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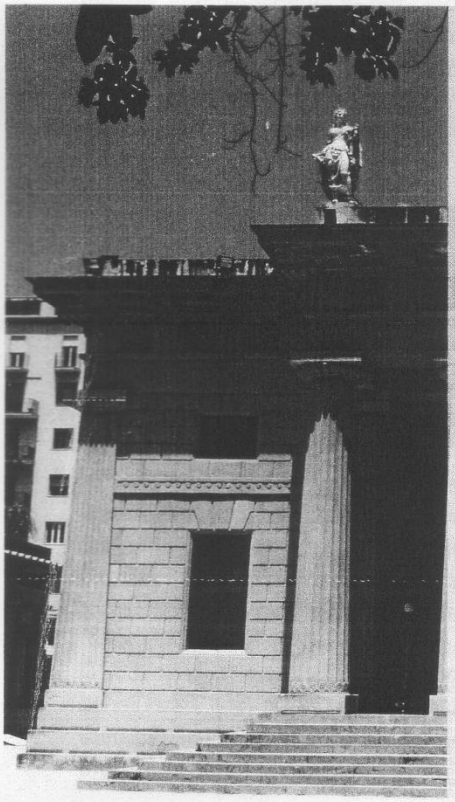

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PHYTOCHEMICAL INDICAXANTHIN PREVENTS 7-ketoCHOLESTEROL-INDUCED OXIDATIVE STRESS AND CELL CYCLE ARREST IN MURINE MACROPHAGES

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Dietary phytochemicals are widely investigated in the field of chemistry, biology, pharmacology and medicine for their potential health-promoting effects. Indeed, many *in vitro* studies provide evidence that a number of these compounds may affect redox-sensitive bio-segnaling cell pathways involved in the pathogenesis of chronic disorders such as cancer and cardiovascular diseases, which could finally contribute to their prevention and/or control.

Characteristic phytochemicals of cactus pear (*Opuntia ficus indica*, L.Mill), the betalain pigments betanin and indicaxanthin, have been the object of our studies for years (1). In particular, reducing properties of indicaxanthin (Ind) have been shown to confer the molecule lipoperoxyl radical-scavenging activity in various either chemical or biological models from liposomes to red blood cells and low density lipoproteins (2-4). The cellular effects of antioxidants do not simply depend on their free radical chain-breaking activity. By virtue of their properties these compounds may effectively help to maintaining the cell redox environment thus preserving cell behavior and function. We have recently found that Ind has remarkable anti-inflammatory effects in cells and *in vivo* (5-7). This work investigated the activity of Ind in murine macrophages submitted to the inflammatory action of 7-ketocholesterol (7K), a major dietary oxysterol suggested to have an active role in the development of the human atherosclerotic plaque (8). Indeed 7K, that accumulates in the plaque, can trigger signaling pathways in macrophages leading to cell inflammation and apoptosis. This, not only prevents the phagocytic cells to get rid of cholesterol and other material at the atherosclerotic lesion, but also contributes to further development of the lesion. Our previous studies showed that indicaxanthin is highly bioavailable in humans, reaching micromolar plasma concentrations after ingestion of eight cactus pear fruits (9). Then, in this work we were able to mimic a pathophysiological environment by using amounts of 7K and Ind known to be present at the plaque and plasma level, respectively. Our results show that indicaxanthin at 1.0 to 2.0 μM dose-dependently inhibits the formation of reactive oxygen species induced by 16 μM 7K, prevents depletion of reduced glutathione, the loss of mitochondrial membrane potential and the arrest of the cell cycle at G0-G1. At the same time, the inhibition of nitrite production provides evidence that Ind also modulates the macrophage inflammatory response.

Discovering the activity of phytochemicals at the level of specific pathways is now considered the basis to suggest either preventive dietary strategies or eventually therapeutic interventions. Our previous and present findings contribute to suggest Ind as a promising nutraceutical compound.

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