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# Toxicological Impacts of Benzophenone on the Liver of Guinea Pig (*Cavia porcellus*)

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Benzophenone, a benzene derivative diphenyl ketone is widely used in perfumery industries for its persistant rose like odor ( Bahl and Bahl 1980; Sax 1958 ). This chemical has not been investigated for its possible toxic effects in living organisms. The present study was undertaken to determine the effects of benzophenone on the liver of guinea pig. The assessment was made on the basis of alterations in the gross, microscopic and histochemical levels of liver.

## MATERIALS AND METHODS

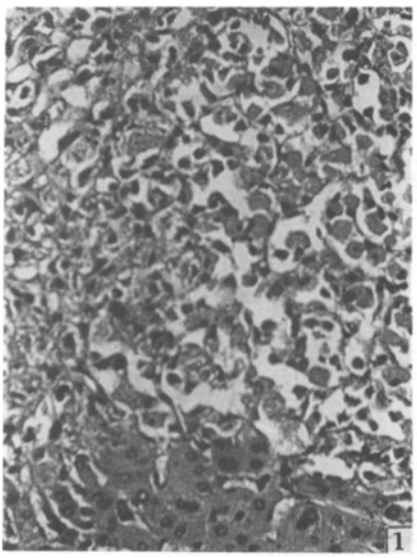
Male guinea pigs weighing approximately 550-600 gms. were used in this study and in experimental setup the animals were randomly divided into two groups and were kept under the same environmental conditions (room temperature 25°c ± 2°c) and nutritional status. The treated group received intraperitoneal injection of benzophenone 5 mg/kg body wt. (dissolved in 1ml. olive oil) and the control group received the same volume of olive oil (1 ml/kg. body wt.) daily for a period of 15 days.

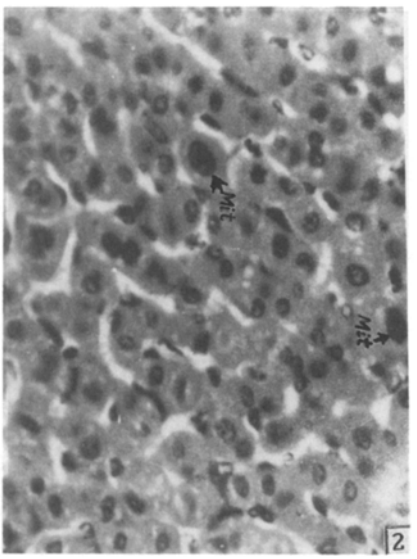
Animals were sacrificed at 24 hours after the last dose. Pieces of liver from both treated and control animals were removed, fixed in carnoy's fluid for histopathological and histochemical studies. Following the standard technique, paraffin blocks were prepared. Sections of 3-4 micron thickness were cut and stained by haematoxylin and eosin method. Histochemical detection of DNA in liver was made by schiff's reagent (Gurr 1958) and detection of glycogen was made by periodic acid-schiff (PAS) reaction (Hotchkiss 1948).

## RESULTS AND DISCUSSION

Guinea pigs exposed to benzophenone daily for 15 days showed slight enlargement and distinct nodular cirrhotic lesions of liver. The liver became slightly rubbery in consistency.

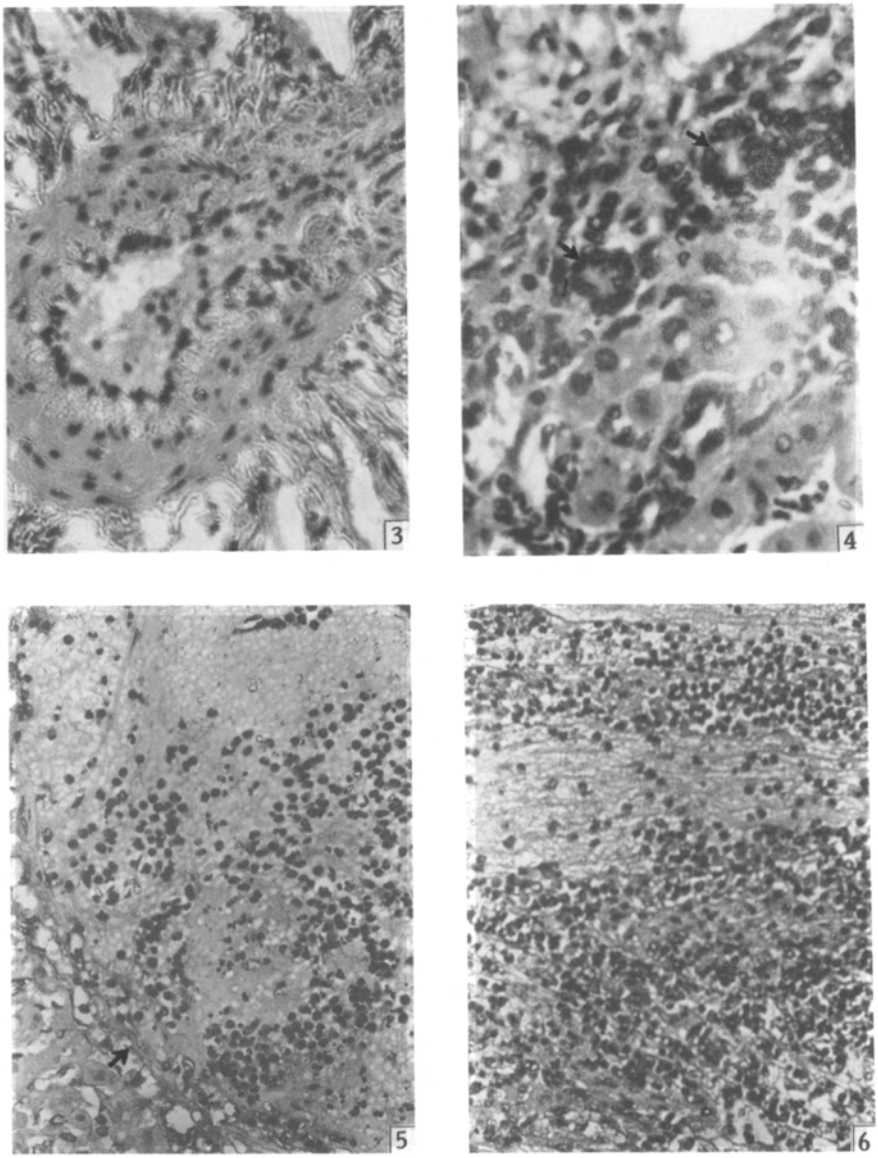
Microscopically the hepatic changes observed were disorganization of lobular architecture and hepatic cords. Perilobular and centrilobular cirrhosis characterized by replacement of






Figures 1-2. Sections of liver from benzophenone treated guinea pig showing (1) Hepatic degeneration with mild fatty changes. (2) Mitotic figure [Photomicrograph 400X].

hepatocytes with connective tissue were noted. These pathological changes resembles that of chronic hepatitis. Nuclear hyperchromatia and various grades of degenerative changes in association with mild to moderate fatty changes were observed in the hepatic cells ( Fig.1). Hepatocellular necrosis was prominent in different parts of the liver, mainly at the periportal areas. At places, areas of regeneration characterized by unusually larger size of the cells and their nuclei, occasional presence of more than one nuclei in a single cell and presence of a few mitotic figures could be noticed (Fig.2). Thickening of the wall of the blood vessels along with swollen endothelial cells led to the constriction of their lumina (Fig.3). Proliferation of the bile duct epithelial cells were observed in the periportal areas. These proliferated cells showed either clumping or led to the development of new bile canaliculi (Fig.4). At some places the hepatic capsule protruded out due to the pressure exerted by the underlying proliferating bile duct epithelial cells. Fibrinous thrombi with a large amount of leucocytic infiltration was noted within the blood vessels leading to obliteration of the vessel lumen (Fig.5), and exerted its influence on microcirculation in this highly vascularized organ. Slowing or stagnation of blood flow is a predisposing factor in venous thrombosis. Zalokar, et al.(1981) established the correlation between the circulating leucocytes and the risk of ischemia and necrotic events due to major disturbances in microvascular flow. Subcapsular areas were filled with fibrinous



Figures 3-6. Sections of liver from benzophenone treated guinea pig showing (3) Endothelial hypertrophy (4) Proliferation of bile duct epithelial cells leading to the formation of bile canaliculi (5) Fibrinous thrombus crowded with leucocytes within the blood vessel (6) Fibrinous exudate with a large number of leucocytes [Photomicrograph 400X].

exudate with a large number of leucocytes. Lymphocytes, macrophages and plasma cells were abundantly seen in the inflammatory areas (Fig.6).

Macrophages and kupffer cells laden with bile pigments were frequently encountered within the hepatic sinusoids. Robbins and Cotran (1981) suggested that presence of leucocytes at the site of inflammation, constitute the prime defensive feature of the inflammatory response.

Histochemical studies revealed a decline in stored glycogen in liver cells characterized by irregular distribution and lower intensity of PAS-positive granules indicating active glycolysis. A weak Fuelgen reaction was observed in the hepatic cells, whereas the biliary epithelial cells exhibited a strongly positive reaction indicating active mitotic divisions in these cells at the expense of metabolites from other hepatic cells. These changes may be indications of future carcinogenic transformation. Similar changes following intoxication with the dye p-dimethyl aminobenzene (butter yellow) are reported by Jennings and Florey (1970). They suggested that these changes eventually produce liver carcinoma. Alterations in the metabolic processes in the liver may be another factor for histopathological changes. Depletion in stored glycogen in liver indicated the interference of the chemical treatment with carbohydrate metabolism.

Analyses of the results of the present investination clearly revealed the hepatotoxic nature of the chemical. As benzophenone is widely used in perfumery industries, a long term exposure study on the exact role of the chemical needs further investigation.

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