

« Botanicals for skin aging »

by Dr Alessandra HADDAD, MD PhD



Patrizia A d'Alessio, MD PhD

QoL is becoming an issue in aesthetic treatments



According to Dr Haddad,

(EPM/Rosenberg), and a pain scale. The minimally invasive procedures resulted in improvement in quality of life and self-esteem, which were stronger the first 3 months after the procedures but remained at a higher level than that before treatment, even after

Original Article | [Published: 22 March 2013](#)

Assessment of Quality of Life in Patients Who Underwent Minimally Invasive Cosmetic Procedures

[Marcello Simão de Aquino](#) ✉, [Alessandra Haddad](#) & [Lydia Masako Ferreira](#)

[Aesthetic Plastic Surgery](#) **37**, 497–503 (2013) | [Cite this article](#)

939 Accesses | **24** Citations | **1** Altmetric | [Metrics](#)

What will be talking about?

According to Pr Kerscher,

major targets of anti-aging ingredients

- oxidative stress;
- **collagen** metabolism;
- supplementing effective **sunscreens**;
- maximized skin care.

Leitthema | [Published: July 2004](#)

Dermatokosmetische Wirkstoffe

Active ingredients in dermatocosmetics

[T. Reuther](#) ✉ & [M. Kerscher](#)

[Der Hautarzt](#) **55**, 630–636 (2004) | [Cite this article](#)

605 Accesses | **3** Citations | [Metrics](#)

Botanical ingredients



... may contribute to mood modulation and skin amelioration vs rejuvenation addressing some medical issues

In ancient times the food / skin link had already been observed



Dr George Cheyne
(1671-1743)

At the edge of the 17th – 18th century, **vegetarianism** became a treatment for obesity and gout for rich people consuming a lot of meat.

It turned out as a solution to **prevent wrinkles and the fading of radiance of the skin.**

Opuntia Ficus Indica

Pigments **Betanine and Indicaxanthine**,
plus Flavonoïdes,

- metabolic markers, glycemia, cholesterol and triglycerides,
 - anti-oxydant & neuroprotective,
- Anti-inflammatory & cicatrisation



Antioxidant Betalains from Cactus Pear (*Opuntia Ficus Indica*) inhibit endothelial ICAM-1 expression. Gentile C, Tesoriere L, Allegra M, Livrea MA, **d'Alessio P**. Annals **NY Acad Sci**, **2004**, vol.1028, "Signal Transduction and Communication in Cancer Cells", pp 481-486.

BIO-GUIDED

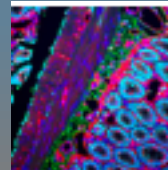
RESEARCH



More than 20 years of research
2000 molecules analyzed
out of 100 plant extracts

- ✓ Initially discovered in the *Halfordia kendack* plant in Vietnam at the border with China,
- ✓ the AISA molecular complex was then identified in orange peel extracts





AIMS Molecular Science

2022, Volume 9, Issue 2: 46-65. doi: [10.3934/molsci.2022003](https://doi.org/10.3934/molsci.2022003)

Research article

[⏪ Previous Article](#)

d-Limonene challenging anti-inflammatory strategies

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2. Hematology Biology, CHU de Nantes & Inserm 1232 CRCINA, Nantes, France

3. IBMM, Univ Montpellier, CNRS, ENSCM, Montpellier, France

Received: 12 November 2021 | Revised: 09 January 2022 | Accepted: 07 April 2022 | Published: 20 April 2022

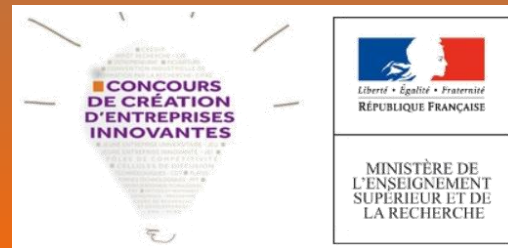
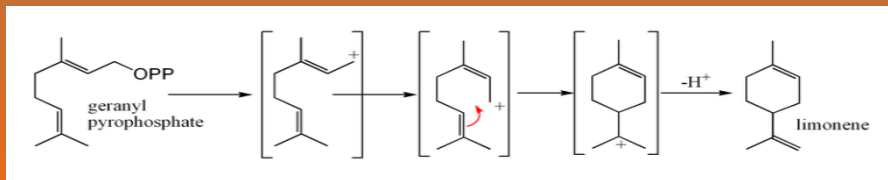
From the *Rutacea* *Halfordia kendack* of the rain forests in Asia to the *Citrus Sinensis* of the same Genus, peel extract as rich in *d*-Limonene



At the end of this extensive screen, four molecules were finally identified with the expected activity on all cell types (organ-derived) and in all animal species tested. They were respectively: geranyl acetate, geraniol, *d*-Limonene and isomenthone. Notably, *d*-Limonene was present in the tested extract of *Halfordia kendack* (*Rutaceae*). This tree, initially discovered in New Caledonia, has a natural habitat in Australasia and in tropical and subtropical rainforests [33]. In fact, *d*-Limonene is also present in numerous species of the *Citrus* genus that belongs also to the *Rutaceae* family. Oranges (*Citrus sinensis* L) are safe to obtain, compared to the first exotic plants holding the rare terpenoid tested. Last but not least, this choice was also driven by the necessity to protect rare Asian plants. Further studies were therefore conducted with orange peel extract (OPE) obtained by cold

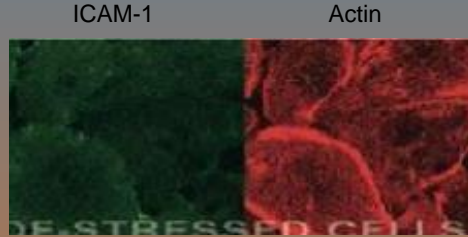


- ◆ In collaboration with Pierre Potier (discoverer of Taxoter®), we identified anti-inflammatory anti-senescence monoterpenes....
- ◆ ...in the *Halfordia kendack* plant, collected yearly by ethno-botanists of Hanoi University (Vietnam).
- ◆ First patent on cell degeneration reversibility
- ◆ National award for innovative research



Stress, pollution, lifestyle, nutrition, epigenetics

Normal



Activation
by $\text{TNF-}\alpha$



Reset by
AISA



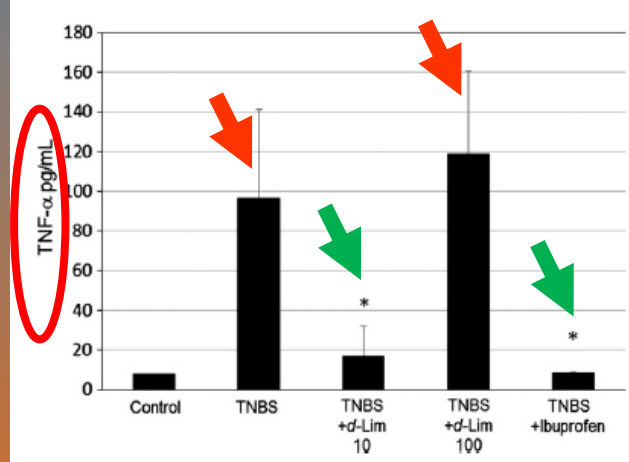
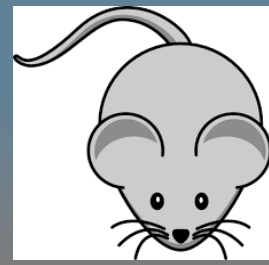
- ✓ will contribute to install chronic silent inflammation;
- ✓ altering the immune system and accelerating cell senescence;
- ✓ a reversible process

Mech Ageing Dev. 2020 Jan 2;186:111206. doi: 10.1016/j.mad.2019.111206. [Epub ahead of print]

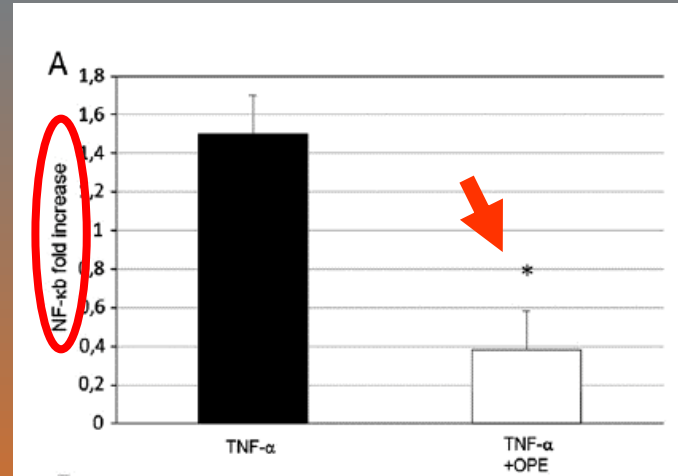
AISA can control the inflammatory facet of SASP.

d'Alessio PA¹, Béné MC².

What about transcription factor NF- κ B



Effect comparable to ibuprofen
for low-dose *d*-Limonene

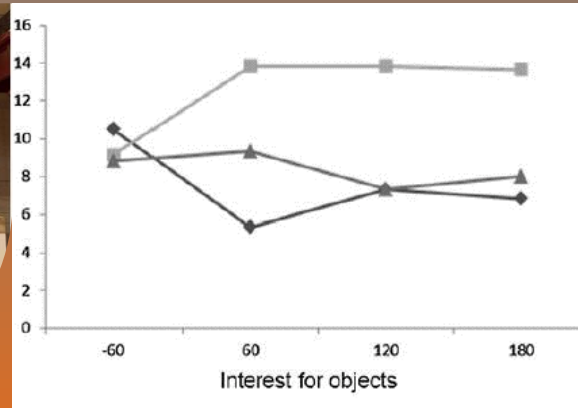


Anti TNF- α , IL-6, IL-1 β , IFN- γ effect
& Inhibition of NF- κ B

Life Sciences. 2013;92:1151-1156

Anti-inflammation RESULTS in mood modulation

Motivational effect in rodents



Rejuvenation Res.
2014;17:145-149

PRIME 2012; 30-37

Mood modulation effect in humans

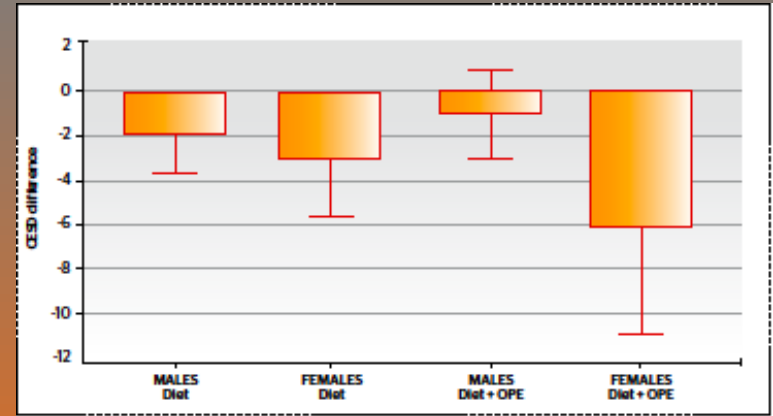
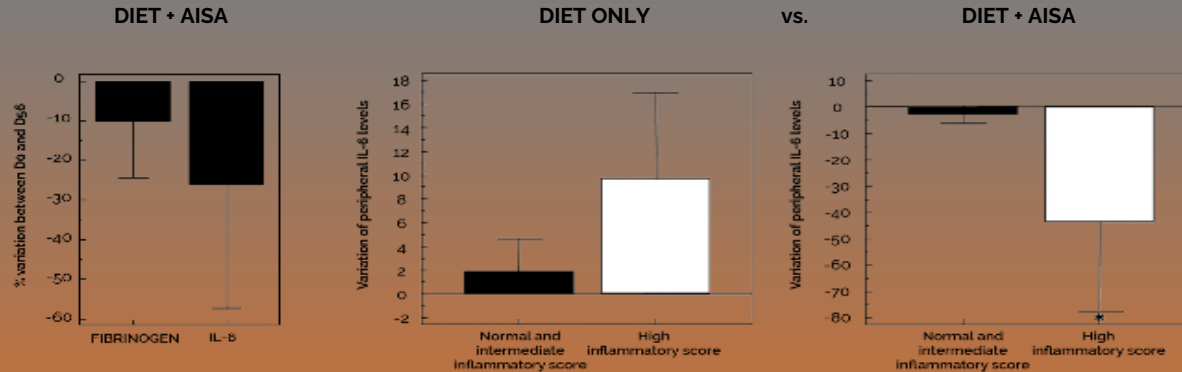


Figure 3 Gender partition and CES-D variation in diet versus diet plus OPE

Inflammation markers

Anti-IL-6 efficacy as food supplementation



Significant modifications of inflammation markers
(fibrinogen and IL-6) were observed in individuals with baseline moderate inflammation (**RISTOMED diet + AISA**) between D0 and D56.

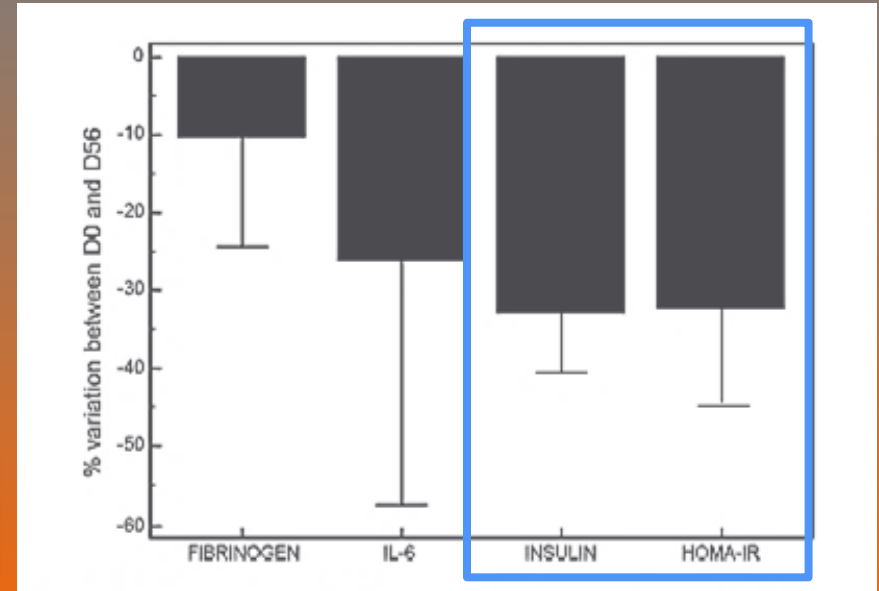


Markers of cardio-metabolic syndrome, diabetes, thrombosis



Monoterpenes target IL-6 and fibrinogen, but also insulin and **markers** of insulin resistance*

* Homeostatic model assessment of insulin resistance HOMA-IR



Clin Nutr. 2016;35:812-818.

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Monoterpenes repair gut barrier and modulate microbiota

Clostridium cluster IV / *Bifidobacteria* ratio

Barrier function restoration

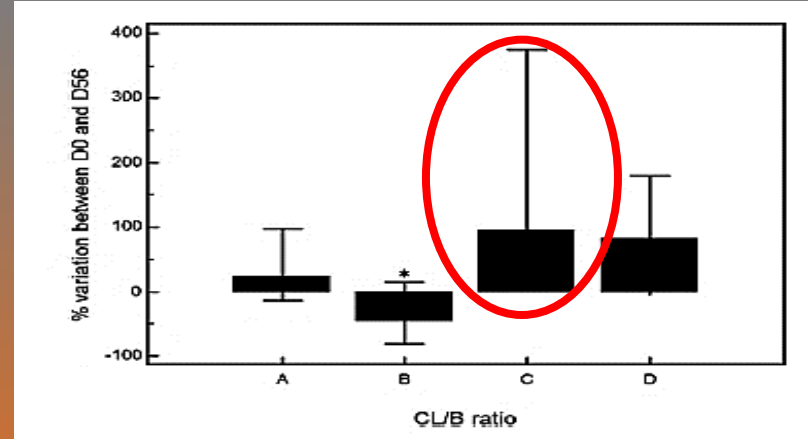
Table 1

AISA: significant effect on strengthening the epithelial barrier function

	Control	AISA			
		75 μ M	150 μ M	750 μ M	1500 μ M
R ^t	107 \pm 3%	106 \pm 4%	112 \pm 3%	132 \pm 3%	153 \pm 4%
n	9	6	6	6	6
p		n.s.	n.s.	<0.001	<0.001

Evaluation of the electrical resistance (Ω -CM²)
percentage of the initial resistance : R^t.

Life Sciences **2013**;92:1151-1156



Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: <http://www.elsevier.com/locate/clnu>

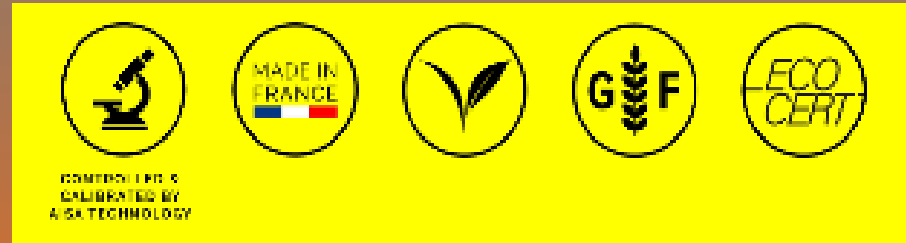
Randomized control trials

Impact of diet and nutraceutical supplementation on inflammation in elderly people. Results from the RISTOMED study, an open-label randomized control trial^a

R. Ostan^a, M.C. Béné^b, L. Spazzafumo^c, A. Pinto^d, L.M. Donini^d, F. Pryen^e, Z. Charrouf^f, L. Valentini^g, H. Lochs^h, I. Bourdel-Marchasson^{i,j,k}, C. Blanc-Bisson^{j,k,l}, F. Buccolini^j, P. Brigidì^m, C. Franceschi^{n,o}, P.A. d'Alessioⁿ

Protect & repair the gut barrier !

Are nutraceuticals an option for skin embellishment ?



CONTROLLED &
CALIBRATED BY
AISA TECHNOLOGY

SKIN RELAXATION

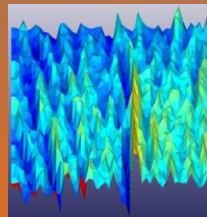
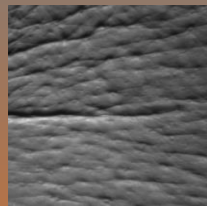
Day 0



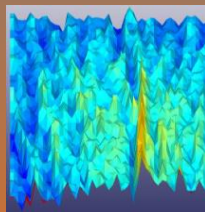
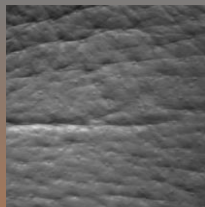
Day 56



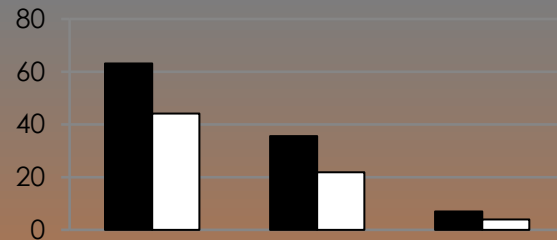
Before



After



Observational study



■ Do

WRINKLES
NUMBER
-30,2%

WRINKLES
LENGTH
-38,5%

WRINKLES
SURFACE
-43,3%

PRIME 2015;11:19-25



Skin dishydrosis of the elderly

Gut dysbiosis
directly compromises the
barrier function of the **skin**



Anti-inflammatory
nutraceuticals can preserve
gut barrier function restoring
skin compliance



INTERMEDIATE PSORIASIS

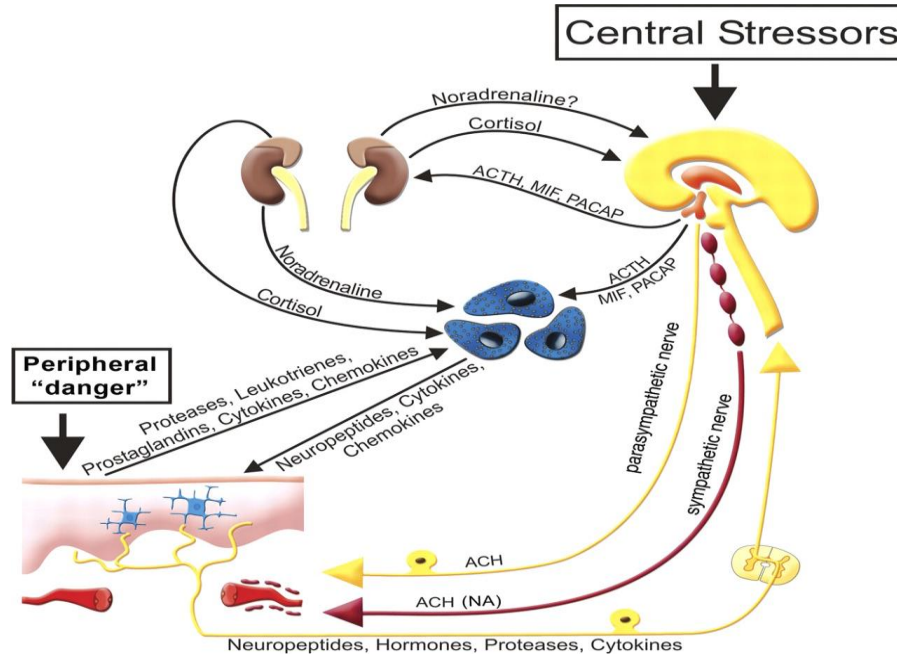


D0

D45

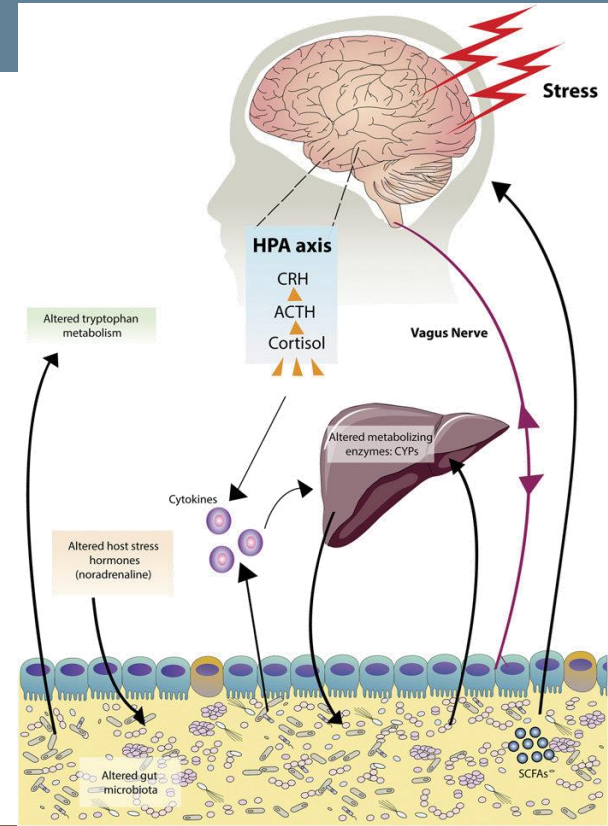
Global Journal of Dermatology & Venereology, 2015, 3, 1-4

The brain-gut connexion is CONCOMITANT to the brain-skin connexion



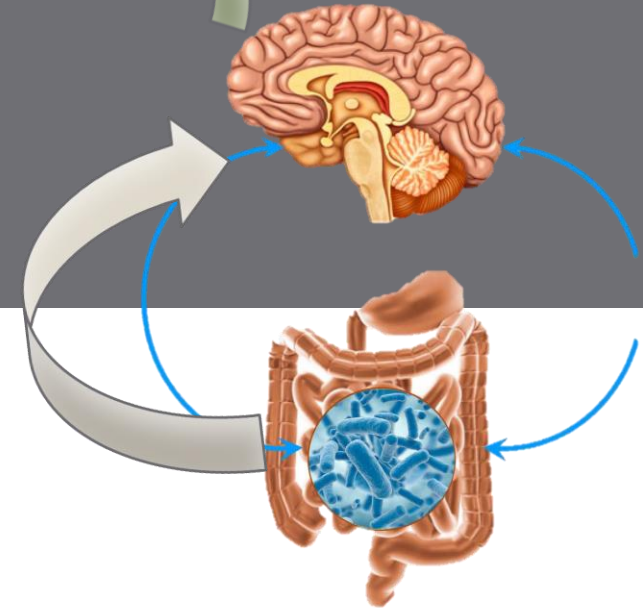
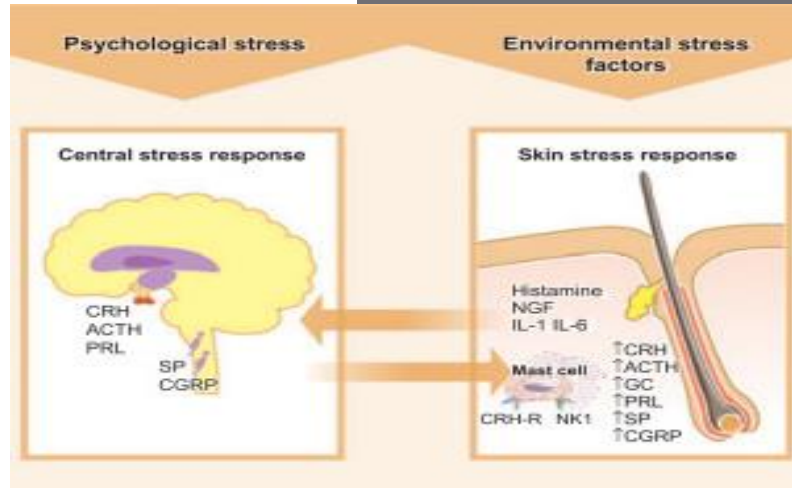
Bioengineering in Wound Healing: A Systems Approach (book), 2017

Pharmacological Reviews 2019;71:198-224



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The brain whispers microbiota secrets to the skin



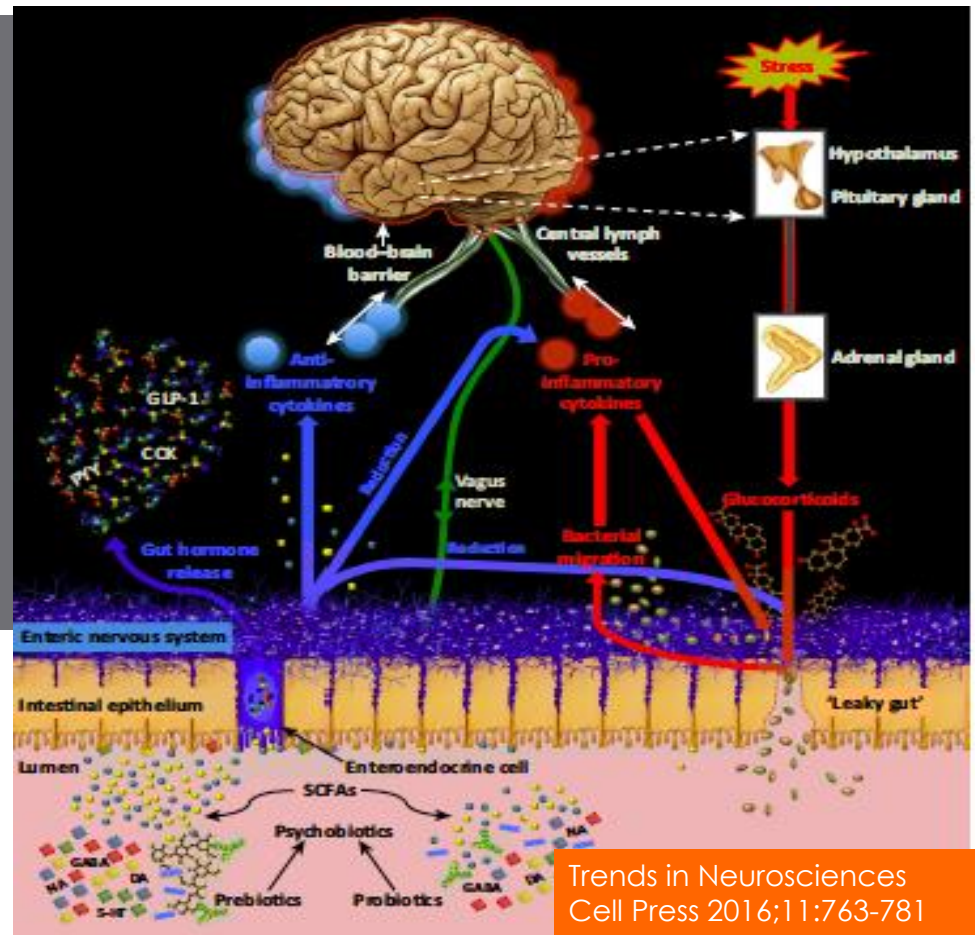
Neuroimmunology of Stress: Skin Takes Center Stage

Petra C. Arck¹, Andrzej Slominski², Theoharis C. Theoharides³, Eva M. J. Peters¹ and Ralf Paus⁴

Journal of Investigative Dermatology (2006) 126, 1697-1704. doi:10.1038/sj.jid.5700104

PSYCHOBIOOTICS

- ◆ Pre-and probiotics compose **psychobiotics**
- ◆ induce short chain fatty acids (SCFA)
- ◆ Provide anti-inflammation in gut and skin
- ◆ « *bacterial taxa are potential leads for **psychobiotics**—confering health benefits in patients suffering from **psychiatric illness*** »



Case study : atopic dermatitis

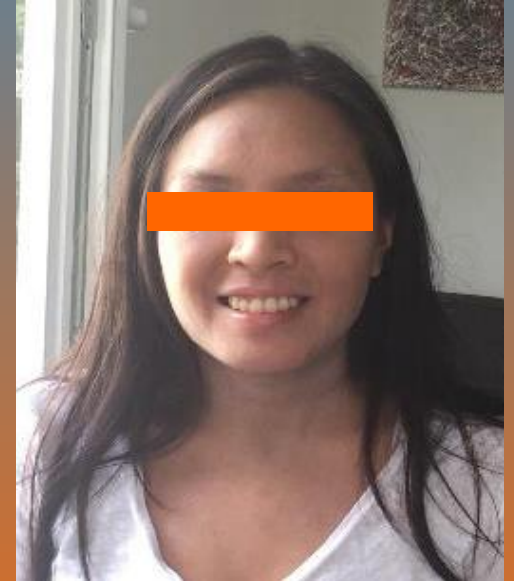
(eczema) worsened by repeated topic cortisol treatment

High levels of zonulin /
anti-food IgG

Partial restoration after 10 days cure with
anti-inflammatory terpenoids

Gut barrier repair, with
restitution of skin quality

Visible **mood** amelioration
Rejuvenation effect





Review

Terpenoids as Potential Geroprotectors

Ekaterina Proshkina ¹, Sergey Plyusnin ^{1,2}, Tatyana Babak ¹, Ekaterina Lashmanova ¹, Faniya Maganova ³, Liubov Koval ^{1,2}, Elena Platonova ^{1,2}, Mikhail Shaposhnikov ¹ and Alexey Moskalev ^{1,2,*}

Food and Chemical Toxicology 123 (2019) 233–257

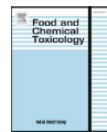


ELSEVIER

Contents lists available at ScienceDirect

Food and Chemical Toxicology

journal homepage: www.elsevier.com/locate/foodchemtox



Monoterpenes modulating cytokines - A review

Jullyana S.S. Quintans^a, Saravanan Shanmugam^a, Luana Heimfarth^a, Adriano Antunes S. Araújo^b, Jackson R.G.da S. Almeida^c, Laurent Picot^d, Lucindo J. Quintans-Júnior^{a,*}

^a Laboratory of Neuroscience and Pharmacological Assays, Department of Physiology, Federal University of Sergipe, São Cristóvão, Sergipe, Brazil

^b Department of Pharmacy (DFA), Federal University of Sergipe, São Cristóvão, SE, Brazil

^c Center for Studies and Research of Medicinal Plants (NEPLAME), Federal University of San Francisco Valley (UNIVASF), Petrolina, Pernambuco, Brazil

^d UMRI CNRS 7266 LIENSs, University of La Rochelle, 17042, La Rochelle, France



« Cytokine storm »

*“The fact is that the real morbidity and mortality of this disease is probably driven by **this out-of-proportion inflammatory response** to the virus...”*



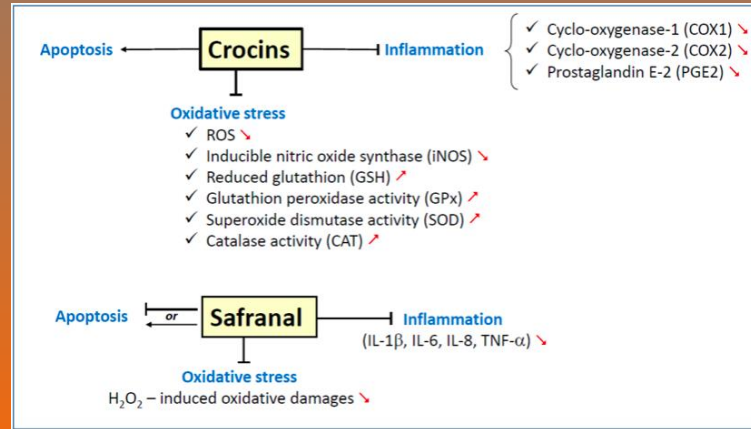
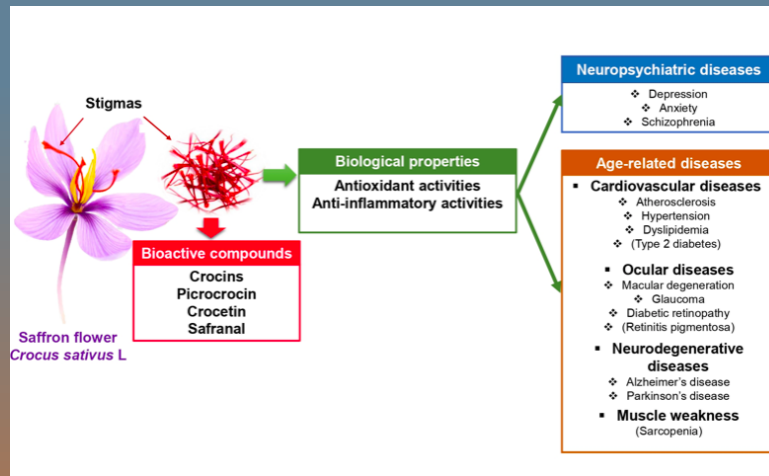
Jamie Garfield,
Temple University Hospital

Questions arise



- Psychotropic effects due to
- cannabinoids or
 - terpenoids ?

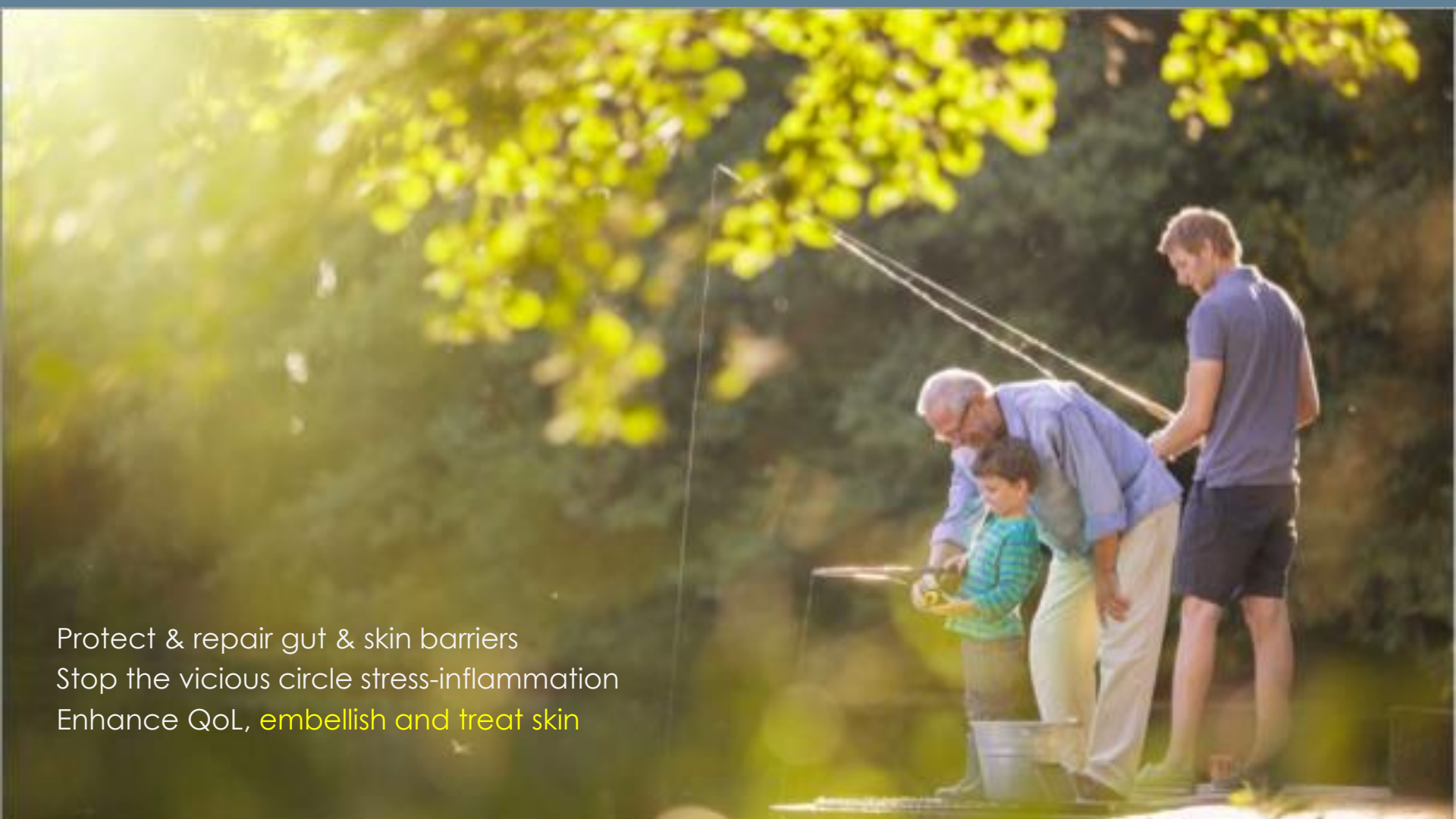
The spice Safran



TAKE HOME MESSAGE

*In med cometics - the new trend
in dermatology - botanicals
thanks to their **active ingredients**
have definitely their place*



A photograph of a family of three fishing in a pond. An older man with glasses and a blue shirt is bent over, holding a small yellow bucket. A young boy in a green and blue striped shirt stands next to him, also looking at the bucket. A younger man in a blue polo shirt and dark shorts stands behind them, holding a fishing rod. They are all standing on a wooden dock or pier. The background is filled with lush green trees and foliage, with sunlight filtering through the leaves, creating a warm, golden glow. The overall scene is peaceful and suggests a family outing in nature.

Protect & repair gut & skin barriers
Stop the vicious circle stress-inflammation
Enhance QoL, **embellish and treat skin**



Thank you for your attention
Questions & Credits



Consiglio Nazionale delle Ricerche
Institute of Genetics and Biophysics
Adriano Buzzati-Traverso

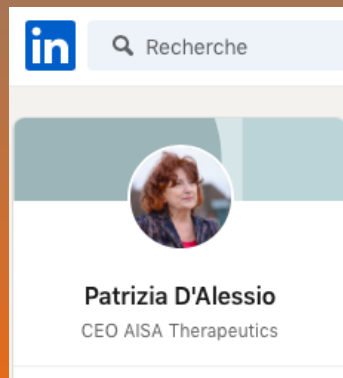


Life Sciences **2013**;92:1151-1156; Global Journal of Dermatology & Venereology, **2015**, 3, 1-4;
Clinical Nutrition **2016**;35:812-818; Nutrients **2020**;12,800; AIMS Molecular Science **2022** 9 (2): 46-65.

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