Studies on the Evaluation of Adsorbent for Primary Treatment in Paraquat Poisoning

Manabu Kitakouji, Tamotsu Miyoshi, Seiki Tanada and Takeo Nakamura

Department of Public Health, School of Medicine, The University of Tokushima, Tokushima

INTRODUCTION

Paraquat (1, 1'-dimethyl-4, 4'-dipyridyl chloride) is a non-hormonal, non-selective herbicide. In Japan, paraquat was registered as an agricultural chemical in 1965. However, since paraquat is widely used because of its superior herbicidal effect, many people have died through accidental, suicidal or homicidal ingestion of paraquat, and the number of dead has increased every year. In order to reduce the number of accidental poisonings caused by doses or mis-ingestion, emetics, blue azo dye and specific odor substances were added to paraquat preparations in 1979, 1982 and 1985, respectively.

Paraquat has a local irritant effect and causes contact dermatitis. In the case of oral ingestion, paraquat stimulates the mucous membrane of the digestive tract, resulting in vomiting, hematemesis and so on. Paraquat is rapidly absorbed through the digestive tract and affects the central nervous system by inducing disturbances of consciousness, convulsions, etc. when a large quantity is ingested. Furthermore, in the state of shock, some cases of death have occurred. Emergency treatment for paraquat poisoning involves methods which minimize the internal absorption by excretion of paraquat through the digestive tract and methods which remove paraquat in the blood. The former method involves gastrointestinal lavage and the administration of a purgative. The latter utilizes activated carbon hemoperfusion, with reported survival cases. On the other hand, a method which hinders the absorption of paraquat by adsorbents has been discussed. As adsorbents, the effectiveness of aluminium silicate, bentonite, activated carbon and cation exchange resin among others, have been reported.

In this study, we discussed the characteristics of removal of paraquat in vitro by adsorbent in the primary treatment of paraquat poisoning and the efficacy of various adsorbents was examined.

MATERIALS AND METHODS

1. Materials

The paraquat used was a commercial preparation (Gramoxone S, Nihon Nohyaku Co., Ltd.) and its concentration was indicated as 24%.

Thirteen kinds of activated carbons (Hokutan Kogyo Ltd., Sigma Chemical Co., Fujisawa Chemical Ind. Ltd., Kanto Chemical Co., Kurare Chemical Ltd., Takeda Chemical Ind. Ltd., Nakarai Chemical Ltd., Kureha Chemical Ltd., Wako Pure Chemical Ind. Ltd., and Tsurumi Coal Ltd.), two kinds of bone charcoals (Naruto Chemical Ltd. and Wako Pure Chemical Ind. Ltd.), natural zeolite (San Zeolite Ind. Ltd.), five kinds of synthetic zeolites (Wako Pure Chemical Ind. Ltd. and Mizusawa Chemical Ind. Ltd.), four kinds of molecular sieves (Fuji-Davison Chemical Ltd. and Wako Pure Chemical Ind. Ltd.), five kinds of cation exchange resins (Organo Ltd.), kayakalexate (Torii Co. Ltd.), vitachange (Wako Pure Chemical Ind. Ltd.), alumina gel (Mizusawa Chemical Ind. Ltd.), silica gel (Mizusawa Chemical Ind. Ltd.), diatomaceous earth (Wako Pure Chemical Ind. Ltd.), bentonite (Wako Pure Chemical Ind. Ltd.), gelatin (Wako Pure Chemical Ind. Ltd.), agar (Wako Pure Chemical Ind. Ltd.) and dialdehyde starch (Nakarai Chemical Ltd.) were commercially obtained to be used as adsorbents.

2. Methods

1) Removal Capacity of Paraquat

The removal capacity of each of the forty materials was determined in vitro. Five hundred
milligrams of adsorbent were shaken with 50 ml of paraquat solution which was diluted with artificial gastric juice (ca. 800 mg/l) at a constant temperature of 37°C for 24 hrs. Artificial gastric juice was prepared according to the method described in the Japanese Pharmacopoeia. After extraction using a Sep-Pak C₁₈ cartridge for the filtrate, the paraquat concentration was measured photochemically according to the method of Calderbank and Yuen.

2) Removal Rate of Paraquat

The removal rate of the paraquat-artificial gastric juice/adsorbent system was measured at 37°C. Five grams of adsorbent were placed in one liter of a stirred paraquat solution (ca. 800 mg/l). Five milliliters of the suspension were taken up at regular intervals, and the paraquat concentration was measured.

RESULTS AND DISCUSSION

1. Capacity for Removal of Paraquat by Various Removers

Table 1 shows the paraquat removal ratios of fifteen types of carboneous materials. Table 2 shows the removal ratios of ten types of zeolites and molecular sieves, and Table 3 shows the ratios of fifteen kinds of cation exchange resins and other materials. The removal ratio of activated carbon was 22.91-42.14 %, and that of bone charcoal was 10.61-23.13 %. Although we tried to correlate the removal ratio and physicochemical properties of activated carbon, no correlation was found. In the case of zeolite or molecular sieves, the removal ratios were indicated as 2.25-29.24 %, and their values were lower than that of activated carbon. It seems that the removal ratio of paraquat is relative to pore size of the zeolite or the molecular sieve. When cation exchange resins including káyexalate were used, the removal ratios were higher than those of the activated carbon, bone charcoal, zeolite and molecular sieve. It was shown to be 82.45-98.57 %. The removal ratio of vitachange, which is used for the measurement of vitamin B₁, was 51.77 %. This value is also higher than that of activated carbon. In the cases using alumina gel and silica gel, the removal ratio was the same as that of the synthetic zeolite and the molecular sieve. The

<table>
<thead>
<tr>
<th>No.</th>
<th>Adsorbent</th>
<th>Removal Ratio (%)</th>
<th>No.</th>
<th>Adsorbent</th>
<th>Removal Ratio (%)</th>
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<tbody>
<tr>
<td>1</td>
<td>Activated Carbon 4-8 mesh</td>
<td>22.91</td>
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<td>Activated Carbon 4-7 mesh</td>
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<td>Activated Carbon 4-14 mesh</td>
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<td>Activated Carbon 4-7 mesh</td>
<td>40.90</td>
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<td>3</td>
<td>Activated Carbon 4-8 mesh</td>
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<td>Activated Carbon 4-7 mesh</td>
<td>40.99</td>
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<td>12</td>
<td>Activated Carbon 4-7 mesh</td>
<td>41.32</td>
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<td>13</td>
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<td>42.14</td>
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<td>6</td>
<td>Activated Carbon 4-8 mesh</td>
<td>33.57</td>
<td>14</td>
<td>Charcoal Bone 7-20 mesh</td>
<td>10.61</td>
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<td>7</td>
<td>Activated Carbon 4-7 mesh</td>
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<td>15</td>
<td>Charcoal Bone powder</td>
<td>23.13</td>
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<td>8</td>
<td>Activated Carbon 32-48 mesh</td>
<td>39.92</td>
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Initial conditions: Co; 781.348 mg/l, pH; 1.52

<table>
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<tr>
<th>No.</th>
<th>Adsorbent</th>
<th>Removal Ratio (%)</th>
<th>No.</th>
<th>Adsorbent</th>
<th>Removal Ratio (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>Natural Zeolite</td>
<td>13.54</td>
<td>21</td>
<td>Synthetic Zeolite F-9 14-30 mesh</td>
<td>29.24</td>
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<td>17</td>
<td>Synthetic Zeolite A-3 4-8 mesh</td>
<td>3.72</td>
<td>22</td>
<td>Molecular Sieve 4A 4-8 mesh</td>
<td>11.21</td>
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<tr>
<td>18</td>
<td>Synthetic Zeolite 4A 4-8 mesh</td>
<td>2.25</td>
<td>23</td>
<td>Molecular Sieve 5A 1/16</td>
<td>3.78</td>
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<tr>
<td>19</td>
<td>Synthetic Zeolite A-4 4-8 mesh</td>
<td>5.82</td>
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<td>Molecular Sieve 5A 4-8 mesh</td>
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<tr>
<td>20</td>
<td>Synthetic Zeolite F-9 4-8 mesh</td>
<td>19.58</td>
<td>25</td>
<td>Molecular Sieve 13X 4-8 mesh</td>
<td>18.94</td>
</tr>
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</table>

Initial conditions: Co; 781.348 mg/l, pH; 1.52
Table 3 Removal Ratio of Paraquat by Cation-exchange Resins and Other Materials.

<table>
<thead>
<tr>
<th>No.</th>
<th>Adsorbent</th>
<th>Removal Ratio (%)</th>
<th>No.</th>
<th>Adsorbent</th>
<th>Removal Ratio (%)</th>
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<tbody>
<tr>
<td>26</td>
<td>Amberlite IR-124T</td>
<td>82.45</td>
<td>34</td>
<td>Silica Gel</td>
<td>4.25</td>
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<td>27</td>
<td>Amberlite IR-120B</td>
<td>88.44</td>
<td>35</td>
<td>Diatomaceous Earth</td>
<td>21.11</td>
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<tr>
<td>28</td>
<td>Amberlite CG-120</td>
<td>88.46</td>
<td>36</td>
<td>Aluminum Silicate</td>
<td>34.44</td>
</tr>
<tr>
<td>29</td>
<td>Amberlite 200C</td>
<td>91.43</td>
<td>37</td>
<td>Bentonite</td>
<td>45.78</td>
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<tr>
<td>30</td>
<td>Amberlite IR-122</td>
<td>98.57</td>
<td>38</td>
<td>Gelatin</td>
<td>0.25</td>
</tr>
<tr>
<td>31</td>
<td>Kayexalate</td>
<td>98.55</td>
<td>39</td>
<td>Agar Powder</td>
<td>0.00</td>
</tr>
<tr>
<td>32</td>
<td>Vitachange</td>
<td>51.77</td>
<td>40</td>
<td>Dialdehyde Starch</td>
<td>0.00</td>
</tr>
<tr>
<td>33</td>
<td>Alumina Gel 4-8 mesh</td>
<td></td>
<td></td>
<td></td>
<td>4.15</td>
</tr>
</tbody>
</table>

Initial conditions: Co; 781.348 mg/l, pH; 1.52

removal ratios of diatomaceous earth, aluminum silicate and bentonite were 21.11, 34.44 and 45.78%, respectively, and were comparable to that of activated carbon. Gelatin, agar and dialdehyde starch hardly removed paraquat.

Activated carbon has been used as medicated carbon for the purpose of detoxification. In direct hemoperfusion, activated carbon is the main material, and its effectiveness has been sufficiently assessed. However, the amount of paraquat removed by activated carbon is not sufficient. In our investigation, no significant correlation between the physicochemical properties of activated carbon and the ratio of paraquat removal was found. However, from the fact that the ratio of paraquat removal is different for different activated carbons, it is assumed that an increase in the ratio of paraquat removal by a modification of the properties of activated carbon may be possible.

Although zeolites and molecular sieves have been used in paraquat removal on the basis of the fact that paraquat is inactivated by contact with clay in the soil. It was found that the removal ratio was affected by the pore size of the zeolite or the molecular sieve, and using vitachange, a kind of synthetic zeolite, the removal ratio was also affected by the particle size of the remover.

In recent years, sodium polystyrene sulfonate (kayexalate, kalimate) has been used for the treatment of paraquat poisoning, however, it has the drawback that the electrolyte balance of the body fluid is disrupted.

Dialdehyde starch has been used in the removal of urea. It utilizes a bonding mechanism between its aldehyde group and urea. We expected that there would be removed by bonding between dialdehyde starch and paraquat, but paraquat removal by dialdehyde starch was not found.

2. Removal Rate of Paraquat by Various Removers

Fig. 1 shows the variations of paraquat concentration with elapsed time with five kinds of activated carbons (Nos. 1, 4, 7, 8, 10), Fig. 2 the variations with synthetic zeolite (No. 20), a molecular sieve (No. 24), vitachange (No. 32), aluminum silicate (No. 36) and bentonite (No. 37), and Fig. 3 the variations with four kinds of cation exchange resins (Nos. 26, 27, 29, 30) and kayexalate (No. 31). Activated carbon No. 8 had a faster removal rate than other activated carbons. The difference could be based upon the difference in particle size. Synthetic zeolite and molecular sieves had slow removal rates because their
removal ratios were small. In the case of vitachange (No. 32), the paraquat concentration decreased in the first 5 minutes; however, the subsequent paraquat concentration gradually increased. After 60 minutes of elapsed time, it reached a plateau. Aluminum silicate (No. 36) also showed the same tendency. These phenomena of decreases and then increases in the concentration of paraquat are explained by ion exchange action that occurs between vitachange or aluminum silicate and the paraquat cation. It is considered that the binding force is weak and the cation which was exchanged is recombined. In the cases using cation exchange resins, the paraquat removal rate was faster than with any other remover; i.e., activated carbon, zeolite and the others. The removal rate by kayexalate (No. 31) was the fastest and it reached at plateau after 5 minutes of elapsed time. The concentration of paraquat at that time was 11.5 mg/l. The reason that kayexalate shows the highest removal rate may be thought that the finer the mesh size, the greater the external surface area. The removal rates by cation exchange resins (Nos. 26, 27, 29, 30) were successively faster in the order No. 27 > No. 30 > No. 26 > No. 29. The degrees of cross-linkage (divinylbenzene contents) were 8% (No. 27), 10% (No. 30), 12% (No. 26) and 20% (No. 29). It was concluded that the removal rate was dominated by the degree of cross-linkage of the cation exchange resin. The removal rate using No. 29 was slower than that of other cation exchange resins. This result can be explained by the fact that No. 29 is macroreticular, while Nos. 26, 27 and 30 are gel-type cation exchange resins.

No suitable antidote has been found for the treatment of paraquat poisoning. Therefore, it is a key point that paraquat be excreted as rapidly as possible. At present, gastrointestinal lavage, administration of an adsorbent, forced diuresis and blood purification have been performed. In this investigation, we tried to evaluate paraquat removal using forty kinds of materials. A small amount of fundamental study has been done on paraquat removal. Okoneck, et al. proposed activated carbon as a suitable adsorbent. Donald, et al. proposed cation exchange resin. The results from our investigation show that cation exchange resin was a suitable remover from the standpoint of removal ratio and rate. But, because of its poor selectivity, it causes an electrolyte imbalance in the body fluid. With some surface modification, activated carbon has the possibility of removing greater amounts of paraquat. We will discuss this subject at a later time.

SUMMARY

An evaluation of adsorbent for the treatment of paraquat poisoning was performed. Forty kinds of materials (activated carbons, zeolites, molecular sieves, cation exchange resins, etc.) were used as removers, and the removal ratios and removal rates in vitro were discussed. The results show that cation exchange resin had a high removal ratio and rate. It was concluded that the removal rate of paraquat
was mainly dominated by the degree of cross-linkage in the cation exchange resin. Moreover, it was found that cation exchange resins of the gel-type were more advantageous than those of the macroreticular type. Sodium polystyrene sulfonate, kayexalate, showed the greatest removal ratio and rate because of its great external surface area.

REFERENCES

パラコート中毒における初期治療を
目的とした吸着剤の評価に関する研究

北 小 路 学・三 好 保・棚 田 成 紀・中 村 武 夫

パラコート中毒を目的として吸着剤の評価に関する研究を行った。40種の材料（活性炭、ゼオライト、モレキュ
ラーサー、陽イオン交換樹脂等）を除去剤として使用し、in vitro における除去率、除去速度について検討した。
その結果、陽イオン交換樹脂が除去率、除去速度とも高値を示した。陽イオン交換樹脂によるパラコートの除去速度
は、主に樹脂の架橋度によって支配されることが示唆された。また、ゲル型の陽イオン交換樹脂の方がポーラス (MR)
型の樹脂より有利であることが見出された。特に、ポリスチンスルホン酸ナトリウムであるケイキサレートは、そ
の外部表面積が大きいことにより、最大の除去率、除去速度を示した。

Key words: Paraquat, Removal by adsorption, Removal ratio, Removal rate

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