

Materials and methods

Chemicals. Practical grade BP (approximately 98% purity) was obtained from Sigma Chemical Company, St. Louis, Missouri.

Animals and diets. Female A/HeJ mice (ages 7, 6 and 5 weeks) were purchased from Jackson Laboratory, Bar Harbor, Maine. They were housed in plastic cages (5 mice per cage) and fed on Formulab Chow 5008 (Ralston Purina Company, St. Louis, Missouri) *ad libitum* until each batch attained 9 weeks of age. At 9 weeks of age, each batch was weighed, randomized and divided into two groups: one group as BP control and the other as test group. The control group was continued on stock pellets while the test group was switched over to food containing 1% AA10 (w/w), prepared from the same pellets used for the control animals. The test group continued to receive AA10 in the diet for the entire period of the experiment.

Tumour induction. Each animal was given 3 mg of BP in 0.25 ml of corn oil through an intragastric tube on the 8th day (10 weeks of age) and 22nd day (12 weeks of age) following the beginning of AA10 feeding. This dosing regimen was shown to yield over 95% incidence of lung tumour in control animals after 18 weeks (14).

Tumour determination. Animals were sacrificed 157 days later (from the initial dose of BP) and the lungs were removed and placed in Telleysniczky's acetic bichromatic solution for two days and examined grossly (15). Lung tumours appeared as pearly white nodules, while the normal tissue was stained darker. The relative susceptibility to BP-induced tumours is expressed by the "Tumorigenic Index" proposed by Shimkin (16). The type of tumour was confirmed by histopathological examination.

Statistical analysis. All data in this study were statistically analysed by Student's t-test.

Results

The effect of AA10 on pulmonary adenoma formation by acute exposure to BP is summarized in Table I. One per cent of AA10, fed in the diet for one week prior to the challenge of carcinogen and continued thereafter, resulted in a 70% reduction in the total number of pulmonary adenoma in A/HeJ mice. In this instance all the tumours irrespective of size were counted.

Weight gain occurred in each group during the period of experiment as depicted in Table II. The weight gain in batches 2 and 3 of the AA10 group is smaller when compared to the corresponding batches of the controls. The overall weight difference is not statistically significant. In fact, there was no significant weight difference between the test and the control groups at any given time during the test period.

Microscopically the lungs showed pulmonary tumours with typical histopathology characteristics of pulmonary adenomas as described previously in similar experiments (16, 17).

Discussion

The findings in the present study demonstrate that AA10 fed in the diet for one week prior to the challenge of BP and continued thereafter will inhibit pulmonary adenoma formation. A possible mechanism of protective action of AA10 may include binding to DNA.

AA10 and BP are small molecules of size and shape similar to a DNA base pair (11). The complexes of BP with DNA have already been isolated (18). It was proved in our previous studies that AA10 specifically interacts with DNA and had the greatest effect on poly(dA-dG) · poly(dC-dT) (19-21). It has been postulated, therefore, that AA10 may compete with BP and exert its chemopreventive effect this way (11).

Associated risks are the main consideration for