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abstract

In today's world consumers aim for a sustainable and healthy lifestyle. Therefore, a modern cosmetic product must not only be safe to use but is formulated and produced with an aspiration for a low environmental footprint. These demands call for efficient and safe ingredients without compromising the microbial safety.

The options for microbial stabilization are increasingly limited due to legislative restrictions and changing consumer expectations. Furthermore, the increased use of natural ingredients can pose a higher risk of contamination. High raw material standards and a sound microbial quality management (e.g. Ashland's MQM™) applied throughout the entire production process lay ground for a hygienic product. However, to safeguard the integrity of a cosmetic product during its transport, storage and use, an adequate broad-spectrum antimicrobial is essential.

Ashland's latest launch sensiva™ sc 80 multifunctional meets multiple needs. The synergistic blend is a powerful antibacterial and fungicide, safe to use, sustainable, and nature-derived (ISO 16128). Additionally, sensiva™ sc 80 multifunctional provides skin functionalities that contribute to well-aging and a healthy skin.

Antimicrobial activity of sensiva™ sc 80 multifunctional

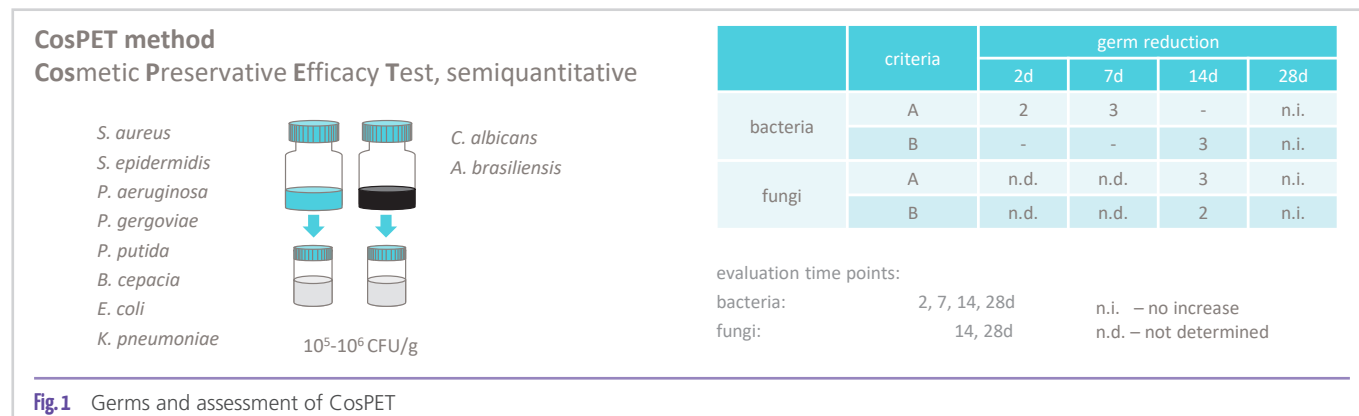
The new synergistic blend sensiva™ sc 80 multifunctional provides outstanding broad-spectrum efficacy without pH limitations. Especially its fungicidal activity ensures a well-protected product at use-concentrations between 0.3 - 1.5%.

The antimicrobial activity has been proven by the Ashland CosPET (Cosmetic Preservation Efficacy Test). This method is used to determine the efficacy of antimicrobials in cosmetic formulations, e.g. creams, lotions and shampoos. During CosPET, two samples of a test product are separately inoculated with a bacterial and a fungal suspension. Simultaneously, streak cultures of each batch are made before inoculation. The microbial growth is evaluated semi-quantitatively. After inoculation the germ count is expected to decrease over time. The final assessment is performed in accordance with European Pharmacopoeia (Figure 1).

The synergism of an optimized combination of caprylyl glycol with caprylhydroxamic acid solubilized in natural 1,3-propanediol is displayed in Table 1. The tested formulation is an oil-in water natural body lotion (Table 2). The results of the challenge test show the strong fungicidal capacity of caprylhydroxamic acid alone at only 0.05%. Caprylyl glycol alone or boosted with 1,3-propanediol is sufficiently bactericidal but fails against fungi. A low concentration of 0.75% sensiva™ sc 80 multifunctional already achieves a criteria A in this formulation tested at pH 5.3.

Table 3 shows the pH independent activity of sensiva™ sc 80 multifunctional exemplary tested in an oil-in-water cream (Table 4). A criteria A is fulfilled at both pH values 5.0 and 8.0 with 0.5% of the antimicrobial stabilizer.

sensiva™ sc 80 multifunctional is also suitable for wet-wipe emulsions. Table 5 shows the results of an oil-in -water natural wipe emulsion (Table 6) sufficiently protected by using 0.75% of the active blend.



natural body lotion (o/w) FL-22-0154	pH	sterility control	evaluation									assessment
			bacteria				fungi					
			2d	7d	14d	28d	assessment	14d	28d	assessment		
unpreserved	5.3	-	C	C	C	C	f	C	C	f	f	
+ 0.05% Caprylhydroxamic Acid	5.3	-	C	C	C	C	f	+	-	A	f	
+ 0.35% Caprylyl Glycol	5.3	-	++	-	-	-	A	C	+++	f	f	
+ 0.35% Caprylyl Glycol + 0.60% 1,3-Propanediol	5.3	-	+	-	-	-	A	C	C	f	f	
+ 0.50% sensiva™ sc 80 multifunctional	5.3	-	+++	+++	C	C	f	++	-	A	f	
+ 0.75% sensiva™ sc 80 multifunctional	5.3	-	++	-	-	-	A	-	-	A	A	

assessment
 f = failed
 A = pass criteria A
 B = pass criteria B
 - = free of microbial growth
 + = slight growth
 ++ = moderate growth
 +++ = heavy growth
 ++++ = massive growth
 C = completely overgrown

Tab.1 CosPET results in a natural body lotion (o/w)

phase	INCI name	trade name	function	% w/w
A	Sucrose Polystearate (and) Cetyl Palmitate	Emulgade Sucro Plus ¹⁾	emulsifier	3.00
	Sodium Stearoyl Glutamate	Emulglin SG ²⁾	emulsifier	0.20
	Cetearyl Alcohol	Lanette O ²⁾	consistency factor	2.00
	Cocoglycerides	Myrilol 331 ³⁾	emollient	4.00
	Prunus Amygdalus Dulcis (Sweet Almond) Oil	Sweet Almond Oil ⁴⁾	emollient	1.50
	Dicaprylyl Ether	Cetiol OE ²⁾	emollient	4.00
	Cetyl Palmitate	Cufina CP ²⁾	consistency agent	1.00
B	Aqua			ad 100
	Glycerin	Glycerin (99%)	humectant	5.00
	Xanthan Gum	Keltrol CG-SF ³⁾	stabilizer	0.30
C	Tocopherol	Covl-ox T 90 EU C ²⁾	antioxidant	0.50
D	Propanediol (and) Caprylyl Glycol (and) Caprylhydroxamic acid	sensiva™ sc 80 multifunctional ¹⁾	antimicrobial stabilizer	0.75
	Citric Acid	Citric Acid (50% aq. Solution)	pH-adjuster	q.s.

¹⁾ Ashland ²⁾ BASF ³⁾ CP Kelco ⁴⁾ Gustav Heess

Tab.2 Formulation of natural body lotion (o/w) FL-22-0154

o/w cream FL-19-0135	pH	sterility control	evaluation									assessment
			bacteria				fungi					
			2d	7d	14d	28d	assessment	14d	28d	assessment		
unpreserved	5.0	-	C	C	C	C	f	C	C	f	f	
unpreserved	8.0	-	C	C	C	C	f	C	C	f	f	
+ 0.50% sensiva™ sc 80 multifunctional	5.0	-	-	-	-	-	A	+	-	A	A	
+ 0.50% sensiva™ sc 80 multifunctional	8.0	-	-	-	-	-	A	-	-	A	A	

Tab.3 CosPET results in o/w cream at different pH values

phase	INCI name	trade name	function	% w/w
A	Aqua			ad 100
	Glycerin	Glycerin (99%)	humectant	2.30
B	Glyceryl Stearate (and) PEG-30 Stearate	Arlacel 983 PW ²⁾	emulsifier	3.00
	Stearic Acid		consistency factor	4.00
	Cetyl Alcohol	Lanette 16 ³⁾	consistency factor	3.00
	Mineral Oil	Paraffinum Liquidum	emollient	6.00
	Dimethicone	Xiameter PMX-200 Silicone Fluid 50cs ⁴⁾	emollient	5.00
	Ethylhexyl Palmitate	Cegesoft C 24 ³⁾	consistency agent	1.50
C	Propanediol (and) Caprylyl Glycol (and) Caprylhydroxamic acid	sensiva™ sc 80 multifunctional ¹⁾	antimicrobial stabilizer	0.50
	Sodium Hydroxide	Sodium Hydroxide (10% aq. solution)	emollient	0.80

¹⁾ Ashland ²⁾ Croda ³⁾ BASF ⁴⁾ Dow Chemical

Tab.4 Formulation of o/w cream FL-19-0135

natural wipe emulsion (o/w) FW-13-0121	pH	sterility control	evaluation								
			bacteria				assessment		fungi		assessment
			2d	7d	14d	28d	14d	28d	14d	28d	
unpreserved	7.0	-	C	C	C	C	f	C	C	f	f
+ 0.50% sensiva™ sc 80 multifunctional	7.0	-	C	C	C	C	f	-	-	A	f
+ 0.75% sensiva™ sc 80 multifunctional	7.0	-	+	-	-	-	A	-	-	A	A

assessment
 - = free of microbial growth
 f = failed
 A = pass criteria A
 B = pass criteria B
 + = slight growth
 ++ = moderate growth
 +++ = heavy growth
 ++++ = massive growth
 C = completely overgrown

Tab. 5 CosPET results in natural wipe emulsion (o/w)

phase	INCI name	trade name	function	% w/w
A	Glycerin	Glycerin (99%)	humectant	5.00
	Aqua (and) Sucrose Laurate (and) Alcohol	Sisterna L70-C ²⁾	emulsifier	3.75
B	Caprylic/Capric Triglyceride	Myritol 318 ³⁾	emollient	5.00
	Tocopherol	Tocopherol	antioxidant	0.10
C	Aqua		thickener	ad 100
	Microcrystalline Cellulose, Cellulose Gum	Avicel PC 611 ⁴⁾	thickener	1.50
D	Propanediol (and) Caprylyl Glycol (and) Caprylhydroxamic acid	sensiva™ sc 80 multifunctional ¹⁾	antimicrobial stabilizer	q.s.
E	Citric Acid		pH adjuster	q.s.

¹⁾ Ashland ²⁾ Sisterna ³⁾ BASF ⁴⁾ FMC Corporation

Tab. 6 Formulation of natural wipe emulsion (o/w) FW-13-0121

Skin protection and well-aging

Several scientific *in-vitro* cell-free tests were performed to investigate the antioxidant and enzyme inhibition capability of sensiva™ sc 80 multifunctional [1].

Antioxidant properties

The active ingredient caprylhydroxamic acid included in sensiva™ sc 80 multifunctional acts as a chelating agent. It reacts and forms complexes with metal ions. Free metal ions can induce oxidation reactions and can affect the stability and appearance of cosmetic products. Caprylhydroxamic acid is also known to provide free radical scavenging activity [2, 3, 4].

sensiva™ sc 80 multifunctional is a powerful chelator. Iron chelators function as antioxidants by scavenging reactive oxygen species (ROS) and reduce the amount of available iron by decreasing the quantity of hydroxide generated by Fenton reactions. Iron and hydrogen peroxide can oxidize a wide range of substrates and causing biological damage. The reaction in this assay, referred to as the Fenton reaction, can generate both hydroxyl radicals and higher oxidation states of the iron.

The method used was the *in tubo* chelating assay with copper sulfate. sensiva™ sc 80 multifunctional in propanediol at pH 5.5 was tested against control and the well-known chelator EDTA in water at pH 10.5 as a benchmark. Chelating activity leads to green or blue staining dependent on the pH of the sample. The results show that sensiva™ sc 80 multifunctional possesses significant and dose-dependent chelating power reflected by the formation of green aggregates after copper solution addition. The benchmark EDTA also chelates ions leading to

increase in blue staining (Figure 2).

In addition, sensiva™ sc 80 multifunctional acts as an iron

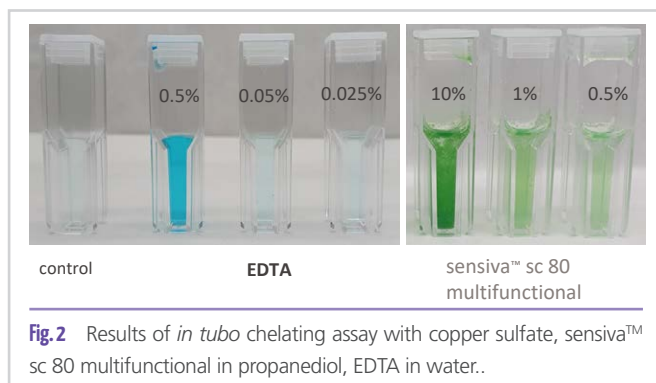


Fig. 2 Results of *in tubo* chelating assay with copper sulfate, sensiva™ sc 80 multifunctional in propanediol, EDTA in water.

protection shield. The FRAP (ferric reducing ability of plasma) assay is a widely used method where in Fe³⁺ is reduced to Fe²⁺; which then reacts with ferric chloride to form ferric-ferrous complex that has an absorption maximum at 700 nm. The ingredient antioxidant activity depends on the potential to form complexes with metal ions, particularly iron and copper [2]. 0.5% sensiva™ sc 80 multifunctional diluted in propanediol provides significant reducing power comparable to ascorbic acid (AA), 1.0% even stronger. Thus, sensiva™ sc 80 multifunctional can prevent metal ion catalyzed generation of reactive species leading to reductive cascades. No reducing effect was detected by hydroxyacetophenone (HAP) which was tested in comparison (Figure 3).

A lipid peroxidation study was performed to investigate the ability of sensiva™ sc 80 multifunctional to protect lipids in cells and membranes against oxidative stress. Lipid peroxi-

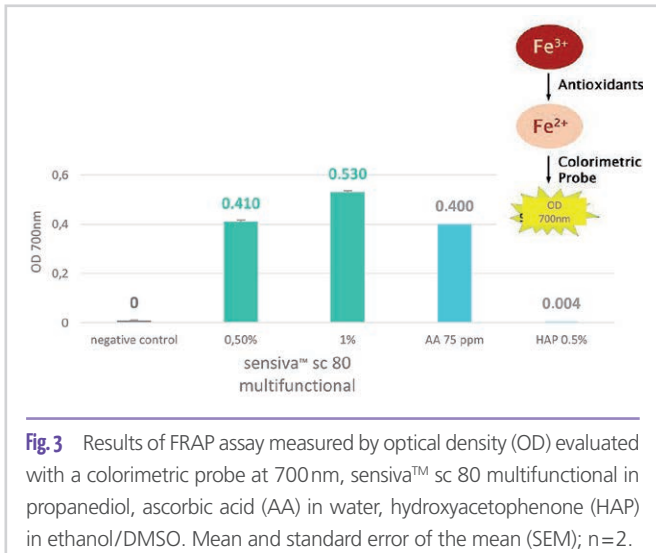


Fig. 3 Results of FRAP assay measured by optical density (OD) evaluated with a colorimetric probe at 700 nm, sensiva™ sc 80 multifunctional in propanediol, ascorbic acid (AA) in water, hydroxyacetophenone (HAP) in ethanol/DMSO. Mean and standard error of the mean (SEM); n=2.

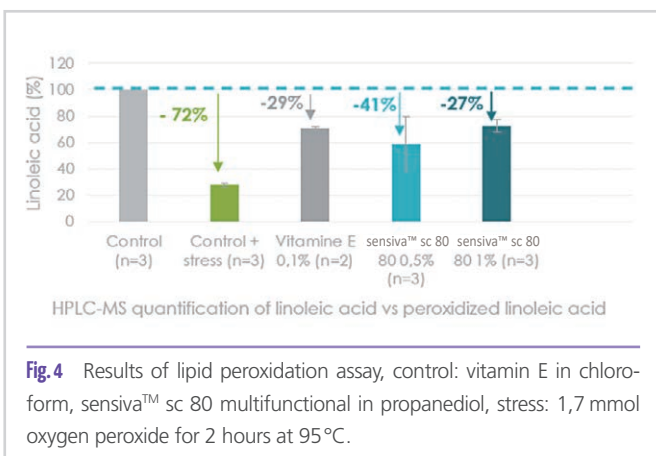


Fig. 4 Results of lipid peroxidation assay, control: vitamin E in chloroform, sensiva™ sc 80 multifunctional in propanediol, stress: 1,7 mmol oxygen peroxide for 2 hours at 95 °C.

oxidation is the oxidative degradation of lipids. In this process free radicals initiate a cascade of reactions attacking the lipid membranes resulting in cell damage. Lipid peroxidation is involved in premature aging and in the progression of comedogenesis which can lead to clogged pores and possibly to acne. The positive control in the assay was vitamin E and stress was induced by hydrogen peroxide and heating. The results (Figure 4) show the HPLC-MS quantification of linoleic acid before peroxidation (control) and after application of stress conditions. 72% of linoleic acid becomes oxidized under stress conditions. With addition of sensiva™ sc 80 multifunctional the peroxidation is reduced at 41% using 0.5% of the active blend. 1.0 % sensiva™ sc 80 multifunctional achieves the same good protection (27% of oxidation) like 0.1% of the benchmark vitamin E (29% of oxidation).

Well-aging benefits

Dermal matrix components such as collagen and hyaluronic acid are playing a key role in well-aging and skin repair. Collagenases are part of enzyme-family Matrix-Metalloproteinases (MMPs) involved in proteins degradation of the skin connective tissue. They act as transmembrane zinc endopeptidases that break the peptide bonds of collagen, the most abundant constituent of the extracellular matrix (ECM). Hyaluronidases

are classes of enzymes degrading predominantly the polysaccharides hyaluronan (hyaluronic acid), a voluminous polysaccharide found in ECM. It binds to the surface of cells and provides elasticity, hydration, and protection, which contributes to healthy-looking skin.

Under normal physiological conditions, the activity of these enzymes is precisely regulated to ensure skin tissue homeostasis. Under oxidative stress or UV light exposure, they are over-expressed, resulting in skin disorders such as premature skin aging, inflammation, or, more seriously, degenerative diseases. sensiva™ sc 80 multifunctional exhibits strong inhibition of both collagenase and hyaluronidase proven in the *in tubo* assays at both tested concentrations 0.5% and 1.0% (Figure 4, 5). The prevention from degradation of collagen and hyaluronan can help to sustain strength and flexibility of the skin.

Summary

The new innovative blend sensiva™ sc 80 multifunctional offers broad-spectrum activity to protect the microbiological stability of cosmetic application. Its excellent fungicidal capacity makes it a perfect solution for different formulations especially those which are difficult to preserve. It is easy to use, pH independent and compatible with typical cosmetic ingredients. In addition, sensiva™ sc 80 multifunctional acts as chelator and antioxidant and contributes to a healthy-looking skin by guarding collagen and hyaluronan.

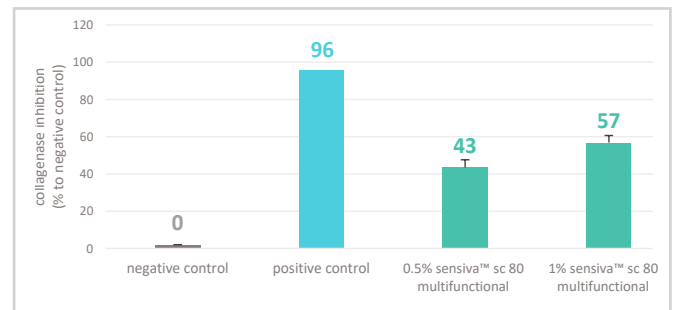


Fig. 5 Results of collagenase inhibition *in tubo* assay, control: 0.1% gallic acid, sensiva™ sc 80 multifunctional in propanediol, analysis of collagen fluorescent digested fragment. Mean and standard error of the mean (SEM); n=2.

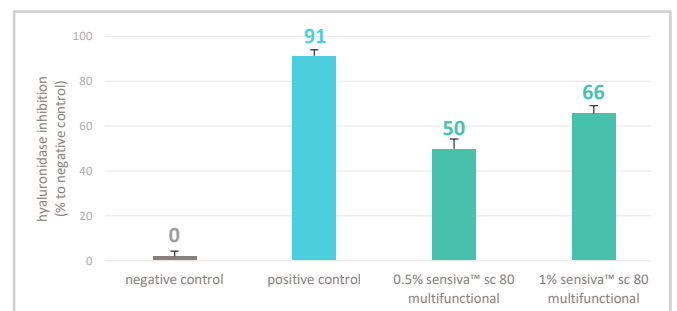


Fig. 6 Results of hyaluronidase inhibition *in tubo* assay, control: 0.03% tannic acid, sensiva™ sc 80 multifunctional in propanediol, analysis of turbidity (reactivity between remaining hyaluronan and acidic albumin solution). Mean and standard error of the mean (SEM); n=2.

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