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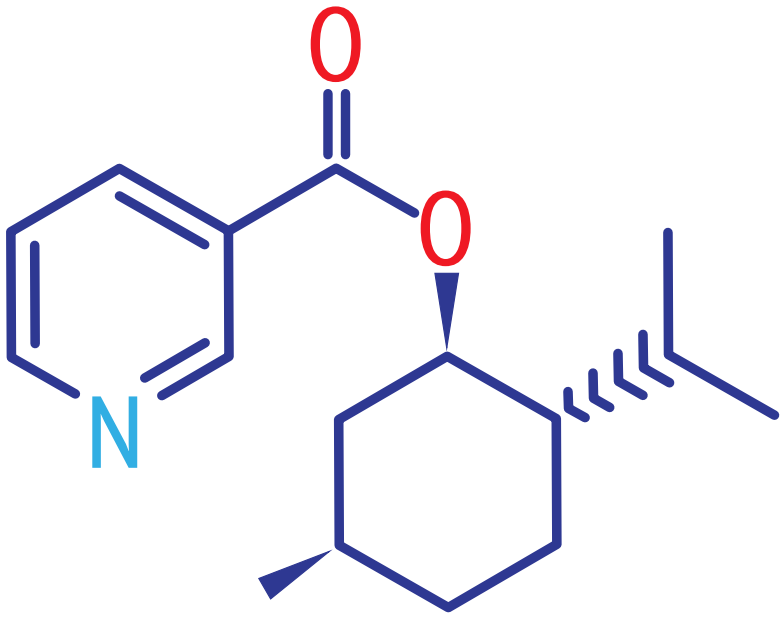
(310) 782-0282

nicomenthyl®

menthyl nicotinate

DETOX POWER



multi chem R&D

nicomenthyl®

menthyl nicotinate

MICROCIRCULATION ENHANCER

AND MUCH MORE...

NICOMENTHYL® (pure Menthyl Nicotinate) is derived from two natural components:

- **MENTHOL**, widely used in personal care refreshing and soothing preparations.
- **NIACIN (Vitamin B3)**, optimizing skin microcirculation and enhancing skin barrier integrity.

NICOMENTHYL represents a new and revolutionary substance for cosmetic use that significantly activates the cutaneous microcirculation **WITHOUT CAUSING ANY BOTHERSOME FLUSH OR IRRITATION**.

Its exceptional **HIGH DEGREE OF PENETRATION** through the skin barrier and **HIGH TRANSDERMAL DELIVERY OF NIACIN**, make NICOMENTHYL

THE MOST POWERFUL AND SAFE SKIN DETOX AGENT so far known

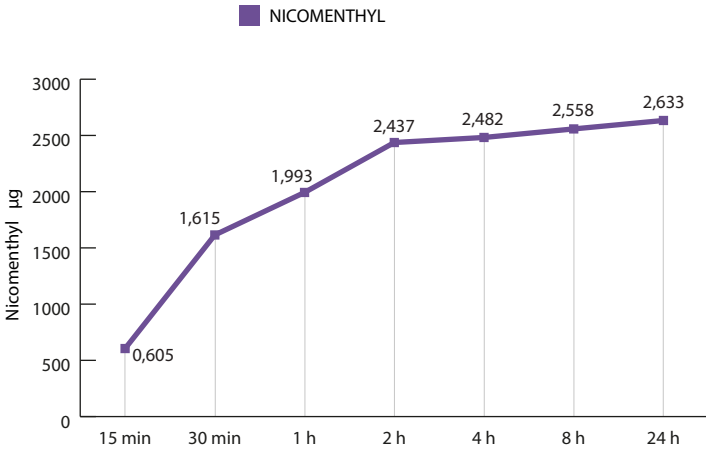
Recent scientific studies, hereafter presented (reports available on request), have revealed that NICOMENTHYL is the ideal active ingredient for all cosmetic applications aiming at **RAPID AND EFFECTIVE SKIN DETOX** and **REPAIR**.

NICOMENTHYL, already known as a powerful microcirculation enhancer and a pleasant beneficial sensate, has demonstrated to be as well

HIGHLY PROTECTIVE, ANTIOXIDANT, ANTIPOLLUTANT, DETOXIFYING, REPAIRING

NICOMENTHYL SKIN ABSORPTION IN VITRO STUDY

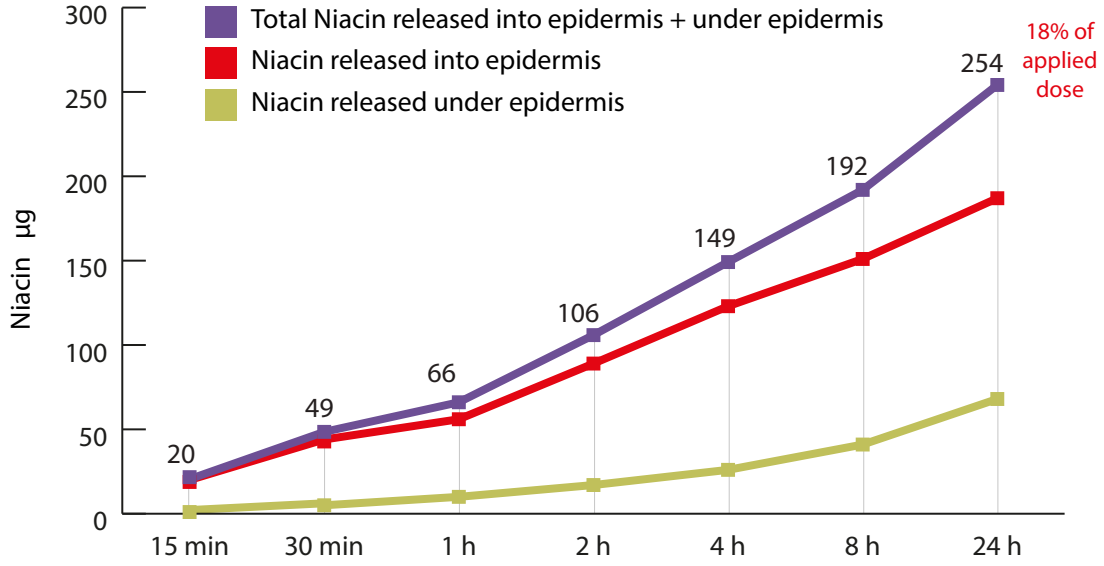
A quantity of 3000 µg of Nicomenthyl was applied to a sample of RHE (in vitro Reconstructed Human Epidermis). A very high rate of penetration through the stratum corneum was observed, reaching an amount of 53.8% of the applied dose in only 30 minutes. The whole process of absorption and hydrolysis into its two components, Menthol and Niacin, gets practically completed in a period of 24 hours after application.



The Niacin so released gets immediately distributed both in the epidermis and under the epidermis.

HPLC analysis revealed **a total amount of 254 µg of released Niacin having penetrated the skin barrier** (from the initial 1413 µg contained in the 3000 µg applied dose of Nicomenthyl), i.e. **a Niacin absorption rate of approx. 18% of the applied dose in 24 hours**. These results are very significant, especially if compared to the absorption rate of the commonly used *Nicotinamide* (another form of Vit. B3), which is only 11% of the applied dose in 120 hours (i.e. 2.2% in 24 hours); or to the absorption rate of pure *Niacin itself*, which is less than 1% of the applied dose in 120 hours (i.e. less than 0.2% in 24 hours).*

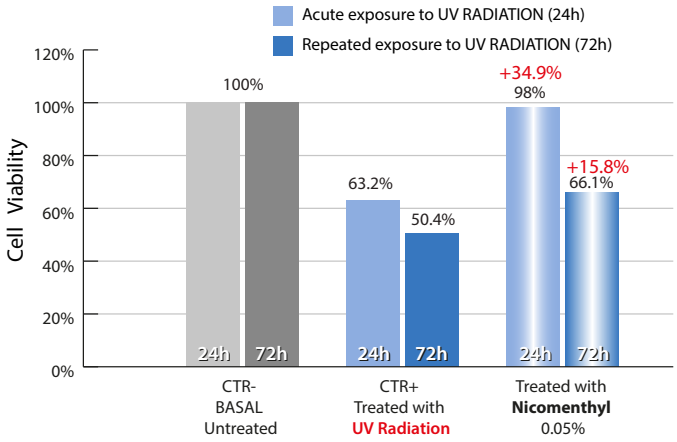
YOUR SKIN NEEDS NIACIN – NICOMENTHYL PROVIDES IT !



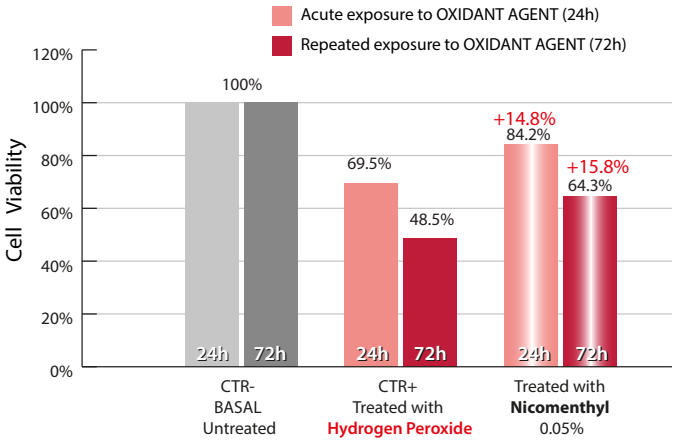
*Cfr.: ABSORPTION OF SOME ORGANIC COMPOUNDS THROUGH THE SKIN IN MAN - Robert J. Feldmann, Howard J. Maibach. *The Journal of Investigative Dermatology* – © 1970 The Williams & Wilkins Co.

Skin Penetration Study Protocol: this test method has been designed to provide information on absorption of a test substance applied to the surface of a skin sample separating the two chambers (a donor chamber and a receptor chamber) of a diffusion cell. In vivo viable human skin has been used. The skin has been shown to have the capability to metabolize some chemicals during percutaneous absorption. In this case, metabolites of the test chemical in the epidermis and under epidermis may be analyzed by appropriate methods. A quantity of 3000 µg of Nicomenthyl (in Caprylic Capric Triglyceride) is applied to a 0.5 cm^2 surface of RHE (i.e. equivalent to an exposure of 6000 µg/cm^2 of the test substance). Temperature must be kept constant throughout the whole test. The absorption of Nicomenthyl during a given time period (24h) is measured by HPLC analysis of the receptor fluid. Furthermore, the distribution of Nicomenthyl and its main metabolite (Niacin) in the test system and their absorption profiles are presented in appropriate graphic formats at intervals of 15 min, 30 min, 1h, 2h, 4h, 8h, 24 h after application.

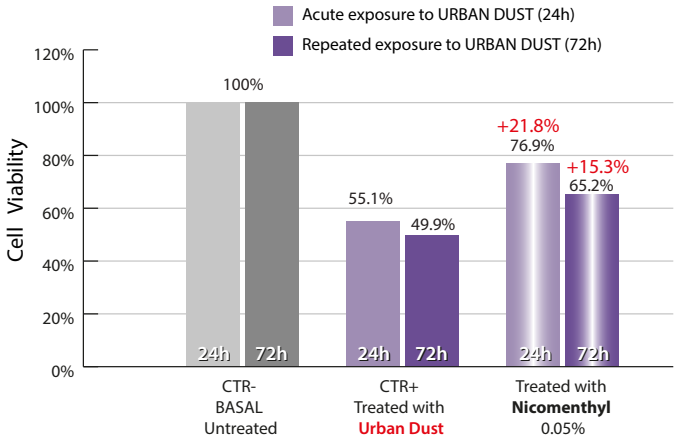
NICOMENTHYL – Keratinocytes Viability Study (MTT Assay)
Acute (24h) & Repeated Exposure (72h) to 4 damaging agents*



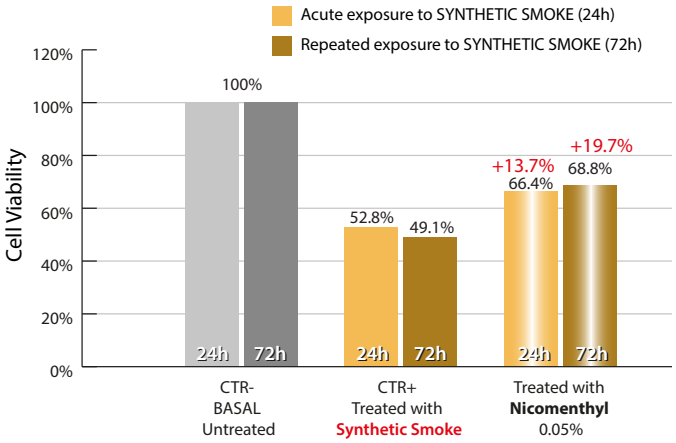
Nicomenthyl treated keratinocyte culture (on the right) had a nearly complete recovery (98%) of cell viability for acute exposure and approx. 66% recovery for repeated exposure vs CTR- (basal condition); that's to say a +34.9% recovery for acute exposure and +15.8% recovery for repeated exposure vs CTR+



Nicomenthyl treated keratinocyte culture (on the right) had an excellent recovery (84.2%) of cell viability for acute exposure and 64.3% recovery for repeated exposure vs CTR- (basal condition); that's to say a +14.8% recovery for acute exposure and +15.8% recovery for repeated exposure vs CTR+



Nicomenthyl treated keratinocyte culture (on the right) had an excellent recovery (76.9%) of cell viability for acute exposure and 65.2% recovery for repeated exposure vs CTR- (basal condition); that's to say a +21.8% recovery for acute exposure and +15.3% recovery for repeated exposure vs CTR+



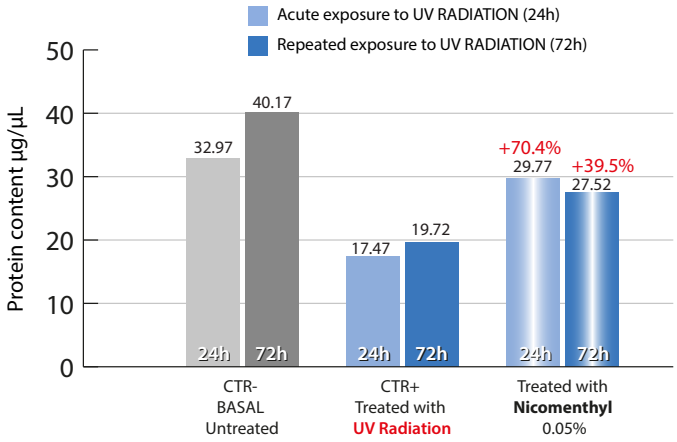
Nicomenthyl treated keratinocyte culture (on the right) had a good recovery (up to 66.4%) of cell viability for acute exposure and 68.8% recovery for repeated exposure vs CTR- (basal condition); that's to say a +13.7% recovery for acute exposure and +19.7% recovery for repeated exposure vs CTR+

***damaging agents used:**

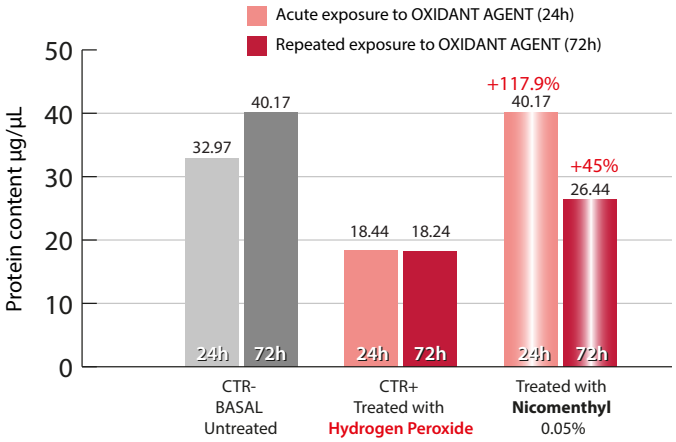
1. UV Radiation: UVB, UVA, visible and infrared radiation emitted by *Sun Simulator Suntest CPS+* (total energy irradiated 300 J/m^2).
2. Oxidant Agent: Hydrogen peroxide, 50 µM in culture medium for acute exposure, 25 µM in culture medium for repeated exposure.
3. Urban Dust: certified urban particulate material, mixture of PAHs, PCB congeners, and Chlorinated Pesticides, average PM10, conc. 0.25% for acute exposure, 0.125% for repeated exposure.
4. Synthetic Smoke: mixture of nicotine, cadmium, formaldehyde and ethyl carbamate in equal parts, conc. 0.00125% for acute exposure, 0.0006% for repeated exposure.

The tetrazolium dye (MTT) assay is a standard, simple and accurate colorimetric method for cell viability assessment. The assay is based on the intracellular reduction of the yellow tetrazolium salts by the mitochondrial enzyme succinate dehydrogenase in blue/purple formazan crystals. The reaction may therefore take place only in metabolically active human keratinocyte cells and the value of the optical density obtained by photometric reading can be correlated to the amount of viable cells. After isopropanol incubation absorbance readings was performed at 570 nm by microplate reader (isopropanol was used as blank for reading). For each test condition the ratio of the average optical density of the treated cultures on the average optical density of negative controls determines the viability rate. The % protection, intended as cell viability % increase compared to positive control condition, treated only with the damaging agent, is also calculated.

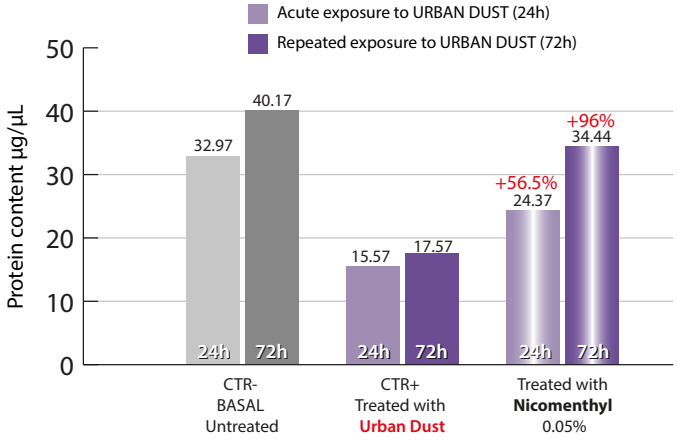
NICOMENTHYL – Keratinocyte Cells Metabolism Study (Lowry Assay)
Acute (24h) & Repeated Exposure (72h) to 4 damaging agents



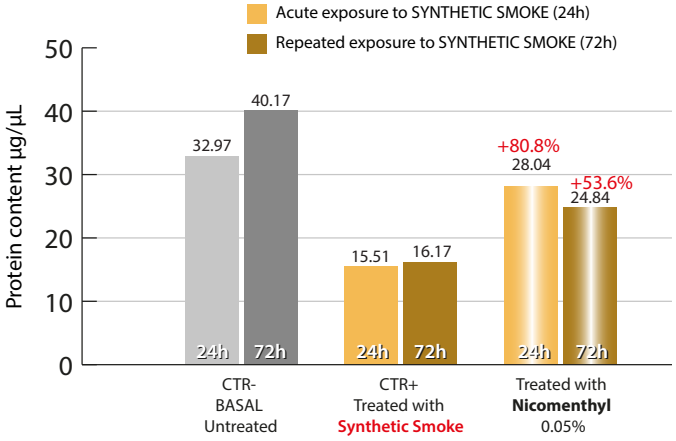
Nicomenthyl treated keratinocyte culture had a very high recovery of protein synthesis up to 29.77 µg/µL (90.3% of basal) for acute exposure and up to 27.52 µg/µL (68.5% of basal) for repeated exposure vs CTR- (basal condition); that's to say a +70.4% recovery for acute exposure and +39.5% recovery for repeated exposure vs CTR+



Nicomenthyl treated keratinocyte culture had an extraordinary recovery of protein synthesis up to 40.17 µg/µL (121.8% of basal value) for acute exposure and up to 26.44 µg/µL (65.8% of basal) for repeated exposure vs CTR- (basal condition); that's to say a +117.9% recovery for acute exposure and +45% recovery for repeated exposure vs CTR+



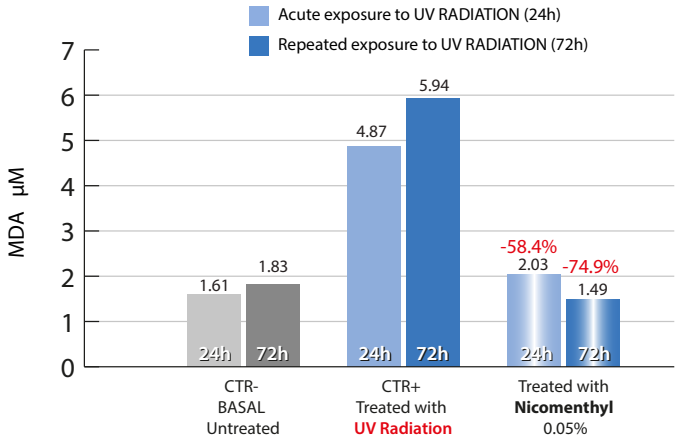
Nicomenthyl treated keratinocytes had an excellent recovery of protein synthesis up to 24.37 µg/µL (73.9% of basal value) for acute exposure and up to 34.44 µg/µL (85.7% of basal) for repeated exposure vs CTR- (basal condition); that's to say a +56.5% recovery for acute exposure and +96% recovery for repeated exposure vs CTR+



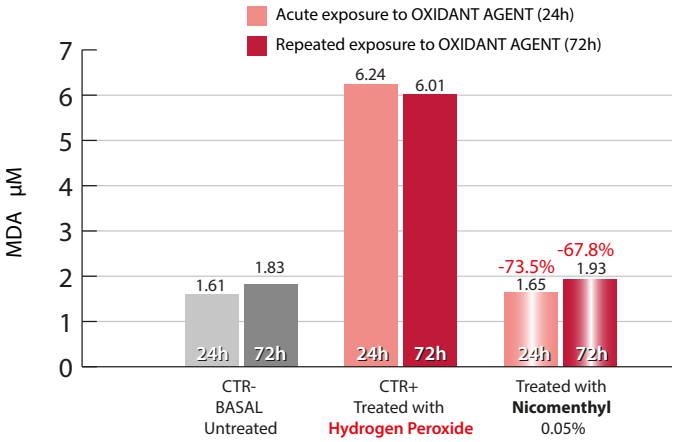
Nicomenthyl treated keratinocytes had an excellent recovery of protein synthesis up to 28.04 µg/µL (86% of basal value) for acute exposure and up to 24.84 µg/µL (61.8% of basal) for repeated exposure vs CTR- (basal condition); that's to say a +80.8% recovery for acute exposure and +53.6% recovery for repeated exposure vs CTR+

Cell metabolism study – Protein synthesis determination by Lowry assay. The determination of protein synthesis was carried out by colorimetric method. Like in biuret method, in alkaline condition Copper(II) ions complex with proteins and catalize the oxidation of tyrosine and tryptophan residues. This oxidation causes the reduction of Folin-Ciocalteau reactive that changes its colour from yellow to blue. The colour intensity is proportional to the protein content. The results are expressed as % protein synthesis increase compared to an untreated control cell culture (CTR-).

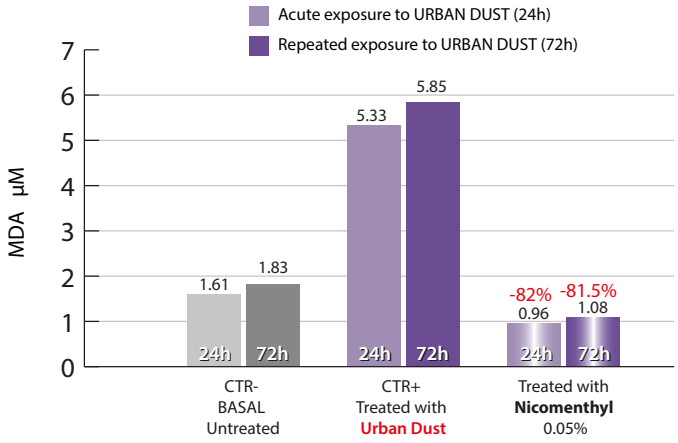
NICOMENTHYL – Lipid Damage Study (MDA Dosage)
Acute (24h) & Repeated Exposure (72h) to 4 damaging agents



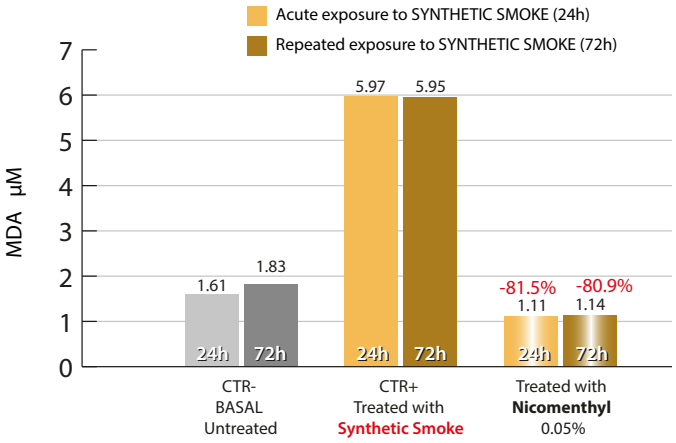
Nicomenthyl treated keratinocyte culture showed a very significant drop of MDA down to 2.03 µM in 100 µM(126% of basal) for acute exposure and down to 1.49 µM of MDA (81.4 % of the basal) for repeated exposure vs CTR- (basal condition); that's to say a -58.4% of MDA for acute exposure and -74.9% for repeated exposure vs CTR+



Nicomenthyl treated keratinocyte culture had an extraordinary drop of MDA down to 1.65 µM (102.5% of basal value) for the acute exposure and down to 1.93 µM (105.5% of basal) for repeated exposure vs CTR- (basal condition); that's to say a -73.5% drop of MDA for acute exposure and -67.8% for repeated exposure vs CTR+



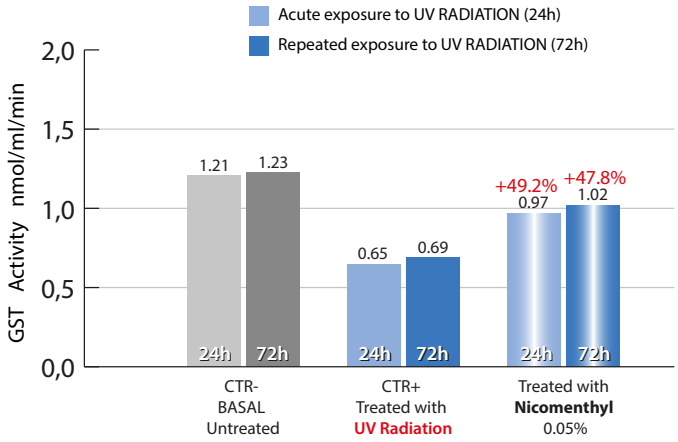
Nicomenthyl treated keratinocyte culture had an extraordinary drop of MDA down to 0.96 µM (59.6% of basal value) for acute exposure and down to 1.08 µM (59% of basal) for repeated exposure vs CTR- (basal condition); that's to say a -82% drop of MDA for acute exposure and -81.5% for repeated exposure vs CTR+



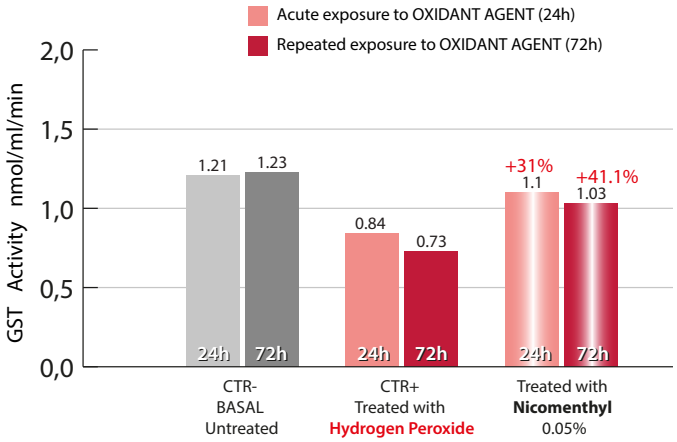
Nicomenthyl treated keratinocyte culture had an extraordinary drop of MDA down to 1.11 µM (69% of basal value) for acute exposure and down to 1.14 µM (62.3% of basal) for repeated exposure vs CTR- (basal condition); that's to say a -81.5% drop of MDA for acute exposure and -80.9% for repeated exposure vs CTR+

Lipid damage study- MDA (Malondialdehyde) dosage. MDA content determination was used as oxidative stress index linked to the lipid components. The malondialdehyde is in fact a specific biomarker of oxidative stress for lipids indicating the state of lipid peroxidation. This phenomenon begins at the level of polyunsaturated fatty acids of the membrane phospholipids; free radicals react with phospholipids by oxidizing them and thus lead to the formation of unstable lipid hydroperoxides that decompose producing a number of secondary products such as aldehydes and ketones recognized as toxic or carcinogenic substances. Malondialdehyde (MDA) is one of the main products of lipid peroxidation, and its concentration in biological systems is a good index of lipo-peroxide damage. To determine the lipoperoxides levels the colorimetric method tested by Erdelmeier and collaborators (1998) was assayed: the test is based on the capability of a chromogen, N-methyl -2-phenylindole (NMPI), to react with MDA at 45°C with acid pH to produce a stable blue chromophore that has an absorption pick at 586 nm. The quantitative determination uses a calibration curve made-up of known and growing concentrations of standard MDA. The results are expressed as MDA concentration (µM) in 100 µL cell homogenate. The difference in MDA content between positive control/ sample and negative control is calculated.

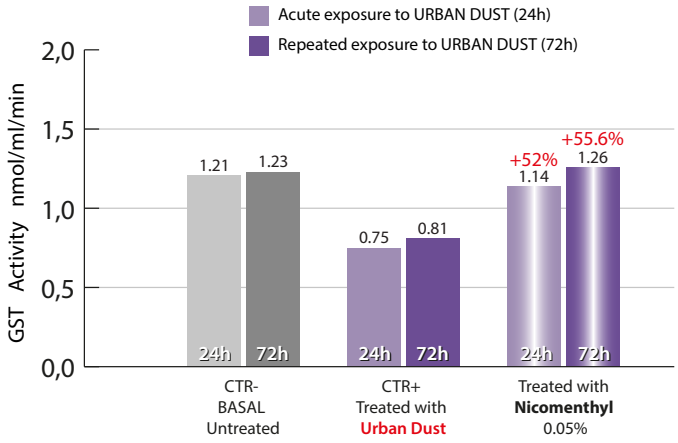
NICOMENTHYL – Detoxifying Activity Study (GST) Assay
Acute (24h) & Repeated Exposure (72h) to 4 damaging agents



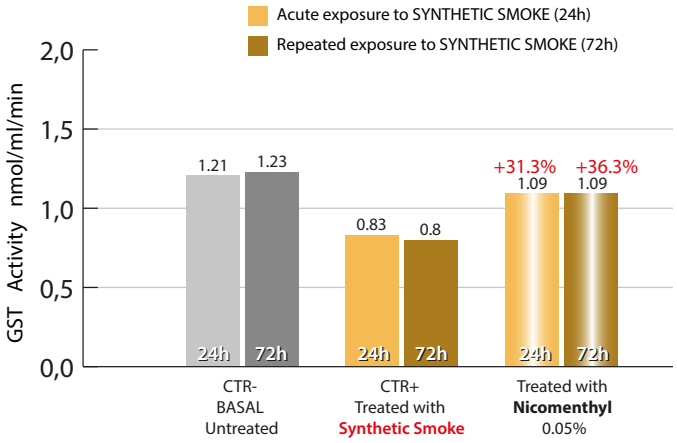
Nicomenthyl treated keratinocyte culture showed a very significant recovery of GST activity up to 0.97 nmol/ml/min (80.1% of basal) for acute exposure and up to 1.02 nmol/ml/min (83% of basal) for repeated exposure vs CTR- (basal condition); that's to say a +49,2% of GST activity increase for acute exposure and +47.8% for repeated exposure vs CTR+



Nicomenthyl treated keratinocyte culture had a very significant recovery of GST activity up to 1.1 nmol/ml/min (91% of basal) for acute exposure and up to 1.03 nmol/ml/min (83.7% of basal) for repeated exposure vs CTR- (basal condition); that's to say a +31% of GST activity increase for acute exposure and +41.1% for repeated exposure vs CTR+



Nicomenthyl treated keratinocyte culture had a very significant recovery of GST activity up to 1.14 nmol/ml/min (94,2% of basal) for acute exposure and up to 1.26 nmol/ml/min (102.4% of basal) for repeated exposure vs CTR- (basal condition); that's to say a +52% of GST activity increase for acute exposure and +55.6% for repeated exposure vs CTR+



Nicomenthyl treated keratinocyte culture had a significant recovery of GST activity up to 1.09 nmol/ml/min (90% of basal) for acute exposure and up to 1.09 nmol/ml/min (88.6% of basal) for repeated exposure vs CTR- (basal condition); that's to say a +31.3% of GST activity increase for acute exposure and +36.3% for repeated exposure vs CTR+

Detoxifying activity study – Glutathione S-transferase (GST) Assay - Glutathione S-transferases are a group of isoenzymes important in the detoxication of the tissues. These enzymes protect the cells against toxicants by conjugating to the thiols of glutathione and subsequent elimination. Starting from the cell homogenates in the different experimental conditions, the detoxifying activity of Nicomenthyl was determined by monitoring the capability of the enzyme to conjugate the glutathione to 1-chloro-2,4-dinitrobenzene (CDNB) to produce a stable complex with absorption at 340 nm.

The above studies and assays have been carried out by Complife Italia Srl – Via Guido Rossa, 1 – 20024 Garbagnate (MI) - Italy

nicomenthyl®

menthyl nicotinate

MICROCIRCULATION ENHANCER

AND MUCH MORE...

These new discoveries place NICOMENTHYL at the cutting edge of the Science of Cosmetics and open new horizons over a broad scenario of innovative and powerful applications, aiming at the achievement of the most basic and important cosmetic claim:

SKIN BARRIER INTEGRITY RECOVERY & ENHANCEMENT

Recommended dosage in **Face Products: 0.5 – 1%**
in **Body Products: 0.5 – 3%**

Particularly indicated for:

- Anti-age and anti-pollutant, skin detox formulations
- Sun care products
- Hair loss prevention treatment
- Cellulitis treatment
- Sport products
- Spa treatment products
- Refreshing products for feet and legs
- Intimate hygiene products
- Cosmetic lip plumping treatments
- Deodorant/antiperspirants
- Pre/after shave products
- Body lotions

multi chem R&D

MULTICHEM R&D SRL - Via G. Marconi 37 - 20089 Rozzano (Milan) - ITALY
+39 02 8262192 - www.multichem.it - info@multichem.it