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Carotenoids from microalgae to block oxidative stress

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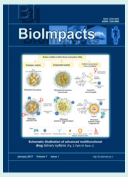

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Summary

Reactive oxygen species (ROS) are produced under normal physiological conditions and involved in several cellular biochemical processes. Their external or endogenous overproduction induces a disruption of redox signaling and control known as oxidative stress. Under oxidative stress, the cell membrane structures, enzyme functions and gene expression are compromised leading to the pathogenesis of several chronic inflammatory diseases including the cardiovascular pathologies. Attempts to find new therapeutic molecules capable of blocking the oxidative stress are of crucial importance.
Owing to their anti-inflammatory and antioxidant properties, carotenoids have been proposed for the prevention and treatment of chronic diseases. In particular, microalgae carotenoids such as astaxanthin and lutein have shown promising results. Due to their protective action, these carotenoids could have a high potential to treat ROS-related pathologies. However, a better understanding of their biological mechanisms of action and the appropriate administration and uses of delivery systems are needed in the prevention and treatment of chronic pathologies.

Author's Biosketch

Professor D. Letourneur, material engineer, PhD in chemistry/biomaterials is research Director at CNRS. He is the Head of the Laboratory for Vascular Translational Science INSERM U1148-University Paris Diderot-University Paris 13 (160 persons), and the President of the French Association for Biomaterials (Biomat) since 2009. As the Director of a multidisciplinary laboratory, Dr. Letourneur is interested in the interface between chemistry, materials engineering, biology, biomedical imaging and cardiovascular research. He has developed several industrial biomedical projects, patent developments, as well as a start-up creation for reparative medicine.

Reactive oxygen species (ROS) are normal products of aerobic metabolism involved in cellular biochemical processes, including: signal transduction, gene expression and transcription and the activation of cell signaling cascades.[1] ROS are reactive chemical species having a single unpaired electron in an outer orbit. The increase of external ROS exposure, the decrease of antioxidant levels and the high ROS endogenous production induce excess levels of ROS, a disruption of redox signaling and control - known as oxidative stress.[2] This state leads to lipid peroxidation, protein oxidation and nitration, and DNA fragmentation that ultimately affect cell membrane structures, enzyme functions and gene expression.

Oxidative stress have widely been implicated in the pathogenesis of many chronic diseases such as cardiovascular pathologies, neurodegenerative pathologies,[3] cancer and age related diseases.[4,5] New therapeutic molecules capable of blocking the oxidative stress are of crucial importance. Because of their anti-inflammatory and antioxidant properties carotenoids have been proposed for the prevention of chronic diseases.[6,7] Epidemiological studies suggest that carotenoids prevent the oxidation of free radical-dependent of LDL, cholesterol, proteins or DNA, by capturing free radicals and by reducing stress induced by ROS.[8]

Carotenoids are fat-soluble pigments. Over 750 structurally defined compounds are present in nature, plants and microorganisms. They are directly accumulated from food or partially modified by metabolic reactions in animals. Carotenoids are divided into two major classes based on their structural elements; carotenes, constituted by carbon and hydrogen (e.g. β-carotene, α-carotene and lycopene), and xanthophylls, constituted

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by carbon, hydrogen, and additionally oxygen (e.g. lutein, b-cryptoxanthin, zeaxanthin, astaxanthin and fucoxanthin).[9] The presence of conjugated double bonds allows carotenoids to accept electrons from reactive species, and then neutralize free radicals.[10] Besides, some carotenoids have been shown not only to have a direct action but also the ability to modulate gene expression of endogenous antioxidant pathways.

Some of strains of microalgae have extensively been studied for their carotenoid production, including: astaxanthin from *Haematococcus pluvialis*, β-carotene from *Dunaliella salina* and Spirulina, zeaxanthin from *Synechocystis* sp., lutein from *Chlorella protothecoides*, etc. Specific advantages in the use of microalgae include simple and fast cultivation, processing and harvesting cycle. However, the existence of a rigid cell walls in some algal species limits the efficiency in recovery of bioactive compounds. This is, therefore, a significant bottleneck in the overall bioprocess materials.[8]

One of the well-known carotenoid is astaxanthin, a natural molecule that shows strong antioxidant activity.[11] Astaxanthin protective action involves an antioxidant mechanism based on the activation of its hydroxyl groups, which results in the formation of an ortho-dihydroxy-conjugate polyene system acting as a chain-breaking antioxidant. This molecule has shown promising results in animals and also in human experiments by the decrease of blood pressure and the increase of HDL rate. A number of studies show that natural astaxanthin extracted from *H. pluvialis* is more active than synthetic one and could present therapeutic properties for the treatment of atherosclerosis and cardiovascular disease.[11,12] Moreover, growing evidences suggest that astaxanthin has potential health-promoting effect in the prevention and treatment of other diseases such metabolic syndrome,[13] skin disease,[14] neurodegenerative pathologies.[15]

Lutein is another prominent carotenoid found in several algae species, i.e. in *Scenedesmus almeriensis*, *Chlorella*, *Chlorella vulgaris*, *Scenedesmus obliquus*, *Dunaliella salina* and *Mougeotia* sp.[16] Lutein has similar physicochemical properties to astaxanthin, and it has been used for applications related to human health such as age-related macular degeneration and cardiovascular diseases. It has been stated that in a typical diet the lutein intake is lower than the daily need, and it is recommended to use a supplement containing lutein.[17-19]

A combination of two or more lipophilic antioxidants could also allow synergistic effects, like the elimination of reactive nitrogen species and inhibition of lipid peroxidation.[6] Natural extracts of carotenoids are a mixture of molecules with higher activities when compared to synthetics ones. Combination of phycocyanin and β-carotene contributed to antioxidant, immunomodulatory, and anti-inflammatory properties of Spirulina,[20] while, the ERK1/2, JNK, p38, and IκB signaling pathways are mediators in its beneficial properties.[21]

Several studies have confirmed the antioxidant and anti-inflammatory properties might attribute to carotenoids. In addition, treatment with carotenoids showed a reduction in markers of oxidative stress and inflammation without adverse effects.[12] Nevertheless, the optimal administration and delivery systems needed to improve carotenoid bioavailability are still under investigation. Since most of the researches carried out have been based on animals and in vitro models, the efficiency of microalgae carotenoids in human remains to be established. Future clinical surveys should focus on large patients cohorts. Besides, it is still needed to improve the understanding of their biological mechanisms of action to determine their efficacy in the potential prevention and treatment of chronic diseases.

Ethical approval
There is none to be declared.

Competing interests
The authors declare no competing interests.

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