
Effect of Cadmium and Parathion on Renal Function in Rat

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Individuals are simultaneously exposed to several contaminants such as pesticides (parathion) and heavy metals (cadmium) that are found in environmental pollution. Parathion is a widely used organophosphorus insecticide. Its acute toxicity is due to the inactivation of acetylcholinesterase [1]. Parathion is eliminated by the kidney through the secretory pathway for organic anions [2]. Cadmium is a toxic metal with many applications. It is a by-product of zinc and lead mining and smelting, which are important sources of environmental pollution [3]. Cadmium concentration in kidney is 7-10 times higher than that in liver [4]. The major excretion pathway of both contaminants is the kidney. Metabolism and concentration is carried out in the liver. The purpose of the present study was to evaluate the effects produced by the contaminants on the renal and hepatic functions on the adult rat.

METHODS:

Cadmium and parathion on renal function in the adult rat. The experiments were carried out in female Wistar adult rats (200 ± 20 g body weight), fed on a standard diet (Purina chow) with free access to water. The rats were divided into three groups: one control group (vehicle) and two cadmium-parathion-treated group, cadmium-parathion (10/0.5 mg/kg) and 18.0/1.0 mg/kg body weight, for 15 and 21 days. The rats were allocated by means of a table of random numbers and were kept in a quiet and warm environment (21-23°C) during the treatment. The administration was per os.

At the end of these periods, the rats were installed in metabolic cages to obtain urine samples. Volume was measured in calibrated pipettes (Dade, Miami, Fl., USA) as previously described [5]. The animals were decapitated and blood samples were collected into tubes that were centrifuged at 6,000 rpm for 20 min to separate cells from serum.

Cadmium and parathion on p-aminohippuric acid uptake. Paraaminohippuric acid (PAH) has been extensively used as an indicator of the renal secretory pathway of organic anions. Cortical slices were obtained from rats of the different experimental groups. Slices from each treated group were incubated in Ringer solution containing PAH (1 mM) for 1 h. At the end of this period, the slices were retired from incubation media, wet weight of tissue pieces were recorded on a Sartorius Handy H 100 balance and results were expressed as tissue/medium ratio. PAH was measured according to the method of Bratton and Marshall [6].

Effects of cadmium and parathion on glucose and protein urinary excretion. Glucose concentration in urine samples was measured with a standard kit (Merck). The protein determination was carried out according to the Bradford method [7].

RESULTS:

Effect of cadmium and parathion on PAH uptake and glucose and protein urinary excretion. Cadmium and parathion reduced the PAH uptake at the 10/0.5 dose in the 15 days treatment (p < 0.05; Table 1). Both contaminants increased the PAH uptake at the 18/1.0 dose in the 15 and 21 days treatments. These increments reached statistical significance (Table 1).

Effect of cadmium and parathion on glucose and protein urinary excretion. The glucose urinary excretion was augmented in all treated-groups in the two experimental periods (Table 1). At the 10/0.5 dose in the 15 days treatment, urinary excretion of protein was increased (p < 0.05; Table 1). The protein concentration in urine was not modified in the other treated groups (Table 1).

Effects of cadmium and parathion on hepatic function. The values of bilirubin concentration were similar among groups. Cadmium and parathion treatment did not modify these values (Table 2). The GOT and GPT activities were increased in all treated-groups (Table 2 and Figure 1), while the alkaline phosphatase and glucose was only augmented in the treated group at the 10/0.5 dose in the 21-day period (p < 0.05; Table 2).

LD₅₀ for cadmium and parathion administered simultaneously in the rat. The value of LD₅₀ obtained in the adult rat for cadmium in the presence of parathion was 107.1 mg/kg body weight and for parathion in the presence of cadmium it was 4.5 mg/kg body weight.
DISCUSSION: Toxicological responses to contaminants are modified by several factors. Among them are the simultaneous presence of two or more toxins, the dose and treatment period, and the age and the sex of the animal [8,9]. It has reported that adult female rats showed higher sensitivity than male rats to parathion. Due to this fact, we only used female adult rats. The LD$_{50}$ obtained for parathion alone was similar to that reported by other authors (4 mg/kg) [5]. The simultaneous presence of cadmium slightly lowered lethality to an LD$_{50}$ of 4.5 mg/kg. Similar results were obtained for cadmium in the presence of parathion, the LD$_{50}$ changing from 100 to 107.1 mg/kg body weight (absence and presence of parathion respectively). These results suggest that the simultaneous presence of both toxins only modestly affected

Table 1. Effect of cadmium and parathion on renal tubular secretion and glucose and protein urinary excretion

<table>
<thead>
<tr>
<th>Cadmium/Parathion (10/0.5 mg/kg body weight)</th>
<th>glucose concentration (mg/dl)</th>
<th>protein concentration (µg/dl)</th>
<th>PAH uptake (t/m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>treatment-days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>control</td>
<td>20.9 ± 3.9 (20)</td>
<td>4.9 ± 0.4 (20)</td>
<td>1.9 ± 0.1 (40)</td>
</tr>
<tr>
<td>15 days</td>
<td>68.3 ± 8.5** (10)</td>
<td>6.4 ± 0.7* (10)</td>
<td>1.3 ± 0.0* (20)</td>
</tr>
<tr>
<td>21 days</td>
<td>40.6 ± 5.1* (10)</td>
<td>5.8 ± 0.3 (10)</td>
<td>1.8 ± 0.0 (20)</td>
</tr>
</tbody>
</table>

Cadmium/Parathion (18/1.0 mg/kg body weight)

| 15 days                                     | 42.1± 3.8** (10)              | 4.0 ± 0.3 (10)               | 2.7 ± 0.0** (20) |
| 21 days                                     | 49.8 ± 6.8** (10)             | 4.1 ± 0.8 (10)               | 2.7 ± 0.0** (20) |

Mean ± SEM are shown. Figures in parentheses indicate number of animals. **p < 0.01; *p < 0.05

Table 2. Effect of cadmium and parathion on the hepatic function

<table>
<thead>
<tr>
<th>Cadmium/Parathion (10/0.5 mg/kg body weight)</th>
<th>bilirubin concentration (mMol/l)</th>
<th>GOT activity (U/l)</th>
<th>Alkaline phosphatase (U/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment-days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>13.2 ± 0.7 (40)</td>
<td>170.2 ± 5.6 (40)</td>
<td>18.1 ± 0.9 (40)</td>
</tr>
<tr>
<td>15 days</td>
<td>9.5 ± 0.8 (20)</td>
<td>180.9 ± 4.7 (20)</td>
<td>18.6 ± 1.1 (20)</td>
</tr>
<tr>
<td>21 days</td>
<td>13.0 ± 1.1 (20)</td>
<td>210.6 ± 4.3** (20)</td>
<td>20.9 ± 0.9* (20)</td>
</tr>
</tbody>
</table>

Cadmium/Parathion (18/1.0 mg/kg body weight)

| 15 days                                     | 13.2 ± 1.5 (20)                   | 193.9 ± 12.3* (20)  | 18.4 ± 1.0 (20)            |
| 21 days                                     | 13.1± 0.6 (20)                    | 243.2 ±10.8** (20)  | 18.7 ± 1.2 (20)            |

Mean ± SEM are shown. Figures in parentheses indicate number of animals. **p < 0.01; *p < 0.05.
the lethality observed when the agents were administered alone.

PAH uptake was measured in the presence of both toxins. Parathion had a stimulating effect, which was also seen when this insecticide was administered alone [8]. A reduction in PAH uptake was induced by cadmium when was administered alone [10]. However this effect was not produced in the presence of parathion. It is known that parathion is eliminated by the kidney through the secretory pathway for organic anions [2]. This excretory pathway could be stimulated by the administration of parathion for 21 days. As a consequence, an increase in PAH uptake was observed even though cadmium was present [5]. A selective site for the toxic action of cadmium and parathion is the proximal tubule. This is presumably the basis for the increase in glucose urinary excretion and proteinuria [5,10].

Recent studies have described lipid peroxidation to be an early and sensitive consequence of cadmium exposure. Free radical scavengers and antioxidants have been reported to attenuate cadmium induced toxicity [11]. These observations are consistent with the effects observed on GOT and GPT activities, due to altered hepatic cellular membranes in the presence of cadmium.

SUMMARY: Our results suggest that parathion induces a stimulating effect on PAH uptake. The simultaneous presence of cadmium does not modify this effect. The simultaneous presence of cadmium and parathion produced an hepatotoxic effect in the rat.

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REFERENCES