological studies. Once approved, preservatives are subject to supervision by local authorities. They collect data about observed side effects and hand in this information to the 'Scientific Committee on Consumer Safety' (SCCS) of the European Commission. The SCCS consists of experts in the field. They evaluate the existing data and, if necessary, recommend to restrict the application of a preservative or even to delete it completely from Annex V.

The lifecycle of a preservative on Annex V can be illustrated using the example of methyldibromoglutaronitrile (MDBG) (Fig. 1). In 1983, after its admission, MDBG was well-accepted among cosmetic formulators, due to its reliable antimicrobial properties and good price-performance ratio. In the course of its popularity, MDBG was increasingly applied in cosmetic products. But its extensive use correlated with an increased number of reported cases of contact allergies. In 2005, the SCCS recommended a restriction of MDBG application to rinse-off products, which in 2007 led to a general ban of MDBG and its deletion from Annex V.[3]

So far, the SCCS has conducted a number of reports on other popular preservatives on Annex V. It is well conceivable that these reports might also lead to restrictions or prohibitions in the future. Another important factor determining the fate of a preservative lies in the hand of public perception. Media reports and theme-based internet blogs can quickly discredit the reputation of a preservative in the eyes of the consumer. In the case of parabens, this happened even though scientific data reaffirmed

Table 1: Dermosoft multifunctional additives.

Dermosoft	INCI multifunctional additives	Characteristics	Cosmetic properties	Natural cosmetics	pH range	Dermosoft blends
Organic Acids						
688 Anisate / 688 eco Anisate eco	*p*-Anisic Acid / Sodium Anisate	Fungicidal, mild and skin-friendly organic acid	Masking, pH-regulating	✓	4.0–6.5	1388 / 1388 eco
700B	Levulinic Acid/ Sodium Levulinate	Bactericidal, plant-derived, mild and skin-friendly organic acid	Perfume, skin conditioning, pH-regulating	✓	4.0–6.0	
Surface Actives						
PEA / Phenethylalcohol nat.	Phenethyl Alcohol	Water-soluble masking agent with rose-like scent; good antimicrobial activity	Masking	✓	Unlimited / Unlimited	
250	Phenylpropanol	Fragrance with antimicrobial activity. Synergistic effect with dermosoft octiol	Perfume		Unlimited	OMP, LP
Octiol	Caprylyl Glycol	Wetting agent with strong antimicrobial properties; synergistic with organic acids	Wetting, co-emulsifier		Unlimited	LP, MCA variant
GMCY	Glyceryl Caprylate	Vegetable-derived; strong against bacteria and yeast	Wetting, refatting, co-emulsifier	✓	4.0–7.0	
GMC	Glyceryl Caprate	Vegetable-based, selective antimicrobial; suitable for W/O-emulsions	Wetting, refatting	✓	4.0–7.0	
SLL	Sodium Lauroyl Lactylate	Vegetable-based, selective antimicrobial; low influence on viscosity and stability of emulsions	Wetting, refatting	✓	4.0–7.0	

their safety. As a consequence, marketing departments of cosmetic companies are forced to react. They pressure their product development team in order to find alternative preservative systems for their products. Not surprisingly, under such pressure and in a short time range, many formulators resort to preservatives whose skin intolerance has simply been forgotten. A good example is the renaissance of methylisothiazolinone (MIT). Since the early 1980s, MIT, as a part of Kathon CG, has been known as a contact allergen. Nevertheless, in the mid-2000s, MIT was advertised intensively as an alternative for the comparably harmless parabens. Not surprisingly, after a short period of marketing, MIT received the title 'Contact allergen of the year'.[4] Ever since, the opinion has prevailed that readjustment of preservative systems has to be accompanied by competent partners.

Cosmetic developers principally have two possibilities of adjusting their preservative system in a cosmetic formulation. They can either alter their existing preservative system according to the new regulations (i.e. by lowering concentrations) or they exchange problematic preservatives and rebuild their preservative system from scratch. At the beginning, the latter solution is definitely more labour-intensive, but in the long term some interesting marketing opportunities may arise. In the end, a smartly designed preservative concept helps to avoid bad press and prevents cosmetic consumers to adapt to future regulatory or public pressure. Which raises the question: what does such a smart preservative system look like?

Multifunctional product range

One way to circumnavigate legislative regulations of preservatives is to use multifunctional additives. Multifunctionals,

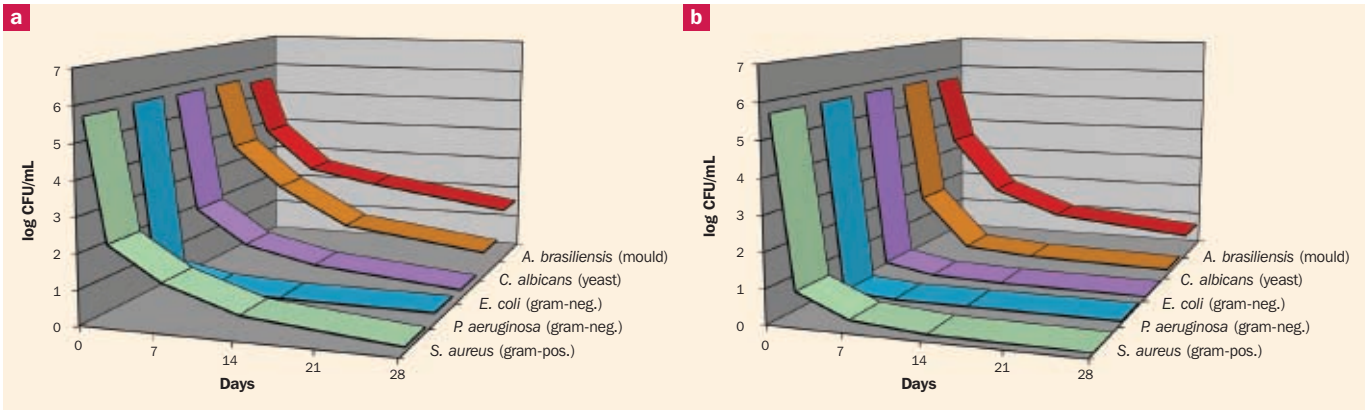

Figure 2: *Average reduction of microorganisms during various challenge tests of different market-typical formulations, containing either* **a)** *1% Phenonip (INCI: Phenoxyethanol, Methylparaben, Ethylparaben, Butylparaben, Propylparaben, Isobutylparaben) (from Clariant), a listed benchmark preservative blend (in total 66 challenge tests) or* **b)** *3% (0.5% active matter) dermosoft OMP (INCI: Methylpropanediol, Caprylyl Glycol, Phenylpropanol) a multifunctional-based preservative blend (in total 271 challenge tests).*

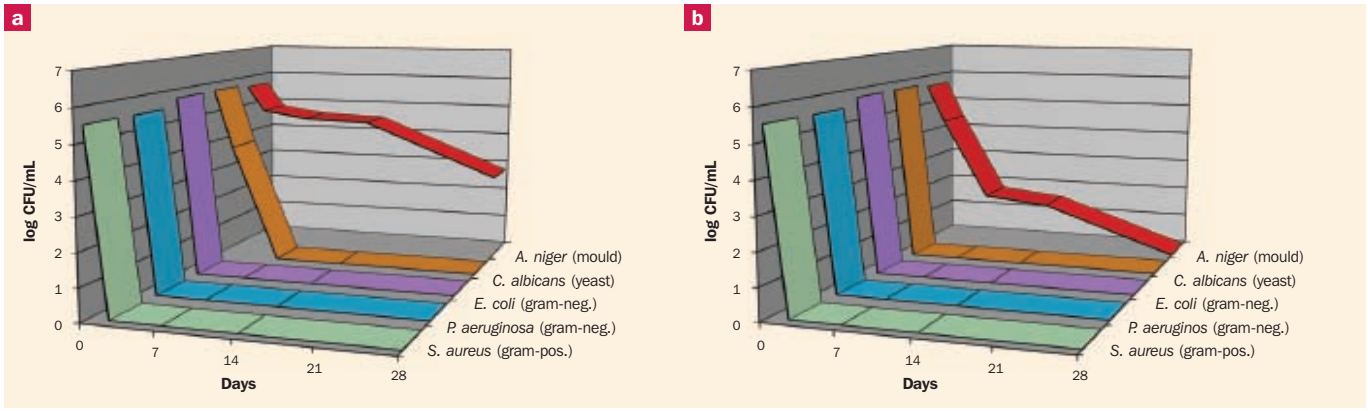

Figure 3: *Challenge Test with a natural O/W-emulsion (pH 5.35) stabilised with* **a)** *0.7% dermosoft GMCY and* **b**) *with additional 0.2% dermosoft 688 eco. Note the strong effect of dermosoft 688 eco on* Aspergillus niger *(red curve), changing the result from B to A-criteria (criteria for the test of sufficient preservation according to European Pharmacopeia 5.1.3).*

in addition to their cosmetic properties, possess an antimicrobial activity. Under the name dermosoft, Dr. Straetmans offers a variety of reliable and secure multifunctional raw materials and blends (Table 1). Choosing the right ingredients for a cosmetic preservative system is a challenging task for every formulator. Marketing claims, regulatory demands for globally approved raw materials, economic interests, and expectations about the production process all influence the decision. The dermosoft (now referred to as 'DS') multifunctionals, however, offer the formulator a safe and simple solution to address all kinds of demands and to enable the preservation of all types of cosmetic formulations without any listed preservatives.

The antimicrobial efficacy of DS multifunctionals was examined and compared to benchmark preservatives in numerous challenge tests according to the procedure described in Chapter 5.1.3. of the European Pharmacopeia. Tests were conducted for different market-typical formulations under similar conditions. The results demonstrate that multifunctionals in a broad variety of formulations can serve as an excellent alternative to listed traditional preservatives (Fig. 2).[5]

These products comprise two major groups of multifunctionals: organic acids and surface-actives (Table 1). Thanks to their amphiphilic molecule structure, with a hydrophilic and a lipophilic part, the surface-actives are capable of destabilising the microorganism's cell membrane. DS's organic acids, p-anisic acid and levulinic acid, dissociate into the microorganisms through the membrane, where they lower the pH-value of the cell. This ultimately leads to the death of the microorganism. In combination, organic acids and surface active compounds reveal a synergistic, antimicrobial effect. The surface active species penetrate the cell membrane and destabilise its structure. This causes the formation of pores in the membrane and allows the organic acids to dissociate more easily into the microorganisms.

The diversity of DS products enables the combination of multifunctionals with complement antimicrobial properties and synergistic effects. The range comprises both single multifunctionals with selective antimicrobial activity as well as single multifunctionals or convenience blends with a broad antimicrobial activity. For example, glyceryl caprylate (DS GMCY) is a surface active glycerol fatty acid ester with an excellent bactericidal activity (Fig. 3). For a complete preservative system an ingredient with fungicidal properties is missing. In Figure 3, the beneficial, fungicidal effect after addition of *p*-anisic acid (DS 688 eco) into the natural O/W emulsion (with 0.7% glyceryl caprylate) is demonstrated.

An example for a ready-to-use, broad-spectrum preservative blend is DS 1388 and its natural version DS 1388 eco (INCI: Glycerin, Aqua, Sodium Levulinate, Sodium Anisate). This blend combines the fungicidal activity of sodium anisate from DS anisate with the bactericidal acitivity of sodium levulinate from DS 700B. The broad-spectrum antimicrobial activity of DS 1388 eco was demonstrated in a challenge test for a surfactant-based, natural shampoo formulation (Fig. 4).

DS multifunctionals can be used for conventional and/or natural cosmetic concepts (see Table 1). DS GMCY (INCI: Glyceryl Caprylate), DS GMC (INCI: Glyceryl Caprate), DS SLL (INCI: Sodium Lauroyl Lactylate), DS 688 eco (INCI: p-Anisic Acid), DS anisate eco (INCI: Sodium Anisate), Phenethylalcohol nat. (INCI: Phenethyl Alcohol) and the blend DS 1388 eco (INCI: Glycerin, Aqua, Sodium Levulinate, Sodium Anisate) are all produced from 100% renewable resources and are fully compliant with natural cosmetic standards, like Ecocert, BDIH and Natrue. Cosmetic products with this range of ingredients as their preservative system can be claimed "free from listed preservatives" or "Formaldehyde-, Parabene-, Isothiazolinone-free". These claims are very popular in Europe, since the general perception of preservatives in the public opinion is not very positive. Nevertheless, the claims have been the subject of many heated debates. Some voices in the industry call them misleading, while others emphasise their role in the promotion of less-irritating alternatives. Some countries, like Canada, already reacted and allowed the use of these marketing claims only under stringent conditions. In Europe, the European Commission has not yet made a final judgement about the future of specific claims in advertising and packaging.

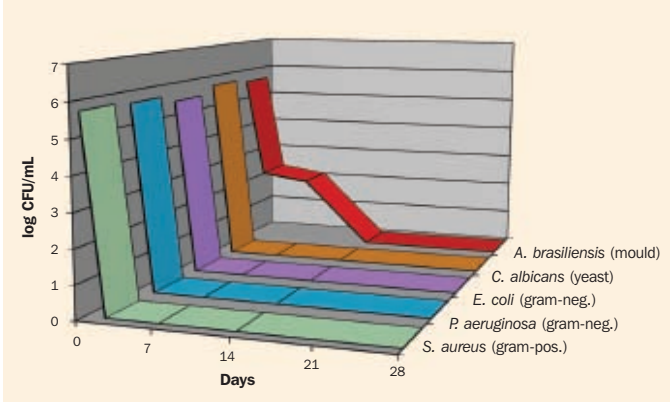

Figure 4: *Challenge test with Shampoo Baby Care stabilised with 3.5% dermosoft 1388 eco.*

Table 2: Verstatil blends of listed preservatives and multifunctional additives.

Verstatil	Characteristics	Cosmetic properties	Natural cosmetics	pH range	Multifunctional additives	Listed (Annex V) preservatives
PC	Economic blend for skin care products; pH-independent	Wetting, humectant		Unlimited	Caprylyl Glycol	Phenoxy-Ethanol
BP	Preservative with no discoloration of product	–		4.0–6.0		Benzoic Acid
BOB	Preservative for all cosmetic products	Perfuming, wetting		4.0–7.0		Benzyl Alcohol
TBO	Mild preservation for emulsions, tonics and gels	Wetting		4.0–6.0	Triethyl Citrate	
TBG	Preservation of certified natural cosmetics (emulsions, tonics, hydrogels)	Solvent, masking, wetting	✓	4.0–6.0	Glyceryl Caprylate	
BL non GMO	Perfectly suitable preservative for surfactant based products and tonics	Perfuming	✓	4.0–6.0	Sodium Levulinate	
SL non GMO	Preservative with optimised skin compatibility	Masking	✓	4.0–6.0		Sorbic Acid

Another essential factor in the selection of the right preservative system is the product concept. In general, in surfactant-based products like shower gels, the most effective preservative system is based on organic acids. Organic acids from DS products, to which this rule applies, are levulinic acid and its salt sodium levulinate (DS 700B), *p*-anisic acid (DS 688/688 eco) and its salt sodium anisate (DS anisate/anisate eco), or sodium levulinate and sodium anisate in the convenience blend DS 1388/1388 eco. The organic acids in these products act synergistically with the highly concentrated surfactants in the formulation. The surface-active multifunctionals instead get bound and inactivated by the micelle structures of the highly concentrated surfactants in the product.

An exception to this rule is DS OMP (INCI: Methylpropanediol, Caprylyl Glycol, Phenylpropanol). This blend is an outstanding multifunctional preservative against all kinds of microorganisms in all types of conventional cosmetic products. The combination of caprylyl glycol (DS octiol) and phenylpropanol (DS 250) has been known as an effective preservative system against bacteria and yeast with a synergistic effect against moulds for a long time.[6] The methylpropanediol in DS OMP further improves the preservative efficacy of the surface-active multifunctionals. As a hydrophilic matrix, methylpropanediol is shifting their distribution coefficient towards the aqueous phase, in which the microorganisms reside. The blend thus combines a synergistic antimicrobial system with a booster, pulling the system into the aqueous phase, where it is required.

In emulsions the concentration of surfactants is much lower. Therefore, a combination of organic acids and surface-active multifunctionals is recommended. Suitable surface-actives are, dependent on the marketing strategy of the product, glyceryl caprylate (DS GMCY), sodium lauroyl lactylate (DS SLL), glyceryl caprate (DS GMC) or caprylyl glycol (DS octiol). In aqueous systems, blends of organic acids (DS 1388) combined with a convenient solvent are recommended. Another possibility is the water-soluble, natural Phenethylalcohol nat. with its broad antimicrobial efficacy.

A crucial factor in the formulator's decision is the pH-value of the product. In general, organic acids are more likely to be pH-restricted than surface-actives, because of their dissociation in aqueous solutions. The organic acid and its salt are in an equilibrium state which is influenced by the pH value of the solution. Only the neutral acid can dissociate into the cell, whereas the salt remains in the medium. These products with a pH-independent activity comprise DS octiol (INCI: Caprylyl Glycol), Phenethylalcohol nat. (INCI: Phenethyl Alcohol) and DS OMP (INCI: Methylpropanediol, Caprylyl Glycol, Phenylpropanol) (Table 1).

The budget of a cosmetic product does not always allow for the application of multifunctional additives. So the question is: what preservatives from Annex V are safe and can be used with a clear conscience? A closer look at the science, legislation and public perception of some of the regularly used raw materials can

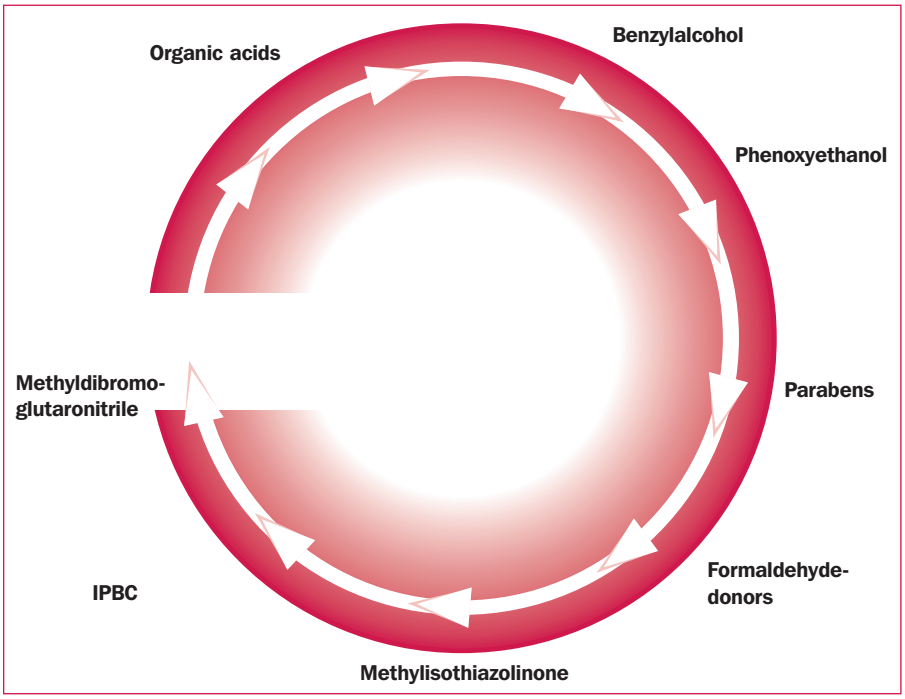

Figure 5: *Future perspectives of selected preservative systems.*

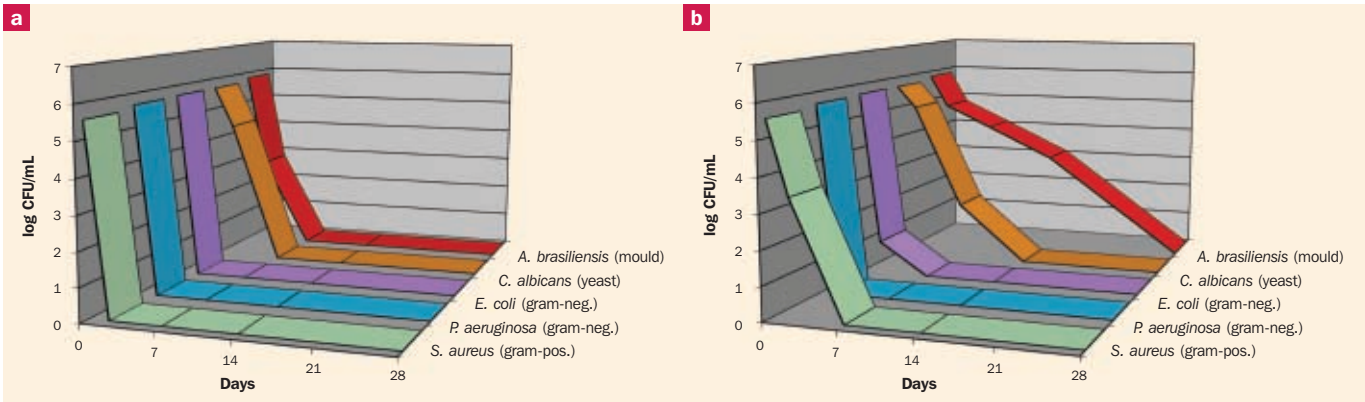

Figure 6: *Challenge test with an O/W-emulsion stabilised with 1% Verstatil TBO at* **a)** *pH 5.5 and* **b)** *pH 7.0.*

result in the picture shown in Figure 5. IPBC and methylisothiazolinone are already heavily restricted in their application and formaldehyde-donors and parabens suffer under a bad reputation among the general public. However, in comparison, organic acids and aromatic alcohols are quite safe in their assessment. For phenoxyethanol first inquiries for SCCS toxicological assessments have emerged.[7] However, the pressure to seek for alternatives is yet relatively low.

Formulators who wish to implement a long lasting system based on listed preservatives, should search for systems with a long history without side effects and negative press reports. To minimise the risk of upcoming skin side effects, a decrease in preservative concentrations, by exploiting synergistic effects of raw materials, is recommended.

Listed preservative product range

Dr. Straetman's Verstatil blends apply to these goals. Within this range, only listed preservatives with a clean record are implemented. They are combined with multifunctional additives in a way that synergistic effects occur (Table 2). Lower possible preservative concentrations are the result, which do not solely minimise the risk of undesired side effects but likewise decrease the cost of the final cosmetic product.

Four listed preservatives, comprising aromatic alcohols and organic acids, are implemented in the Verstatil (now referred to as 'VT') blends. Two conventional blends contain the well-known and established preservative Phenoxyethanol. In VT BP (INCI: Phenoxyethanol, Benzoic Acid) the synergistic combination of phenoxyethanol with benzoic acid allows for the effective preservation of surfactant based products and wet wipes at low concentrations between 0.5% and 1.0%. With VT BP, unlike other traditional preservatives, no discoloration of the final cosmetic products occurs. VT PC (INCI: Phenoxyethanol, Caprylyl Glycol) combines phenoxyethanol with caprylyl glycol, whose superior wetting ability boosts its preservative efficacy. The synergistic effect explains VT PC's broad-spectrum activity without any pH limitations in O/W- and W/O-emulsions, gels and tonics.

The product range of these blends, free of phenoxyethanol, enables the natural and the conventional formulation of cosmetic products. The group of natural blends include VT TBG (INCI: Triethyl Citrate, Glyceryl Caprylate, Benzoic acid), VT BL non GMO (INCI: Aqua, Sodium Levulinate, Sodium Benzoate) and VT SL non GMO (INCI: Aqua, Sodium Levulinate, Potassium Sorbate). VT TBG and VT TBO introduce triethyl citrate as an innovative solvent system for preservation blends in cosmetics. Together with the listed preservative benzoic acid and a surface-active wetting agent (glyceryl caprylate or caprylyl glycol, respectively) the two VTs are applicable in emulsions, tonics and gels. VT TBG's unique feature is its natural compliance, whereas the big advantage of VT TBO lies in the absence of any fragrance components. The blend itself has no noticeable odour and therefore suits perfume-free product concepts perfectly. Moreover the effective performance of VT TBO is covering the pH range of most cosmetic products (pH 4-7) (Fig. 6).

VT BL non GMO and VT SL non GMO each combine the multifunctional skin conditioner sodium levulinate with either benzoic acid or sorbic acid. Both are natural blends and suited to surfactant-, as well as water-based products.
In emulsions a combination with a wetting agent is recommended. The choice for one of the two blends is at last a question of personal preferences and marketing concepts.

Two 'phenoxyethanol-free' conventional blends use the synergistic combination of benzoic acid and the multifunctional wetting agent caprylyl glycol. One is the already described VT TBO, the other is VT BOB.

BOB is the economic all-rounder for all kinds of conventional cosmetic concepts and pH-values. The blend is a well-adjusted mixture of two listed preservatives, benzyl alcohol and benzoic acid combined with the boosting activity of caprylyl glycol. It has an excellent activity against all kinds of microorganisms. No further combination with other antimicrobials is needed

Conclusion

Future-proof cosmetic preservative systems with listed preservatives are becoming more and more restricted. In response to this negative trend, Dr. Straetmans developed two product lines for cosmetic preservation, dermosoft and Verstatil. Both product lines comprise raw materials and blends, which can be matched with the cosmetic formulations and their special features and claims. Dermosoft offers formulators multifunctional additives with antimicrobial properties for preservation without any listed preservatives, whereas Verstatil combines well established, inexpensive preservatives from Annex V with modern multifunctional additives to exploit synergies. PC

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