



HAL
open science

Marine microalgae used as food supplements and their implication in preventing cardiovascular diseases

Virginie Mimouni, Lionel Ulmann, Adil Haimeur, Frédérique Guéno, Nadia Meskini, Gérard Tremblin

► To cite this version:

Virginie Mimouni, Lionel Ulmann, Adil Haimeur, Frédérique Guéno, Nadia Meskini, et al.. Marine microalgae used as food supplements and their implication in preventing cardiovascular diseases. OCL Oilseeds and fats crops and lipids, 2015, 22 (4), pp.D409. 10.1051/ocl/2015015 . hal-02001045

HAL Id: hal-02001045

<https://univ-lemans.hal.science/hal-02001045v1>

Submitted on 21 Apr 2024

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

**12TH EURO FED LIPIDS CONGRESS: OILS, FATS AND LIPIDS:
FROM LIPIDOMICS TO INDUSTRIAL INNOVATION**

Marine microalgae used as food supplements and their implication in preventing cardiovascular diseases

Virginie Mimouni^{1,2,3,*}, Lionel Ulmann^{1,2,3}, Adil Haimeur^{1,2,3,4}, Frédérique Guéno¹, Nadia Meskini⁴ and Gérard Tremblin^{2,3}

¹ IUT Département Génie Biologique 53020 Laval, France

² Faculté des Sciences et Techniques 72085 Le Mans, France

³ EA 2160-MMS, Mer Molécules Santé, IUML-FR 3473 CNRS, Université du Maine, Le Mans, France

⁴ Université Hassan II, Equipe Nutrition, Environnement, Santé. Laboratoire de Virologie, Microbiologie, Qualité/Écotoxicologie et Biodiversité, Faculté des Sciences et Techniques, Mohammedia, Université de Casablanca, Morocco

Received 19 February 2015 – Accepted 31 March 2015

Abstract – Marine microalgae are photosynthetic microorganisms producing numerous bioactive molecules of interest for health and disease care such as lipids rich in omega-3 fatty acids -as eicosapentaenoic acid (EPA, 20:5 n-3) and docosahexaenoic acid (DHA, 22:6 n-3)- and carotenoids (*e.g.*, β -carotene, fucoxanthin, astaxanthin). It has already been shown that these molecules, individually used, are benefic in the prevention of diseases such as those associated with the cardiovascular risks, but also in some carcinomas. When these molecules are combined, synergistic effects may be observed. Microalgae, as a dietary supplement, can be used to study these synergistic effects in animal models in which dyslipidemia can be induced by a nutrition treatment. Different marine microalgae of interest are studied in this context to determine their potential effect as an alternative source to marine omega-3 rich fish oils, actually widely used for human health. Actually, the pharmaceutical and nutrition industries are developing health research programs involving microalgae, trying to limit the dramatic reduction of fish stocks and the associated pollution in the marine environment. The aim of this review is threefold: (1) to present research on lipids, particularly long chain polyunsaturated fatty acids, as components of marine microalgae used as food supplements; (2) to present the health benefits of some microalgae or their extracts, in particular in the prevention of cardiovascular diseases and (3) to highlight the role of *Odontella aurita*, a marine microalga rich in EPA used as food supplement with the aim of preventing cardiovascular diseases.

Keywords: Microalgae / *Odontella aurita* / omega-3 polyunsaturated fatty acids / food supplement / cardiovascular diseases

Résumé – Microalgues marines utilisées comme compléments alimentaires et leur rôle dans la prévention des maladies cardiovasculaires. Les microalgues marines sont des micro-organismes photosynthétiques produisant de nombreuses molécules bioactives d'intérêt dans le domaine de la santé, tels que des lipides riches en acides gras oméga-3, comme l'acide eicosapentaénoïque (EPA, 20 :5 n-3) et l'acide docosahexaénoïque (DHA, 22 :6, n-3), et des caroténoïdes (par exemple, le β -carotène, la fucoxanthine, l'astaxanthine). Il a déjà été démontré que ces molécules ont un effet positif dans la prévention de maladies notamment celles qui sont associées au système cardiovasculaire, mais aussi dans certains carcinomes. Lorsque ces molécules sont combinées, des effets synergiques peuvent être observés. Les microalgues, utilisées en tant que compléments alimentaires, peuvent contribuer à étudier les effets synergiques de ces composés chez des modèles animaux pour lesquels apparaît une dyslipidémie d'origine nutritionnelle. Différentes microalgues marines sont utilisées dans ce contexte afin de déterminer leur potentiel d'action et de rechercher une source de lipides alternative aux huiles de poissons, ces dernières étant largement utilisées dans le domaine de la santé humaine en tant que sources marines riches en acides gras oméga-3. En fait, les industriels du secteur de la santé développent des programmes de recherche impliquant des microalgues en raison de la réduction spectaculaire des stocks de poissons et des polluants qui sont de plus en plus présents dans le milieu marin. Les objectifs de cette revue sont triples : (1) mettre l'accent sur les lipides, notamment les acides gras polyinsaturés à longue chaîne d'intérêt présents chez les microalgues

* Correspondence: virginie.mimouni@univ-lemans.fr

utilisées en tant que compléments alimentaires ; (2) présenter les effets bénéfiques sur la santé de quelques microalgues ou de leurs extraits notamment dans la prévention des maladies cardiovasculaires et (3) mettre en exergue le rôle de *Odontella aurita*, une microalgue marine riche en EPA, commercialisée en tant que complément alimentaire dans la prévention des maladies cardiovasculaires.

Mots clés : Microalgues / *Odontella aurita* / acides gras polyinsaturés oméga-3 / compléments alimentaires / maladies cardiovasculaires

1 Introduction

Food supplements are used to provide nutrients that can improve metabolic reactions involved in bioactive molecule synthesis. Among these nutrients, polyunsaturated fatty acids (PUFA) are needed as precursors of molecules related with cardiovascular regulation such as prostaglandins, thromboxanes or leucotriens (Guesnet *et al.*, 2005). Actually, fish oils are used to provide omega-3 PUFA, specifically eicosapentaenoic and docosahexaenoic acids (EPA and DHA, respectively) for human nutrition. However, new plant marine sources can be used for the production of these fatty acids. Marine microalgae have the ability to synthesize these fatty acids and received special attention for aquaculture or for food supplement use by pharmaceutical and nutrition industries. Actually, few microalga species are used for human nutrition. Moreover, crude extracts or whole cell can be provided as ingredient in different food. As microalgae are known for lipid storage, extraction of lipid droplets provides oil that can be integrated in food preparation. In this case, only the effect of lipid could be beneficial, while when the whole cell is used, as freeze-dried biomass, all compounds of microalgae could interact in human metabolic pathways. Indeed, in addition to lipids, high levels of pigments or phytosterols present in microalgae can have synergic effects in the regulation of parameters involved in cardiovascular or metabolic diseases.

The aim of this review is to bring information about the potential role of microalgae as food supplements in replacement of commonly used marine sources such as fish oils. This information will be focused on the use of microalgae as alternative lipid and PUFA sources and their health benefits. Original results will also be presented on the dose effect of freeze-dried biomass of a marine diatom, *Odontella aurita*, on omega-3 PUFA tissue enrichment.

2 Microalgae as lipid and PUFA sources

Microalgae are photosynthetic microorganisms found in marine and freshwater. These organisms are characterized by biochemical molecules with potential for different industrial activities such as biofuel production, pharmaceuticals, cosmetics or nutraceuticals use (Mimouni *et al.*, 2012).

The biochemical composition of microalgae reveals interesting levels of organic molecules such as proteins, polysaccharides, lipids, phytosterols and pigments, but also of mineral salts.

Although isolated from natural marine or freshwater, microalgae can be cultured through different scales, from erlenmeyer flasks (laboratory scale) to photobioreactors or open

ponds and raceways (industrial scale). In order to maintain a constant biochemical composition, the photobioreactor culture is preferentially used in order to control parameters involved in the microalgal culture such as carbon source, nutrients, pH, light and temperature.

Among bioactive molecules, even if lipids from microalgae are actually used for animal nutrition in aquaculture, these molecules could be also used for human nutrition.

Indeed, marine microalgae are characterized by high levels of PUFA especially from the n-3 series, eicosapentaenoic and docosahexaenoic acids (EPA and DHA, respectively). The fatty acids are incorporated into neutral lipids (triacylglycerols) as storage but also into polar lipids such as phospholipids and galactolipids as membrane constituents of chloroplast and endoplasmic reticulum compartments, respectively.

According to this specificity in lipids and fatty acids, microalgae could be considered as an alternative to usual marine source used in human nutrition such as fish oils. Indeed, fish and fish oil are the main sources of omega-3 long chain polyunsaturated fatty acids (LC-PUFA) but it has been raised that pollutants or toxins could be accumulated in fish. Moreover, the use of fish oil is quite poor partially due to problems linked with odor, taste and oxidative stability. Due to these disadvantages, researches have been developed for an application of microalgae (marine or freshwater) in human nutrition, specifically with fatty acid new source.

The main constituents of the lipid fraction of the fresh water microalga *Chlorella vulgaris* are oleic (18:1 n-9), palmitic (16:0) and linolenic (18:3 n-3) acids, accounting for 41, 22 and 9% of the total amount, respectively (Mendes *et al.*, 1995). In another species, *Dunaliella salina*, these fatty acids account for more than 80% of the total of fatty acids (Herrero *et al.*, 2006). The diversity of fatty acids that can be produced by microalgae are also function of length or unsaturation. For example, in the green fresh water microalga *Haematococcus*, short chain fatty acids have been characterized (Rodriguez-Meizoso *et al.*, 2010). Some microalgae are able to synthesize LC-PUFA which could present some health benefits. Some are producing omega-6 fatty acids: the *Arthrospira* and *Porphyridium* species have the ability to synthesize respectively gamma-linolenic and arachidonic acids. Some others are producing omega-3 fatty acids: EPA has been proved to be synthesized in genus *Nannochloropsis*, *Phaeodactylum*, *Nitzschia*, *Odontella*, *Isochrysis* and *Pavlova* species while DHA was only present in the *Cryptocodinium*, *Pavlova* and *Schizochytrium* ones.

Among these microalgae, only few species have been authorized for a commercial used as food supplements. These species are *Arthrospira*, *Chlorella*, *Cryptocodinium*, *Dunaliella* and *Odontella*.

Table 1. Lipid content and the main omega-3 PUFA of interest of microalgae authorized for human nutrition.

Microalga species	Lipid content* (% dry weight biomass)	PUFA of interest
<i>Dunaliella</i> sp.	10–70	ALA + EPA (Sheffer <i>et al.</i> , 1986) (Chen <i>et al.</i> , 2011) (Bhosale <i>et al.</i> , 2010)
<i>Chlorella</i> sp.	5–58	ALA + EPA (Petkov and Garcia, 2007) (Buono <i>et al.</i> , 2014)
<i>Odontella aurita</i>	8–10	
<i>Cryptocodinium cohnii</i>	20–51	
<i>Isochrysis</i> sp.	7–40	EPA (Guihéneuf <i>et al.</i> , 2010) DHA (De Swaaf <i>et al.</i> , 1999) EPA + DHA (Lin <i>et al.</i> , 2007)

* Results are from Mata *et al.* (2010). ALA, alpha-linolenic acid; EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid.

Table 2. Use of biomass or crude extracts from some microalgae approved for human nutrition on some lipid parameters.

Lipid parameters	Microalgae	Human studies	Animal studies
Lipidemia	<i>Arthrospira</i>	(Torres-Duran <i>et al.</i> , 2012) (Samuels <i>et al.</i> , 2002) (Parikh <i>et al.</i> , 2001)	(Ponce-Canchihuaman <i>et al.</i> , 2010)
	<i>Cryptocodinium</i>		(Ryan <i>et al.</i> , 2009)
	<i>Chlorella</i>		(Cherng and Shih, 2005)
Tissue fatty acid	<i>Arthrospira</i>		(Torres-Duran <i>et al.</i> , 2006)
Composition	<i>Cryptocodinium</i>		(Lin <i>et al.</i> , 2011)
Lipoprotein	<i>Dunaliella</i>	(Shaish <i>et al.</i> , 2006)	
Metabolism	<i>Isochrysis</i>		(Nuno <i>et al.</i> , 2013)
Lipidemia	<i>Odontella aurita</i>		(Haimeur <i>et al.</i> , 2012)

In Table 1 are reported the lipid content and the main omega-3 PUFA of interest of microalgae authorized for human nutrition.

3 Health benefits of microalgae in preventing cardiovascular diseases

Health benefits of microalgae are being increasingly recognized and appreciated within the last three to four decades since the introduction of probiotic nutritional supplements. Health benefits of food ingredients and dietary supplements are attributed essentially to long chain polyunsaturated fatty acids (LC-PUFA). Various microalgae, as outlined in the previous section, have the ability to synthesize LC-PUFA with particular interest, specifically the omega-3 and omega-6 series such as EPA, DHA and ARA (Pulz and Gross, 2004).

Freshwater and marine microalgae have been found to have health benefits on cardiovascular diseases, inflammatory diseases, cancer and viral infections. We focused this section on the role of some microalgae in the prevention of cardiovascular diseases.

The microalga or more exactly cyanobacteria *Athrospira* sp. has been shown to increase the plasminogen activating factor in endothelial cells with a positive impact on cardiovascular disease prevention. This cyanobacteria is also known to enhance the immune system with a prevention in both viral and cancer infections, or to increase the gastrointestinal microorganism flora (Barrow and Shahidi, 2008). This microalga

alleviates hyperlipidemia, decreases hypertension and glucose level (Spolaore *et al.*, 2006). It also has been stated that another freshwater microalga, *Chlorella* sp. was able to have several health benefits such as a decrease of glycemia and cholesterolemia. These species could also be used to increase the cytokine production to stimulate immune response (Barrow and Shahidi, 2008).

Even if few microalga strains have been approved for human nutrition, some experiments with other microalgae have been conducted on animal models. Indeed, a lyophilisate of *Porphyridium cruentum* strain have been used as a food supplement for Syrian golden hamsters. In this experiment, it has been shown that the use of this microalga biomass reduced the circulating cholesterol (dose dependently) and body fat (expressed as percentage) in hypercholesterolaemic animals (Harding *et al.*, 2009). In diabetic rats, it has been shown that groups fed with the microalga *Isochrysis galbana* exhibited decreased glucose and lipid values (triacylglycerol and cholesterol) and weight loss. Concerning the lipoprotein metabolism, this microalga increased the low density lipoproteins and decreased the high lipoprotein concentrations (Nuno *et al.*, 2013).

In Table 2 are summarized the health effects investigated for microalgae biomass, extracts or metabolites in human and animal studies. Reported data are focused on regulation of lipid parameters with microalga approved for human nutrition. According to these data it appears that the use of diatoms in nutrition studies has only been poorly developed. In the last section of this review data will be provided with the use of

Table 3. Animal characteristics after 7 weeks of treatment.

Parameters (g)	Control	1% OA	3% OA	9% OA	12% OA
Body weight	392 ± 43.7	400 ± 9.0	379 ± 17.4	401 ± 17.9	395 ± 32.2
Liver weight	10.98 ± 1.35	10.09 ± 1.37	10.01 ± 0.59	10.03 ± 0.75	10.21 ± 1.28
Adipose tissue	3.22 ± 0.53	4.57 ± 0.77	4.78 ± 1.99	3.97 ± 1.23	4.21 ± 1.27
Heart weight	1.28 ± 0.16	1.47 ± 0.24	1.27 ± 0.12	1.32 ± 0.10	1.32 ± 0.16
Kidneys weight	2.52 ± 0.16	2.68 ± 0.22	2.51 ± 0.08	2.79 ± 0.35	2.67 ± 0.40

Results are expressed as mean ± SD ($n = 4$). After a one-way ANOVA and a Student-Newman-Keuls multiple comparison test, results were arranged in increasing order $a > b > c$ ($p < 0.05$). Means assigned with superscript letters are statistically different.

Table 4. Glycemia and plasma lipids determinations after 7 weeks of treatment.

Parameters (g/L)	Control	1% OA	3% OA	9% OA	12% OA
Glycemia	1.65 ± 0.13	2.39 ± 0.09	2.03 ± 0.38	1.70 ± 0.15	2.30 ± 0.91
Triacylglycerols	0.86 ± 0.12	0.84 ± 0.14	0.83 ± 0.11	0.87 ± 0.11	0.95 ± 0.29
Cholesterol	0.64 ± 0.30	0.66 ± 0.16	0.50 ± 0.03	0.62 ± 0.11	0.64 ± 0.13

Results are expressed as mean ± SD ($n = 4$). After a one-way ANOVA and a Student-Newman-Keuls multiple comparison test, results were arranged in increasing order $a > b > c$ ($p < 0.05$). Means assigned with superscript letters are statistically different.

the marine microalga *O. aurita*, a diatom rich in EPA used as dietary supplement.

4 The role of *O. aurita*, a marine diatom, used as dietary supplement, in preventing cardiovascular diseases

Metabolic syndrome including dyslipidemia, obesity and insulin resistance is a major public health problem. The modern lifestyle of an increased intake of palatable high-fat diet associated with decreased energy expenditure contribute to the current rising prevalence of the metabolic syndrome. Omega-3 PUFA contained in fish oils are well known to reduce the incidence of risk factors of metabolic syndrome (Poudyal *et al.*, 2011). However, an alternative source of omega-3, from marine microalga, could have a similar effect. *O. aurita* is a marine diatom known to contain high levels of eicosapentaenoic acid (EPA, 25 to 26% of total fatty acids) which is recognized to be involved in the prevention of cardiovascular risks. The use of this microalga was approved in 2002 for human nutrition by AFSSA (Agence Française pour la Sécurité Sanitaire des Aliments).

First, will be presented results concerning the influence of the doses of *O. aurita* as food supplement in order to determine the minimal effective dose for incorporation of EPA and its conversion into DHA in plasma and liver tissues, and second, a synthesis of results obtained on effects of *O. aurita* used as dietary supplement on risk factors linked to metabolic syndrome installation in high fat-fed rats will be reported (Haimeur *et al.*, 2012).

4.1 Effect of different doses of *O. aurita* supplemented to a standard diet on biochemical parameters involved in lipid metabolism in healthy rats

A preliminary study has been performed to investigate the effects of a standard diet supplemented with different doses

of lyophilized *O. aurita* on biochemical parameters involved in lipid metabolism in rats, in order to determine the minimal effective dose for a positive effect on these biochemical parameters.

For this preliminary experiment, 30 Wistar rats were fed a standard diet for a week (acclimatation); then the rats were divided into 5 groups each receiving the standard diet supplemented with 0, 1, 3, 9, 12% of lyophilized *O. aurita*. After 7 weeks of diet the rats were sacrificed and the impact of different diets on some plasmatic biochemical parameters such as glucose, triglycerides and cholesterol, and the enrichment of plasma and tissue lipids in omega-3 are measured in order to find the lowest effective dose on these parameters.

Doses of *O. aurita* tested have no effect on the evolution of animal weight (Tab. 3). Also for plasma parameters, no significant dose effect on glycemia or on the plasma triglycerides and cholesterol levels were observed (Tab. 4).

As one of the interest of food supplement is to increase levels of molecules that can enhance metabolic reactions, we investigated the plasma and liver omega-3 PUFA enrichment. Main results are reported on Tables 5 and 6. In plasma the lipid EPA content was increased according to the dose supplied and the contents of docosapentaenoic acid (DPA) and DHA were significantly higher over 3% of *O. aurita* tested. In the liver a similar trend was observed with EPA provided by the microalga, with a conversion into DPA and DHA from a 3% weight/weight diet supplementation. According to these preliminary observations, it seemed that a 3% level of *O. aurita* biomass was enough to have omega-3 PUFA increase from EPA conversion. Even if EPA is incorporated into triacylglycerols or phospholipids, it seems that microalga fatty acids are available for tissue enrichment. So, it can be considered that the diatom *O. aurita* can be used as an alternative to fish oil sources for tissue lipid EPA supplementation. Therefore, the rate of 3%, which induced a high content of DHA in the liver, was used for subsequent experiments investigating the effect of freeze-dried *O. aurita* used as a food supplement, on the risk factors for high-fat diet induced metabolic syndrome in rats (Haimeur *et al.*, 2012).

Table 5. Effect of different doses of *O. aurita* (OA) supplemented to a standard diet on fatty acid composition of the plasmatic lipids after 7 weeks of diet (in % molar).

Fatty acids	Control	1% OA	3% OA	9% OA	12% OA
20:5 n-3	0.28 ± 0.06 ^c	0.36 ± 0.08 ^b	0.51 ± 0.02 ^b	1.55 ± 0.22 ^a	1.95 ± 0.57 ^a
22:5 n-3	0.37 ± 0.07 ^c	0.39 ± 0.07 ^c	0.49 ± 0.03 ^b	0.67 ± 0.05 ^a	0.79 ± 0.11 ^a
22:6 n-3	3.90 ± 0.27 ^b	3.63 ± 0.36 ^b	4.56 ± 0.20 ^a	3.45 ± 0.38 ^b	4.74 ± 0.63 ^a
AGPI n-3	4.56 ± 0.24 ^c	4.48 ± 0.39 ^c	5.57 ± 0.23 ^b	5.66 ± 0.37 ^b	7.48 ± 0.94 ^a

Results are expressed as mean ± SD ($n = 4$). After a one-way ANOVA and a Student-Newman-Keuls multiple comparison test, results were arranged in increasing order $a > b > c$ ($p < 0.05$). Means assigned with superscript letters are statistically different.

Table 6. Effect of different doses of *O. aurita* (OA) supplemented to a standard diet on fatty acid composition of the liver lipids after 7 weeks of diet (in % molar).

Fatty acids	Control	1% OA	3% OA	9% OA	12% OA
20:5 n-3	0.13 ± 0.02 ^d	0.16 ± 0.05 ^d	0.29 ± 0.10 ^c	0.82 ± 0.10 ^b	1.18 ± 0.15 ^a
22:5 n-3	0.42 ± 0.04 ^b	0.51 ± 0.12 ^b	0.67 ± 0.06 ^a	0.92 ± 0.20 ^a	0.97 ± 0.18 ^a
22:6 n-3	5.76 ± 0.95 ^b	5.52 ± 0.77 ^b	7.23 ± 0.36 ^a	6.69 ± 0.59 ^a	6.55 ± 0.83 ^a
AGPI n-3	6.30 ± 0.92 ^c	6.19 ± 0.75 ^c	7.42 ± 0.34 ^b	8.43 ± 0.14 ^a	9.12 ± 1.63 ^a

Results are expressed as mean ± SD ($n = 4$). After a one-way ANOVA and a Student-Newman-Keuls multiple comparison test, results were arranged in increasing order $a > b > c$ ($p < 0.05$). Means assigned with superscript letters are statistically different.

Table 7. Main results obtained with a 3% freeze-dried *O. aurita* food supplement in high-fat fed rats in some biochemical parameters. Results are from Haimeur *et al.*, 2012.

Parameters ¹	Control diet	High fat diet	High fat diet + <i>O. aurita</i>
Rat characteristics			
Body weight (g)	359 ± 18 ^b	389 ± 13 ^a	379 ± 2 ^{ab}
Adipose tissue weight (g)	4.5 ± 1.6 ^b	6.9 ± 0.8 ^a	4.3 ± 0.9 ^b
Blood			
Glycemia	4.30 ± 0.49 ^b	5.17 ± 0.74 ^a	4.57 ± 0.51 ^{ab}
Triglyceridemia (mmol/L)	0.84 ± 0.07 ^b	1.06 ± 0.04 ^a	0.91 ± 0.09 ^b
Cholesterolemia (mmol/L)	1.49 ± 0.22 ^b	1.87 ± 0.17 ^a	1.51 ± 0.13 ^b
Platelet total aggregation (%) ²	68.35 ± 3.56 ^b	80.29 ± 3.59 ^a	72.42 ± 1.09 ^{ab}
Platelet TXB2 level (ng/5 × 10 ⁸ cell)	12.16 ± 0.19 ^b	16.14 ± 1.51 ^a	12.30 ± 0.21 ^b
Liver			
Triacylglycerols (mg/g)	12.04 ± 2.48 ^b	28.28 ± 4.97 ^a	16.62 ± 4.15 ^b
Total cholesterol (mg/g)	2.97 ± 0.49 ^b	4.19 ± 0.66 ^a	2.88 ± 0.10 ^b
MDA level (nmol/mg prot)	4.64 ± 0.2 ^b	5.15 ± 0.22 ^a	4.57 ± 0.20 ^b
GPx activity (nmol ROOH/min/mg prot)	148.1 ± 3.4 ^a	108.6 ± 11.5 ^b	133.6 ± 5.7 ^a

¹ Results were expressed as mean ± SD ($n = 5$). After a one-way ANOVA and a Student-Newman-Keuls multiple comparison test, results were arranged in increasing order $a > b$ ($p < 0.05$). Means assigned with superscript letters are statistically different. ² After stimulation with collagen (5 µg/mL).

4.2 Effects of *O. aurita*, used as food supplement, on risk factors linked to metabolic syndrome installation in high fat-fed rats

In this study, the effects of *O. aurita* as dietary supplement on risk factors linked to metabolic syndrome installation in high fat-fed rats were reported (Haimeur *et al.*, 2012).

For this experiment, male Wistar rats were randomly divided into groups of 6 animals and were fed with a standard

diet (Control), with a high-fat diet (HF) or with the high-fat diet supplemented with 3% of freeze dried *O. aurita* (HFOA).

After 7 weeks of treatment, we evaluated in these animals, the effects of these different diets on the risk factors for metabolic syndrome, such as hyperlipidemia, platelet aggregation, thromboxane B2 production and oxidative stress.

The overview of the major results obtained in this study were reported in Table 7.

Despite no modification in body weight, it was noticed a decrease in adipose tissue weight in HFOA-fed rats.

Even if a slight decrease in glycemia was observed (ns), *O. aurita* intake decreased significantly triacylglycerol (TG) and total cholesterol (T-Chol) levels in plasma and liver compared to HF group levels which became similar to those obtained in controls. These modifications are similar to those already obtained with EPA in high fat-fed-mice, which reduced plasma and liver levels of triacylglycerol and total cholesterol (Nemoto *et al.*, 2009).

Platelet aggregability tended to decrease with *O. aurita* intake in association with a decrease in the TXB2 level. The high amounts of EPA in this microalga could explain the crucial role of this fatty acid in reducing platelet aggregability (Lagarde *et al.*, 2013). Concerning the oxidative stress parameters, it has been reported lower MDA levels and increased GPx activity in the liver after consumption of *O. aurita*, in high fat fed rats.

In conclusion, our results showed the efficiency of *O. aurita* as food supplement in regulation of physiological and biochemical parameters involved in metabolic syndrome installation, platelet aggregability and oxidative stress status.

5 Concluding remarks

The main dietary sources of omega-3 (precursors) originate from oils produced by plants (Colza, walnuts, etc.) but LC-PUFAs came from seafood products. The omega-3 LC-PUFAs such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are primarily derived from oily fish (Nichols, 2010) or arising from use of some marine microalgae as a dietary supplement (Ulmann *et al.*, 2014). Indeed, some species of microalgae are of particular interest and are used as a rich dietary source of EPA and DHA, but the consumption of complete microalgae or lipid extracts in the form of commercial food supplements is restricted to some genera, such as *Arthrospira*, *Chlorella*, *Cryptocodinium*, *Dunaliella*, and *Odontella*; however many other microalgae have been tested as potential food supplements, but are not yet authorized for commercial use (De Jesus *et al.*, 2013).

The marine diatom *O. aurita* presents high levels of EPA, a central fatty acid in the prevention of cardiovascular risks, and has been approved as a dietary supplement. Preliminary results obtained in healthy rats on the dose effect of freeze-dried biomass of *O. aurita* have shown an omega-3 PUFA plasma and liver enrichment from a dose of 3%. Our results concerning the effect of freeze dried *O. aurita*, used as dietary supplement might help to focus on the interest of using this microalga to prevent cardio-metabolic risks.

Our findings also suggest that the effects of *O. aurita* intake could be related to a synergistic effect between EPA and other microalgal bioactive compounds, such as pigments, fibers, and phytosterols, which are known to have beneficial effects on human health (Lattimer *et al.*, 2010; Peng *et al.*, 2011).

Acknowledgements. This study was supported by the PHC-Volubilis program No. MA/21/61 with joint financial support from the French Foreign Affairs Ministry, the Moroccan Ministry of Research and Higher Education and the FP 7 European Project GIAVAP (Genetic Improvement of Algae for Value Added Products).

Conflict of interest

The authors declare no conflict of interest.

References

- Barrow C, Shahidi F. 2008. Marine nutraceuticals and functional foods. Taylor & Francis Group: CRC Press.
- Bhosale RA, Rajabhoj M, Chaugule B. 2010. *Dunaliella salina* Teod. As a prominent source of eicosapentaenoic acid. *Int. J. Algae* 12: 185–189.
- Buono S, Lagellotti AL, Martello A, Rinna F, Fogliano V. 2014. Functional ingredients from microalgae. *Food Funct.* 5: 1669.
- Chen M, Tang H, Ma H, Holland TC, Ng KYS, Salley SO. 2011. Effects of nutrients on growth and lipid accumulation in the green algae *Dunaliella tertiolecta*. *Bioresour. Technol.* 102: 1649–1665.
- Cheng JY, Shih MF. 2005. Preventing dyslipidemia by *Chlorella pyrenoidosa* in rats and hamster after chronic high fat diet treatment. *Life Sci.* 76: 3001–3013.
- De Jesus Raposo MF, De Moraes RM, De Moraes AM. 2013. Health applications of bioactive compounds from marine microalgae. *Life Sci.* 15: 479–486.
- De Swaaf ME, De Rijk TC, Eggink G, Sijtsma L. 1999. Optimisation of docosahexaenoic acid production in batch cultivations by *Cryptocodinium cohnii*. *Prog. Ind. Microbiol.* 35: 185–192.
- Guesnet P, Alessandri JM, Astorg P, Pifferi F, Lavielle M. 2005. Les rôles physiologiques majeurs exercés par les acides gras polyinsaturés (AGPI). *OCL* 12: 333–343.
- Guiheneuf F, Fouqueray M, Mimouni V, Ulmann L, Jacqueline B, Tremblin G. 2010. Effect of stress UV on the fatty acid and lipid class composition in two marine microalgae *Pavlova lutheri* (Pavlovophyceae) and *Odontella aurita* (Bacillariophyceae). *J. Appl. Phycol.* 22: 629–638.
- Haimeur A, Ulmann L, Mimouni V, *et al.* 2012. The role of *Odontella aurita*, a marine diatom rich in EPA, as a dietary supplement in dyslipidemia, platelet function and oxidative stress in high-fat fed rats. *Lipids Health Dis.* 11: 147.
- Herrero JM, Ibáñez E, Cifuentes A, Reglero G, Santoyo S. 2006. *Dunaliella salina* microalga pressurized liquid extracts as potential antimicrobials. *J. Food Protein* 69: 2471–2477.
- Lagarde M, Calzada C, Guichardant M, Vericel E. 2013. Dose effect and metabolism of docosahexaenoic acid: Pathophysiological relevance in blood platelets. *Prostaglandins Leukot. Essent. Fatty Acids* 88: 49–52.
- Lattimer JM, Haub MD. 2010. Effects of dietary fibers and its components on metabolic health. *Nutrients* 2: 1266–1289.
- Lin YH, Chang FL, Tsao CY, Leu JY. 2007. Influence of growth phase and nutrient source on fatty acid composition of *Isochrysis galbana* CCMP 1324 in a batch photoreactor. *Biochem. Eng. J.* 37: 166–176.
- Lin YH, Shah S, Salem N. 2011. Altered essential fatty acid metabolism and composition in rat liver, plasma, heart and brain after microalgal-DHA addition to the diet. *J. Nutr. Biochem.* 22: 758–765.
- Mata TM, Martins AA, Caetano NS. 2010. Microalgae for biodiesel production and other applications: A review. *Renew. Sust. Energ. Rev.* 14: 217–232.
- Mendes RL, Fernandes HL, Coelho JP, *et al.* 1995. Supercritical CO₂ extraction of carotenoids and other lipids from *Chlorella vulgaris*. *Food Chem.* 53: 99–103.
- Mimouni V, Ulmann L, Pasquet V, *et al.* 2012. The potential of microalgae for the production of bioactive molecules of pharmaceutical interest. *Curr. Pharm. Biotechnol.* 13: 2733–2750.

- Nemoto N, Susuki S, Okabe H, Sassa S, Sakamoto S. 2009. Ethyl-eicosapentaenoic acid reduce liver lipids and lower plasma levels of lipids in mice fed a high-fat diet. *In vivo* 23: 685–690.
- Nichols PD, Petrie J, Singh S. 2010. Long-chain omega-3 oils-An update on sustainable sources. *Nutrients* 2: 572–585.
- Nuno K, Vilaruel-Lopez A, Puebla-Perez AM, Romero-Velarde E, Puebla-Mora AG, Ascencio F. 2013. Effects of the marine microalgae *Isochrysis galbana* and *Nannochloropsis oculata* in diabetic rats. *J. Funct. Foods* 5: 106–115.
- Peng J, Yuan JP, Wu CF, Wang JH. 2011. Fucoxanthin, a marine carotenoid present in brown seaweeds and diatoms: metabolism and bioactivities relevant to human health. *Marine Drugs* 9: 1806–1828.
- Parikh P, Mani U, Iyer U. 2001. Role of *Spirulina* in the control of glycemia and lipidemia in type-2 diabetes mellitus. *J. Med. Food* 4: 193–199.
- Petkov G, Garcia G. 2007. Which are fatty acids of the green alga *Chlorella*? *Biochem. System. Ecol.* 35: 281–285.
- Ponce-Canchihuaman JC, Perez-Mendez O, Hernandez-Munoz R, Torres-Duran PV, Juarez-Oropeza A. 2010. Protective effects of *Spirulina maxima* on hyperlipidaemia and oxidative-stress induced by lead acetate in the liver and kidney. *Lipid. Health Dis.* 9: 35.
- Poudyal H, Panchal SK, Diwan V, Brown L. 2011. Omega-3 fatty acids and metabolic syndrome: effects and emerging mechanisms of action. *Prog. Lipid Res.* 50: 372–387.
- Pulz O, Gross W. 2004. Valuable products from biotechnology of microalgae. *Appl. Microbiol. Biotechnol.* 65: 635–648.
- Rodriguez-Meizoso L, Jaime L, Santoyo S, Senorans FJ, Cifuentes A, Ibanez E. 2010. Subcritical water extraction and characterization of bioactive compounds from *Haematococcus pluvialis* microalga. *J. Pharm. Biomed. Anal.* 51: 456–463.
- Ryan AS, Bailey-Hall E, Nelson EB, Salem N. 2009. The hypolipidemic effect of an ethyl ester of algal docosahexaenoic acid in rats fed a high-fructose diet. *Lipids* 44: 817–826.
- Samuels R, Mani UV, Iyer UM, Nayak US. 2002. Hypocholesterolemic effect of *Spirulina* in patients with hyperlipidemic nephrotic syndrome. *J. Med. Food* 5: 91–96.
- Shaish A, Harari A, Hanashvili L, *et al.* 2006. 9-cis-carotene rich powder of alga *Dunaliella bardawil* increases plasma HDL-cholesterol in fibrate-treated patients. *Atherosclerosis* 189: 215–221.
- Sheffer M, Fried A, Gottlieb HE, Tietz A, Avron M. 1986. Lipid composition of the plasma-membrane of the halotolerant alga, *Dunaliella salina*. *Biochim. Biophys. Acta* 857: 165–172.
- Spolaore P, Joannis-Cassan C, Duran E, Isambert A. 2006. Commercial applications of microalgae. *J. Biosci. Bioeng.* 101: 87–96.
- Torres-Duran PV, Paredes-Carbajal AMC, Mascher BD, Zamora-Gonzalez BJ, Diaz-Zagoya CJD, Juarez-Oropeza MA. 2006. Protective effect of *Arthrospira maxima* on fatty acid composition in fatty liver. *Arch. Med. Res.* 37: 479–483.
- Torres-Duran PV, Ferreira-Hermosillo A, Ramos-Jimenez A, Hernandez-Torres RP, Juarez-Oropeza MA. 2012. Effect of *Spirulina maxima* on postprandial lipemia in young runners: a preliminary report. *J. Med. Food* 15: 753–757.
- Ulmann L, Mimouni V, Blanckaert V, Pasquet, Schoefs B, Chénais B. 2014. The polyunsaturated fatty acids from microalgae as potential sources for health and disease. In: Catalá A, ed. *Polyunsaturated Fatty Acids*. Nova Science Publishers: New York.
- Wendell SG, Baffi C, Holguin F. 2014. Fatty acids, inflammation and asthma. *J. Allergy Clin. Immunol.* 63: 1255–1264.

Cite this article as: Virginie Mimouni, Lionel Ulmann, Adil Haimeur, Frédérique Guéno, Nadia Meskini, Gérard Tremblin. Marine microalgae used as food supplements and their implication in preventing cardiovascular diseases. OCL 2015, 22(4) D409.