A New Generation of Preservatives for Cosmetic Formulations – Nipaguard® PO 5, Nipaguard® POB and Nipaguard® POM

Authors: S. Klein, Dr P. Klug, Clariant Produkte (Deutschland) GmbH, Germany

Abstract

Several currently used preservative classes have been under discussion during recent years because of safety concerns. Therefore a need has arisen for new, highly effective preservative blends which are easily incorporated into cosmetic formulations and which have a good toxicological profile. We have developed three new preservative blends which meet our customer needs concerning safety, efficacy, ease of incorporation, long term stability and antimicrobial activity for personal care products: Nipaguard® PO 5, Nipaguard® POB and Nipaguard® POM.

Introduction

Most cosmetic and personal care products present an ideal environment for microorganisms to grow and multiply quite easily. All the vital components such as temperature, nutrients, pH (slightly acidic to neutral) and water are present in cosmetic products which would make contamination highly likely if preservatives were not used. In most countries around the world, the use of preservatives in cosmetic and personal care formulations is not compulsory. However, the supplier/manufacturer is responsible for ensuring that consumer products such as cosmetics and personal care do not cause harm to the end user if used under normal conditions. Clearly, microbiological contamination would cause harm to the consumer. As several currently used preservative classes have been under discussion, there is a need for new highly effective preservative blends which are easily incorporated into cosmetic formulations and which have a good toxicological profile.

Octopirox®[1] (INCI: Piroctone Olamine) is a highly effective antifungal and antidandruff agent which has been used for over 30 years in the field of personal care formulations. Octopirox® has been reported[2] in the past to be not sufficiently effective as a single preservative for cosmetic formulations. The reason for this may have been inadequate incorporation especially into leave-on personal care products due to its low water solubility. Octopirox® provides its full activity only when completely dissolved and homogeneously distributed in the cosmetic formulation.

Phenoxyethanol is a commonly used solvent for liquid preservative blends but is also a preservative itself with particular efficacy against gram-negative bacteria.

A combination of the antifungal activity of Octopirox® with the antibacterial activity of Phenoyethanol results in a synergistic, broad spectrum activity preservative blend. This blend Nipaguard®[3] PO 5 (INCI: Piroctone Olamine (and) Phenoxyethanol) is a clear liquid. It is easily incorporated into cosmetic formulations and ensures homogeneous distribution of the active Piroctone Olamine, so that both Octopirox® and Phenoxyethanol can instantaneously provide their full activity.

Nipaguard® POB (INCI: Piroctone Olamine (and) Phenoxyethanol (and) Benzoic Acid) and Nipaguard® POM (INCI: Piroctone Olamine (and) Phenoxyethanol (and) Methylparaben) are two further developments with outstanding efficacy. The additional Benzoic Acid and Methylparaben lead to even higher efficacy.

Antimicrobial Activity of Nipaguard® PO 5, Nipaguard® POB and Nipaguard® POM

These blends exhibit micro biostatic activity against a wide range of bacteria, yeasts and molds. This is illustrated by Table 1, which shows the minimum inhibitory concentration (MIC) of Nipaguard® PO 5, Nipaguard® POB and Nipaguard® POM against examples of different groups of microorganisms.

	MIC level (%)		
Microorganisms	**Nipaguard® PO 5**	**Nipaguard® POB**	**Nipaguard® POM**
Bacteria			
Pseudomonas aeruginosa	0.125	0.08	0.063
Staphylococcus aureus	0.125	0.08	0.063
Yeasts			
Candida albicans	0.125	0.08	0.063
Molds			
Aspergillus niger	0.125	0.08	0.063

Table 1

The determined MIC values clearly demonstrate that the combination of Piroctone Olamine and Phenoxyethanol represent a synergistic blend. The values are lower in comparison to the calculated values based on the MIC values of the single ingredients Piroctone Olamine and Phenoxyethanol.

Cosmetic formulations contain preservatives in order to prevent proliferation or to limit microbial contamination which, during normal conditions of storage and use, particularly for multidose containers, could occur in a product and present a hazard to the consumer. The efficacy of an antimicrobial preservative may be enhanced or diminished by the different ingredients present in the formulation in which it is incorporated. It shall be demonstrated that the antimicrobial activity of the cosmetic formulations with the addition of Nipaguard® PO 5, Nipaguard® POB or Nipaguard® POM provide adequate protection from adverse effects that may arise from microbial contamination or proliferation during storage and use of the preparation. The antimicrobial efficacy was demonstrated by the test described in the European Pharmacopoeia[4].

The test consists of challenging the preparation, with a prescribed inoculum of suitable micro-organisms, storing the inoculated preparation at a prescribed temperature, withdrawing samples from the container at specified intervals of time and counting the organisms in the samples so removed. The preservative properties of the preparation are adequate if, in the conditions of the test, there is a significant fall or no increase, as appropriate, in the number of microorganisms in the inoculated preparation after the times and at the temperatures specified. The criteria of acceptance, in terms of decrease in the number of microorganisms with time, vary for different types of preparations.

Pseudomonas aeruginosa, Staphylococcus aureus, Candida albicans and *Aspergillus niger* represent likely contaminants of cosmetic formulations and therefore are typically used in the challenge test.

The criteria for evaluation of antimicrobial activity are given in Table 2 in terms of the log reduction in the number of viable microorganisms against the value obtained for the inoculum.

The A criteria express the recommended efficacy to be achieved. In justified cases where the A criteria cannot be attained the B criteria must be satisfied.

Parenteral and ophthalmic preparations					
		Log reduction			
		2 d	**7 d**	**14 d**	**d 28 d**
Bacteria	A	2	3	-	NI*
	B	-	-	3	NI
Fungi	A	-	-	2	NI
	B	-	-	1	NI

*NI: no increase

Table 2

The following four examples of cosmetic formulations represent typical classes of cosmetics, rinse-off and leave-on and have been chosen to investigate the efficacy of Nipaguard® PO 5 according to the criteria of the European Pharmacopoeia: BI 6146 Conditioning Shampoo, AI 8117 Basic Shower Gel, AVI 1711 OW Night Cream, AVI 2806 WO Cream. The Basic Shower Gel AI 8117 is a rather difficult to preserve formulation because of its low active content/high water content, its neutral pH of approx. pH = 7 and because the surfactants used do not themselves contain a preservative.

BI/ 6146, Conditioning Shampoo

Recipe

A	Genapol® LRO liquid	(Clariant)	30.00 %
	Sodium Laureth Sulfate		
B	Belsil® DMC 6032		0.50 %
	Dimethicone Copolyol Acetate		
	Fragrance		0.30 %
C	Allantoin	(Clariant)	0.30 %
D	Water		ad 100.00 %
E	Dyestuff solution		q.s.
	Panthenol		1.00 %
	Genagen® CAB	(Clariant)	8.00 %
	Cocamidopropyl Betaine		
	Genapol® L-3	(Clariant)	1.50 %
	Laureth-3		
F	Sodium Chloride		1.50 %

Procedure

I. Stir the components of B one after another into A.
II. Dissolve C in D under stirring while heating slightly and then stir into I.
III. Stir the components of E one after another into II.
IV. If necessary adjust the pH.
V. Finally adjust the viscosity with F.

AI/ 8117, Basic Surfactant Formulation

Recipe

A	Genapol® LRO paste	(Clariant)	13.70
	Sodium Laureth Sulfate		
B	Water		ad 100 %
C	Genagen® KB	(Clariant)	6.00 %
	Coco Betaine		
	Sodium Chloride		1.40 %
D	Citric Acid (10 % in water)		0.08 %

Procedure

I. Mix A and B.
II. Add C to I.
III. Adjust the pH with D to approx. 7

AVI/ 1711, heavy O/W– Night Cream

Recipe

A	Hostaphat® KW 340 D	(Clariant)	2.00 %
	Tricetearet-4 Phosphate		
	Hostacerin® DGMS	(Clariant)	3.00 %
	Polyglyceryl-2 Stearate		
	Stearic Acid		2.00 %
	Cetyl Alcohol		2.00 %
	Cetyl Palmitate		1.00 %
	Lunacera® M		1.00 %
	Microcrystalline Wax		
	Miglyol® 812		7.00 %
	Caprylic/Capric Triglyceride		
	Abil® 100		1.00 %
	Dimethicone		
	Mineral Oil, low viscosity		5.00 %
	Jojoba Oil		2.00 %
	Tocopheryl Acetate		1.00 %
B	Carbopol® 980		0.20 %
	Carbomer		
C	Sodium Hydroxide solution (10 % in water)		0.80 %
	Glycerin		3.00 %
	Water		ad 100 %
D	Fragrance		0.40 %

Procedure

I. Melt A at approx. 70°C, then add B. II. Heat C to approx. 70°C. III. Stir II into I and stir until cool. IV. At approx. 35°C add D to III. V. Homogenize the emulsion.

AVI/ 2806, Classic W/O– Cream

Recipe

A	Hostacerin® DGI	(Clariant)	4.00 %
	Polyglyceryl-2 Sesquiisostearate		
	Beeswax		2.00 %
	Lunacera® M		3.00 %
	Micrycrystalline Wax		
	Magnesium Stearate		1.00 %
	Mineral Oil, low viscosity		5.00 %
	Vaseline		10.00 %
	Cetiol® V		5.00 %
	Decyl Oleate		
B	1,2-Propylene glycol		3.00 %
	Water		65.20 %
C	Fragrance		

Procedure

I. Melt A at 80°C. II. Heat B to 80°C. III. Stir II into I. IV. Stir until cool. V. At 35°C add C to IV.

All four formulations without preservative fail the challenge test, but pass the challenge test according to the European Pharmacopoeia with criteria A when the indicated amounts of Nipaguard® PO 5 are added.

The results for surfactant based formulations are given in Table 3. The results for an O/W and an W/O cream are given in Table 4.

Nipaguard® POB and Nipaguard® POM have been tested in comparison to Nipaguard® PO 5 in the basic shower gel

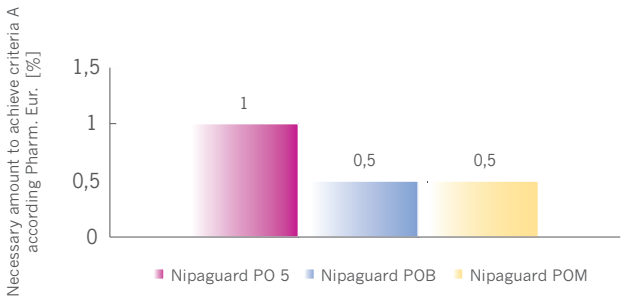
Test species	Colony forming units per g after 2 days	7 days	14 days	28 days
0.5 % Nipaguard® PO 5 in BI 6146 Conditioning Shampoo				
Pseudomonas aeruginosa	< 10	< 10	< 10	< 10
Staphylococcus aureus	< 10	< 10	< 10	< 10
Candida albicans	-	-	< 10	< 10
Aspergillus niger	-	-	< 10	< 10
1 % Nipaguard® PO 5 AI 8117 Basic Shower Gel				
Pseudomonas aeruginosa	< 10	< 10	< 10	< 10
Staphylococcus aureus	< 10	< 10	< 10	< 10
Candida albicans	-	-	< 10	< 10
Aspergillus niger	-	-	< 10	< 10

Table 3

Test species	Colony forming units per g after 2 days	7 days	14 days	28 days
0.5 % Nipaguard® PO 5 in AVI 1711 OW Night Cream				
Pseudomonas aeruginosa	< 10	< 10	< 10	< 10
Staphylococcus aureus	1×10^4	4.2×10^3	8×10^2	< 10
Candida albicans	-	-	< 10	< 10
Aspergillus niger	-	-	< 10	< 10
0.8 % Nipaguard® PO 5 in AVI 2806 Classic WO Cream				
Pseudomonas aeruginosa	8×10^3	< 10	< 10	< 10
Staphylococcus aureus	6×10^4	4×10^2	< 10	< 10
Candida albicans	-	-	< 10	< 10
Aspergillus niger	-	-	< 10	< 10

Table 4

formulation AI 8117 at pH 7. These two novel blends achieved criteria A according to the European Pharmacopoeia already at a use concentration of 0.5%. These findings (Figure 1) show the outstanding efficacy of Nipaguard® POB and Nipaguard® POM. Nipaguard® PO 5, Nipaguard® POB and Nipaguard® POM are broad spectrum liquid preservatives designed for the



Challenge Test, basic shower gel AI 8117, pH 7

Fig. 1

preservation of a wide range of cosmetics and toiletries, such as creams, lotions, shower gels, shampoos, cream rinses, liquid soaps and foam baths. The recommended use level to preserve most product types is normally in the range of 0.5 - 1.0% based on the total weight of the finished product.

Due to the low aqueous solubility, Nipaguard® PO 5, Nipaguard® POB and Nipaguard® POM are best added to any emulsifiers or solvents prior to the addition of water. In hot emulsification processes it is preferable to add the product during the cooling stage of the process, ideally below 40°C. In surfactant based formulations all three products are readily soluble. Nipaguard® PO 5, Nipaguard® POB and Nipaguard® POM are clear, pale yellow liquids, which remain fully stable over a wide pH range from 4-10.

Regulatory status

Piroctone Olamine is listed on Annex VI of the cosmetic directive 76/768/EEC in Europe with a maximum concentration of 1% for rinse-off products and 0.5% for leave-on products and is not restricted in the USA (no Cosmetic Ingredient Review (CIR) report available), but is not permitted for Japan as a preservative.

Phenoxyethanol is listed on Annex VI of the cosmetics directive 76/768/EEC in Europe with a maximum concentration of 1% for cosmetic products, is not restricted in the USA (CIR report is available) and permitted for Japan up to a maximum use concentration of 1%.

Based on the above information Nipaguard® PO 5 is permitted for both leave-on and rinse-off cosmetic products up to a maximum concentration of 1.05% in Europe according to Annex VI of the cosmetics directive 76/768/EEC. Nipaguard® POB and Nipaguard® POM are permitted for both leave-on and rinse-off cosmetic products up to a maximum concentration of 1.2% in Europe according to Annex VI of the cosmetics directive 76/768/EEC. All three blends Nipaguard® PO 5, Nipaguard® POB and Nipaguard® POM are not restricted in the USA but are currently not permitted for Japan.

Summary

Nipaguard® PO 5 (INCI: Piroctone Olamine (and) Phenoxyethanol), Nipaguard® POB (INCI: Piroctone Olamine (and) Phenoxyethanol (and) Benzoic Acid) and Nipaguard® POM (INCI: Piroctone Olamine (and) Phenoxyethanol (and) Methylparaben) are our company's novel, synergistic liquid and eas-to-handle preservative blends based on Piroctone Olamine and Phenoxyethanol, which provide excellent broad spectrum activity against most bacteria, yeasts and moulds. These blends are especially suitable for the preservation of creams, lotions, sun screens, deodorant formulations, cream rinses, shampoos, shower gels, liquid soaps and a lot more cosmetic formulations. Nipaguard® PO 5, Nipaguard® POB and Nipaguard® POM are active at low use concentrations, provide long term preservative and antimicrobial activity, are easily incorporated into personal care products and stable within a wide pH- range.

Bibliography

1. Preservatives for Cosmetics, by David C. Steinberg, Allured Publishing Corporation, 2006, ISBN 978-1-932633-12-2
2. Dr. Andreas Domsch: Konservierungsmittel und ihre praktische Anwendung in kosmetischen Produkten, in Seifen- Öle- Fette-Wachse, Vol. 116, No. 9/1990, S. 345- 356.
3. Clariant Patent- No. DE 10 2005 005 009
4. European Pharmacopoeia Online im Internet: URL:http://online.pheur.org/entry.htm [Stand 08.03.2006]

Biography

Sonja Klein holds a Bachelor of Chemical Engineering and has been R&D Manager Personal Care within Clariant for the product group of Personal Care Preservatives since 2004.

Dr. Peter Klug holds a Ph.D. in Organic Chemistry and has been global R&D Director Personal Care within Clariant since 2000.