SUPPLEMENTAL CAROTENOIDS PREVENT SKIN CANCER BY BENZO(a)PYRENE, BREAST CANCER BY PUVA, AND GASTRIC CANCER BY MNNG. Relevance in human chemoprevention.

L. Santamaria 1, A. Bianchi 2, A. Arnaboldi 1, L. Andreoni 1, G. Santagati 3, C. Ravetto 1, L. Bianchi 1, R. Pizzala 1, P. Bermond 1.

1 C. Golgi Institute of General Pathology, Centro Tumori; 2 Institute of Pharmacology II; 3 Medical Clinic; University of Pavia, 27100 Pavia, Italy. 4 Centre Hospitalier, 51100 Reims, France.

INTRODUCTION

In 1980, the results of an experiment carried out on female mice with the methodology used to show a photoenhancement of benzo(a)pyrene (BP) carcinogenicity, demonstrated that supplemental dietary carotenoids prevent BP skin cancer, both following long UV irradiation and in the dark (29). Such experiment was stimulated by the fact that carotenoids produce a reduction in the UV-B induced sunburn erythema response (14,15) and delay skin tumor induction in hairless mice exposed to UV-B (16).

Since BP must be activated to oxidative derivatives to perform its carcinogenic activity (42), the above results pointed out that the mechanism of carotenoids protection was most probably consistent with their activities as oxyradical scavengers and/or singlet oxygen (O2) quenchers (10), rather than as pro-vitamin A precursors.
Later, in 1984, the same experimental procedure was applied to photocarcinogenesis by 8-methoxypsoralen (8-MOP), a drug used in photochemotherapy, whose photodynamic mechanism is questionable, as far as oxygen requirement is concerned (19,17).

In such experiment, supplemental dietary carotenoids protected female mice against the onset of a mammary carcinoma (32). In vitro investigations on photomutagenesis on Salmonella typhimurium, TA 102 by 8-MOP in the presence of carotenoids, indicated a two-step photoreaction by this drug; namely, an anoxic 8-MOP-DNA photobinding followed by an oxygen dependent enhancement of genotoxicity, which can be prevented by carotenoids (33).

Finally, in 1985, an experimental attempt was completed on gastric carcinogenesis induced in rats by the direct carcinogen N - methyl - N' - nitro - N - nitrosoguanidine (MNNG), to verify whether supplemental carotenoids can affect such carcinogenesis, where neither light excitation nor oxidative metabolic processes were presumably involved. The results demonstrated that supplemental carotenoids did not affect any dysplasia arising from the glandular part of rat gastric mucosa, but dramatically prevented the progression of dysplasias to infiltrating gastric carcinomas (34).

All the above data are presented here in different sections (each one carrying the initials of the responsible authors) with reference to both methodology and results to put forward possible applications in human cancer chemoprevention.