indena®

INDUSTRIA
DERIVATI
NATURALI

GLI ESTRATTI DI PIANTE: DA TUTTO IL MONDO UN SOSTEGNO ALLA BELLEZZA E ALLA SALUTE

FROM ALL OVER THE WORLD, PLANT EXTRACTS SUPPORT BEAUTY AND HEALTH

Con il patrocinio di

LE UNIVERSITÀ PER EXPO 2015
COMITATO SCIENTIFICO DEL COMUNE DI MILANO

Giada Maramaldi

MORE THAN ONE METABOLISM

COMPOUNDS OF **PRIMARY** METABOLISM

Primary metabolism refers to compunds absolutely necessary for life such as:

- Energy sources
- Genetic material
- Proteins
- Components of cells membranes

COMPOUNDS OF **SECONDARY** METABOLISM

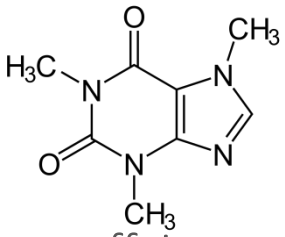
Secondary metabolism refers to molecules that are NOT required for the short term functioning of an organism.

- Toxic to the animals that eat the plant
- Pigments in flowers to attract pollinators

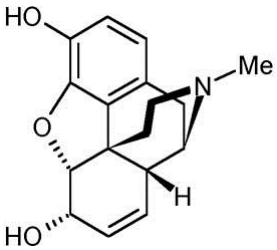
indena®

MORE THAN ONE METABOLISM: MANY COMPOUNDS!

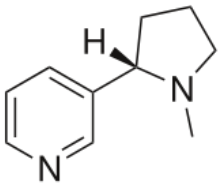
ALKALOIDS



caffeine

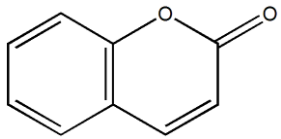


morphine

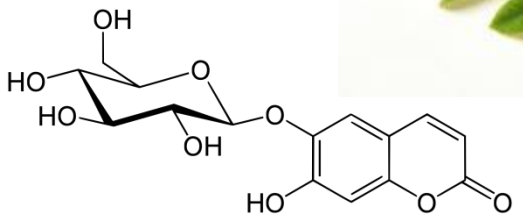


nicotine

COUMARINS

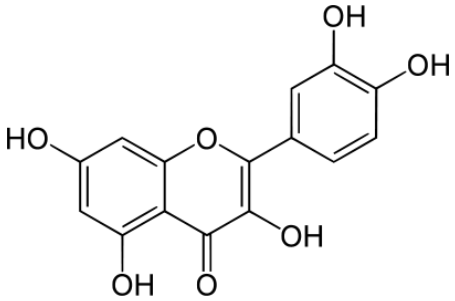


coumarin



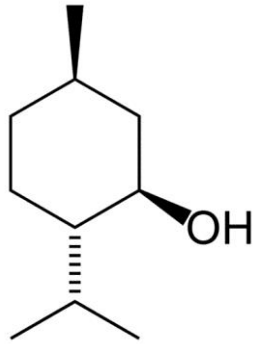
aesculin

AND FLAVONOIDS!

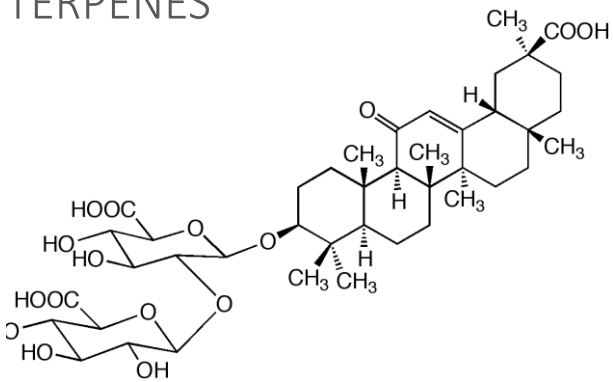


quercetin

TERPENES



menthol



glycyrrhizin

indena®

PROLOGUE

Plants for beauty

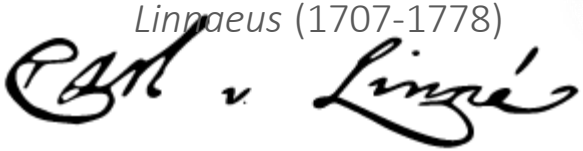
indena®

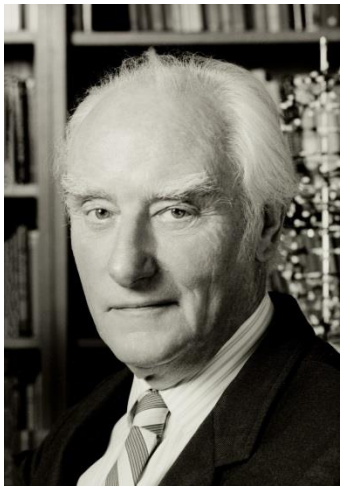
PROLOGUE

Understanding of life

«Herbs and plants are medical jewels gracing in the woods, fields and lanes which few eyes see and few minds understand.»

Linnaeus (1707-1778)





«Almost all aspects of life are engineered at the molecular level, and without understanding molecules we can only have a very sketchy understanding of life itself.»

Francis Crick

(Nobel Prize for Medicine in 1962)

indena®

INTRODUCTION

Nomadic hunter-gatherer societies passed on, by oral tradition, their **empirical observations** about the different kinds of **plants** that they used for food, shelter, but also poisons, **medicines**, for ceremonies and rituals etc.

The nomadic life-style was drastically changed when settled communities were established Neolithic Revolution which extended from about 10,000 to 2500 years ago depending on the region. With these communities came the development of the technology and skills needed for the **domestication of plants** and animals and the emergence of the **written word** provided evidence for the passing of systematic knowledge and culture from one generation to the next.

indena®

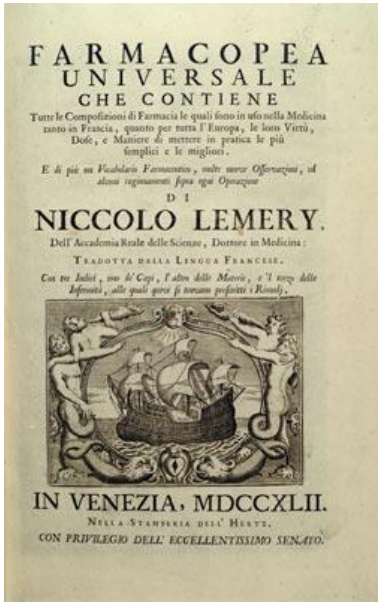
INTRODUCTION

Natural products for health care: medicinal plants (V-X cent)

Hortus simpliciorum (ca 1500)

Pharmacognosy is the study of medicines derived from natural sources. The ASP defines pharmacognosy as "*the study of the physical, chemical, biochemical and biological properties of drugs, drug substances or potential drugs or drug substances of natural origin as well as the search for new drugs from natural sources.*"

EXTRACT DEFINITIONS ACCORDING TO PH. EUR.


FARMACOPEA
UNIVERSALE
CHE CONTIENE
Tutte le Compositioni di Farmacia le quali sono in uso nella Medicina tanto in Francia, quanto per tutta l'Europa, le loro Virtù, Dose, e Maniere di mettere in pratica le più semplici e le migliori.
E di più un Vocabolario Farmaceutico, molte nuove Osservazioni, ed alcuni ragionamenti sopra ogni Operazione
DI
NICCOLO LEMERY.
Dell' Accademia Reale delle Scienze, Dottore in Medicina:
TRADOTTA DALLA LINGUA FRANCESE.
Con tre Indici, uno de' Capi, l'altro delle Materie, e l'terzo delle Infermità, alle quali quest si trovano profittevoli i Rimedj.
IN VENEZIA, MDCCXLII.
NELLA STAMPERIA DELL' HERTZ.
CON PRIVILEGIO DELL' ECCELLENTISSIMO SENATO.

Extracts (Extracta)

Different types of extract may be distinguished.

Standardised extracts:

are adjusted within an acceptable tolerance to a given content of constituents with known therapeutic activity; standardisation is achieved by adjustment of the extract with inert material or by blending batches of extracts.

Quantified extracts:

are adjusted to a defined range of constituents; adjustments are made by blending batches of extracts.

Other extracts:

are essentially defined by their production process (state of the herbal drug or animal matter to be extracted, solvent, extraction conditions) and their specifications.

(Ph. Eur. 6.2)

indena®

ADVANTAGES OF EXTRACTS VS DRUGS

Extracts, unlike drugs (part of plants):

- Have a **higher amount** of active compounds
- **Toxic** or undesired compounds may be **removed**
- Long shelf life
- Greater availability
- Final **form** is **easier** to manage

"Drug" in pharmacognosy means the part of the plant used – it derives from the German word "**troken**"= dried

indena®

EXTRACTION: WHAT IS IT ABOUT?

Maceration: the solvent and the drug are put in contact until the saturation balance is reached

K= a. p. conc in extracting solution/a.p. conc in residual drug

Percolation: the drug is treated with the solvent until exausted: fresh solvent on residual drug – balance is moved.

indena®

WHERE DO WE FIND EXTRACTS?

From the plant: Plant – extraction industry – extracts for:

- Drugs
- Food and **supplements**
- **Cosmetics/**Medical devices

Let us not forget additives, feed, eccipients…

Quality issues, although regulated by different laws in the different sectors, are **very similar**.

indena®

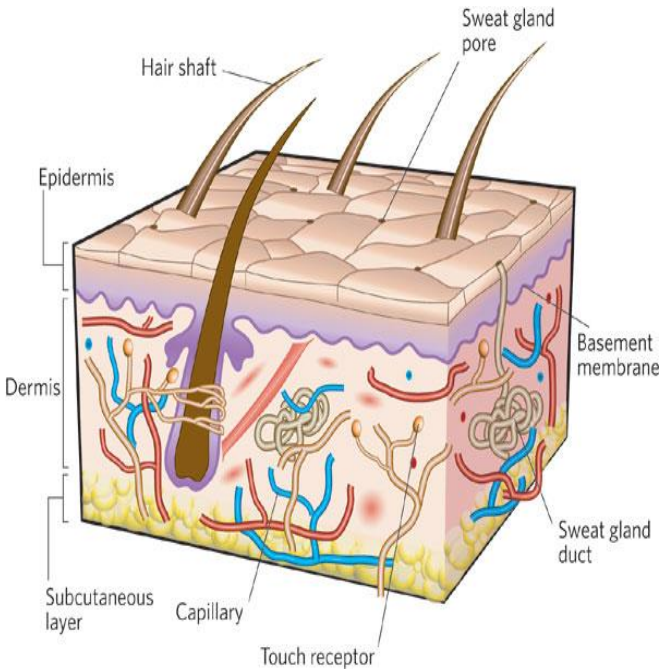
SKIN BIOLOGY

SKIN HYDRATION

Hydration and moisture are essential for a healthy biological activity, and being the skin the largest organ of our body, it is very sensitive to dehydration.

ANTI-AGEING

Anti-ageing strategy comprises **anti oxidants**, **free radical scavengers**, **cells renewal promoters**, UV protection, ect.



CONNECTIVE TISSUE PROTECTION

In the dermis, cells are immersed into an extra-cellular matrix which contains **collagen**, **elastin** as proteic fibers, hyaluronic acid as polysaccharide for **mechanical** properties.

RESTRUCTURING SKIN

The **skin barrier function** is crucial in protecting our organism from external threats.

SOOTHING, LENITIVE

Over reactive and sensitive skin is to be **soothed** by lenitive products

indena®

SKIN CARE

SKIN HYDRATION

XILOGEL®

CONNECTIVE TISSUE PROTECTION

CENTELLA ASIATICA DERIVATIVES

ANTI-AGEING

SILIPHOS®

RESTRUCTURING SKIN

OMEGABLUE®

SOOTHING, LENITIVE

BOSEXIL®

indena®

XILOGEL®

GENERAL OVERVIEW

Tamarind is considered as one of the most beautiful trees growing in the South East of Asia.

Belonging to the Leguminosae family, it is also called Tamar-hindi, referring to its presence in the Indian regions.

Its young pods are used for nutrition (savory, sour and acidic) and for manufacturing spices. As an example, the well known Worcester sauce contains spices derived from tamarind.

Tamarind is used in Indian Ayurvedic Medicine for gastric and digestive problems.

indena®

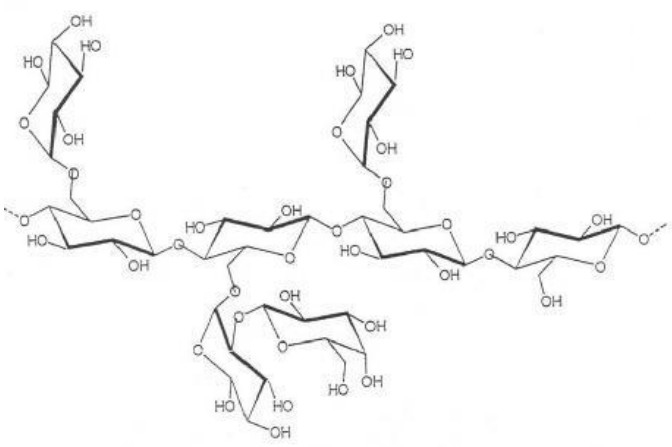
XILOGEL®

GENERAL OVERVIEW

The tamarind seed appears as a broad bean covered with a dark brown hull.

The seed of tamarind has a high content of polysaccharide:

The main component is a branched polysaccharide consisting of a cellulose-type backbone (β-(1→4)-D glucose) which carries xylose and galactoxylose substituent. Other sugar groups could be present in lower concentration (i.e. arabinose).



A novel **film-forming** and **moisture-regulating** polysaccharide

indena®

XILOGEL®

THE EFFICACY

Study name:	**Hydrating, Elasticizing, Anti-age and re-densifying efficacy of Xilogel®**
Experimental model	Xilogel® at 0.5% is applied versus a positive reference (Hyaluronic acid, MW 1.1 -1.7 mioDa, purity 95-100%) on 20 female volunteers (mean age 45-50) on a long term treatment of 4 weeks + immediate hydration measurement at 30 min
Concentrations tested	0.5%
Measured parameters	Hydration (Corneometric units), Elasticity, Roughness (3D digital imaging) and ecogenicity (density)
Results	**Cutaneous hydration** immediately improved by **+59.2%,** over long term increased by **35.8%**; **Overall elasticity** (R2 parameter) improved by **+19.4%**; **Average roughness** : **-27.6%**; **Maximum roughness**: **-21.3%**; **Density** improved by **+7.9%**;
Indications	Hydrating, antiage, elasticizing, moisturizer, re-densifying. It also improves the sensorial feeling of finished forms.

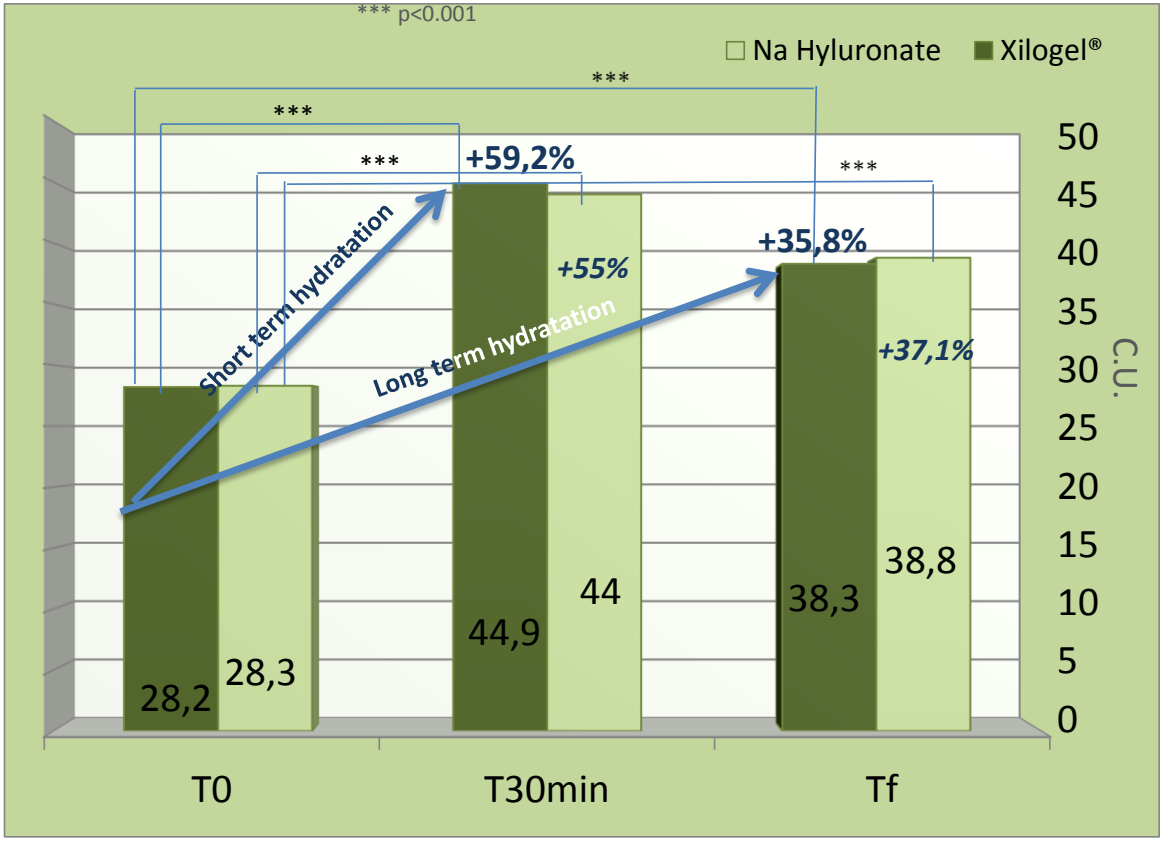
Study conducted @:
ISPE, Italy

indena®

XILOGEL®

THE EFFICACY

Hydration: short and long term



Xilogel® induced an immediate increase in hydration (measured by Corneometric Units) by **59.2%,** which is even **higher than** the positive reference **hyaluronic acid** (55.5%); p=0.001

Instrument:
CORNEOMETER CM 825
by Courage&Khazaka

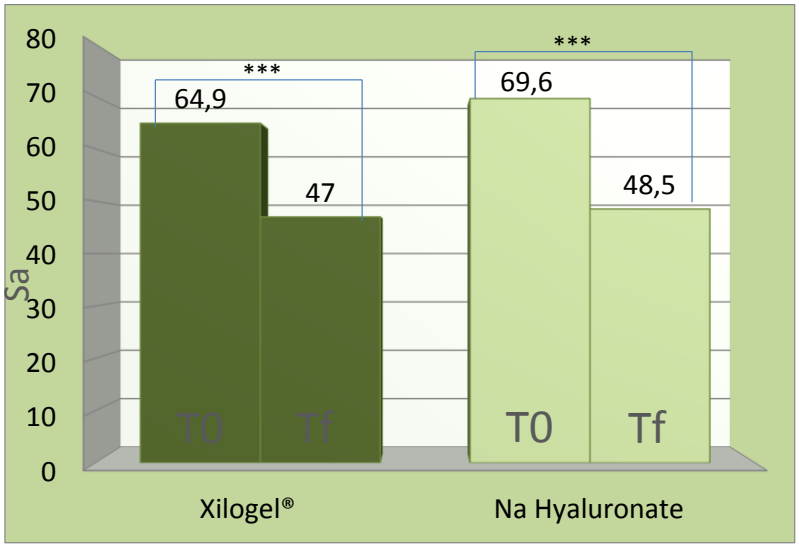
Over 4 weeks' application, Xilogel® gives the same impressive results as the positive reference (**35.8% - 37.1% hydration increase**) .

indena®

XILOGEL®

THE EFFICACY

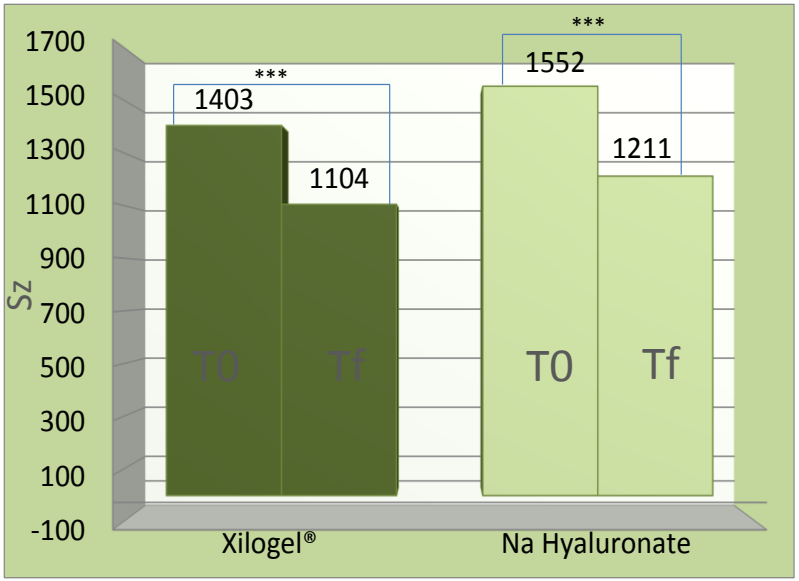
Skin Roughness: anti wrinkle



Xilogel® induced a decrease in the **average roughness** parameter (Sa) by **27.6%.** The data are comparable with the challenging positive reference.

*** p<0.001

Xilogel® induced a decrease in the **maximum roughness** parameter (Sz) by **21.3%**. The data are comparable with the challenging positive reference.



*** p<0.001

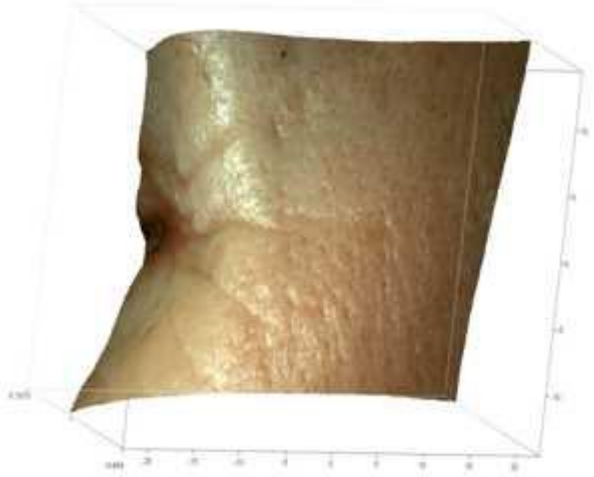
Instrument:
PRIMOS PICO OPTICAL 3D
by GFM

indena®

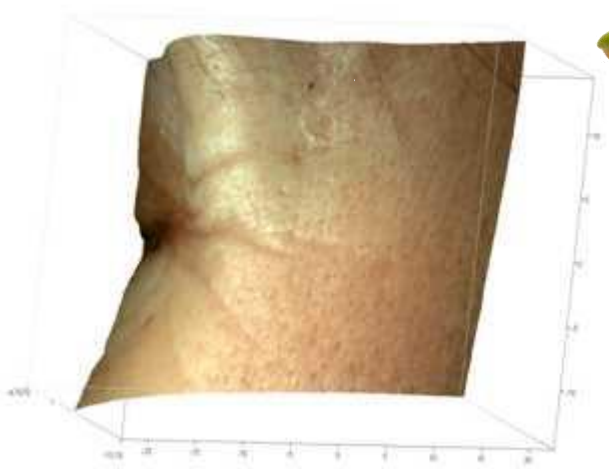
XILOGEL®

THE EFFICACY

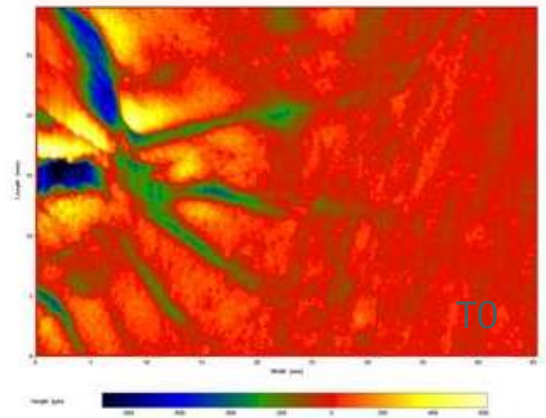
Skin Roughness: anti wrinkle

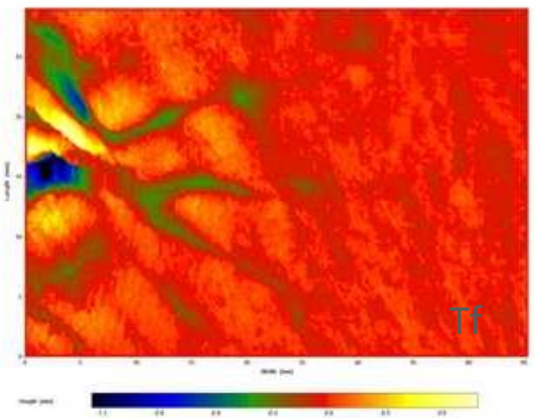


Skin Roughness
Subject 14 – T0



Skin Roughness
Subject 14 – Tf



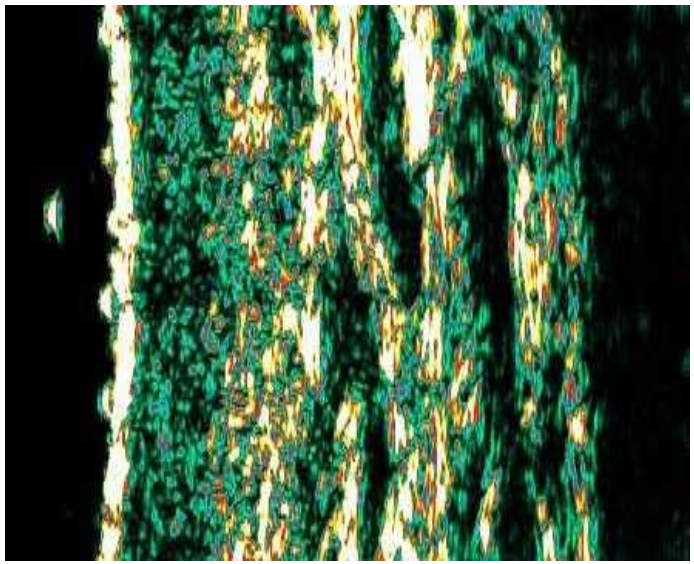


indena®

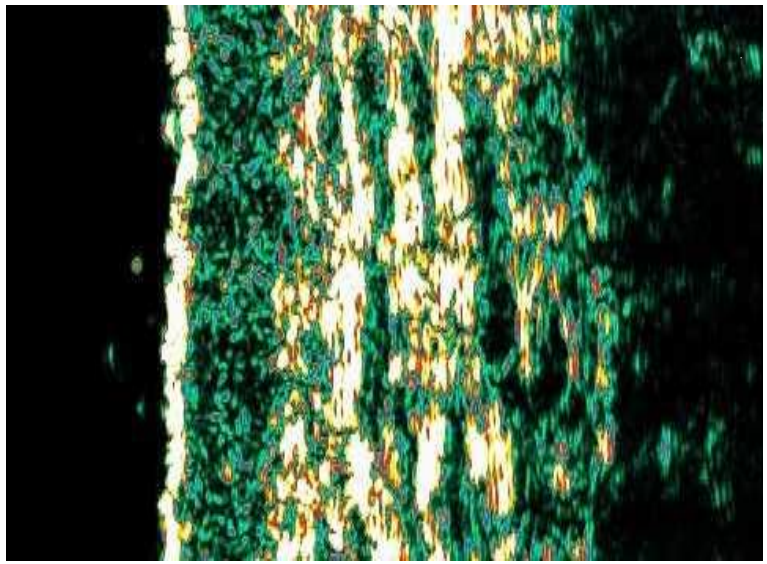
XILOGEL®

THE EFFICACY

Skin Roughness: anti wrinkle



Skin Density
Subject 6 – T0



Skin Density
Subject 6 – Tf

It is measured the intensity of the ecogenic band (the colored one).
0%= black
100%= white

indena®

MILK THISTLE

GENERAL OVERVIEW

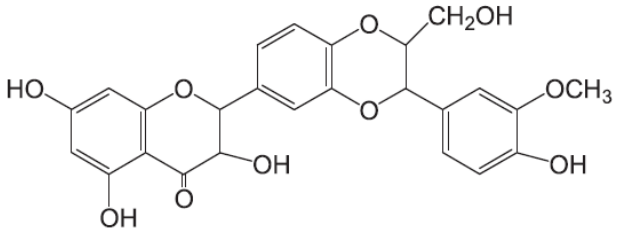
- Botanical products have been known since ancient times and have been traditionally used by all cultures for **supporting milking** both in nursing mothers as well as in animals.
- In the US around 15% are reported to use botanical supplements to improve milking
- In the European traditional medicine, milk thistle has been associated to improved milking.
- Milk thistle (o lady's thistle), is believed to either refer to the milky sap or to the traditional use for milking.
- Traditionally, the medicinal use of milk thistle is liver protection.
- Milk thistle contains silymarin

indena®

SILIPHOS®

SILYBIN PHYTOSOME®

INCI NAME: LECITHIN (SYN.PHOSPHATIDYLCHLINE), SILYBUM MARIANUM EXTRACT



Silymarin is a standardized mixture of **flavanolignans** (silybin, silydianin and silycristin) extracted from silybum marianum fruits

Silybin is the most active phytochemicals and is largely responsible for the claimed benefits of silymarin
Siliphos® is a phytosome complex of Silybin and Phosphatidilcholine.

It has been recently demonstrated as having a retinoic acid like activity.

Siliphos® induces morphological changes and prevents differentiation of keratinocytes. it reduces expression of keratinocytes terminal differentiation markers and stimulates the basement membrane protein expression.

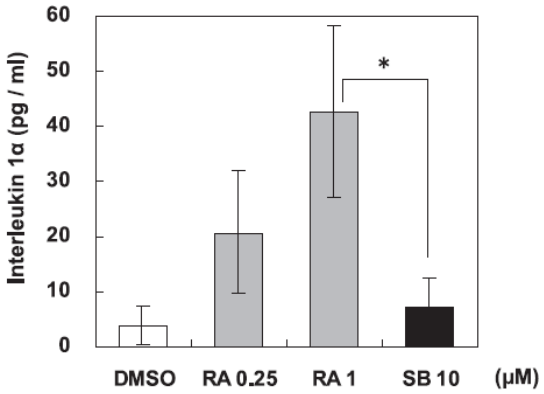
Differently from retinoic acid, siliphos® does not stimulate the secretion of proinflammatory cytokines, (skin irritation mediators).

indena®

SILIPHOS®

RETINOIC-LIKE ACTIVITY

Study name:	**Silybin inhibits confluent induced keratinocytes differentiation as effectively as retinoic acid**
Experimental model	Various botanicals incubated with normal human epidermal keratinocytes; after 4 days incubation, cellular media are collected and analyzed.
Measured parameters	Cell morphological changes; cell differentiation (differentiation associated markers as RA) markers; Basement protein membranes (laminin-5 and laminin-5 receptor); IL1 production
Results	Cells treated with Siliphos showed morphological changes as the ones treated with RA. Siliphos reduced the expression of differentiation associated markers but did not increase the IL1secretion (not proinflammatory).
Indications	Antiaging, retinoic acid like, skin renewal

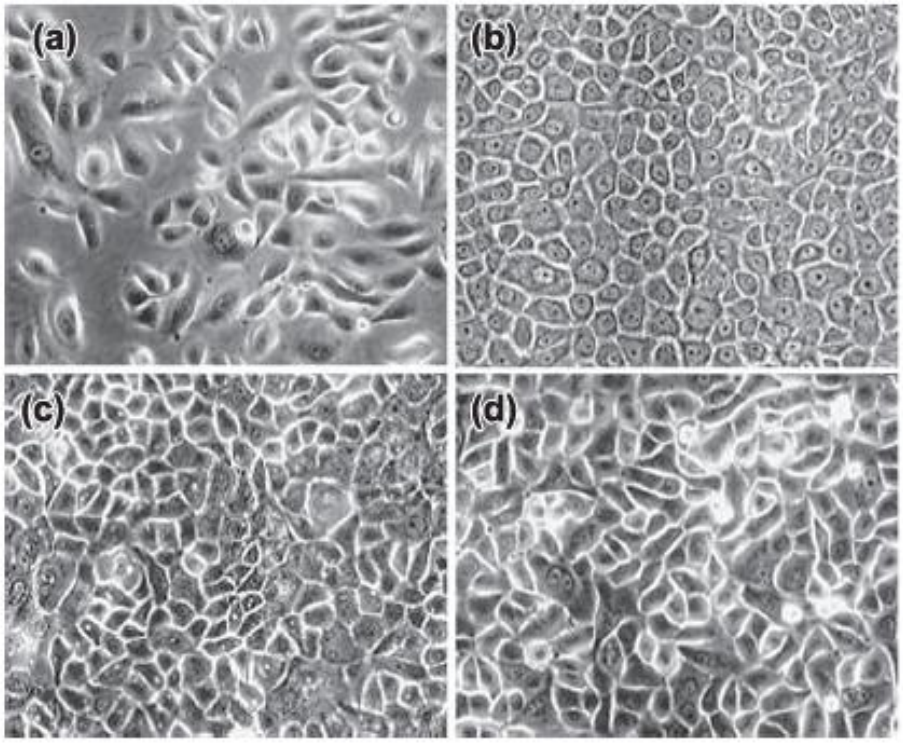


indena®

SILIPHOS®

RETINOIC-LIKE ACTIVITY

A



Original Article *J. Clin. Biochem. Nutr.*, **45**, 178–184, September 2009

Silybin from *Silybum Marianum* Seeds Inhibits Confluent-Induced Keratinocytes Differentiation as Effectively as Retinoic Acid without Inducing Inflammatory Cytokine

Seiji Kitajima, and Kohji Yamaguchi*

FANCL Research Laboratories, FANCL Corporation, 12-13 Kamishinano, Totsuka-ku, Yokohama, 244-0806, Japan

Received 19 February, 2009; Accepted 9 March, 2009

Phase-contrast image of keratinocytes treated with RA or SILIPHOS® on Confluent-induced differentiation:

a) Non confluent proliferative keratinocytes
b) Keratinocytes incubated in KGM with DMSO
c) RA 1 µmolar
d) Siliphos® 10 µmolar

indena®

SILIPHOS®

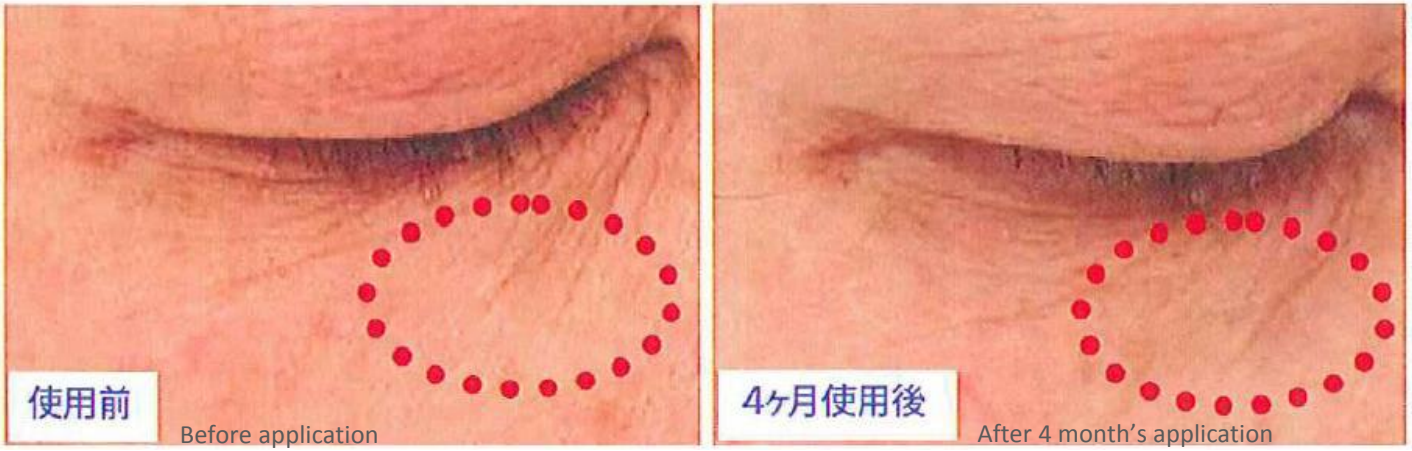
CLINICAL EFFICACY

Application for 4 months in women of over 40 years of age of:
- a cosmetic containing Siliphos® on half her face
- a cosmetic containing retinol on the other half.

At the end a comparison was made of the skin conditions:
- tendency to enhanced elasticity and wrinkle improvement on either side of the face.

BUT

- **On the retinol side the skin barrier function appeared in worse conditions, while on the Siliphos® side skin barrier REMAINED UNCHANGED.**



Even if Siliphos® has been demonstrated to **induce** the **same improvement** as retinol on sunlight-induced skin ageing, it **maintained** the **skin barrier function unchanged**, thus proving to be a safer ingredient.

IFSCC (International Federation of Societies of Cosmetic Chemists) 2005

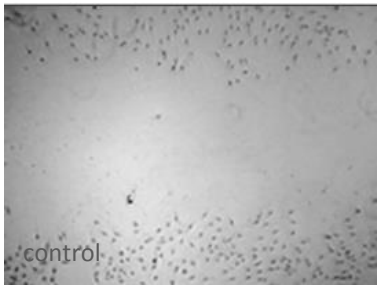
indena®

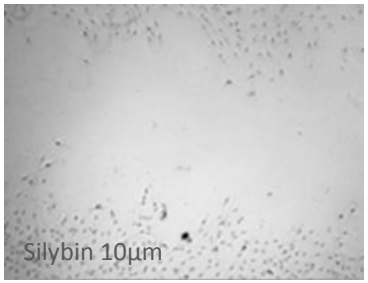
SILIPHOS®

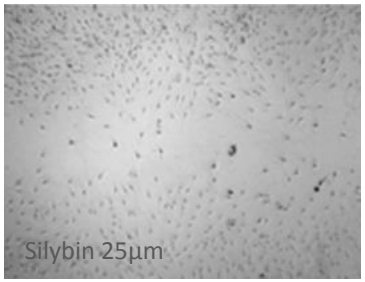
FIBROBLAST PROLIFERATION AND MIGRATION

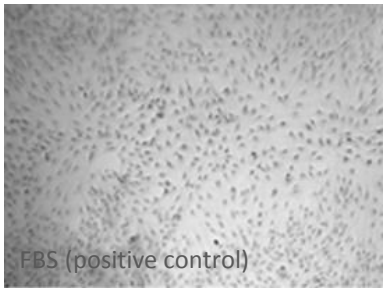
During skin ageing, the epidermal turnover begins to slow down, keratinocytes forms accumulations and the skin appearance gets translucent, wrinkled and dull.

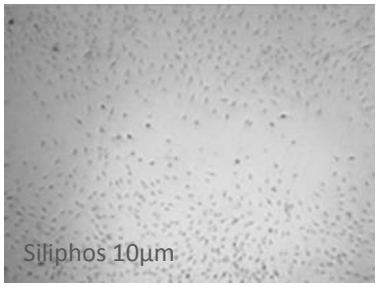
The capacity of Siliphos® to induce fibroblasts migration was analyzed in a **scratch test** simulating a wound repair during 48 hours.

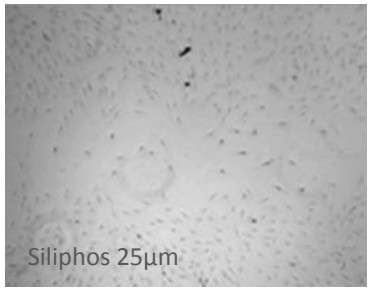












Siliphos® has shown the capacity to **increase cell migration** in a dose dependent manner, even higher that the pure silybin.

BEROS Consulting, report 26 June 2012

indena®

CENTELLA DERIVATIVES

HISTORY AND BOTANY

Centella is a perennial, creeping herbaceous **plant** belonging to

the Apiaceae (Umbelliferae) family. It has been **widely used both in Indian ayurvedic medicine** and as a traditional herbal medicine in Asia and India.

The traditional medicine of Madagascar has used for immemorial time as an agent **favouring cicatrization**, but also orally to treat stomach ulcers.

Centella grows easily in open warm, low and wet areas.

To ensure the content of active compounds, the **source of the plant** needs to be carefully evaluated.

Following to repeated botanical researches, although centella is present not only in Madagascar but also in most of Asia, the **Centella leaves from Madagascar are the most reliable source**.[1]

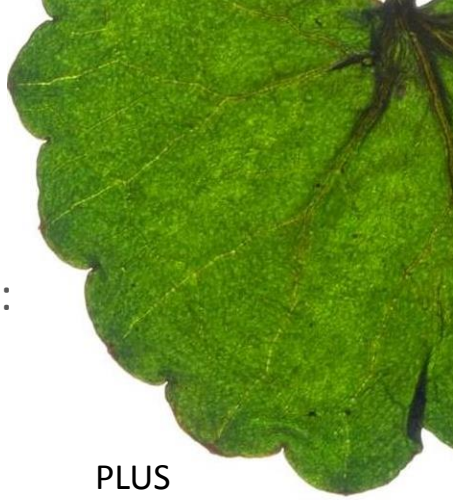
They have the most constant quality and the highest content of biologically active triterpenes.

indena®

CENTELLA DERIVATIVES

GENERAL OVERVIEW

Centella asiatica derivatives are available with different characteristics:



	INCI/CFTA NAME	PLUS
CENTEVITA™	CENTELLA ASIATICA LEAF EXTRACT	Ecocert validated, contains triterpenes including madecassoside and polyphenols
MADECASSOSIDE	MADECASSOSIDE	Pure molecule, promotes collagen III synthesis, water soluble
ASIATICOSIDE	ASIATICOSIDE	Pure molecule, promotes collagen I synthesis
CENTEROX™	MADECASSOSIDE, ASIATICOSIDE	Combination of glycosilated terpenoids, freely water soluble
CENTELLA ASIATICA SELECTED TRITERPENES	ASIATICOSIDE, ASIATIC ACID, MADECASSIC ACID	Combination of pure terpenoids, high cenc. of bioavtive components
CENTELLA ASIATICA SELECTED TRITERPENES PHYTOSOME®	LECITHIN (SYN. PHOSPHATIDYLCHOLINE), ASIATICOSIDE, ASIATIC ACID, MADECASSIC ACID	Enhanced bioavailability, improved formulability

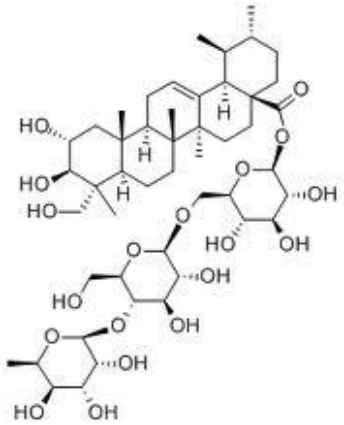
indena®

CENTEVITA®

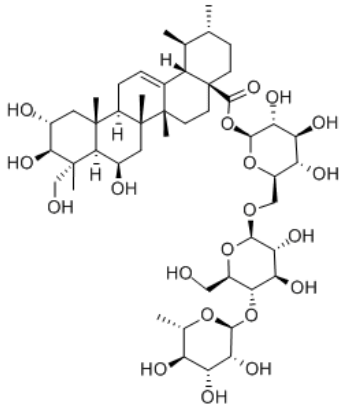
ACTIVE COMPOUNDS

THE TERPENIC FRACTION

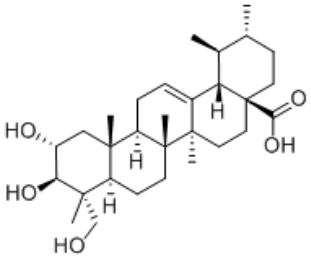
≥45.0% of the sum of asiaticoside, **madecassoside**, asiatic and madecassic acids by HPLC
Almost 7.5% of the remaining part accounting for biologically active **polyphenols**



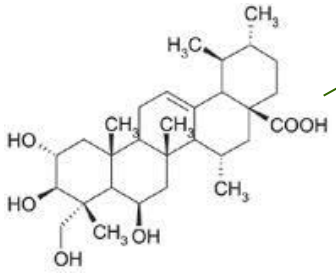
Asiaticoside



Madecassoside



Asiatic acid



Madecassic acid

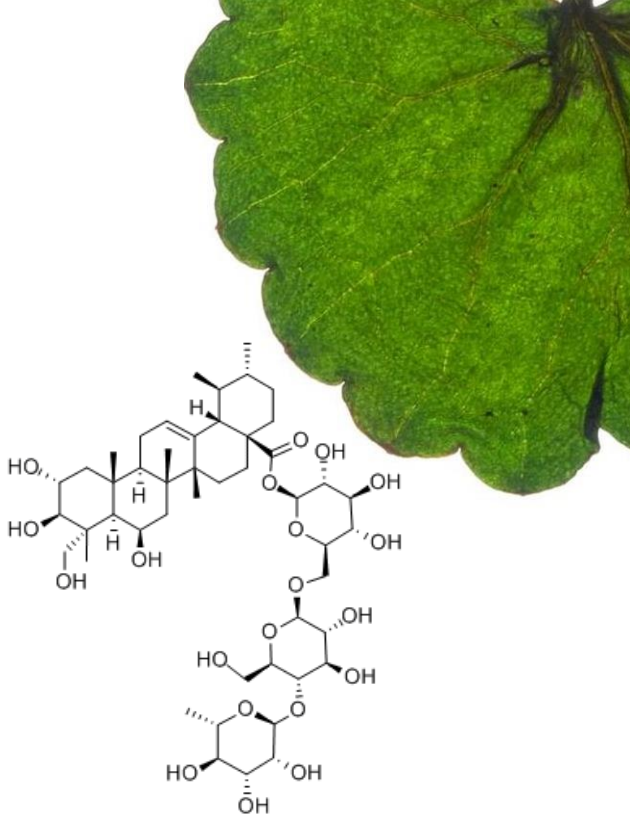
indena®

CENTELLA DERIVATIVES

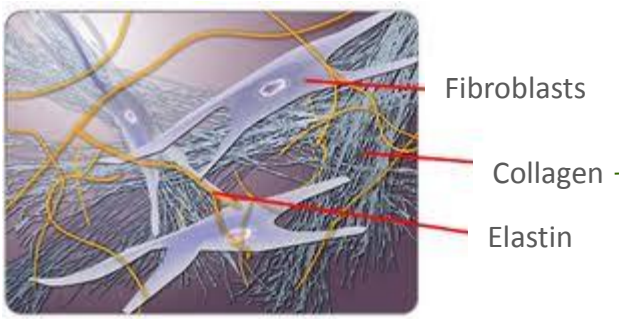
GENERAL OVERVIEW

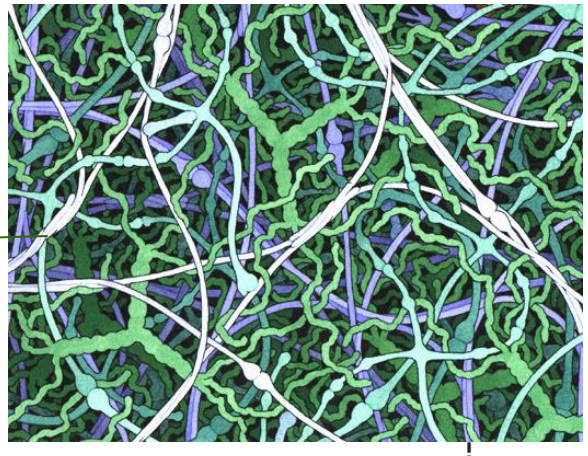
While both asiaticoside and madecassoside stimulate collagen type I, so far only **madecassoside** has been shown to significantly **increase type III collagen** synthesis.

Type III collagen is a fibrillar forming collagen comprising three alpha1(III) chains and it is a major component of the extracellular matrix in a variety of internal organs and in skin.



MADECASSOSIDE





Bonte F. et al, Ann Pharm Fr 53, 1995, 38-42

indena®

CENTEVITA®

THE EFFICACY IN VITRO

Study name:	**Evaluation of the anti-photoaging, anti-inflammatory and DNA protecting activity of CENTEVITA™ extract on human skin explants**
Experimental model (IN VITRO)	Centevita ™ applied on day 0,2,3,4,5 (2mg per explant) on human skin explants; on day 5 treatment followed by UV irradiation (UV A+B 18 J/cm^2). Evaluations taken on day 6 (day 5 for MDA).
Samples num.	6 skin explants of an average diameter of 11 mm
Tested concentrations	An aqueous solution of Centevita™ at 1% was topically applied on day 0, and from day 2 to day 5 (2mg/explant)
Measured parameters	- General cells morphology observed on paraffinized sections - Thymine dimers evaluated by anti-thymine dimers antibody, quantified by image analysis - MDA assay evaluated by ELISA - IL-1$^\alpha$ assay evaluated by ELISA
Results	General cells morphology; good morphology, thick collagen bundles, quite dense network, well cellularized Thymine dimers; decrease by **28% (*)** MDA assay; tendential decrease by **38%** IL-1$^\alpha$ assay: decrease of IL1α induction by **26%(**)**

indena®

CENTEVITA®

THE EFFICACY IN VITRO

Aim of the test is to evaluate the **anti-inflammatory**, **anti-aging** and **DNA protecting capacity** of Centevita™ directly on human skin.

Cells morphology: sun burned cells (SBC) will be evaluated and counted

Thymine dimers: gives in indication on DNA protection counteracting the photodimerization induced by UV irradiation

MDA assay: gives and indication on free radical scavenging capacity

IL-1α: gives an indication on anti-inflammatory properties

Indications: Anti aging, photoageing prevention; anti-inflammatory; DNA protection

Study conducted @:
Bio-EC, France

indena®

CENTEVITA®

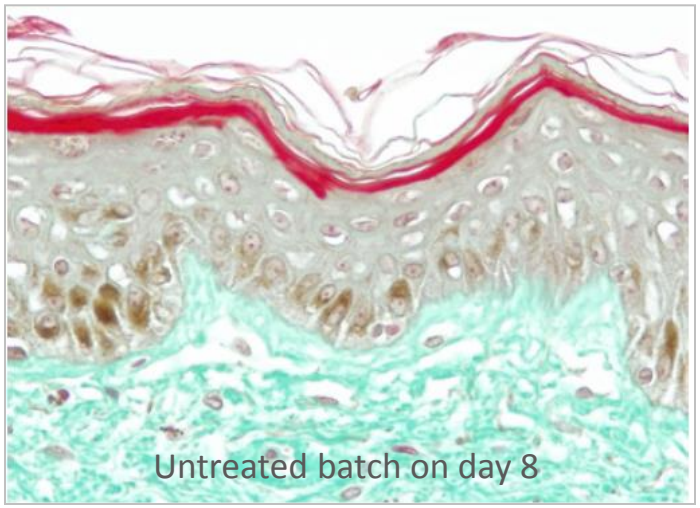
THE EFFICACY IN VITRO

Study name:	**Evaluation of the anti-glycation activity of Centevita™ on human skin explants**
Experimental model (IN VITRO)	Centevita™ incubated human skin explants; glycation will be induced by methoxyglyoxal in culture medium
Samples numerosity	12 skin explants of an average diameter of 11 mm
Tested concentrations	An aqueous solution of Centevita™ at 1% was topically applied every day (2mg/explant); MG at 500µM incorporated in the medium on day 3, 5 and 7. Final sampling on day 8.
Measured parameters	General cells morphology; N-Carboxy-Methyl-Lysine (CML) immunostaining (microscopical observation)
Results	A **total inhibition of carboxymethyl lysine** induced by methylglyoxal; Centevita™ application induces a clear increase of the collagen network density in the papillary dermis.
Indications	Anti aging, counteracting inflammaging

indena®

CENTEVITA®

THE EFFICACY IN VITRO



Untreated batch on day 8

Centevita™ treated batch on day 8

The general morphology is similar to the one observed on day 0.

Centevita® treated batch shows a very slight dermal stimulation with a clear increase of the collagen network denbsity in the papillary dermis.

A **clear densification** of collagen network in the papillary dermis is visible.

indena®

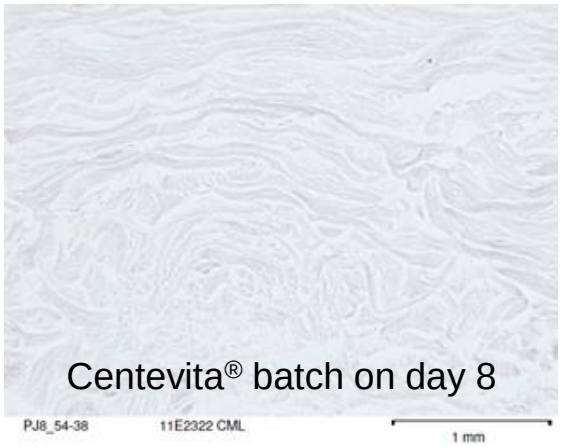
CENTEVITA®

IN VITRO EFFICACY: ANTI-GLYCATION

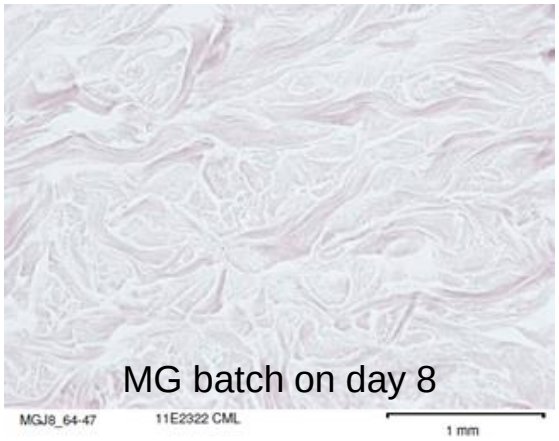
Control batch on day 0

Control batch on day 8

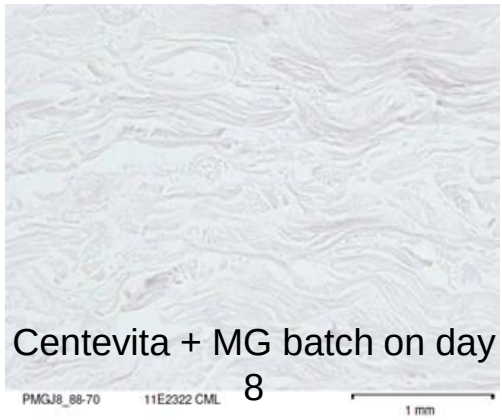
Centevita® has shown a clear inhibition of CML expression both in the MG treated and in the non–MG treated batches (immunostaining).



Centevita® batch on day 8



MG batch on day 8



Centevita + MG batch on day 8

indena®

CENTEVITA®

THE CLINICAL EFFICACY

Study name:	**Evaluation of the anti-ageing activity and activity on the MED of Centevita™ vs placebo on a panel of volunteers**
Experimental model	Centevita™ at 0.5% formulated in a simple o/w emulsion vs placebo over 6 weeks' application twice daily.
Number of subjects	20 volunteers aged 45 and over (55±9), treating half face and forearms with each product (active or placebo) each one being its own control
Tested concentration	0.5% in o/w emulsion
Measured parameters	Anti ageing activity by replica analysis; firming and elasticity assessments by Cutometer; evaluation of collagen density by siascope; evaluation of MED variation on day D0+24h and day D42+24h
Results	Collagen redensification observed **in 70% of volunteers** ($p<0.05$), tendential **improvement of wrinkles appearance**, significant **improvement in skin elasticity and firmness**
Indications	Antiageing, photoaging protection

indena®

CENTEROX®

IN VITRO EFFICACY

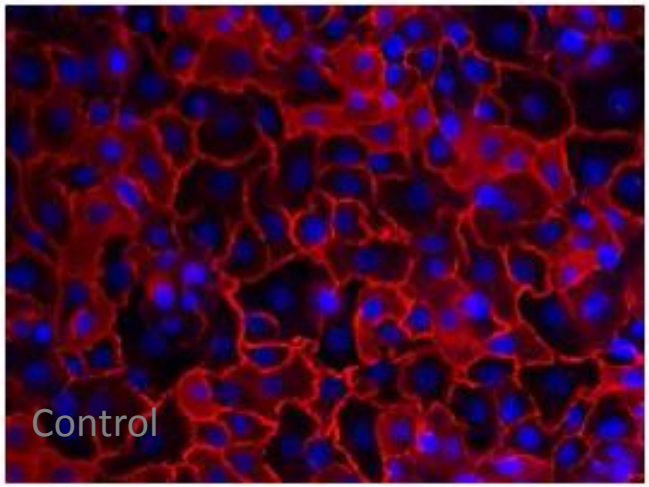
Study name:	**Dermo-epidermal junction proteins expression**
Experimental model	Centerox at 0.05 and 0.1% applied on human epidermal keratynocytes (NHEK) compared to a control (medium) and a positive control (TGF-b). All experimental conditions were performed in n=3. 24 + 72 hours.
Measured parameters	Physio-pathology by dermal cohesion, dermo-epidermal junction; laminin -5 expression by in situ- immunolabelling. Primary antibody detected by fluorescence.
Results	Laminin-5 improved by **33%** ($p<0.05$)
Indications	Hair care, skin care, body care. Laminin-5 improvement suggests a reinforcing function on the **attachment of epidermis to dermis**.

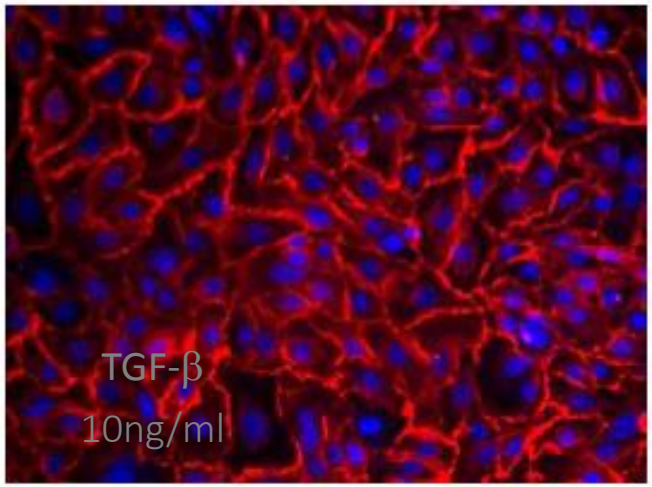
Bioalternatives study
BM131207, 2014

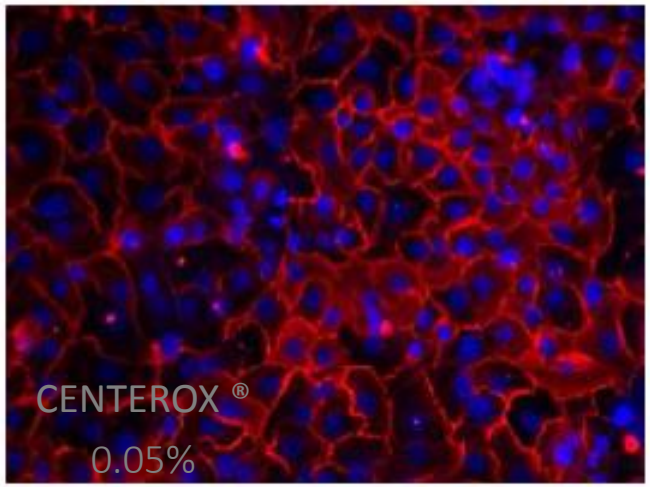
indena®

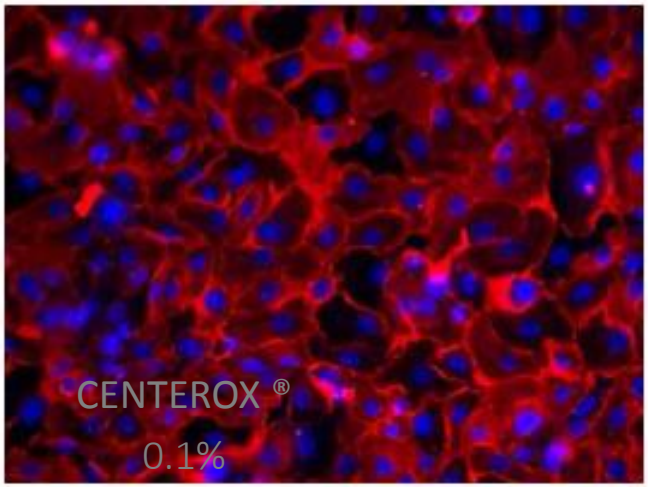
CENTEROX®

IN VITRO EFFICACY









+33% laminin-5 expression

Cells are labelled using a primary antibody which is then revealed with a fluorescent secondary antibody and staining cells nuclei.

indena®

CENTEROX®

CLINICALLY PROVEN EFFICACY – HAIR STRENGTHENING

Study name:	**Clinical evaluation of a topical hair strengthening treatment**
Experimental model	Volunteers were asked to apply the topical product (active or placebo) daily for 8 weeks.
Number of subjects	30 volunteers (15 females and 15 males) suffering from telogel effluvium and androgenic alopecia
Measured parameters	Resistance of hair to traction (**pull test**); hair lost during washing (**wash test**); hair diameter by scanning electron microscope (SEM)
Results	Hair resistance to traction improved by **125%** ($p<0.05$); hair lost during wasing (wash test) decreased significantly by **41.2%** ($p<0.01$)
Indications	Hair strengthening, hair envigorating
Treatment	Two ml of a formulation containing Centerox®0.5% (or corresponding placebo) was applied on two groups of volunteers (15 volunteers each group) daily for 8 weeks. Application directions involved: application on hair root by dividing hair in sections; distribution over the entire scalp; massage gently for a few minutes.

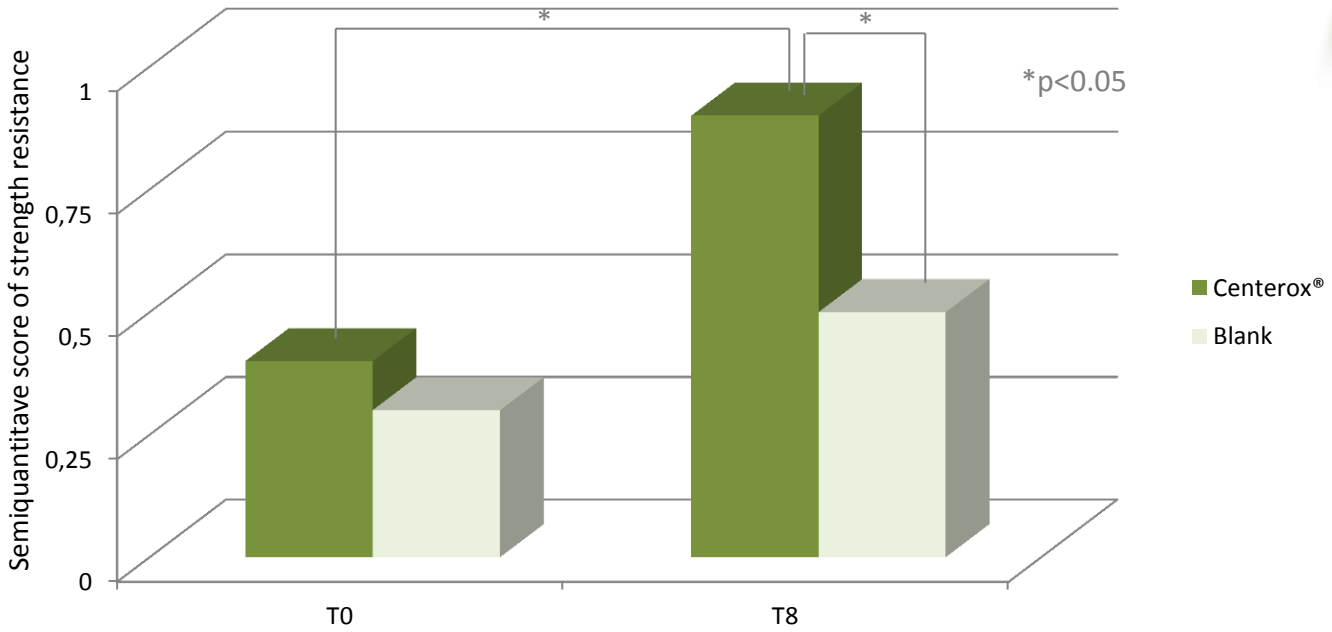
Ispe Study 205/13/10-02, 2013

indena®

CENTEROX®

CLINICALLY PROVEN EFFICACY – **PULL TEST**

Pull test (resistance of hair to traction)



The **hair resistance** to **traction** was evaluated on the basis of the total number of removed hair in all three areas (temporal, frontal, occipital).

A statistically significant reduction of pulled hair was observed in the Centerox® treated group: pulled hair resistance increased by **over two folds** (+125%).

indena®

CENTEROX®

CLINICALLY PROVEN EFFICACY – **WASH TEST**

Wash test (hair lost during washing)

The fallen hair have been counted after washing under controlled conditions.

Clinical assessment

The presence of dandruff, seborrhea and erythema were also clinically evaluated. Volunteers were required to report potential itching of burning sensations perceived on the scalp.

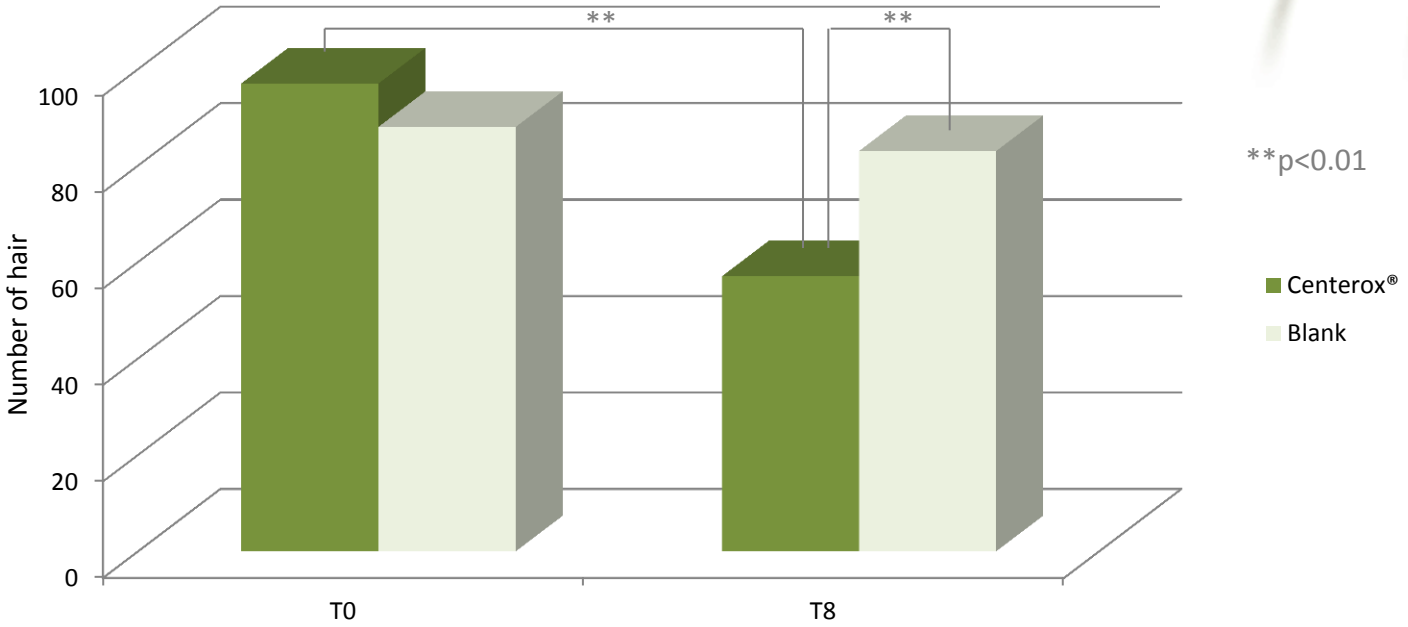
A score was assigned on a 4-point scale. No significant variations in the investigated parameter were observed, thus the treatment might be considered **well tolerated**.

indena®

CENTEROX®

CLINICALLY PROVEN EFFICACY – **WASH TEST**

Wash test (hair lost during washing)



The hair resistance to washing was evaluated on the basis of the total number of hair lost during a standardized washing.

A statistically significant reduction hair lost during washing was observed in the Centerox® treated group by **41.2%**

indena®

BOSEXIL®

HISTORY AND FACTS

Frankincense is associated to religious ceremonies in both Judaism and Christianity.

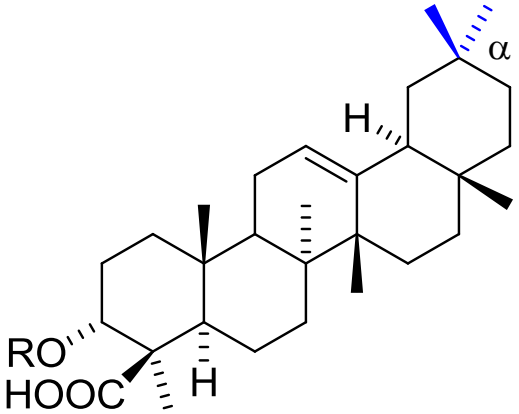
The early church during Roman times forbade the use of incense in services, and the practice was reintroduced in Europe by the Frankish Crusaders (Frankincense).

The resin is also known as olibanum, from the Arabic al-lubān (“the result of milking”).

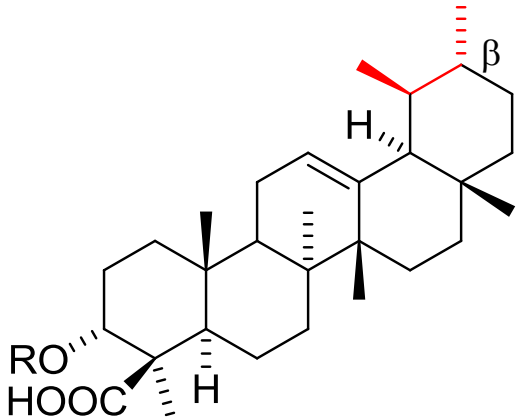
indena®

BOSEXIL®

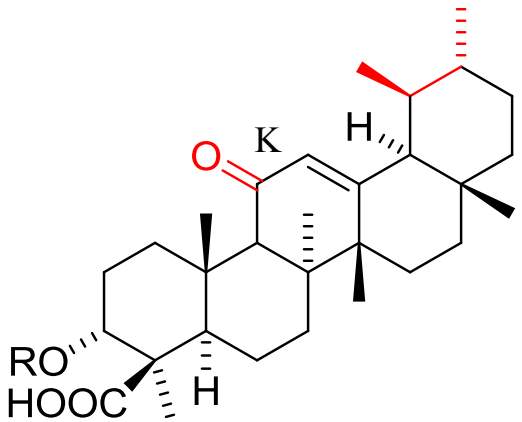
THE BOSWELLIC ACID ALPHABET



	R
αBA	H
AαBA	Ac



	R
βBA	H
AβBA	Ac



	R
KBA	H
AKBA	Ac

The six boswellic acids accounting for the large majority of BA compounds in Bosexil™.

βBoswellic acid (βBA)
Acetyl βboswellic acid (AcβBA)

are the most abundant in Bosexil®.

indena®

BOSEXIL®

THE CLINICAL EFFICACY

Clinical, Cosmetic and Investigational Dermatology

Dovepress
open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

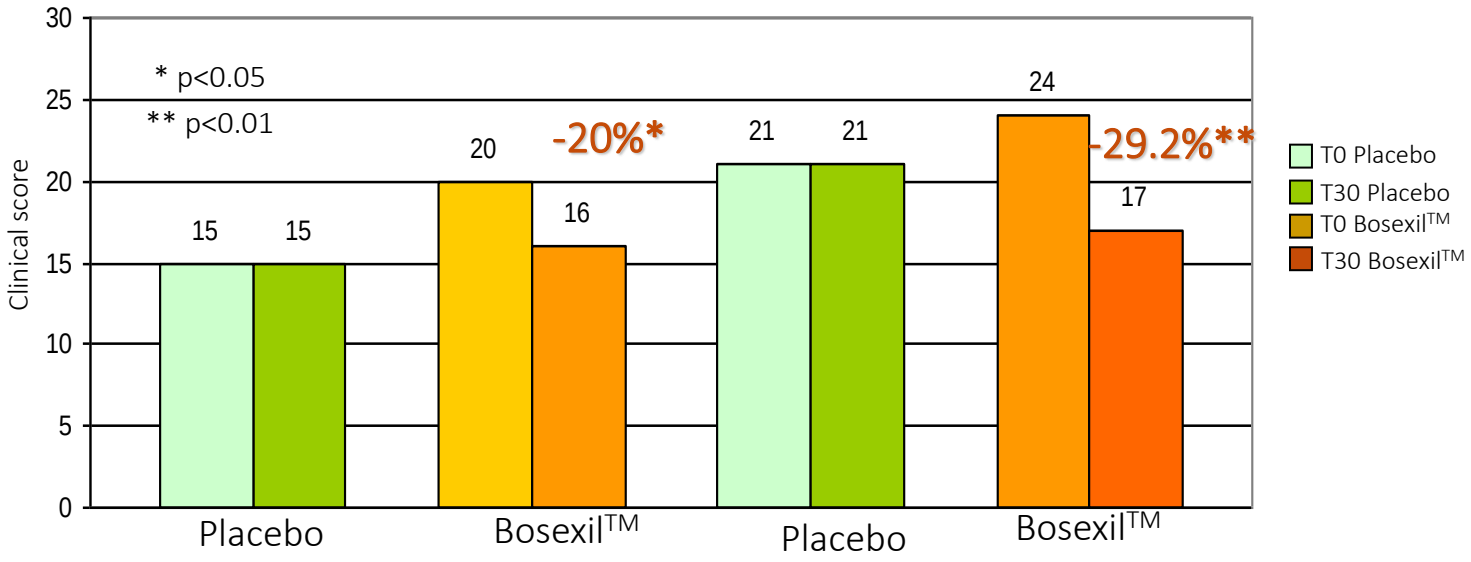
A cosmeceutical formulation based on boswellic acids for the treatment of erythematous eczema and psoriasis

Study name:	**Evaluation of Bosexil® containing formulation in patients affected by psoriasis and eczema versus placebo**
Experimental model	After basal evaluation of psoriasis, erythema and eczema conditions, a double blind trial is conducted with topical application twice daily on the affected areas for 30 days.
Number of subjects	40 patients, 20 belonging to the placebo groups, 10 affected by psoriasis and 10 affected by eczema
Measured parameters	Clinical evaluation (assessement scale) on: Scales and erythema for psoriasis Itch and erythema for eczema
Results	Clinical evaluation improved by **20% (erythema, $p<0.05$) and 29.2% (scales formation, $p<0.01$)** in patients affected by prsoriasis, **improved by 30.4% (erythema, $p<0.05$) and 31.8% (itch, $p<0.05$)** in patients affected by eczema
Indications	Soothing, anti-irritant, lenitive, anti-redness, restructuring
Treatment	Topical application of O/W emulsion containing **BOSEXIL® at 0.5%** in comparison to a placebo twice daily over a 30 days' period.

BOSEXIL®

CLINICALLY PROVEN EFFICACY ON PSORIASIS AND ECZEMA

Patients affected by PSORIASIS



ERYTHEMA

SCALES

Observed skin erythema decreased by 20% (p<0.05)

Observed scales formation decreased by 29.2% (p<0.01)

Clinical evaluation scale for skin manifestations:

0=absent

1=mild

2=marked

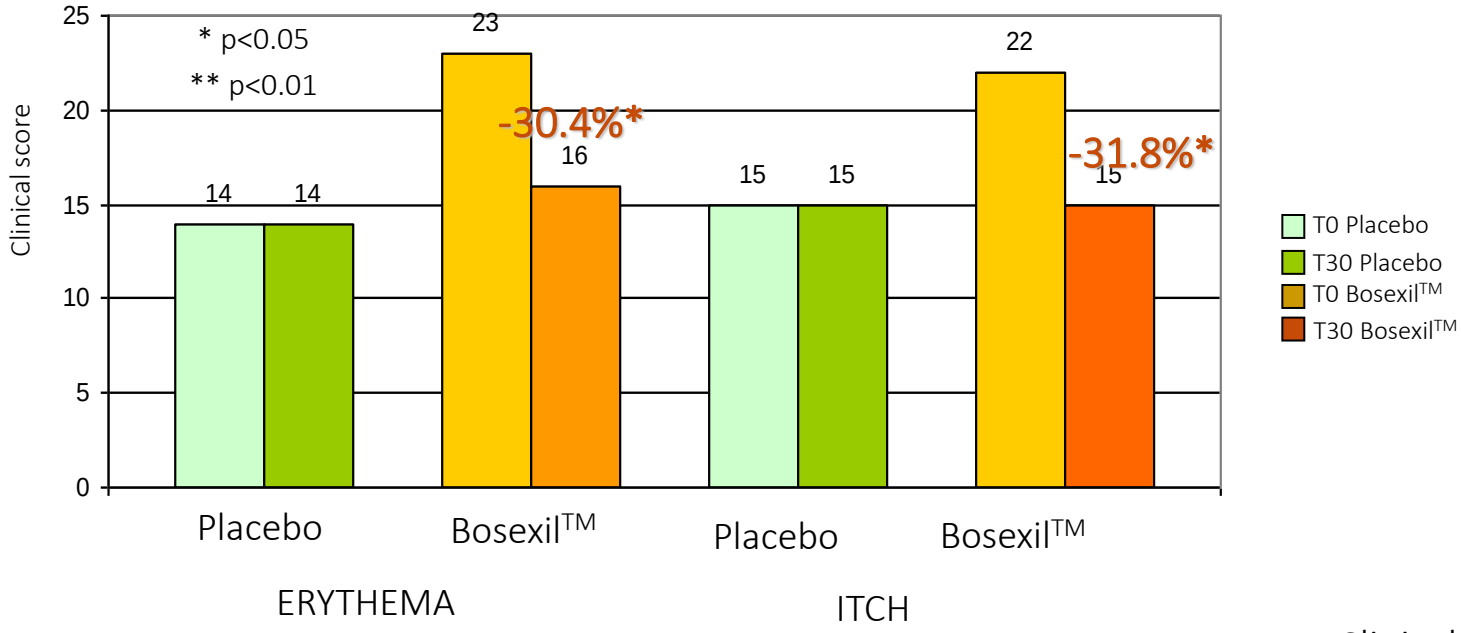
3=severe

indena®

BOSEXIL®

CLINICALLY PROVEN EFFICACY ON PSORIASIS AND ECZEMA

Patients affected by ECZEMA



Observed skin erythema decreased by 30.4% (p<0.05)

Observed scales formation decreased by 31.8% (p<0.01)

Clinical evaluation scale for skin manifestations:

0=absent

1=mild

2=marked

3=severe

indena®

BOSEXIL®

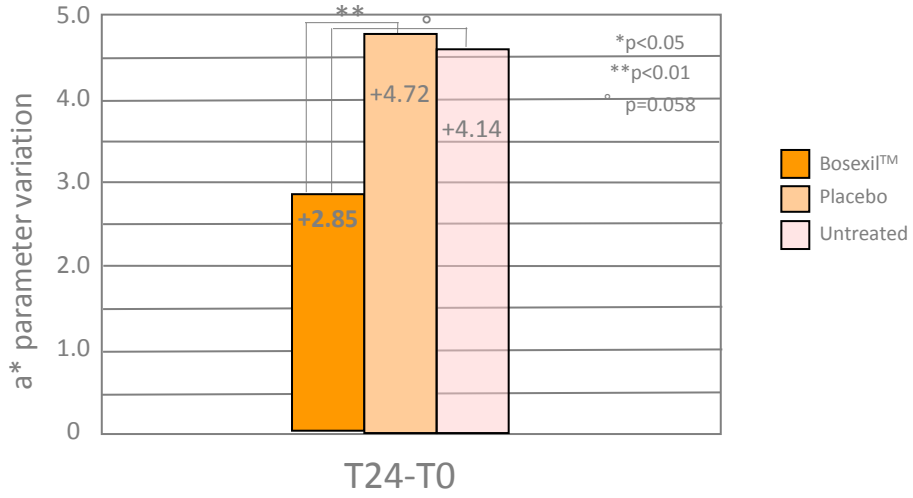
THE CLINICAL EFFICACY

Study name:	**Single blind instrumental evaluation of the lenitive and recovery properties of Bosexil™ on mechanical, physical and chemical skin damages**
Experimental model	PREVENTION: twice daily applications, 1w prior to UV (2MED) damage. Evaluations at T0 (basal) and T24, T48, T72 and T96. SOOTHING: after PHYSICAL (2MED) skin damage CHEMICAL (by SLS occlusion for 24h), evaluations at T0 (basal) T24, T48, T72 and T96; MECHANICAL: stripping until TEWL 15 g/h m^2, measurements at 30, 60 120’
Number of subjects	30 subjects aged 18-60 (mean 36.6), each testing substance/placebo/untreated area for two different skin damages. 20 volunteers subject to each challenge
Measured parameters	**CHEMICAL** damage: TEWL; skin redness (a* parameter); skin blood micro-flow. **PHYSICAL** damage: TEWL; skin redness (a* parameter); skin blood micro-flow. **MECHANICAL** damage: TEWL; skin redness (a* parameter); skin blood micro-flow.
Results	See following slides
Indications	Soothing, anti-irritant, lenitive, anti-redness, restructuring
Treatment	O/W emulsion containing **BOSEXIL™ at 1%** vs placebo and non treated area in acute and short term treatment (few minutes/few days depending on induced damage)

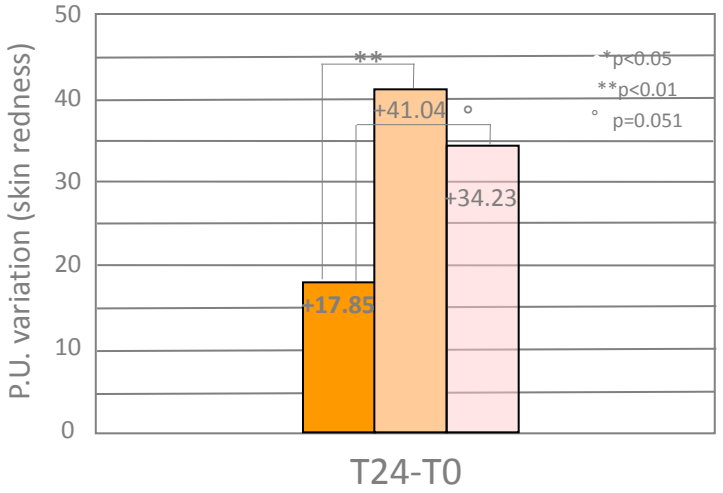
indena®

BOSEXIL™: **PREVENTIVE** EFFICACY ON **UV** DAMAGE (PHYSICAL DAMAGE) - results

SKIN REDNESS



MICRO-FLOW



The PREVENTIVE efficacy is represented the data **T0-T24** where the erythema intensity is evaluated.

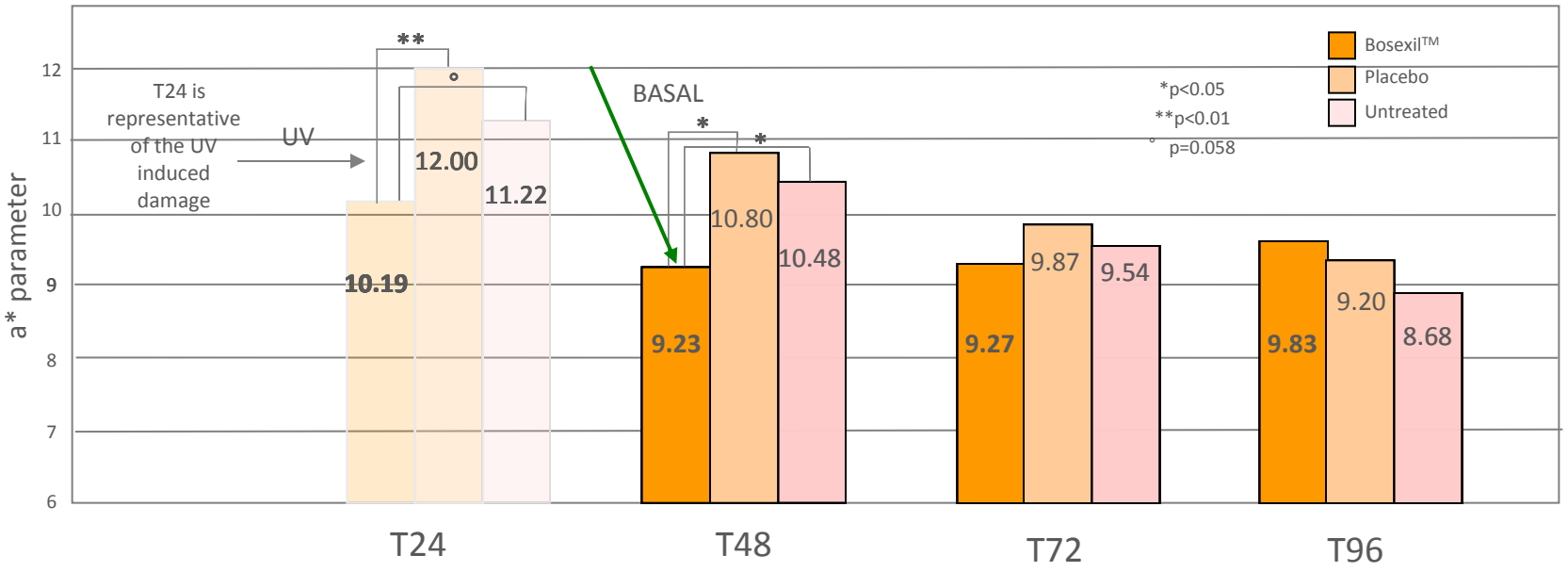
Observed variation in skin redness in the Bosexil™ treated area was **39.6%** (p<0.01) lower at T24 compared to the placebo, thus showing a **preventive** efficacy on UV induced challenge.

Observed variation in micro-flow (P.U.) in the Bosexil™ treated area was **56.6%** (p<0.01) lower at T24 compared to the placebo, thus showing a **preventive** efficacy on UV induced challenge.

indena®

BOSEXIL™: **SOOTHING** EFFICACY ON **UV** DAMAGE (PHYSICAL DAMAGE) - Results (1/2)

SKIN REDNESS



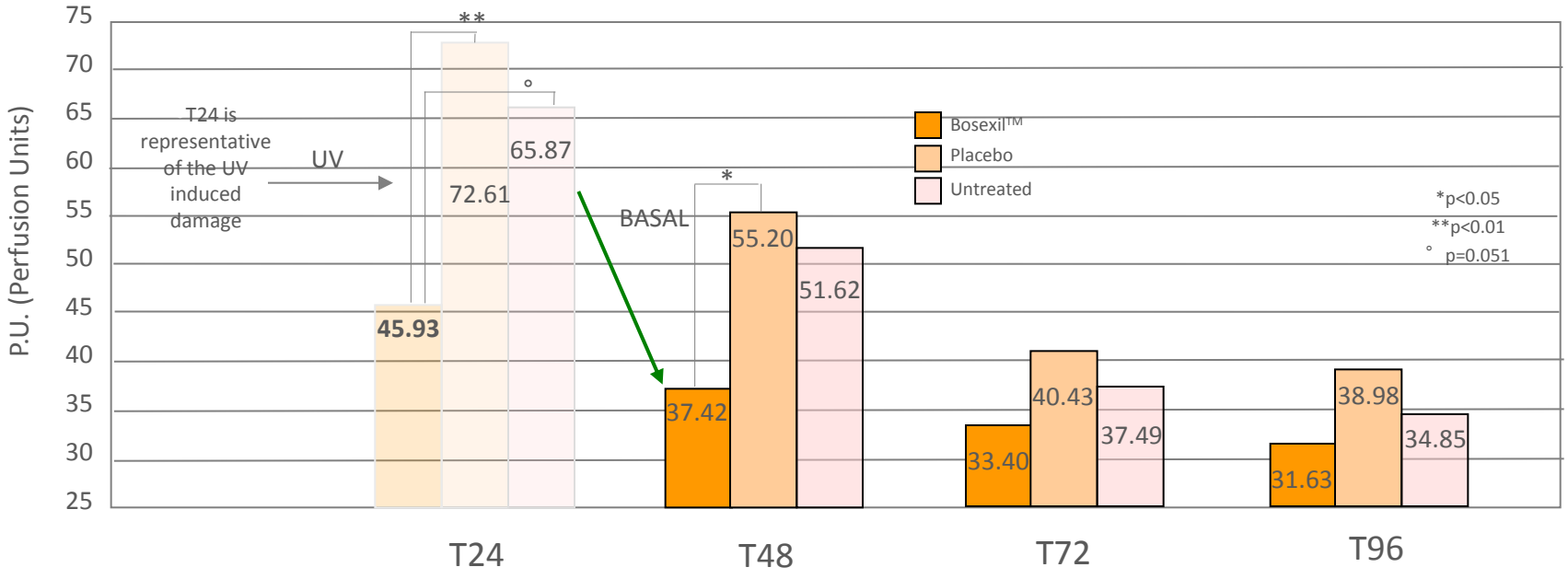
Observed skin erythema in the Bosexil™ treated area decreased by **14.5%** ($p<0.05$) at T48 showing a soothing efficacy on UV induced challenge.

The efficacy of the SOOTHING activity was shown in the faster recovery at T48.

In fact, the intensity of erythema was not significantly different from baseline at T48 and T72, meaning that in two days the erythema parameter had already completely gone back to basal.

BOSEXIL™: **SOOTHING** EFFICACY ON **UV** DAMAGE (PHYSICAL DAMAGE) - Results (2/2)

MICRO-FLOW



Observed micro-flow in the Bosexil™ treated area decreased by **32.2%** ($p<0.05$) at T48 showing a soothing efficacy on UV induced challenge micro-flow increase.

The intensity of micro-flow was not significantly different from baseline at T48, in the treated area, meaning that in two days the erythema parameter had already completely gone back to basal, whereas it took three days for the other two areas to recover.

BOSEXIL®

CLINICALLY PROVEN EFFICACY – SUPPORTIVE CARE

European Review for Medical and Pharmacological Sciences 2015; 19: 1338-1344

Clinical evaluation of safety and efficacy of *Boswellia*-based cream for prevention of adjuvant radiotherapy skin damage in mammary carcinoma: a randomized placebo controlled trial

S. TOGNI[1], G. MARAMALDI[1], A. BONETTA[2], L. GIACOMELLI[3], F. DI PIERRO[4]

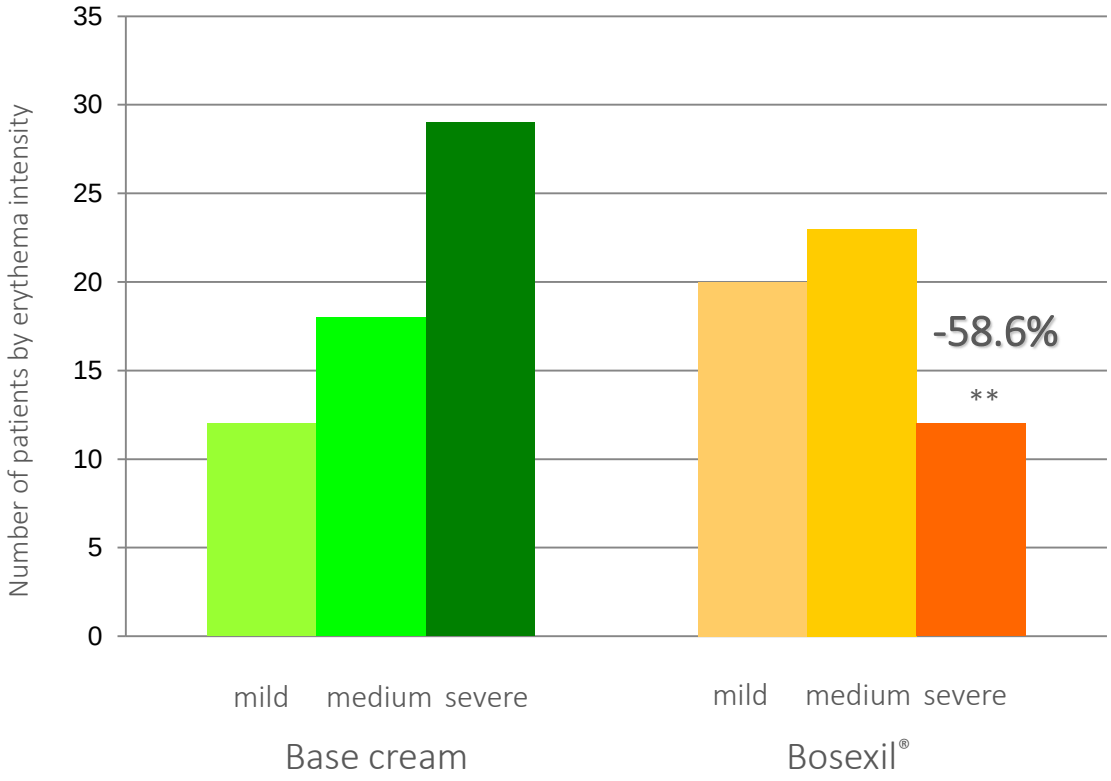
[1]Indena S.p.A., Milan, Italy
[2]Radiotherapy Unit, Istituti Ospedalieri, Cremona, Italy
[3]Free Researcher, Milan, Italy
[4]Scientific Department, Velleja Research, Milan, Italy

Study name:	Single blind evaluation of a lenitive cream as part of a radiotherapy protocol : SUPPORTIVE CARE
Experimental model	79 patients with a diagnosis of breast cancer and surgical intervention and undergoing radiotherapy alone or radiotherapy and chemotherapy use the topical product (boswellia or base cream) twice daily: just after radiotherapy and at night (during radiotherapy) and morning and night in no radiotherapy days. New data: + 35 patients tot 114
Number of subjects	114 Patients: 55 in the Bosexil® group; 59 in the base cream group
Measured parameters	Erythrema intensity; need to use cortison derived drugs.
Results	Severe rythema intensity dropped by 58.6%($p<0.001$) in the Bosexil group vs the placebo group; 74.55% of patients in the Bosexil® group had no need of cortisonic drugs, whereas only 37.29% in the base cream group.
Indications	Soothing, anti-irritant, lenitive, anti-redness, restructuring in supportive care
Treatment	O/W emulsion containing **BOSEXIL™ at 2%** vs base cream for 12 weeks according to the radiotherapy clinical protocol.

BOSEXIL®

CLINICALLY PROVEN EFFICACY – SUPPORTIVE CARE

Reduced erythema intensity



** p<0.01

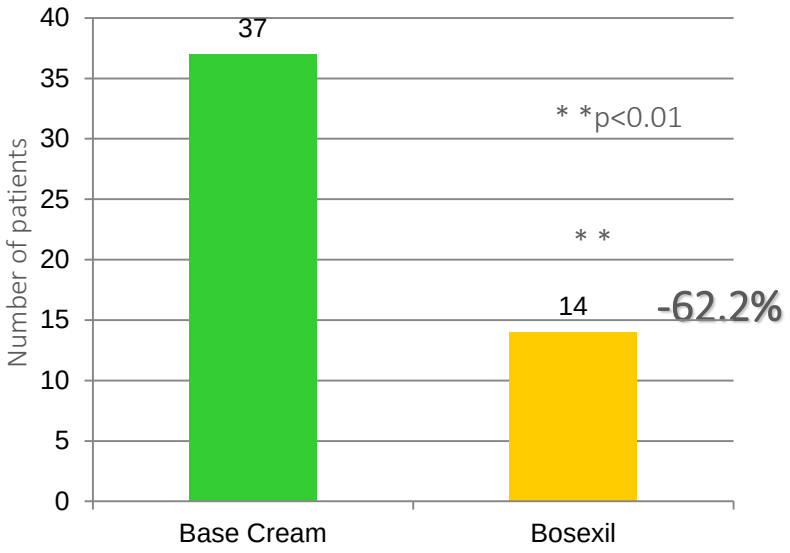
The number of patients that a severe skin erythema dropped by **58.6%** in the Bosexil® group compared to the base cream (p<0.001).

indena®

BOSEXIL®

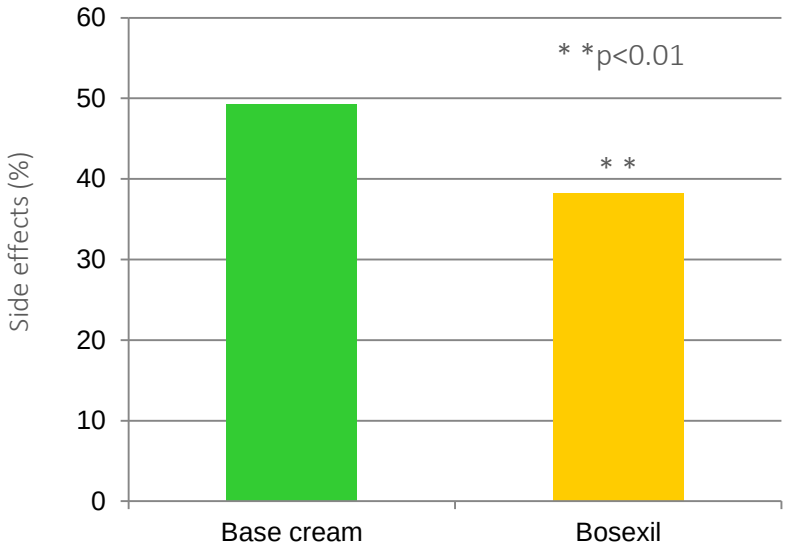
CLINICALLY PROVEN EFFICACY – SUPPORTIVE CARE

Reduced need to use cortisone drugs



The number of patients that had no need of cortisone increased by **62.2%** in the Bosexil® group compared to the base cream (p<p.001).

Reduced side effects



The percentage of patients that has various skin effects dropped from 49.2% to 38.2% in the base cream group (p<0.001).

indena®

OMEGABLUE®

GENERAL OVERVIEW

INCI NAME: VACCINIUM MYRTILLUS SEED OIL

- Bilberry grows **wild** in the North-Eastern parts of Europe
- Bilberries are not produced in clusters, but **only as single or rarely twin fruits**
- Bilberries are **difficult to harvest**
- Bilberries are susceptible to damage using picking rakes, they are **mostly hand-picked**
- Bilberries **can not be cultivated**
- Bilberries are softer and juicer than other berries
- Bilberries are difficult to transport and **must be kept frozen** until extraction
- Bilberries **can not be processed unfrozen**, since tissue damage triggers the deglycosilation of antocyanosides.

Wild bilberry contains many and very small seeds.

indena®

OMEGABLUE®

GENERAL OVERVIEW

Indena is one of the major producer of Bilberry extracts, processing every year **3500 tons** of fresh (frozen) fruits. **Up to 26.000 kg** of bilberry fruits processed every day.

From Bilberry we obtain:

Extraction process

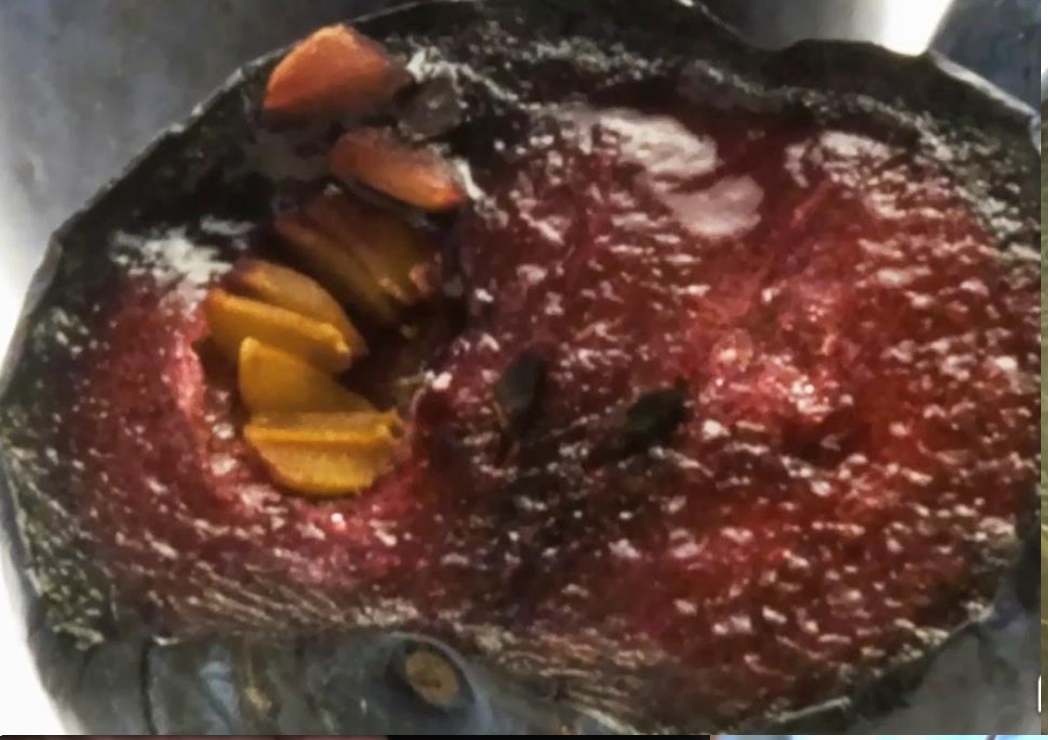
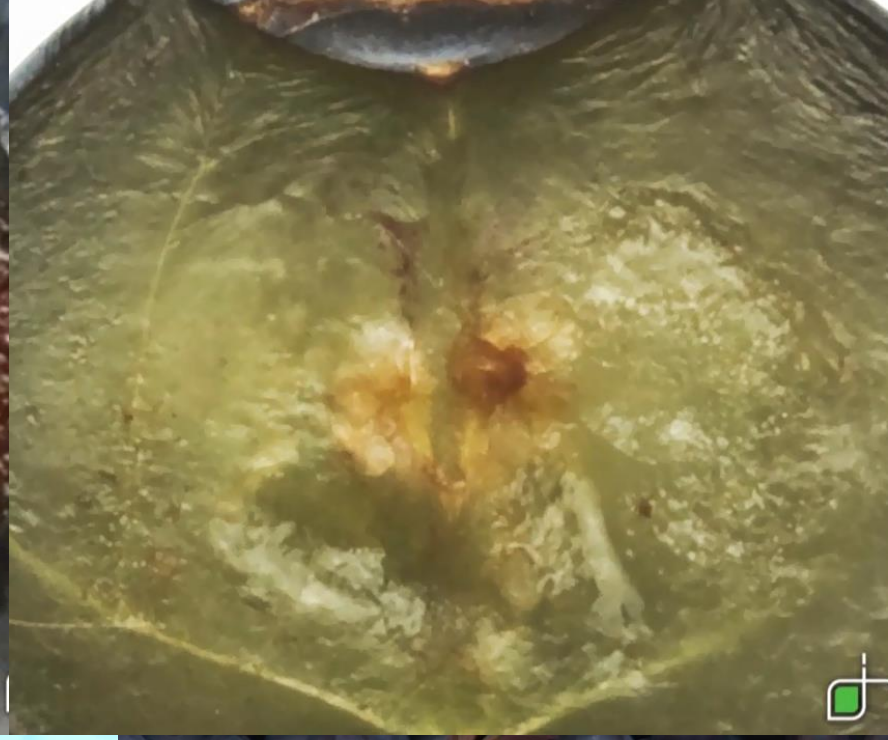
Seeds

Bilberry extracts:
Mirtoselect®
Mirtocyan®

OMEGABLUE®: Vaccinium myrtillus seed oil

Total fatty acids > 80 % -- PUFA > 50 % (α-linolenic acid (ALA) ω-3: -- Linoleic acid (LA) ω-6)
-Compared to the other sources of unsaturated fatty acids, bilberry seed oil has also an optimal **omega-6/omega-3 ratio** (around 1) it is a **great source of essential fatty acids:** omega-3 and omega-6 and of oleic acid.

indena®


OMEGABLUE®

THE CLINICAL EFFICACY

Study name:	**Evaluation of the barrier repairing and soothing efficacy of OMEGABLUE® after irritative damage induced by SLS**
Experimental model	After basal measurements on the inner part of the forearm, an occlusive SLS patch is applied for 24 hours. Measurements are taken to quantify the barrier damage; formulations are then applied on the tested areas twice daily for 3 days. Evaporimetry and colorimetry measurements taken at 24, 48 and 72 hours from patch removal.
Number of subjects	12 volunteers
Measured parameters	**TEWL; skin colour (*a parameter indicating the red/green axis, directly proportional to skin redness)**
Results	Skin barrier completely respred at 72 hours (three days. Placebo skin barrier still damaged.
Indications	Soothing, anti-irritant, lenitive, anti-redness, restructuring
Treatment	Topical application of O/W emulsion containing OMEGABLUE at 2% or 5% in comparison to a placebo and a non treated area, twice daily for 3 days.

The product efficacy is shown in a quicker return to the original cutaneous parameters in correspondence of the areas treated with OMEGABLUE®

indena®

OMEGABLUE®

THE CLINICAL EFFICACY

Articoli

Giada Maramaldi[1], Stefano Togni[1], Martino Meneghin[1], Giovanni Appendino[2]
Massimo Biondi[3], Francesco Di Pierro[4]
[1]Indena, Milano - giada.maramaldi@indena.com, [2]Università del Piemonte Orientale, Novara,
[3]Dipartimento Dermatologia ASL, Piacenza, [4]Velleja Research, Pontenure, Piacenza

Olio di semi di mirtillo

Un cosmeceutico nel trattamento di soggetti con cute eczematosa o psoriasica

Bilberry seeds oil

A cosmeceutical treatment for eczema and psoriasis

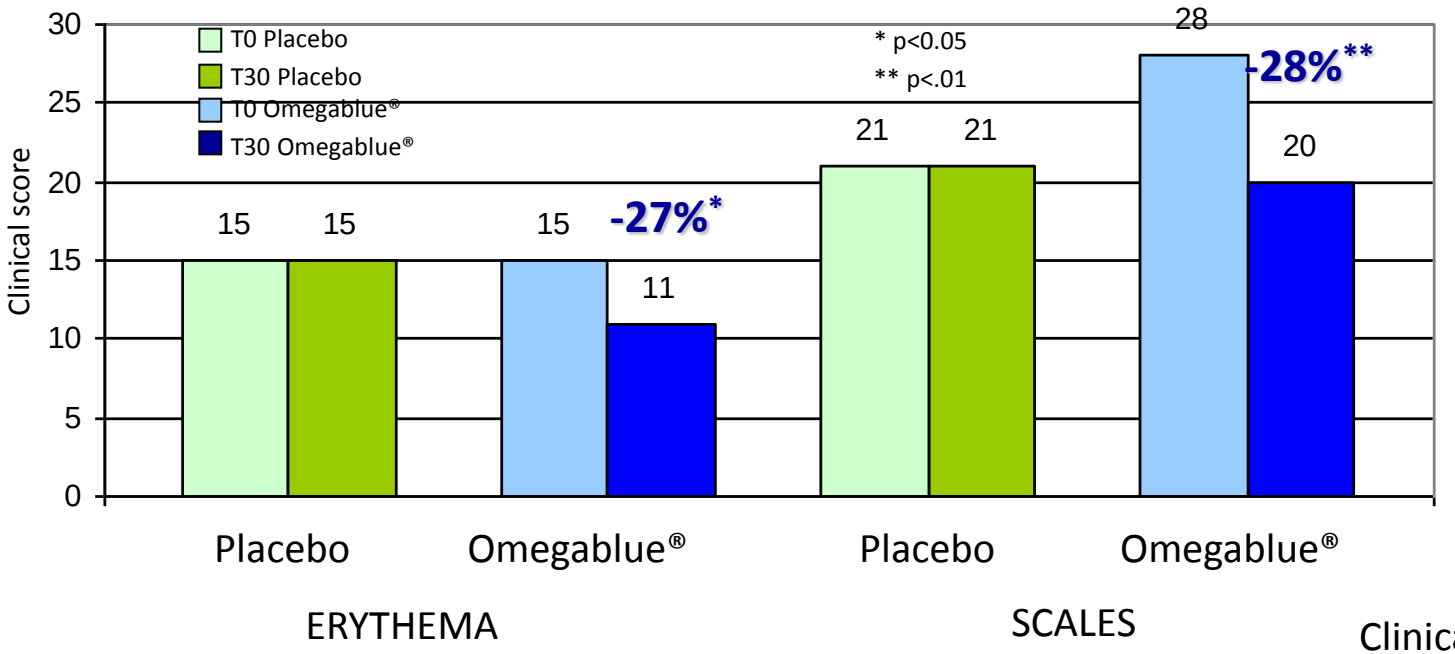
Parole chiave
Vaccinium myrtillus seed oil - Lenitivi - Ristrutturanti
Protettivi della barriera cutanea - Eczema - Psoriasi

Study name:	**Evaluation of the Omegablue® formulation in patients affected by psoriasis and eczema versus placebo**
Experimental model	After basal evaluation of psiriasis, erythema and eczema conditions, a double blind trial is conducted with topical application twice daily on the affected areas.
Number of subjects	40 patients, 20 belonging to the placebo group, 10 affected by psoriasis and 10 affected by eczema
Measured parameters	Clinical evaluation (assessemnt scale) on: Scales and erythema for psoriasis Itch and erythema for eczema
Results	Clinical evaluation improved by **27% (erythema) and 28% (scales formation)** in patients affected by prsoriasis, **improved by 37.5% (erythema) and 42.8% (itch)** in patients affected by eczema
Indications	Soothing, anti-irritant, lenitive, anti-redness, restructuring
Treatment	Topical application of O/W emulsion containing OMEGABLUE® at 2% in comparison to a placebo twice daily over a 30 days' period

OMEGABLUE®

THE CLINICAL EFFICACY

PATIENTS AFFECTED BY PSORIASIS



Observed skin erythema decreased by 27% (p<0.05)
Observed scales formation decreased by 28% (p<0.01)

Clinical evaluation scale for skin manifestations:

0=absent

1=mild

2=marked

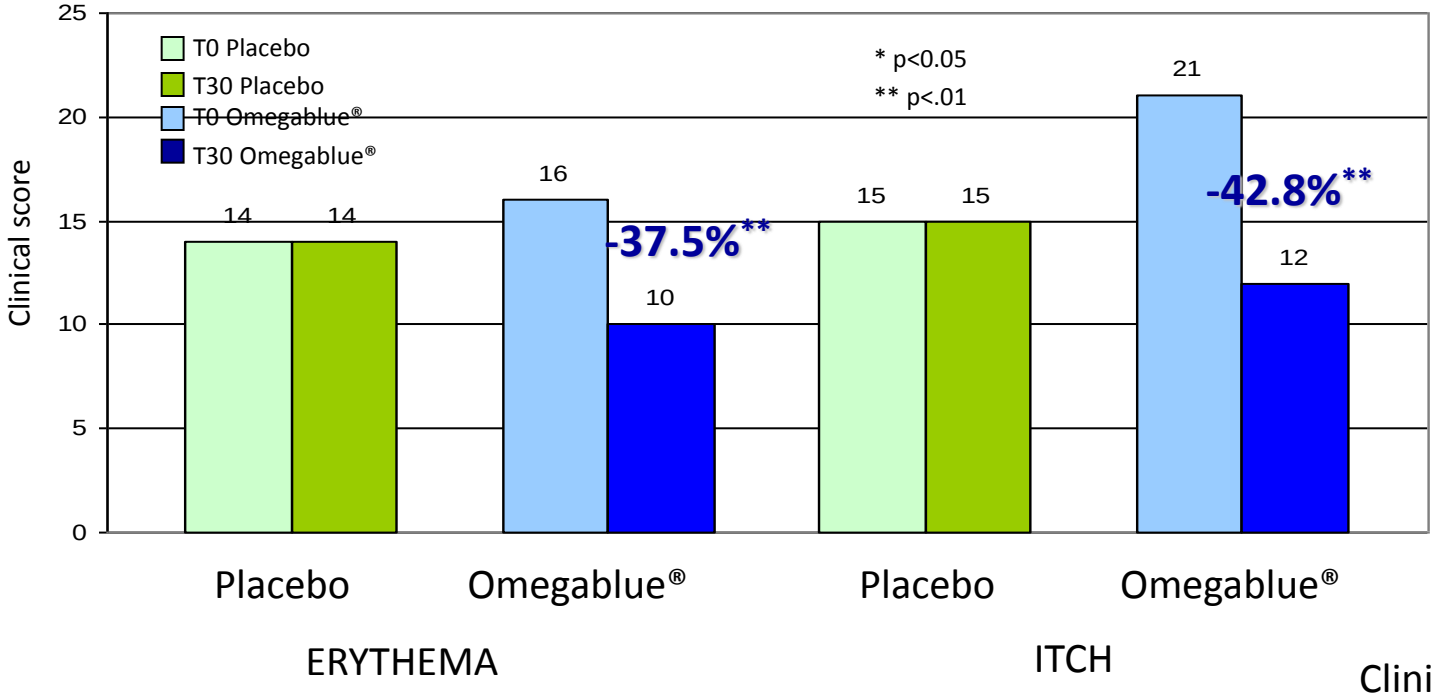
3=severe

indena®

OMEGABLUE®

THE CLINICAL EFFICACY

PATIENTS AFFECTED BY ECZEMA



Observed skin erythema decreased by 37.5% (p<0.01)
Observed and reported itch decreased by 42.8% (p<0.01)

Clinical evaluation scale for skin manifestations:

0=absent

1=mild

2=marked

3=severe

indena®

INDENA TODAY

Follow us on: