

APIVITA



# Microalgae in Cosmetics

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Konstantinos Gardikis, MSc, PhD  
R&D Director



Project co-financed by the European  
Regional Development Fund

International learning Camp

Technical Session on Blue BioTech

26 March 2021 | 10-12,30



# APIVITA



## NATURAL BEAUTY CARE

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BORN OF BEES IN GREEK NATURE,  
RAISED BY SCIENCE



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## POLLINATE BEAUTY

[www.apivita.com](http://www.apivita.com)



# EFFECTIVE & NATURAL PRINCIPLE TRANSLATION TO LAB METHODS



- All ingredients from natural sources
- Processes (solvents, preservatives etc) from natural sources
- Where possible from organic sources
- Development of new ingredients to increase the % naturality of products

- All ingredients chosen and assessed for the human skin with state-of-the-art biochemistry methods (Biolab)
- All ingredients analyzed for their ingredients and chosen for the maximum biomarkers concentration (Phytolab)

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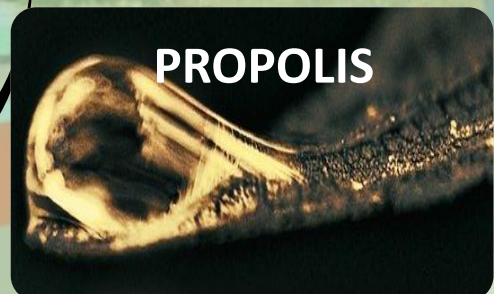
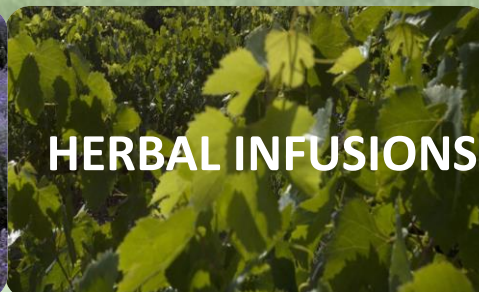




# INGREDIENTS FROM THE MEDITERRANEAN AREA

ORGANIC PLANTS

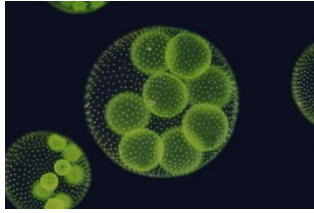
BEE



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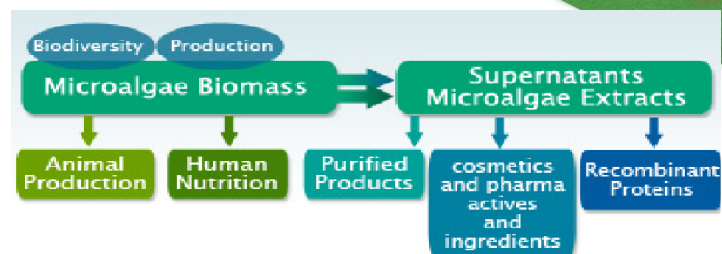




## Micro Algae Facts

- Evolved ~500 Million years ago.
- >300,000 species.
- Large contributor to fossil fuel deposits.
- Produce ~50% of atmospheric oxygen.
- Account for ~50% of Earth's carbon fixation.
- Lipids can account for 60-70% of biomass.
- Can grow both photosynthetically and heterotrophically.
- Ability to grow solely on sunlight, CO<sub>2</sub> and brackish water.

50x greater biomass productivity than fastest growing terrestrial plant



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EUROPEAN  
COMMISSION



# AlgaeCom

Exploitation of microalgae diversity for the development of novel high added-value cosmeceuticals



**FRENCH**  
National Centre for  
Scientific Research



AGRICULTURAL UNIVERSITY OF ATHENS |

**APIVITA**



# Participants

Participant	Country	Dept.	Scientist in charge
1 Agricultural University of Athens (AUA)	Greece	Dept. Agric. Biotechn. Lab. Molec. Biology	Dr. Emmanouil Flemetakis
2 Centre National de Recherches Scientifique (CNRS)	France	Marine plant and biomolecules	Dr. William Helbert
3 APIVITA S.A.	Greece	Scientific Affairs-R&D	Dr. Konstantinos Gardikis
4 FITOPLANCTON MARINO	Spain	Molecular Biology & Manufacturing	Dr. Carlos Unamunzaga



# Core Idea

## MICROALGAE

### Bioactive Ingredients

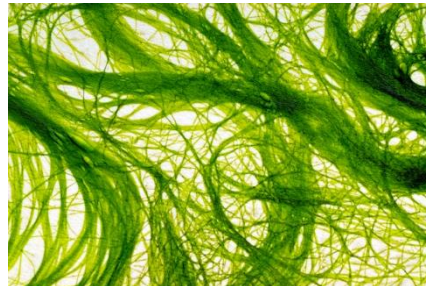
Proteins

Ω3

### Sugars

Rhamnose

Carageenan



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# Innovation –AlgaeCom



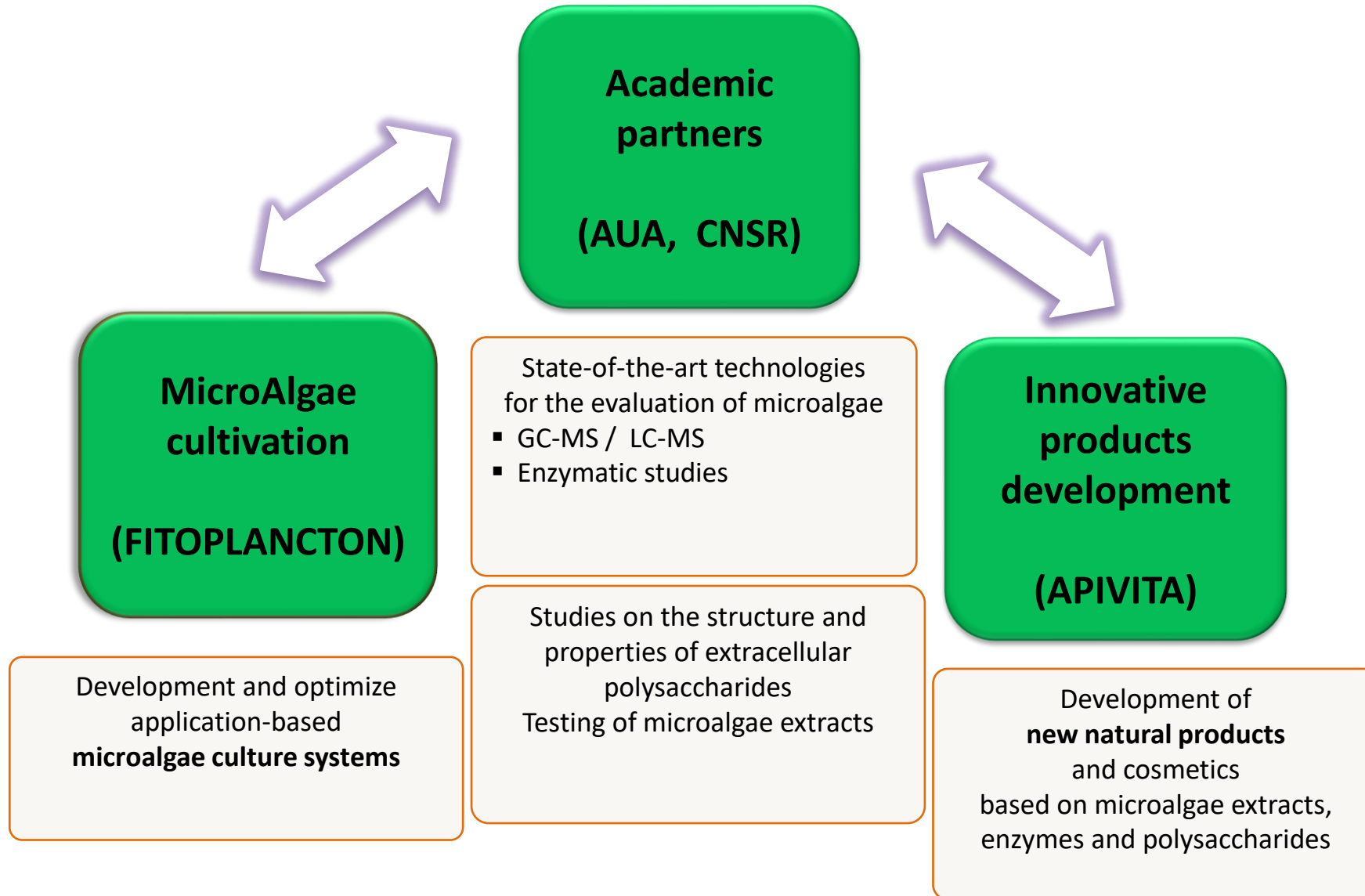
**Ingredients for the Cosmetic  
Industry**  
**Antioxidants**  
**Colorants**  
**Vitamins**  
**Polysacharides**

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# Workflow



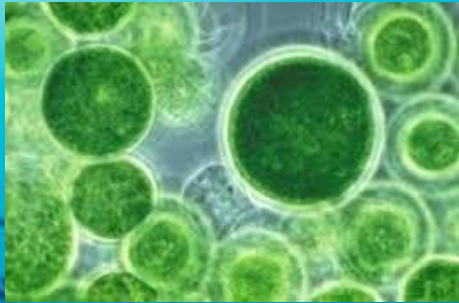
APIVITA



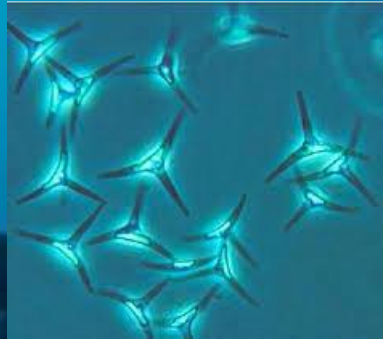




# Microalgae Extracts



*Nannochloropsis gaditana*



*Phaeodactylum tricornutum*

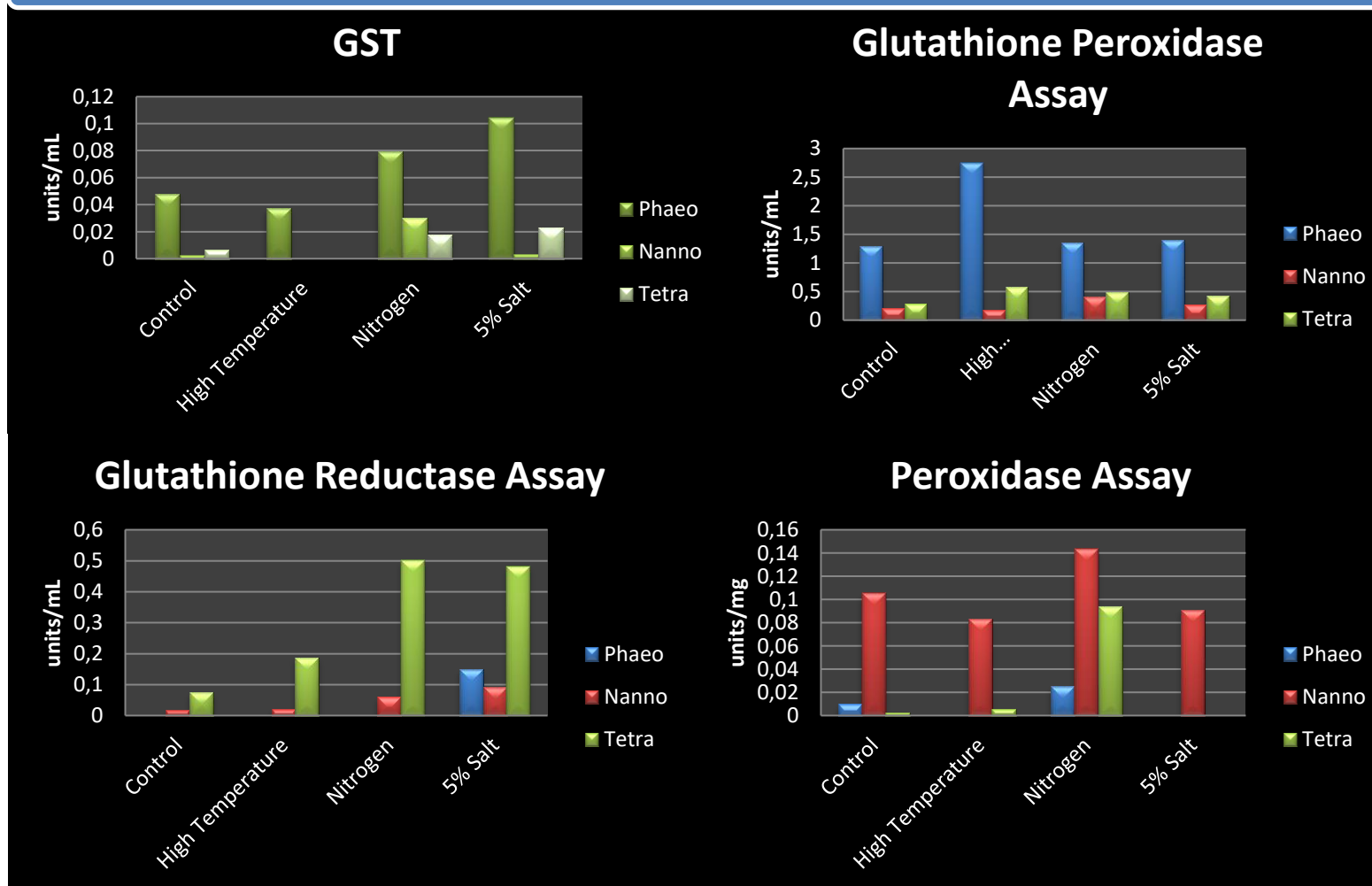


*Tetraselmis chuii*

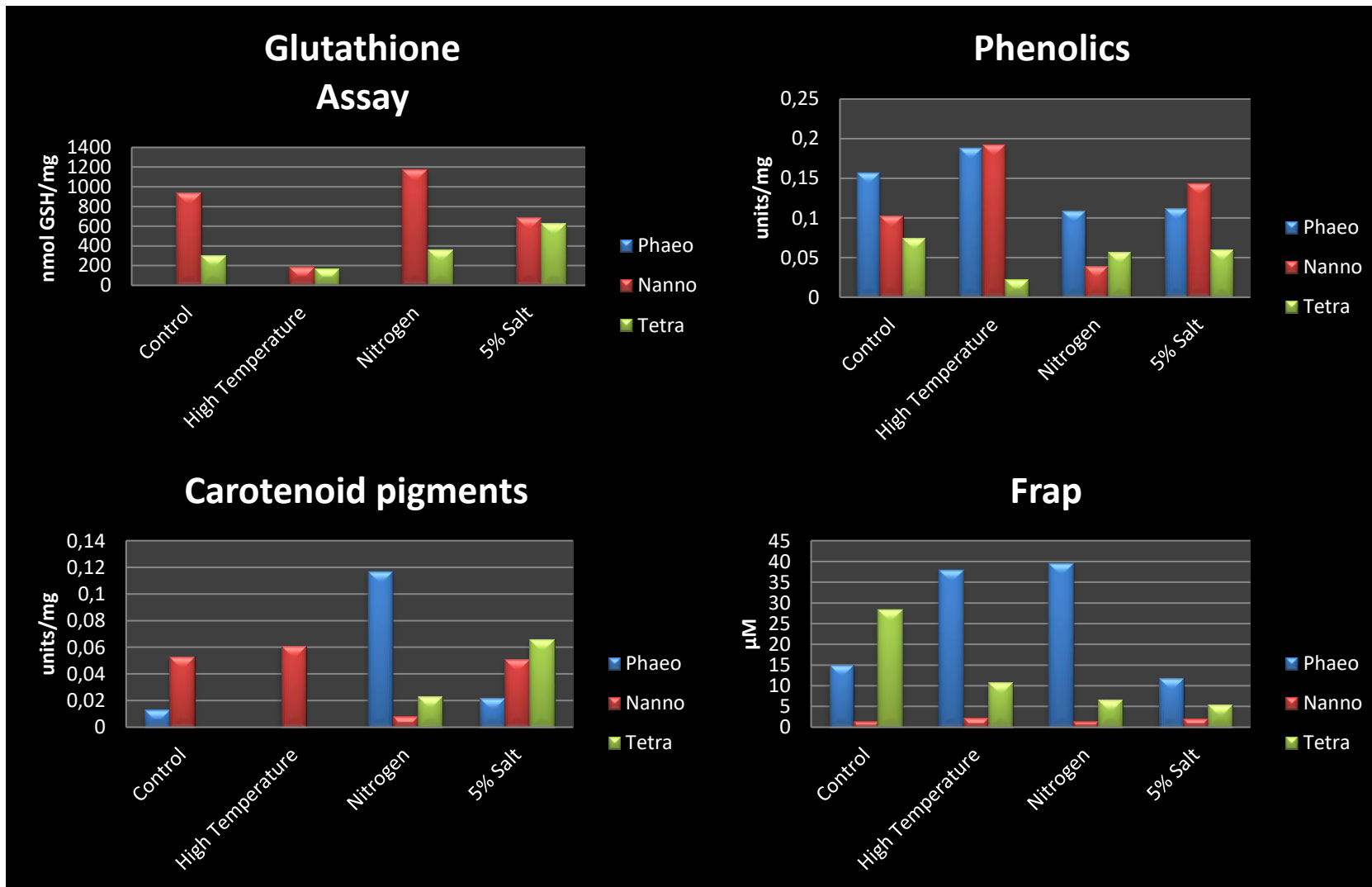


# Catalomic analysis of microalgae under different culture conditions

Antioxidant enzymes (Glutathione transferase, glutathione peroxidase, glutathione reductase, peroxidase)



# Catalomic analysis of microalgae under different culture conditions

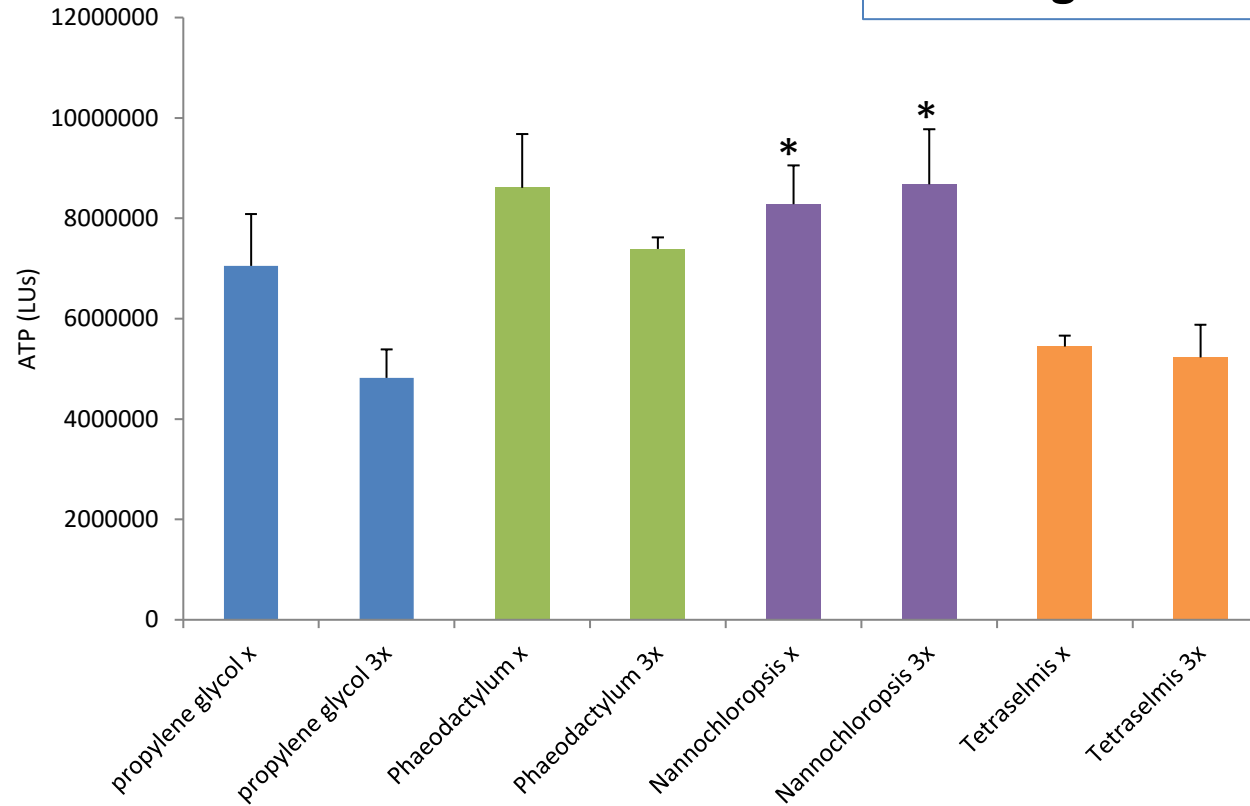




# Cell viability- Cell proliferation Test

## Primary human dermal cell line

### Microalgae extracts



\* Statistical significant from solvent level,  $p < 0.05$

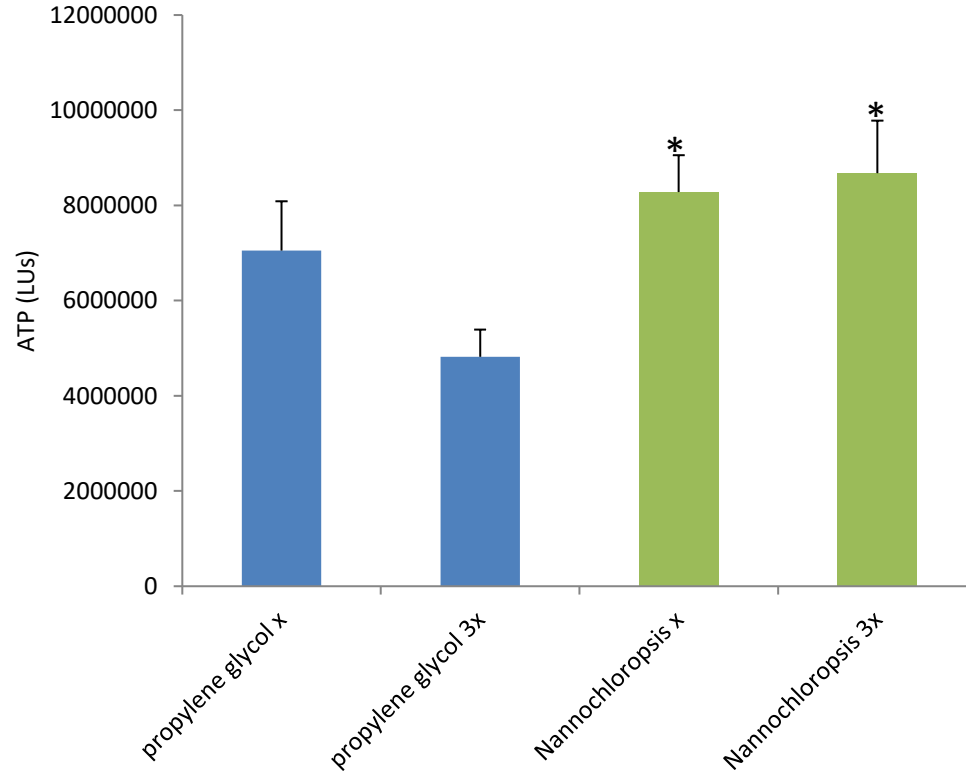
X = Apivita's concentration  
3X = Toxicity level.

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# Cell viability- Cell proliferation Test

## Primary human dermal cell line



*Nannochloropsis Gaditana increases Cell viability /cell proliferation in both Concentrations.*

X = 1%  
3X = Toxicity level.

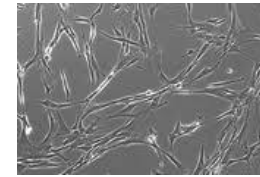
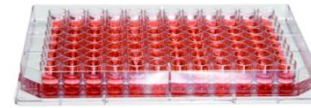
\* Statistical significant from solvent level,  $p < 0.05$

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# Oxidative Stress ----Skin aging



Primary Human Normal Dermal Fibroblasts

*In Vitro* Approach

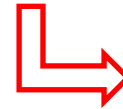


Incubation for 48h under : 5% CO<sub>2</sub> , 37 °C

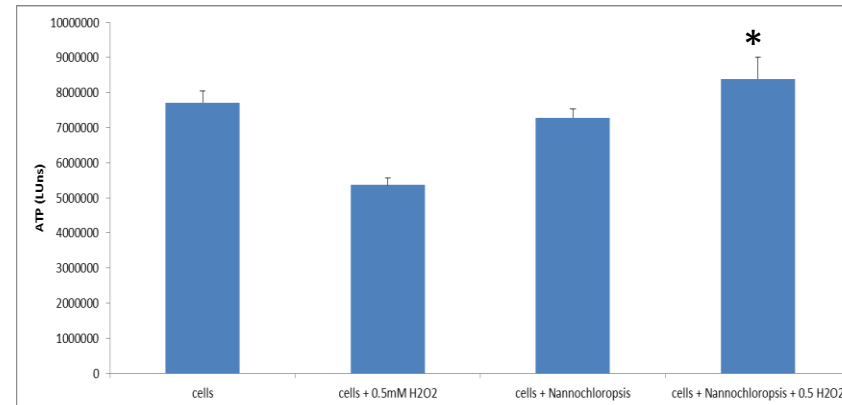
Wash two times with PBS and insertion of stressor H<sub>2</sub>O<sub>2</sub> for 3h

Insertion of cell medium for 3h

**Cell viability (ATP)**



*Nannochloropsis Gaditana* has a cytoprotective role against oxidative stress using 0.5mM H<sub>2</sub>O<sub>2</sub> as stressor in primary human normal dermal fibroblasts



\* Statistical significant ,p<0.05 Vs cells + H<sub>2</sub>O<sub>2</sub>

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# Transcriptomics Analysis

Gene Symbol			
SOD1	EPS8	Col1A1	BTG2
TNF	FGF23	Caspase 14	p21
VEGFA	PMCH	Involucrin	socs3
SELE	FOXO3	HSPA5	rfpl4a
ITGB2	FOXO1	MMP1	SIRT2
IL1 R1	CASP7	NRF2	SIRT3
IL1 R2	CLOCK	CCL2	GHRH
NFKB1	COL4A1	CCR1	POLG
NOS3	COL6A1	BCL2	ABL1
IL4	EGF	CD44	NFE2L2
GPX 1	CAT	VCAM1	HGF
GPX4	TXN	SPP1	FGFR2
KL	ATM	Apo A	PCNA
GUSB	HSPB1	Apo B	VWF
GAPDH	AR	Fibrinogen A	SERPINE1
SDHA	CRABP2	Fibrinogen F2	ACE
TBP	MC1R	HBEGF	BAX
HPRT1	POMC	IL3	IFNG
ACTB	ANGPTL1	KLF2	NFE2L2
PPARG	MC5R	FLG	BIRC3
SITR1	MC2R	FBN 1	CFLAR
MMP9	TIMP1	CDH5	FAS
IL8	MMP13	Keap 1	TNFAIP3
PTGER2	MMP8	NOG	BID
AQP3	GDF15	KRT5	TYR

**Cells + Solvent**  
**Cells + Nannochloropsis Gaditana**  
**Cells + H<sub>2</sub>O<sub>2</sub>**  
**Cells + H<sub>2</sub>O<sub>2</sub> + Nannochloropsis Gaditana**



Gene Symbol	
COL4A1	FAS
COL6A1	BIRC3
FBN 1	BTG2
ITGB2	SERPINE1
VEGFA	PCNA
HSPB1	ABL1
CRABP2	HGF
PTGER2	AQP3
PPARG	Fibrinogen F2
GPX 1	FOXO3
GPX4	BID
IL1 R1	HBEGF
MMP1	KLF2
VCAM1	SIRT3
SPP1	NFKB1

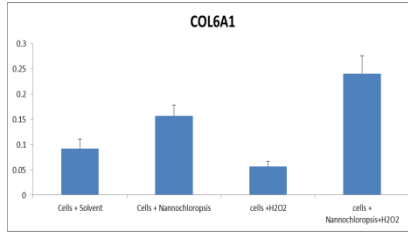
Angiogenesis
ECM protease inhibitor
DNA repair
Apoptosis
Epidermal Function
Aging
Growth factors
Skin Hydration
Elastin Synthesis
Cell adhesion
Antioxidant Pathway
Collagen Synthesis
Collagen Breakdown
Retinoid Metabolism
Cell metabolism
Skin Homeostasis

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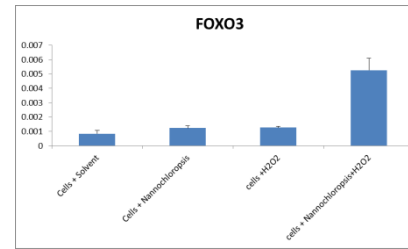




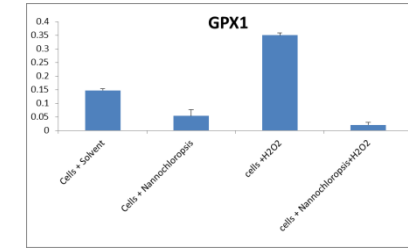
# Targeted Activity – qPCR – Genes expression



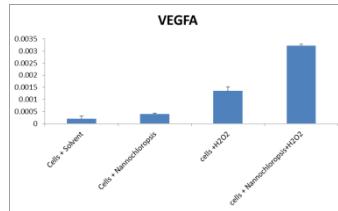
**Collagen Synthesis**



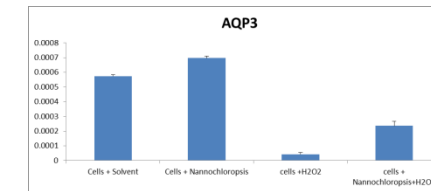
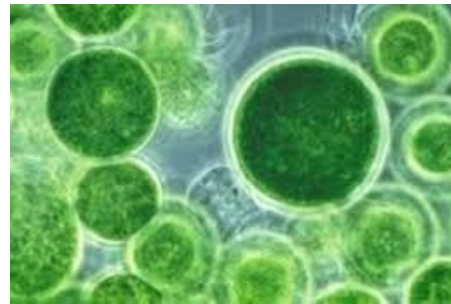
**Aging process**



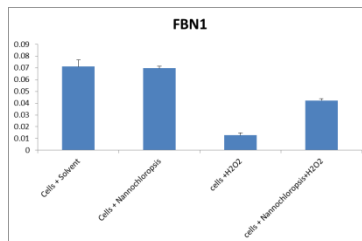
**Antioxidant Defense**



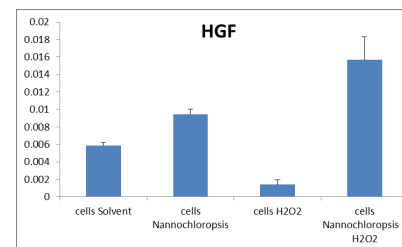
**Angiogenesis**



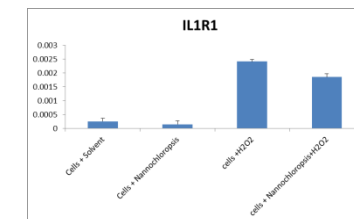
**Hydration**



**Elastin synthesis**



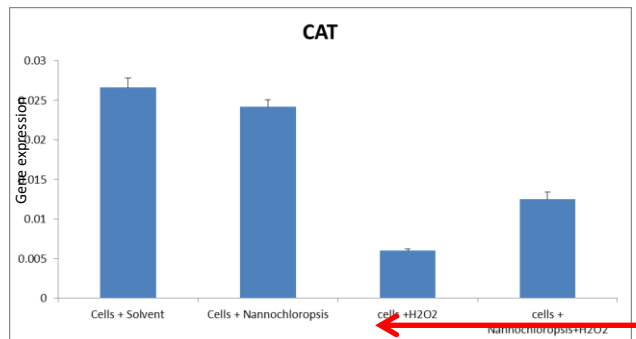
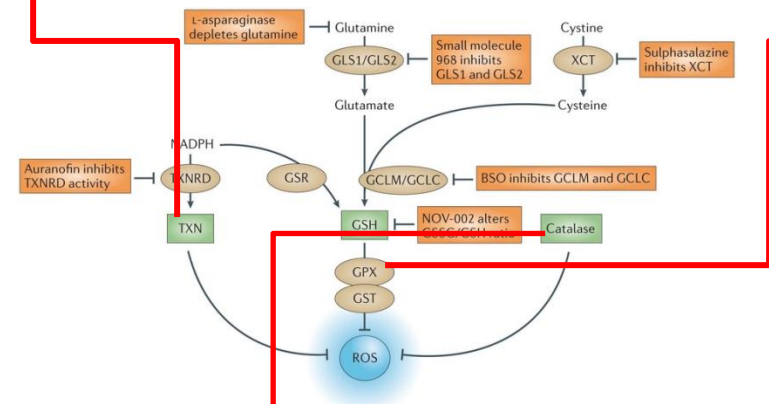
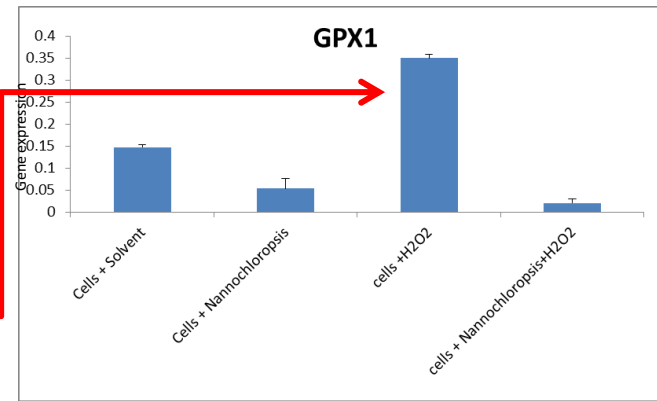
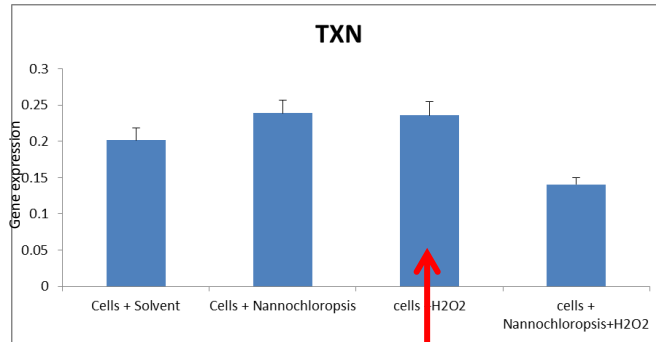
**Skin Homeostasis**



**Inflammation**

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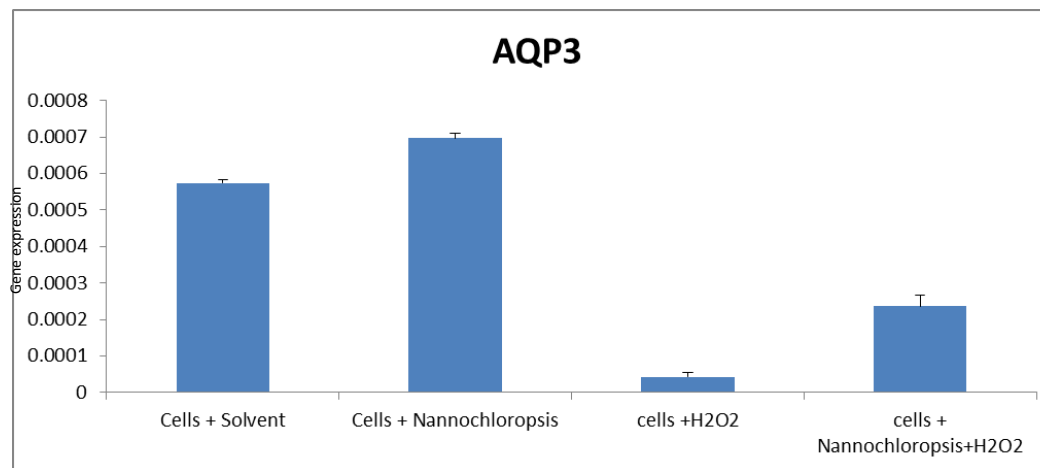
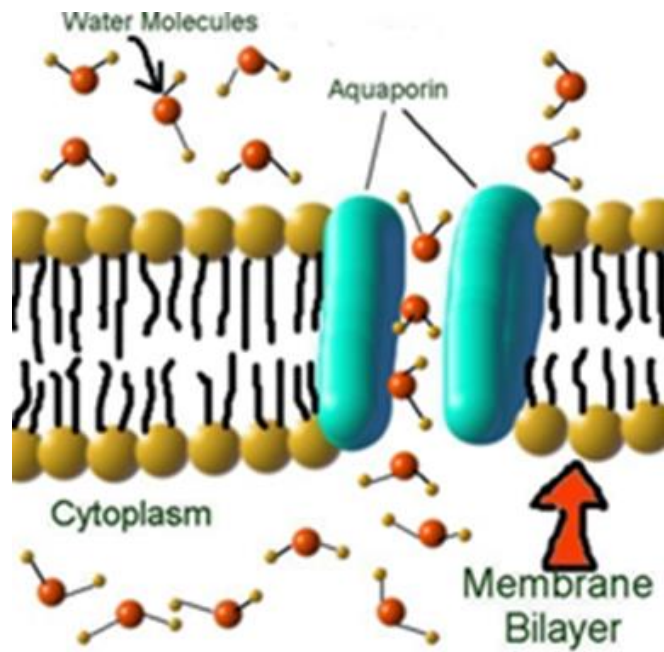
The transcript of CAT are increased in NHDF treated with Nannochloropsis gaditana extract under oxidative stress.

Nature Reviews | Drug Discovery

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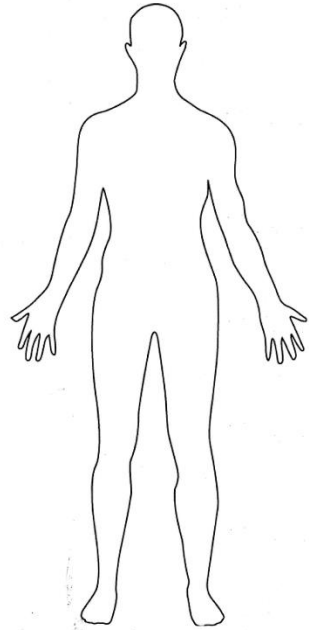




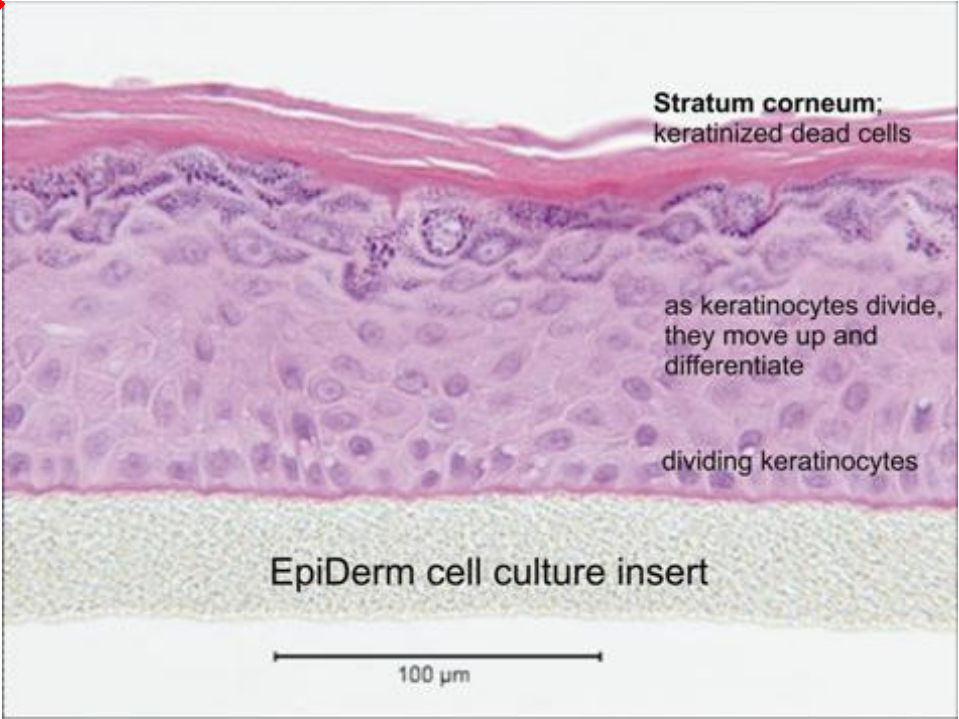


**The transcript of AQP3 are increased in NHDF treated with Nannochloropsis gaditana extract under oxidative stress**

# 3D reconstructed human tissue model



**In Vitro**

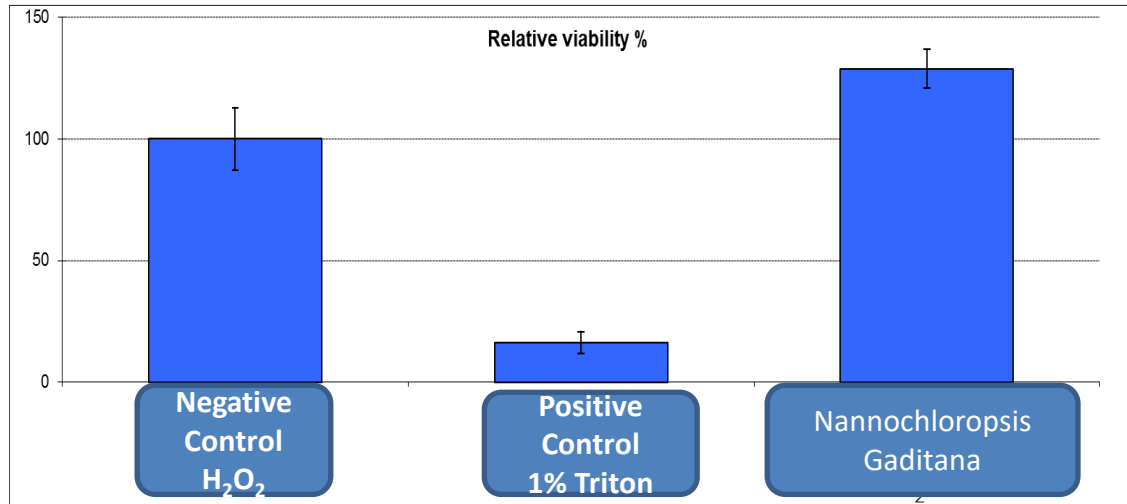


EpiDerm™ cell culture insert. Quelle & Rechte: MatTek Corporation

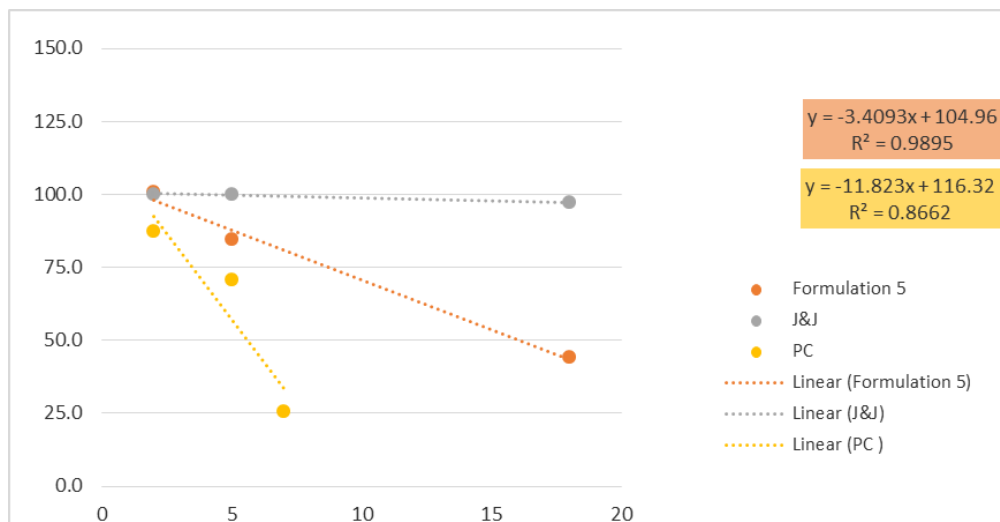




# Results on 3D reconstructed human tissue model



- **MTT Tissue Viability Assay**  
Nannochloropsis Gaditana Extract was proven not skin irritant (Relative Viability >50 %)



Application of Cosmetic formulation with Nannochloropsis Gaditana was tested into 3 time points (2 hours / 5 hours / 18 hours).

Cosmetic formulation with Nannochloropsis Gaditana was proven very mild (ET-50 > 16.1)

# ALGAECOM DISSEMINATION

- Marine Drugs conference

<http://ecmnp2015.com/>



***In Vitro* efficacy of *Nannochloropsis gaditana* extract on primary human dermal fibroblasts as cosmeceutical bioactive ingredient.**

Sophia Letsiou<sup>1</sup>, Konstantinos Gardikis<sup>1</sup>, Lalia Mantecón<sup>2</sup>, Carlos Unamunzaga<sup>2</sup>, Emmanouil Fletmetakis<sup>3</sup>

1. APIVITA S.A., Scientific Affairs, Industrial Park of Markopoulo Mesogaïas, 19003 Markopoulo Attiki, Athens, Greece.
2. Fitoplanton Marino, S.L. Dársena Comercial s/n (Muelle Pesquero), 11500 El Puerto de Santa María (Cádiz), Spain.
3. Laboratory of Molecular Biology, Department of Biotechnology, School of Food, Biotechnology and Development, Agricultural University of Athens, Athens, Greece.

- Newletters

[http://www.algaecom.aua.gr/AlgaeCom\\_files/Page1057.htm](http://www.algaecom.aua.gr/AlgaeCom_files/Page1057.htm)

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< Articles

ORIGINAL RESEARCH ARTICLE

Front. Mar. Sci., 11 July 2017 | <https://doi.org/10.3389/fmars.2017.00221>



# Skin Protective Effects of *Nannochloropsis gaditana* Extract on H<sub>2</sub>O<sub>2</sub>-Stressed Human Dermal Fibroblasts

 Sophia Letsiou<sup>1</sup>,  Katerina Kalliampakou<sup>2</sup>,  Konstantinos Gardikis<sup>1</sup>,  Lalia Mantecon<sup>3</sup>,  Carlos Infante<sup>3</sup>,  Marianna Chatzikonstantinou<sup>4</sup>,  Nikolaos E. Labrou<sup>4</sup> and  Emmanouil Flemetakis<sup>2\*</sup>

<sup>1</sup>Laboratory of Biochemistry, Scientific Affairs Department, APIVITA S.A., Athens, Greece

<sup>2</sup>Laboratory of Molecular Biology, Department of Biotechnology, School of Food, Biotechnology and Development, Agricultural University of Athens, Athens, Greece

<sup>3</sup>Fitoplanton Marino, Cádiz, Spain

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# International INNOVATION

Disseminating science, research and technology

## AlgaeCom

WWW.INTERNATIONALINNOVATION.COM

## Restorative powers of microalgae

The collaborative European **AlgaeCom** project is mining the vast, yet so far untapped, potential of microalgae extracts for new cosmetic products with promising restorative and nourishing properties

**FOR THOUSANDS OF** years, people have used balms, emollients and cosmetics to improve the protective qualities and appearance of the largest organ of their bodies, the skin. Use of cosmetics specifically to achieve a more youthful look, however, is relatively recent, dating from the 1930s. Today, the global anti-ageing skin care market is huge, valued at more than US \$60 billion. Of that market, the share taken by cosmetics that deliver highly effective and efficient active substances with anti-ageing benefits is growing rapidly at an annual rate of 8.60 per cent, and is expected to reach \$9.3 billion by 2019.

The historical use of damaging ingredients, such as lead, and the dubious sustainability and ethics of certain animal and microbial ingredients, have made safety and ingredient traceability key purchasing factors for modern cosmetics consumers. Natural enzymes, amino acids and botanical extracts are perceived as preferable to oils and surfactants from large-scale engineering as, for example, in the petrochemical industry. Global demand for natural, organic ingredients in cosmetics without attributable, negative environmental impacts or animal cruelty is significantly rising, supporting the philosophy of green growth and sustainable development.

### TRUE ACADEMIC-INDUSTRIAL PARTNERSHIP

APIVITA, a cosmetic company based in Greece, combines naturally derived active ingredients with medicinal and aromatic plant extracts, bee products and organic essential oils to deliver beauty products that do not contain silicone, parabens, mineral oil, propylene glycol, polycyclic musk, nitromusk, phthalates – or any other ingredient associated with adverse health or environmental effects. APIVITA is one of two industrial partners in AlgaeCom, a multinational collaboration between academic researchers and industry innovators, which aims to develop novel anti-ageing and other cosmetics – cosmetics with beneficial effects – from microalgae.

The other industrial partner is Floeplankton Marino, based in southern Spain, who has expertise in high-value microalgae products and production systems. In fact, Floeplankton Marino is the first microalgae production company to receive ISO22000 and FSSC22000 certification for microalgae production. It is also the first company to receive a novel food authorisation from the EU for a marine microalgae species, and their products are rated as "generally recognised as safe" in the US.

Led by biochemist Dr Emmanouil Flamietakis and enzyme technologist Dr Nikolaos Labrous of the Agricultural University of Athens, AlgaeCom is exploring the huge value of cosmetics by exploiting the diversity of microalgae in Europe. From the perspective of academic involvement in AlgaeCom, the Agricultural University of Athens is partnering with Dr William Helbert at the University of Grenoble-associated Centre for Research on Plant Macromolecules (CERMAP), part of the French National Centre for Scientific Research (CNRS), who bring expertise in biopolymers, especially polysaccharides, and application-targeted transformation of biomass. "AlgaeCom is a success story because of its multidisciplinary approach," explains Flamietakis.

### MICROALGAE PROMISES

As an abundant, renewable, natural and non-toxic alternative to fossil materials, with equivalent mechanical, thermal and optical properties, biomass is becoming increasingly attractive as a resource for new materials and products, such as biofuel. According to Flamietakis, biomass from microalgae has the potential to revolutionise a bioeconomy in fields beyond biofuels, as a source of novel, high added value biomolecules in such applications as healthcare, materials, cosmetics, nutraceuticals, aquaculture, pharmaceuticals and cosmeceuticals. Importantly, microalgae extracts offer the same functionality as microbial and animal-derived proteins, and are considered for cosmeceuticals.



Phases of the production facilities of APIVITA (1,2,3) and the laboratory and pilot-plant facilities at Floeplankton Marino (4,5).

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# PRO-ALGAE PATENT

## A combination of a nannochloropsis gaditana extract and a propolis extract as active component in cosmetic formulations for dermal use

### Abstract

A combination of a Nannochloropsis gaditana extract and a propolis extract as an active component in cosmetic formulations for dermal and in particular anti-aging use, wherein an active component of the formulation is constituted of the combination of an extract of Nannochloropsis gaditana in water and 1,3-propanediol and an extract of propolis in water, glycerol and  $\beta$ -hydroxypropyl cyclodextrin at a content of 0.1 to 20% w/w, which is added into the mixture after having been incorporated in a citric acid buffer solution pre-mixture adjusted to pH = 7 with its conjugate base, in order to ensure the stability of the final product, and pH is then checked and adjusted as required by the addition of pH adjusters, which are either a 20% w/w sodium hydroxide (NaOH) solution or a 20%w/w citric acid ( $C_6H_8O_7$ ) solution for the final adjustment to pH = 7.

### Classifications

• **A61K8/927** Oils, fats or waxes; Derivatives thereof, e.g. hydrogenation products thereof of insects, e.g. shellac

[View 2 more classifications](#)

WO2017216588A1

WIPO (PCT)

 Download PDF  Find Prior Art  Similar

Other languages: [French](#)

Inventor: [Nikolaos Koutsianas](#), [Sofia LETSIU](#), [Konstantinos GARDIKIS](#), [Panagiota Dragani](#)

### Worldwide applications

2016 • [GR](#) [WO](#)

### Application PCT/GR2016/000063 events

2016-06-13 • Priority to GR20160100314A

2016-06-13 • Priority to GR20160100314

2016-11-21 • Application filed by Apivita S.A.

2017-12-21 • Publication of WO2017216588A1

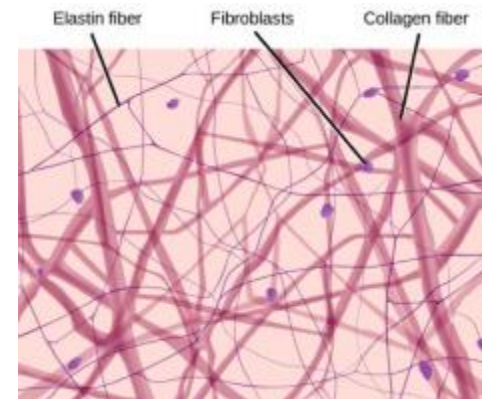
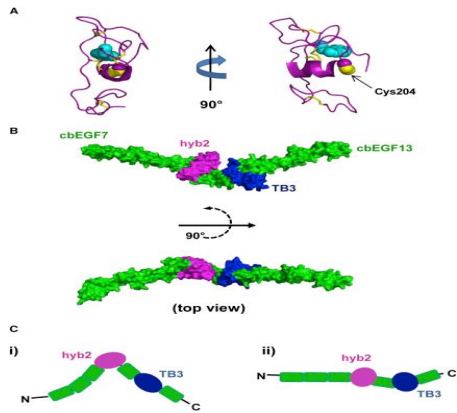
PIVITA





# PRO-ALGAE PATENT

- Nannochloropsis gaditana extract (1<sup>st</sup> time in cosmetics) +
- Propolis patent



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# SUNCARE FACE



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# HORIZON 2020 PROGRAMS



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# HORIZON 2020: TASCMAR

**Title:** Tools And Strategies to access to original bioactive compounds from Cultivation of MARine invertebrates and associated symbionts

- Call: H2020- Blue Growth---3---2014
- Topic: Novel marine derived biomolecules and industrial biomaterials
- **Type of action:** *Research and Innovation actions*
  
- **Target:** Isolation and production of new antioxidant molecules or enhanced extracts from plants of sea
- **APIVITA interest:** New sustainable and effective raw materials derived with innovative green methods of extraction
- **Total Budget:** 6760000 euro
- **APIVITA budget:** 400000 euro
- **Reimbursement rate:** 100%
- **Duration:** 48 months



# PARTICIPANTS

## List of participants:

Participant	Participant organization name	Type of institution	Country
1 CNRS	CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE	RESEARCH ORGANIZATION	FRANCE
2 UoA	NATIONAL AND KAPODISTRIAN UNIVERSITY OF ATHENS	ACADEMIA	GREECE
3 TAU	TEL AVIV UNIVERSITY (ASSOCIATED COUNTRY)	ACADEMIA	ISRAEL
4 CU-CEMB	CHULALONGKORN UNIVERSITY. Center Of Excellence For Marine Biotechnology . (THIRD COUNTRY).	RESEARCH ORGANIZATION	THAILAND
5 UR	UNIVERSITE DE LA REUNION (OCT OVERSEAS)	ACADEMIA	FRANCE
6 I2C	CRELUX-4SC join venture (I2C, Ideas to Candidate)	INDUSTRY - SME	GERMANY
7 BICT	BICT BIOINDUSTRY INNOVATION	INDUSTRY - SME	ITALY
8 PGT	PIERRE GUERIN TECHNOLOGIES	INDUSTRY	FRANCE
9 IMARE	IMARE NATURAL SL	INDUSTRY - SME	SPAIN
10 ASTAREAL	ASTAREAL AB	INDUSTRY - SME	SWEDEN
11 APIVITA	APIVITA	INDUSTRY - SME	GREECE
12 T6ECO	T6 ECOSYSTEMS SRL	CONSULTING - SME	ITALY
13 ECOOCEAN	ECOOCEAN (ASSOCIATED COUNTRY)	NGO	ISRAEL



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**Group 1. Marine invertebrates**




**Group 2. Microorganisms**



**Group 3. Microalgae**



**Group 4. Chemistry**



**Group 5. Bio-essays**



**Group 6. Tech Equipment**



**Group 7. Enzymes**



**Group 8. Industrial developments**



**Group 9. Socio-Eco-Environ**



**Group 10. Management**



# HORIZON 2020: ALGAE4A-B

**Title:** Development of Microalgae-based novel high added-value products for the Cosmetic and Aquaculture industry

- Call: H2020-MSCA-RISE-2015
- Topic: MSCA-RISE
- **Type of action:** *Marie-Curie actions*
  
- **Target:** New -omic technologies and new strains for the production of high added value cosmeceuticals
- **APIVITA interest:** New multifunctional enhanced extracts and isolated enzymes
- **Total Budget:** 972000 euro
- **APIVITA budget:** 216000 euro
- **Reimbursement rate:** 100%
- **Duration:** 48 months

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# PARTICIPANTS

PARTICIPANT NO	PARTICIPANT ORGANIZATION NAME	COUNTRY
1 (Coordinator)	FITOPLANCTON MARINO	SPAIN
2	APIVITA	GREECE
3	CNRS	FRANCE
4	AGRICULTURAL UNIVERSITY OF ATHENS	GREECE
5	IFAPA	SPAIN
6	CCMAR	PORTUGAL
7	LIFESEQUENCING	SPAIN



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**Title:** Novel, sustainable marine bio-surfactant / bio-emulsifiers for commercial exploitation

- Call: H2020- Blue Growth---3---2014
- Topic: Novel marine derived biomolecules and industrial biomaterials
- **Target:** Isolation and production of new bio-surfactants and bio-emulsifiers by environmental pollution degrading bacteria (green biotechnology and sustainability)





# GREENTECH EXPERTISE

Cutting-edge research, partnership & innovation programs

## RESEARCH PROGRAMS



Long-term research collaborations

Four “2020 horizon” international research programs

## UNIVERSITIES PARTNERSHIPS



Partnerships with international Academia

Active collaborations with 25 countries around the world

## CONFERENCES & PUBLICATIONS



Recognition & publications

Keynote speaker in the most prestigious conferences.  
Numerous scientific publications in the most advanced & recognized revues.

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Thank you!