Studies on the Detoxicating Hormone of the Liver (Yakriton).

94th Report.
Effect of Yakriton upon Detoxication of Sodium Santonate by the Liver. Part 2.

By

Fumio Ohta.

(From the Department of Pediatrics, Faculty of Medicine, Tohoku Imperial University, Sendai.
Director: Prof. A. Sato.)

Introduction.

In Part 1) of the present study, I reported that yakriton, the detoxicating hormone of the liver, has the ability to strengthen the detoxication of sodium santonate by the liver, as Takasugi and Miyamoto2) have already stated. Prof. Sato3) is of opinion that yakriton will exert detoxicating action on different poisons with different numbers of units or different phases of "yakritisation." So I performed further experiments, with different uses of yakriton which might influence the santonine dye excretion, or the conversion of sodium santonate into that dye by the liver differently.

Method of Experiment.

1. Animals used for experiment.

Healthy, adult male rabbits were used. They were put to Sato and Sakurada's4) liver function test 3 times (once a day) every other day in all, and only b-classed (low-classed) rabbits were used. They were put to the experiment proper only after a lapse of more than 10 days after the liver function test.

2) T. Takasugi and E. Miyamoto, Nippon Shokakibyo Gakkai Zassi, 1937, 36, 935.
4) A. Sato and H. Sakurada, Tohoku J. Exp. Med., 1927, 8, 347.
2. The method of santsol* test.
   It was the same as described in Part 1\(^\text{1)}\) of the present study.

3. The general schedule of experiment.
   Rabbits were put to the santsol test 2 times—the control experiment (without use of yakriton) and the yakriton experiment (with use of it). The yakriton experiment was performed just a week after the control. The 10 experiments were performed according to different ways of "yakritisation."

   Experiment 1. In this experiment yakriton was used for 5 consecutive days. It was injected on rabbits in the amount of 1/5 R.A.U.\(^\uparrow\) per kilo of body weight at 4 p.m. each day from the 2nd day of the control experiment on, and on the morning of the next day of the last yakriton injection rabbits were put to the yakriton experiment, as is shown in Fig. 1.

   **Fig. 1. Schedule of Experiment 1 or 3.**

   ![Diagram](image)

   Experiment 2. This experiment differed from Exp. 1 only in the time of yakriton injection. Yakriton was used on rabbits in the amount of 1/5 R.A.U. per kilo of body weight for 5 consecutive days. It was injected at 9 a.m. each day from the 3rd day of the control experiment on. The yakriton experiment was performed 30 minutes after the last yakriton injection, as is shown in Fig. 2.

   **Fig. 2. Schedule of Experiment 2 or 4.**

   ![Diagram](image)

   Experiment 3. This experiment differed from Exp. 1 only in the unit of yakriton used. 2/5 R.A.U. were used instead of 1/5 R.A.U.

   \(^*\) Santsol is a preparation of sodium santonate.

   \(^\uparrow\) R.A.U. = Rabbit-Ammonia-Unit.
Experiment 4. This experiment differed from Exp. 2 only in the unit of yakriton used. 2/5 R.A.U. were used instead of 1/5 R.A.U.

Experiment 5. In this experiment yakriton was used in the amount of 1 R.A.U. per kilo of body weight at 4 p.m. on the 6th day of the control experiment on, and at 9:30 a.m. the yakriton experiment was performed, as is shown in Fig. 3.

Fig. 3. Schedule of Experiment 5 or 7.

Experiment 6. This experiment differed from Exp. 5 only in the time of yakriton injection. It was used in the same amount as in Exp. 5 at 9 a.m. on the 7th day of the control experiment on, and 30 minutes after it the yakriton experiment was performed, as is shown in Fig. 4.

Fig. 4. Schedule of Experiment 6 or 8.

Experiment 7. This experiment differed from Exp. 5 only in the unit of yakriton used. 2 R.A.U. were used instead of 1 R.A.U.

Experiment 8. This experiment differed from Exp. 6 only in the unit of yakriton used. 2 R.A.U. was used instead of 1 R.A.U.

Experiment 9.

In this experiment yakriton was used for 4 consecutive days in the amount of 1 R.A.U. per kilo of body weight. It was used at 4 p.m. each day from the 3rd day of the control experiment on, and the yakriton experiment was performed at 9 a.m. on the next day of the last yakriton injection, as is shown in Fig. 5.

Experiment 10. This experiment differed from Exp. 9 only in the time of yakriton injection. It was injected in the same amount as in Exp. 9 at 9:00 a.m. each day for 4 consecutive days from the 4th day of the control experiment on. The yakriton experiment was performed 30 minutes after the last yakriton injection, as is shown in Fig. 6.
Fig. 5. Schedule of Experiment 9.

![Diagram of Experiment 9 schedule]

Fig. 6. Schedule of Experiment 10.

![Diagram of Experiment 10 schedule]

Result of Experiment.

The results obtained are shown in Tables 1-10.

**Table 1.**

Result of Experiment 1.

Yakriton was used in the amount of 1/5 R.A.U. per kilo of body weight at 4 p.m. for 5 consecutive days from the 2nd day of the control experiment.

<table>
<thead>
<tr>
<th>No. of rabbits</th>
<th>Date of experiment</th>
<th>Experiment</th>
<th>Body weight (in kilos)</th>
<th>Amount of santonine dye excreted</th>
<th>Ratio of increase by use of yakriton</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. 1</td>
<td>30. IV</td>
<td>Control</td>
<td>2.20</td>
<td>12 14 2 + + + + + + + + + + + + +</td>
<td>28 1.0</td>
</tr>
<tr>
<td>(6420)</td>
<td></td>
<td>Yakriton</td>
<td>2.33</td>
<td>13 14 2 + + + + + + + + + + + + +</td>
<td>29 1.0</td>
</tr>
<tr>
<td>No. 3</td>
<td>7. V</td>
<td>Control</td>
<td>2.15</td>
<td>10 10 1 + + + + + + + + + + + + +</td>
<td>16 1.0</td>
</tr>
<tr>
<td>(6422)</td>
<td></td>
<td>Yakriton</td>
<td>2.08</td>
<td>12 2 1 + + + + + + + + + + + + +</td>
<td>12 1.0</td>
</tr>
<tr>
<td>No. 5</td>
<td>8. V</td>
<td>Control</td>
<td>2.55</td>
<td>18 4 + + + + + + + + + + + + +</td>
<td>22 1.0</td>
</tr>
<tr>
<td>(6424)</td>
<td></td>
<td>Yakriton</td>
<td>2.44</td>
<td>15 4 + + + + + + + + + + + + +</td>
<td>20 1.0</td>
</tr>
<tr>
<td>No. 7</td>
<td>9. V</td>
<td>Control</td>
<td>2.62</td>
<td>22 13 12 6 + + + + + + + + + + +</td>
<td>24 1.0</td>
</tr>
<tr>
<td>(6428)</td>
<td></td>
<td>Yakriton</td>
<td>2.60</td>
<td>23 18 6 1 + + + + + + + + + + +</td>
<td>22 1.0</td>
</tr>
<tr>
<td>No. 9</td>
<td>10. V</td>
<td>Control</td>
<td>2.15</td>
<td>32 18 6 1 + + + + + + + + + + +</td>
<td>27 1.2</td>
</tr>
<tr>
<td>(6428)</td>
<td></td>
<td>Yakriton</td>
<td>2.25</td>
<td>32 18 6 1 + + + + + + + + + + +</td>
<td>29 1.2</td>
</tr>
</tbody>
</table>

* Dye was identified by means of amylic or butylic alcohol in an amount as small as negligible.
† Dye was not identified.
TABLE 2.

Result of Experiment 2.

Yakriton was used in the amount of 1/5 R.A.U. per kilo of body weight at 9 a.m. for 5 consecutive days from the 3rd day of the control experiment.

<table>
<thead>
<tr>
<th>No. of rabbits</th>
<th>Date of experiment</th>
<th>Experiment</th>
<th>Body weight (in kilos)</th>
<th>Amount of santonine dye excreted</th>
<th>Lapse of time after santonine injection</th>
<th>Total</th>
<th>Ratio of increase by use of yakriton</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. 2 30. IV  (6421) 7. V</td>
<td>Yakriton 1.97</td>
<td>24 10 2 + - - -</td>
<td>36 11 2 + - - -</td>
<td>36 1.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. 4 1. 8.  (6425)</td>
<td>Yakriton 2.05</td>
<td>32 27 4 + + - -</td>
<td>54</td>
<td>Decrease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. 6 2. 9.  (6425)</td>
<td>Yakriton 2.25</td>
<td>16 12 4 + + - -</td>
<td>32</td>
<td>1.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. 8 3. 10.  (6427)</td>
<td>Yakriton 2.20</td>
<td>26 12 5 + + - -</td>
<td>43</td>
<td>1.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. 10 4. 11.  (6429)</td>
<td>Yakriton 2.25</td>
<td>24 12 1 + + - -</td>
<td>48</td>
<td>1.2</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*, † = Cf. Foot note to Table 1.

TABLE 3.

Result of Experiment 3.

Yakriton was used in the amount of 2/5 R.A.U. per kilo of body weight at 4 p.m. for 5 consecutive days from the 2nd day of the control experiment.

<table>
<thead>
<tr>
<th>No. of rabbits</th>
<th>Date of experiment</th>
<th>Experiment</th>
<th>Body weight (in kilos)</th>
<th>Amount of santonine dye excreted</th>
<th>Lapse of time after santonine injection</th>
<th>Total</th>
<th>Ratio of increase by use of yakriton</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. 11 17. V  (6430) 24.</td>
<td>Yakriton 2.02</td>
<td>32 8 1 + - - -</td>
<td>41</td>
<td>1.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. 18 18.  (6432) 25.</td>
<td>Yakriton 1.87</td>
<td>48 13 4 1 + - -</td>
<td>66</td>
<td>Decrease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. 19 19.  (6434) 26.</td>
<td>Yakriton 2.18</td>
<td>54 27 12 2 + - -</td>
<td>95</td>
<td>Decrease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. 17 20.  (6436) 27.</td>
<td>Yakriton 2.23</td>
<td>21 6 + + - -</td>
<td>27</td>
<td>Decrease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. 19 21.  (6439) 28.</td>
<td>Yakriton 2.07</td>
<td>24 4 + - - -</td>
<td>28</td>
<td>Decrease</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*, † = Cf. Foot-note to Table 1.

In the following I shall relate on the results of my own experiments, making a point of the whole amount of santonine dye excreted:

Experiment 1. As is shown in Table 1, the whole amount of santonine dye excreted in the yakriton experiment was almost the same as in the control experiment, except for No. 9.

Experiment 2. As is shown in Table 2, the whole amount of
Result of Experiment 4.

Yakriton was used in the amount of 2/5 R.A.U. per kilo of body weight at 9 a.m. for 5 consecutive days from the 3rd day of the control experiment.

<table>
<thead>
<tr>
<th>No. of rabbits</th>
<th>Date of experiment</th>
<th>Experiment</th>
<th>Body weight (in kilos)</th>
<th>Amount of santonine dye excreted</th>
<th>Ratio of increase by use of yakriton</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. 18</td>
<td>17. V</td>
<td>Control</td>
<td>2.21</td>
<td>25 18 2  +  -  -  -</td>
<td>48 1.2</td>
</tr>
<tr>
<td>(6451)</td>
<td></td>
<td>Yakriton</td>
<td>2.27</td>
<td>35 14 2  1  -</td>
<td>53 1.5</td>
</tr>
<tr>
<td>No. 14</td>
<td>18. V</td>
<td>Control</td>
<td>2.65</td>
<td>12 6  -  -  -</td>
<td>18 2.5</td>
</tr>
<tr>
<td>(6453)</td>
<td></td>
<td>Yakriton</td>
<td>2.63</td>
<td>36 2  -  -</td>
<td>46</td>
</tr>
<tr>
<td>No. 16</td>
<td>19. V</td>
<td>Control</td>
<td>1.87</td>
<td>52 18 2  +  +</td>
<td>87 3.5</td>
</tr>
<tr>
<td>(6455)</td>
<td></td>
<td>Yakriton</td>
<td>1.88</td>
<td>45 45 5  2</td>
<td>85</td>
</tr>
<tr>
<td>No. 18</td>
<td>20. V</td>
<td>Control</td>
<td>2.30</td>
<td>33 24 6  1  -</td>
<td>69 2.5</td>
</tr>
<tr>
<td>(6457)</td>
<td></td>
<td>Yakriton</td>
<td>2.26</td>
<td>33 33 8  2  -</td>
<td>72</td>
</tr>
<tr>
<td>No. 20</td>
<td>21. V</td>
<td>Control</td>
<td>1.97</td>
<td>14 6  3  +  -</td>
<td>26 1.3</td>
</tr>
<tr>
<td>(6458)</td>
<td></td>
<td>Yakriton</td>
<td>1.97</td>
<td>22 8  2  -  -</td>
<td>22 1.5</td>
</tr>
</tbody>
</table>

*; + = Cf. Foot note to Table 1.

Result of Experiment 5.

Yakriton was used in the amount of 1 R.A.U. per kilo of body weight at 4 a.m. on the day before the yakriton experiment.

<table>
<thead>
<tr>
<th>No. of rabbits</th>
<th>Date of experiment</th>
<th>Experiment</th>
<th>Body weight (in kilos)</th>
<th>Amount of santonine dye excreted</th>
<th>Ratio of increase by use of yakriton</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. 21</td>
<td>3. VI</td>
<td>Control</td>
<td>2.23</td>
<td>12 4 3  +  +  -  -</td>
<td>19 1.9</td>
</tr>
<tr>
<td>(6440)</td>
<td></td>
<td>Yakriton</td>
<td>2.24</td>
<td>15 15 3  1  +</td>
<td>35</td>
</tr>
<tr>
<td>No. 23</td>
<td>6. V</td>
<td>Control</td>
<td>2.39</td>
<td>10 12 3  1  +</td>
<td>32</td>
</tr>
<tr>
<td>(6442)</td>
<td></td>
<td>Yakriton</td>
<td>2.38</td>
<td>27 18 4  2  +</td>
<td>51</td>
</tr>
<tr>
<td>No. 25</td>
<td>9. V</td>
<td>Control</td>
<td>2.30</td>
<td>14 3  1  -  -</td>
<td>21</td>
</tr>
<tr>
<td>(6444)</td>
<td></td>
<td>Yakriton</td>
<td>2.33</td>
<td>33 31 7  1  +</td>
<td>39</td>
</tr>
<tr>
<td>No. 27</td>
<td>12. V</td>
<td>Control</td>
<td>2.30</td>
<td>33 7  3  +  -</td>
<td>45</td>
</tr>
<tr>
<td>(6448)</td>
<td></td>
<td>Yakriton</td>
<td>2.32</td>
<td>33 31 7  1  +</td>
<td>87</td>
</tr>
<tr>
<td>No. 28</td>
<td>15. V</td>
<td>Control</td>
<td>2.07</td>
<td>37 17 12 3  +</td>
<td>69 1.9</td>
</tr>
<tr>
<td>(6450)</td>
<td></td>
<td>Yakriton</td>
<td>2.12</td>
<td>32 48 14 3  +</td>
<td>77 1.1</td>
</tr>
</tbody>
</table>

*; + = Cf. Foot note to Table 1.

Santonine dye excreted in the yakriton experiment increased as compared with that in the control experiment in rabbits Nos. 2 and 10, while it was almost the same as in the control experiment in the other animals.

Experiment 3. As is shown in Table 3, the whole amount of santonine dye excreted in the yakriton experiment was almost the same.
TABLE 6.

Result of Experiment 6.

Yakriton was injected in the amount of 1 R.A.U. per kilo of body weight 30 minutes prior to the yakriton experiment.

<table>
<thead>
<tr>
<th>No. of rabbits</th>
<th>Date of experiment</th>
<th>Experiment</th>
<th>Body weight (in kilos)</th>
<th>Amount of santonine dye excreted</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lapse of time after santonine dye injection</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0°-1°</td>
</tr>
<tr>
<td>No. 22 (6441)</td>
<td>3. VI</td>
<td>Control</td>
<td>2.33</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>10.</td>
<td>Yakriton</td>
<td>2.34</td>
<td>34</td>
</tr>
<tr>
<td>No. 24 (6443)</td>
<td>4.</td>
<td>Control</td>
<td>1.95</td>
<td>48</td>
</tr>
<tr>
<td></td>
<td>11.</td>
<td>Yakriton</td>
<td>2.06</td>
<td>32</td>
</tr>
<tr>
<td>No. 26 (6445)</td>
<td>4.</td>
<td>Control</td>
<td>1.96</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>11.</td>
<td>Yakriton</td>
<td>2.04</td>
<td>10</td>
</tr>
<tr>
<td>No. 28 (6447)</td>
<td>7.</td>
<td>Control</td>
<td>2.20</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>14.</td>
<td>Yakriton</td>
<td>2.22</td>
<td>37</td>
</tr>
<tr>
<td>No. 30 (6449)</td>
<td>7.</td>
<td>Control</td>
<td>2.38</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>14.</td>
<td>Yakriton</td>
<td>2.37</td>
<td>48</td>
</tr>
</tbody>
</table>

Average 1.7

*, † = Cf. Foot note to Table 1.

TABLE 7.

Result of Experiment 7.

Yakriton was used in the amount of 2 R.A.U. per kilo of body weight at 4 p.m. on the day before the yakriton experiment.

<table>
<thead>
<tr>
<th>No. of rabbits</th>
<th>Date of experiment</th>
<th>Experiment</th>
<th>Body weight (in kilos)</th>
<th>Amount of santonine dye excreted</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lapse of time after santonine dye injection</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0°-1°</td>
</tr>
<tr>
<td>No. 31 (6426)</td>
<td>13. VI</td>
<td>Control</td>
<td>2.52</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>36.</td>
<td>Yakriton</td>
<td>2.45</td>
<td>14</td>
</tr>
<tr>
<td>No. 33 (6449)</td>
<td>15.</td>
<td>Control</td>
<td>2.33</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td>22.</td>
<td>Yakriton</td>
<td>2.24</td>
<td>24</td>
</tr>
<tr>
<td>No. 35 (6428)</td>
<td>17.</td>
<td>Control</td>
<td>2.40</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td>24.</td>
<td>Yakriton</td>
<td>2.25</td>
<td>24</td>
</tr>
<tr>
<td>No. 37 (6430)</td>
<td>18.</td>
<td>Control</td>
<td>2.37</td>
<td>36</td>
</tr>
<tr>
<td></td>
<td>25.</td>
<td>Yakriton</td>
<td>2.19</td>
<td>23</td>
</tr>
</tbody>
</table>

*, † = Cf. Foot-note to Table 1.

as in the control experiment in rabbit No. 11, while it decreased in relation to the control experiment in the others.

Experiment 4. As is shown in Table 4, the whole amount of santonine dye excreted in the yakriton experiment was larger than that in the control experiment in all the rabbits without exception, especially remarkably in rabbit No. 14.

Experiment 5. As is shown in Table 5, the whole amount of san-
TABLE 8.
Result of Experiment 8.
Yakriton was used in the amount of 2 R.A.U. per kilo of body weight 30 minutes prior to the yakriton experiment.

<table>
<thead>
<tr>
<th>No. of rabbits</th>
<th>Date of experiment</th>
<th>Experiment</th>
<th>Body weight (in kilos)</th>
<th>Amount of santonine dye excreted</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lapse of time after santsol injection</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0°-1°</td>
</tr>
<tr>
<td>No. 32</td>
<td>9. VI</td>
<td>Control</td>
<td>2.25</td>
<td>15</td>
</tr>
<tr>
<td>(6421)</td>
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<td>Yakriton</td>
<td>2.26</td>
<td>23</td>
</tr>
<tr>
<td>No. 34</td>
<td>13. *</td>
<td>Control</td>
<td>2.12</td>
<td>8</td>
</tr>
<tr>
<td>(6427)</td>
<td></td>
<td>Yakriton</td>
<td>2.14</td>
<td>22</td>
</tr>
<tr>
<td>No. 36</td>
<td>14. *</td>
<td>Control</td>
<td>2.52</td>
<td>14</td>
</tr>
<tr>
<td>(6429)</td>
<td></td>
<td>Yakriton</td>
<td>2.60</td>
<td>24</td>
</tr>
<tr>
<td>No. 38</td>
<td>16. *</td>
<td>Control</td>
<td>2.80</td>
<td>20</td>
</tr>
<tr>
<td>(6450)</td>
<td></td>
<td>Yakriton</td>
<td>2.81</td>
<td>36</td>
</tr>
<tr>
<td>No. 40</td>
<td>17. *</td>
<td>Control</td>
<td>3.55</td>
<td>22</td>
</tr>
<tr>
<td>(6452)</td>
<td></td>
<td>Yakriton</td>
<td>2.49</td>
<td>39</td>
</tr>
<tr>
<td>*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* [*] = Cf. Foot-note to Table 1.

Average 1.8

TABLE 9.
Result of Experiment 9.
Yakriton was used in the amount of 1 R.A.U. per kilo of body weight at 4 p.m. for 4 consecutive days from the 3rd day of the control experiment.

<table>
<thead>
<tr>
<th>No. of rabbits</th>
<th>Date of experiment</th>
<th>Experiment</th>
<th>Body weight (in kilos)</th>
<th>Amount of santonine dye excreted</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lapse of time after santsol injection</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0°-1°</td>
</tr>
<tr>
<td>No. 41</td>
<td>22. VI</td>
<td>Control</td>
<td>2.13</td>
<td>48</td>
</tr>
<tr>
<td>(6435)</td>
<td></td>
<td>Yakriton</td>
<td>2.14</td>
<td>66</td>
</tr>
<tr>
<td>No. 43</td>
<td>23. *</td>
<td>Control</td>
<td>2.03</td>
<td>24</td>
</tr>
<tr>
<td>(6438)</td>
<td></td>
<td>Yakriton</td>
<td>2.06</td>
<td>44</td>
</tr>
<tr>
<td>No. 45</td>
<td>24. *</td>
<td>Control</td>
<td>2.50</td>
<td>24</td>
</tr>
<tr>
<td>(6442)</td>
<td></td>
<td>Yakriton</td>
<td>2.52</td>
<td>36</td>
</tr>
<tr>
<td>*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* [*] = Cf. Foot-note to Table 1.

Average 1.7

tonine dye excreted was larger in the yakriton experiment than in the control experiment in all the rabbits without exception.

Experiment 6. As is shown in Table 6, the whole amount of santonine dye excreted was larger in the yakriton experiment than in the control experiment in all the rabbits without exception, and the influence of yakriton was more remarkable in this experiment than in Exp. 5 (Cf. Table 5). This result was completely coincident with that of my own experiment reported in Part 1) (Cf. Table 1 of Part 1) and with that of Takusugi's and Miyamoto's 2) experiment.
Studies on the Detoxicating Hormone of the Liver (Yakriton). XCIV.

TABLE 10.

Result of Experiment 10.

Yakriton was used in the amount of 1 R.A.U. per kilo of body weight at 9 a.m. for 4 consecutive days from the 4th day of the control experiment.

<table>
<thead>
<tr>
<th>No. of rabbits</th>
<th>Date of experiment</th>
<th>Experiment</th>
<th>Body weight (in kilos)</th>
<th>Amount of santonine dye excreted</th>
<th>Ratio of increase by use of yaktron</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lapse of time after santonol injection</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0°-1° 1°-2° 2°-3° 3°-4° 4°-5° 5°-6°</td>
<td></td>
</tr>
<tr>
<td>No. 4942. VI</td>
<td>(6454) 29.</td>
<td>Control</td>
<td>2.18</td>
<td>32 8 3 1 - - 1</td>
<td>44 Decrease</td>
</tr>
<tr>
<td>No. 4423.</td>
<td>(6455) 30.</td>
<td>Yakriton</td>
<td>2.18</td>
<td>28 6 2 + + -</td>
<td></td>
</tr>
<tr>
<td>No. 4634. 1 V</td>
<td>(6445)</td>
<td>Control</td>
<td>2.10</td>
<td>18 5 1 + + +</td>
<td>24 1.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Yakriton</td>
<td>2.13</td>
<td>18 8 2 + + +</td>
<td></td>
</tr>
</tbody>
</table>

* Almost no change.

Experiment 7. As is shown in Table 7, the whole amount of santonine dye was almost unchanged in rabbits Nos. 31, 35 and 39, but slightly decreased in the others.

Experiment 8. As is shown in Table 8, the whole amount of santonine dye excreted increased remarkably more in the yakriton experiment than in the control experiment in all the rabbits without exception. This result was completely coincident with that of my own experiment reported in Part 11 of the present study (Cf. Table of Part 1).

Experiment 9. As is shown in Table 9, the whole amount of santonine dye excreted was remarkably larger in the yakriton experiment than in the control experiment in all the rabbits without exception.

Experiment 10. As is shown in Table 10, the whole amount of santonine dye was smaller in the yakriton experiment than in the control experiment in all the rabbits without exception.

The results of my own experiments above mentioned, are shown briefly in Table 11.

According to these results it will be known that the effect of yakriton will be different, if the way of "yakritisation" is different. Now we shall see the results, not in different individuals, but also in one and the same* rabbit.

TABLE 11.

Difference of effect of yakriton according to different ways of yakritisation.

<table>
<thead>
<tr>
<th>No. of experiments</th>
<th>Average ratio of increase by use of yakriton</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. 1</td>
<td>*</td>
</tr>
<tr>
<td>No. 2</td>
<td>+</td>
</tr>
<tr>
<td>No. 3</td>
<td>+</td>
</tr>
<tr>
<td>No. 4</td>
<td>1.5</td>
</tr>
<tr>
<td>No. 5</td>
<td>1.5</td>
</tr>
<tr>
<td>No. 6</td>
<td>1.7</td>
</tr>
<tr>
<td>No. 7</td>
<td>+</td>
</tr>
<tr>
<td>No. 8</td>
<td>1.8</td>
</tr>
<tr>
<td>No. 9</td>
<td>1.7</td>
</tr>
<tr>
<td>No. 10</td>
<td>*</td>
</tr>
</tbody>
</table>

* One and the same rabbits used in my experiment were: No. 2 and No. 32, No. 7 and No. 31, No. 8 and No. 34, No. 9 and No. 36, No. 10 and No. 38, No. 11 and No. 37, No. 12, and No. 39, No. 16 and No. 41, No. 19 and No. 43, No. 20 and No. 45, and, No. 26 and No. 46.
Discussion.

From the results of experiments in Part 1\(^1\) and Part 2 of the present study, in which the ability of yakriton to strengthen the detoxication of sodium santonate by the liver was studied, the following facts will be known:

1. Yakriton is more effective when used in a large amount than when used in a small amount. Because, in Exp. A in Part 1, yakriton was more effective when used in 1 or 2 R.A.U. per kilo of body weight than when used in 1/5 or 1/2 R.A.U. per kilo (Cf. Table 1 of Part 1). In Part 2, it was more effective in Exp. 4 than in Exp. 2 (Cf. Tables 2, 4 and 11). Yakriton was used in the amount of 2/5 R.A.U. per kilo of body weight in the former and used in the amount of 1/5 R.A.U. per kilo in the latter.

2. Yakriton is more effective when the interval between its use and santsol injection is short than when it is long. Because it was more effective in Exp. 6 and Exp. 8 than in Exp. 5 and Exp. 7 (Cf. Tables 5, 6, 7, 8 and 11). Santsol was injected 30 minutes after yakriton injection in the former two, and 17 hours and 30 minutes after it in the latter two. And yakriton was more effective in Exp. 4 than in Exp. 3 (Cf. Tables 3, 4 and 11). Santsol was injected 30 minutes after the last yakriton injection in Exp. 4, and it was injected 17 hours and 30 minutes after the last yakriton injection in Exp. 3 (Cf. Figs. 1 and 2).

3. When yakriton is repeatedly used, its effect is piled up or accumulated. Because, in Exp. A in Part 1,\(^1\) yakriton used in the amount of 1/2 R.A.U. per kilo of body weight at one time was not always effective, while its use in the same amount for 4 consecutive days was remarkably effective (Cf. Table 1 of Part 1). In Exp. 4 of Part 2, yakriton used in the amount of 2/5 R.A.U. per kilo of body weight for 5 consecutive days was remarkably effective (Cf. Table 4).

4. When yakriton is used in a too large amount, it will probably not be so effective. Because yakriton was more effective in Exp. 9 than in Exp. 10. Santsol was injected 30 minutes after the last yakriton injection in Exp. 10 and it was injected 17 hours and 30 minutes after the last yakriton injection in Exp. 9 (Cf. Figs. 5 and 6). Yakriton was not effective in Exp. 10, probably because the amount used was too large, while it was effective in Exp. 9, undoubtedly because in that experiment santsol was injected when the effect of yakriton was weakened as the time passed.
As has been shown in a number of reports* published from this Laboratory, yakriton is the most effectual when used in an appropriate amount (R.A.U.). It does not follow that a larger amount is better than a small amount. There are instances in which 1/5 R.A.U. is much more efficacious than 1 R.A.U.

Remarks.

In 1929 Prof. Sato5) reported that yakriton has two contrary effects, the pro-effect and the con-effect, which may seem completely contrary to each other, and that some poisons are detoxicated by the pro-effect, some by the con-effect and others by the combined effect of them.

From these results of my own experiments, the effect of yakriton to strengthen the detoxication of sodium santonate by the liver exists probably in the con-effect. For more precise study of it, many more experiments would be necessary.

It may also be remarked that yakriton was effective in Exp. 5, while it was not in Exp. 7 (Cf. Tables 5, 7 and 11). So it will not necessarily follow the late effect of yakriton used in 2 R.A.U., for instance, is stronger than 1 R.A.U.

It is to be remarked here that, if the present experiments had not been done in a fasting state, the effect of yakriton might have been somewhat different, if Prof. Sato's6) study concerning hunger is taken into consideration.

* For instance;
He reported that, in his study on the Effect of Yakriton against Acute Phosphorus Poisoning, yakriton used in the amount of 1/4 R.A.U. was more effective than in that of 1/2, 1, 5 or 50 R.A.U.
He reported that, in his study on the Effect of Yakriton on Uranyl Nephritis, yakriton used in the amount of 1/2 R.A.U. was more effective than in that of 1 R.A.U.
He reported that, in his study on the Effect of Yakriton upon Chromic Nephritis, yakriton used in the amount of 1/2 R.A.U. was more effective than in that of 1 R.A.U.
1) The pro-effect is weak in its strength at the time of injection, while its maximum will occur much later, after the maximum of the con-effect is over.
2) The con-effect manifests itself most strongly at the time of injection, and leaves only a moderate effect thereafter, while its late effect will still be seen even after the pro-effect is over.
Wakakuri reported that he could strengthen the detoxication of sodium santonate by the liver in rabbits, administered perorally with vitamin B complex in a large amount for a long time, but Takasugi and Miyamoto, and myself could attain the same result as his by a single use of yakriton. It is most likely due to the direct effect of yakriton upon the liver than to its vitamin B mobilizing or sparing effect.

It was reported by Lewin, Miura, Ogata, Hayashi, Takakame, Asada, Kato and Ito that santonine or sodium santonate would exert an action as an antihelminthic, after it was transformed into the santonine dye or satogenin (oxisantonine) by the liver. Ito stated that he could strengthen the action of santonine or sodium santonate as an antihelmintic by means of decholen, a chologogue, which increased the amount of santonine dye produced by the liver. So I presume that the antihelminthic action of santonine or sodium santonate can be strengthened by means of yakriton too, which is used in a relatively large amount a short time before an administration of santonine or sodium santonate.

Summary.

I investigated the effect of yakriton upon strengthening the detoxication of sodium santonate by the liver in different phases of "yakritisation," and obtained results as follow:

1. In cases of a single use of yakriton 30 minutes prior to santsol injection, it was not always effective when it was used in the amount of 1/5 or 1/2 R.A.U. per kilo of body weight, while it was remarkably effective when used in the amount of 1 or 2 R.A.U. per kilo (Cf. Table 1 of Part I).

2. In cases of yakriton used for 5 consecutive days, it was not always effective when used in the amount of 1/5 R.A.U. per kilo of body weight, while it was effective when used in the amount of 2/5 R.A.U. per kilo (Cf. Tables 1, 2, 3, 4 and 11).

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7) K. Wakakuri, Jikken Shokwakibyo Gaku, 1937, 12, 1597.
11) H. Hayashi, Jikken Iho, 1920, 6, 504.
13) Ky. Takakame, and J. Asada, Okayama Igakkai Zassi, 1928, No. 400, 73.
15) Sh. Ito, Keio Igaku, 1932, 12, 2053.
16) Sh. Ito, Keio Igaku, 1933, 13, 73.
3. In the case of a single use of yakriton in the amount of 1 or 2 R.A.U. per kilo of body weight, it was not always remarkably effective when used 17 hours and 30 minutes prior to santsol injection, while it was always decidedly effective when used 30 minutes prior to santsol injection (Cf. Tables 5, 6, 7, 8 and 11).

4. In cases of yakriton used in the amount of 2/5 R.A.U. per kilo of body weight for 5 consecutive days, it was not always effective when the last yakriton injection was performed 17 hours and 30 minutes prior to santsol injection, but it was remarkably effective when the last yakriton injection was performed 30 minutes prior to santsol injection (Cf. Tables 3, 4 and 11).

5. In cases of yakriton used for 4 consecutive days, it was effective when it was used in the amount of 1/2 R.A.U. per kilo of body weight and the last injection of it was performed 30 minutes prior to santsol injection (Cf. Table 1 of Part 1), also when it was used in the amount of 1 R.A.U. per kilo and the last injection was performed 17 hours and 30 minutes prior to santsol injection, while it was not effective when it was used in the amount of 1 R.A.U. per kilo and the last injection of it was performed 30 minutes prior to santsol injection (Cf. Table 9, 10 and 11).

6. Where yakriton was used in the amount of 1/2 R.A.U. per kilo of body weight once a week for a month, it was effective, and the liver power strengthened by use of yakriton in this way remained potent even after a lapse of a month, in spite of no additional use of it (Cf. Table 2 A of Part 1)1).

Conclusions.

The results of my experiments, described above, concerning the effect of yakriton upon strengthening the detoxication of sodium santonate by the liver led me to the following conclusions:

1. The effect of yakriton will be remarkable when it is used in a relatively large amount and not long before the administration of sodium santonate.

2. If yakriton is used in a moderate amount repeatedly, the effect in question will be piled up or accumulated.

3. If yakriton is used in an excessive amount, its effect will show itself after a long lapse of time from its injection.

4. Effect of yakriton, used in a moderate amount and way, will remain potent for a long time.