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#### The conception

- Problem of discoloration
- Post-sclerotherapy

| An | Fast Action<br>Windown - Urown | <text></text> |
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# Developments of the idea ...



On the pharmaceutical market existed :

Mercaptoacetic acid: keratolytic and exfoliating

✓Heparinoids: wrongly used being anticoagulants

✓ Oxide of vitamin K along with vitamins A, C and E, and other active agents: bland antioxidant action.





# Our research is focused on a new concept : substances iron chelators

The chelation of metals is the uptake of a metal-ion through anionic radical of a molecule.

The chelating activity is an important biological mode in all living organisms, is sufficient to recall the Hemoglobin, the protein that contains within it the groups Eme, polypeptides which in turn include a chelate, in this case the Iron.





## Which chelator?

#### **Chelating agents of Synthesis**

#### EDTA DEFEROXAMIN CLIOCHINOLO

(hard to handle the first, and toxic the seconds)

#### **Endogenous chelating agents**

# LACTOFERRIN

Ideal Chelating agent?





We focused our attention on lactoferrin derived from cow's milk (structurally similar to the human one).

The Lactoferrin is a glycoprotein mainly present in breast milk, but is present in many secretions such as tears and saliva with a strong chelating action of the iron.

Until now, it was investigated for topical use, only from a microbiological point of view: showing antibacterial, antiviral, antifungal and anti-inflammatory activity. Not always iron-dependent

Advanced studies, for systemic use of lactoferrin as antianaemic, are currently available.





### General information on Lactoferrin

### The Lactoferrin is a chelator endogenous which belongs to the family of transferrins.

The Lactoferrin is able to chelate iron (two atoms) at neutral or alkaline pH and of release at acidic pH.





#### THREE DIMENSIONAL STRUCTURE OF LACTOFERRIN



The three-dimensional structure of lactoferrin, consists of a single polypeptide chain of 692 amino acids, is organized in two globular lobes joined by a alpha-helix.

Each of the two lobes of the protein consists of two domains. The protein is structured in such a way such as to have a single binding site for the iron for each lobe, located in each of the faces internal of intra-dominial space.

The binding properties of lactoferrin are developed through the combined action of 4 residues amino acid identical for each lobe and and include, in addition to the ferric ion, a counter ion (normally a CO32-), synergistic for each Fe3 +. This set of ligands is chemically and geometrically ideal for a high binding affinity reversible with iron and the presence of a non-protein element (CO3 2 -) seems to be a necessary condition both for the bond, and for the release of iron.





## **OBJECTIVES** Our goal was to make it:

# ✓ more bioavailable✓ more stable for topical use

The denaturation leads to chelator inactivity of lactoferrin.





## LIPOSOMES The system of vehiculation at controlled-release most recent is represented by LIPOSOMES.

The liposome term comes from the Greek "lipos" (fat) and "soma" (body). So literally means "body fat."





# NANOTECHNOLOGY



The inclusion of the substance in functional Nanolipids provides excellent protection and bioavailability.





# Analogy between the structure of the cell membrane and Nano LPD's









# USE AND BENEFITS

- Increase the effectiveness and reduce the side effects of the active ingredients (toxicity).
- They are similar to the structure of cell membranes.
- Extension of the bioavailability of the active ingredient.
- Better absorption, penetration and diffusion of the active ingredient.
- Stabilization of the active ingredient.





# Design and development of a natural Chelating cream in nanolipids for topical use.

# <u>Chelaskin</u>

lactoferrin in nanolipids

Patented





# "Primum non nocere" Patch-test

University of Naples Faculty of Pharmacy

> result: NOT IRRITATING





# **Chelaskin Action**

Chelaskin performs immediate removal of bruises, post-filler, post-mesotherapy, post-sclerotherapy, postlaser, post skin-roller, post-dermoabrasion, post-rhinoplasty, and so on...

It allows to extend filler's half-life, thanks to the anti-metal protease chelating action.

It performs an efficient purifying action, removing all dermal deposits of heavy metals (iron, lead and zinc) which concur to skin aging.





## Mode of action

Main characteristic of Lactoferrin is to have a molecular conformation such as to host within itself two ions iron thus allowing to adjust the transport and absorption, as well as increase its bioavailability.

It is believed that this is the only system for integrating the iron in every cell of the human body and the use of Lactoferrin permitting its introduction in much lower dosages than those used up to now, since it increases the bioavailability and then absorption.





## **Anti-inflammatory Activities**

As regards the ability anti-inflammatory of the Lactoferrin, significant traces have been noticed in the circulation during the inflammatory phase, resulting from activated neutrophils.

This evidence suggests that the Lactoferrin put into circulation acts in such a way as to inhibit the excessive production of cytokines and preventing the excessive recruitment and activation of leukocytes in the inflamed areas.





## FIRST APPLICATION TREATMENT OF A BRUISING WITH CHELASKIN CREAM



RESULT AFTER 48 HOURS with partial application on half bruising











#### STATUS OF THE ECCHYMOSIS AFTER 72 HOURS OF TREATMENT WITH CHELASKIN CREAM







# AFTER SCLEROTHERAPY

## APPLYING CHELASKIN AT THE SAME TIME, NO ECCHYMOSIS ANYMORE.







# ACCUMULATION OF IRON

Iron is essential for life.

Used for the transport of oxygen in the blood to keep it stored in the muscles, the cellular respiratory activity, for cell replication and to build the structure of tissues and organs.

Furthermore is the constituent of many metal-enzymes (without the iron the enzyme loses its capacity) including catalysis and cytochromes.

### But when it is in excess?

Iron in excess is toxic and can be fatal.







# HEMOSIDERIN

The hemosiderin is a form of parenchymal stable storage of iron.

The hemosiderin accumulates and causes the skin discolourations in particular when the vascularity of the tissue is not effective.

Instead, in a well-vascularized tissue, hemosiderin does not have the time nor the way to be produced, because the ferric iron is immediately chelated by proteins such as transferrins, which shall remove it from the area.





# CHRONIC VENOUS INSUFFICIENCY and IRON

The accumulation of iron in tissues, in case of CVI, is evidenced by the presence of brown hemosiderinic discoloration but also by pathophysiological conditions previously exposed and it is likely that this accumulation interacts with the surrounding structures, see extracellular matrix, motivating at least in part, the 'activation of a reactive sequence which causes over-expression of metalloproteinases, mainly responsible for the remodeling of the matrix (lipodermatosclerosis).

The sequence that justifies the presence and accumulation of iron (which we remind as a metal ion it does not possess autonomous bioavailability), is represented by the extravasation of formed elements, in particular the red blood cells. These latter are degraded by interstitial macrophages and iron is liberated and subsequently incorporated by Hemosiderin that gives rise to clinically evident discoloration.





# SYNERGY OF ACTION:

# Lactoferrin in nanolipids

# Development of the Product in CREAM





# GREAT SYNERGY REMODELING OF THE MATRIX

## Skin much more toned

Revascularization





# THE SYNERGY LEADS TO:

## $\checkmark$ Chelation of zinc and calcium

 Inhibition of metalloproteinase (zinc-calcium dependent)





it's obvious that

## lactoferrin chelates iron in depth

it contributes to the healing by using its many <u>activities</u> :

- chelating
- antibacterial
- antivirals
- antifungal
- anti-inflammatory





# Synergy with HYALURONIC ACID FILLER

- Avoids Ecchymosis
- Strengthen The System For The Presence Of Antimetal-protease.
- Greater Permanence In Situ Of The Hyaluronic Acid.





#### INDICATIONS

<u>Aesthetic Medicine</u>: bruises after filler, mesotherapy, needling, laser, RF, discoloration of sclerosing.

Aesthetic surgery: rhinoplasty, liposuction, blepharoplasty, lifting.

<u>Home indications</u>: dark circle, vascular sign (couperose, teleangectasie, rosacea), dark spot.

#### HOW TO USE

To apply on the skin and massage gently.

#### DOSE

Each dose is of 0,15mL. The quantity to use it depends by the dimension of the area to treat.

#### FREQUENCY

For aesthetic medicine indications one application is enough immediately after the session.

For aesthetic surgery, it needs the applications at home by the patient. For homecare indications: apply twice (morning and evening) on the area.

It is suggetsed to wait for the total absorption before makeup or bandages to use.







# THANK YOU FOR YOUR ATTENTION