

Discussion

A considerably higher percentage of animals in the control group had multiple and advanced neoplastic lesions, suggesting the multifocal origin and early onset of tumours in this group. On the other hand, a majority of the animals in the test group had only single, discrete and small tumours even after continuing the experiment for a long duration. The absence of multiple tumours in the A10-fed group indicates a significant inhibitory action at the early stage of carcinogenesis and the absence of advanced lesions is a sign of slow tumour formation or a late onset induced by A10. These results prove that the inhibitory effect of A10 on hepatic tumourigenesis induced by AFB₁ in Fischer rats is remarkable.

The mechanism of action may be related to the interaction of A10 with DNA (35, 36). A10 appears to fit stereospecifically between base pairs at several sites in DNA. This interaction is weak and readily reversible, unlike the case of many known intercalating carcinogens (37). It has been postulated, therefore, that A10 may compete with AFB₁ and exert its chemopreventive action in this manner (18).

In this experiment, an increased frequency of testicular interstitial cell tumours was seen in rats fed on A10. Development of Leydig cell tumours is an age-related strain-specific natural phenomenon in Fischer rats (38–40). Hence, it should be assumed that A10 had some action on Leydig cells of this strain leading to an early onset of tumours. Chronic exposure to oestrogens and cryptorchidism, which produce Leydig cell tumours in mice (41, 42), have an opposite effect in Fischer rats (43). This indicates that the tumourigenesis in Leydig cells of Fischer rats has a different biochemical mechanism. So it is probable that this side-effect of A10 is also a strain-specific phenomenon. Since A10 is not a natural constituent of the rat (44), some form of adverse reaction may be anticipated in some strains on prolonged admin-

istration. In any case, this phenomenon will be closely studied in a number of species of animals in the future.

The weight gain for A10-fed animals was found to be less, during the AFB₁ dosing and immediate post-dosing period, than with animals in the control group (Group 2). After that period, both the groups had more or less equal weight gains. The difference in weight between the two groups was not statistically significant at any stage of the experiment. Chronic toxicity studies did not reveal a decrease of weight gain in animals fed A10 compared to the controls (34). Furthermore, a comparison of average weights in tumour-bearing and non-tumour-bearing rats in the A10 group showed no difference. Hence, it should be understood that, under the present experimental conditions, the reduced weight in the A10 group was not an important determining factor for decrease in tumours in that group.

Chemoprevention or anticarcinogenesis has become a popular strategy in the combat against cancer (45). Associated risks are the main hindrance for accepting any agent for chemoprevention since these agents have to be administered for a long duration to be effective (46). In this regard, A10 appears to be a promising agent for intensive research due to its wide spectrum of antitumour action, effectiveness as a therapeutic agent, and low toxicity.

References

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