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STUDIES ON GRISEOFULVIN: PART-II EFFECTS ON THE LIVER AND KIDNEY OF ALBINO RAT

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ABSTRACT

Studies were performed on albino rats to investigate any untoward effects of griseofulvin on their liver and kidneys. Animals weighing between 200-250g were selected and divided into control and test groups. Griseofulvin was ad-ministered to the test groups at a dose level of 20 mg/Kg/day for 2, 4 6 and 8 weeks respectively. Animals wee sacrificed at the end of their respective study periods for collection of blood and removal of the liver and kidneys. Histopathological examination of the liver and kidneys of the treated animals at the end of 4 and 8 weeks of griseofulvin administration showed no cytotoxic changes. It was, therefore, concluded that griseofulvin has no hepatotoxic effects in albino rats at a dose level of 20 mg/Kg/day.

Introduction

Griseofulvin is wisely used in treating fungal infections in local population. There are reports of some side effects of this drug like nausea, diarrhea, anorexia, vomiting, abdominal cramps, dizziness, drowsiness, insomnia, fatigue, confusion, depression, irritability, head ache etc., in patients taking the drug (Nater & Groot, 1983; Goodman & Gilman, 1991). In mice, administration of griseofulvin led to protoporphyrin deposition in the liver causing liver cirrohosis and development of hepatomata (Hurst & Paget, 1963). It has also been shown to act as a co-carcinogen to methyl cholenthrene in mice. Thus tumours developed more rapidly when both the drugs were given simultaneously (Barish *et al*, 1962). Mitchel *et al*, in 1973, noted irnmuno-suppressive effect of griseofulvin in mice and rats leading subsequently to formation of tumours in the liver. Paget and Alcock (1960), found no evidence of carcinogenic action of either griseofulvin or colchicine in rats when administered with 500µg compound/Kg body weight. Paget and Walpole (1960), observed colchicine-like effects in the rats after intra-venous and intra-peritoneal administration of griseofulvin in large doses. These effects were noted in testes, bone marrow and intestinal walls. In view of these diverse reports, it was decided to investigate the effect of the therapeutically effective dose of griseofulvin on the liver and kidney of albino rats.

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Material and Methods

Fifty albino rats weighting between 200-250 g were divided into five groups, each containing ten animals. The animals had free access to feed and water. One group served as control while the other four groups A, B, C and D, received a daily oral dose of griseofulvin equal to 20 mg/Kg/day by stomach tube for 2, 4, 6 and 8 weeks duration respectively. The animals were observed for the manifestation of any aberrant behaviour during the drug administration period. Blood was collected from the animals by d[i]rect cardiac puncture after which they were autopised and the[i]r vital organs were examined for any gross changes. The[i]r livers and kidneys were removed and fixed in *10%* formalin. After dehydration and dealcoholization, the tissues were embedded in paraffin wax. Sections, 5 µg in thickness, were cut and stained with Ham's hacmatoxylin and eosin. The sections were then examined under light microscope and photographed.

Results and Discussion

Animals were observed during the drug administration period of 4 to 8 weeks. Throughout this period, the animals behaved normally and did not show any signs of discomfort or aberrant behaviour. No gross change in the vital organs like heart, lungs, liver, kidneys and GMT was observed in the drug-treated rats. Ovaries, uterus and testes were also without any noticeable abnormality. Liver and kidneys were examined in detail. There was no congestion or abnormality in colour.

Microscopic examination of the liver sections of the treated rats did not manifest any change in the morphology or the cellular structure as compared with the normal controls. Thus, the bile duct, central vein, hepatic artery, portal vein and the hepatic cells under the microscope appeared perfectly normal in shape Figs. A, C, and E. Similarly, microscopic examination of the kidney sections of the treated rats showed no change in the morphology and cellular structure and there was no infiltration with polymorphonuclear leukocytes or extravasation of erythrocytes in the cortical and medullary regions of the kidney Figs. B, D and F. Paget and Walpole (1960), have reported no histological abnormality in the liver and kidneys of the griseofulvin treated rats. On the other hand, Hurst and Paget (1963), have reported the formation of hepatomata in the mice treated with griseofulvin. Enlargement of livers and histopathological changes in the liver after prolonged administration of griseofulvin has also been reported (Demattis *et al*, 1966). Epstein et al, 1967, observed hepatocarcinogenecity in infant mice after parenteral administration of griseofulvin. In another report by Rustia and Shubic (1978), griseofulvin treatment was found to cause hepatic cell tumours in mice and thyroid tumours in rats. Thus, it becomes evident that there is a great deal of variation in the manifestation of untoward effects of this drug depend*ing on varied* factors like size of the dosage, duration of treatment, absorption of the drug, as well as, the metabolism and the excretion of the drug. Our studies have shown that a dose level of 20 mg/Kg/day, griseofulvin administered orally produces no un-

toward effects in rats, and therefore, should be safe for use at this level as a therapeutic agent.

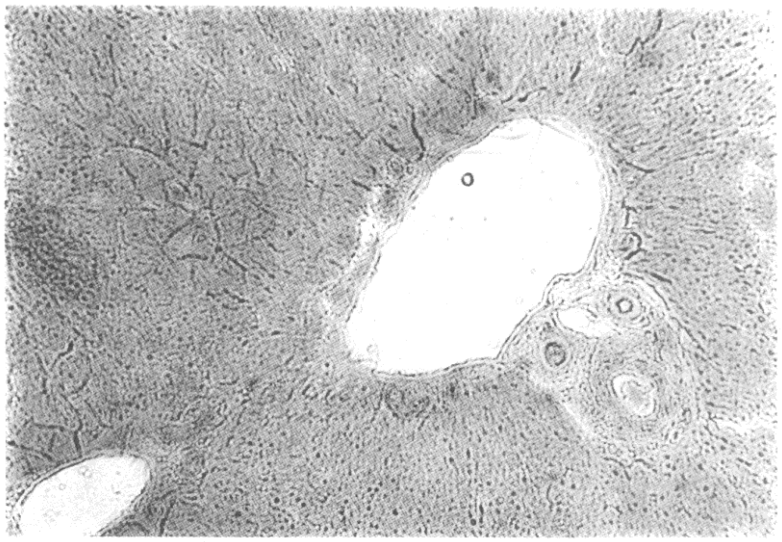

Fig. A: Normal liver tissue showing bile duct and central vein.

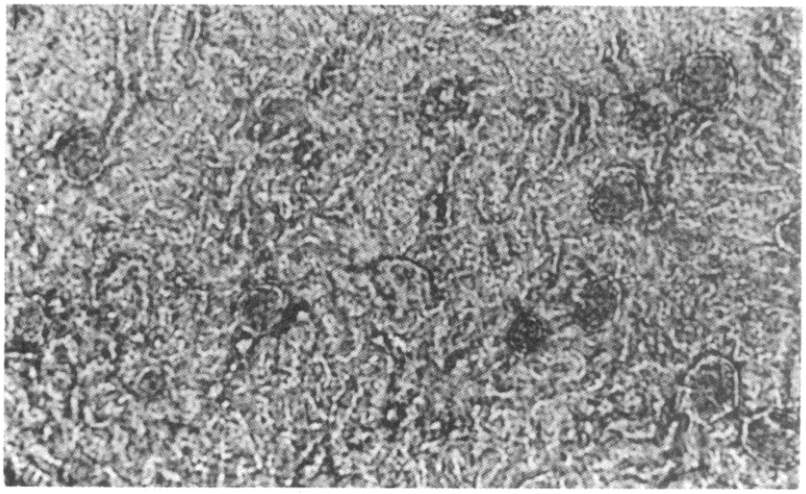

Fig. B: Normal kidney tissue showing Bowman's capsule and medullary rays.

GRISEOFULVIN TREATMENT

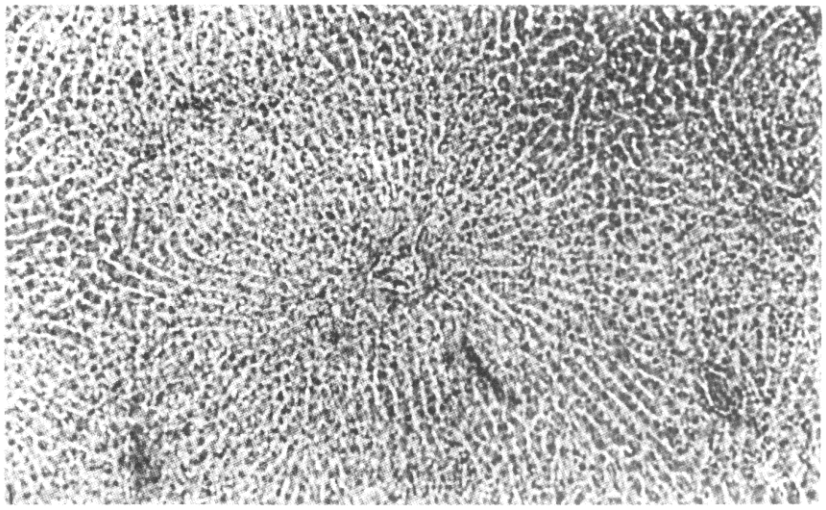

Fig. C: Liver tissue after 4 weeks treatment.
Central vein and hepatic cells are normal.

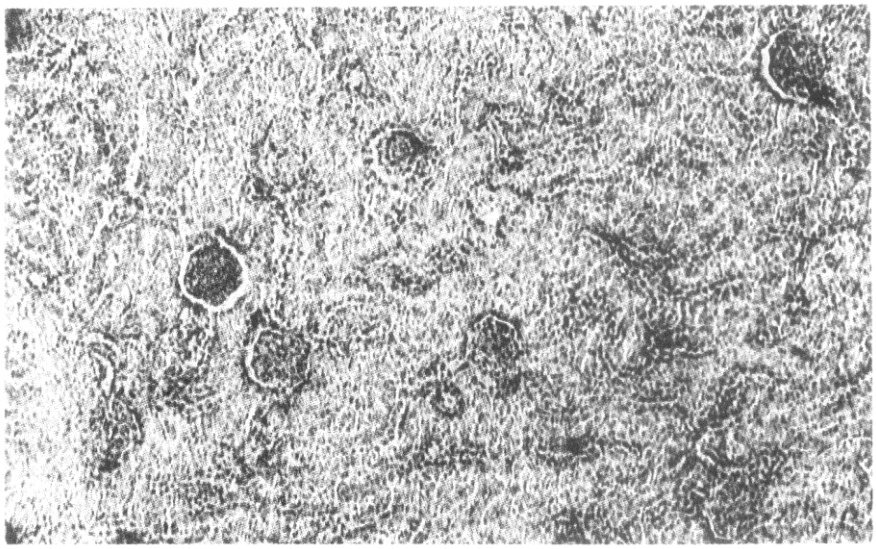

Fig. D: Kidney tissue after 4 weeks treatment.
Bowman's capsules and medullary rays normal.

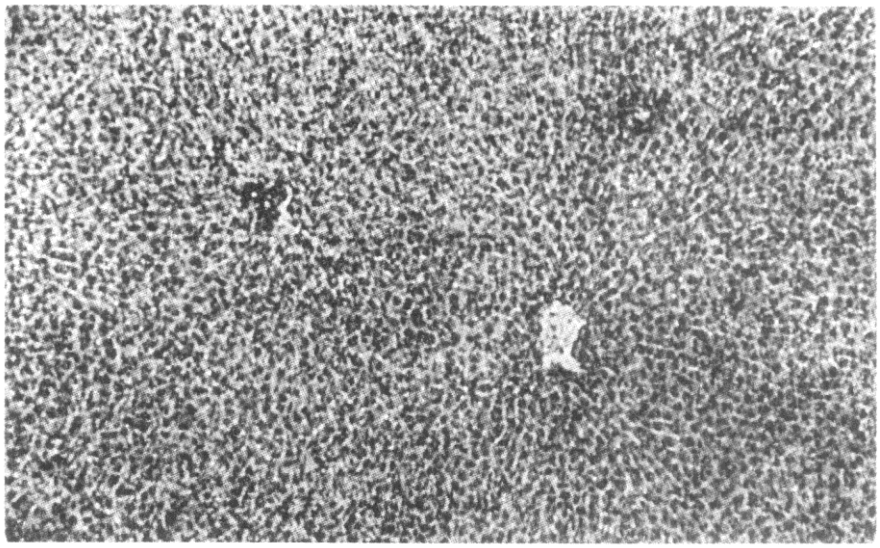

Fig. E: Liver tissue after 8 weeks treatment.
Central vein and hepatic cells are normal.

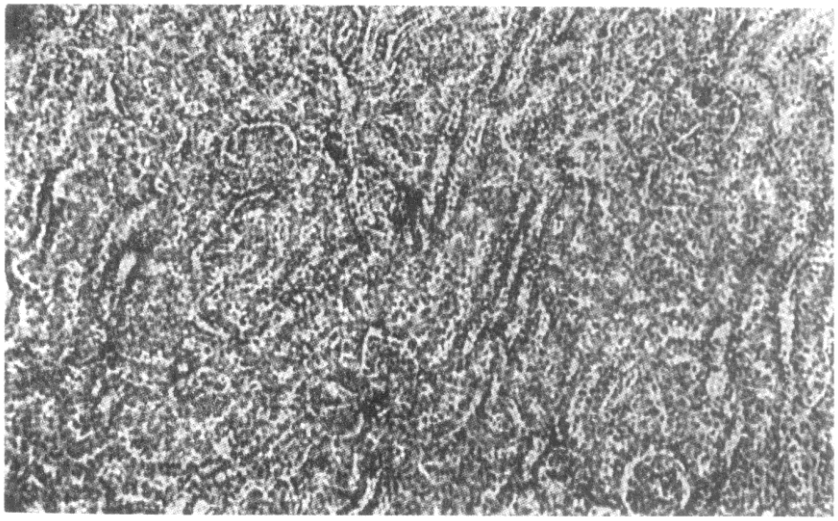

Fig. F: Kidney tissue after 8 weeks treatment.
Bowman's capsules and medullary rays normal.

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