Evaluation of the protective activity of beta-carotene *and l-carnitine on doxorubicin -induced genotoxicity in rats*

(Received: 25.02.2003; Accepted: 02.04.2003)

Aida El-makawy and H.M.EL-Ashmaoui
Cell Biology Department-National Research Center Dokki-Giza,Egypt.

ABSTRACT

Doxorubicin is a potent antitumor agent used worldwide against many forms of human cancers. It has been demonstrated to have the potential for initiating genetic events in non-tumor cells in human and in animal systems. Due to the importance of doxorubicin in chemotherapy for the treatment of many types of cancer, it is important to reduce its toxicity to the normal cells. This goal can be achieved by concurrent administration of free radical scavenging agents, such as antioxidants. Beta-carotene and L-carnitine antioxidants were used to evaluate their ability to reduce the induction of genetic damage (MNPCEs) by the anticancer drug (doxorubicin) in bone marrow cells of male and female rats. Results indicated that the treatment with beta-carotene and L-carnitine concurrently with doxorubicin induced reduction in the frequencies of MNPCEs. No significant difference was recorded between the frequency of MNPCEs in male and in female rats within each group. Treatment of rats with beta carotene did not induce any significant variation in the incidence of MNPCEs as compared to control values, while, L-carnitine induces significant increase in the frequency of MNPCEs when compared to control.Therefore, it is concluded that Beta- carotene and L-carnitine may act as positive modulators of cytotoxic anticancer agents.

Key words: *Doxorubicin - beta-carotene - L-carnitine- MNPCEs -bone marrow cells - rat.*

INTRODUCTION

Antitumor agents are common therapy against many of human cancers. However, as with many agents that have mammalian cell toxicity as a target, physiological side effects can occur, and genotoxic effect rise to secondary tumors (Beretta, 1991). The anthracycline antibiotic adriamycin (doxorubicin) is one of the most effective chemotherapeutic agents against a wide variety of cancers. The tumors that respond better to adriamycin are breast and esophageal carcinomas, asteosarcoma Kaposi's Sarcoma, soft-tissue sarcomas, hodgkin's and non-hodkin's lymphoma. There are other cancers that, despite being less responsive to adriamycin, are still treated with this compound because of its benefitial effects, such as gastric liver, bile-duct, pancreatic and endometrial carcinomas (Quiles *et al.*, 2002).

Doxorubicin induces mutations and chromosome aberrations in normal and tumor cells. The capacity of doxorubicin to inhibit DNA synthesis has been proposed as a mode of action of this drug (Gewirtz, 1999).