SUSCEPTIBILITY OF RATS TO PALMOTOXINS B_0 AND G_0

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1. Introduction

The various isolates of *Aspergillus flavus* have been shown to differ remarkably in their toxicity to different species of animals [1]. However, aflatoxin B_1 has been recognized as the most potent of the hitherto isolated metabolites of *Aspergillus flavus*. Palmotoxins B_0 and G_0 represent a group of new isolates from *Aspergillus flavus* grown on palm sap [2]. Their toxicities have been assessed only on chick embryos and have been shown to induce death, liver lesions and other morphological changes in chick embryos similar to those of aflatoxin B_1, [3–5]. Possible toxic effects of palmotoxins B_0 and G_0 on mammalian species are yet unknown. The present paper reports the effects, in small doses, of these toxins on young rats.

2. Materials and methods

Methods applied for the assessment of toxicity were similar to those of Chang et al. [6] and Rao and Ghering [7] and involved determination of loss in body weight due to administration of the toxins; reduction in liver size and changes in some serum enzyme activities. 20 day-old male rats (Wistar strain) 31–31.5 g body wt. were selected from litter mates and arranged into five groups of five animals each. Animals were housed in cages and supplied with food and water 'ad. libitum'. They were starved overnight prior to the initial administration of the toxins. Each animal in the first group received a dosage of palmotoxins B_0 and G_0, respectively, corresponding to 1.6 mg/kg body wt. (50 μg); the second and third groups each received 3.2 mg/kg body wt. (100 μg) and 6.4 mg/kg body wt. (200 μg) respectively. The fourth group received 0.5 mg/kg body wt. (15 μg) of aflatoxin B_1 while the fifth group served as control being administered with propylene glycol – the carrier solvent only. Injections were administered intraperitoneally every morning for 15 days. Weights of the animals were taken on alternate days in most cases. Animals were sacrificed one hour after the last injection. Blood from each group was pooled in centrifuge tubes cooled to about 4°C in an ice–water mixture. Serum was obtained immediately, from the blood by centrifugation. Serum alkaline phosphatase activity was determined by the method of Bessey et al. [8], serum glutamic oxaloacetic acid transaminase (SGOT) activity was determined by the method of Reitman and Frankel [9]. Sections of the excised livers of the respective rats were prepared, stained with haematoxylin and eosin, and subjected to histological studies.

3. Results

Rats treated with palmotoxin B_0 showed a consistent loss in weight with respect to the control. This response varied with the dosage. (fig. 1). However palmotoxin G_0 treated animals did not exhibit any significant loss in total body weight with respect to control, although lower mean weights were consistently recorded for the group of animals dosed with 200 μg of palmotoxins G_0. Palmotoxin B_0 and aflatoxin B_1 treated rats showed a reduction in their respective liver sizes in relation to the total body weight (table 1). Palmotoxin

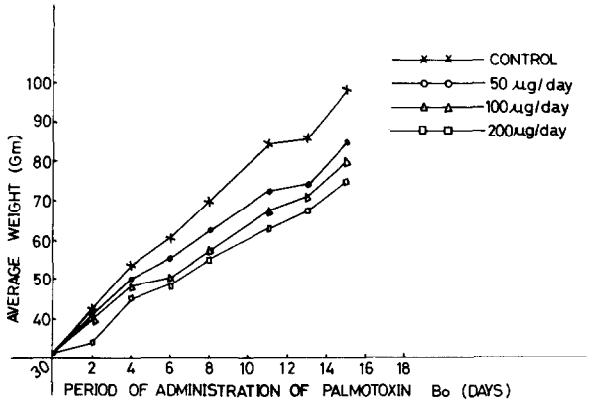

Fig. 1. Effect of administration of palmotoxin Bo on the body weight of 20 day old rats (Wistar strain).

Table 1
Relationship between liver weights and body weights of the palmotoxin B_0 treated rats

Dose/rat/day	(Average) initial weight of rats (g)	(Average) final weight (g)	Liver weight (g)	% age liver wt/ body wt
Control	31.5 ± 0.5	98.0 ± 1.0	5.0	5.1
50 µg	31.8 ± 0.4	85.0 ± 0.7	4.1	4.8
100 µg	31.5 ± 0.4	81.0 ± 0.5	3.16	3.9
200 µg	31.5 ± 0.5	75.0 ± 0.4	2.6	3.4
15 µg Aflatoxin B_1	31.4 ± 0.3	84.0 ± 1.0	3.83	4.5

G_0 treated rats did not show any reduction in liver sizes when compared with the control. No deaths were recorded throughout the period of study. Examination of liver sections from palmotoxin G_0 treated animals, did not reveal any marked pathological changes when compared with the control. Aflatoxin B_1 and palmotoxin B_0 treated rats showed a peripheral necrosis of the liver cells. Table 2 shows the serum alkaline phosphatase activity and serum glutamic oxaloacetic acid transaminase activity for both palmotoxin B_0 and G_0 treated rats. Values for aflatoxin B_1 treated animals under the same experimental conditions have been included for comparison. Palmotoxin B_0 treated rats showed a remarkable increase in the glutamic oxaloacetic acid transaminase activity over the control. Increase in alkaline phosphatase activity for this group was not very significant. Alterations in the activity of these enzymes were not significant in palmotoxin G_0 treated groups. The values are compared with those of both the control and the aflatoxin B_1 treated animals.

4. Discussion

The results obtained indicate that palmotoxin B_0 might induce toxicity syndromes in mammals in a similar manner as aflatoxin B_1. Palmotoxin G_0 does not appear to exhibit similar potency at the dose levels studied. Increase in the activities of serum glutamic oxaloacetic acid transaminase and alkaline

Table 2
Glutamic oxaloacetic acid transaminase and alkaline phosphatase activity in the serum of rats treated with palmotoxin B_0 and G_0 and aflatoxin B_1

	Palmotoxin B_0 treated rats		Palmotoxin G_0 treated rats	
Dose/rat	GOT level (international units/litre)	Alkaline phosphatase level (Mu)*	GOT level (international units/litre)	Alkaline phosphatase level (Mu)
Control	12.5 ± 1.0	204.0 ± 3.0	12.4 ± 0.5	203.0 ± 3.0
50 µg	19.0 ± 1.5	214.0 ± 2.0	11.9 ± 1.0	205.0 ± 2.5
100 µg	24.5 ± 0.5	226.0 ± 1.5	12.5 ± 1.0	204.0 ± 2.6
200 µg	33.0 ± 3.5	230.0 ± 1.0	13.0 ± 1.5	206.0 ± 3.0
15 µg Aflatoxin	26.0 ± 2.5	215 ± 1.6	26.0 ± 2.0	215.0 ± 1.5

* Mu = milliunits = 0.06 mole units (Bessey et al., 1949).

phosphatase are indicative of the onset of necrosis of hepatic cell and myocardial infarction [8–10]. Barnes [11] has given the LD_{50} of aflatoxin B_1 for 21-day old male rats as 5.5 mg/kg body wt. The fact that no deaths were recorded for palmotoxins B_0 and G_0 even at a dose of 6.4 mg/kg body wt. is indicative of the fact that the toxins might not be of comparable potency with aflatoxin B_1. However evidence is obtained to show that palmotoxin G_0 is less toxic than palmotoxin B_0 in the rat and this is in line with previous reports from Bassir and Adekunle [3]. Barnes and Butler [12] and Barnes [11], have demonstrated a slow onset of carcinogenesis in the rat arising from aflatoxin B_1 poisoning. The inextensive morphological changes observed with the palmotoxins might be in conformity with the observed delayed onset of carcinogenesis in the rat and mice.

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