

LACTONYL©

"Milk Lacto peptides"
Cosmetic Grade Ingredient



"LONG LIFE SKIN ELIXIR"

Milk lacto peptides *LACTONYL*®



Peptides – Cosmetic interest

Peptides are very small pieces of proteins consisting of various numbers of amino acids. They are the most important part of all body and cellular activity.

All proteins and enzymes which regulates metabolism are composed of peptides. They have various functions and multiple activities on the skin (epidermis).

Naturally occurring water soluble biological molecules with low molecular weight

They are short chains of <u>amino acid monomers</u> linked by <u>peptide</u> (<u>amide</u>) bonds formed when the <u>carboxyl</u> group of one amino acid reacts with the <u>amino</u> group of another.

Peptides are distinguished from <u>proteins</u> on the basis of size, and as an arbitrary benchmark can be understood to contain approximately 50 or fewer amino acids.

Proteins consist of one or more polypeptides arranged in a biologically functional way, often bound to ligands such as coenzymes and cofactors, or to another protein or other macromolecule

Amino acids that have been incorporated into peptides are termed "residues" due to the release of either a hydrogen ion from the amine end or a hydroxyl ion from the carboxyl end, or both, as a water molecule is released during formation of each amide bond. [2] All peptides except cyclic peptides have an N-terminal and C-terminal

Lacto peptides

Milk Lacto peptides, derived from milk protein, are bio active peptides found in milk under Tri-peptidic form (Casein):

- Isoleucine-Proline-Proline (IPP)
- Valine -Proline-Proline (VPP)

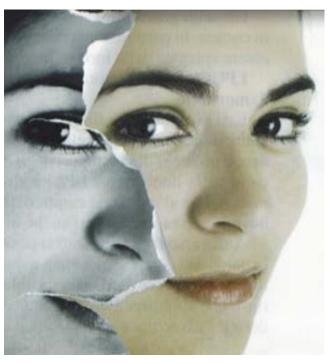
With age collagen fibers are becoming weaker until being destroyed and not replaced. The consequence is that your skin appears thinner and wrinkled over time.

Cosmetic concept

Peptides are effective in improving the appearance of fine lines (wrinkles).

Human collagen content decrease with age and pre-matured wrinkles start to appear. One cosmetic way to minimize pre-matured winkles appearance and make your skin looking younger could be to replace "lost or deteriorated collagen" by new native collagen (stimulation of new collagen). Which formation decreases with age. When collagen breaks down, it forms specific peptides. Those peptides act as a signal to tell your skin it was damaged and to induce the production of new collagen.

Applying peptides directly to your skin is a way to trick your skin into thinking that it has lost collagen recently and needs to make more new collagen. By dermal application in an appropriated cosmetic base, Lacto peptides will re-activate the native collagen production



Because peptides are small, they can penetrate the skin's protective barriers to get to the deeper layers.

- IPP: tri-peptides complex acting as skin conditioner improving skin softness and smoothness
- **VPP**: tri-peptides complex improving skin feeling acting as **skin and Hair conditioner**

Proline can break down protein to help create healthy cells and connective tissues, promoting firmer, glowing skin and reducing sagging, wrinkles and aging of skin due to sun exposure.

This amino acid is seen in cosmetics and beauty products primarily as a hair and skin conditioning agent, but also as a fragrance ingredient. It can

also be used in formulas to act as a **moisturizer** when mixed with water. Proline has also been used in hair trials as one of four amino acids to help strengthen the hair shaft.

Donkey milk contains many elements such as amino acids, tri-peptides, minerals and Vitaminic complex. It has been established also that copper if found into the composition of DM (copper (mg/100 g : 0.35/0.38)

When copper is attached to a peptide, the peptide can deliver copper to the living layers of the skin. It has been shown that copper is an effective agent in skin healing. **Copper peptides** seem to promote collagen production and act as antioxidants. They are needed for natural healing and regeneration of your skin and to help remove damaged collagen.

The synergy between Donkey milk lacto peptides and Minerals contributes to accelerate all the metabolic reactions and participates to maintain your skin in good health conditions

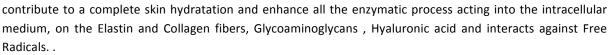
Lacto peptides from Donkey milk in Dermo-cosmetics

Since Hippocrates period, many studies on Donkey's milk have been conducted focusing on skin benefit. Today with all the scientific background it has been demonstrated the following properties:

- Stimulation of Fibroblast metabolism (Elastin and Collagen)
- · Activation of the endogen production of Collagen fibers
- Enhancement of Skin moisturization
- Protection against Free Radical production

Some visible results can be observed within 10 days.

All the components contained in the milk are biocompatible with the human skin and easily absorbed. They participate and



In the Donkey's milk we find an amino acid such as "Lysine" having a nutritive activity on the Fibroblast and increasing skin vitality.



Can be used as Fresh milk by mixing 100 g of Lyophilized Milk powder with 900 gr of pure water (1 liter of Fresh milk). In this case the product obtained is active and can be used immediately and directly in an appropriated formulation. The final formula must be microbiologically stabilized to avoid any kind of possible contamination.

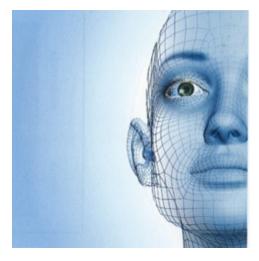
Or

can be used under powder form (Lyophilized) in any type of formulation under the same conditions. The final formulation must be well protected (appropriated preservative system) and filling must be done under strict hygiene conditions (Laminar Flux for example)

The lyophilisation process is made at -50/70°C under specific conditions to maintain all the components active. The Powder milk is filled into a special tin under vacuum.

Main Characteristics of Milk Lacto peptides from She-Donkey's milk for Cosmetic use

- Specific agreement from European administration and ASL
- Documents with Traceability from producer to identify the origin
- Control of the cold chain
- Complete Quality control
- · analytical and microbiological Analysis quali quantitative of all the elements contained in the milk



Skin Care benefits of each components

Minerals, Amino acids, Vitamins, Fatty acids, Proteins, peptides, enzymes, co enzymes, Growth factors are presents in the Donkey's milk milk.

Vitamins found in Donkey's milk

Vitamins into the Lyophilized version are :, Vit B, Vit C, , They contributes to :

- 1. Increase of water into the interstitial liquid Enhance water retention
- 2. Maintain a good trans epidermal water balance / Hydro lipidic film
- 3. Maintain a good skin elasticity
- 4. Skin repair activity (cicatrization wound healing)
- 5. Vit A: Cellular protection Skin regeneration
- 6. Vit B12: Participates in DNA synthesis

Amino acids

The main amino acids found in Donkey's milk powder are

Arginine, Cisteine, Istidine, Isoleucine, Leucine, Lisyn, Methionine, Phenylalanine, Threonine, Triptophane, Tyrosine and Valinine

- 1. Threonine: Participates at collagen and Elastin formation
- 2. Leucine: Acts at the wound healing processes
- 3. Arginine: improve collagen synthesis
- 4. Lysine: Cell's repair actions. Participates in collagen synthesis

Minerals

The main minerals found in the milk are: Calcium, Sodium, Potassium, Phosphor, Magnesium, Iron, Selenium, Zinc, Copper, Iode, Manganese, Chrome..

- 1. Participate to the cells regeneration mechanism, enter in the Repair process,
- 2. anti inflammatory and anti irritation mechanism .
- 3. Calcium: Reinforces cell's membranes
- 4. **Copper:** stimulation of new collagen fibers
- 5. **Selenium**: Free Radical protection Reduction of aging process
- 6. Magnesium: Basic for Calcium and Vit C assimilation
- 7. Sodium: Facilitates cell's metabolisms
- 8. **Phosphorous**: Essential role at energy transfers

Proteins, Enzymes and Co enzymes

Lyzozyme (Specific Protein) having

- 1. Anti inflammatory activity
- 2. Skin repair activity (Treatment of cutaneous wound)
- 3. Anti irritant properties

Lactoferrine (Glyco protein)

- 1. Anti bacterial activity
- 2. Anti viral activity
- 3. Anti fungal
- 4. Stimulation of Fibroblast and Epithelial cells
- 5. Interact into the cicatrization process Wound healing

Leptin (Protein hormone)

- 1. Acts on cutaneous metabolism- Improve micro relief
- 2. Decrease the excess of fatty components into the interstitial fluid
- 3. Inhibits lipogenesis
- 4. Reduce oily skins
- 5. Astringent Pore reducer

Growth Factors

- 1. Improves and accelerate Cells renewals mechanism
- 2. Participate to a deep Dermo purification Detoxication- Emollient
- 3. Recommended for Atopic skin Sensitive skins and dry skins
- 4. Reduce itching sensations

Fatty acids (Omega 3 and 6)

- 1. Participates to the Fillagrin synthesis
- 2. Re densification of subcutaneous layers
- 3. Protects epidermis against water loss
- 4. Facilitates the absorption of liposolubles vitamins (A; D, E)

Lacto albumin and lacto globulin

- 1. Skin Tensor effect
- 2. Improvement of skin brightness

Lattosio (Di-saccharides)

- 1. Emollient and Hydrating factor
- 2. Cutaneous Anti inflammatory
- 3. Reduce skin irritation



Cosmetic activity of Milk Lacto peptides Lactonyl®

- Reduce Eye Wrinkles (see graph 4)
- Quick visible and perceivable tensor activity
- New collagen and New Elastin precursor
- Rebalance the Hydro lipidic film
- Reduce itching and skin irritation Calming effect
- Prevent skin inflammation
- Restore skin microrelief
- Protect the epidermins against Free Radicals action
- Improve and enhance Hydroretention mechanism
- Give to your skin a better skin appearance and elasticity
- Recommended for sensitive and Atopic skins

Cosmetic formulation / Advises and suggestions

Milk lacto peptides are obtained from Farmed She Donkey milk and lyophilized after collection Recommended use dosage :

- Anti Age Nourisching cream: around 5%
- Daily Facial Moisturizing cream or lotion: around 3%
- Baby anti irritant cream : around 3%
- Hand Cream around 1%
- Soap for sensitive dry skins: around 0.5%

Cosmetic application

- Sensitive atopic skins
- Aged tired skins
- Irritated skins
- Baby irritated skins

Skin's benefit

- Anti irritant and Anti inflammatory properties / Prevent Skin inflammation/Hypoallergenic skins
- Enhance Skin moisturizing process /Rebalance Hydro lipidic film/ Improve skin appearance
- Protection agains Free Radicals / Stimulation of New collagen (fibroblasts)

Milk Lacto Peptides LACTONYL© **DERMO COSMETIC ACTIVITY / TEST PROTOCOL**

Test conducted at the University of Sciences of Bale and Magdeburg (section Biology-Chemistry) by Doctor- Pharmacologist

A. ORSINGHER

1 - REVITALIZING - SENSORIAL clinical TEST (In vivo)

Number of Human (Females) on which the test has been conducted → 36 Females

Age group → 25 up to 68

Skin Type: Caucasian (Europe/Italy)

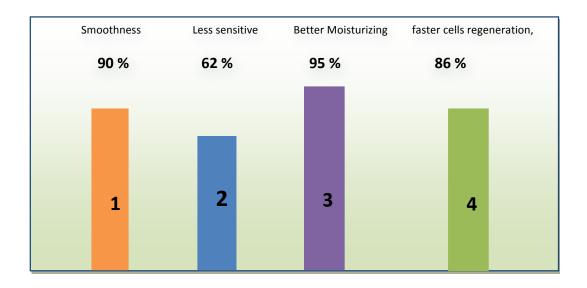
Duration: The cream has been applied during 4 weeks everyday versus a Placebo cream

Active substance used in the Formula: Lyophilized Donkey Milk (Lactonyl)

Concentration: 55% of diluted 5% Lyophilized Lactonyl in sterile water(Donkey Milk) /2.75% of Lactonyl in the formula

(water phase 55%) Emulsion type w/o

Test Result conducted by Dermatologist (cream versus Placebo)



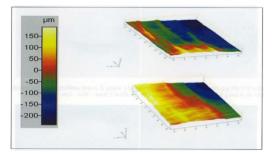
- $1 \rightarrow$ Skin appears to be smoother (90%)
- 2 → Skin is less dried / less Sensitive (62%)
- 3 → Moisturizing and hydro retention skin feeling (95%)
- 4 → Quicker skin regeneration (86%)

2 - Wrinkles Reduction (In vivo test on 3 patients)

Test Protocol: same as Test 1:

Comparative observation between 3 Patients treated 28 days with a 2.75% Milk Lacto peptides Cream

- Comparative Test D0 and D28
- Reduction of small wrinkles



- Patient 1 / Female 50 years
- Patient 2 / Female 58 years
- Patients 3 / Female 60 years

Results

Micro Photos taken before and after daily application

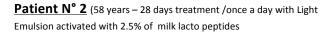


Before application (D0)

After 4 weeks application (D30)

<u>Patient N° 1</u> (50 years – 28 days treatment /once a day with Light Emulsion activated with 2.5% milk lacto peptides

Wrinkle Reduction around 62% \Rightarrow (deepness reduction)



Wrinkles Reduction around 42% (deepness and length)



After 4 weeks application (D30)



<u>Patient N° 3</u> (60 years – 28 days treatment / one a day with light emulsion activated with 2.5% of milk lacto peptides

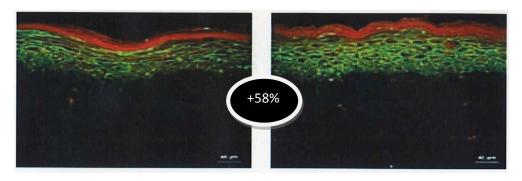
Wrinkles Reduction around 40% (deepness reduction)

3 - Cells Migration/ in Vitro Test (colorimetric test)

In Vitro Lab Test (Human skins)

Analysis of Skin reconstitution after 12 days

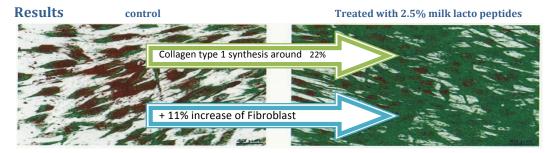
- Stimulation of Proteoglycan (Repair Process Migration of Proteoglycans into the extra cellular matrix
- Color Phosphorescence



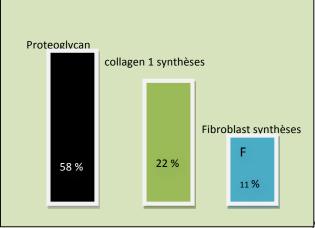
4 - FIBROBLAST / COLLAGEN Synthesis in Cellular Membrane

DERMICAN Laboratory Clinical Test under Dermatologist control

- 4 months application
- Cream used: 2.5% Milk lacto peptides cream (Lyophilized Donkey Milk) diluted in 55 % water phase



All those tests have been conducted on Human skins using a light emulsion activated with 2.5>% of Milk lacto peptides from She Donkey



- 1 Stimulation of **Proteoglycan** synthesis (pseudo derma) 58 % : **P**
- 2 stimulation of Collagen synthesis + 22 % : C
- 3 Stimulation of Fibroblast synthesis + 11%: F

Results after Daily application during 4 weeks

5 - Anti Inflammatory Skin Activity

Many publications indicates that the Lactoferrine fraction of Milk lacto peptides inhibits the production of pro inflammatory cytokines (TNF- α and IL-6) reducing skin inflammation mechanism.

Figure 1: Anti Inflamatory activity / Re equilibrium of Hydro lipidic Film (Fig 1)

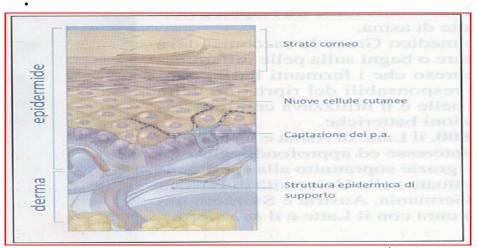
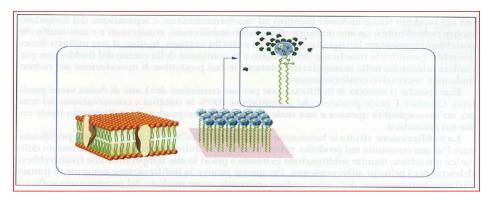


Figure 2 Milk lacto peptides distribution into the stratum corneum/
Diffusion into the extra cellular matrix (Regeneration process)



Figure 3 (Migration and release process of Fatty Components of Milk lacto peptides (Lactonyl®)into epidermis acting against Free Radicals



Annexes

Milk LACTO PEPTIDES "Lactonyl®"



« Vitamins content »

Vitamin B1	Vitamin B2	Vitamin B5	Vitamin B6	Vitamin B9	Vitamin B12	Vitamin C
Thiamine	Riboflavin	Pantothenic acid	Pyroxidine	Total Folacines	Cabolamines	Ascorbic acid
mg/kg	mg/kg	mg/kg	mg/kg	ug/kg	ug/kg	mg/kg
0.6	1.1	14.8	1	85	2	230

SKIN and HAIR Benefits

Vitamin B1	Contains sulfur – key element of Keratin. Gives energy to the Hair follicles
Vitamin B2	Acts on Keratin elasticity and improves Keratin resistance. Reinforces Hair structure
Vitamin B5	Participates and enhances Hair growth process. Prevents Hair loss.
Vitamin B6	Vit B6 combined with Vit B12 play an essential role in reduction of Hair loss
Vitamin B9	Enters in the synthesis of methionin (Sulfur amino acid)playing an important role in the synthesis of Keratin (precursor and activator of Keratin synthesis)
Vitamin B12	direct action on Hair when combined with B6 , Folic acid, biotin
Vitamin C	Aids iron absorption

Shedonkey milk lacto peptides « Minerals content »

Calcium	Iron	Magnesium	Copper	Selenium	Zinc	Phosphor
mg/100g	mg/100g	mg/100g	mg/100g	ug/100g	mg/100g	mg/100g
815	2.09	93.5	0.36	7.8	1.56	486

SKIN and HAIR Benefits

Calcium	There are many factors that affect hair loss. Calcium and magnesium imbalance is a common contributor. Reinforces the cell membranes and activates certain enzymes vital for the skin's metabolism
Iron	Iron is important in hair health , and these foods are rich in it. An iron deficiency causes hair loss
Magnesium	There are many factors that affect hair loss . Calcium and magnesium imbalance is a common contributor. It is a basic mineral for human nutrition. It has metabolic functions a key role at the production and transport of energy. This mineral participates at the protein synthesis and at the activation of certain enzymes. It is indispensable for the correct assimilation of calcium and vitamin C. It is also a good moisturizer .
Copper	The metal copper controls hair growth and hair loss. Healthy tissue concentrations of copper lie between 1.7 and 3.5 milligrams
Selenium	Selenium is a mineral that has been shown to be essential for hair and skin health. Recent study showing the benefits of selenium for hair and scalp. Selenium, along with zinc, can help your body properly utilize proteins and hormones to produce more hair. It has also been found that vitamin A, C, E and vitamin B6 aid these two minerals in promoting hair regrowth. Along with vitamin E, it has an anti-oxidant activity. It protects the cellular membranes by neutralizing the oxidative free radical actions, delaying the tissues aging process
Zinc	Deficiency in zinc can contribute a lot to hair shedding because without zinc and other related minerals, you hair shafts get weakened, causing hair breakage and very slow hair regrowth. Zinc benefits for hair include promotion of cell reproduction, tissue growth and repair broken tissues . It also maintains the oil-secreting glands that are attached to your hair follicles, thus decreasing their chances of falling off
Phosphorus:	For every form of life, phosphates play an essential role in all energy-transfer processes such as metabolism, photosynthesis, nerve function, and muscle action. The nucleic acids which among other things make up the hereditary material (the chromosomes) are phosphates, as are a number of coenzymes