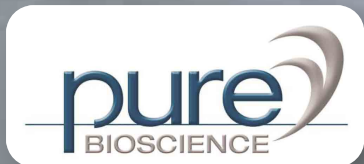




SILVÉRION 2400

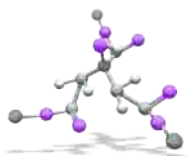


**A Versatile Antimicrobial for
Personal Care Applications**



www.purebio.com





SILVÉRIION 2400 – Versatile Antimicrobial



Effective deodorant ingredient

- SILVÉRIION 2400 exhibits strong activity against *Corynebacteria* and significantly reduces body malodor



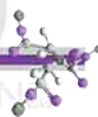
Fast killing antimicrobial active

- SILVÉRIION 2400 shows reduction of gram-negative and gram-positive bacteria on skin.



Broad spectrum preservative for personal care products

- SILVÉRIION 2400 works as stand-alone preservative in many cosmetic formulations
- SILVÉRIION 2400 can be combined with a broad range of preservatives due to its excellent compatibility with cosmetic ingredients



Ionic Silver Technology

SILVÉRION 2400 combines ionic silver and citric acid to provide a highly stable and active antimicrobial

- Silver's as an antimicrobial benefits known for centuries:
 - highly effective
 - safe for use on humans
 - natural origin
- Silver used successfully in water treatment and medical applications, including wound care



- Previous attempts using silver in personal care unsuccessful due to limited compatibility and stability of market products in cosmetic formulations leading to precipitation, discoloration and reduced efficacy

SILVÉRION 2400 resolves compatibility, aesthetic and performance challenges

SILVÉRIION 2400 – Overview

Clear product with high water solubility

- Beneficial for clear formulations such as shampoos and gels
- Does not migrate into the oil phase of emulsions causing reduced efficacy against microorganisms in the water phase
- Good stability in a broad range of personal care products types

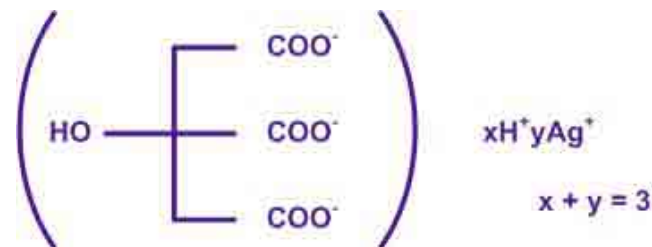
Broad spectrum antimicrobial activity

- Deodorant Active - Effective against malodor-causing *Corynebacteria*
- Fast-acting Active - Quickly reduces pathogenic bacteria
- Excellent preservative - Effective against bacteria and fungi that cause deterioration and/or pose health risks for consumers

SILVÉRIION 2400 – Chemistry

Composition

- **INCI Name:** Citric Acid (and) Silver Citrate
- **Active Ingredient:** Silver ions (2400 ppm) stabilized in citric acid (20%)



- **pH of product:** 1.5
- **Appearance:** clear aqueous solution, colorless, odorless, low viscosity
- **Solubility:** highly soluble in water

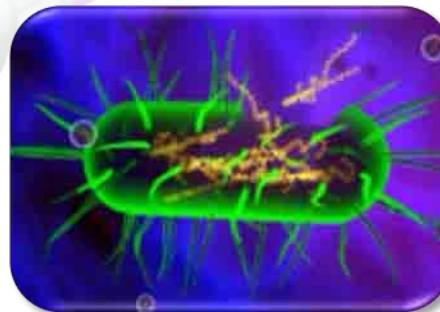
SILVÉRIION 2400 – Efficacy

Minimal Inhibitory Concentrations (MIC)

Microorganism	MIC of SDC % SDC (ppm Ag ⁺)
<i>Corynebacterium xerosis</i> ATCC 373	0.12 (2.88 ppm)
<i>Corynebacterium minutissimum</i> ATCC 23348	0.12 (2.88 ppm)
<i>Propionibacterium acnes</i> ATCC 6919	0.25 (6.00 ppm)
<i>Staphylococcus aureus</i> ATCC 6538	0.16 (3.84 ppm)
<i>Escherichia coli</i> ATCC 10536	0.08 (1.92 ppm)
<i>Pseudomonas aeruginosa</i> ATCC 15442	0.16 (3.84 ppm)
<i>Candida albicans</i> ATCC 10231	0.12 (2.88 ppm)
<i>Malassezia furfur</i> DSM 6171	0.25 (6.00 ppm)
<i>Aspergillus niger</i> ATCC 16404	0.50 (12 ppm)
<i>Trichophyton mentagrophytes</i> ATCC 9533	0.50 (12 ppm)

Minimal Biocidal Concentrations (MBC)

Microorganism	MBC of SDC % SDC (ppm Ag ⁺)
<i>Staphylococcus aureus</i> ATCC 6538	0.31 (7.44 ppm)
<i>Escherichia coli</i> ATCC 10536	0.16 (3.84 ppm)
<i>Pseudomonas aeruginosa</i> ATCC 15442	0.08 (1.92 ppm)
<i>Klebsiella pneumoniae</i> 4352	0.16 (3.84 ppm)
<i>Corynebacterium minutissimum</i> ATCC 23348	0.16 (3.84 ppm)
<i>Candida albicans</i> ATCC 10231	>1.25 (30 ppm)
<i>Aspergillus niger</i> ATCC 16404	>2.5 (60 ppm)
<i>Trichophyton mentagrophytes</i> ATCC 9533	0.08 (1.92 ppm)
<i>Epidermophyton floccosum</i> DSM 10709	0.63 (15.12 ppm)



SILVÉRIION 2400 is effective against all groups of microorganisms

SILVÉRIION 2400 – Safety

Study Design	Species	Test Article	Results
Dermal Sensitization (Buehler Method)	Guinea Pig	SDC Concentrate ¹ (Aqueous)	Not a contact sensitizer
Primary Skin Irritation	Rabbit	SDC Concentrate ¹ (Aqueous)	PDI Score 1.7, Slightly irritating
Acute Dermal Toxicity	Rat	SDC Concentrate ¹ (Aqueous)	LD ₅₀ > 5000mg/kg
Acute Oral Toxicity	Rat	SDC Concentrate ¹ (Aqueous)	LD ₅₀ > 5000mg/kg
Primary Eye Irritation	Rabbit	SDC Concentrate ¹ (Aqueous)	Draize MTS 10.7, Mildly Irritating
Primary Eye Irritation	Rabbit	Diluted SDC Solution ² (Aqueous)	Draize MTS 1.3, Practically nonirritating

1. Aqueous formula containing 2438 ppm ionic silver and 21% citric acid; 2. Formulated dilution with 5% citric acid

Independent Scientific Opinion

SILVÉRIION 2400 was evaluated by the Scientific Committee on Consumer Safety (SCCS) of the European Commission which concluded that the product, when used up to 24 ppm silver, does not pose a risk to the health of consumers when used as a preservative in cosmetics and that it is safe when used as a preservative or active in deodorants and anti-perspirants.

SCCS (Scientific Committee on Consumer Safety), Opinion on citric acid (and) silver citrate, 13 October 2009

Use Recommendations

- **Recommended concentration**
 - 0.1% - 0.3%
- **Incorporation methods**
 - **Direct incorporation**
 - SILVÉRIION 2400 directly added to the final formulation at temperatures of $< 50^{\circ}\text{C}$. pH value of the formulation to be adjusted
 - **Indirect incorporation**
 - SILVÉRIION 2400 pre-diluted with water and pH is adjusted to the target pH (i.e. $\text{pH} < 7$)
 - Addition of diluted SILVÉRIION 2400 to final formulation at temp. of $< 50^{\circ}\text{C}$
 - Keep the pH of the formulation < 7 prior to incorporation of SILVÉRIION 2400 in order to avoid discoloration
 - Indirect method preferred for pH-sensitive formulations



SILVÉRIION 2400 easy to incorporate in many types of Personal Care formulations

Compatibility

Surfactants

- SILVÉRIION 2400 compatible with anionic, nonionic and amphoteric surfactants up to 15 – 20%

Neutralizer

- SILVÉRIION 2400 containing formulations can be neutralized by the use of any base. Recommended NaOH or KOH rather than amines like AMP

Thickener System

- Good compatibility with xantham gum, associative acrylate polymers, carbomers

Emulsifier System

- SILVÉRIION 2400 compatible with most nonionic emulsifiers and anionic emulsifiers
- Cationic emulsifiers may cause incompatibilities depending on charge of the ingredient and concentration
- Chlorides may cause discoloration and should be avoided

Emollients

- No impact seen from formulating with emollients

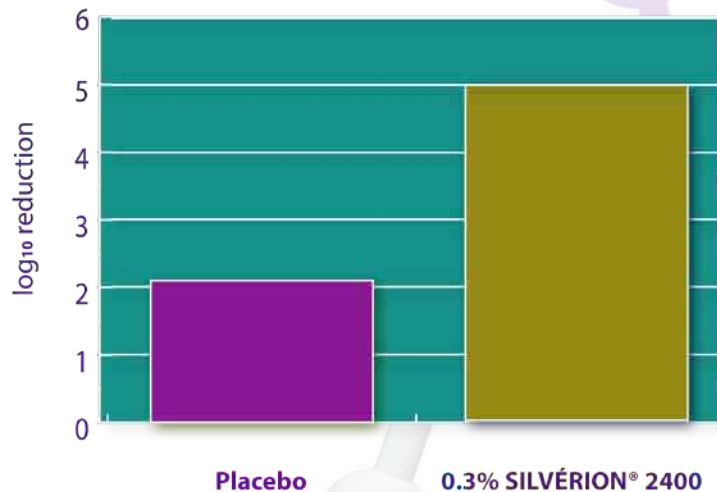
Other Antimicrobial Agents

- | | |
|---------------------|-----------------------|
| • Benzoic Acid | • Isothiazolinone |
| • Parabens | • DMDM Hydantoin |
| • Pheonxyethanol | • Triclosan |
| • Potassium Sorbate | • Imidazolidinyl Urea |
| • Sodium Benzoate | |



Deodorant Ingredient

- **SILVÉRIION 2400 shows strong bactericidal efficacy against body malodor generating *Corynebacteria* with 0.3% SILVÉRIION 2400**



Test Bacteria:

Corynebacterium minutissimum
(ATCC 23348)

Test conditions:

EN1040, 5 minutes contact time,
90% concentration

- **0.3% SILVÉRIION 2400 Deodorant Spray Consumer Preference Study**

- Double blind, placebo-controlled, 18 volunteers (females and males)
- 5-day in-use study; BID: 1 armpit treated with placebo; other armpit treated with active
- Preference rating recorded 24-hours after last use
- 50% preferred SILVÉRIION 2400 formulation; none preferred placebo.



Antimicrobial Active

Liquid Hand Soap

Significant inhibition of pathogenic bacteria with liquid hand soap containing 0.2% - 0.3% SILVÉRIION 2400

- *Staphylococcus aureus* (ATCC 9144)
- *Enterococcus hirae* (ATCC 10541)
- *Salmonella choleraesuis* (ATCC 9184)

Antiseptic Hand Cream

Growth inhibition of pathogenic bacteria even with 10% dilution of hand cream containing 0.3% SILVÉRIION 2400

Staphylococcus aureus (ATCC 9144))



Control

Hand Cream (10%)

Salmonella choleraesuis (ATCC 9184))



Control

Hand Cream (10%)

Antimicrobial Active

Hair Care

SILVÉRIION 2400 shows significant inhibition of *Malassezia furfur*, providing anti-dandruff efficacy

- Compatible with clear tonics and mild shampoo formulations

Hair and Scalp lotion

Growth inhibition with 10% diluted lotion containing 0.3% SILVÉRIION 2400

Malassezia furfur DSM 6171



Water Control



Lotion (placebo)



Lotion + 0.3% SILVÉRIION 2400



Broad Spectrum Preservative

Strong concerns over widespread use of traditional preservatives in personal care product create need for natural alternatives

- **Parabens**

- Under pressure due to endocrine activity and sensitization issues
- Customers looking for alternatives or refuse raw materials containing parabens
- “Paraben Free” products are gaining popularity in market

- **Formaldehyde donors (Diazolidinyl urea and Imidazolidinyl urea)**

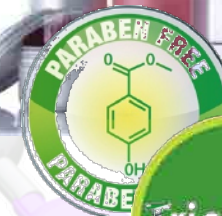
- Strong concerns of carcinogenicity of formaldehyde donors
- High concentrations required
- Often combined with other preservatives to achieve sufficient efficacy

- **Bronopol/Bronidox**

- Halogen compounds can form carcinogenic nitrosamines in combination with nitrite and amines.

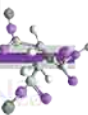
- **Isothiazolinones (MIT/CIT)**

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



SILVERION®

SILVERION



Broad Spectrum Preservative

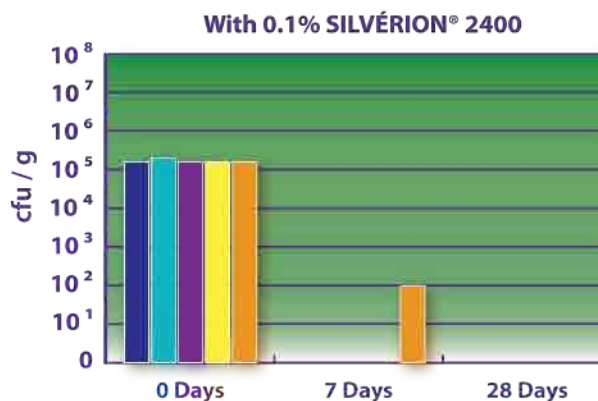
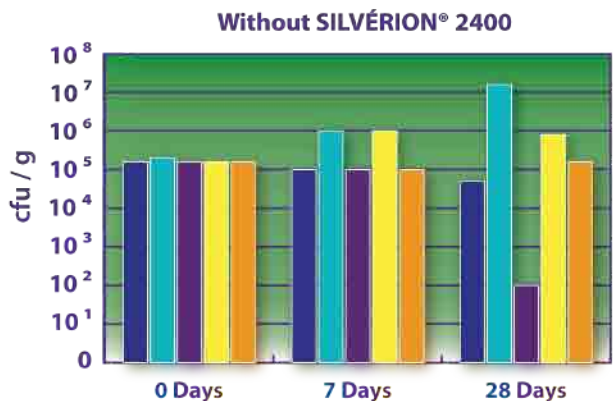
- **SILVÉRIION 2400 shows excellent preservative activity at low concentrations (0.1 – 0.3%)**
 - Provides preservative activity in addition to deodorant and antimicrobial effects
 - Demonstrated preservative activity in preservative challenge testing against Gram negative and Gram positive bacteria, yeast and mold (USP <51> and Ph Eur 5.1.3)
 - Use alone or in combination with other preservatives
 - Can be combined with wide range of preservatives to improve efficacy and lower concentrations of less desirable preservatives
- **Formaldehyde and paraben-free**
- **Non-halogenated**
- **No phenols**
- **No quaternary ammonium compounds**
- **Favorable toxicity and environmental profile**
- **Natural ingredients**



Broad Spectrum Preservative

Preservative Challenge Test

Face Lotion



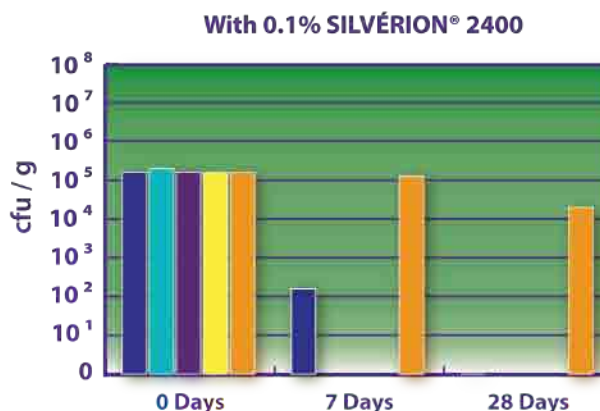
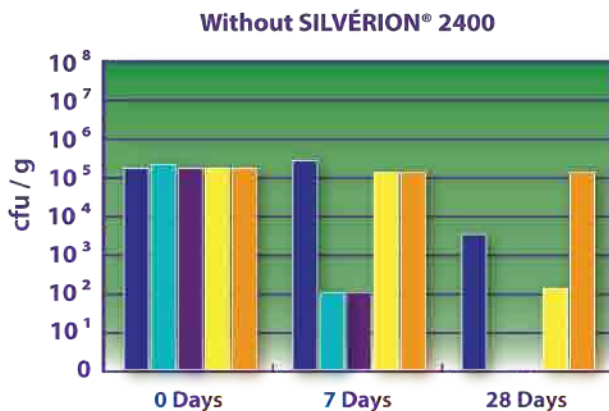
- Escherichia coli ATCC 8739
- Pseudomonas aeruginosa ATCC 9027
- Staphylococcus aureus ATCC 6538
- Candida albicans ATCC 10231
- Aspergillus niger ATCC 16404

Samples were inoculated at time zero with the test bacteria to obtain 10⁵ - 10⁶ CFU per gram products.

The contaminated products were stored at 22°C for the duration of the test.

The survival rate of microorganisms was determined at set time intervals by taking aliquots and counting the number of viable cells by means of the plate count method.

Shampoo



Preservation requirements of Pharm. Eur. and USP fulfilled with SILVÉRIION SD



Regulatory Status

	Preservative In Cosmetics	Deodorants	Cosmetic products with hygienic/antimicrobial claims ^c
EU	(0.2% ⁰)	0.2%	Only secondary
Switzerland	Withdrawn	Withdrawn	Withdrawn
Indonesia ^a	see EU ³	Allowed ³	Allowed ³
Hong Kong	Allowed ¹	Allowed ¹	Not allowed (end products to be registered)
Thailand ^a	see EU ³	Allowed ³	Only secondary ³
Taiwan	Allowed *	Allowed *	Not allowed
S. Korea	Not allowed	Not allowed	Not allowed
Japan	Not allowed	Not allowed	Use restrictions apply depending upon claim
China	Not allowed	Allowed ¹	Allowed only in soaps
Australia	Allowed ²	Allowed ²	Not allowed
Malaysia	see EU ³	Allowed ¹	Only secondary ³
Phillippines	see EU ³	Allowed ¹	Only secondary ³
Vietnam	see EU ³	Not allowed	Only secondary ³
USA	Allowed ^{1b}	Allowed ^{1b}	Not allowed
Canada	Allowed **	Allowed **	Allowed **
Mercosur	Not allowed	Allowed	Allowed
Brazil	see EU	Allowed ¹	Allowed ¹
Chile	see EU	see EU	Allowed ^b
Mexico	0.30%	0.30%	0.30%
Andean Community	Registration for the final cosmetic product. Proof of safety or new ingredient (inclusion of data in the submission and (materias primas) ingredients to be registered too.		

0 - EU - Approved for use in all cosmetics according to European Cosmetics Regulation Annex III, IV and V (EU Regulation 1223/2009) The 0.2% concentration limit for SDC for Europe is based on the lyophilisate of SDC and is equivalent to 24 PPM silver.

1 - No volume restrictions

2 - Low volume permit required by importer

3 - Registration/Certification of finished products and active ingredients required prior to marketing

* - TW - allowed in cosmetic products but no preservation claim. Allowed in deodorants for claims such as anti-odor; freshness. Not allowed in antiperspirants. Not allowed in cosmetics with antimicrobial claim

** - Canada - allowed up to 4 t/yr (Import restriction based on citric acid (and) silver citrate). Label to bear following warnings: "This product contains silver and/or silver salts. Avoid contact with broken or abraded skin."

Mercosur - Cosmetic products to be registered by health authority

a - ASEAN Cosmetics Directive follows the positive listings of the EU Cosmetics Directive 76/768/EEC Annex VI

b - Safety in product is warranted

c - Antimicrobial claims are regulated by different authorities and each country should be checked individually depending upon the claim sought. Strong claims may be regulated under Biocidal regulations.

Regulatory Status

In the USA, SDC is not allowed for use in cosmetics making hygienic or antiseptic claims.

Approval as and over-the-counter (OTC) antiseptic drug would be required for this allowance, meaning an approved new drug application (NDA)

Additionally, compliance with the new FDA proposed safety data requirements and “clinical significance” criteria would be expected.

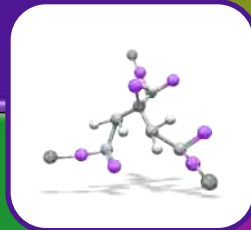
Regulation of Consumer Antiseptics

Consumer antiseptics are OTC drugs and currently are being evaluated under the Healthcare Antiseptic rulemaking. However, in the Final Rule for Healthcare Antiseptic Drug Products, consumer antiseptics may be placed in a separate category from healthcare antiseptics if they are deemed different from healthcare antiseptics. This way, FDA can address any differences in active ingredients, labeling, and testing criteria for consumer and hospital products. A separate category may also be made for food handler antiseptics.

Testing: Products approved by a new drug application must also undergo extensive testing. The required testing focuses on whether the product is safe and effective and includes both in vitro and animal studies. FDA has issued specific testing guidelines titled "Guidelines for the Format and Content of the Clinical and Statistical Sections of an Application." This document is available over the Internet at FDA's web site: <http://www.fda.gov/cder/guidance/index.htm>.

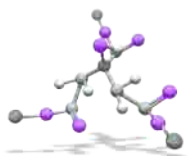
**Versatile
Antimicrobial for
Personal Care**

**Deodorant
Efficacy**



**Supports
Preservative
System**

**Rapid Efficacy
for Hand &
Skin Care**



SILVÉRION 2400- Ideal for PC products

Builds on silver's reputation as well known biocide

High water solubility

Good compatibility

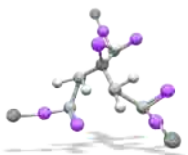
Effective against wide range of microorganisms

Favorable safety profile

NO Parabens, Formaldehyde, Halogens or quats

Versatile use in personal care

Transparent solution suitable for clear formulations



Company Information



1725 Gillespie Way. El Cajon, CA 92020 USA Phone: 619-596-8600

www.purebio.com

<http://silverion.purebio.com>

PURE Bioscience, Inc. develops and markets technology-based bioscience products that provide solutions to numerous global health challenges, including Staph (MRSA) and Carbapenem-resistant Enterobacteriaceae (CRE)/NDM-1+. PURE's proprietary high efficacy/low toxicity bioscience technologies, including its silver dihydrogen citrate-based antimicrobials, represent innovative advances in diverse markets and lead today's global trend toward industry and consumer use of "green" products while providing competitive advantages in efficacy and safety. Patented SDC is an electrolytically generated source of stabilized ionic silver, which formulates well with other compounds. As a platform technology, SDC is distinguished from competitors in the marketplace because of its superior efficacy, reduced toxicity and the inability of bacteria to form a resistance to it. PURE is headquartered in El Cajon, California (San Diego metropolitan area). Additional information on PURE is available at www.purebio.com.