EFFECT OF ETHANOL PRETREATMENT ON HEPATOTOXICITY AND FAT ACCUMULATION INDUCED BY AFLATOXIN B₁ IN THE RAT

BY

PANTIP LOHAKACHONPAN

A THESIS SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF SCIENCE (TOXICOLOGY)

IN THE

FACULTY OF GRADUATE STUDIES OF MAHIDOL UNIVERSITY

1986
EFFECT OF ETHANOL PRETREATMENT ON HEPATOTOXICITY AND FAT ACCUMULATION INDUCED BY AFLATOXIN B₁ IN THE RAT

PANTIP LOHAKACHONPAN

Toxicology Program, Department of Physiology, Faculty of Science, Mahidol University, Rama VI Road, Bangkok 10400

ABSTRACT

Effect of ethanol pretreatment on aflatoxin B₁-induced necrosis, fat accumulation and glycogen depletion in liver of rats was investigated. Adult rats were pretreated with four oral doses of ethanol (4.0 g/kg) at 48, 45, 24 and 21 hours prior to a single i.p. administration of aflatoxin B₁ (2.0 mg/kg). Ethanol pretreatment enhanced severity of aflatoxin B₁-induced hepatic necrosis as shown by an increase in the activities of plasma glutamic pyruvic transaminase (PGPT) (P < 0.001) and plasma glutamic oxaloacetic transaminase (PGOT) (P < 0.001) at 72 hours after aflatoxin B₁ administration. It also had an enhanced effect on the accumulation of liver triglycerides (P < 0.001) and had an additive effect on liver cholesterol (P < 0.05) and cholesterol esters (P < 0.01). In time-course study, it was shown that hepatic necrosis, triglycerides, cholesterol and cholesterol esters occurred simultaneously in both groups of rat treated with aflatoxin B₁ alone and ethanol and aflatoxin B₁. These toxicological parameters were gradually increased to 36 hours and sharply increased to maximum response at 48 and 72 hours after aflatoxin B₁ administration. It seems that fat accumulation in liver induced by aflatoxin B₁ and ethanol and aflatoxin B₁ is probably not the possible causative factor of hepatic necrosis. Another important factor, hepatic glycogen as energy source was
also depleted by ethanol pretreatment (P < 0.05) at 48 hours after afla-
toxin B₁ administration. The reduction in energy source of liver cell
is suspected to interfere with cell volume regulation which would lead
to cell swollen. It is likely that ethanol pretreatment might enhance
aflatoxin B₁-induced hepatic necrosis by lowering cell capability to
perform volume regulation.