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## Algal Research

journal homepage: [www.elsevier.com/locate/algal](http://www.elsevier.com/locate/algal)Insights on the safety of carotenogenic *Chlorella vulgaris* in rodentsCristina de Mello-Sampayo<sup>a</sup>, M. Luisa Corvo<sup>b</sup>, Rogério Mendes<sup>a</sup>, Diana Duarte<sup>c</sup>, Joana Lucas<sup>a</sup>, Rui Pinto<sup>a</sup>, Ana Paula Batista<sup>d,e</sup>, Anabela Raymundo<sup>e</sup>, Beatriz Silva-Lima<sup>a</sup>, Narcisa M. Bandarra<sup>c</sup>, Luisa Gouveia<sup>d,\*</sup><sup>a</sup> Pharmacol. Sci. Group, iMed.UL, Faculdade de Farmácia Universidade de Lisboa, Av. Prof. Gama Pinto, 1649-019 Lisboa, Portugal<sup>b</sup> InTraCell ADD Group, iMed.UL, Faculdade de Farmácia da Universidade de Lisboa, Campus do Lumiar-Estrada do Paço do Lumiar, 22, 1649-038 Lisboa, Portugal<sup>c</sup> Divisão de Aquacultura e Valorização, Instituto Português do Mar e da Atmosfera, Av. Brasília, 1449-006 Lisboa, Portugal<sup>d</sup> LNEG, Unidade Bioenergia, Estrada do Paço do Lumiar, 1649-038 Lisboa, Portugal<sup>e</sup> Núcleo de Investigação em Engenharia Alimentar e Biotecnologia, Instituto Piaget–ISEIT de Almada, Quinta da Arreina de Cima, 2800-305 Almada, Portugal

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## ABSTRACT

*Chlorella vulgaris* (Cv) biomass is widely used as a traditional food in the Orient and its safety for human consumption has been proved. However, carotenogenic biomass (orange), resulting from induced stresses, needs further safety evaluation, which is the aim of this study.

The preliminary toxicological characterization of Cv consisted of a single dose (mice), repeated dose studies (mice and rats) and a biodisposition evaluation (rats).

No mortalities nor relevant clinical signs or behavioural changes were observed in mice or in rats. The carotenoids in the rat faecal matter suggest that the carotenoids contained in Cv have been absorbed through a potentially saturated transport across the intestinal wall. No safety concerns were identified based on clinical signs, biochemical parameters, and liver and spleen histopathology. No significant differences in food/water intake, blood-pressure, blood glucose levels, glucose tolerance and plasticity of erythrocytes were observed over one month with both supplemented and control animals.

The intake of carotenogenic Cv did not reveal any signs of toxicity for doses far exceeding the proposed carotenoid human-diet dose. Therefore these preliminary results suggest that the orange Cv microalgae can be used as a source of carotenoids and could be used for human consumption with possible health benefits.

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## 1. Introduction

Microalgae are able to enhance the nutritional content of conventional food and hence to positively affect human health, due to an almost unlimited, natural source of functional ingredients.

*Chlorella vulgaris* (Cv) has been used in a variety of practical applications in biotechnology and medical science. This microalga has been used as an alternative medicine in the Far East since ancient times and it is known as a traditional food in the Orient [1]. *Chlorella* has been reported to potentially prevent or reduce the impact of several lifestyle-related diseases [2–4] with antiviral (including anti-HIV), antibacterial, anti-tumour properties. *Chlorella* has also been used for infant malnutrition and neurosis [5], as well as food additive. These algae are believed to have a positive effect on the reduction of cardio-circulatory and coronary diseases, atherosclerosis, gastric ulcers, wounds, constipation, anaemia, hypertension, and diabetes [5,6].

In addition to health aspects, *Chlorella* is also important as a source of natural pigments such as carotenoids (powerful antioxidants), and can be used as a natural colouring agent. These carotenoids can accumulate in high concentration in *Chlorella* under certain culture conditions (light

stress, nutrient depletion and high salinity) [7]. The resulting orange coloured biomass can be used as an ingredient in animal feed and human food, with increasing quality and attractiveness, which has already been successfully tested by the authors in many feed and food products [8–13].

The study of carotenoids is of interest not only because of their provitamin A function in some cases, but also because these compounds have been associated to reducing the risk of: (1) certain cancers [14–19], (2) cardiovascular diseases [20–23], and (3) macular degeneration and cataract formation [22,24,25] and possibly may have an effect on immune function and chronic diseases [26–29].

It has also been recognized that carotenoids can be used as antioxidant molecules in health foods. They have the capacity to quench free radicals, thereby protecting cells and tissues from oxidative damage. They are useful in preventing the deterioration of food during processing and storage and also to influence cellular signalling which may trigger sensitive regulatory pathways [30].

It is now recognized that different carotenoids have different functions and they may reduce the impact of certain diseases. The hydrocarbon carotenoids, such as beta-carotene, may be markers to reduce the risk of cancer and heart disease, whereas xanthophylls, such as lutein and zeaxanthin, may be more important for age related macular degeneration and cataract formation [22,24,25]. The most plausible reason for

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