



OPEXTAN®

# OPEXTAN®

## HISTORY AND FACTS: NOT ALL OLIVES ARE THE SAME



OPEXTAN® is a **patented olive fruit extract** for beauty supplements and cosmetics, obtained with aqueous ethanol as the unique solvent.

From a selected variety of Italian olives, OPEXTAN® has a **unique polyphenolic profile**, containing **verbascoside** and hydroxytyrosol as major phenolics.

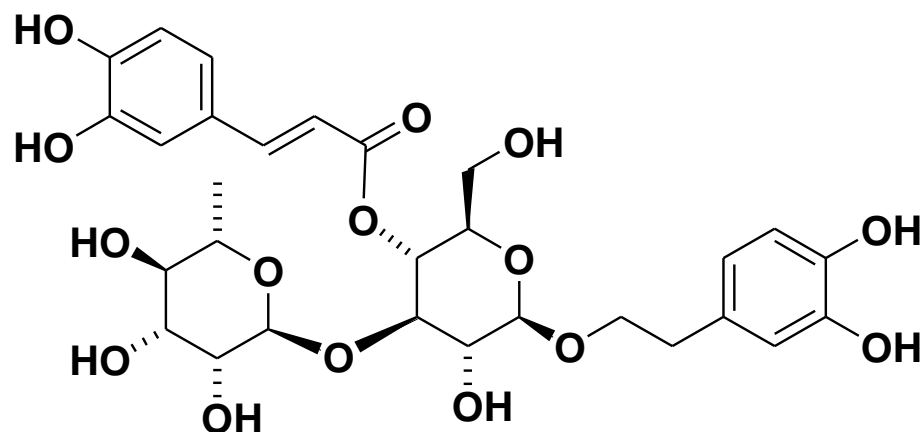
Verbascoside (>2%), a strong free radical scavenger molecule present in the olive pulp, is used topically to protect skin from a variety of oxidative attacks.

**Verbascoside** was found as the **most potent phenol** from the olive tree compared to the other reference compounds (caffeic acid, hydroxytyrosol, oleuropein).



# OPEXTAN®

HISTORY AND FACTS: NOT ALL OLIVES ARE THE SAME



There are over **300 different varieties** of olive tree, and a high concentration of **verbascoside** is typical of some South-Italian and French varieties characterized by a very high antioxidant concentration.

# MED DIET

## HEALTH



- Mediterranean diet: a modern nutritional recommendation originally inspired by the traditional dietary patterns of Greece, Southern Italy, and Spain
- Proportionally high consumption of olive oil, legumes, unrefined cereals, fruits, and vegetables
- Recognized in 2003 as an Intangible Cultural Heritage of Italy by UNESCO
- Olive oil as the principal source of fat is characteristic of this diet

# MED DIET

## HEALTH



- The strongest evidence for a beneficial health effect and decreased mortality after switching to a largely plant based diet comes from studies of Mediterranean diet (e.g. from the NIH-AARP Diet and Health Study)
- Strongly related to the **health effect of olive oil** (polyphenols)
- Inclusion of red wine is considered a contributing factor (flavonoids)
- Med diet is associated with **50% cardiovascular risk reduction**

# MED DIET

## HEALTH



Only rumors?

- In one of the few diet-beauty epidemiological correlations published so far, people consuming olive products (fruits and oil) have shown fewer wrinkles than those of the same age and ethnic group who do not, or rarely, consume olive oil

### Original Research

### Skin Wrinkling: Can Food Make a Difference?

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Martalena br Purba, BSc, MCN, Antigone Kouris-Blazos, PhD, Naiyana Wattanapenpaiboon, PhD, Widjaja Lukito, MD, PhD, Elizabet M Rothenberg, PhD, Bertil C. Steen, MD, PhD, and Mark L. Wahlqvist, MD, FACN  
*International Health and Development Unit, Faculty of Medicine Nursing and Health Sciences and Asia Pacific Health and Nutrition Centre, Monash University, Melbourne, Victoria, AUSTRALIA (M.b.P., A.K.-B., N.W., M.L.W.), SEAMEO-TROPMED Regional Center for Community Nutrition, University of Indonesia, Jakarta, INDONESIA (W.L.), Department of Geriatric Medicine, Vasa Hospital, Goteborg University, SWEDEN (E.M.R., B.C.S.)*

**Key words:** food intake, nutrients, Caucasian elderly, actinic skin wrinkling, photoaging

# OPEXTAN®

## HISTORY AND FACTS: OLIVE OIL AS A BEAUTY OIL



Olive oil has always been associated to beauty, and, in antiquity, it was at the basis of all cosmetic practices. Today, many actresses and models attribute the perfection of their skin to the swallowing of at least one tablespoon of extra-virgin olive oil each morning<sup>1</sup>

*“The secret of my beauty?  
Extra-virgin olive oil!”*

**Sophia Loren**, voted, at 71, the world’s most naturally beautiful person, and rumored to take two spoonfuls of olive oil every day<sup>2</sup>



1. C. Firenze: The passionate olive, Ballantine Books, New York, 2005, p. 90

2. BBC News, 13 August 2006

# OPEXTAN®

## HISTORY AND FACTS: OLIVE OIL AS A BEAUTY OIL



**Jeanne Louise Calment** holds the record for the longest confirmed lifespan (***122 years and 164 days***). On turning 121, she was asked the secret of her longevity and attributed it to her calm disposition (as befits her name) and to olive oil, which she poured on each meal and rubbed into her skin. **She claimed not to have any wrinkle on her face<sup>3</sup>**



3. Daily Telegraph, August 4, 2007



FEBRUARY 23, 2004

BUSH'S  
MILITARY RECORDS  
IS DISNEY MOUSETRAPPED?

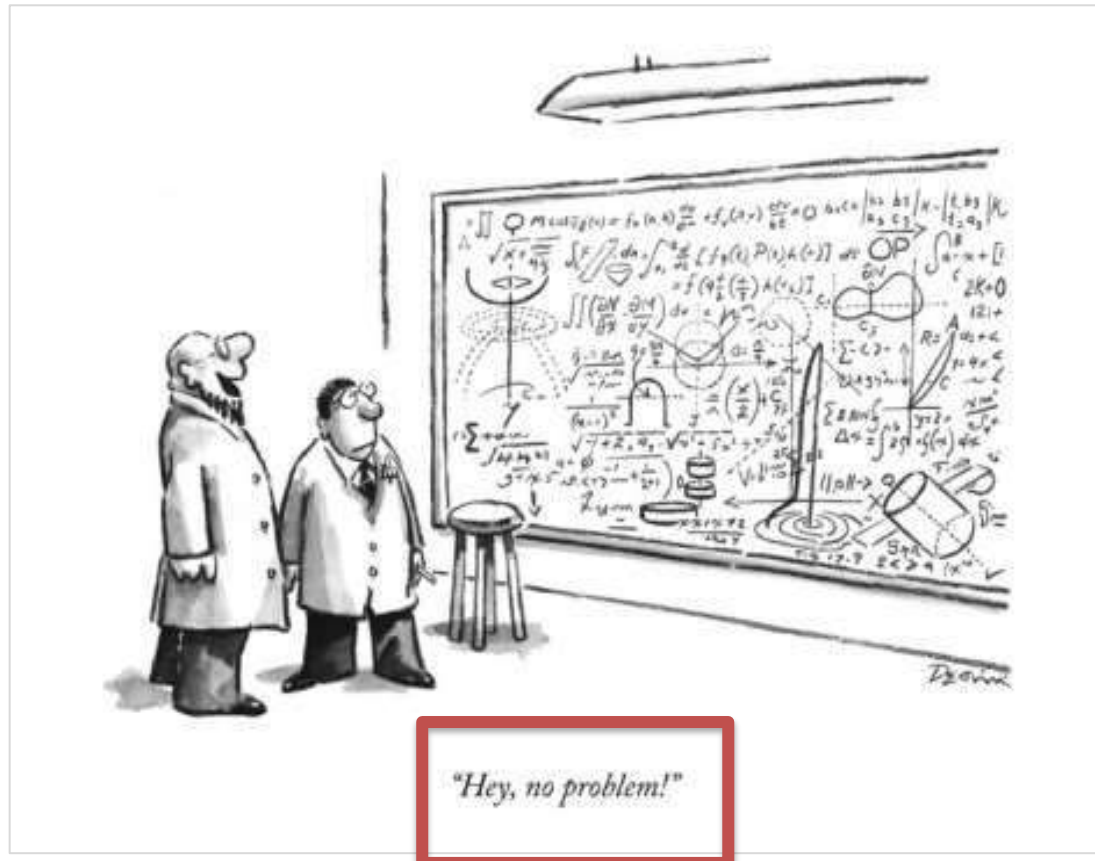
# TIME

## THE SECRET KILLER

- The surprising link between **INFLAMMATION** and **HEART ATTACKS, CANCER, ALZHEIMER'S** and other diseases
- What you can do to fight it

# INFLAMMATION?

- Acute (it hurts)
- Chronic and low-grade (it kills)



# INFLAMMATION?

**Acute inflammation** is a normal physiological response critical to maintain homeostatic control,

but

when it becomes **chronic**, inflammation contributes to the pathophysiology of a range of diseases.

# INFLAMMATION AND SKIN INFLAMMAGING

“Inflammaging”= was coined by C. Franceschi and colleagues, characterizes the fact that ageing is accompanied by a low-grade chronic up-regulation of certain pro-inflammatory responses.

What is the difference between inflammation and inflammaging?

Inflammation= tumor, rubor, dolor, calor  
(and functio laesa))



Inflammaging= differs significantly from acute inflammation in that it is a  
(a) low-grade, (b) controlled, (c) asymptomatic, (d) chronic, and (e) systemic state of inflammation



In skin, chronic inflammation causes the known phenomena of skin aging such as wrinkles and loss of elasticity.

The end result of this cycle is a chronic and systemic pro-inflammatory state where both tissue damaging and healing mechanisms operate simultaneously. Over decades, the opposing forces are likely critical perpetrators of ageing and age related disease, leading to an accumulation of subtle tissue damage.



# SOME EVIDENCES FROM SCI-PAPERS



## Hydroxytyrosol as anti-inflammatory agent

### 1. In vitro

#### INHIBITION OF LEUKOCYTE LEUKOTRIENE B<sub>4</sub> PRODUCTION BY AN OLIVE OIL-DERIVED PHENOL IDENTIFIED BY MASS-SPECTROMETRY

Anna Petroni, Milena Blasevich, Nadia Papini, Marco Salami, Angelo Sala  
and Claudio Galli

Institute of Pharmacological Sciences, University of Milan, Milan, Italy

*Thrombosis Research*, Vol. 87, No. 3, pp. 315–322, 1997

#### Inhibition of Leukocyte 5-Lipoxygenase by Phenolics from Virgin Olive Oil

Rocio de la Puerta,\*† Valentina Ruiz Gutierrez‡ and J. Robin S. Hoult\*§

*Biochemical Pharmacology*, Vol. 57, pp. 445–449, 1999.

#### Inhibition of Arachidonate Lipoxygenase Activities by 2-(3,4-Dihydroxyphenyl)ethanol, a Phenolic Compound from Olives

Noriko KOHYAMA, Tadahiro NAGATA,\* Shin-ichi FUJIMOTO, and Keizo SEKIYA†

*Biosci. Biotech. Biochem.* **61** (2), 347–350, 1997

# SOME MORE



## Hydroxytyrosol as anti-inflammatory agent 2. In vivo

### Effects of Hydroxytyrosol-20 on Carrageenan-induced Acute Inflammation and Hyperalgesia in Rats

Dezheng Gong<sup>1</sup>, Chengyan Geng<sup>1</sup>, Liping Jiang<sup>1</sup>, Jun Cao<sup>1</sup>, Hiroyuki Yoshimura<sup>2</sup> and Laifu Zhong<sup>1\*</sup>

PHYTOTHERAPY RESEARCH  
*Phytother. Res.* 23, 646–650 (2009)

### Hydrolyzed Olive Vegetation Water in Mice Has Anti-Inflammatory Activity<sup>1</sup>

Catherine M. Bitler,<sup>2</sup> Tiffany M. Viale, Bassam Damaj,<sup>\*</sup> and Roberto Crea

*J. Nutr.* 135: 1475–1479, 2005.

# AND MORE

**Hydroxytyrosol** as anti-inflammatory agent

## 3. Clinically

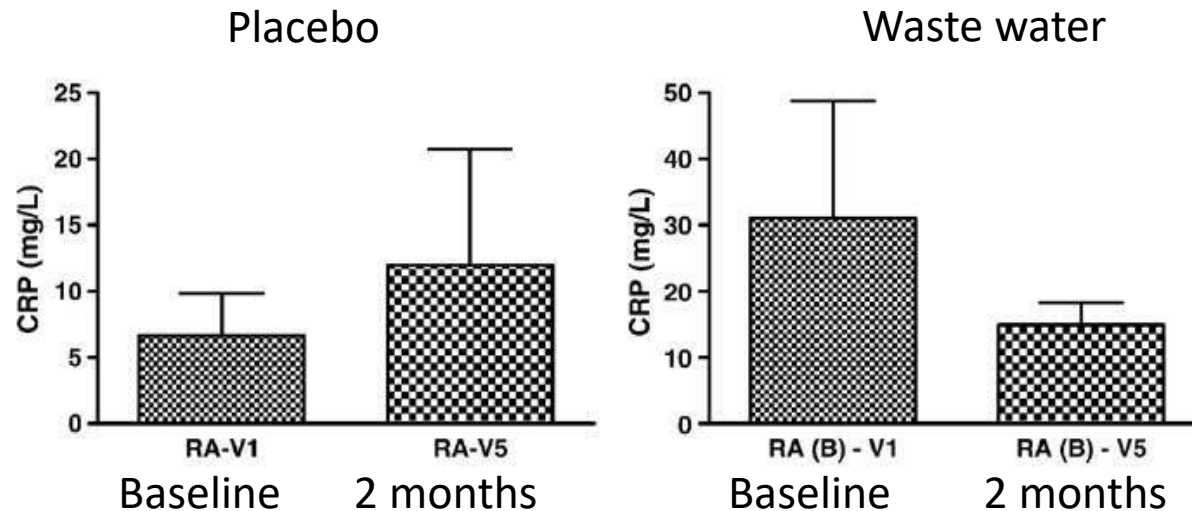
Olive extract supplement decreases pain and improves daily activities in adults with osteoarthritis and decreases plasma homocysteine in those with rheumatoid arthritis<sup>☆</sup>

Catherine M. Bitler<sup>b,\*</sup>, Kathleen Matt<sup>a</sup>, Mary Irving<sup>a</sup>, Ginger Hook<sup>a</sup>, Joseph Yusen<sup>a</sup>, Forrest Eagar<sup>a</sup>, Ken Kirschner<sup>a</sup>, Brian Walker<sup>a</sup>, Roberto Crea<sup>b</sup>

Nutrition Research 27 (2007) 470–477



## CRP levels in rheumatoid arthritis patients



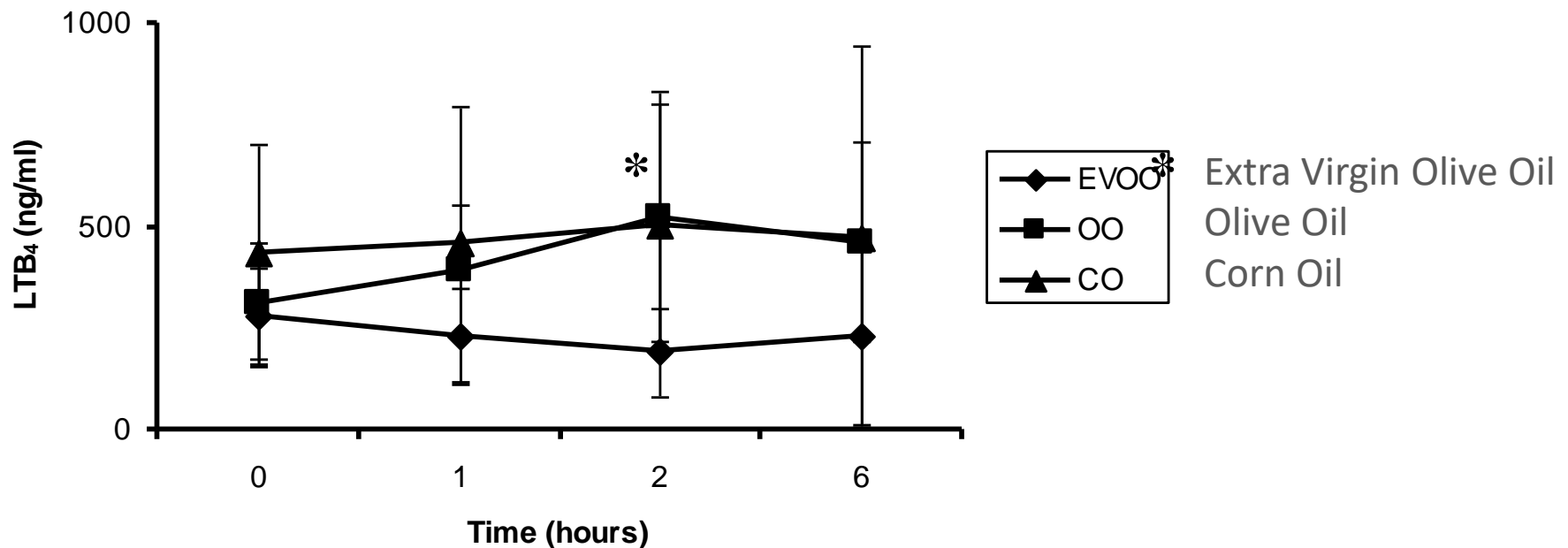
# AND MORE

**EVOO** as anti-inflammatory agent

## 3. Clinically



EVOO lowers postprandial increase in LTB<sub>4</sub> production





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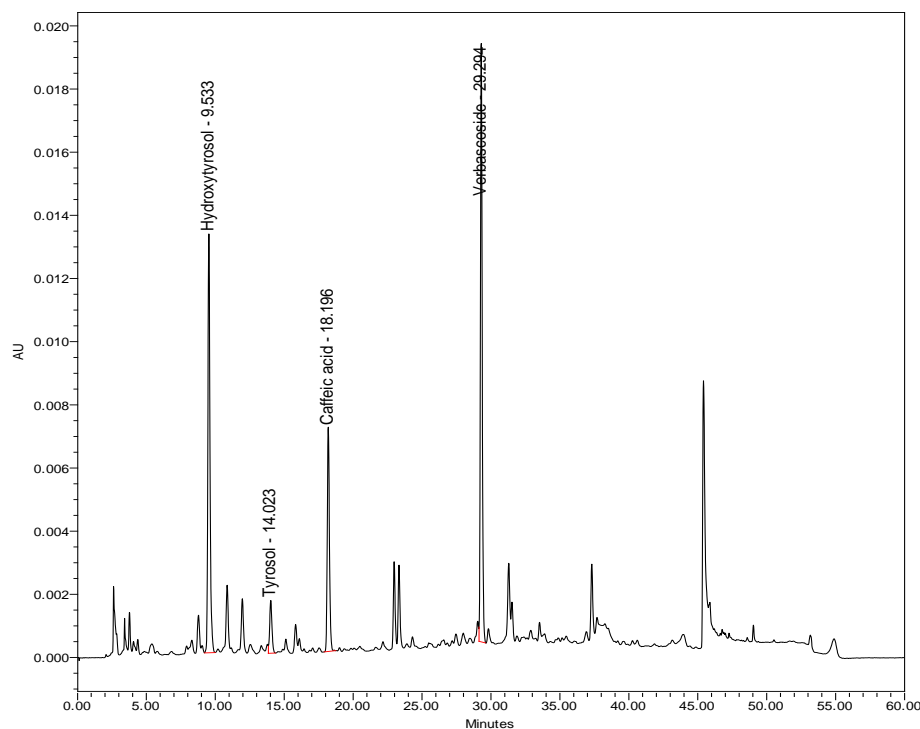
**Verbascoside** was found as the **most potent phenol** from the olive tree compared to the other reference compounds (caffeic acid, oleuropein).

# OPEXTAN<sup>®</sup>

## ACTIVE COMPOUNDS AND HPLC ANALYSIS



Opextan<sup>®</sup> contains all major phenolics of the olive fruit, and it is standardized in 10% polyphenolics, with **verbascoside** (>2%) as the major constituent and **hydroxytyrosol** and derivatives >4.5%



# OPEXTAN®

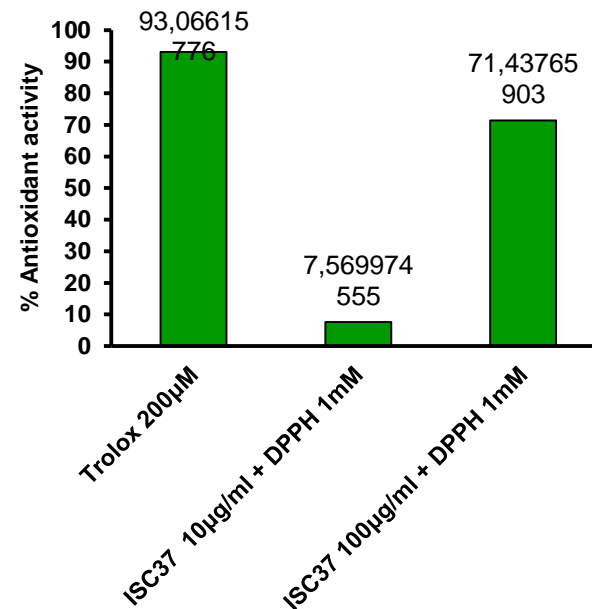
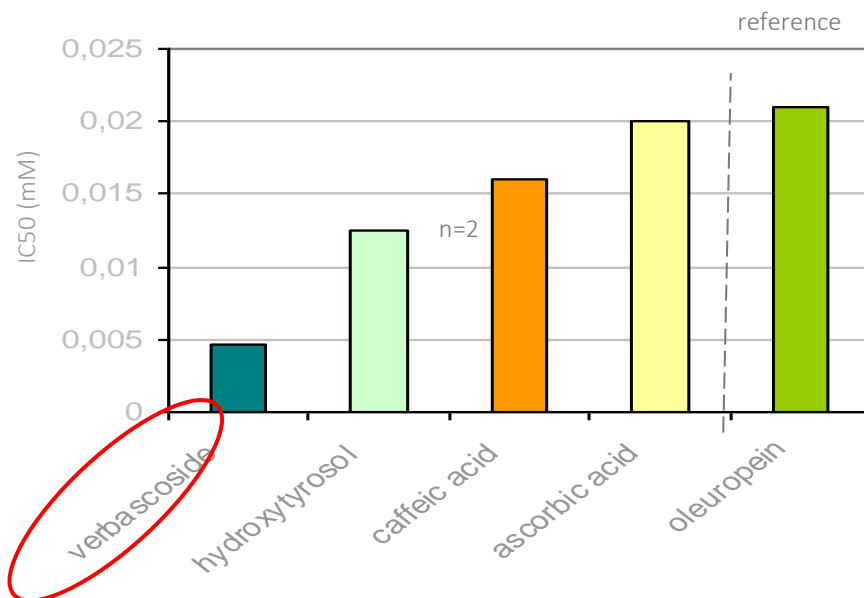
## IN VITRO EFFICACY



Study name:	DPPH radical scavenging activity of OPEXTAN® and OPEXTAN® polyphenols
Experimental model	OPEXTAN® in 500µM DPPH (1,1diphenyl-2-picryl-hydrazyl); absorbance at 517 nm measured after 20 minutes (solution left in the dark after shake) – lower the absorbance, higher the antioxidant activity; Single OPEXTAN® polyphenols have been tested for DPPH radical scavenging activity
Measured parameters	IC50 (Inhibitory concentration 50) has been detected – lower the IC50, higher the radical scavenging by absorbance at 517 nm; single Opextan® polyphenols have been compared to standards as oleuropein (abundant in olive leaf extracts) and ascorbic acid (Vitamin C)
Results	Verbascoside <b>over four times</b> more active than the standard oleuropein considered as an olive stuff benckmark
Indications	Topical antiaging, antioxidant

# OPEXTAN<sup>®</sup>

## IN VITRO EFFICACY- DPPH



### Test results

- Verbascoide was over **four times** more potent than oleuropeine, the typical olive molecule, in reducing DPPH formation
- Opextan<sup>®</sup> has shown relevant antioxidant properties in the DPPH model at 100 mcg/ml



# OPEXTAN®

## IN VITRO EFFICACY

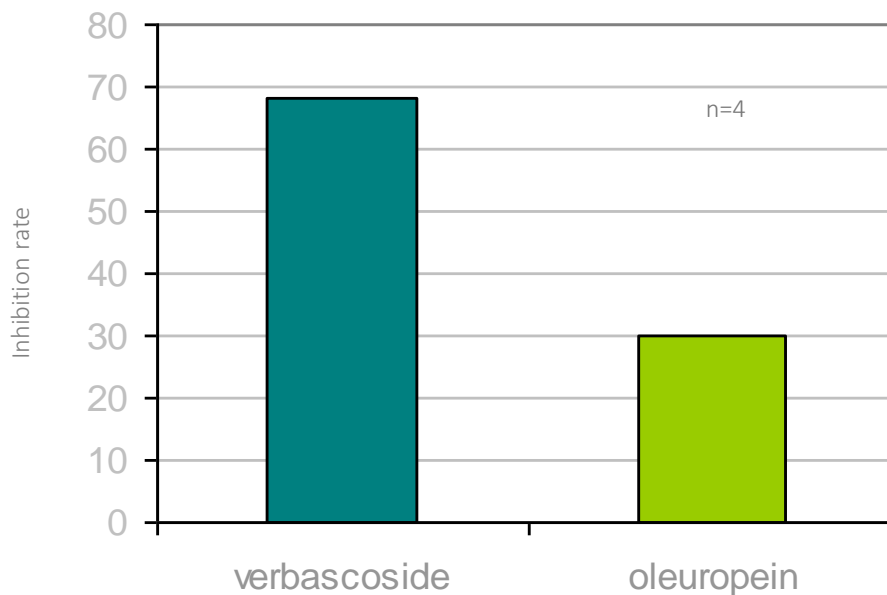


Study name:	O <sup>2-</sup> radical scavenging activity of OPEXTAN® and OPEXTAN® polyphenols
Experimental model	<p>1ml of 250µM hypoxanthine and 0.2ml of xanthine oxidase (0.06 units/ml) were used to initiate the generation of O<sup>2-</sup></p> <p>The mixtures without xanthine oxidase were used as controls</p>
Measured parameters	<p>The rate of increase in absorbance at 560nm for 12 min was measured</p> <p>Flavonoids were tested at a concentration 0.016mM</p>
Results	<p>Verbascoside at 0.016mM <b>inhibits O<sup>2-</sup> formation by 68%</b></p> <p>Verbascoside inhibition rate is <b>more than double</b> than oleuropein</p>
Indications	Topical antiaging, antioxidant

6. Maramaldi *et al.* “Estratto standardizzato di frutti di Olea Europea”, Integr Nutr 2006, 9(3)

# OPEXTAN<sup>®</sup>

## IN VITRO EFFICACY



### Test results

- The  $O^{2-}$  radical scavenging models confirm verbascoside scavenging activity
- Verbascoside at 0.016mM inhibits  $O^{2-}$  formation by **68%**
- Verbascoside inhibition rate is more than double than oleuropein
- $O^{2-}$  radical scavenging model is the one that best mimics the *in vivo* situation

# OPEXTAN®

CLINICALLY PROVEN EFFICACY – PER OS



Study name:	Effect of Opextan® on skin sensitivity to UV (observational study)
Experimental model	UV exposition, MED evaluated for each subject
Number of subjects	13 male volunteers subjects
Measured parameters	MED (Minimal Erythematol Dose) following to UV irradiation
Results	<b>+14.5%</b> MED increase
Indications	Antioxidant
Treatment	160 mg/day for 4 weeks



# OPEXTAN®

CLINICALLY PROVEN EFFICACY – PER OS



Study name:	Effect of Opextan® on oxidative status
Experimental model	Evaluation of the oxidative markers
Number of subjects	19 subjects
Measured parameters	8-isoprostane in the urine evaluated as a marker of oxidative stress (oxidative marker of arachidonic acid)
Results	<b>-47%</b> in the urine content of 8-isoprostane
Indications	Antioxidant
Treatment	400 mg/day for 4 weeks



# OPEXTAN®

## BENEFITS ON SKIN – (SUPPLEMENT)



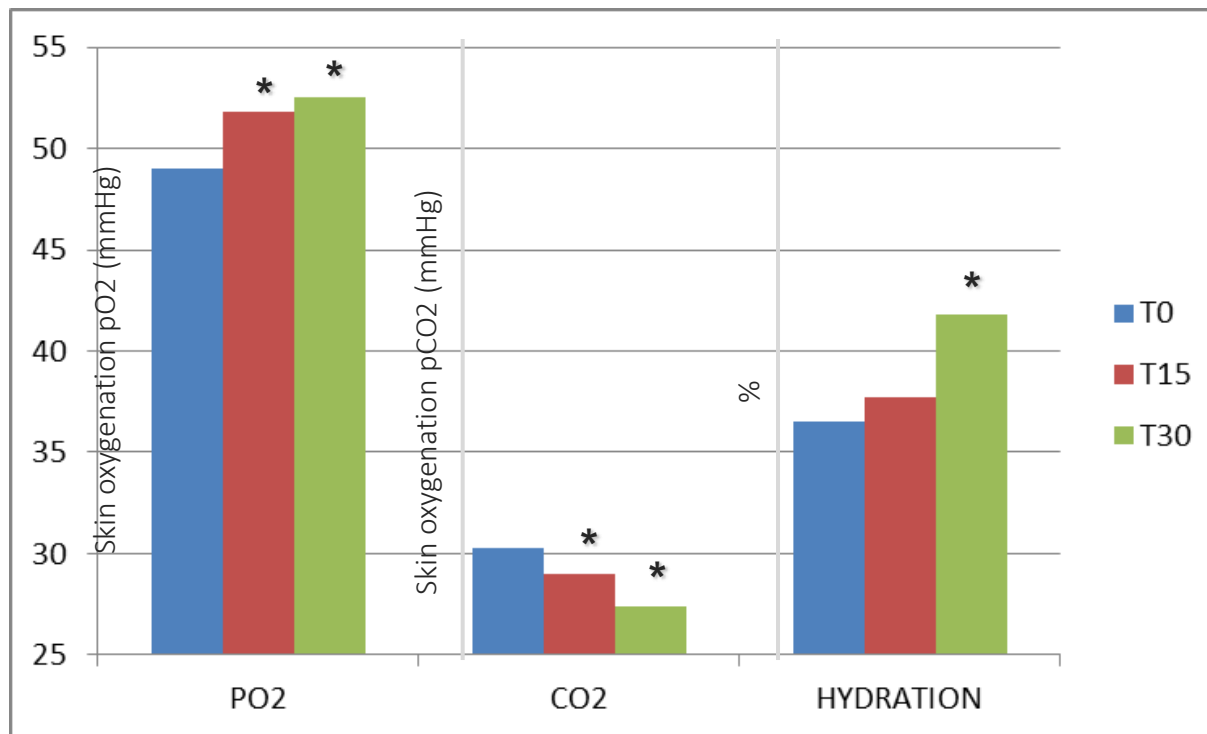
Study name:	Evaluation of the skin benefits induced by Opextan® based supplement
Experimental model	Opextan® taken at 300mg daily by normal subjects with a higher oxidative stress rate (moderate)
Number of subjects	67 volunteers (women) treated with Opextan® supplement over 4 weeks (n=34) vs control (n=33)
Dosage	Coated tablets 150mg Opextan®(2xdie), 300mg/die
Measured parameters	Skin oxygenation, water/lipids content of the skin barrier, skin hydration, oxidative stress, blood lipids
Indications	Nutricosmetics, healthy ageing

# OPEXTAN<sup>®</sup>

## BENEFITS ON SKIN – (SUPPLEMENT)



### Skin parameters



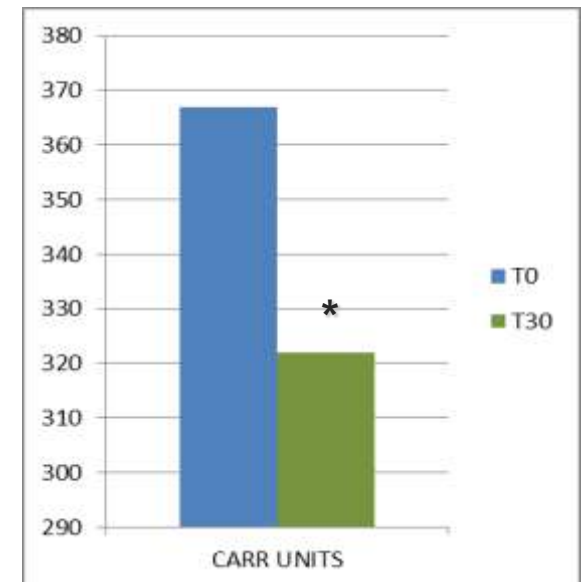
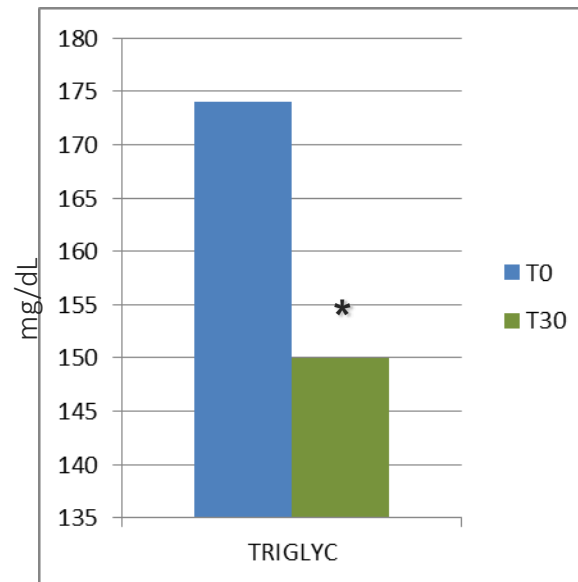
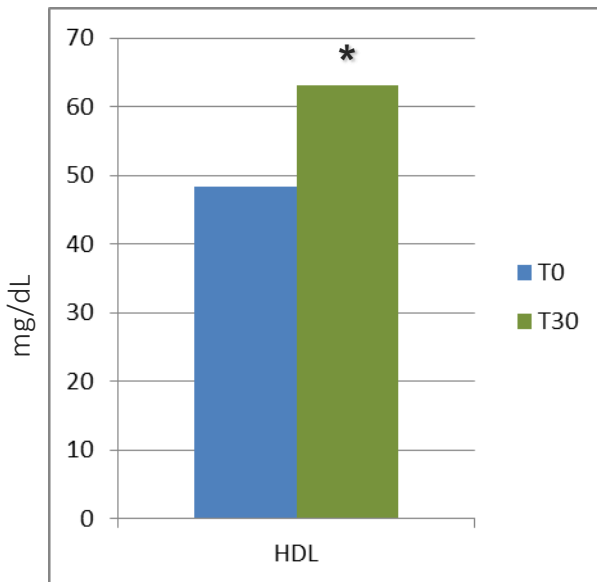
Skin oxygenation (measured by laser doppler flowmetry) improved by 6% ( $p < 0.05$ ) in as short a time as 30 days. Conversely, pCO<sub>2</sub> decreased accordingly in the Opextan<sup>®</sup> group.

# OPEXTAN®

## BENEFITS ON SKIN – (SUPPLEMENT)



### Blood parameters



A statistically significant improvement of blood lipids parameters as well as the oxidative stress has been observed.

# A MILESTONE IN INFLAMMATION HISTORY

## ATHEROSCLEROSIS — AN INFLAMMATORY DISEASE

RUSSELL ROSS, PH.D.

**A** THEROSCLEROSIS is an inflammatory disease. Because high plasma concentrations of cholesterol, in particular those of low-density

# INFLAMMATION AND CARDIOVASCULAR HEALTH

- Heart Health
- Blood Vessels
- High Blood Pressure
- Plaques, Clots, Strokes



# INFLAMMATION AND JOINT HEALTH

- Joint Pain and Swelling
- Arthritis
- Performance
- Recovery





# INFLAMMATION AND SKIN HEALTH

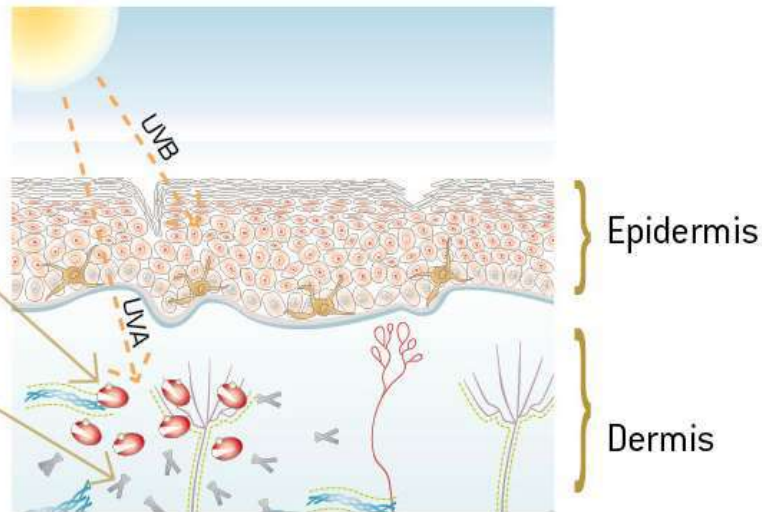


## Photo-aged skin

UVA = aging  
UVB = burning

Increase in free radicals

Over-production of enzymes



Damage caused to the structural elements of the dermis.

- Photoageing
- Skin wrinkling
- Free radical scavenger damage
- Skin elasticity
- Skin homeostasis

# GROWING EVIDENCES

## Elevated pre-treatment levels of plasma C-reactive protein are associated with poor prognosis after breast cancer: a cohort study

Kristine H Allin<sup>1,2</sup>, Børge G Nordestgaard<sup>1,2</sup>, Henrik Flyger<sup>3</sup> and Stig E Bojesen<sup>1,2\*</sup>

Higher levels of fatigue are associated with higher CRP levels in disease-free breast cancer survivors

Ingrid J. Orre<sup>a,\*</sup>, Kristin V. Reinertsen<sup>b,c</sup>, Pål Aukrust<sup>d,e</sup>, Alv A. Dahl<sup>b</sup>, Sophie D. Fosså<sup>b</sup>, Thor Ueland<sup>d,f</sup>, Robert Murison<sup>a</sup>

## Effect of high-dose intravenous vitamin C on inflammation in cancer patients

Nina Mikirova<sup>\*</sup>, Joseph Casciaro<sup>†</sup>, Andrea Rogers<sup>†</sup> and Paul Taylor<sup>†</sup>

pro-inflammation cytokines in cancer patients. In our study, we found that modulation of inflammation by IVC correlated with decreases in tumor marker levels.

GROWING EVIDENCES CORRELATE

High inflammation

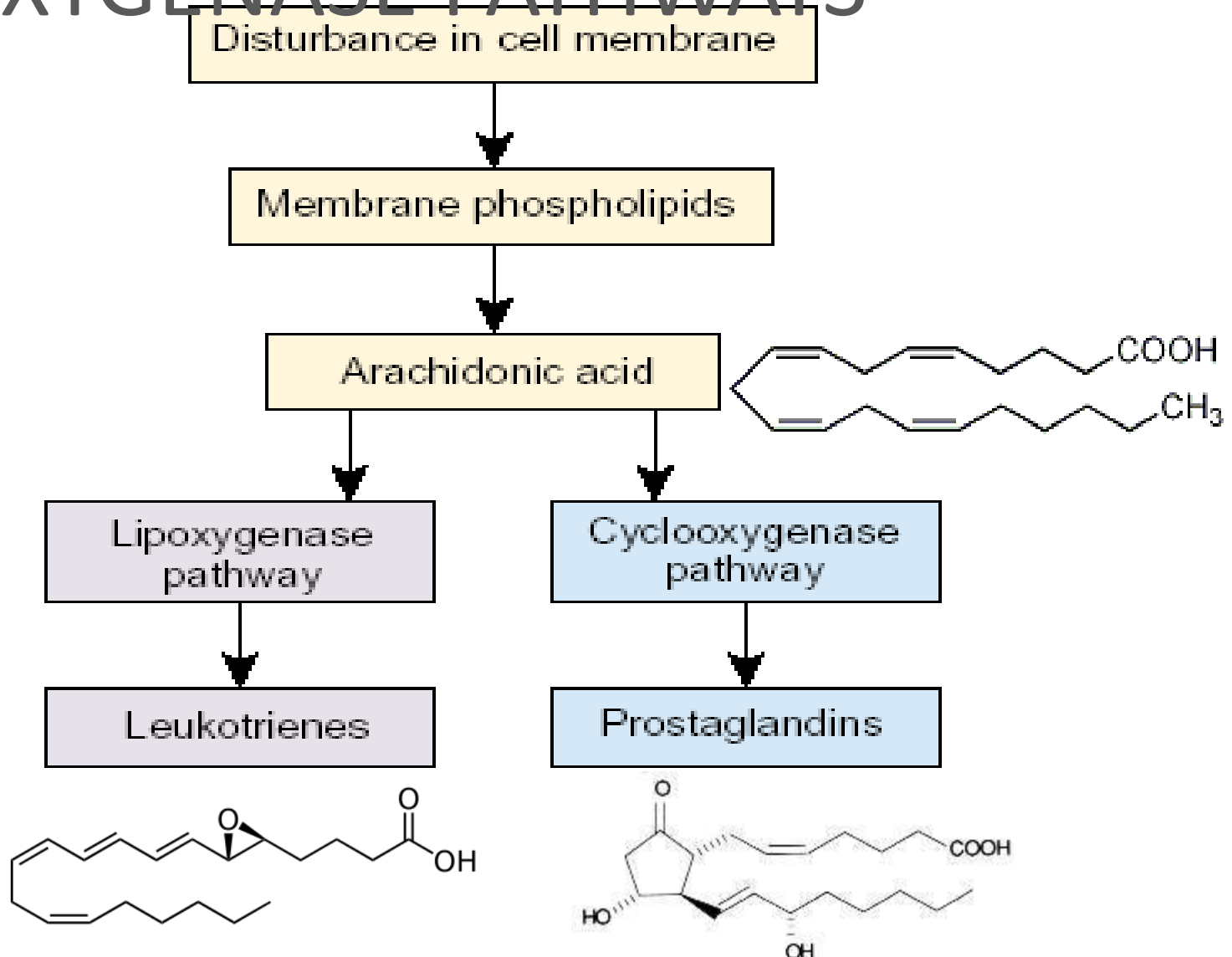
=

poor prognosis

# INFLAMMATORY MEDIATORS

- **Cytokines**, especially IL-6, stimulate the release of acute-phase reactants such as C-reactive protein (**CRP**).
- The proinflammatory **interleukins** either function directly on tissue or work via secondary mediators to activate the coagulation cascade, complement cascade, and the release of nitric oxide, platelet-activating factor, prostaglandins, and leukotrienes.

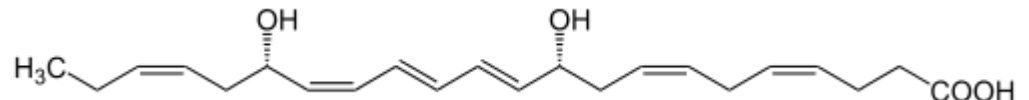
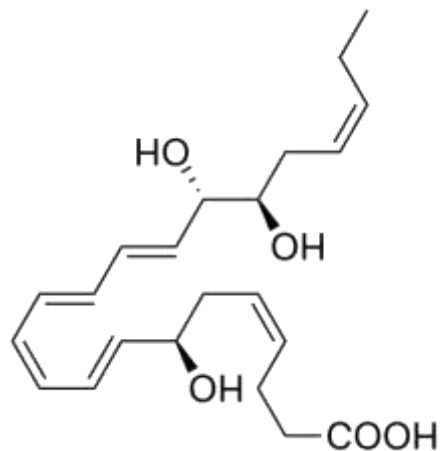
# THE CYCLOXYGENASE AND LIPOXYGENASE PATHWAYS



# HOW DOES INFLAMMATION RESOLVE?

## Production of anti-inflammatory lipoxins

- An active, coordinated program of resolution initiates in the first few hours after an inflammatory response begins.
- These events coincide with the biosynthesis, from omega-3 polyunsaturated fatty acids, of **resolvins** and **protectins**, which dramatically shorten the period of neutrophil infiltration by initiating apoptosis.





# ANY CHANCES WE MAY CHANGE THINGS?

Eat



Move  
differently



Think



# SO FAR

- Inflammation is a MAJOR contributor to health/disease.
- Underdiagnosed.
- Difficult to diagnose/quantify.
- Chance to keep it low with lifestyle, food, supplements.
- Especially when disease is present.

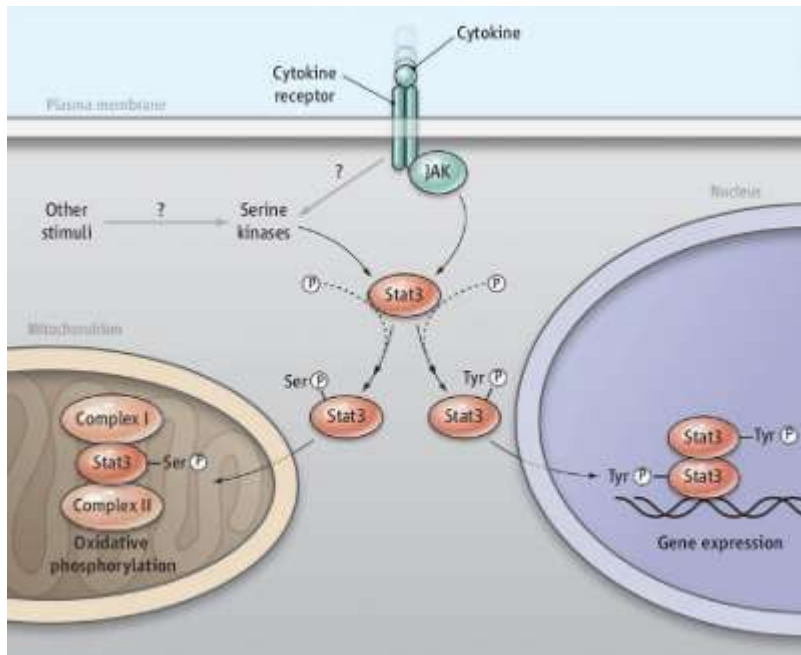
# CAN OPEXTAN<sup>®</sup> BE BENEFICIAL?

## STAT3



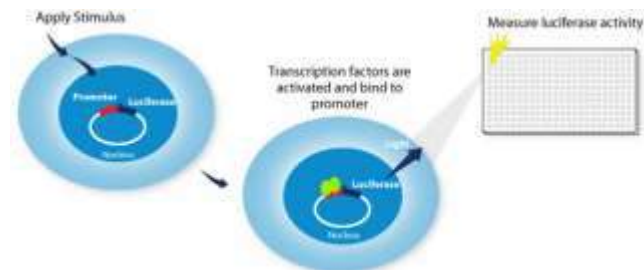
### THE MODEL

STAT-3 is a **transcriptional factor** involved in the **pro-inflammatory** responses of the body. It responds in fact to inflammatory stimulus as cytokines and interferons.



The **inhibition of STAT-3 activation** has a relevance in **inflammatory-associated reactions**.

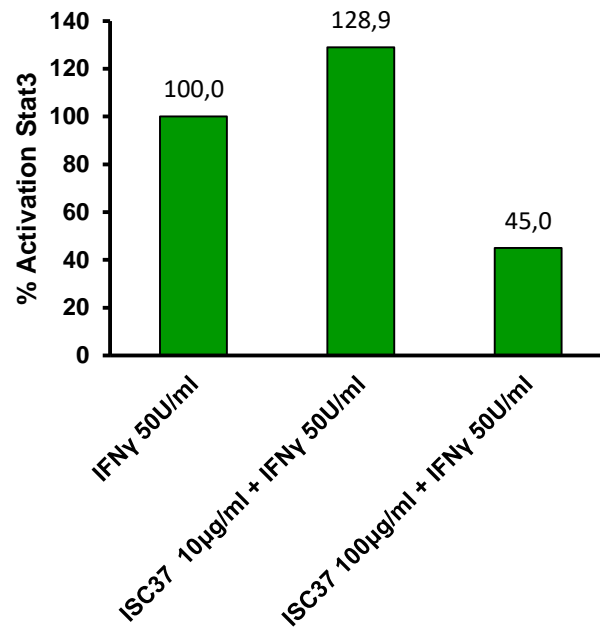
The evaluation has been made by luciferase activity.



# OPEXTAN<sup>®</sup>

## IN VITRO EFFICACY: STAT-3

Study name:	Opextan <sup>®</sup> inhibits INF gamma induced STAT-3 activation (in in HeLa cells).
Experimental model	Cells(transfected with the plasmid pTATA TK -Lucplasmid) are treated with IFN gamma in the absence or presence of Visnatine.
Number of subjects	2 + 2 experiments/ 3 conc.
Measured parameters	STAT-3 activation(%) measured on a 100% IFN gamma activated scale.



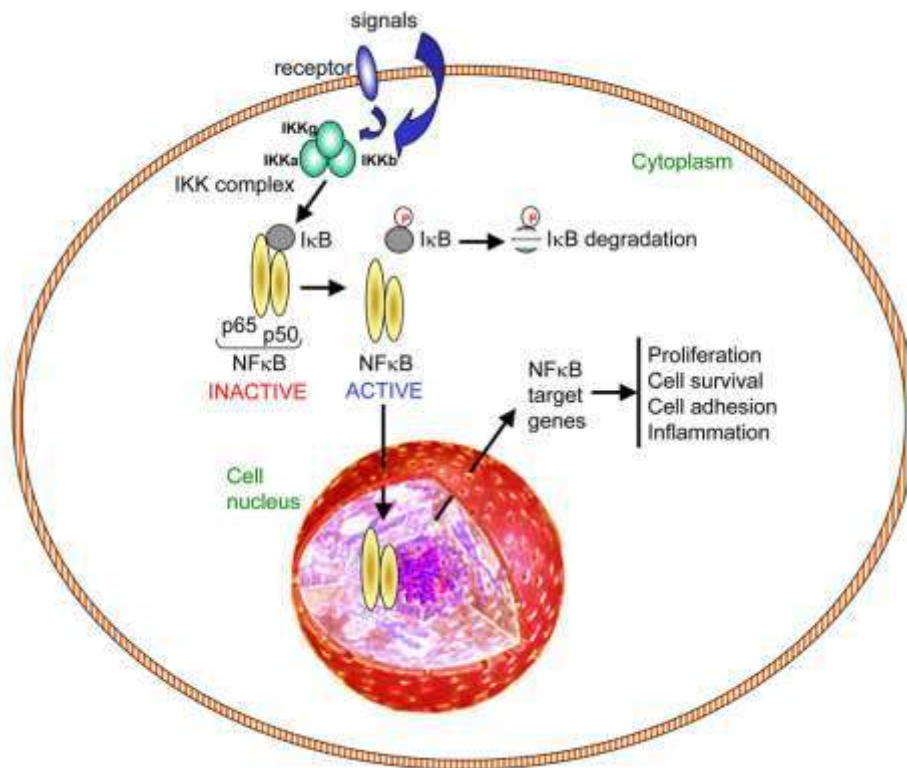
Opextan<sup>®</sup> has been shown to **reduce** STAT-3 activation.

# OPEXTAN<sup>®</sup>

NFκB

## THE MODEL

NF-κB is a transcriptional factor located in all cells and is involved in the **pro-inflammatory** responses of the body. It is involved in cells reaction to cytokines, ROS, UV, immune challenges.



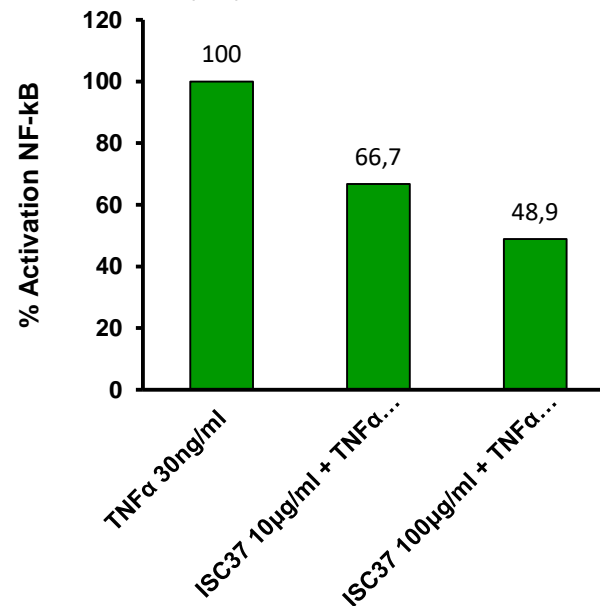
The **inhibition** of NFκB activation has a relevance in **inflammatory-associated reactions**.



# OPEXTAN<sup>®</sup>

## IN VITRO EFFICACY: NFkB

Study name:	Opextan <sup>®</sup> inhibits TNF alpha induced NFkB activation in vitro.
Experimental model	Cells(transfected with a three copies of NFkB binding site plasmid) are incubated with Visnadine and TNF alpha.
Number of subjects	2 + 2 experiments/ 3 conc.
Measured parameters	NFkB activation(%) measured on a 100% TNF alpha activated scale.

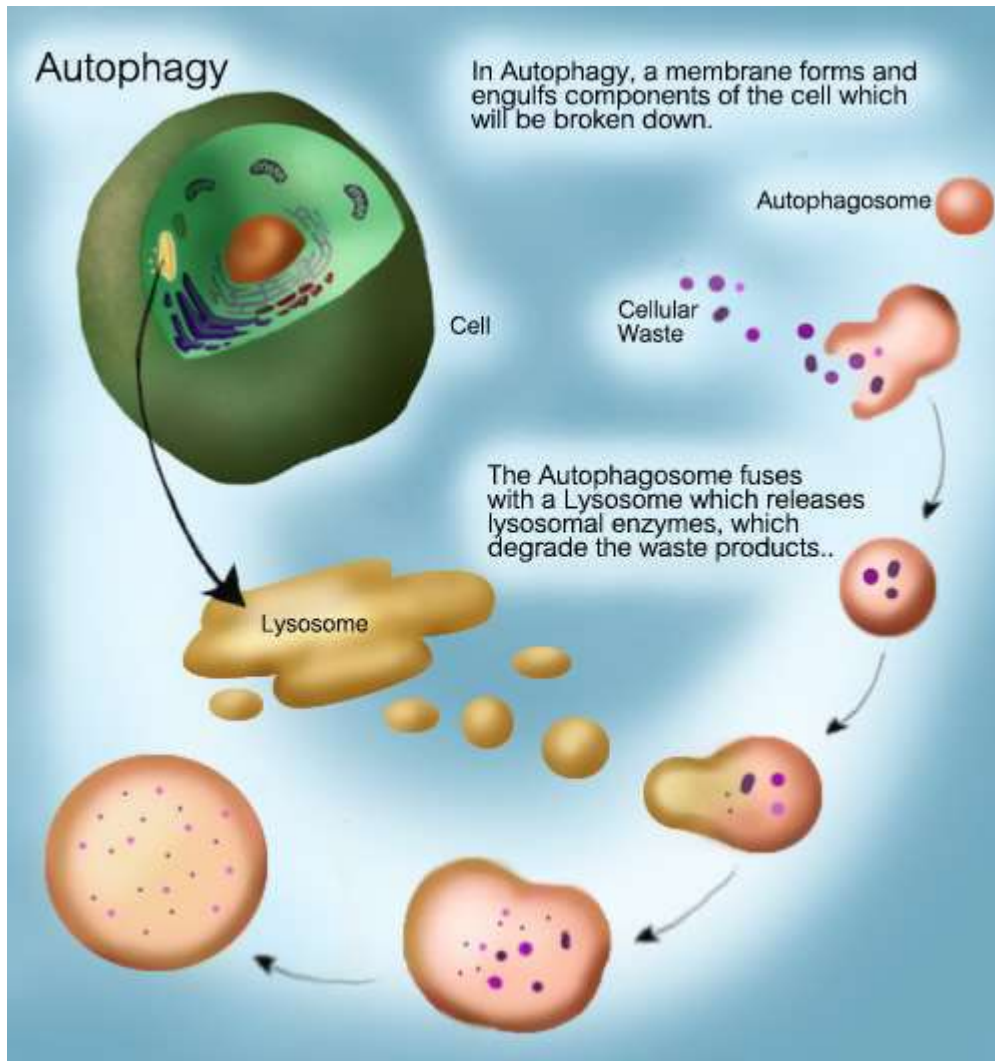


Opextan<sup>®</sup> has been shown to **reduce** TNF Alpha induced NFkB activation.



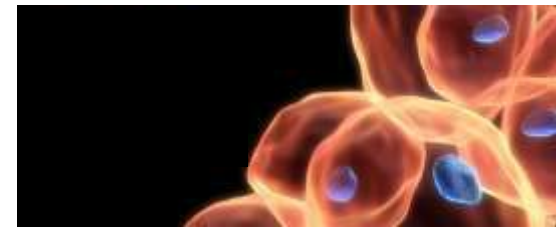
# OPEXTAN<sup>®</sup>

## AUTOPHAGY



### THE MODEL

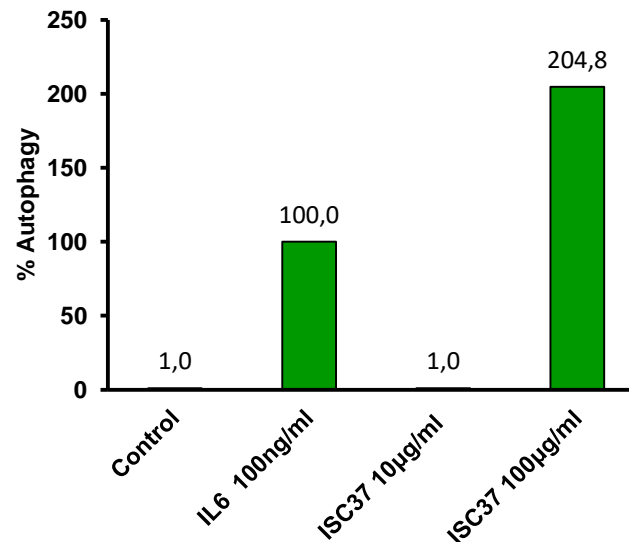
Autophagy is evaluated as the capacity of cells of **collecting** and **degrading waste products**. It may thus suggest a detox function.



# OPEXTAN®

## IN VITRO EFFICACY: **AUTOPHAGY** on keratinocytes

Study name:	Opextan® induces autophagy in keratinocytes
Experimental model	Fluorescent vesicles are produced during autophagy in HaCaT (Human keratinocytes).
Number of subjects	2 + 2 experiments/ 3 conc.
Measured parameters	Autophagy induction (%) measured on a 100% IL-6 activated autophagy by fluorescence.

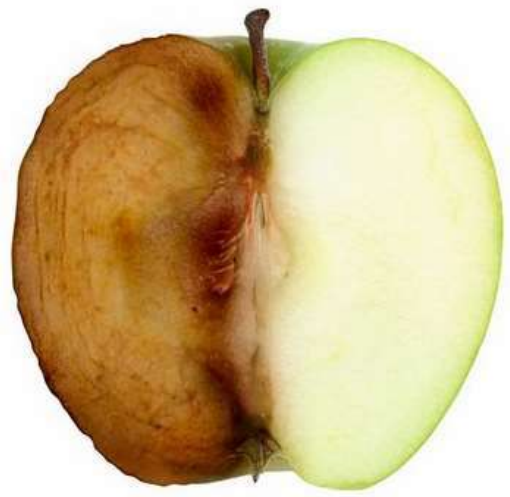


Opextan® has been shown to **induce autophagy**.

ECOCERT

# OPEXTAN®

## TAKE HOME MESSAGE



# OPEXTAN®

## SUM UP -> MECHANISMS

Opextan® acts on skin aspect/closely entangles with function, on the basis of several mechanisms:



ANTIOXYDANT



FREE RADICAL SCAVENGER



ANTI-INFLAMMATORY/ANTI-INFLAMMAGING



SUN CARE/ANTI-PHOTOAGEING

- Effects of a standardized olive (*Olea europaea*) extract on healthy skin aging parameters, *Minerva Medica* 2019, in press

# OPEXTAN®

160-400 mg/die

## SUM UP -> FINAL OUTCOMES

Opextan® acts on skin aspect/closely entangles with skin function, on the basis of several mechanisms:

- Clinically assessed **skin oxygenation**
- Clinically assessed **skin hydration**
- Clinically assessed **skin resistance to sun damage**
- Clinically assessed **oxidative status**
- **Food grade** ingredient (solvent and **contaminants**)
- Standardized in **verbascoside** and **HT**
- (In vitro) and clinically assessed **anti oxidant** efficacy

# OPEXTAN®

## IN A NUTSHELL



- Olive pulp extract (**non caloric**) titrated in 10% polyphenolics
- Obtained from the edible part of an **Italian cultivar** of olive characterized by a high and unique polyphenolic contents.
- Contains **verbascoside**, a caffeoylated glycosyl conjugate of hydroxytyrosol, as major constituent (ca. 3%).
- The mixture of olive polyphenolics provides benefits from their proven synergistic activity.
- Is obtained from an edible olive biomass in a process that does not imply acids or bases, and only uses water and alcohol.
- Standardized in >10% phenolics, and its major constituent is **verbascoside** (<2%), the most potent anti-oxidant of the olive tree
- **USE: Skin protection against UV exposure and radical damage** with an oral supplement/amelioration of **skin oxygenation** and in situ oxidative status/cardiovascular protection by inhibition of LDL oxidation.
- Toxicological profile, in vivo anti-oxidant activity (excretion of isoprostanes), protection against glycemic and radiation offense (healthy ageing), **amelioration of skin conditions** (taken orally) are available.
- **USP:** contains a mixture of genuine phenolic conjugates from olives and not Hydroxytyrosol alone. Its major constituent is the olive's most potent antioxidant.

**AVAILABLE FOR ORAL + TOPICAL APPLICATION**

160-400 mg/die





ANTI-AGEING, SKIN RESTRUCTURANT, BODY SHAPING



 **indena®**  
INDUSTRIA  
DERIVATI  
NATURALI

COSMETIC

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C E N T E V I T A <sup>TM</sup>

ANTI-INFLAMMAGING AND ANTI-GLYCATION AGENT

**CENTEVITA™** is an Ecocert validated extract from the leaves of *Centella asiatica*, also known as *Gotu kola* or India Pennyworth.

It is characterized not only by all the biologically active triterpenes, including madecassoside, but it also contains a polyphenolic fraction contributing to the biological efficacy of the extract.

The *Centella asiatica* leaf is characterized by the content of extremely biologically active molecules, known as triterpenes, asiaticoside, asiatic acid, madecassoside and madecassic acid. They all contribute to enhance the collagen synthesis, mainly accounting for the type I collagen.

Madecassoside, accounting as the major component of this extract, is also able to enhance collagen type III formation<sup>1</sup>, being type I and type III collagens the major components of skin dermis.



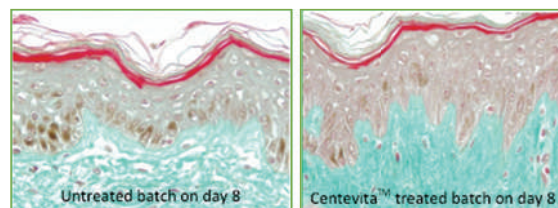
## CENTEVITA™ - PROPERTIES

*Centella asiatica* is widely used both in the Indian Ayurvedic medicine and as a traditional herbal medicine in Asia and India. The traditional medicine of Madagascar has used it for immemorial time as an agent favouring cicatrization, but also orally to treat stomach ulcers and leprosy. The triterpenic fraction of *Centella asiatica* has been shown to enhance collagen synthesis in fibroblast cultures,<sup>2</sup> and more recently they were reported to have an action on factors controlling the regulation of inflammation.<sup>3</sup>

### EVALUATION DATA

Novel in vitro studies confirm the biological activity of CENTEVITA™ and suggest a synergy between the triterpenes and the polyphenolic fraction. Several biological mechanisms have been elucidated:<sup>4,5</sup>

- applied on human skin explants at 1% for five consecutive days (once a day) has reduced the UV induced photodimerization of thymine, evaluated by immunostaining, by **28%** ( $p < 0.05$ ), thus indicating a **DNA protection efficacy**;
- applied on human skin explants at 1% for five consecutive days (once a day) has reduced the IL-1 $\alpha$  expression by **26%** ( $p < 0.01$ ), thus suggesting an efficacy in **counteracting inflammaging**;
- induced a **total glycation prevention** of the reaction induced by methylglyoxal in culture medium on human skin explants;
- induced a **marked densification** of the collagen network in the papillary dermis;
- topically applied on human adipocytes induced an increase by **39%** of the **smaller adipocytes** sized 0-40  $\mu\text{m}$  and compared to the untreated batch has induced a total fatty acids release in the medium 155% ( $p < 0.05$ ) higher than the untreated batch, in line with the caffeine positive reference.



CENTEVITA™ on human keratinocytes

### CLINICAL EVALUATION DATA

A double blind, placebo controlled clinical trial on 20 volunteers<sup>6</sup> (each representing its own control) has underlined the following results: CENTEVITA™ applied twice daily for 6 weeks in a cosmetic formulation at 0.5% improved **skin clinical elasticity** (R5 parameter) by **29%** ( $p = 0.001$ ) as well as **skin firmness** (R7 parameter) by **17%** ( $p = 0.003$ ).

**Collagen density** was evaluated by the means of a siascope and increased in a statistically significant manner in **70% of tested volunteers**.

#### CHARACTERISTICS

**≥45.0%** ≥45.0% of the sum of asiaticoside, madecassoside, asiatic acid and madecassic acid.

**INCI NAME** Centella asiatica leaf extract

**CAS** 283-640-5

**EINECS** 84696-21-9

#### APPLICATIONS

CENTEVITA™ is a recommended active ingredient to counteract visible skin aging and invisible inflammaging and collagen glycation. It promotes collagen synthesis, prevents inflammation and UV damages. It has also shown interesting lipolytic properties. It is Ecocert validated, manufactured with "clean" food grade solvents and the raw material is sourced with a full sustainable supply chain from the African biodiversity.

**RECOMMENDED DOSAGE: 0.1-1%**

#### References

- <sup>1</sup> Bonte F, Dumas M, Chaudagne C, Meybeck A, Ann Pharm. Fr: 53, 38-42 1995.
- <sup>2</sup> Maquart FX, Bellon G, Gilleri P, Wegrowski Y, Borel JP, Connect Tissue Res. 24, 107-120 1990.
- <sup>3</sup> Loiseau A, Theron E, Degueray A, Lepetit JC, Proceed. SCC New York, December 2001.
- <sup>4</sup> Indena, data on file, study 11E2321-P1.
- <sup>5</sup> Indena, data on file, study 11E2339.
- <sup>6</sup> Indena, data on file, study 11E2402.