

PROTECTIVE ROLE OF PHYTOCHEMICALS ON IMMUNE SYSTEM DERANGEMENT DURING CHEMOTHERAPY: AN EXPERIMENTAL STUDY IN YOUNG AND AGED ANIMALS

*AICR 2010, Annual Research Conference
Food, Nutrition, Physical Activity and Cancer
Washington DC, USA. 21st~ 22nd October 2010*

F. Marotta 1), M. Harada 2), E. Minelli 1), P. Signorelli 3), A. Polimeni 3), U. Solimene 1)
WHO-Cntr for Biotech. & Trad. Medicine, University of Milan, Italy
MCH Hospital, Saitama, Japan
ReGenera Research Group for Aging-Intervention, Milan, Italy

Background:

Aging is associated with immune system impairment which make elderly more vulnerable to cancerous, infectious, inflammatory disease and oxidative stress- related diseases. Anticancer agent cyclophosphamide (CPA) exerts its cytotoxicity through direct damage of DNA and immunocompetence which is likely to be more pronounced in the elderly. The aim of this study was to test the possible beneficial effect of a phytochemical, endowed with antioxidant and immuno-modulating properties, in young and old animals under CPA chemotherapy.

Method:

Young (Y) and aged (A) mice, raised on a standard laboratory diet, were given intraperitoneally, 10 dose of CPA (25mg/kg/bw) or CPA plus 150mg/kg/bw of a quality-controlled phytochemical (DTS: panax pseudo ginseng, *Eucommia ulmoides*, ginseng radix, Kyotsu Jigyo, Tokyo, Japan). After sacrifice, it was determined: macrophage chemotaxis, serum level of IFN- γ , IL-2, GM-CSF and substance P receptor in the bladder by RT-PCR and Western blot analysis. Liver and urinary bladder were examined histologically and the liver and kidney for redox enzymes.

Results:

There was a significant ($p < 0.01$) weight loss in young and aged animals treated with CPA, besides of the liver (24%), kidney (33%), and spleen (61%). However, DTS administration abolished this phenomenon allowing a physiological weight increase in both groups ($p < 0.05$). CPA significantly decreased macrophage chemotaxis and all tested cytokines ($p < 0.05$, A \gg Y). Animals receiving CPA showed moderate-to-severe oedema and marked hemorrhagic damages in the bladder with higher substance-P receptor gene expression than in control ($p < 0.001$). However, these alterations were significantly reduced ($p < 0.05$) by DTS at the same extent in both groups. DTS restored also macrophage function and cytokine concentration ($p < 0.001$) and redox status in liver and kidney ($p < 0.05$).

Conclusion:

Such data suggest that DTS effectively prevents CPA-induced immune suppression and oxidative-inflammatory damage which were particularly enhanced in aged organisms, thus envisaging an integrative approach in chemotherapeutic strategies especially in old organisms.

Keywords: Cyclophosphamide, oxidative stress, immune-modulation, phytochemicals