



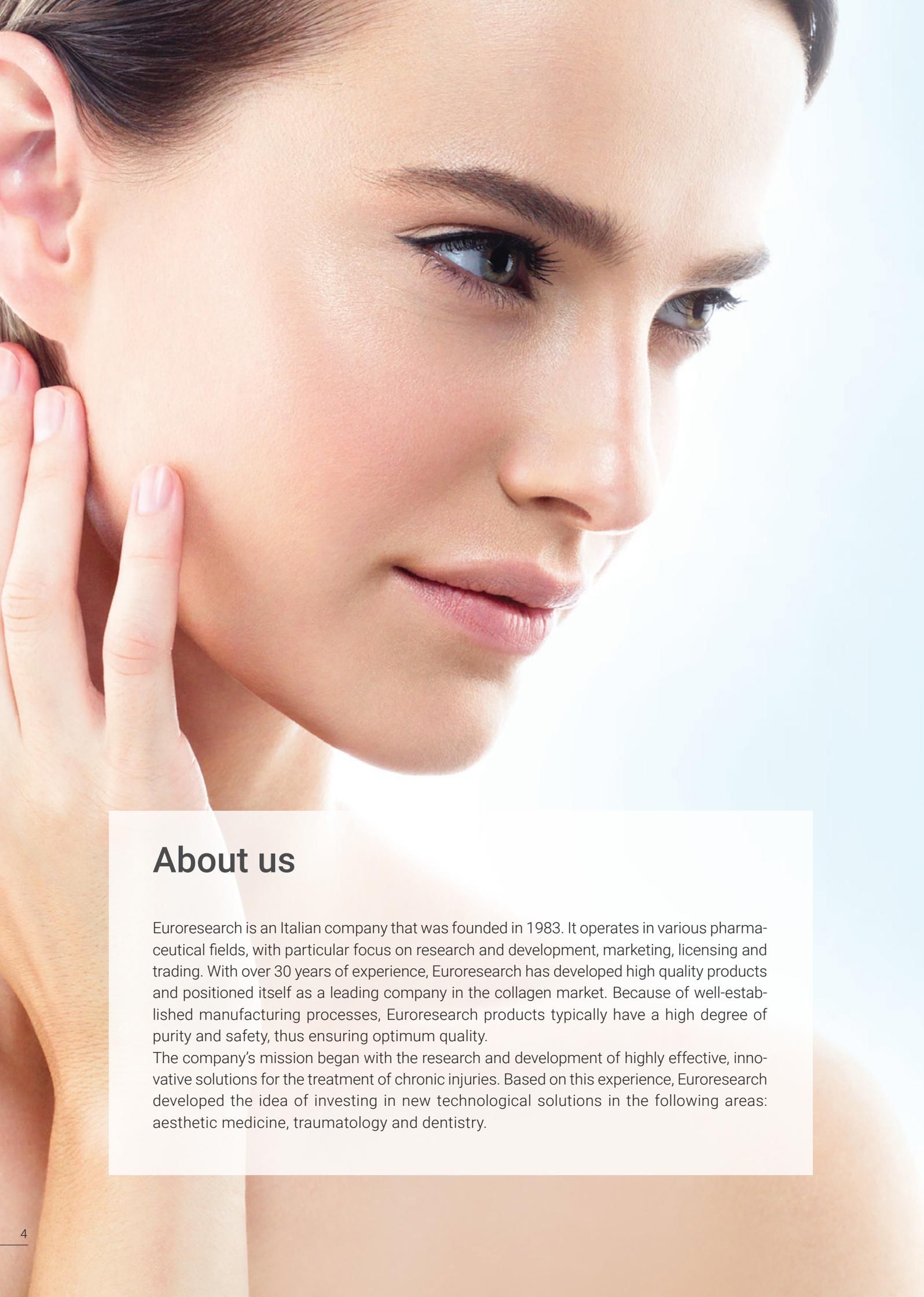
Safety and clinical
experience



nithya

Endless beauty

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About us

Euroresearch is an Italian company that was founded in 1983. It operates in various pharmaceutical fields, with particular focus on research and development, marketing, licensing and trading. With over 30 years of experience, Euroresearch has developed high quality products and positioned itself as a leading company in the collagen market. Because of well-established manufacturing processes, Euroresearch products typically have a high degree of purity and safety, thus ensuring optimum quality.

The company's mission began with the research and development of highly effective, innovative solutions for the treatment of chronic injuries. Based on this experience, Euroresearch developed the idea of investing in new technological solutions in the following areas: aesthetic medicine, traumatology and dentistry.

Nithya Collagen

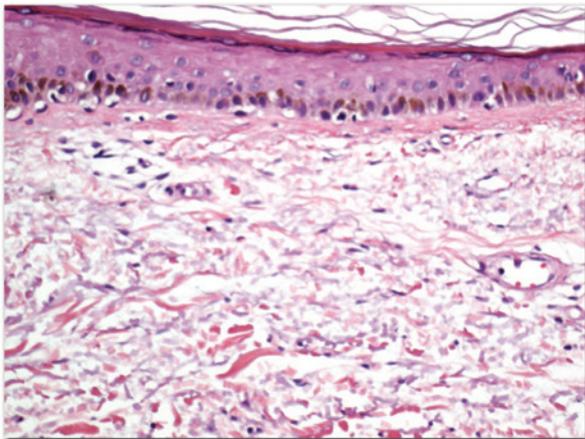
The mechanism of action of type I collagen is currently the subject of renewed interest thanks to the discovery of new molecular mechanisms involved in homeostasis of the ECM. The most recent findings regarding the ECM highlight the importance of molecular analysis in understanding the mechanisms ensuring homeostasis and the alterations occurring in fibrotic processes.

Nithya is composed of heterologous type I collagen micro-particles. A proprietary extraction technology produces a collagen with biomimetic properties that simulate polymerized collagen breakdown and thus stimulate fibroblast clustering and the deposition of procollagen and, as a consequence, type IV endogenous collagen.

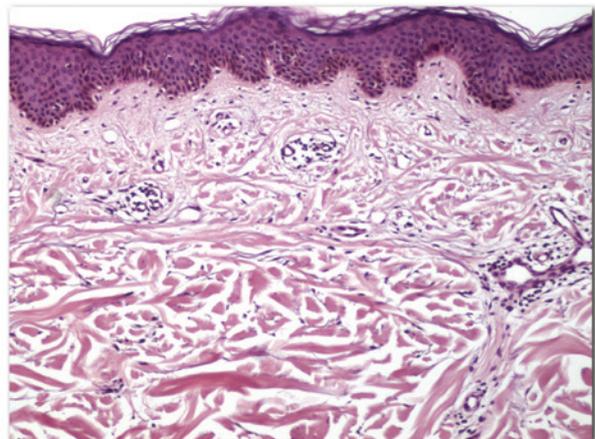
Starting from the premise that normal skin has an overall negative ionic charge while the cellular membranes in aging skin has a greater positive ionic charge, the process of micronization - producing biomimetic collagen microfibrils - improves the hydrophylic properties of type I collagen, giving a negative charge to the molecule. Thus charged, the collagen binds with tissue and remains bound longer, thus optimizing the disaggregation process of its triple helix structure.

Type I collagen binds to and exerts traction on type IV collagen fibrils on the surface of the fibroblast membrane, transducing this mechanical action into the production of new ECM (mechanotransduction). The type I collagen binds to type IV collagen in the ECM, giving rise to the process of mechanotransduction.

After 6 hours



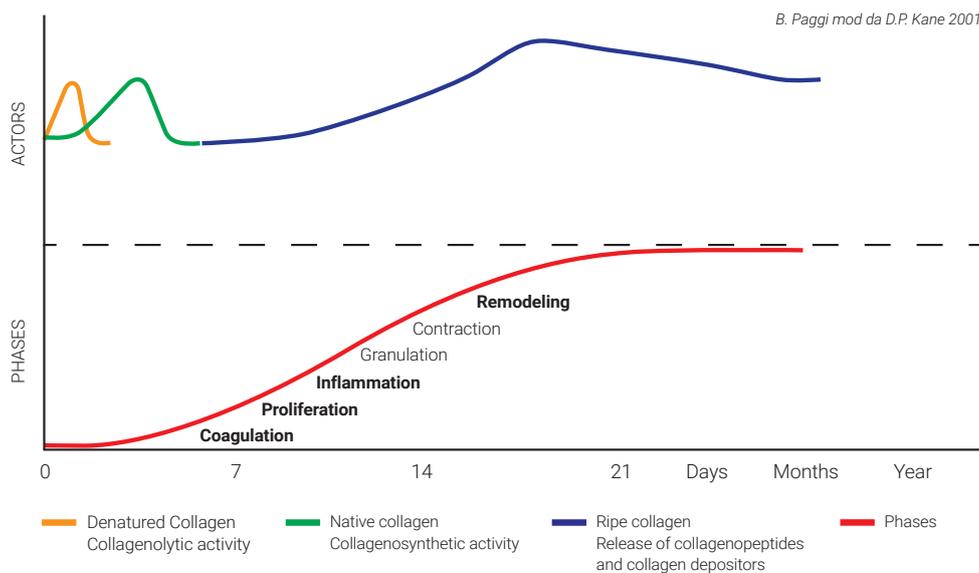
After 15 days



Collagen

The word collagen derives from the Greek kolla, meaning “glue” and the suffix - gen, “producing”. The term accurately characterizes the action of this protein within the structural matrix of the skin and organs. Collagen provides a structural matrix for various parts of the body such as connective tissue, cartilage, ligaments, tendons, bones, and teeth. It is insoluble in water and easily biodegradable and/or digestible in contact with acids or bases. There are more than 28 distinct types of collagen, with collagen types I, II and III making up the greatest portion (80 - 90%). Collagen is a protein taking the form of elongated fibrils found in abundance in the extracellular matrix (ECM).

Each type of collagen is made up of three alpha chains based on regular arrangements of the amino acids glycine, proline, hydroxyproline and hydroxylysine, with a glycine residue at every third position. Collagen may be considered a glycoprotein because some of its hydroxylysine residues are covalently bonded (glycosidic linkage) to a carbohydrate molecule. Anabolic processes predominate in collagen during growth and development of the body (as well as in scarring and fibrotic pathologies) but slow at a directly proportional rate as the body ages, leading to fragmentation, disorientation, and increasing rigidity of the fibrils. This theory is supported by experimental data demonstrating that collagen becomes increasingly insoluble with age. Repairing damaged tissues and the associated formation of new ECM are not the only recognized functions of collagen. It also plays a key role in regeneration processes, taking part in many different cellular functions. The roles most commonly attributed to collagen in tissue regeneration are those associated with an early and a late action. Collagen and fragments deriving from its breakdown regulate many cellular functions. Of primary importance among these is: cellular proliferation and the synthesis, differentiation, and migration of a certain number of proteins. We may thus state that collagen plays a key role in all phases of tissue regeneration.

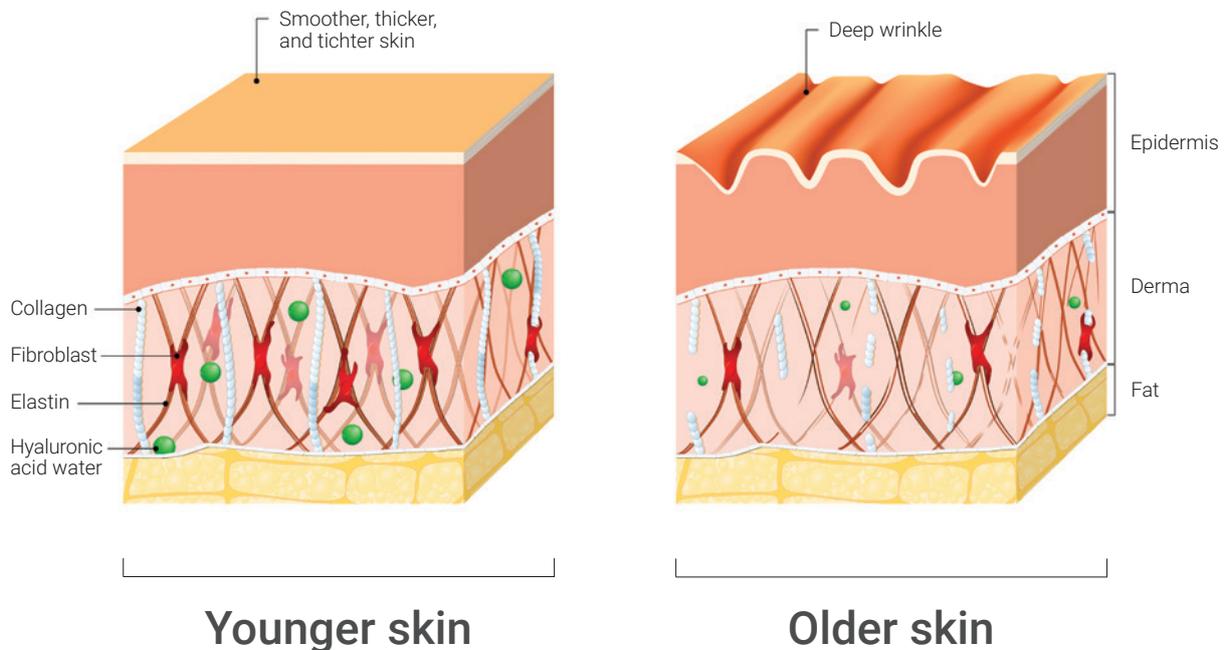


Dermal-Connective Bioregeneration

The goal of this process is structural regeneration via both physiological reaction and a sufficient chemical/mechanical stimulation to trigger a regenerative reaction without leading to chronic or granulomatous inflammation, both supporting and relaxing the skin. Type I collagen exerts a mechanical action on the fibroblasts, which are thus stimulated to produce new ECM and thus new collagen, elastin, and endogenous glucosaminoglycans.

This process, by means of which the cells regulate the mechanical properties of their environment, converts mechanical impulses into biochemical signals and thus leads to deposition, rearrangement or removal maintaining form and function.

Hence, the ultimate goal of the complex cell-matrix-cell interconnections in connective tissue is to develop and maintain homeostasis in order to promote and prolong structural and functional integrity of tissue. This is why we speak of dermal-connective bioregeneration. The action of Nithya collagen faithfully reproduces the physiological process of regeneration of the ECM, creating the necessary preconditions for restoring wellness.





Nithya protocol face

Medical Device CE, Class III. Injectable Nithya is available in packages of three 70 mg vials.

Indications

- For treating chrono - and photoaging of face, neck and hands
- For the regeneration of dermal and subdermal connective tissue via stimulation of fibroblasts and neocollagenesis
- For remodelling genetic deformations, such as dermal hypotrophy and hypotonia, and compromised skin elasticity

Instructions for use

Suspend the micronized collagen contained in one vial in 5 ml of physiological solution. Each vial of micronized collagen powder must be put into suspension immediately before use.

Protocol: Injection points

Divide the 5 ml of collagen suspension into five 1 ml syringes. This will facilitate distribution of the product: face (2-3 cc), neck (0.5-1 cc), décolleté (0.5-1 cc), and hands (0.5 cc). The product should be injected around the mouth and eyes in micro-punctures (0.1-0.2 cc and/or 0.05 cc each). Administer using fine needles (30-32 G) at the deep dermal level or at the dermal-subdermal interface (4 mm needle).

Frequency of treatment

Every 15-20 days from the first administration for a total of 30 days. The protocol is geared to cell regenerative turnover, which is characterized by an average cycle of 14-15 days, and thus it is very important to observe the treatment timeline to ensure a constant cell regeneration rate. A recall dose should be administered one month after the end of the protocol, and the treatment cycle should be repeated 3-6 months later depending on physician's judgement and results.





Nithya protocol face - mousse

Medical Device CE. Nithya mousse is available in 50 ml bottles.

Indications

- For use following aesthetic skin treatments, including minor operations, laser treatments, dermabrasion and peeling
- Nithya Mousse is the ideal complement to injection treatments because it promotes normalization and enhances outcomes

Instructions for use

Clean skin before application. Apply 2 to 4 times a day until skin is completely regenerated.

Thanks to its formulation and consistency, the mousse is the ideal complement to other therapies where collagen administration is necessary to support tissue regeneration.





Nithya protocol body

Medical Device CE, Class III. Injectable Nithya is available in a package containing one 200 mg vial.

Indications

- For treating cellulite, scars, stretch marks, sagging following aesthetic surgery such as liposuction
- Nithya Body is also indicated for treating body blemishes arising from chronoaging

Instructions for use

Suspend the micronized collagen in the vial in 10 ml of physiological solution.

Protocol: Injection points

Each vial of micronized collagen powder must be put into suspension immediately before use.

Divide the 10 ml of collagen suspension into four 2.5 cc syringes.

This will facilitate distribution of the product:

- Inner arm and thigh, inject 0.1 cc of suspension at each puncture point at the deep dermal level using a 4 mm 30 G needle;
- Stretch marks, tunnelling technique, injecting 1 cc of suspension using a 13 mm, 30 G needle;
- Abdomen, micro injections of 0.2 cc every 2 cm using a 4 mm 30 G needle.

Frequency of treatment

Results are already visible from the first application; however, to achieve a longer-lasting effect, it is recommended to perform at least three treatments at three-week intervals with a recall dose one month later.

The frequency of treatment depends on objectives, conditions of the patient and clinical assessment.





Nithya protocol body - cream

Medical Device CE. Available as a lotion in a 100 ml tube.

The fluid cream made of collagen and elastin is indicated for the firming and moisturising of all skin types. It is suitable for use after aesthetic surgery treatments such as liposuction, abdominoplasty or body sculpture, once the skin has fully healed.

Indications

Collagen helps to provide the necessary support structure to the dermis, moisturising it and contrasting the relaxation processes, giving tone and elasticity to the skin.

In addition to collagen, Nithya Body Cream contains:

- Elastin, which helps keep the skin supple;
- Jojoba, which counteracts two major causes of skin aging: dryness and lipid peroxidation.

Instructions for use

Apply the product morning and evening, promoting its absorption with a light massage.

Only for external use.





Anti-Age Activity and Tolerance Evaluation of Collagen Micro-Injection Treatment Associated to Topical Application of a Cosmetic Formulation (Investigator-Initiated Multicentre Trial)

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Received date: March 20, 2017; Accepted date: April 11, 2017; Published date: April 14, 2017

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Abstract

Objective: A novel equine type I collagen treatment consisting of an intradermal injection associated with the use of a topical mousse was developed with characteristics especially suited for global face rejuvenation. A multicenter, investigator-initiated, open clinical trial, conducted by 6 Italian centers, was carried out to evaluate the anti-age performance of this combined treatment.

Methods: The study was conducted on 72 female healthy subjects, age range 40-65 years, asking for midface volume restoration and presenting cutaneous aging/photoaging signs. The 1st injection treatment with the injectable product was performed immediately after the basal evaluation (T0). Two touch-up treatments were performed after 2 (T1) and 4 weeks (T2). Collagen mousse was to be applied by the volunteers on the face (including the submental area) twice a day, with a mild massage. Subject returned 2 (T3), 3 (T4) and 6 months (T5) after the 1st injection treatment for the follow-up evaluation. The aesthetics results were established through the use of clinical evaluations (Wrinkle Severity Rating Scale (WSRS), Facial Volume Loss Scale (FVLS), and wrinkles grade of the area around the eyes (Glogau's reference photographic scale)) and instrumental assessments (profilometry on skin replicas) supported by photographic documentation and face volume image analysis. Secondary endpoints were tolerance evaluation, performance duration and subjects' efficacy judgement.

Results: The study treatment determined a very significant reduction of all clinical parameters considered (Crows' feet grade, FVLS and WSRS) at every study time. Profilometry on crows' feet skin replicas and face volume image analysis confirmed the clinical evaluation, showing a statistical/clinical significant reduction of all the profilometric parameters (anti-wrinkle efficacy) and a consistent improvement of cheek volume (bio-revolumetric effect).

Conclusion: Obtained results confirm the anti-aging activity of the associated collagen treatment (injectable dermal filler and topical mousse). The aesthetic performance resulted persistent up to the final follow-up visit, sign of a long-lasting stimulating activity on cellular functionality of the associated treatment. The majority of volunteers underlined a very marked reshaping of face contour as well as an important improvement of skin smoothness, brightness and hydration. The study treatment was well tolerated, no unexpected adverse reaction related to the tested products/injection procedure occurred during the trial.

| | Sum of Medium, Marked and very Marked Judgements (Subject %) |
|-------------------------------------|---|
| Improvement of cheeks volume | 95% |
| Reshaping of face silhouette | 88% |
| Improvement of deep wrinkles | 87% |
| Improvement of superficial wrinkles | 95% |
| Lifting effect | 89% |
| Improvement of skin suppleness | 94% |
| Improvement of skin smoothness | 95% |
| Improvement of skin brightness | 93% |
| Improvement of skin hydration | 89% |

Summary table: Subject's judgements on the treatment efficacy (sum of subject % who expressed a medium, marked and very marked judgements).



Scientific literature

1. MENICAGLI C.
CHIMICA OGGI 1989; 4; 13.
2. MENICAGLI C.
II FARMACO 1988; 43; 381.
3. JASMAN J. ET AL.
CURR THER RES 1987; 42: 1066.
4. ABBOTT WM, ET AL.
SURG 1974; 75: 925.
5. CORVIN JY, ET AL.
CURR THER RES 1987; 42: 1066.
6. VISIER M. ET AL.
RIV IT STOM 1980; 6; 477.
7. MOTTA G, ET AL.
IT J SURG SCI 1983; 13; 101.
8. POSTLETHWAITE AE, ET AL.
J EXP MED 1976; 143; 1299.
9. DANON D, ET AL.
PROC NOTI ACOD SCI 1989; 86; 2018.
10. SCARMUZZI M, ET AL.
XII CONGR. NAZ. SOC. IT. RIC. CHIR.
MODENA, 20-22 NOVEMBRE 1986.
11. CHAVAPIL M, ET AL.
J SURG RES 1986; 41: 410.
12. OLUWASANMI J, ET AL.
J TRAUMA 1976; 16; 348.
13. COLLINS J, ET AL.
SURG FORUM 1976; 27; 551.
14. MIAN E, ET AL.
INT J TISS REOC 1992; 14: 27-34.
15. CANGIOTTI L, ET AL.
CONGR INT. DI ISTAMBUL.
ISTAMBUL, 23-24 MARZO 1990.
16. PALMIERI B, ET AL.
INT J TISS REAC 1992; 19; 21-25.
17. DI MAURO, ET AL.
DRUGS EXPTL CLIN RES 1991, XII (7): 371-373.

Matarasso SL. Injectable collagens: lost but not forgotten--a review of products, indications, and injection techniques. *Plast Reconstr Surg.* 2007 Nov [cited 2015 Sep 9]; 120 (6 Suppl): 17S – 26S.

Cukier J, Beauchamp RA, Spindler JS, Spindler S, Lorenzo C, Trentham DE. Association between bovine collagen dermal implants and a dermatomyositis or a polymyositis-like syndrome. *Ann Intern Med.*

1993;118:920–8

Klein AW. Techniques for soft tissue augmentation: An "A to Z." *American Journal of Clinical Dermatology.* 2006. p. 107–20.

Wong T, McGrath JA, Navsaria H. The role of fibroblasts in tissue engineering and regeneration. *British Journal of Dermatology.* 2007. p. 1149–55.

Brown RA, Phillips JB. Cell Responses to Biomimetic Protein Scaffolds Used in Tissue Repair and Engineering. *International Review of Cytology.* 2007. p. 75–150.

J.D. Humphrey, E.R. Dufresne, M.A. Schwartz "Mechanotransduction and extracellular matrix. Homeostasis" *Nat.Rev.Mol.Cell.Biol.*; Dec.2014



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