Cosmetic Preservation
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Because of public misconceptions and marketing pressures about the preservatives that have safely protected cosmetics for many decades formulators are constantly seeking alternatives. This feature is going to present some possible answers to the problem of providing cosmetic products with adequate preservation within the confines of current EU legislation while conforming to current marketing trends.

The starting point is to look at existing preservatives of proven efficacy and examine whether they can be made more efficient so that less is required. This may be achieved by better solubilising into the aqueous phase or by finding materials that appear to work in synergy.

Methylparaben possesses a broad spectrum of antibacterial activity. The activity of parabens increases with the increase in alkyl chain length, however their solubility in water is inversely proportional to the length of alkyl chain. Even methylparaben is only soluble at 0.25% in water and this is very close to its lower limit of effective concentration and if oils are present its partition coefficient will favour migration into the oil phase. By adding 0.02% propylparaben to the emulsion methylparaben is kept in the aqueous phase and this explains the need for more than one type of paraben in a single formulation.

Propylene glycol is known to enhance the activity of the majority of preservatives and is a preservative in its own right for most bacterial strains at a level of 10%. Much has been published about its ability to potentiate parabens through its co-solvent action. Methyl and propyl paraben are only effective at their limit of solubility but a study showed that a 2% and concentration of propylene glycol allowed the minimum inhibitory concentration of methylparaben to be reduced from 0.18% to 0.1% when combined with 0.02% propylparaben [Ref. 1].

Methylparaben is soluble at about 30%$^{w}/_{v}$ in ethanol but ethanol could upset the emulsion and it does introduce handling problems. If it can be tolerated then it is an effective preservative at about 15%$^{w}/_{w}$ related to the water content. Methylparaben is also soluble in glycerin but although glycerin preserves at concentrations ≥50%, at lower concentrations it may actually act as a nutrient for some microorganisms. This is because glycerin's antimicrobial activity depends solely on an osmotic effect rather than any innate toxicity to microorganisms.

Phenoxyethanol is a favoured solvent for parabens. Other materials that enhance activity by promoting solubility are benzyl alcohol and ethylhexylglycerin and these three materials plus propylene glycol frequently appear in preservative systems offered as alternatives to parabens because of their antimicrobial activity and solvent properties.

Benzyl alcohol is water soluble up to about 3g/L and is bactericidal at between 1% and 2% but is most effective below pH 5 and is virtually inactive above pH 8. It is incompatible with methylcellulose and its activity is reduced by non-ionic surfactants, such as the polysorbates. It is approved as a preservative by Ecocert and COSMOS but its level of use is restricted by Regulation (EC) No 1223/2009 to 1% in the final composition. There are anomalies about this material: it is approved as a preservative at a maximum level of 1% and it is often used in perfumery as a solvent but because it is a potential irritant its presence must be indicated on the label when its concentration exceeds 0.001 % in leave-on products and 0.01 % in rinse-off products. The anomaly is that despite these concerns it can be used above 1% for purposes other than inhibiting the development of microorganisms in the product but this purpose has to be apparent from the presentation of the product.

Ethylhexylglycerin has no such restrictions under current EU legislation and is a weak preservative in its own right. It works by reducing interfacial tension on the cellular walls of micro-organisms, enhancing the effect of other preservatives by increasing their penetration through the cell membrane. Its HLB is approximately 7.5 and this can upset some emulsifier systems. Its water solubility is about 1.8g/L but it is soluble to about 30% in propylene glycol. Interestingly it has demonstrable emollient properties and is increasingly used as a multifunctional component in preservative mixtures.

Phenoxyethanol is permitted to a maximum level of 1% under EC 1223/2009 and has bactericidal activity across the total pH range likely to be found in cosmetics. Its solubility in water is about 2.4% and it is compatible with cationic and anionic surfactants but it may be inactivated by ethoxylated surfactants. Although it has a wide spectrum of activity it is usually found in combination with other preservatives; traditionally these were parabens but other mixtures are now widely available.

The re-emergence of organic acids as preservatives is very much driven by the wish to avoid parabens and by their approval by Ecocert and COSMOS. Generally their activity is not wide spectrum and their efficacy is very pH dependent. Benzoic acid is effective at a concentration of 0.1% to 0.3%, which is the limit of its solubility in water. Its $pK_a = 4.19$ and it is ineffective in solutions with a pH above 5. Because of its insolubility in water it is often used as the very soluble sodium salt but its effectiveness may be reduced by non-ionic surfactants such as the polysorbates.

Another favourite is sorbic with an effective concentration of 0.05% to 0.2%. Sorbic acid has properties and problems that are similar to those of benzoic acid and like benzoic acid, sorbic acid has an effective concentration that is very close to its limit of solubility. Because of this, potassium sorbate is often used. Sorbic acid may be used at a higher pH than benzoic acid but is said to have little antimicrobial activity above pH 6.

Dehydroacetic acid is permitted to 0.60% but is almost insoluble in water (≥0.1%) however it remains effective to pH 6. Salicylic acid is permitted to 0.50% and may be used at higher levels if its primary purpose is not as a preservative. It is soluble in water to about 0.2% but the effectiveness of salicylic acid and its salts declines rapidly above pH 2.

The challenge to find alternative preservatives has led to the use of materials that are not classified as preservatives yet have antimicrobial activity. Glyceryl monoesters are a good example and are to be found in many of the alternative systems. Lowering the water activity of the final composition is also postulated as a possible route to avoid the use of traditional preservatives however it is rarely practical with an oil-in-water composition or with other water-based products. Materials used to achieve lower water activity include glycols such as glycerin and propylene glycol. Higher diols like pentylene glycol, 1,2-hexanadiol and caprylyl glycol appear to have an antimicrobial effect beyond their water-binding capacity but they also become less water-soluble.

Chelating agents like the sodium salts of EDTA are not preservatives but may provide a synergistic effect for the overall preservative system. They contribute to the partial solubilising of the cell membrane, which allows preservatives a pathway into the cell.

Nipaguard Zero is a new range of preservatives from **Clariant International Ltd.** based around sorbitan caprylate, which acts as a preservative booster. It is said to enable lower use concentrations of preservatives and increase performance of alternatives to traditional preservative actives. There are four blends: Nipaguard SCE [INCI: Sorbitan caprylate, 1,3-propane diol, benzoic acid] that claims high efficacy for leave-on formulations at pH 6.5 and superior results to parabens for rinse-off formulations at low pH. Nipaguard SCM [INCI: Sorbitan caprylate, methylisothiazolinone, propylene glycol] that, because of the strong synergistic effect of the sorbitan caprylate, it enables a lower level of methylisothiazolinone to be used. Nipaguard SC [INCI: Sorbitan caprylate, phenoxyethanol] delivers comparable results to parabens for both rinse-off and leave-on formulations. Finally Nipaguard SCV [INCI: Sorbitan caprylate, phenoxyethanol, benzyl alcohol, benzoic acid] is a selection of

actives geared towards fungal preservation at low pH and is said to provide comparable results to parabens for both leave-on and rinse-off formulations.

Salicylates & Chemicals Ltd. supply numerous preservative ingredients based on caprylyl glycol, 1,3-propanediol and ethylhexylglycerin. An example is Saliguard EZ [INCI: Ethylhexylglycerin, 1,3-propanediol] that is said to be effective at a pH level of 4 – 9 and to have good solvent properties for natural extracts. Another example is Saliguard EU, which is a preservative blend of ethylhexylglycerin and undecylenic acid. It is suitable for leave on as well as rinse off applications at pH 3 – 10 and its content of undecylenic acid imparts effective fungicidal properties.

Many of the possible alternative preservative systems show weak anti-fungal activity. Two materials that are on the permitted EU preservative list could be of interest to fill this gap. They are iodopropinylbutyl carbamate (IPBC) and dichlorobenzyl alcohol. IPBC is a highly effective fungicide which is functional over a wide pH and temperature range. It is non-irritating or sensitising and can be effective at low usage levels from as little as 15ppm. An example of its use is TroyCare FE02 from **Troy Products** comprising 2% IPBC, and 98% phenoxyethanol to give broadband anti-microbial protection.

From **Induchem**, Unigard BJ-93 is based on a combination of sodium benzoate, potassium sorbate and IPBC in a glycol-water solution that is effective at pH ≤5. Dichlorobenzyl alcohol is available as Unikon A-22 from **Induchem** and is permitted in the EU to 0.15%. It is described as is a broad spectrum antifungal preservative with good bacteriostatic properties over a pH-range of 3 – 10. Unigard OA-94 is a liquid preservative mixture from **Induchem** comprising benzoic acid and dehydroacetic acid in phenoxyethanol and is effective at pH≤6.

The **drstraetmans** company has long been associated with alternative preservative systems and the use of materials that although not on the EU permitted list they have antimicrobial activity. It has now added a new range of mixtures under its Verstatil trade name that is said to close the gap between safety, economy and positive image. It does this by combining mild preservatives with multifunctional ingredients to provide four liquid blends: Verstatil BOB is a mixture of benzyl alcohol, benzoic acid and caprylyl glycol; Verstatil TBO is a mix of triethyl citrate, benzoic acid and caprylyl glycol; Verstatil TBG is benzoic acid with glyceryl caprylate and Verstatil BL is a solution of benzoic acid and sodium levulinate in water.

Avoiding all listed preservatives are the Dermosoft products from **drstraetmans**. Dermosoft 688 is p-anisic acid that is effective against moulds over a pH range from 4.5 to 5.5. Easier to

use because of increased water solubility is Dermosoft Anisate [INCI: Sodium anisate] that can be used with Dermosoft 700B [INCI: Levulinic acid, sodium levulinate, glycerin, aqua] to provide complete protection at an optimum pH of 4.5 – 5.5. Dermosoft GMYC is glyceryl caprylate and it is recommended as a preservative booster and Dermosoft SLL is sodium lauroyl lactylate that has deodorant and anti-dandruff properties.

Cosphatec provides a number of ingredients with antimicrobial activity under its Cosphaderm trade name. An example is Cosphaderm MultiMEG, which is a mixture of magnolia extract with glyceryl caprylate and pentylene glycol. Magnolia extract is claimed to have antimicrobial, antioxidant, anti-acne and anti-inflammatory properties. Test data shows it to be weak against gram-negative bacteria but to have excellent activity against gram-positive bacteria and strong activity against yeast and mould. However, the glyceryl caprylate has anti-bacteria properties and is also effective against yeast and the pentylene glycol has antimicrobial properties and boosts the effect of the other two components. There are many other single substances and mixtures from Cosphatec with anti-microbial properties that are of interest for alternative preservative systems.

A novel approach to avoid using named preservative materials was launched at In-Cosmetics 2014 by **Lonza** under the name Romacil V [INCI: Parfum]. It was described as a new multi-functional cosmetic ingredient blend that provides a delicate gentle vanilla-like fragrance and it protects against microbiological spoilage. Extensive challenge test results showed it to possess wide-spectrum anti-microbial properties in a variety of formulation types, including o/w & w/o emulsions, make-up remover, mouthwash, and hair-conditioner at an optimum effective pH range of 4 to 7.

Other ingredients of possible interest include Glycapryl Glycine by **Prodotti Gianni**, which is capryloyl glycine and is suggested as a preservative booster. **Shulke Inc.** provides Sensiva PA 40, which is a synergistic blend that combines the antimicrobial activity of phenylpropanol and caprylyl glycol with the boosting and skin care properties of naturally-derived propanediol. The nature-identical fragrance ingredient phenylpropanol acts as an excellent booster for the antimicrobial properties of caprylyl glycol. Sensiva PA 40 has a very faint flowery scent and is suited for leave-on, wet-wipe and sensitive applications.

Vivimed Labs. Ltd., has a range of preservatives including Vivisept CVT [INCI: Glyceryl undecenylate, propylene glycol, chlorphenesin] and Vivisept GC [INCI: Glyceryl caprylate, glyceryl undecenylate] for preservation of skin, hair and body wash formulations. Galguard Trident was patented [WO20123076697A2] by **Galaxy Surfactants** as a three component

synergistic preservative blend for personal care formulations [INCI: N-undecylenoyl glycine, N-capryloyl glycine, phenoxyethanol].

Octiphen BSB-N from **Ashland** is a combination of benzoic acid, sorbic acid and benzyl alcohol and Sharon MX 705 from **Sharon Laboratories** is a blend of sorbic acid, benzyl alcohol, benzoic acid and dehydroacetic acid. *Asparagopsis armata* is a red seaweed gathered off the coast of Brittany that provides natural antimicrobial properties to Ysaline 100 from **A&M Cosmetics.** The active components extracted are a mixture of brominated and iodized compounds with a molecular weight over 10,000 Daltons.

With so many different microbial protection systems from which to make a selection and so many variables that can effect preservative efficacy Formula Protect available on the **Lonza** web site is a great tool for narrowing choice. There is a wide variety of parameters with tick boxes including compliance with different legislative areas, Ecocert approval, pH range, type of product to be protected and compatibilities. For example selecting a preservative system requiring EU and Ecocert approval for an o/w emulsion of pH ≤6 and containing polysorbates it returned Geoguard 221 [INCI: Dehydroacetic acid, benzyl alcohol, aqua] and Geoguard ECT [INCI: Benzyl alcohol, salicylic acid, glycerin, sorbic acid].

Whatever system is selected it must be remembered that preservatives are added to a composition to protect it against chance contamination in use and good production hygiene and raw materials with low microorganism count are a vital part of ensuring microbial safety.

Ref. 1 Prickett PS, Murray HL, Mercer NH. Potentiation of preservatives (parabens) in pharmaceutical formulations by low concentrations of propylene glycol. J Pharm Sci 1961; 50: 316–320

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