

ISP

BIOPEPTIDES

Vinciencia
BIOFUNCTIONALS

Chondricare™ IS

Description

Anti-aging peptide designed to adaptively energize skin or protect mitochondrial DNA, based on the needs of the mitochondria.

Chondricare IS has been developed to slow premature aging and to enhance the appearance of healthy skin. This biofunctional ingredient is a synthetic pentapeptide based upon the moonlighting protein aconitase, a critical functional element of human cells that both stimulates cell metabolism and protects mitochondrial DNA (mtDNA) from oxidative damage. Chondricare IS can help counteract the slowing of cell metabolism and help prevent mtDNA damage, both of which have been described as the origin of the aging process.

The interest in aconitase, in cosmetics, is linked to its capacity to adapt its activity according to the needs of the mitochondria: energy production or mtDNA protection. Chondricare IS is designed to help the skin to switch from energy synthesis to a bodyguard function – protection of mtDNA – as an adaptive response to changing environmental conditions and stresses.

Properties

- Increases aconitase enzymatic activity *in-vitro*
- Stimulates cell vitality *in-vitro*
- Protects mitochondrial DNA *in-vitro*

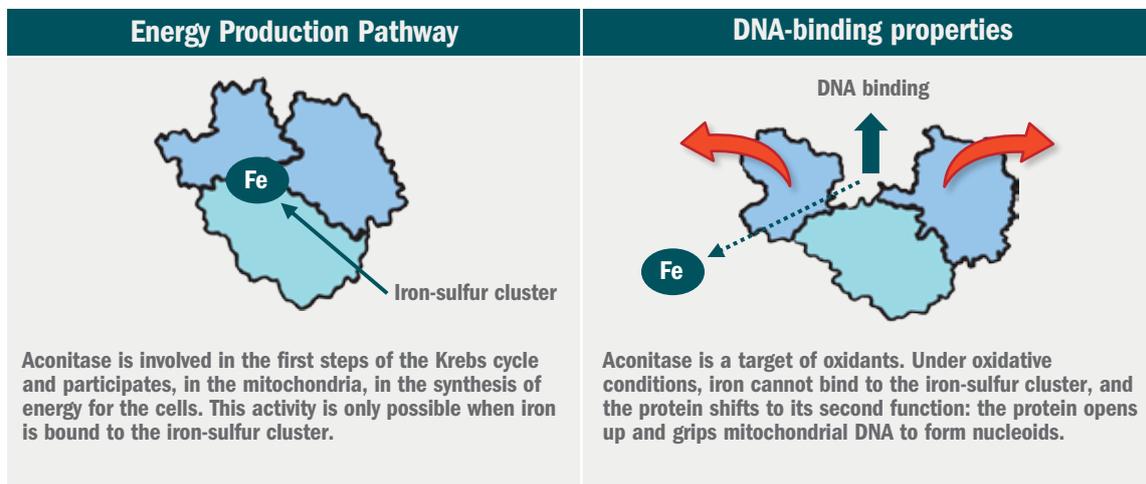
Cosmetic applications

- Anti-aging formulations to help protect mtDNA
- Day formulations to help protect from mtDNA damage
- Night formulations to help regenerate bioenergetic level

Vinciencia™ Biofunctionals

Aconitase, a moonlighting protein

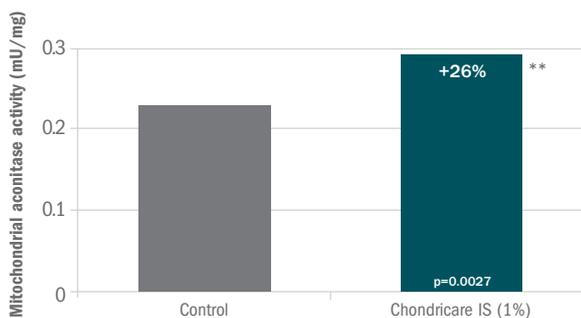
The idea of one protein – one function has become too simple because increasing numbers of proteins are found to have two or more different functions. These proteins, such as aconitase, are called moonlighting proteins. The multiple functions of these moonlighting proteins add another dimension to cellular complexity and benefit cells in several ways, as cells have developed sophisticated mechanisms for switching between the distinct functions of these proteins. Interest in aconitase is linked to its capacity to adapt its activity according to the needs of the mitochondria: energy production or mtDNA protection.



Energy production pathway

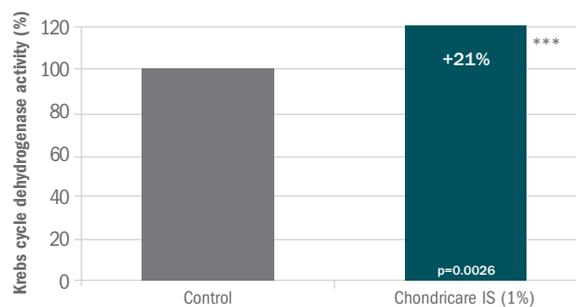
1. Krebs cycle

Aconitase is a key player in the central pathway of energy production (Krebs cycle) and it is suggested that an age-related decrease in aconitase activity is likely to contribute to a decline in the overall efficiency of mitochondrial bioenergetics.



Cell culture: Fibroblasts
 Product application: Chondricare IS (1%)
 Application time: 72 hours (once a day)
 Evaluation: Mitochondrial aconitase activity

** Very significant



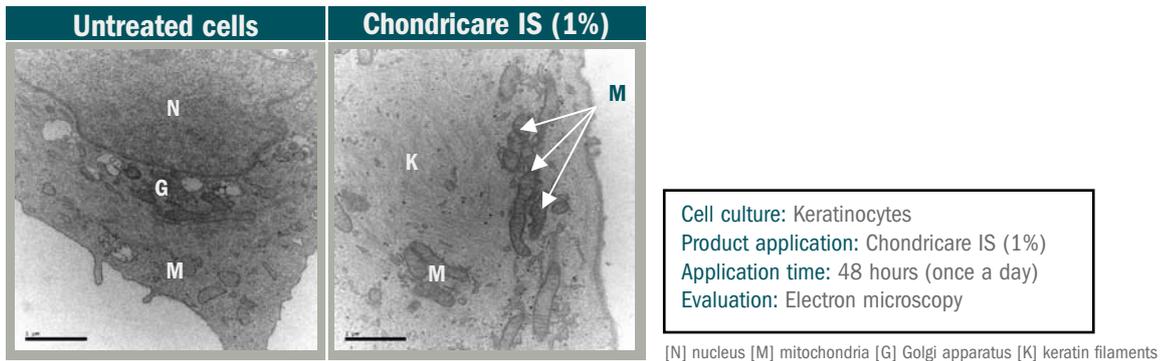
Cell culture: Fibroblasts
 Product application: Chondricare IS (1%)
 Application time: 48 hours (once a day)
 Evaluation: MTT

*** Highly significant

Mitochondrial aconitase activity, essential to the Krebs cycle, is significantly increased (+26%) by Chondricare IS (1%) *in-vitro*. These results also show a significant overall mitochondrial activity increase (+21%) by Chondricare IS *in-vitro* application. Additional tests (not shown here) demonstrate that the application *in-vitro* on fibroblasts of Chondricare IS, maintains mitochondrial aconitase and dehydrogenase activity under UVB stress conditions.

2. Cell metabolism: mitochondria ultra structure

Ultrastructural studies based on electron microscopy on human keratinocytes (and fibroblasts) show that Chondricare IS treated cells exhibit ultrastructural features that support increased metabolic and synthetic activities. This is reflected in the mitochondrial population, their structural attributes, as well as the abundance of Golgi elements.



mtDNA protection

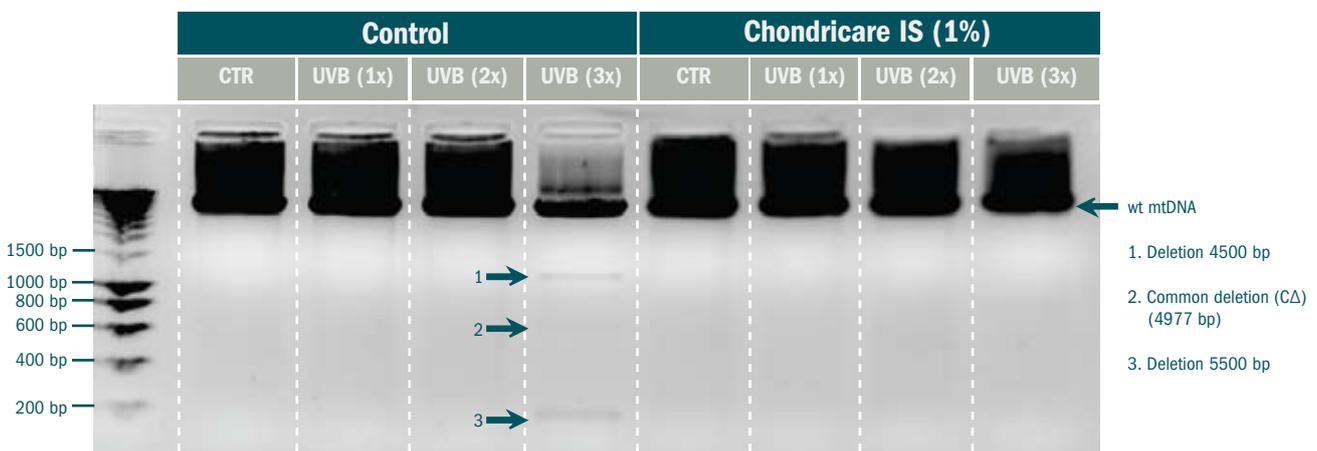
Mitochondrial DNA (mtDNA) codes for some of the mitochondrial proteins essential for the production of energy. During aging, oxidative damage to mitochondrial proteins and DNA increases and the Krebs cycle activity declines. The high vulnerability of mtDNA to reactive oxygen species (ROS) and other damaging agents is due to the absence of histones in mitochondria. Studies have shown that mitochondrial DNA-binding proteins, such as aconitase, were able to shield mitochondrial DNA from oxidative damage, the same way as nuclear histones do. Aconitase has been shown to protect mtDNA from excessive accumulation of mutations.

mtDNA protection: UVB damage

Human keratinocytes are cultivated for 48 hours with or without Chondricare IS 1%. Cells are then irradiated once, twice or 3 times with UVB (75 mJ.cm⁻²). The time between each UVB irradiation is 24 hours. 1 hour after each UVB irradiation, total DNA is prepared for the detection of mtDNA deletion.

The method of evaluation used is a specific long PCR with pfu DNA polymerase, on the extracted DNA, analyzed on 1% agarose gel. The primer set 1/2 PCR specifically amplify:

- 5694 bp fragment in wild type mtDNA (wt mtDNA, the fragment is big and will remain at the top of the gel)
- 717 bp fragment when mtDNA contains the common deletion (fragment 2, indicated as CA)
- Shorter and longer fragment in case of a different induced-deletion (fragment 1 and 3)



Several deletions, including the common deletion, were induced in mtDNA, after 3 UVB irradiations. This mtDNA deletion was not detected *in-vitro* for Chondricare IS (1%) treated cells suggesting a protection of mtDNA.

Specifications

Form:	Aqueous limpid solution
Color:	Colorless
Odor:	Light, characteristic
Solubility:	Water soluble
Preservatives:	Preservative-free

INCI Name

AQUA (WATER), BUTYLENE GLYCOL, PENTAPEPTIDE-28

Formulation Guidelines

- Add to water phase of cold process formulations; in hot process emulsions add on cool down, below 40°C
- Recommended use level: 1%

The above formulation information is for guideline purposes only. Some products may be formulated outside of the parameters of these guidelines. Please contact ISP Vincience for more specific information.

Additional Evaluation Tests

- *In-vitro* measure of ATP after 1 and 3 hours
- Ultrastructural study of fibroblasts
- *In-vitro* viability (MTT) in presence of H₂O₂ or UVB
- *In-vitro* DNA fragmentation (comet assay) after UVB
- *In-vitro* observation of fibroblasts morphology in presence of NO
- *Ex-vivo* observation of skin morphology in presence of H₂O₂ or NO
- Detection of pyrimidines dimers formation (8-OXO dG) after UVB
- *In-vitro* flow cytometry evaluation of free radical production

Tested Prototype Formulations

- Eclipse After Sun Gel: also featuring Stabileze QM and Lubragel CG (prototype #11574-28-2)
- Moonlight Skin Revitalizer: also featuring Ceraphyl and Si-Tec (prototype #11808-21-2)

Ex-vivo testing and sensory evaluation have been carried out on these prototype formulations. The results are summarized and available in our set of prototype formulation brochures.



Vincience

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