EFFECT OF PHENOLIC ANTIOXIDANTS AND METHYLCHOLANTHRENE ON BENZO(A)PYRENE METABOLISM, GENOTOXICITY IN SOS CHROMOTEST AND ITS METABOLITES BINDING TO BACTERIAL DNA

E.Hennig, K.Dobrzański and A.Bębenek

Medical Academy, 01-097 Warsaw, Poland

The effect of buytylated hydroxanisole (BHA), butylated hydroxytoluene (BHT) and 3-methylcholanthrene (MC) on BP metabolism, genotoxicity and its metabolites binding to bacterial DNA was studied using, for activation BP, S9 fractions from the liver of mice fed diet containing BHA or BHT or mice injected i.p. with MC. BHA, BHT and MC-treatment elevated the total BP metabolism. Estimation of the distributions of organic and water soluble products indicated a marked increase of water soluble BP-metabolites formed in the presence of S9 fractions from antioxidant-fed mice. BP genotoxicity was checked in bacterial test SOS Chromotest. Findings from these experiments indicated strong inhibition of BP genotoxicity when the S9 fraction from BHT-fed mice was used for its activation. BHA had only a moderate, but not significant inhibitory effect on BP genotoxicity. The study hs shown that these results were clearly correlated with the effect of antioxidants and MC on BP metabolite binding to bacterial DNA

EXPERIMENTAL LOCAL CHEMOTHERAPY IN BONE TUMOURS

Ph.Hernigou(1), J.P.Thiery(2), J.Benoit(3) M.C.Voisin(1), G.Hagege(4), G.Delepine(1) and D.Goutallier(1)

(1)Hôpital Henri Mondor, 94010 Cretail; (2)Institut Curie, Paris; (3)Pharmacie Galienique Chatenay Malabry; and (4)École Veterinaire, France.

Cement is often used in the treatment of bone tumours. The effects of local chemotherapy produced by adding an antimitotic drug to the acrylic cement have been analysed in the present investigation. Diffusion of methotrexate (MTX) from cement loaded with MTX was studied in vitro; its liberation begins immediately and continues for as long as 3 months. 14 osteosarcomas of dogs were operated and bone loss created by the excision of the tumour was filled with cement containing MTX: this local administration produced a general chemotherapy during 3 to 5 days and seems to reduce local recurrence of the tumour. The effectiveness was tested on 107 rat experimental osteosarcomas (pellets were introduced in the tumour). By the tumour growth and on histological examination, the effectiveness of such a method was confirmed. Pharmacological data, collected from patients who received cement with MTX during surgical treatment have identified the high concentration of MTX in the tumour drainage indicative of the general chemotherapeutic effect during the first days after treatment.

EXPRESSION OF THE N-myc PROTOONCOGENE IN HUMAN FOETAL BRAIN, RETINA AND KIDNEY

H.E.Hirvonen(1), M.M.Sandberg(2), H.Kalimo(3), V.I.Hukkanen(1), E.I.Vuorio(2) and K.Alitalo(4)

Department of (1)Virology, (2)Medical Chemistry and (3)Pathology, University of Turku, Turku, Finland, and (4)Department of Virology, Universty of Helsinki, Helsinki, Finland

The myc family of cellular proto-oncogenes consists of three known members, that are believed to regulate cell growth and differentiation. In embryonic and foetal tissues, distinct tissue and stage specific expression patterns of the myc family genes are observed. This suggests that the differential expression of the myc genes may have a key role in regulating multiple differentiation pathways.

The N-myc gene codes for a nuclear phosphoprotein of yet unknown function. It is expressed mainly in cells of neural origin, but during foetal development also in a variety of other tissues. High expression levels are found also in various tumours displaying neuroectodermal characteristics, such as neuroblastomas, retinoblastomas and in small cell lung carcinomas. Amplifications of the gene have also been found in these malignancies.

We analysed the expression of N-myc in human foetal brain, retina and kidney at 16 to 19 gestational weeks by Northern blotting and by in situ hybridization. By Northern blotting, we found expression of the N-myc gene to be 4 to 10 fold higher in the brain than in the kidney. The in situ hybridizations showed the expression to be rather generalized in the brain, though highest in the ependymal zone where the proliferation of the neuroepithelial cells takes place. The gene was also expressed in neuroblasts already located in the cortex, as well as in cells still migrating there. In the kidney, N-myc mRNA was localised in developing glomeruli and tubular walls. In the retina, N-myc was expressed at high levels in all the retinal cell layers. We conclude that expression of N-myc foetal tissues is