

PROTECTIVE EFFECT OF ANTINEOPLASTON A10 IN HEPATOCARCINOGENESIS INDUCED BY AFLATOXIN B₁

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Summary: Antineoplaston A10 (A10; 3-phenylacetyl-amino-2,6-piperidinedione) has shown a significant modulating effect on pulmonary neoplasia induced by benzo(a)pyrene and urethan, and spontaneous mammary tumour development in the mouse. The purpose of this study was to investigate the applicability of A10 against aflatoxin B₁ (AFB₁)-induced hepatocarcinogenesis. Hepatic neoplasms were induced in male Fischer rats by intragastric administration of AFB₁ at a dose of 25 µg/day for 5 days a week over a period of 8 weeks (total dose 1 mg/rat). This regimen induced an average of 5.84 ± 1.35 macroscopic tumours over a period of 66 weeks. One percent A10; (w/w) given in food 1 week prior to the administration of AFB₁ and continued for 66 weeks reduced the tumour incidence to an average of 0.67 ± 0.53 ($p < 0.001$) in the test group. The relative average weight of the liver in the A10-fed group (4.34 ± 0.35/100 g body weight) was significantly less than that of the control (5.59 ± 0.71/100 g body weight).

Introduction

Aflatoxin B₁ (AFB₁), a pernicious fungal metabolite elaborated by some strains of the saprophytic fungi *Aspergillus flavus*, is the most potent hepatocarcinogen known (1, 2). This virulent hepatotoxin is known to produce neoplasms of various organs in many animal species under experimental conditions (3-7). There is ample evidence to incriminate this mycotoxin as a causative agent of human neoplasms as well, especially primary hepatocellular carcinoma, which occurs at an increased incidence in certain parts of the world where contamination of food with AFB₁ is rampant (8-15). The high risk of human contact with this carcinogen is due to the ubiquitous nature of the fungi that grow on a wide variety of foodstuffs under warm humid conditions,

and AFB₁, being relatively heat stable, is not destroyed by many of the cooking methods (8, 16). So it seems prudent to investigate the applicability of known anticarcinogenic substances like Antineoplaston A10 (A10) against the carcinogenic processes induced by aflatoxin.

A10 (3-phenylacetyl-amino-2,6-piperidinedione), originally isolated from human urine and reproduced by synthesis (17, 18), is a dehydration product of phenylacetylglutamine which is formed *in vivo* by conjugation of phenylacetic acid and L-glutamine (19). It has shown a significant modulating effect on pulmonary neoplasia induced by benzo(a)pyrene (20) and urethan (21), and spontaneous mammary tumour development in the mouse (22). A₁₀ is also remarkable for its trivial toxicity and its effectiveness as a therapeutic agent (23). In view of the interesting results