The administration of xenobiotics, such as PCB, DDT and fat-soluble chemicals having low molecular weight, causes a change in many metabolic states in vivo. When various types of xenobiotics were administered to rats, marked increases in urinary excretion of ascorbic acid and in tissue level of ascorbic acid were observed. Previously, we reported that this phenomenon was caused by stimulation of the biosynthesis of ascorbic acid in the liver; moreover, the turnover of ascorbic acid in the body was accelerated with xenobiotics feeding. In rats, ascorbic acid is synthesized via the glucuronic acid pathway in the liver. We observed marked increases in the activities of hepatic UDP-glucose dehydrogenase and UDP-glucuronyl transferase by the administration of PCB or DDT.

Guinea pig also has a glucuronic acid pathway, but in guinea pig, ascorbic acid cannot be synthesized due to the lack of L-gulonolactone oxidase which catalyzes the reaction of the last step in ascorbic acid synthesis. When xenobiotics are administered to guinea pigs, changes in the urinary excretion of intermediate metabolites and the enzyme activities in the glucuronic acid pathway as units per 100 g of body weight (Fig. 1). Ingestion of PCB significantly increased the activities of all enzymes measured, i.e., UDP-glucuronic acid pyrophosphatase (1.5-fold), when compared with the PCB diet (6.6-fold).

Urinary excretion of glucaric acid was also remarkably increased most remarkably in the aminopyrine group. Urinary excretion of ascorbic acid decreased in the PCB, PCB feeding caused a marked enlargement of the liver. Urinary excretion of glucaric acid increased in the PCB, DDT and aminopyrine groups, especially in the PCB group. On the other hand, the administration of these xenobiotics increased urinary conjugated glucuronic acid, most remarkably in the aminopyrine group. Urinary excretion of glucaric acid was also remarkably increased with the PCB diet (6.6-fold).

We have expressed the hepatic enzyme activities involved in the glucuronic acid pathway as units per 100 g of body weight (Fig. 1). Ingestion of PCB significantly increased the activities of all enzymes measured, i.e., UDP-glucuronic acid pyrophosphatase (3.2-fold), UDP-glucuronyl transferase (2.9-fold), β-glucuronidase (5.8-fold) and UDP-glucuronic acid pyrophosphatase (1.5-fold), when compared with the values of the control group. However, administration of the other xenobiotics caused no significant changes in any enzyme activities.

In rats, the administration of several types of xenobiotics (PCB, DDT, aminopyrine, chloretone, pentobarbital) and on the ascorbic acid metabolism in guinea pigs.

**Note**

**Effect of Some Xenobiotics on the Activities of Enzymes Relating to the Glucuronic Acid Pathway and on the Ascorbic Acid Metabolism in Guinea Pigs†**

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Table 1. Effects of Dietary Addition of Xenobiotics on Body Weight Gain, Urinary Glucuronic Acid, Urinary Glucaric Acid, Urinary Ascorbic Acid and Liver Level of Ascorbic Acid

<table>
<thead>
<tr>
<th>Groups</th>
<th>Control</th>
<th>PCB</th>
<th>DDT</th>
<th>Aminopyrine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial body wt.</td>
<td>259 ± 4</td>
<td>256 ± 6</td>
<td>259 ± 7</td>
<td>253 ± 8</td>
</tr>
<tr>
<td>Body wt. gain for 14 days</td>
<td>78.4 ± 12.8a</td>
<td>-0.8 ± 9.7b</td>
<td>65.4 ± 8.3a</td>
<td>61.8 ± 10.9a</td>
</tr>
<tr>
<td>Liver wt.</td>
<td>4.15 ± 0.26a</td>
<td>5.42 ± 0.29b</td>
<td>4.84 ± 0.19ab</td>
<td>4.31 ± 0.30a</td>
</tr>
<tr>
<td>Urinary glucuronic acid</td>
<td>Conjugated</td>
<td>13.4 ± 0.5a</td>
<td>19.7 ± 1.0ab</td>
<td>19.0 ± 2.7ab</td>
</tr>
<tr>
<td></td>
<td>Free</td>
<td>3.9 ± 1.2</td>
<td>5.5 ± 1.0</td>
<td>2.1 ± 0.5</td>
</tr>
<tr>
<td>Urinary glucaric acid</td>
<td>(mg/100 g body wt./day)</td>
<td>37 ± 14a</td>
<td>244 ± 28b</td>
<td>49 ± 14a</td>
</tr>
<tr>
<td>Urinary ascorbic acid²</td>
<td>(µg/100 g body wt./day)</td>
<td>118 ± 12a</td>
<td>75 ± 13b</td>
<td>86 ± 11ab</td>
</tr>
<tr>
<td>Liver level of ascorbic acid</td>
<td>(µg/g)</td>
<td>42.5 ± 11.2</td>
<td>38.7 ± 8.1</td>
<td>33.7 ± 10.1</td>
</tr>
</tbody>
</table>

1) Means ± SE. Means within a line not followed by the same superscript letter are significantly different (p < 0.05).
2) On day 9 to 10, all guinea pigs were fed an ascorbic acid free diet with or without the addition of xenobiotics to prevent the urine from the contamination by dietary ascorbic acid.
3) Not determined.

If the urinary excretion of a compound generally changes when the animals ingest xenobiotics, it would be useful as an index for showing the ingestion of xenobiotics. We demonstrated that the increase in urinary ascorbic acid in rats was a good index for the ingestion of xenobiotics. However, human cannot synthesize ascorbic acid like guinea pig. We expect that the urinary excretion of glucaric acid or glucuronic acid increases with the ingestion of xenobiotics in human and guinea pigs and that we can use this phenomenon as an index of ingestion of xenobiotics.

REFERENCES
Fig. 1. Effects of the Dietary Addition of Xenobiotics on the Activities of Hepatic UDP-Glucose Dehydrogenase (A), UDP-Glucuronyl Transferase (B), β-Glucuronidase (C) and UDP-Glucuronic Acid Pyrophosphatase (D).

The bars indicate means and the vertical lines above the bars indicate the SE. Bars not followed by the same superscript letter are significantly different ($p < 0.05$). Cont., control group; PCB, PCB group; DDT, DDT group; AP, aminopyrine group.