

Introduction to **Naticol**[®]
marine collagen peptides
for anti-aging and overview
of clinical studies



INTRODUCTION

Naticol® is a natural source of Type I collagen peptides. Type I collagen is a major protein that constitutes more than 75% of the protein found in our connective tissues and skin. This plays an essential role in maintaining skin tone, suppleness, and elasticity. Unfortunately after the age of 25, collagen synthesis in our body reduces at a rate of 1.5% per year. By the age of 45, collagen levels may have fallen by as much as 30%. The external effects of this process are the appearance of wrinkles, fine lines, and dry skin.

Naticol® is a rejuvenating ingredient that provides a pure and concentrated level of Type I collagen. It replenishes the body, providing essential nutrients to rebuild the collagen network due to its small molecular weight and high bioavailability. Uniquely, Naticol® contains more than 16% of essential amino acids (9/10) and around 50% of glycine, proline, and hydroxyproline. These are key amino acids that constitute Type I collagen. No other source of protein can provide this ratio of major skin components. The studies in this report show that regular use of Naticol® may help to slow signs of aging by increasing collagen synthesis, skin elasticity and firmness, and reducing fine lines and wrinkles.

COLLAGEN'S ROLE IN OUR BODIES

Collagen protein is a glycoprotein widely present in our bodies, composing 1/3 of our body's protein! It is present in the connective tissue that makes a framework for our skin, bones, joints, cornea, blood vessels, and the placenta. There are many types of collagen, but 75% of our body's collagen protein is Type I collagen.

Type I collagen is composed of three peptide chains that form a triple helix. One chain represents around 1050 amino acids (100,000 Daltons). These helices form collagen fibers. Glycine, Proline, and Hydroxyproline make up >50% of the amino acids present in hydrolyzed collagen. High contents of Arginine and Glutamic Acid are also present.



A hydrolyzed collagen protein like Naticol® has a low molecular weight to increase bioavailability (<6,000 Daltons). The term "Hydrolyzed collagen" describes native collagen extracted from the connective tissue (e.g. skin) by a technological process (enzymes, T°C, pressure, pH ...). Gelatin is obtained from a very partial hydrolysis of native collagen. Naticol® has no gelling properties or viscosity due to its low molecular weight.

TYPE I COLLAGEN VS. TYPE II COLLAGEN

Type I collagen is composed of two (alpha 1) chains and one (alpha 2) chain. Type I collagen is a higher percentage of the body's collagen protein than Type II collagen, and it is widely present in skin (75-80%), bones (30%), teeth, ligaments (80%), tendons (86%), and the placenta (>70%). While it may play a positive role in skin beauty, Type I collagen is also found in bones, tendons, and ligaments, which are key compounds in articular mechanisms.

Type II collagen is only composed of three (alpha 1) chains and is the basis for articular cartilage and hyaline cartilage alone. It may only help to rebuild cartilage, and its benefits are limited to articular comfort.

Polypeptide collagen chains	Triple helix of collagen molecule	Name	Localisation	
$\alpha 1$ (I)	$[\alpha 1(I)]_2 [\alpha 2(I)]$	Type 1	skin, bones, teeth, joints, cornea, internal organs, artery walls, embryonic tissue, scar and inflammatory tissues	Collagen type 1: two chains are the same (designated as $\alpha 1$ -chains) while the third chain differs ($\alpha 2$ -chains)
$\alpha 2$ (I)				
$\alpha 1$ (II)	$[\alpha 1(II)]_3$	Type 2	Cartilage, vitreous humour of the eye	Collagen type 2: three chains α are the same and the amino acids sequences are near the same of the ($\alpha 1$ -chains) from type 1. This new chain α is called $\alpha 1$ (II).

COLLAGEN PEPTIDES' ROLE IN THE AGING PROCESS

Skin aging is a process that is both Intrinsic and Extrinsic. Intrinsic aging is due to genetic and hormonal processes. Extrinsic aging is caused by external factors like UV radiation, smoking, pollution. They stimulate the production of free radicals, the main enemies of the skin, inducing oxidative stress. Extrinsic and Intrinsic aging reduce the number and the quality of collagen fibers. They also reduce the skin's elasticity and uniformity.

In young skin, the epidermis is thick and structured. The lipid barrier between cells works properly. In the dermis, the fibroblasts synthesize collagen and elastin. These fibers are numerous and dense and give the skin firmness and strength. In mature skin, the epidermis thins and cell renewal is slower. In the dermis, the fibroblasts synthesize is depleted and a decreased number of fibers negatively impacts skin's function.

Dramatization of the dermal layer



Mature skin: increased loss of water



Young skin: water holding

Ingested Naticol® is bioavailable, allowing the body to circulate necessary amino acids used in collagen fibril synthesis and other connective tissues. Studies on Naticol® and fish collagen peptides supplementation suggest health benefits related to skin hydration, antioxidant and anti-inflammatory activity, repair, and UVA protection. The studies below show several of these effects. Naticol® may be used topically or as an ingested supplement.

HOW DOES NATICOL® WORK WITH HYALURONIC ACID and other dietary supplement ingredients?

Hyaluronic acid and hydrolyzed collagen have different functions in the epidermis, but are both moisturizing ingredients that retard water evaporation from the skin and provide a large barrier to trans-epidermal water loss. In the epidermis, hyaluronic acid forms a gel with large amounts of water, which in effect plumps up the skin by resisting the pressure from the collagen fibrils forming skin's matrix. Thus, the size and density of the collagen fibrils and hyaluronic acid in skin have a strong impact on skin's health and function. Fish collagen peptides may also have synergies with other ingredients. Studies have shown synergistic value with antioxidants like Vitamin C, for instance. Marine hydrolyzed collagen has also been shown to accelerate absorption of dietary calcium by increasing calcium bioavailability. (Effect of calcium compounds from oyster shell bound fish skin gelatin peptide in calcium deficient rats. Journal of the Korean Fisheries. Kim, G. H., Jeon, Y. J., Byun, H. G., Lee, Y. S., & Kim, S. K. (1998). Society, 31, 149 -159).



CONSUMER PANEL STUDY

EVALUATION OF NATICOL® (fish collagen peptides) ON JAPANESE CONSUMER PANEL

This study, conducted by Just Research (Tokyo), evaluates the acceptance of Naticol® by women taking part in the study. Collagen peptides are regulated by FOSHU (food for specified health use) in Japan. In this mature market for dietary supplements and nutricosmetics, Japanese consumers are one of the most demanding customers in terms of food ingredient organoleptic and bioactive properties.

I – MATERIAL AND METHODS

Treatment

-Investigated product: NATICOL® (fish collagen peptides, Weishardt group)

Dose: daily intake of 10g for 2 and 4 weeks at the convenience of participants

Study population

Included in the panel were fifty-two (52) healthy, Japanese, female subjects from the Tokyo area, with normal skin and aged between 20 and 60 years old. Participants previously had at least one experience supplementing their diet with collagen.

Study duration

The duration of the study for each subject was 30 days ± 2 days (4 weeks).

Consumer survey

Over the course of the study, the Subject answered a set of questions using the response categories described below. The response categories were: Completely agree, Partially agree, No opinion, Partially disagree, Completely disagree.

The questions pertained to the following: collagen choice criteria, smell of Naticol® after package opening, smell of Naticol® after dissolving in water, taste of Naticol® after dissolving in water, effectiveness of Naticol® after 2 weeks, dissolvability of Naticol®, satisfaction regarding Naticol®, state of the skin at the end of the study, state of the joints at the end of the study, etc...

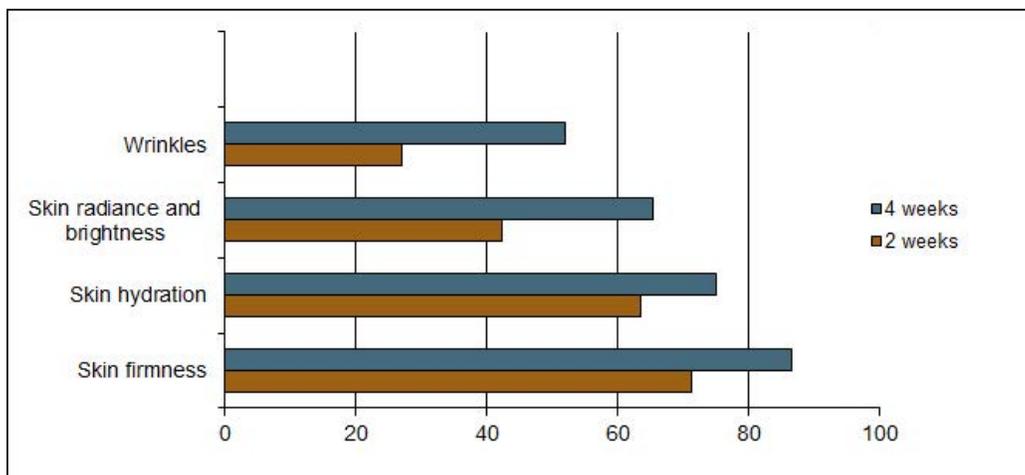
II – RESULTS AND DISCUSSION

A portion of the results pertaining to the survey are presented below. Categories of answers are grouped to form only three categories:

1. Positive (Totally agree and Partially agree); 2. Negative (Partially disagree and Totally disagree); 3. Without opinion. (Fig. 1, 2, & 3)

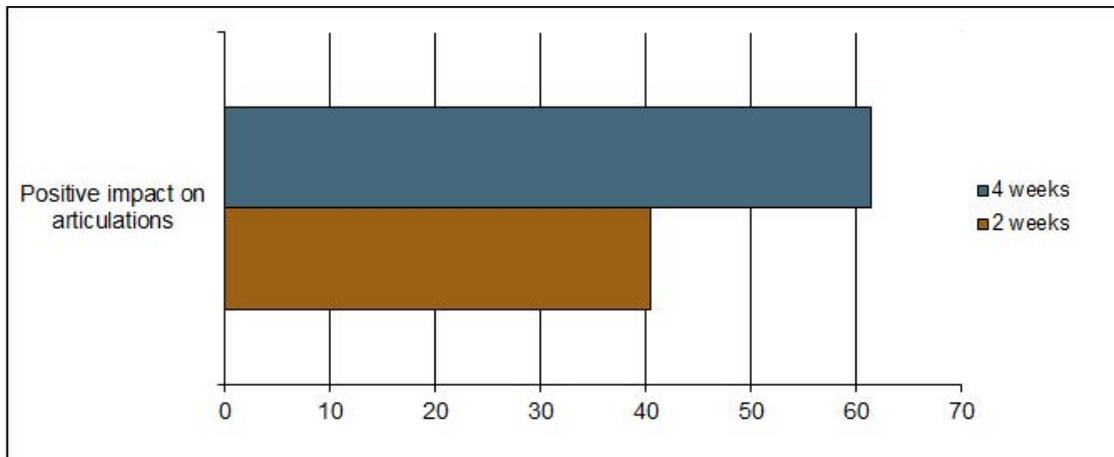
According to the consumers, the oral intake of 10g Naticol®/day may improve skin appearance after only 2 weeks!

After 2 weeks, oral ingestion of 10g Naticol®/day counteracts skin ageing and improves skin appearance (skin firmness, hydration, & brightness)



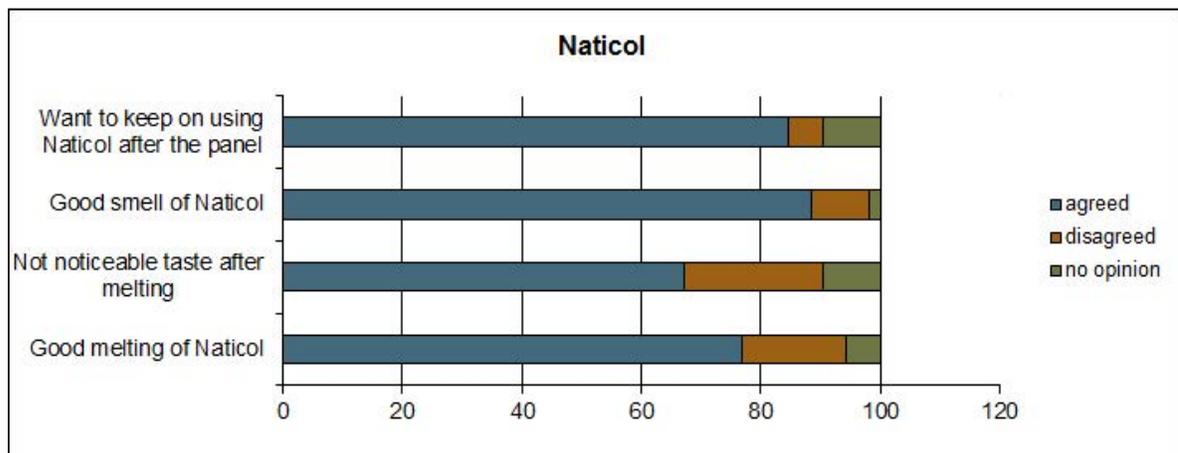
(Fig. 1)

There is a decrease in joint pain after 4 weeks of oral treatment (10g/day Naticol®)



(Fig. 2)

Consumer satisfaction survey of Naticol®



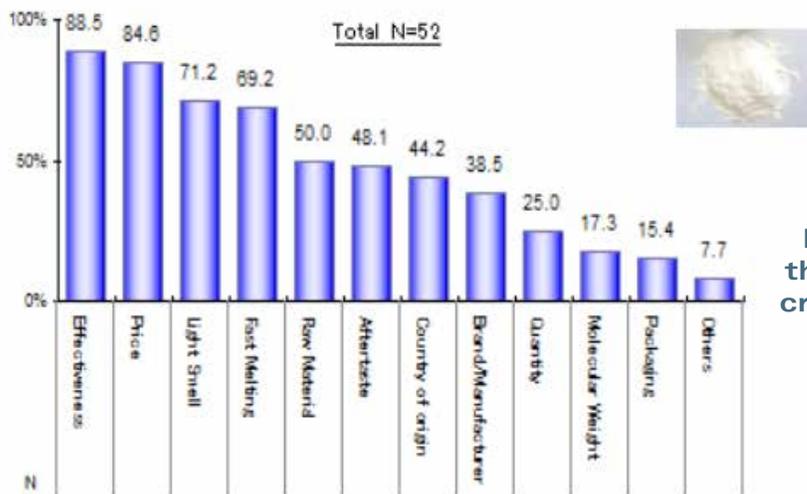
(Fig. 3)

CLINICAL STUDY REPORT

EVALUATION OF THE ANTI-AGING POTENTIAL OF NATICOL® (fish collagen peptides) ON SIGNS OF AGING IN THE FACIAL SKIN OF ASIAN VOLUNTEERS

This clinical study, done by CPCAD (Dermatology laboratory, Nice, France), intends to assess the anti-aging potential for nutritional supplementation of NATICOL® (fish collagen peptides). The study evaluates the aging signs in facial skin of Asian volunteers. Effectiveness is the first consumer choice criteria when buying a nutritional supplement (Fig. 4).

A second objective was to assess, overall, how consumers tolerated supplementation with Naticol® at a 10g/day level over a 12-week period. We asked the volunteers to indicate if any health problems appeared during this treatment, to look at potential adverse effects (headache, nausea, etc.) This objective also focused on the consumer's satisfaction with the product. The study was designed to be a mono-centre, double-blind, placebo-controlled, randomized, interventional Biomedical Research study performed on two parallel groups. For randomization, a person not participating in the study prepared a list by the Biostatistics of the CPCAD using the SYSTAT software version 11.0 (SPSS, USA).



Effectiveness (88.5%) is the first consumer choice criteria to buy a nutritional supplement

(Fig. 4)

I – MATERIAL AND METHODS

Treatment products

-Investigated product: NATICOL® (fish collagen peptides, Weishardt group)

Dose: one daily intake of a 10g bag in 20cl of liquid. Participants ingested Naticol® before breakfast for 12 weeks.

-Comparative product: maltodextrin, placebo of NATICOL®.

Dose: one daily intake of a 10g bag in 20cl of liquid, taken before breakfast for 12 weeks.

Study population

Forty (40) healthy female subjects, aged 59 ± 5 years old, with skin Type II to V according to the Fitzpatrick scale, and meeting the criteria of inclusion/non-inclusion, were included in the study. This study was split into two homogeneous groups of 20 women each.

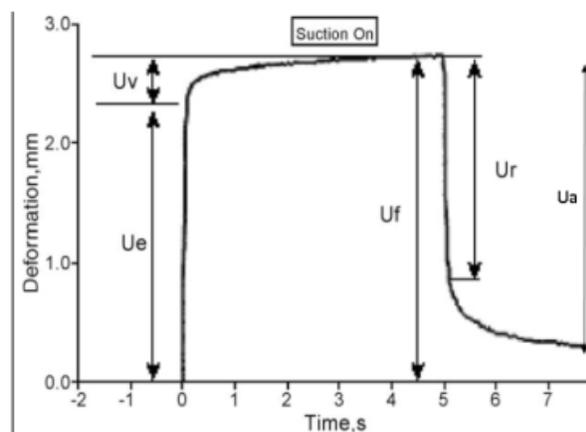
Study duration

The duration of the study for each subject (after a screening period of 2 weeks) was 84 days ± 2 days (12 weeks).

Methodology

Skin biomechanics measurements

- The cutometer® SEM 575 Skin Elasticity Meter® (Courage and KazhKa, Köln, Germany) measures a deformation perpendicular to the skin surface using a suction method. A depression of 400 mbars was applied through the probe onto the skin for 2 seconds, followed by a relaxation period of 2 seconds. This cycle was completed 5 times. The deformation induced on the skin was measured by an optical system placed in the probe, whose aperture has a 2 mm diameter. Three measurements of 5 cycles were performed on the test zone (bony part of the cheek). Each parameter was averaged for analysis. The skin deformation curve as a function of time is described in Fig. 5. This test models the skin stretching from its original state, and measures the time and quality of its ability to return to the original state.



Graph of cutometer® SEM 575 skin elasticity measurement

(Fig. 5)

- The corneometer CM 825® (Courage & Khazaka, Köln, Germany) performs skin hydration measurements. This instrument assesses the hydration state of the outer dermal layers using electrical capacitance measurements. After the probe was placed perpendicularly onto the skin surface, measurements were taken in less than 1 second. Three measurements were taken on each site respectively, and these were averaged for further evaluation.

Skin replica analysis (3D- analysis of wrinkles)

Skin replicas (prints) were analyzed using an image analysis system. This system was composed of a camera (4912-5000/0000, Cohu Inc, San Diego, CA, USA) which was fitted with a Computar macro-objective. The replica was lit with an incident light at 35° which produces shadowing behind each wrinkle or hollow. Digitized, resultant images were recorded by a CCD camera and then analyzed by computer dedicated software (Quantirides software, Monaderm, Monaco).

Consumer Satisfaction Survey by the Subject and Investigator

The Subject and Investigator were surveyed to answer questions in the following response categories:

Completely agree, partially agree, no opinion, partially disagree, completely disagree.

Each subject answered the following question: "Would you say that the Naticol® treatment you underwent has reduced the wrinkles on your face?"

The Investigator and the Subject separately answered the following question:

"Would you say that the treatment you underwent is globally effective in reducing signs of aging in the face?"

Statistical Analyses

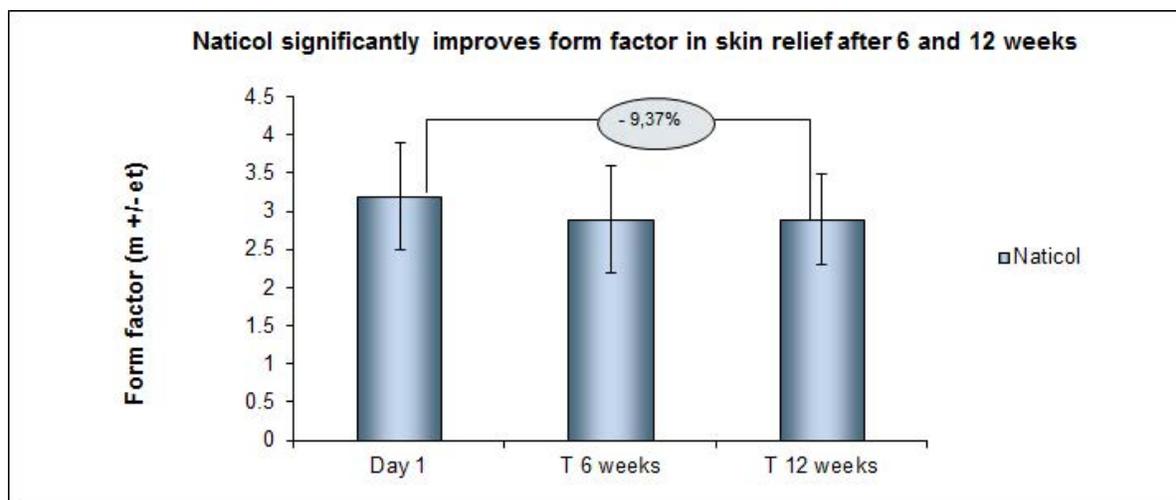
For each normal variable, an analysis of variance (ANOVA) using factors "Subject" and "Treatment" was performed. Significance was determined using a probability level of 0.5.

II – RESULTS AND DISCUSSIONS

Under the conditions of this study, the following was observed:

At the conclusion of the study, compared to Day 1, the level of relief in the periorbital zone (crow's-foot), indicated a significant smoothing in the overlap of the skin and a significant reduction in skin wrinkling (Fig.6) for women in the Naticol® group. No effect was observed in the Placebo group. The clinical score of wrinkles, assessed by the Investigator, decreased significantly under Naticol® at Week 6 and Week 12. The clinical score remained unchanged for the Placebo group.

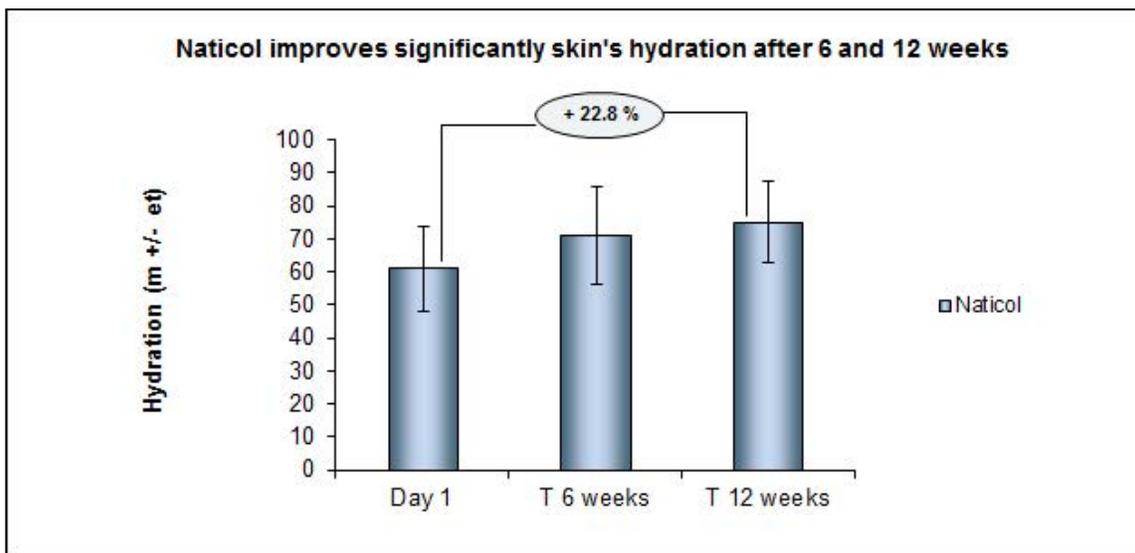
Naticol® significantly reduces skin wrinkles after 12 weeks, $p < 0.05$



(Fig. 6)

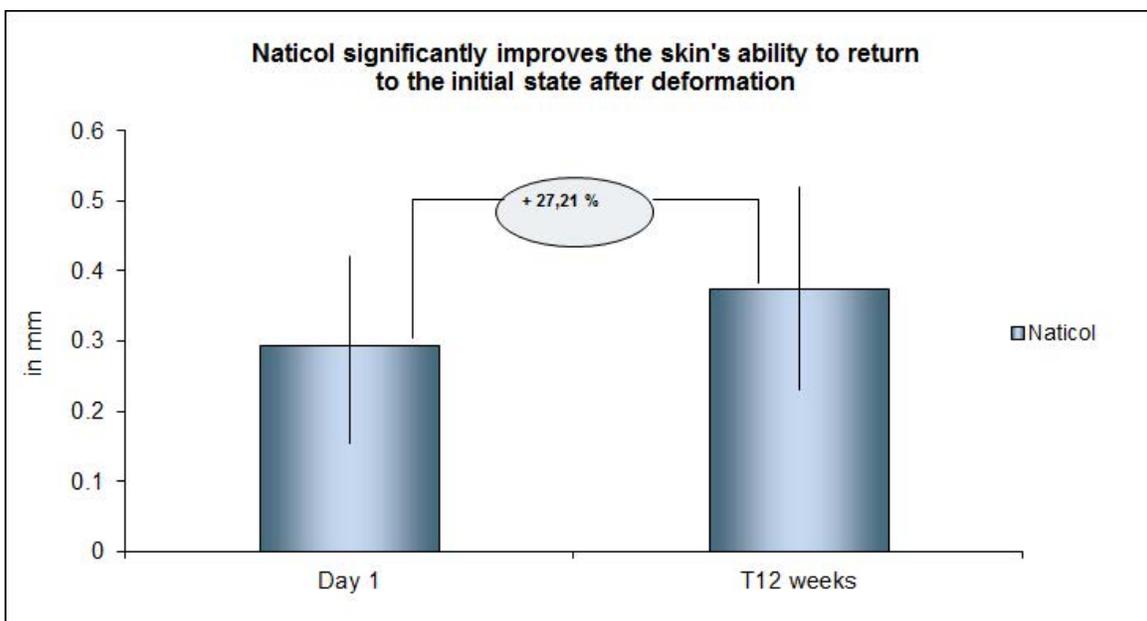
The level of skin hydration increased significantly during the study for the Naticol® group (Fig. 7). Concerning the skin biomechanics parameters, the skin elasticity was found to be significantly improved (+27.2% at Week 12, Fig. 8) for the group Naticol® at both Week 6 and Week 12. In contrast, no significant effect was shown in the Placebo group. Due to the increase of the skin elasticity, the ability of the skin to return to its initial state after deformation by the measurement tool was also increased for women in the Naticol® group.

Naticol® significantly improves skin hydration after 6 & 12 weeks, $p < 0.05$



(Fig. 7)

Naticol® significantly improves skin elasticity, $p < 0.05$

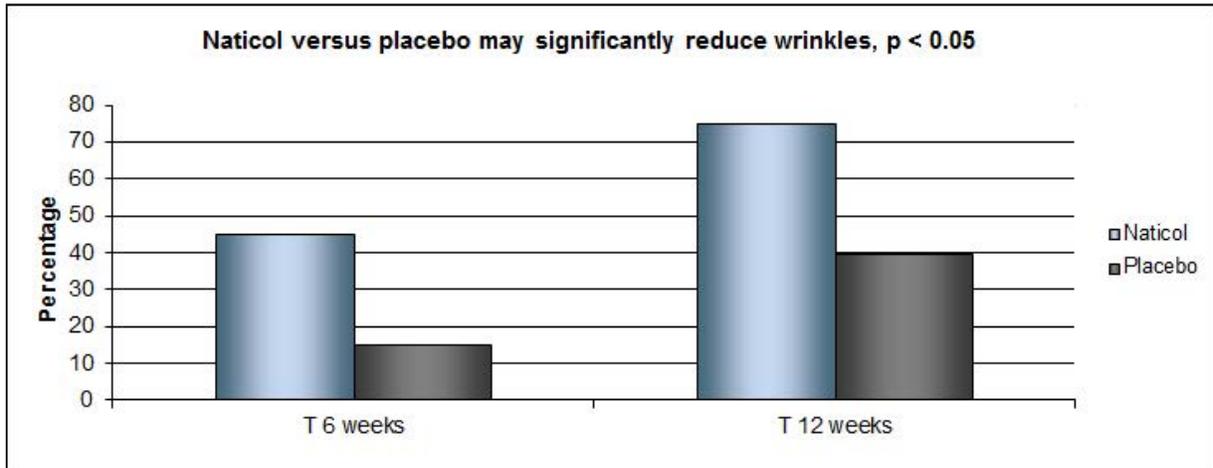


(Fig. 8)

In the consumer satisfaction survey for questions regarding Naticol®'s efficacy, **the number of positive answers was almost always higher in the Naticol® group than in the Placebo group. The difference was significant for the question: "Would you say that the Naticol® treatment you underwent has reduced the wrinkles on your face?" 79% of the subjects in the Naticol® group answered positively**, whereas 58% of the subjects under Placebo gave positive answers (Fig. 9).

In response to the question, "Would you say that the treatment you underwent is globally effective in reducing signs of aging in the face?" the response to the tested products (Naticol® and placebo) was globally excellent.

Naticol® versus placebo may significantly reduce wrinkles, $p < 0.05$



(Fig. 9)

These results indicate that Naticol® expressed significant improvements in the state of the consumer's skin as compared to its baseline, whereas the placebo had no effect. Since a 3-month treatment duration represents a minimum for anti-aging topical actives such as retinoic acid to produce significant effects on fine wrinkling, it could be expected that Naticol® progress is acceptable to consumers. It is also expected that an expanded treatment duration using Naticol® of 4 to 6 months will produce more significant results and a more significant difference vs. the placebo (Image 1).

In conclusion, this clinical study has shown that Naticol® improves the biomechanical properties of the skin compared to its baseline, in particular for skin elasticity and hydration. A smoothing effect of wrinkles observed on the skin imprints of the periorbital zone was confirmed by the clinical observation of the wrinkles as well. In the survey, subjects in the group Naticol® group found Naticol® significantly better for reducing the wrinkles on their face than did subjects in the placebo group.



Clinical study volunteer, before and after results after 12 weeks
(Visia CR Photographs)

(Image 1)

CONCLUSION

QUALITY AND TRACEABILITY

Weishardt's R&D department carefully selects the raw material and enzyme mixture in order to generate peptides with targeted biological activities. The nature of the matrix due to the raw material source, the choice of protease, and the extent of hydrolysis are three main factors in production of peptides with targeted biological activities. These raw materials are selected for:

- High quality standards (production, storage and traceability)
- Amino acid composition

IS NATICOL® SUSTAINABLE?

Yes! Naticol® is made from the skins and scales of fish that would otherwise be discarded in the fillet process. Naticol®'s producer, Weishardt, is very careful to protect the integrity and purity of Naticol® by producing it in a plant that makes fish-derived gelatin and collagen, ensuring your nutraceutical is sourced from a secure, sustainable, and traceable supply chain.

Naticol® is produced from 100% fish skin and scales through a validated and safe process (sterilization and pasteurization, filtration, UF, and demineralization). Naticol® fully conforms to ongoing food and pharmaceutical regulations. Naticol® is not irradiated and is GMO-free, fat free, contaminants free, carbohydrate free, cholesterol free, and preservative free. Naticol® dissolves easily in water or an emulsion, has a neutral taste and smell, has very good clarity and color, and exhibits excellent bioavailability.

Thank you for taking time to learn about Naticol® and fish collagen peptides.



The Scoular Company

The Scoular Company is a supplier of nutritional ingredients to the functional food, dietary supplement, and personal care industry. We work as a sales and marketing arm for companies with high quality ingredients and actives such as Naticol® fish collagen peptides. Scoular supports customer formulations with ingredients that fulfill market needs, providing ingredients with IP & non-GMO traceability, scientifically-backed actives, and certifications for good manufacturing processes.

Count on Scoular People for Quality Food Ingredients
250 Marquette Ave S, Suite 1050
Minneapolis, MN 55401
+1 (612) 851-3737 ph
food@scoular.com



Weishardt

Weishardt International Group

Weishardt is a French company founded in 1839. The world's 4th largest gelatin producer, Weishardt is a growing company with specialty businesses including production of Naticol® fish collagen peptides. Weishardt has facilities in France, Canada, and Slovakia and employees 450 people worldwide.

Rond-point Georges Jolimaitre, BP 259
81305 Graulhet cedex FRANCE

Christelle Bonnet, Health Ingredients Innovation Manager, Weishardt

Christelle Bonnet, technical director at Weishardt, followed classes in the French education system with a Masters degree in Food Science Engineering from Polytech Montpellier/ ISIM and a PhD in Nutrition and Biotechnology from the University of Pharmacy (CIRAD/ UAG). After receiving her Masters degree, Christelle worked for over 5 years in the food industry as a R&D manager. Christelle formulated fruit preparations with added value such as polyphenols, carotenoids, Ca²⁺, vitamins, and other supplementation for dairy products. As she wanted to learn more about how active compounds from a vegetable matrix may add functionality to foods, she embarked on a PhD, researching the effects of polyphenols (dopamine, leucocyanidine, etc) and phytosterols (sitosterols) from Musa cavendish on cardiovascular and anti-ulcerogenic activity. The French Research Ministry awarded Christelle an Innovation Prize for her work in this area. Two years ago, Christelle joined Weishardt in order to support scientific and technical development of Naticol® fish collagen peptides and has completed several research papers and clinical studies on this product during that time.



Christelle Bonnet