
CIBA[®]TINOSAN[®]SDC



A versatile Antimicrobial for Personal Care Applications

Ciba® TINOSAN® SDC: A versatile Antimicrobial

➤ An effective deodorant ingredient

- TINOSAN® SDC exhibits strong activity against Corynebacteria and significantly reduces body malodor

➤ A fast killing antimicrobial active

- TINOSAN® SDC shows reduction of gram-negative and gram-positive bacteria on skin.

➤ A broad spectrum preservative for personal care products*

- TINOSAN® SDC works as stand-alone preservative in many cosmetic formulations
- TINOSAN® SDC can be combined with a broad range of preservatives due to its excellent compatibility with cosmetic ingredients

* TINOSAN® SDC is not registered as a preservative for PC products yet

A new silver-based antimicrobial technology

- The antimicrobial activity of silver is known for more than 100 years
 - effective antimicrobial
 - safe for use on human beings
 - natural biocide
- Various silver-based technologies have been successfully used in technical and medical applications including water purification and wound bandaging
- The use of silver in Personal Care has not been very successful yet due to limited compatibility and stability of market products in cosmetic formulations resulting in precipitation, discoloration and reduction of efficacy



TINOSAN®SDC: Taylor-made silver technology for Personal Care

➤ **Crystal clear product with high water solubility**

- suitable for clear formulations such as shampoos and gels
- does not migrate into the oil phase of emulsions resulting in weak efficacy against microorganisms in the water phase
- good stability in a broad range of PC product types



➤ **Broad spectrum antimicrobial activity**

✓ **Efficient deodorant active:**

active against Corynebacteria which cause body malodor

✓ **Fast killing antimicrobial active:**

reduces pathogenic bacteria within a short time

✓ **Excellent preservative:**

active against bacteria and fungi which can cause product deterioration and/or pose a health risk for consumers

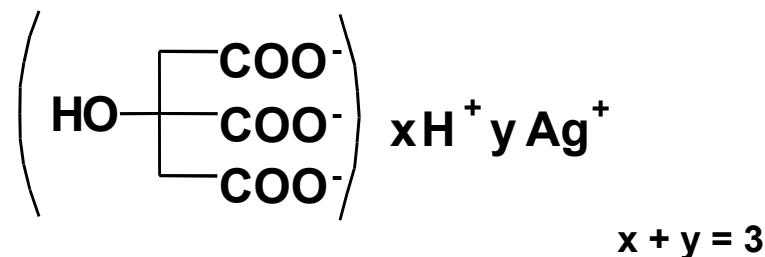


Tinosan[®]SDC, a silver citrate complex

Composition:

INCI Name: Citric Acid (and) Silver Citrate

Active Ingredient: Silver ions (2400 ppm)



pH of product: 1.5

Appearance: transparent aqueous solution, colorless /
slight citrus odor low-viscous liquid

Solubility: highly soluble in water

Efficacy of TINOSAN®SDC / Minimal Inhibitory Concentrations (MIC)

Microorganism	MIC of TINOSAN SDC (%)
Corynebacterium xerosis ATCC 373	0.12
Corynebacterium minutissimum ATCC 23348	0.12
Propionibacterium acnes ATCC 6919	0.25
Staphylococcus aureus ATCC 6538	0.16
Escherichia coli ATCC 10536	0.08
Pseudomonas aeruginosa ATCC 15442	0.16
Candida albicans ATCC 10231	0.12
Malassezia furfur DSM 6171	0.25
Aspergillus niger ATCC 16404	0.50
Trichophyton mentagrophytes ATCC 9533	0.50

TINOSAN®SDC is active against all groups of microorganisms

Mode of Action

- The active in TINOSAN[®]SDC is the silver ion
- Silver ions interact with nucleophilic groups of amino acids in proteins and enzymes and membrane components (e.g. sulfhydryl, amino, imidazole, phosphate and carboxyl groups)
 - Inhibition of transport mechanisms
 - Inhibition of the metabolism of the microbial cell
- ➔ **i.e. unspecific mode of action**
- ➔ **Bacteria have been exposed to silver ions for over 4 billion years and no widespread resistance has been evident to date***

* S.L. Percival et al.: J. Hosp. Infect. 60, 1-7 (2005)

The risk for microbial resistance to Tinosan[®]SDC can be considered as low

TINOSAN®SDC: A Versatile Active for PC

Personal Care

- **Deodorant active**
- **Hand and skin sanitizer**
- **Hair Care**
- **Support of Preservative System**



How to use TINOSAN[®]SDC in PC Products

Recommended conc.: 0.1% - 0.3%

Incorporation methods:

➤ **Direct incorporation:**

- TINOSAN[®]SDC is directly added to the final formulation at temperatures of < 50°C. pH value of the formulation to be adjusted.

➤ **Indirect incorporation:**

- TINOSAN[®]SDC is pre-diluted with water and pH is adjusted to the target pH (i.e. pH < 7). Addition of diluted TINOSAN[®]SDC to the final formulation at temp.of < 50°C.

Indirect method preferred for formulations containing pH-sensitive ingredients.

Keep the pH of the formulation in any case < 7 prior to incorporation of TINOSAN[®]SDC in order to avoid discoloration.

TINOSAN[®]SDC is easy to incorporate in many types of Personal Care formulations

Compatibility of TINOSAN®SDC

- Rinse off formulations (Shampoos, Shower gels, liquid hand soaps, dishwashing liquid, surface cleaner with pH < 7.0)
 - Surfactant systems:
 - TINOSAN®SDC is compatible with anionic, nonionic and amphoteric surfactants up to 15-20%.

TINOSAN®SDC in surfactants after 3 months storage at daylight/22°C

0.3% TINOSAN®SDC
10.0% Sodium Laureth-2
Sulfate

0.3% TINOSAN®SDC
10.0% Cocamidopropyl
Betaine

0.3% TINOSAN®SDC
10.0% Decyl Glucoside

0.3% TINOSAN®SDC
10.0% Laureth-9



Compatibility of TINOSAN®SDC

➤ Neutralizer:

- TINOSAN®SDC containing formulations can be neutralized by the use of any base. To avoid coloration/discoloration, it is recommended to neutralize with NaOH or KOH instead of amines like AMP. The lower the pH value of the formulation the better the light stability of the formulation.

➤ Thickener systems:

- good compatibility with xanthan gum, associative acrylate polymers (eg TINOVIS GTC), carbomers. Chlorides might cause discoloration by formation of Silver Chloride. Use of NaCl as thickener has negative impact on disinfecting activity (i.e. fast killing efficacy). Impact of NaCl on discoloration depend on the composition of the formulation
- Incompatibilities might occur with cellulose derivatives, starch derivatives, cationic thickeners (eg guar derivatives).

TINOSAN®SDC is compatible in common surfactant systems for Personal Care

Compatibility of TINOSAN®SDC

- Leave-on formulations (Creams, Lotions, Gels, Sprays etc.)
 - Emulsifier Systems:
 - TINOSAN®SDC is compatible with most nonionic emulsifiers and anionic emulsifiers. Cationic emulsifiers might cause incompatibilities

O/W Deodorant (AM06069-9)
Fresh
0.3% TINOSAN®SDC

O/W Deodorant (AM06069-9)
After 3 months at daylight/
22°C, 0.3% TINOSAN®SDC

O/W Deodorant (AM06069-9)
After 3 months at 40°C
0.3% TINOSAN®SDC

O/W Deodorant (AM06069-9)
After 3 months at 22°C
in darkness
0.3% TINOSAN®SDC



No discoloration even when exposed to daylight

Compatibility of TINOSAN®SDC

- Leave-on formulations (Creams, Lotions, Gels, Sprays etc.)
 - Neutralizer:
 - TINOSAN®SDC containing formulations can be neutralized by the use of any base. To avoid coloration/discoloration, it is recommended to neutralize with NaOH or KOH instead of amines like AMP. The lower the pH value of the formulation the better the light stability of the formulation.
 - Emollients: No impact was found
 - Thickener systems:
 - good compatibility with xanthan gum, associative acrylate polymers (e.g. TINOVIS GTC), carbomers.
 - Incompatibilities might occur with cellulose derivatives, starch derivatives, cationic thickeners (eg guar derivatives)
 - Chlorides might cause discoloration by formation of Silver Chloride and should be avoided.

TINOSAN®SDC is compatible in common leave-on systems for Personal Care

Compatibility of TINOSAN®SDC

- Cationic Ingredients

- TINOSAN®SDC shows incompatibilities with some cationic ingredients. Incompatibilities depend on the cationic charge of the ingredients used and on the concentration of cationic ingredients.
- Addition of low amounts of cationic conditioners in shampoo or shower products do in most cases not negatively influence the stability of the formulation
- The following cationic ingredients show good compatibility with TINOSAN®SDC

- Polyquaternium-7 (SALCARE® Super 7)
- Polyquaternium-37 (SALCARE® SC96)
- Polyquaternium-11
- Distearyldimonium Chloride

TINOSAN®SDC: A Versatile Active for PC

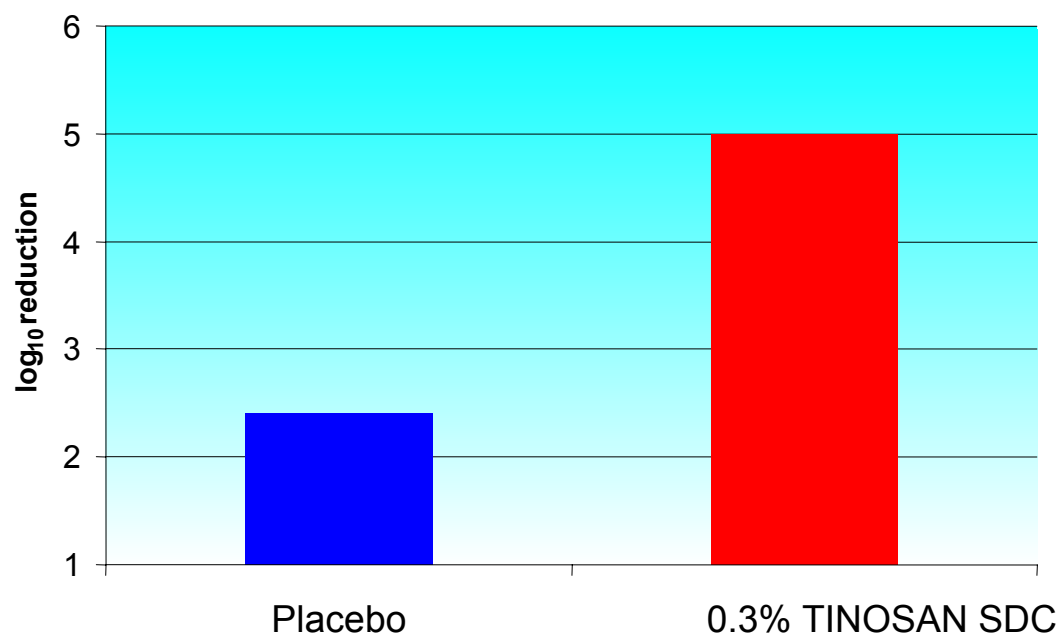
Personal Care

- **Deodorant active**
- Hand and skin sanitizer
- Hair Care
- Support of Preservative System

Deodorant Efficacy of TINOSAN[®]SDC

Bactericidal efficacy of an emulsion roll-on deodorant against *Corynebacterium minutissimum* ATCC 23348

Test conditions: EN1040, 5 minutes contact time, 90% concentration



Strong bactericidal efficacy against body malodor generating *Corynebacteria* with 0.3% TINOSAN[®]SDC

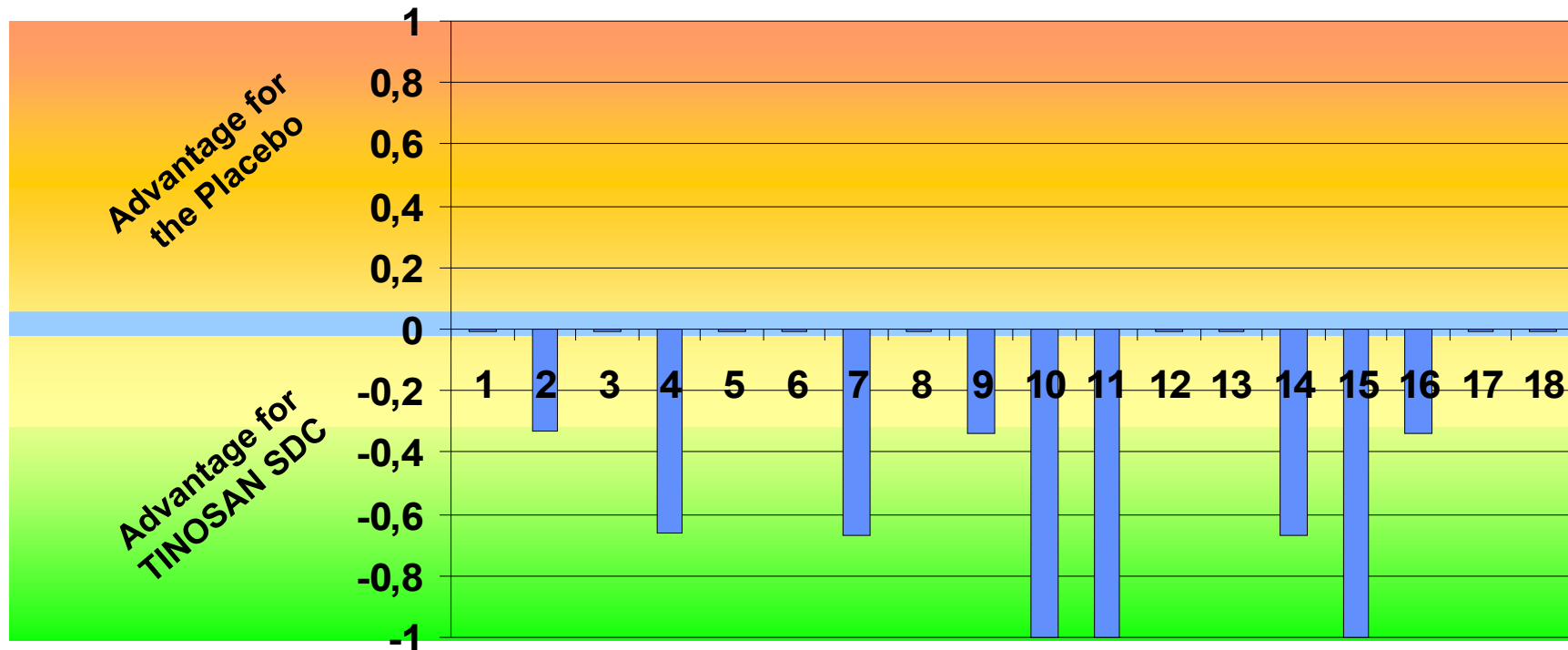
Deodorant Efficacy of TINOSAN[®]SDC: in vivo study

Study Protocol

- Double blind underarm sniffing test with a deodorant spray containing 0.3% TINOSAN[®]SDC against the placebo (without TINOSAN[®]SDC)
- Test panel: 20 volunteers (f & m)
- Volunteers treated one armpit with the placebo and the other armpit with the TINOSAN[®]SDC-containing product.
- Test products were applied twice daily over a period of 5 days
- 24 hours after the last application, the volunteers gave their ratings on performance

Deodorant Efficacy of TINOSAN®SDC

Malodor self-evaluation by volunteers 24 hours after last application



**No volunteer preferred the placebo,
50% of the volunteers preferred the formulation with
TINOSAN®SDC**

TINOSAN®SDC: A Versatile Active for PC

Personal Care

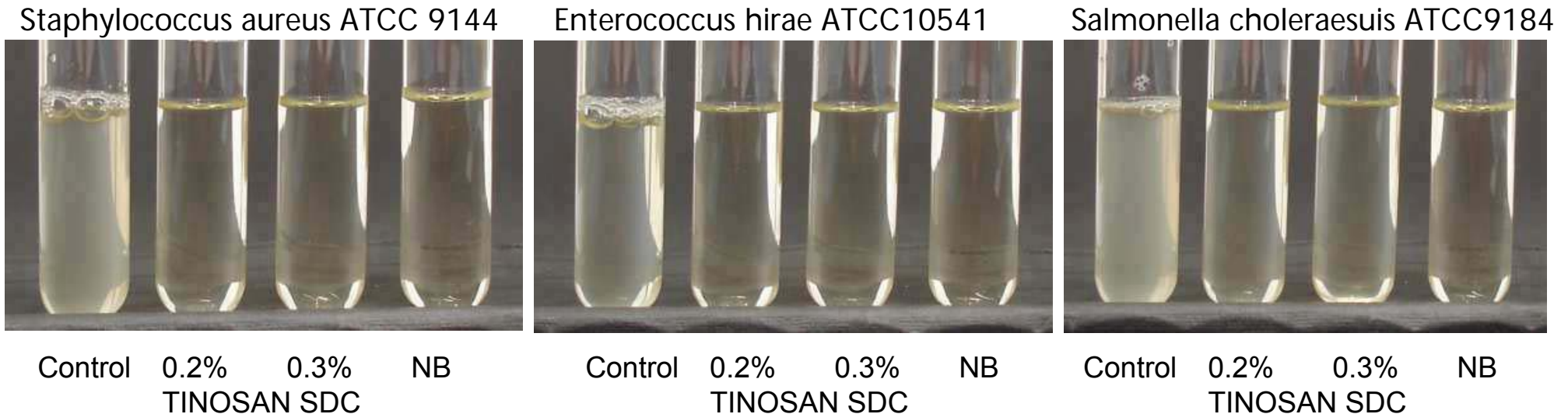
- Deodorant active
- Hand and skin sanitizer
- Hair Care
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TINOSAN®SDC in a Liquid Hand Soap

Formulation: Antibacterial Liquid Soap with TINOSAN®SDC (GEAMPC01/021/04a)

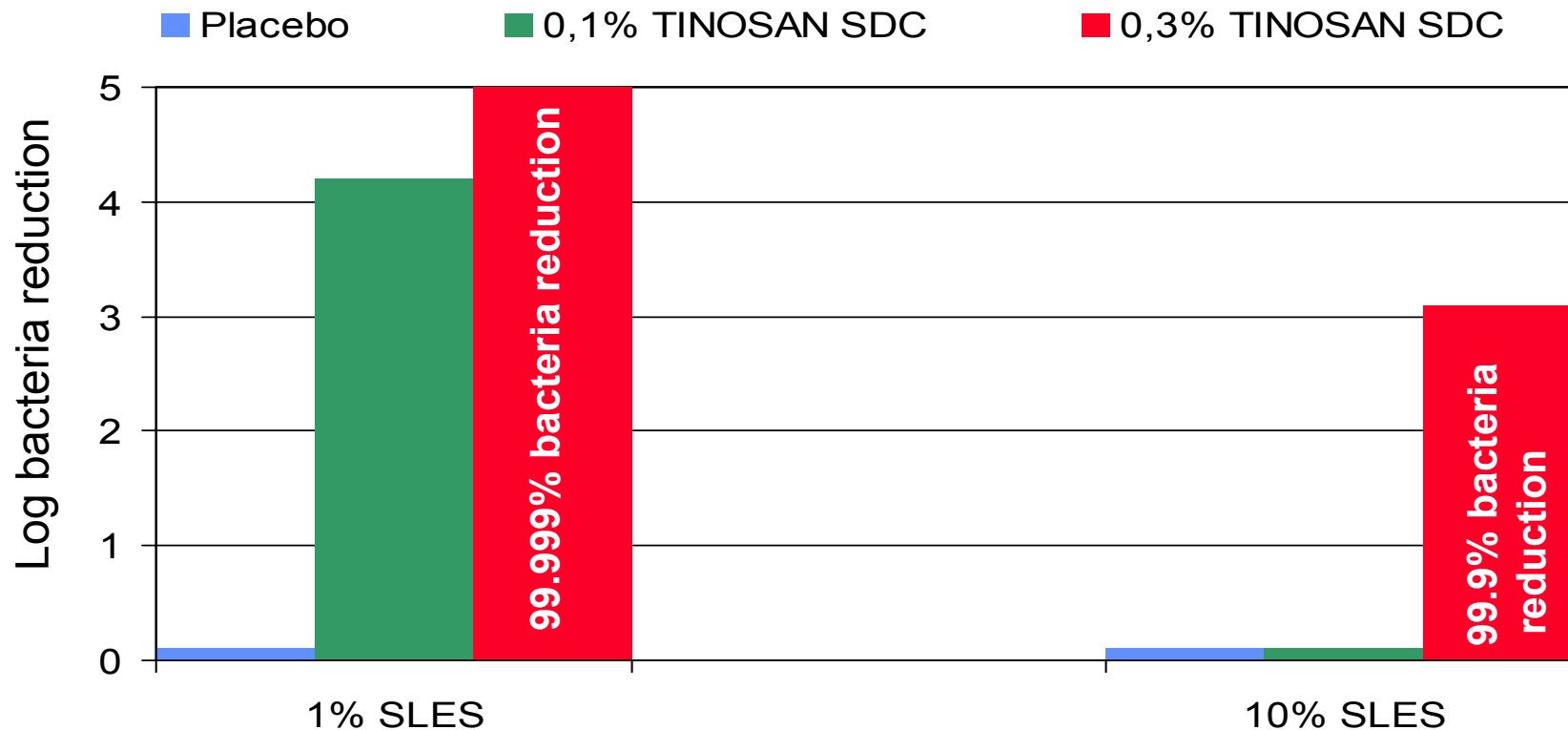
Test Method: The diluted formulation (10%) was contaminated with microorganisms. After incubation, bacterial growth was evaluated visually.



Significant inhibition of bacterial growth of pathogenic bacteria with a liquid soap containing 0.2% - 0.3% TINOSAN®SDC

TINOSAN[®]SDC in a Liquid Hand Soap

Test conditions: Suspension test EN1040, 5 minutes contact time, 90% concentration, Staphylococcus aureus ATCC6583



Depending on the surfactant concentration strong bactericidal effects can be achieved with TINOSAN[®]SDC

TINOSAN®SDC in an Antiseptic Hand Cream

Formulation: Hand cream with 0.3% TINOSAN®SDC

Control: Hand cream without TINOSAN®SDC

Test Method: Diluted formulations were contaminated with bacterial suspensions.

After 24 hours incubation, subcultures were made on agar plates.

Staphylococcus aureus ATCC 9144



Control

Hand Cream (10%)

Salmonella choleraesuis ATCC9184



Control

Hand Cream (10%)

Growth inhibition of pathogenic bacteria even with a 10% dilution of a hand cream containing 0.3% TINOSAN®SDC

TINOSAN®SDC: A Versatile Active for PC

Personal Care

- Deodorant active
- Hand and skin sanitizer
- **Hair Care**
- Support of Preservative System



TINOSAN®SDC in Hair Care

- Correlation between growth of *Malassezia furfur* and formation of dandruff is known
- Anti-dandruff ingredients show antimicrobial efficacy against *Malassezia furfur*
- Anti dandruff ingredients like Zinc Pyrithione can't be formulated in light hair and scalp tonics or are difficult to stabilize in mild hair shampoos

TINOSAN®SDC show significant inhibition of *Malassezia furfur*, provide mild anti-dandruff efficacy and is compatible with clear tonics and mild shampoo formulation

TINOSAN®SDC in a Hair & Scalp Lotion

Formulation: Lotion with 0.3% TINOSAN®SDC
Control: Water + placebo

Test Method: Diluted formulations were contaminated with bacterial suspensions.
After 72 hours incubation, subcultures were made on agar plates.

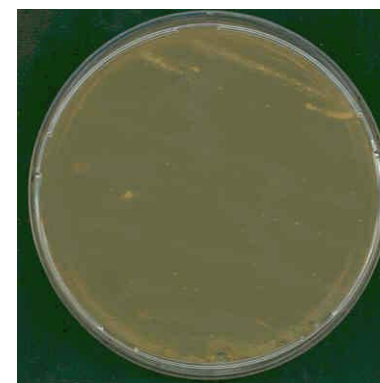
Malassezia furfur DSM 6171



Water Control



Lotion (placebo)



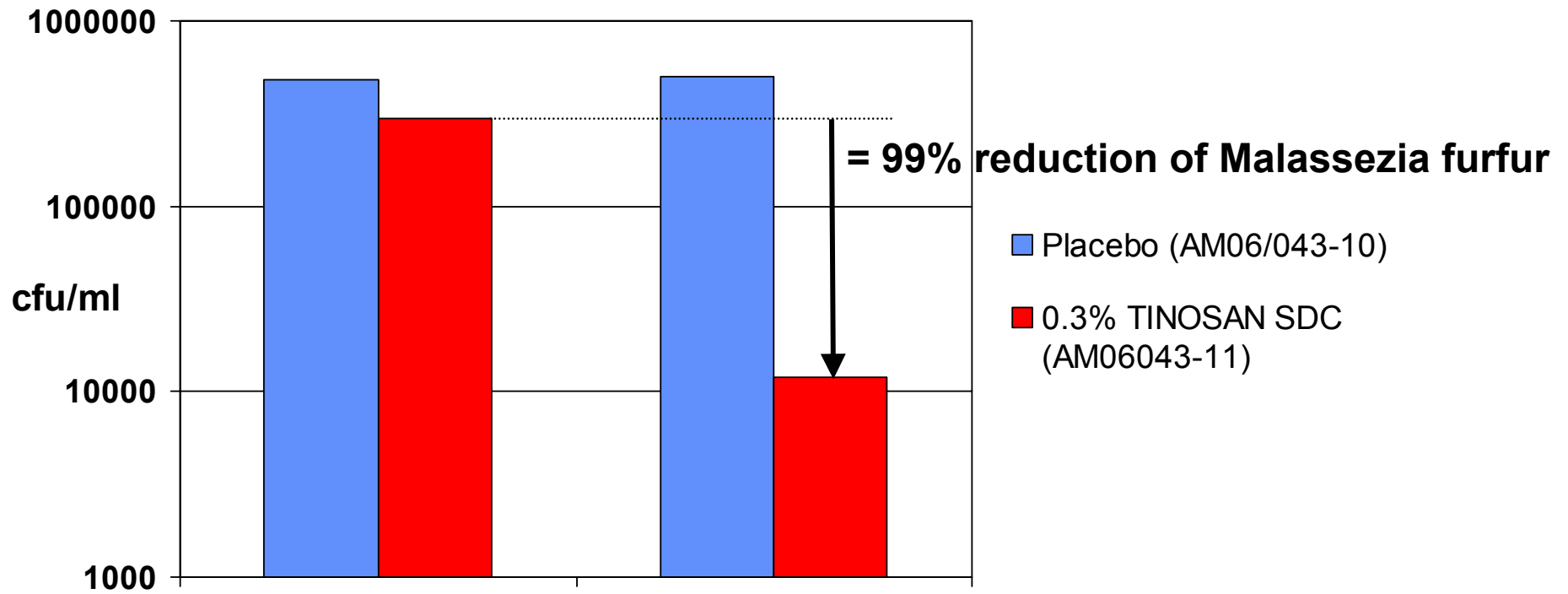
Lotion + 0.3% TINOSAN SDC

Growth inhibition of *Malassezia furfur* with a 10% diluted hair lotion containing 0.3% TINOSAN®SDC



TINOSAN[®]SDC in a Hair & Scalp Lotion

Test conditions: Suspension test EN1040, 30 minutes contact time, 50% concentration, Malassezia furfur DSM 6171



Some microbicidal efficacy were found against Malassezia furfur with a 50% diluted formulation

TINOSAN®SDC: A Versatile Active for PC

Personal Care

- Deodorant active
 - Hand and skin sanitizer
 - Hair care
 - **Support of Preservative System ***
- * Not listed as a preservative on Annex 6
of the European Cosmetic Directive



Preservation: Competitive Products

We observe strong concerns with broadly used preservatives in PC markets

Parabens

- Under pressure due to endocrinic activity and sensitization issues
- Customers ask for alternatives and refuse raw materials preserved with parabens
- „Paraben-free“ PC products are becoming popular

Diazolidinyl urea and Imidazolidinyl urea

- Formaldehyde releasers → strong concerns on cancerogenicity of formaldehyde
- High concentrations needed
- Often combined with other preservatives to achieve sufficient efficacy

Bronopol/Bronidox

- halogenated, can form nitrosamines in combination with nitrite and amines

Isothiazolinones (MIT/CIT)

- Sensitizer
- Chlorinated chemistry
- Instabilities at temperatures of 40°C and higher

TINOSAN®SDC provides preservative activity

- Tinosan®SDC shows excellent preservative activity at low concentrations (0.1% - 0.3%)
 - provides preservative activity besides deodorant and antimicrobial effects
 - can be combined with a wide range of preservatives to improve efficacy
- formaldehyde-free
- non-halogenated
- no phenol
- no quaternary ammonium compound
- favourable human tox and environmental profile
- natural ingredients



Preservative Challenge Test

Test microorganisms

- Gram-negative bacteria
 - Pseudomonas aeruginosa
 - Escherichia coli
- Gram-positive bacteria
 - Staphylococcus aureus
- Yeast
 - Candida albicans
- Mould
 - Aspergillus niger

Test microorganisms should cover a broad range of potential contaminants in the final products

Preservative Challenge Test

15 - 20 gram test product inoculated with microorganisms

S. aureus
 $10^5 - 10^6$



E. coli
 $10^5 - 10^6$



Ps. aeruginosa
 $10^5 - 10^6$



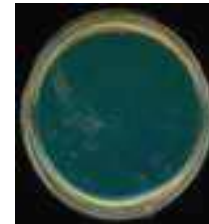
C. albicans
 $10^5 - 10^6$



A. niger
 $10^5 - 10^6$



Determination of viable germs after set time intervals at 20°C-25°C



Agar plates + neutralizer

Test Requirements

Preservative Challenge Test / Pharm. Eur. 5. Edition (5.1.3) Cat.2 (Topica , Cosmetics)

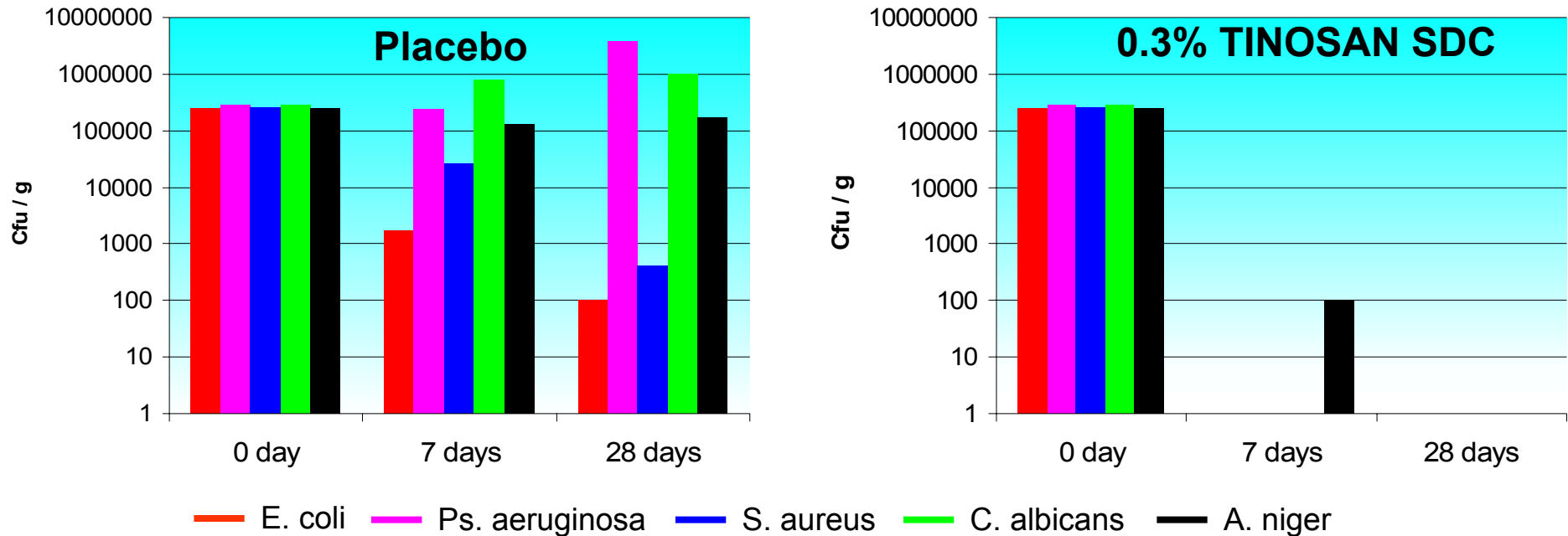
Reduction of MO →	2 days	7 days	14 days	28 days
Bacteria	99% (2 log)	99.9% (3 log)		No increase
Fungi			99% (2 log)	No increase

Preservative Challenge Test (USP 28 <51>)

Reduction of MO →	14 days	28 days
Bacteria	99% (i.e. 2 log)	No further increase
Fungi	No increase	No increase

Preservative Capacity of TINOSAN[®]SDC

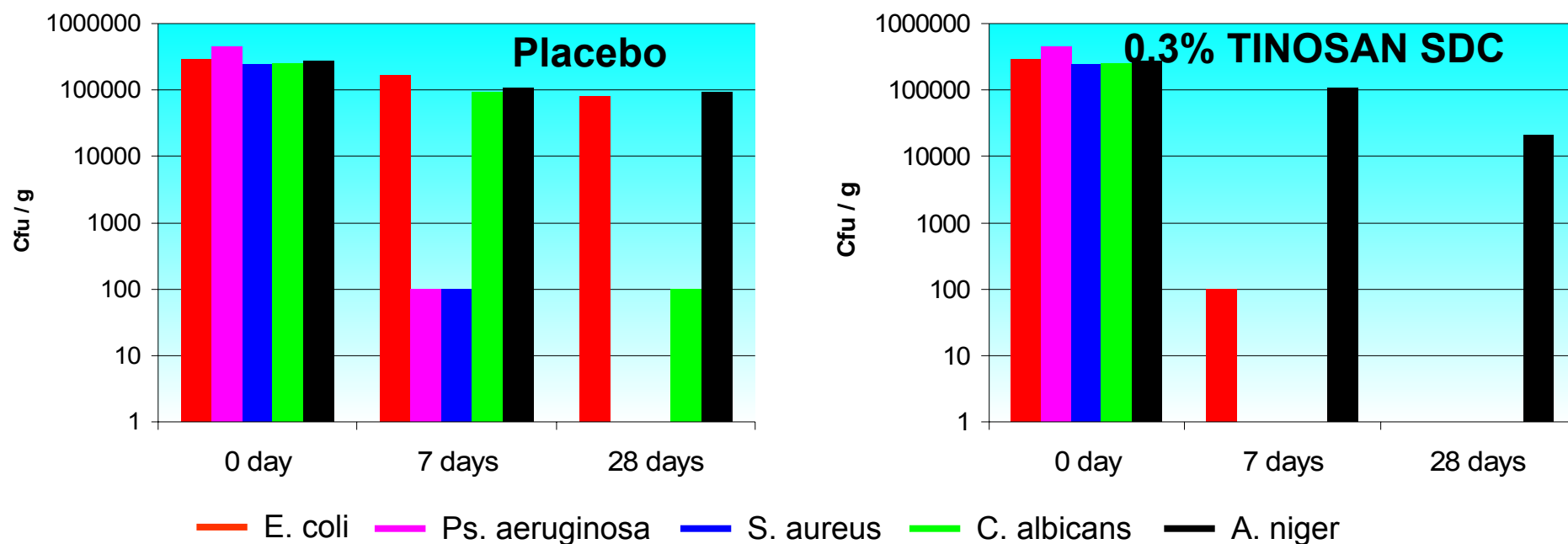
O/W Deodorant based on GMS and Ceteth-20



Preservation requirements of Pharm. Eur. and USP fulfilled with TINOSAN[®]SDC in formulations with nonionic emulsifiers

Preservative Capacity of TINOSAN®SDC

Shampoo Formulation based on SLES, CAPB, Glucoside

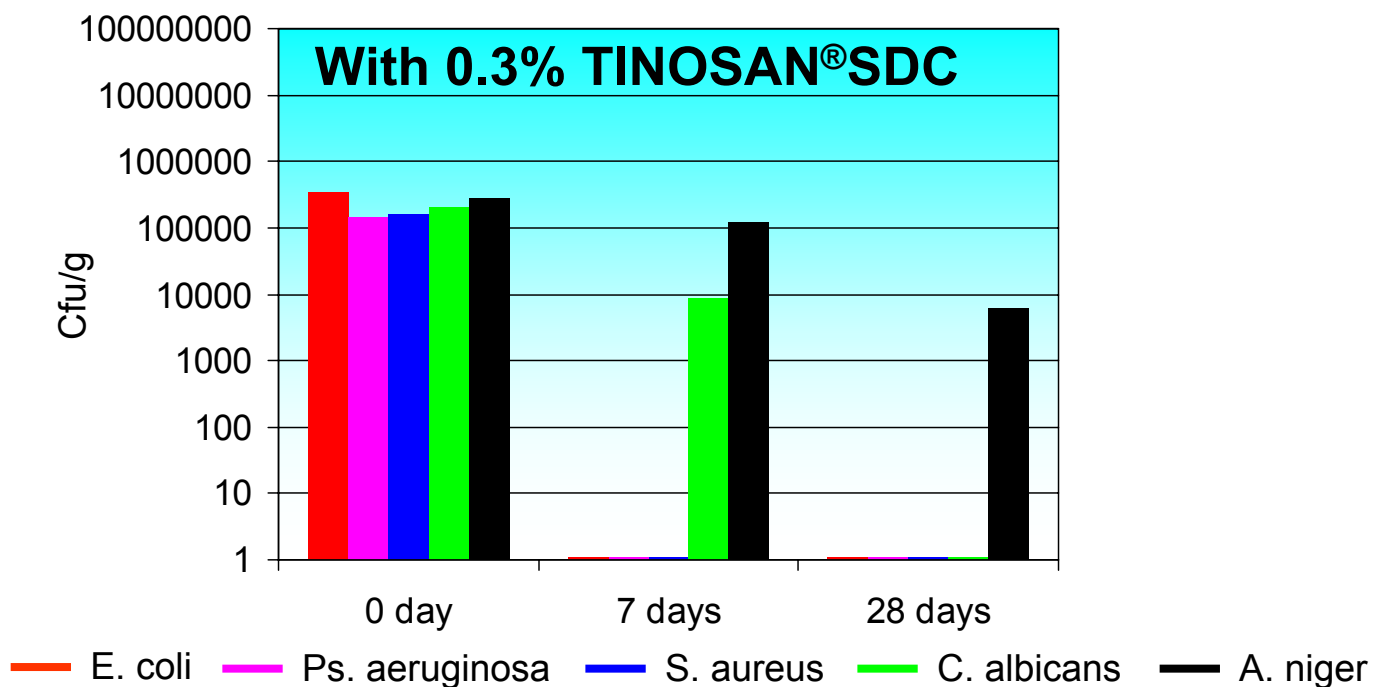


TINOSAN®SDC-preserved shampoo formulation fulfills USP requirements

Preservative Capacity of TINOSAN®SDC in wet wipes

Composition: 2% Ethanol, 5% Glycerin, 1% PEG-40 Hydrogenated Castor Oil, 0.05% Xanthan Gum

Application: Tissue material have been treated with 0.5g liquid /cm² tissue material



Wet wipes treated with TINOSAN®SDC containing lotion are preserved according to USP requirements

Compatibility of TINOSAN®SDC with other antimicrobials

Compatibility of TINOSAN®SDC with:

- Benzoic Acid
- Parabens
- Phenoxyethanol
- Potassium Sorbate
- Sodium Benzoate
- Isothiazolinone (eg Kathon CG)
- DMDM Hydantoin
- Triclosan (IRGASAN DP300)
- Imidazolidinyl Urea (Germall 115)

Incompatibility (precipitation or discoloration) were observed with iodinated and brominated compounds

TINOSAN®SDC can be combined with most antimicrobials/preservatives

Preservative Capacity of TINOSAN®SDC

Natural acids such as benzoic acid, sorbic acid and its salts as well as alcohols such as benzyl alcohol are preferred preservatives due to their good safety profile.

Efficacy at lower concentrations is sometimes insufficient to meet requirements on preservative efficacy. TINOSAN®SDC show synergistic activity when combined with these preservatives

	Formulation with "natural" preservative w/o TINOSAN® SDC	Formulation with 0.1% TINOSAN®SDC alone	Formulation containing 0.1% TINOSAN® SDC with preservative	
0.1% Potassium Sorbate				Eur. Ph requirements & USP28 requirements fulfilled
0.1% Sodium Benzoate				USP28 requirements fulfilled
0.15% Benzylalcohol				Preservation capacity test failed
0.3% Phenoxyethanol				

i.e. Preservation of a body wash formulation (GEAM05049-2-9)

Impact of salt on the performance of TINOSAN®SDC

The impact of salt (NaCl) and chelating agents on the preservative capacity of TINOSAN®SDC have been evaluated.

Test organism: *Pseudomonas aeruginosa* ATCC 15442

The bacterial count was evaluated after 48h, 7 days and 28 days after contamination.

No negative impact by the addition of salt (up to 3% tested) and chelating agents (up to 0.2% tested) on preservative capacity have been observed

Note: Although the preservative capacity of TINOSAN SDC is not negatively impacted by the incorporation of chelating agents and salt, the bactericidal (rapid kill) efficacy is significantly reduced by addition of salt and/or chelating agents. Therefore, the use of salt and chelating agents should be avoided in disinfectants and bactericidal formulations.

Stabilization of TINOSAN[®]SDC

- In most cases TINOSAN[®]SDC does not cause discoloration in formulations when exposed to daylight or elevated temperature.
- In case of formulation incompatibilities, discoloration can be avoided by incorporation of TINOGARD[®] and CIBAFAST[®] product protectants.

O/W Hand cream (AM06069-1)
0.3% TINOSAN SDC
Before storage

O/W Hand cream (AM06069-1)
0.3% TINOSAN[®]SDC
After 3 months storage
at 40°C

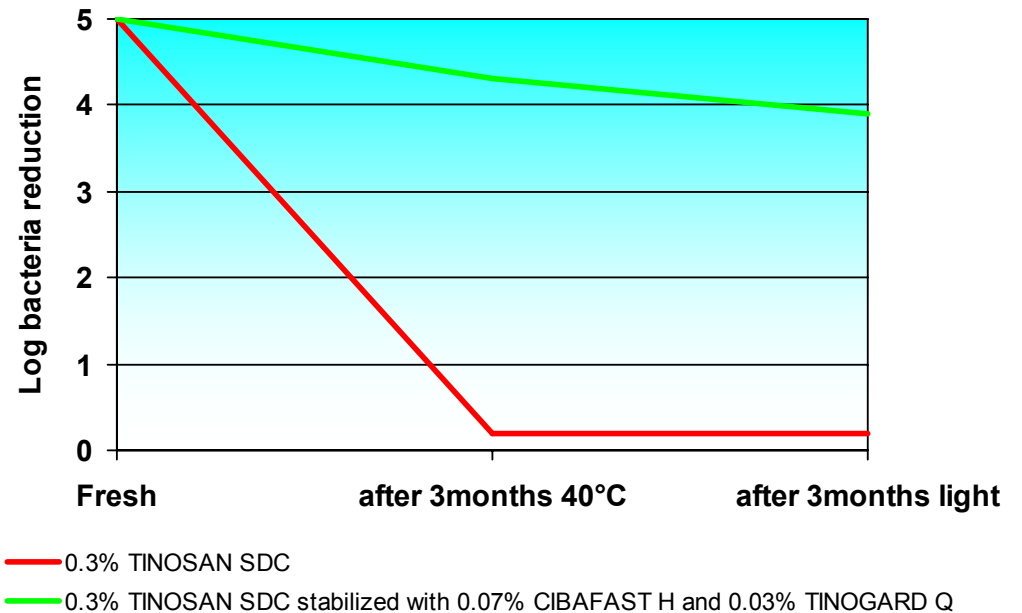
O/W Hand cream (AM06069-1)
0.3% TINOSAN[®]SDC
0.05% CIBAFAST[®]H Liquid
0.05% TINOGARD[®]Q
After 3 months storage at 40°C



Stabilization of TINOSAN[®]SDC

- Bactericidal efficacy of TINOSAN SDC containing formulations might be reduced over time when stored at high temperatures or exposed to daylight. Incorporation of CIBAFAS[®]T H Liquid and TINOGARD[®]Q help to stabilize TINOSAN[®]SDC and keep the bactericidal efficacy on the initial level.

Bactericidal efficacy of 0.3% TINOSAN SDC in water against *S. aureus* ATCC 6538

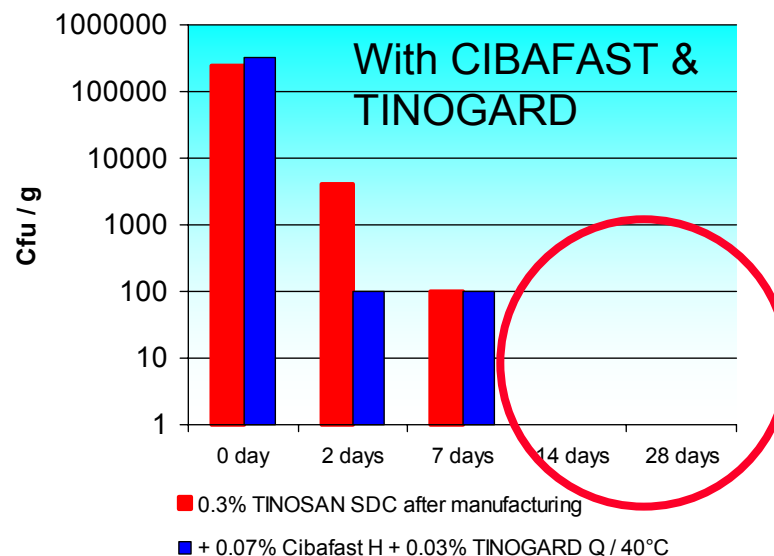
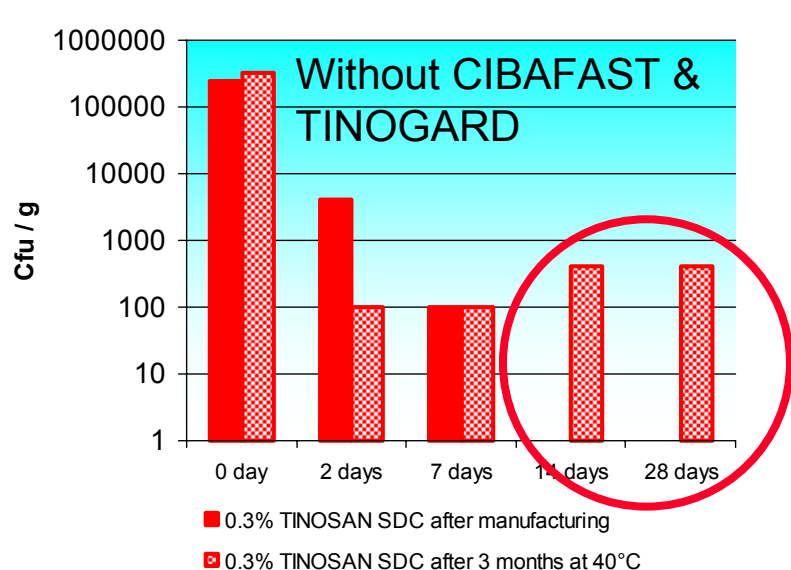


TINOGARD[®]Q and CIBAFAS[®]T H help to stabilize TINOSAN[®]SDC in cosmetic formulations

Stabilization of TINOSAN®SDC

Preservation capacity of TINOSAN®SDC containing formulations might in some cases be slightly impacted over time when stored at high temperatures or exposed to daylight. Incorporation of CIBAFASST®H Liquid and TINOGARD®Q help to stabilize TINOSAN®SDC and keep the preservation capacity on the initial level.

Preservative capacity test vs. *Aspergillus niger* ATCC 16404 before and after 3 months storage at 40°C



Equal performance against *A.niger* after storage at 40°C when stabilized with CIBASFAST and TINOGARD

TINOSAN®SDC, an ideal antimicrobial for PC products

- transparent solution suitable for clear formulations
- no odor problems
- high water solubility
- good compatibility in formulations with pH < 7
- good compatibility with other biocides
- active against a broad spectrum of microorganisms (incl. Pseudomonas)
- versatile use as deodorant and antimicrobial active with a preservative activity
- formaldehyde-free, non-halogenated, no phenol, no quaternary ammonium compound
- favourable toxicological profile



TINOSAN[®]SDC, an ideal antimicrobial for PC products

- Builds on good reputation of silver as a well known biocide and exhibits unique properties in the silver product market:
 - Transparent silver salt product enables incorporation in clear formulations and overcomes formulation/compatibility problems with existing silver technologies (e.g. precipitations in PC formulations with particulate silver technologies)

Tinosan[®]SDC provides silver in an optimized form for Personal Care

TINOSAN®SDC in Personal Care Applications

TINOSAN® SDC provides:

- Deodorant efficacy
- Fast killing activity of hand and skin care
- Support of skin health by
 - skin soothing
 - skin repair
 - prevention of infections of minor skin lesions/abrasions
- Supports the preservative system



TINOSAN®SDC, a versatile antimicrobial, combining strong efficacy of silver with good compatibility in cosmetic formulations

Backup Slides

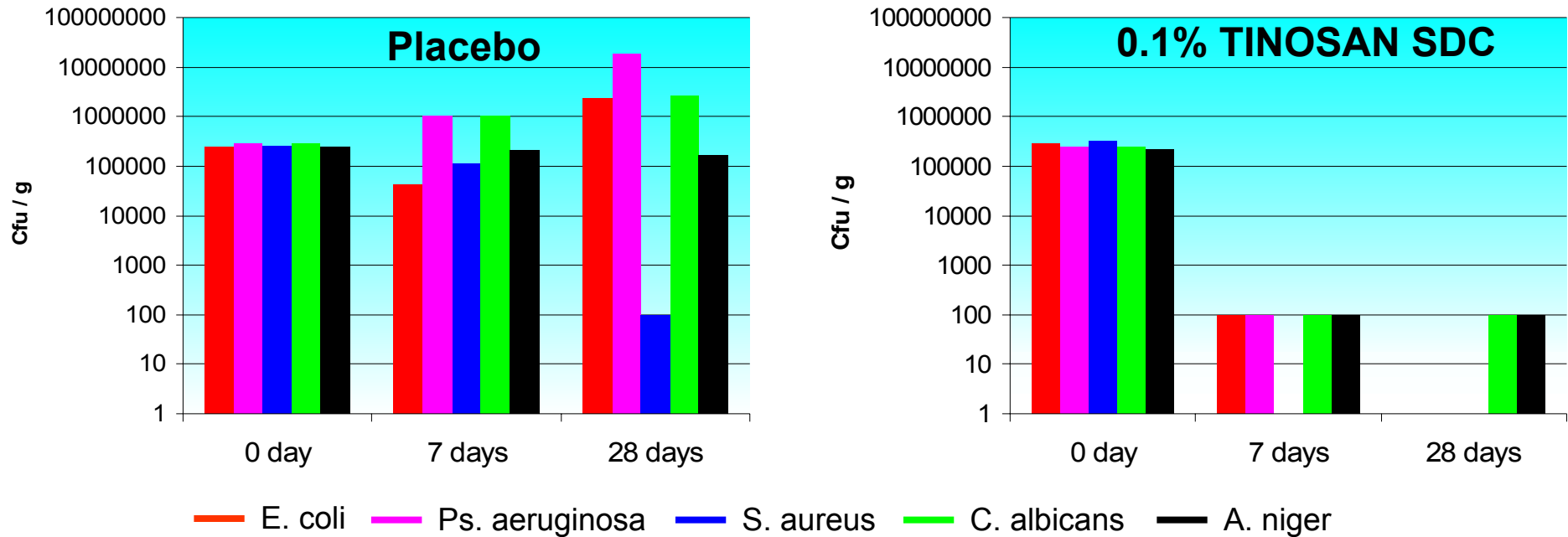
Efficacy of TINOSAN[®]SDC / Minimal Bactericidal Concentrations (MBC)

Microorganism	MBC of TINOSAN SDC (%)
Staphylococcus aureus ATCC 6538	0.31
Escherichia coli ATCC 10536	0.16
Pseudomonas aeruginosa ATCC 15442	0.08
Klebsiella pneumoniae ATCC 4352	0.16
Corynebacterium minutissimum ATCC 23348	0.16
Candida albicans ATCC 10231	> 1.25
Aspergillus niger ATCC 16404	> 2.5
Trichophyton mentagrophytes ATCC 9533	0.08
Epidermophyton floccosum DSM 10709	0.63

TINOSAN[®]SDC is bactericide against a broad spectrum of microorganisms

Preservative Capacity of TINOSAN[®]SDC

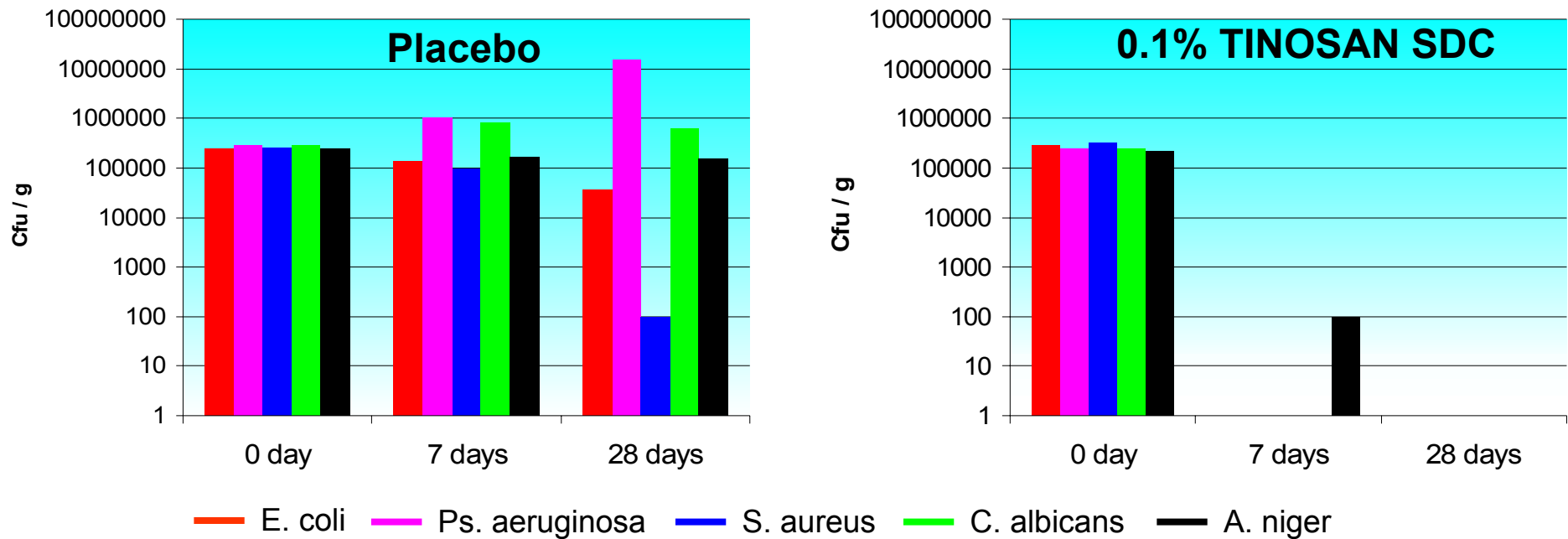
O/W Deodorant based on Glyceryl Stearate Citrate



Pharm. Eur. and USP test requirements fulfilled with TINOSAN[®]SDC in formulations with anionic emulsifiers

Preservative Capacity of TINOSAN®SDC

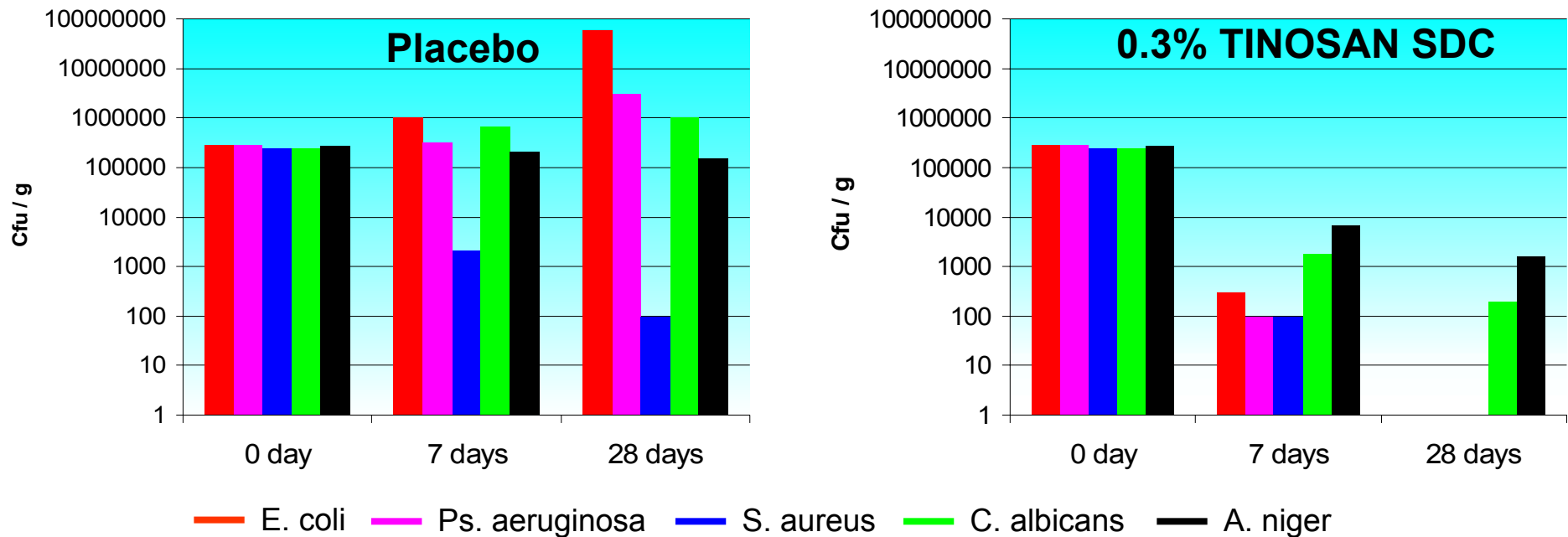
Face Lotion based on Cetearyl Glucoside and Potassium Cetyl Phosphate



Pharm. Eur. and USP test requirements fulfilled with TINOSAN®SDC in formulations with anionic and nonionic emulsifiers

Preservative Capacity of TINOSAN®SDC

Roll-on based on Steareth-10, GMS and PEG-30 Stearate



TINOSAN®SDC fulfills Pharm. Eur. and USP test requirements in formulations with nonionic emulsifiers