RETINOIDS AND CHEMICALLY INDUCED LUNG TUMOURS

P.A. BAGHURST and W. B. LUDERER

The compound 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone or nicotine-derived nitrosamino ketone (NNK) is the most potent tobacco-specific carcinogenic nitrosamine known. Regardless of the route of administration, it induces lung tumours in all species tested, and pancreas tumours in the rat. This would suggest that NNK may be involved in the induction of lung cancer in smokers (Hecht and Hoffman, 1988).

A number of epidemiologic studies have suggested that vitamin A and its precursors (eg β-carotene) or metabolites (eg retinoic acid) may confer a degree of protection against lung cancer.

To test the hypothesis that retinoids may reduce the tumour burden induced by NNK in A/J mice, 61 six-week-old female animals were allocated to one of four groups:- (1) Normal laboratory chow; (2) chow + β-carotene beadlets (10g/kg chow); (3) chow + *cis*-retinoic acid beadlets (200mg/kg chow); (4) chow + placebo beadlets. After two weeks on the allocated diet each animal was given a single dose of 10μmoles of NNK by intraperitoneal injection and then maintained on that diet for a further sixteen weeks after which it was sacrificed, and the lungs excised in order to count the number of pulmonary adenomas.

NNK induced tumours in all animals except one receiving retinoic acid. Assuming tumour counts to have a Poisson distribution, there were statistically significant differences among the tumour burdens recorded for the treatment groups ($\chi^2_3 = 10.9$, $p = 0.012$). The average number of tumours per animal was highest in the control group, 25% lower in the β-carotene group, and 37% lower in the retinoic acid group. However the group receiving only the stabiliser medium used in the preparation of the retinoic acid beadlets showed a similar reduction in tumour burden (35%), throwing doubt on which component of the retinoic acid beadlets was responsible for their apparently protective effect.

Treatment	n	tumours (±se) per mouse
Laboratory chow	15	6.7±0.67
Chow + β-carotene beadlets	16	5.1±0.56
Chow + *cis*-retinoic acid beadlets	14	4.2±0.55
Chow + beadlet-stabilizer	15	4.4±0.54

The antioxidants butylated hydroxyanisole, butylated hydroxytoluene and ascorbyl palmitate were included in the beadlet formulations to stabilize the β-carotene and *cis*-retinoic acid - and further work will be required to determine which of these has tumour-suppressive activity.

HECHT, S.S. and HOFFMAN D. (1988). Carcinogenesis 9: 875.

Division of Human Nutrition, CSIRO, Adelaide, South Australia 5000