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Nicomenthyl® 20 NAD-*Boosting* Lipophilic Derivative of Vitamin B3

MULTICHEM R&D

Nicomenthyl® 20 is a multifunctional sensorial active ingredient derived from vitamin B3 (i.e. niacin or nicotinic acid), manufactured in Italy by Multichem R&D with a patented synthesis process.

Nicomenthyl® 20 significantly enhances skin microcirculation, without causing hyperemia or irritation. Instead, it produces a pleasant localized tingling sensation.

Vitamin B3 is a precursor of the coenzyme NAD (*Nicotinamide Adenine Dinucleotide*), one of the most interesting and important molecules in cellular energetic metabolism. Defined by some researchers as "the molecule of life", NAD is required for over 500 enzymatic reactions and plays a key role in the regulation of almost all major biological processes, including our immune responses and DNA repair against damage caused by aggressive chemicals or radiations (1).

Niacin deficiency in keratinocytes, and consequent lack of NAD, causes intracellular events which can lead to lipid peroxidation, oxidative stress of cell membranes, premature skin ageing, erythema and skin irritation, and eventually to more serious consequences, including irreversible DNA damage, loss of epidermal barrier integrity, mutagenesis, immune suppression, actinic keratosis, and skin cancers. (2 - 4).

A recent study, published in prestigious journal Nature, has also shown that vitamin B3 is highly effective even in preventing lung tissue inflammation damage in COVID-19 patients (5).

Composition and Technical Specifications

The technical characteristics of Nicomenthyl® 20 (INCI Name: Menthyl nicotinate) are reported in *Table 1*.

Menthyl nicotinate is the product of the esterification reaction between nicotinic acid (vitamin B3 or niacin) and natural menthol (**Fig. 1**).

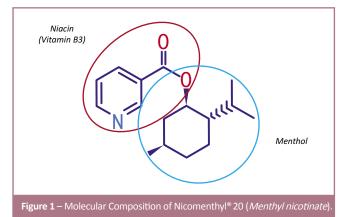
Its physical state (liquid) makes it easier to incorporate into any formulation; moreover, it remains liquid even at very low temperatures (under -20°C).

It is completely thermostable and can be processed either hot or cold, in a pH range between 4 and 8. No incompatibility with other cosmetic ingredients is currently known.

Organoleptic Properties	
Appearance	Liquid
Colour	Transparent and colourless
Odour	Odourless or slight characteristic odour
Physical Chemical Properties	
Specific gravity (at 20°C)	1.031
Solubility	Insoluble in water, soluble in alcohol, polar oils, esters
Boiling point at atm. pressure	292.23°C
Refractive index	1.5074
Composition (ppm)	
Heavy metals	< 10
Arsenic	< 0.02
Microbiological Properties (CFU/g)	
Total bacterial load	< 10
Moulds/Yeasts	< 10
Pathogens	Absent
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Stability and Storage: Thermostable. No added preservatives or antioxidants required nor any special conditions for storage. Shelf life: > 36 months.

Table 1 – Technical characteristics of Nicomenthyl $^{\circ}$ 20



It has a remarkable carrier and booster effect over other liposoluble substances, such as: tocopheryl acetate, retinyl palmitate, vitamin F, omega-3 EPA, DHA, essential oils, etc.

Mechanism of action

Once through the horny layer (stratum corneum), Nicomenthyl® 20 hydrolyzes and splits into its two original components: niacin and menthol.

Thanks to its vasoconstricting activity, the menthol causes a pleasant cooling sensation, within a few minutes after application and acts as a sort of "modulator" of the vasoactive activity of the niacin released by hydrolysis.

The niacin, in turn, triggers a cascade of complex biochemical reactions in the keratinocytes which lead to the synthesis of the NAD, i.e. what may be called the "energy currency molecule" of our organism, as it provides temporary storage to the energy produced by the cellular respiration (Fig. 2).

As already demonstrated in previous studies, Nicomenthyl® 20 shows an extraordinary protective efficacy against the oxidative stress caused by external agents (6, 7) thanks to its rapid penetration through the skin barrier, time-released delivery of niacin, and subsequent significant increase of NAD levels in skin cells (*NAD-booster* effect).

Efficacy

In Vitro Studies

In vitro tests have shown the kinetic profile of the rapid skin penetration of menthyl nicotinate and its slow, time-released delivery of niacin (6).

Further *in vitro* tests have also assessed its protective, antioxidant, and detoxifying efficacy against UV radiation, oxidant chemicals, pollutants, and cigarette smoke, with results clearly confirming how effectively Nicomenthyl® 20 enhances the defense mechanisms of skin cells against all tested damaging agents (7).

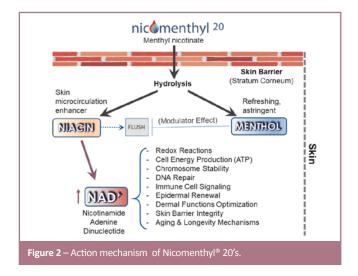
Similar tests have, moreover, assessed the detoxifying power of Nicomenthyl® 20 against skin damage caused by Blue Light and WIFI radiations by monitoring the activity of *Glutathione S-transferase* (GST) i.e. an enzyme which plays a pivotal role in the deactivation and elimination of xenobiotic toxicants. These assessments were made on keratinocytes cultures (*HaCaT*), in a complete medium (*Dulbecco's Modified Eagle Medium, DMEM*) enriched with 10% fetal bovine serum.

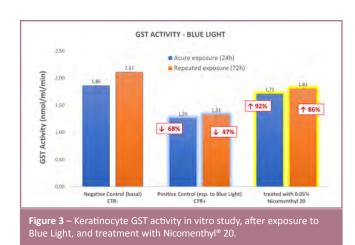
The results showed that both damaging agents cause relevant alterations of the GST's activity in the exposed keratinocyte cultures (CTR+).

On the other hand, the concomitant treatment with Nicomenthyl® 20 has shown a significant recovery of the monitored values of GST activity, almost bringing them back to their baseline levels (CTR-), both in acute (24h) and in repeated exposure (72h) (Fig. 3, 4).

In Vivo Studies

A Laser Doppler blood flowmetry test was carried out on twenty volunteers of both sexes, with a mean age of 44.9, using a topical preparation containing 3% of Nicomenthyl® 20, versus placebo. The results (Fig. 5) showed a significant increase in microcirculatory flow at 15 minutes (+78% compared to T0), and at 30 minutes (+147%). The effect persisted for an hour after being applied (+87%).





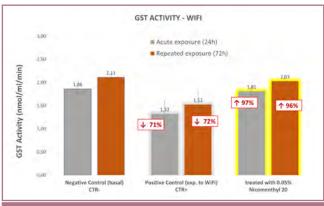


Figure 4 – Keratinocyte GST activity *in vitro* study, after exposure to WIFI, and treatment with Nicomenthyl® 20.

Safety

All tests have confirmed the absence of irritative and/or sensitizing effects, both on skin and vaginal mucosa.

The product is to be considered completely safe at the recommended dosages of use.

Applications and Directions for Use

Its protection from damages caused by external factors and its activity on skin microcirculation qualify Nicomenthyl® 20 as a safe and effective active ingredient, both for *leave-on* or *rinse-off* cosmetic formulations. It is particularly indicated for anti-cellulite formulations, hair loss prevention treatments, intimate hygiene products, detox and anti-pollutant products, tonifying and anti-age treatments, products for oily, impure, and asphyxial skins. Generally suitable for all those cases where enhancing skin microcirculation is particularly needed to promote oxygenation, detoxification and normalization of skin metabolism.

Recommended dosage from 0.5 to 3%.

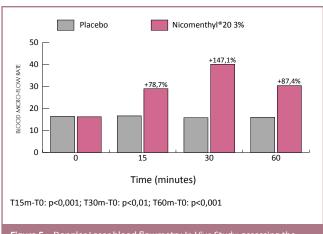


Figure 5 – Doppler Laser blood flowmetry *In Vivo* Study, assessing the effect of a cosmetic product containing 3% Nicomenthyl® 20 on skin microcirculatory flow rate.

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Multichem R&D in a nutshell

With its 30 years of experience and several international patents granted, Multichem R&D pioneered the production of *Menthyl nicotinate-based* ingredients under the trade name Nicomenthyl[®].

Innovation, scientific rigor, safety, sustainability are the values that inspire our passion for research and enlighten our journey toward higher achievements.

Our ultimate goal is to provide our customers with innovative and exclusive solutions that make a real difference and contribute significantly to their success.



NICOMENTHYL 20 (Menthyl nicotinate) is a new multifunctional, sensorial cosmetic ingredient. Liposoluble and thermostable. Skin microcirculation enhancer. Detoxifying, antioxidant, anti-age. Protective against UV radiation, blue light, WIFI, toxins, pollutants and other aggressive agents.

Full scale in vitro and in vivo studies have demonstrated menthyl nicotinate's fast penetration kinetics through the skin, and how its subsequent hydrolysis effectively releases pure niacin (vitamin B3) with consequent increase of NAD coenzyme level (nicotinamide adenine dinucleotide) in the area of application.

NAD plays key roles in the regulation of almost all major biological processes such as electron transport chains, energy metabolism as well as those concerning immune response and DNA repair of damages induced by oxidative stress.

Menthyl nicotinate does not cause any flush, irritation or sensitization, even in cosmetic compositions containing it at concentrations up to 3-5%. Its time-release delivery of niacin is 3 to 8 times higher than the skin absorption rate of the common niacinamide (another form of vit. B3). Such characteristics qualify Nicomenthyl 20 as a powerful, effective and safe percutaneous carrier of Vitamin B3. All efficacy and safety test reports are available to customers upon request.

Particularly indicated for:

- Anti-age, anti free-radicals and anti-pollutant, skin detox formulations
- Protective and repairing treatment against Blue light and WIFI damages
- Sun care products (pre, during and after-sun exposure)
- Hair loss prevention treatment
- Cellulitis treatment
- Sport products
- Spa treatment products
- Refreshing/ reactivating products for feet and legs
- Intimate hygiene product
- Lip plumping treatment
- Deodorant/antiperspirants
- Pre/after shave product
- Oral care products and treatment
- Non irritating hand sanitizers preventing and repairing skin irritation and dryness caused by alcohol based products
- And much more...





