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Cultivated microalgae and the carotenoid fucoxanthin from *Odontella aurita* as potent anti-proliferative agents in bronchopulmonary and epithelial cell lines

Dimitri Moreau [a,*], Christophe Tomasoni [a], Catherine Jacquot [a], Raymond Kaas [b], Roland Le Guedes [b], Jean-Paul Cadoret [b], Arnaud Muller-Feuga [b], Ioanna Kontiza [c], Constantinos Vagias [c], Vassilios Roussis [c], Christos Roussakis [a]

[a] *Laboratoire de Pharmacologie Marine, ISOMer, Faculté de Pharmacie de Nantes, 1 rue Gaston Veil, BP 92208, 44322 Nantes Cedex 03, France*
[b] *Laboratoire de Physiologie et Biotechnologie des Algues, IFREMER, rue de l'île d'Yeu, BP 1105, 44311 Nantes Cedex 03, France*
[c] *University of Athens, Department of Pharmacy, Division of Pharmacognosy and Chemistry of Natural Products, Panepistimiopolis Zografou, Athens 15771, Greece*

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Abstract

The antiproliferative activities of several extracts from cultivated microalgae in France have been studied against bronchopulmonary and epithelial cell lines, respectively (A549, NSCLC-N6 and SRA 01/04). The algal extracts, of Diatomae (*Odontella aurita*, *Chaetoseros* sp.), as well as of Haptophyceae: *Isochrisys aff. galbana*, appeared as the most active among all the assayed species, expressing a broad spectrum of in vitro antiproliferative activity of well-differentiated pathologic cells such as NSCLC-N6 by terminal differentiation. Bio-guided fractionation of the above referred extracts, led us to the isolation, of the carotenoid fucoxanthin. Fucoxanthin has been structurally determined, through modern spectral means and has been studied separately for its activities.

Keywords: *Odontella aurita*; Antiproliferative activities; Bronchopulmonary carcinoma; Secondary cataract; Apoptosis; Fucoxanthin

1. Introduction

Marine microalgae comprise the largest group of living organisms in the oceans, constituting an estimated 10,000 species. Algae are at the base of entire aquatic food chain. Therefore, it is not surprising that the microalgae, which compose the phytoplankton, play a vital role in the rearing of aquatic animals like molluscs; shrimps and fish. Moreover, there are numerous applications for molecules from these phototropic microorganisms in human and animal food, health and cosmetology (Muller-Feuga, 2000).

In recent years, there has been a growing interest in functional foods, that is, foods able to provide additional physiological benefits for human health, other than the basic nutritional and energetic requirements (Bidlack, 1994). Often, functional foods are traditional foods enriched with an ingredient able to provide or promote a specific beneficial action for human health. These are called functional ingredients. These ingredients are preferred to have a natural origin, such as plants or perhaps algae and/or microalgae. These types of marine sources are receiving increasing attention mainly for their content in, for example, polyunsaturated fatty acids and, β-carotene and other pigments (antioxidants), sulphated polysaccharides and sterols (antimicrobials).

One of the main interests in our laboratories is to assess the suitability obtained from extracts and pure compounds from cultivated microalgae, like the ones which they have been studied, as food antioxidants and preventative agents against secondary cataracte and cancer.

In this work, a preliminary screening of ten marine and fresh water species from different orders (Diatomophyceae, Rhodophyceae, Haptophyceae, Cryptophyceae, Prasinophyceae

* Corresponding author. Tel.: +33 2511 25672; fax: +33 2511 25690.
E-mail address: dimitri.moreau@univ-nantes.fr (D. Moreau).

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Table 1
Detail of the different strains studied, with the source and the optimal condition of growing

Order	Species	Source	Medium	pH	T (°C)
Diatomophyceae	*Odontella aurita*	IFREMER	Conway	7.5	20
	Chaetoceros sp.	ccap 1010/11	Conway	7.5	20
	Porphyridium purpureum	SAG 111/79	Hemerick	7	20
Rhodophyceae	*Rhodella violacea*	SAG 115/79	Conway	7	24
	Galdieria sulphuraria[a]	074W	Galdi	2	45
Chlorophyceae	*Chlamydomonas reinhardtii*[a]	PG 27	MMG/TAP	7	24
Haptophyceae	*Isochrysis affinis galbana*	IFREMER	Conway	7	20
Cryptophyceae	*Rhodomonas salina*	ccap 978/24	Conway	7	22
Prasinophyceae	*Tetraselmis suecica*	ccmp 904	Conway	7	20
Dinophyceae	*Heterocapsa triquetra*	IFREMER	ESP	7.8	22

G. sulphuraria source: Institut für biologie, Freie Universität, Berlin.
[a] Fresh water microalgae.

and Dinophyceae) were investigated as natural source of antiproliferative agents in vitro against asynchronous cells of human non-small-cell bronchopulmonary carcinoma line (NSCLC-N6) (Roussakis et al., 1991), human lung epithelial cell line (A549) and against a proliferative human lens epithelial cell line (SRA 01/04). Bio-guided fractionation of the extracts, which appeared as the most active, led us to the isolation of the carotenoid fucoxanthin, which has been also thoroughly assayed. In all cases, the

Table 2
Composition of the different media used for algal culture

Products	Medium				
	Hemerick	Conway	Galdi	MMG/TAP	ESP
$NaNO_3$ (g L^{-1})	1.7	0.1			0.07
$(NH_4)_2SO_4$ (g L^{-1})			1.5		
NH_4Cl (g L^{-1})				0.4	
K_2HPO_4, $3H_2O$ (g L^{-1})	0.175			0.106	
KH_2PO_4 (g L^{-1})	0.175		0.3	0.053	
NaH_2PO_4, H_2O (g L^{-1})		0.02			
$Na_2C_3H_7O_6P$, $5H_2O$ (g L^{-1})					0.01
Na_2SiO_3, $5H_2O$ (g L^{-1})		0.1			
FeEDTA	0.05		0.014		
Na_2EDTA, $2H_2O$ (g L^{-1})	0.049	0.045			0.008
$CaCl_2$, $2H_2O$ (g L^{-1})	1.47		0.02	0.05	
KCl (g L^{-1})	0.75				
$MgSO_4$, $7H_2O$ (g L^{-1})	12.3		0.3	0.1	
$MgSO_4$, H_2O (g L^{-1})					0.00082
NaCl (g L^{-1})	29.0				
Tris (g L^{-1})					0.1
$Co(NO_3)_2$, $6H_2O$ (μg L^{-1})			0.08		
$CoCl_2$, $6H_2O$ (μg L^{-1})		20.0	80	2.927	
$CoSO_4$, $7H_2O$ (μg L^{-1})	0.091				24
$CuSO_4$, $5H_2O$ (μg L^{-1})	0.08	20.0	160	2.855	
$Fe(NH_4)_2(SO_4)_2$, $6H_2O$ (μg L^{-1})					3510
$FeCl_3$, $6H_2O$ (μg L^{-1})		1.3			245
$FeSO_4$, $7H_2O$ (μg L^{-1})				9.073	
H_3BO_3	2.0	33.6	5720	20.73	5700
$MnCL_2$, $4H_2O$ (μg L^{-1})	1.8	0.36	3640	9.2	
$Mo_7O_{24}(NH_4)_6$, $4H_2O$ (μg L^{-1})	20	9.0	260	2.0	
$NaVO_3$, $4H_2O$ (μg L^{-1})			80		
O_5SV, $5H_2O$ (μg L^{-1})	0.043				
$ZnCl_2$ (μg L^{-1})		21			
$ZnSO_4$, $7H_2O$ (μg L^{-1})	0.213		0.44	40	11000
Vitamin B12 (μg L^{-1})		10			2
Thiamin (μg L^{-1})		200			100
Biotin (μg L^{-1})					1
QSP L (μg L^{-1})	FW	MW	FW	FW	MW

Mineral nutrient and their concentration (1×).