GADITANA

Phytoplankton

COMPOSITION

Gaditana Phytoplankton

Balanced nutrient composition

- Good quality of proteins (47%) and lipids ~19%)
- Source of essential amino acids (~1/3 of total amount)
- Adequate fatty acid profile (~49% PUFAs)
- EPA represents ~43% of total fatty acids, and ~5% dry weight
- Ratio w6/w3<1

Bioactive micronutrients

- Carotenoids: b-carotene (0.10 mg/g), zeazanthin (0.16 mg/g), astaxanthin (up to 7% dw); antioxidant and antiinflammatory properties
- Chlorophyll a (~2 mg/g); antioxidant properties
- Polyphenolic compounds (~38 ppm): quercetin, caffeoyl gluco side, protocatechuic acid, caffeic acid, feruloyl glucaricacid acid; antioxidant properties
- Vitamin C (2.4 mg/g) and E (0.4 mg/g); antioxidant properties

Bioactive compounds with antiproliferative/ cytotoxic properties:

- Trihydroxyanthra-quinone
- Heteronemin
- Iasonolide G
- Sitoindoside IX
- Withalongolide J
- Physapubenolide

Bioactive compounds with antiinflammatory properties:

- Asperulosidic acid
- Klymollin E

Bioactive compounds with antibiotic properties:

- Petrosynone
- Monensin B

OXIDATIVE STRESS & GADITANA

ROS Overproduction ↓

Metabolic byproducts
- Xantina oxidases
- NO synthetase
- Mitochondria

Enzymatic synthesis
- NADPH oxidases

Cellular respiration
- Mitochondrial semi-ubiquinone

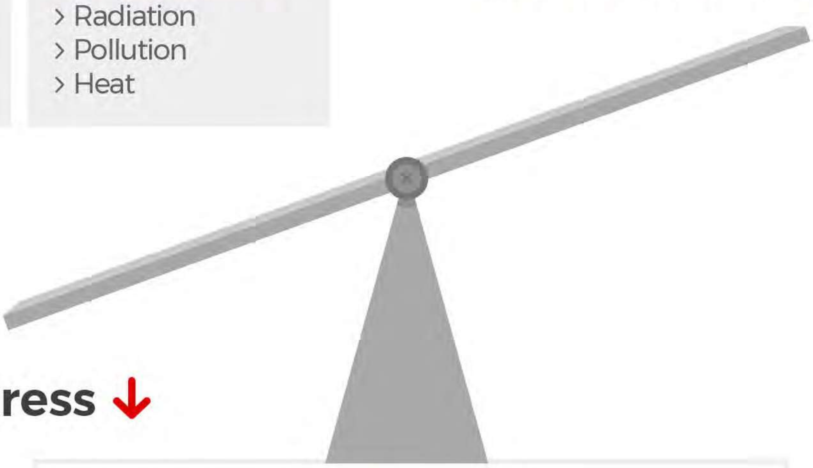
Physical/Chemical
- Radiation
- Pollution
- Heat

Phytoplankton

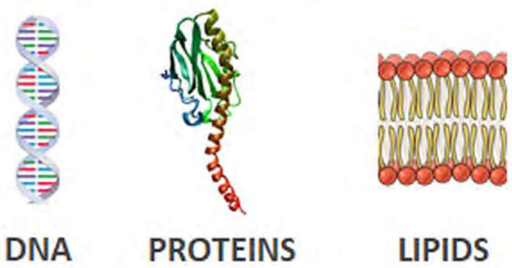
Enzymatic defenses
- SOD, CAT, GPx
- TXN
- PRX
- GSH pathway

Non-Enzymatic scavengers
- Vitamins (C, E)
- Carotenoids
- Polyphenols

Antioxidant defences ↓



Oxidative Stress ↓



↓

Cell Injuries → Tissue Damages → DISEASES

Living organisms on Earth are exposed during lifetime to oxygen, sunlight, and a range of different chemicals present in atmosphere, soil, and water. Moreover, apart from these exogenous environmental factors, endogenously produced chemical and metabolites often perturb cellular and organismal functions. To cope with such perturbations, we all display defence mechanisms specialized in an individual stress to respond to the stress for adaptation and maintenance of homeostasis. All cells produce reactive oxygen species (ROS) as a consequence of the own metabolic processes, the superoxide anion being the precursor of all other ROS.

The three main in vivo sources for superoxide anion are the mitochondrial respiratory chain complexes, the nicotinamide adenine dinucleotide phosphate-oxidase, and xanthine oxidases. Ultimately, ROS can provoke damages in proteins, lipids, and DNA when antioxidant capabilities are overwhelmed by the burden of ROS, and this state is known as **oxidative stress.**

Phytoplankton is a DIRECT antioxidant

In vitro testing: Demonstrated free-radical scavenging activity to combat oxidative damage

B-CAROTENE BLEACHING

DPPH

FRAP

Phytoplankton

ANTIOXIDANT ACTIVITY

ORAC

ABTS

Fe^{2+} CHELATING ACTIVITY

DPPH 2,2-Diphenyl-1-picrylhydrazyl
FRAP Ferric Reducing Antioxidant Power
ORAC Oxygen Radical Absorbance Capacity
ABTS 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid

Direct antioxidant: Demonstrated free-radical scavenging activity to combat oxidative stress by in vitro testing

B-CAROTENE BLEACHING

Percentage: 96.55 (Millao and Uquiche, 2016)

DPPH ASSAY

IC_{50} (μg/ml extract): 365 (Maadane et al., 2015)

μg TE/g: 254.6 (Martinez et al., 2022)

mmol TE/Kg oil: 1.8 (Millao and Uquiche, 2016)

IC_{50} (mg/ml extract): 2.02 (Kherraf et al., 2017)

IC_{50} (mg/ml extract): 44.37 (Mekdade et al., 2016

IC_{50} (μg/ml extract): 400 (Haoujar et al., 2019)

ORAC

IC_{50} (μg/ml extract): 0.026 (Maadane et al., 2015)

Fe^{2+} CHELATING ACTIVITY

IC_{50} (mg/ml extract): 3.52 (Haoujar et al., 2019)

ABTS

μg GAE/g: 193.68 (Martinez et al., 2022)

IC_{50} (mg/ml extract): 0.336 (Letsiou et al., 2017)

FRAP ASSAY

Units OD (5 mg/ml extract): 0.414 (Kherraf et al., 2017)

μM AAE/mg: 2.76 (Letsiou et al., 2017)

IC_{50} (mg/ml extract): 15.5 (Mekdade et al., 2016)

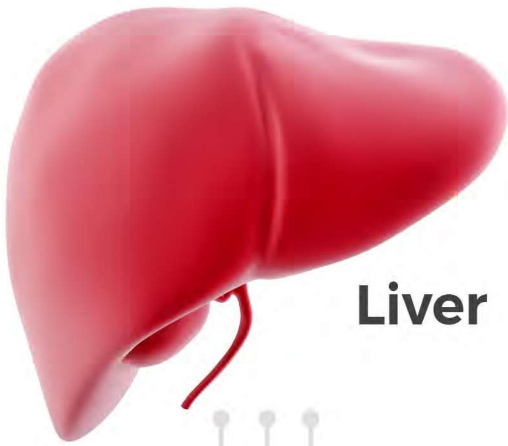
AAE/ml extract: 32.71 (Haoujar et al., 2019)

mmol Fe(II)/Kg oil: 85.52 (Millao and Uquiche, 2016)

Phytoplankton is a INDIRECT antioxidant

In vivo testing: Demonstrated activation of cellular antioxidant mechanisms in animal models

Phytoplankton



Increase antioxidant enzyme activities

Nacer et al., 2020
Martínez et al., 2022

CAT GST GPx
Cu,ZnSOD MnSOD

Increase GSH content

Nacer et al., 2020

Decrease MDA & carbonyl proteins

Nacer et al., 2020

MDA: Malondialdehyde, biomarker of lipid peroxidation
Carbonyl proteins: Biomarker of protein oxidation
GSH: Reduced Glutathione

Phytoplankton is a INDIRECT antioxidant

In vivo testing: Demonstrated activation of cellular antioxidant mechanisms in animal models

Phytoplankton

Plasma (P)
Erythrocytes (E)

Increase GSH content (E)

Nacer et al., 2019

Increase antioxidant enzyme activities (P&E)

Nacer et al., 2019

CAT SOD

Decrease MDA & carbonyl proteins (P&E)

Nacer et al., 2019

Increase Vitamin C content (E)

Nacer et al., 2019

In vivo testing: Demonstrated hypolipidemic effects in animal models

Phytoplankton

Plasma

Decrease in VLDL-C & LDL-C
Nacer et al., 2019

Increase in HDL-C
Nacer et al., 2019
Martínez et al., 2022

Decrease in cholesterol
Nacer et al., 2020

Decrease in triglycerides
Nacer et al., 2020

Liver, Pancreas, Adipose tissue

Decrease in total cholesterol
Nacer et al., 2019

Decrease in triglycerides
Nacer et al., 2019
Bendimerad-Benmokhtar et al., 2019

Increase in LPL activity
Nacer et al., 2019

Liver

Decrease in fat content
Martínez et al., 2022

VLDL-C: very low density lipoprotein-cholesterol
LDL-C: low density lipoprotein-cholesterol
HDL-C: high density lipoprotein-colesterol
LPL: Lipoprotein lipase is an enzyme that degrades circulating triglycerides in the bloodstream. These triglycerides are embedded in very low-density lipoproteins (VLDL) and chylomicrons traveling through the bloodstream. Fatty acids liberated from the triglycerides are then used for storage in adipose tissue or fuel in skeletal or cardiac muscle.

In vivo testing: Demonstrated hypolipidemic effects in animal models

Plasma

Decrease in glucose levels

Nacer et al., 2019

Nacer et al., 2020

Martínez et al., 2022

Nacer et al., 2019
Bendimerad- Benmokhtar et al., 2019

Decrease in glycated hemoglobin

Nacer et al., 2019

Nacer et al., 2020

In vivo testing: Demonstrated hepatoprotective effect in an animal model

Decrease in serum levels of ALT, AST, ALP, and LDH

Nacer et al., 2020

DEMONSTRATED anti-inflammatory effect

Phytoplankton

In vivo (animal model)

Decrease in serum levels of IL-6 and TNFa

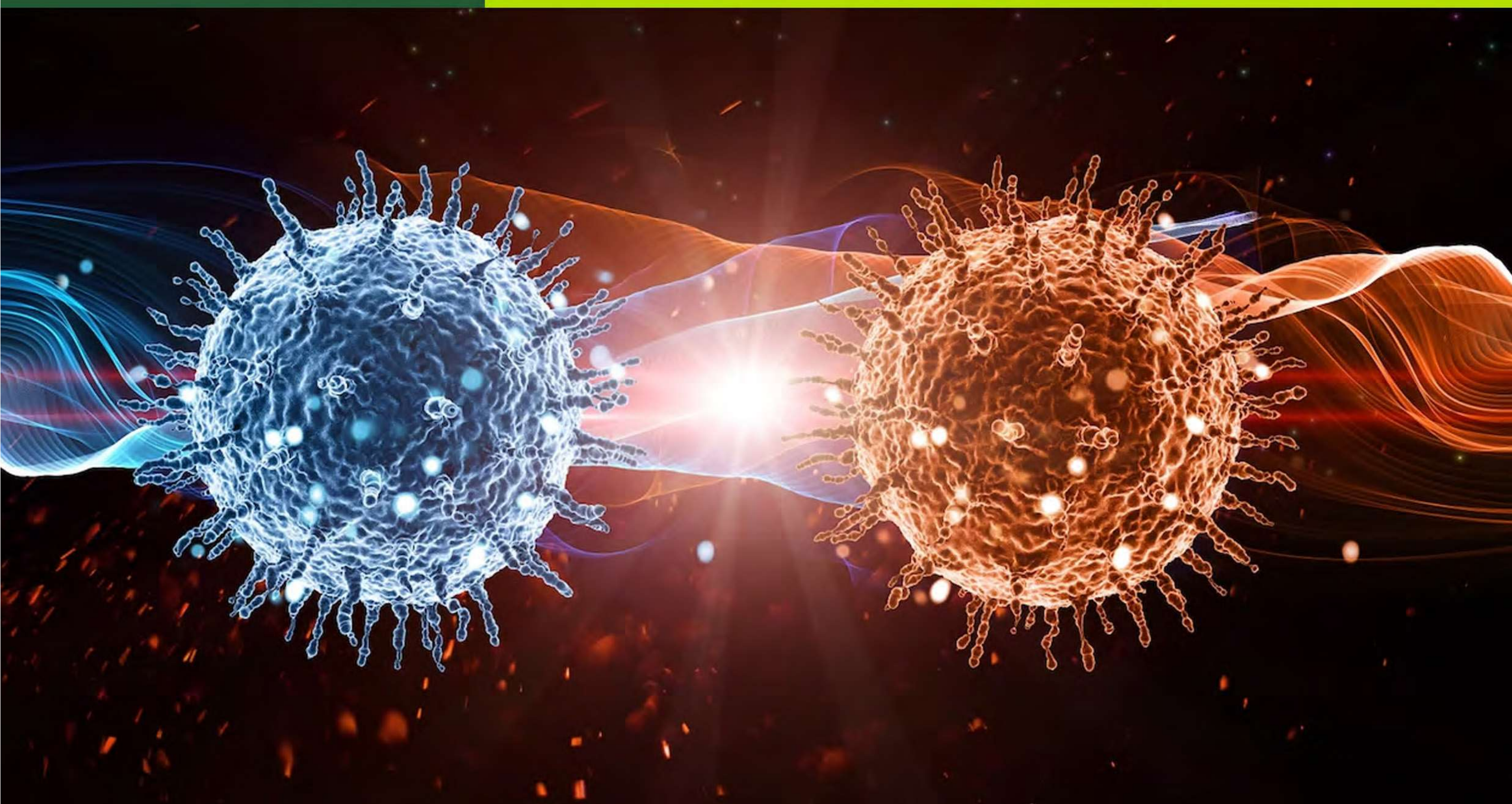
Martínez et al., 2022

In vitro

Inhibited production of TNFa induced by LPS in differentiated macrophagues

de los Reyes et al., 2014

- IL-6 (Interleukin 6) and TNFa (Tumor Necrosis Factor alpha) are two of the major pro-inflammatory cytokines



In vitro: Demonstrated anti-proliferative effect in tumor cells

Caco-2

(human colorectal adenocarcinoma)
Carrasco-Reinado et al., 2021

UACC-62

(human skin melanoma)
Ávila-Román et al., 2016

HepG2

(human liver cancer)
Carrasco-Reinado et al., 2021

HCT-116

(human colon cancer)
Castejón and Marko, 2016

T84

(human colorectal carcinoma)
Martínez et al., 2022

HT-29

(human colon cancer)
Ávila-Román et al., 2016

A549

(adenocarcinomic human alveolarbasal epithelial cells)
Martínez et al., 2022

Phytoplankton
SUPPLY COMPANY

Other potential bioactivies exhibited by in vitro testing

Phytoplankton

Anti-steatotic effect

Anti-steatotic effect
Prevented the accumulation of triglycerides induced by palmitic acid in cultured hepatocytes (AML-12 cells)

(González-Arceo et al., 2023)

Skin protection against oxidative damage

Increased cell viability under oxidative stress in NHDF cells

(Letsiou et al., 2017)

Anti-hypertensive effect

Inhibition of ACE-1

(de los Reyes et al., 2014)

ACE-1 is a key enzyme that helps to regulate the salt-water balance and blood pressure within the renin-angiotensin-aldosterone system. It converts Ang-I in Ang-II, which is considered the main active peptide, which acts on target tissues and regulates blood pressure through renal reabsorption of sodium and water and systemic vasoconstriction.

NHDF: Normal Human Dermal Fibroblasts

Other potential bioactivies exhibited by in vitro testing

Phytoplankton

Antioxidant effect

Up-regulation of GPX1 and FOXO3 genes in NHDF cells

(Letsiou et al., 2017)

Immunomodulatory effect

Up-regulation of FOXO3 and KLF2 genes in NHDF cells

(Letsiou et al., 2017)

Anti-adipogenic effect

Up-regulation of KLF2 gene in NHDF cells

(Letsiou et al., 2017)

Anti-inflammatory effect

Up-regulation of FOXO3, KLF2, and IL-1R genes in NHDF cells

(Letsiou et al., 2017)

Phytoplankton