Behavioral Effects on Juvenile Rats From Perinatal Exposure to Low Levels of Toxaphene, and Its Toxic Components, Toxicant A, and Toxicant B

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Abstract. Behavioral effects of toxaphene, and its toxic components, toxicant A and toxicant B, were studied by perinatally exposing juvenile rats. Toxaphene was given daily to pregnant rats (and their offspring) at 50 μg/kg body weight via their diet. The daily dietary levels of toxicants A and B were 2.0 μg/kg body weight. Behavioral tests were performed on the offspring. All rats fed toxaphene, as well as toxicants A and B, showed retarded maturation as judged by the swimming test during their early development. However, the treated rats eventually attained normal swimming ability. The maze retention test demonstrated significant differences between the toxicant A group and all other groups. The toxicant A animals had no difficulty in learning the test problems but were inferior to the other groups in retaining that knowledge.

Toxaphene, a chlorinated terpene insecticide, is a complex mixture of more than 177 polychloro compounds (Holmstead et al. 1974). Currently, it is the major chlorinated insecticide used in the United States. During the last 25 years, over one billion pounds of toxaphene have been applied to crops and livestock for pest insect control (Matsumura et al. 1975).

Because of the chemical complexity of toxaphene, little is known about its mode of action. However, it is generally agreed that it is a neuropoison affecting the function of the central nervous system. Recently, the two most toxic fractions, toxicant A (Matsumura et al. 1975, Turner et al. 1975) and toxicant B (Casida et al. 1974), have been isolated and identified. Toxicants A and B, which are 14- and 6-fold more toxic than toxaphene to mice, respectively, constitute 2% to 6% of toxaphene (Casida et al. 1974). Subsequent investigations, however, have found that toxicant B is much less toxic than was originally reported (Turner and Casida 1977).

Although toxicological studies on toxaphene are not complete, some of the
adverse effects from chronic toxaphene exposure are known. Chernoff et al. (1976) investigated the fetotoxic potential of toxaphene in rats and mice when administered during gestation. A dose level of 25 mg/kg/day, which had an 8% maternal mortality rate, also resulted in a reduction in fetal weight and a decrease in the degree of skeletal ossification. Kennedy et al. (1973) investigated the reproductive performance of three successive generations of rats fed dietary levels of 25 and 100 ppm toxaphene and found no effects on litter size, pup survival or weaning body weights at either of the two doses. However, animals fed 100 ppm did show liver changes, which consisted of slight cytoplasmic fatty vacuolization. A study of the effects of dietary levels of 10 and 100 ppm of toxaphene fed to white leghorn layers showed a slight decrease in egg production, but no adverse effects of fertility, hatchability, and survival of progeny from treated chickens (Arscott et al. 1976).

A compound called "toxaphene" by the Russian authors (which is similar to its English counterpart) was found to cross the placental barrier (Badayeva and Kiseleva 1976). Rats were fed 12 mg/kg "toxaphene" in the first 14 days of pregnancy. The "toxaphene" level was greater in the fetal organs (2.9 mg/kg) than in the placenta (2.3 mg/kg) which, together with the morphological changes observed in the uterus and placenta, provided evidence that the passage of "toxaphene" into the placenta was due to changes in its permeability. Post-implantation death, stillbirth, decreases in birthweight and disturbances in nervous system embryogenesis indicated that "toxaphene" had a direct toxic effect on the various fetal systems, including the nervous system.

All of the literature thus far on chronic effects of toxaphene exposure has dealt with specific aspects of toxicity. Only one study examined a range of possible toxic effects: physiological, behavioral and ecological changes due to sublethal concentrations of toxaphene. To accomplish this, Warner et al. (1966) selected behavioral tests. The reasoning for this choice reiterated the primary logic behind behavioral research. First, an organism's behavior represents the final integrated result of a diversity of biochemical and physiological processes (Warner et al. 1966). Second, the known sensitivity of behavioral patterns to many environmental contaminants makes them valuable testing parameters for examining environmental levels of contaminants. Finally, behavioral techniques do not require disruption of the normal functioning of an organism. Warner et al. (1966) used a conditioned avoidance response apparatus in testing the effects of toxaphene on behavior. Fish exposed for 96 hr to 1.8 μg/L toxaphene at 25°C showed altered behavior to several response parameters. Specifically, treated fish exhibited an extreme aversiveness to light stimulus and less complete habituation. The authors concluded that the greater avoidance response to light exhibited by the treated fish strongly suggested a hypersensitivity to external stimuli in general and/or a magnification of normal motor patterns, and was not due to a toxicant-induced aversion per se (Warner et al. 1966).

The present study was undertaken to examine the effects of toxaphene, as well as toxaphene components (toxicant A and toxicant B) on a variety of behavioral and developmental parameters. It was reasoned that not only should many behavioral tests increase the potential for detecting any behavioral abnormalities, but these behavioral changes in themselves may help us better understand the impact of these chemicals on the functioning organisms.