EFFECTS OF POLYCHLORINATED BIPHENYLS (KANECHLOR-500) ON SERUM HORMONE LEVELS IN RATS AND MICE

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Introduction

PCBs are ubiquitously present in the environment. PCBs elicit a number of biologic and toxic effects, impairments of immune responses and reproductive function, and the induction of hepatic cytochrome P450 isozymes [1-3]. The susceptibility to PCB-derived toxicity in mammalian species differed each other [2]. However, to our knowledge, only limited data are available on the species difference in alternative level of serum hormone level by PCB treatment in various experimental animals.

In the present study, we examined the species differences between rats and mice in the levels of serum testosterone and thyroid hormone, and in the induction of drug-metabolizing enzymes by Kanechlor-500, commercial PCB mixture.

Methods

Animal treatments. Male Wistar rats, weighing 160-200 g, and male ddy mice, weighing 28-36 g, were housed three or four per cage with free access to commercial chow and tap water, and maintained on a 12-hr dark/light cycle (8:00 a.m.-8:00 p.m. light) in a room with controlled temperature (24.5 ± 1℃) and humidity (55 ± 5%). Rats and mice received an intraperitoneal injection of Kanechlor-500 (100 mg/kg) dissolved in Panacete 810 (5 ml/kg). Control animals received an equivalent volume of vehicle. All animals were killed by decapitation on day 4 after the dosing, and the tissues were removed and weighed. Blood was collected from animals between 10:30 and 11:30 a.m. After clotting at room temperature, serum was separated by centrifugation and stored at -50℃ prior to determination of the levels of total testosterone, total thyroxine (T_4), total triiodothyronine (T_3) and thyroid stimulating hormone (TSH) by radioimmunoassay using Coat A Count Total Testosterone Kit (Diagnostic Products Corporation; Los Angeles, U.S.A.), Amerlex-MT4, Amerlex-MT3 (Ortho-Clinical Diagnostics Co.; Amersham, UK) and Biotrak rTSH [^{125}I] assay system (Amersham Life Science Ltd.; Little Chalfont, UK), respectively.

Preparation of hepatic microsomes and the microsomal enzyme assays. Hepatic microsomes were prepared according to the procedure described previously [4]. The protein content was determined by the method of Lowry *et al.* [5] with bovine serum albumin as a standard. The activity of alkoxyresorufin *O*-dealkylase in microsomes was determined by the method of Burke *et al.* [6]. The microsomal activity of UDP-glucuronosyltransferase (UDP-GT) toward 4-nitrophenol was determined as described by Isselbacher *et al.* [7].

Results and Discussion

Kanechlor-500 treatment resulted in significant decrease in serum total T_4 level in both rats and mice (Fig. 1), while no significant change in serum total TSH level in both species. On the other hand, serum total testosterone level was significantly increased by Kanechlor-500 treatment in mice but not in rats (Fig. 2). Serum total T_3 level was slightly decreased by Kanechlor-500 in mice but not in rats (Fig. 3).

A significant increase in liver weight was observed with Kanechlor-500 treatment in rats and mice. No change was found in the weight of pituitary gland, thyroid gland, thymus gland, adrenal gland, kidney and testis after the administration.

Kanechlor-500 administration resulted in significant increase in hepatic microsomal enzymes; benzyloxyresorufin *O*-dealkylase activity: 86- and 8.9-fold, pentoxyresorufin *O*-dealkylase activity (CYP2B1/2): 25- and 7.8-fold, and ethoxyresorufin *O*-dealkylase activity (CYP1A1/2): 46- and 2-fold in rats and mice, respectively, at 4 days later. The administration of Kanechlor-500 also increased the UDP-GT (UGT1A6) activity toward 4-nitrophenol in rats but not in mice (Fig. 4).

In conclusion, the present findings demonstrated that Kanechlor-500 possess the ability to reduce serum total T_4 level in rats and mice, and further suggested that the reduction of serum total T_4 level in rats might be dependent on increase in the hepatic T_4 glucuronidation through Kanechlor-500-mediated induction of UGT1A1. Furthermore, it is noteworthy that Kanechlor-500 increased the serum total testosterone level in mice but not in rats, although the cause of difference remains unclear.

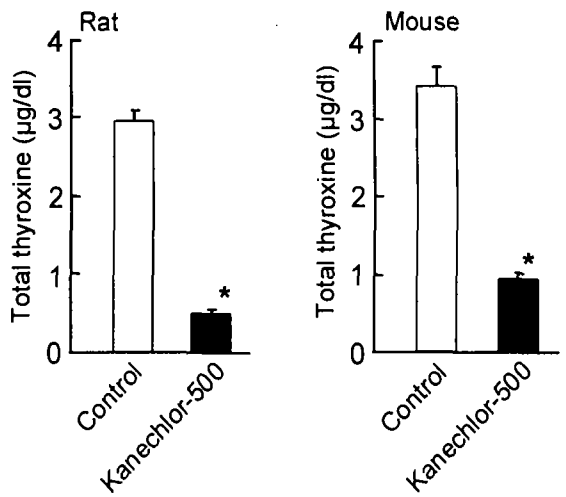

Fig. 1. Effects of Kanechlor-500 on serum total thyroxine concentration in rats and mice. Animals were given i.p. Kanechlor-500 (100 mg/kg) and killed 4 days after the administration. Each column represents the mean ± S.E. (vertical bars) for four to seven animals. *P<0.001, significantly different from the control.

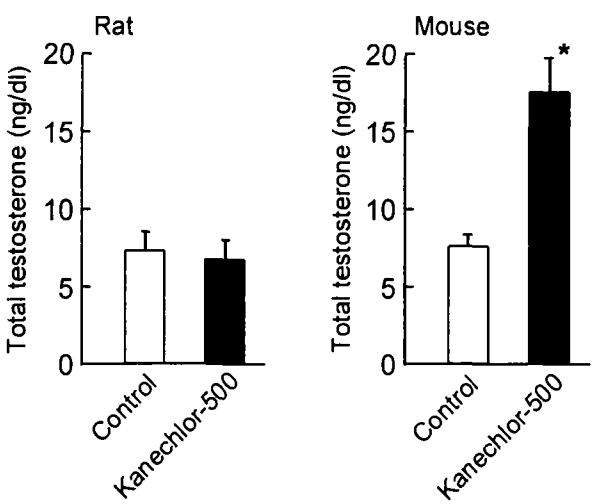

Fig. 2. Effects of Kanechlor-500 on serum total testosterone concentration in rats and mice. The experimental conditions were the same as described in the legend to Fig. 1. Each column represents the mean ± S.E. (vertical bars) for three to seven animals. *P<0.01, significantly different from the control.

Acknowledgements

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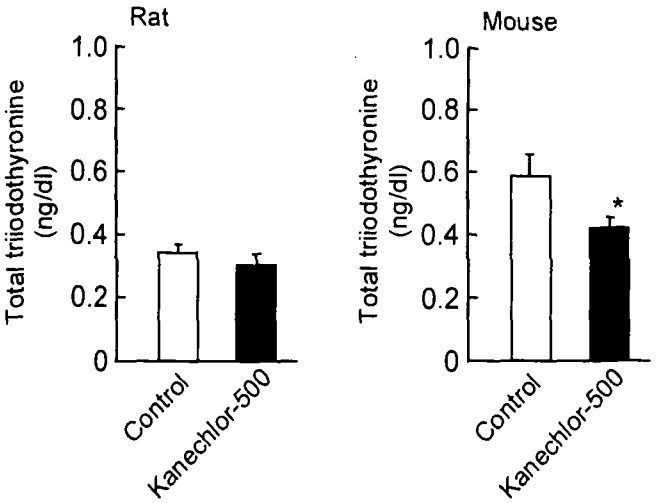

Fig. 3. Effects of Kanechlor-500 on serum total triiodothyronine concentration in rats and mice. The experimental conditions were the same as described in the legend to Fig. 1. Each column represents the mean ± S.E. (vertical bars) for four to eight animals. *$P<0.05$, significantly different from the control.

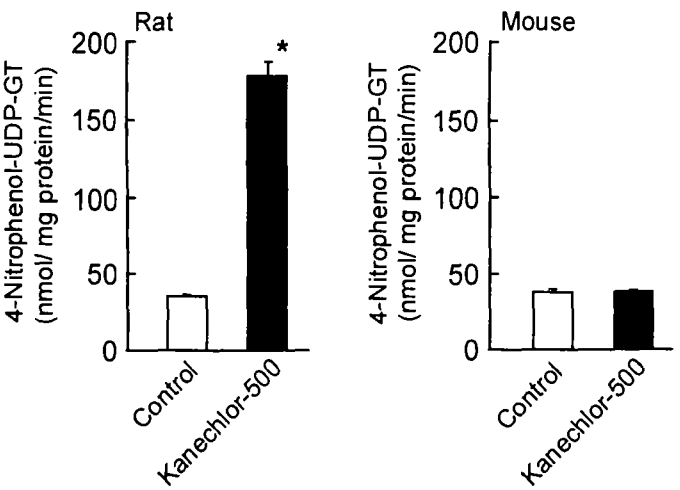

Fig. 4. Effects of Kanechlor-500 on UDP-glucuronosyltransferase activity toward 4-nitrophenol of liver microsomes in rats and mice. The experimental conditions were the same as described in the legend to Fig. 1. Each column represents the mean ± S.E. (vertical bars) for three to five animals. *$P<0.001$, significantly different from the control.