In Vitro Adsorption Characteristics of Diquat by Activated Charcoal for Primary Treatment of Acute Poisoning

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For the evaluation on the efficacy of activated charcoal as an antidote in acute diquat poisoning, the adsorption characteristics of diquat in distilled water and in physiological saline solution were investigated.

The amount of diquat adsorbed onto activated charcoal in physiological saline solution was larger than that in distilled water. The enhancing effect of sodium chloride on diquat removal by activated charcoal was observed.

The adsorption rate of diquat onto activated charcoal was also enhanced by the addition of saline. The correlations between the adsorptivity for diquat and properties of activated charcoal were not significant.

These results suggest that the increase of adsorptivity of activated charcoal for diquat might be due to the increase in electrostatic interaction between the surface on which an electrical double layer was formed by saline and diquat.

Introduction

Diquat (1, 1'-ethylene-2, 2'-dipyridylium dibromide) is a popular herbicide similar in toxicity to paraquat. In Japan, cases of acute poisoning through accidental, suicidal or homicidal ingestion of paraquat occurred frequently from the late 1970s to the early 1980s. Hence, the production of highly concentrated (24%) paraquat preparations was discontinued in July 1986. At present, diquat (30%) and diquat (7%)-paraquat (5%) mixture preparations are marketed as alkylidipyridylium herbicides in Japan.

The oral LD₅₀ of diquat has been reported 400-440 mg/kg in rats. The value is about three times that of paraquat (130 mg/kg). Although the toxic intensity of diquat is weaker than paraquat, the toxicity of diquat is estimated to be equal to that of paraquat when the amounts of diquat and paraquat preparations ingested are the same.

Although many cases of paraquat poisoning have been reported, few reports on diquat poisoning have been published. Seo et al. reported six cases of diquat poisoning and worked out the lethality at 67%.

The principle in the emergency treatment for diquat poisoning is the same as that for paraquat poisoning. The basic care includes the selective excretion of the poison from the gastrointestinal tract by lavage and by the administration of adsorbents. Among adsorbents, activated charcoal is considered a reliable, safe and inexpensive antidote and is recommended for the removal of toxic substances.

Studies on the adsorption characteristics of diquat are few compared with those on paraquat.

To find an effective treatment of acute diquat
poisoning, we studied the adsorption characteristics of diquat by activated charcoal \textit{in vitro}.

\textbf{Methods}

The diquat used in the adsorption experiments was a commercial preparation (Reglox, Nihon Noyaku Co. Ltd., Tokyo) with a concentration of 30\%. The diquat used for the measurement of the calibration curve, purchased from Wako Pure Chem. Ind. Ltd., Osaka, was of a grade suitable for testing agricultural chemical residues.

The three kinds of activated charcoal used were No. 1 from Wako Pure Chem. Ind. Ltd., CDK1269, No. 2 from Kureha Chem. Ltd., BAC-MU, and No. 3 from Bamberg Co., Technicoal. The raw material of each activated charcoal was coconut shell (No. 1), petroleum pitch (No. 2) and coal (No. 3), respectively. Particle sizes ranged from 20 to 32 mesh. The physical properties are shown in Table 1.

Accurately weighed amounts of activated charcoal (about 20—50 mg) were mixed with 50 ml of diquat solutions at the indicated concentration in distilled water and in a physiological saline solution at 37\°C. After 24 hours, the concentration of unadsorbed diquat was determined at 310 nm by a Hitachi model 100-10 spectrophotometer. The amount of diquat adsorbed was calculated from the difference between the initial total amount of diquat and the amount of the unadsorbed diquat. The relationship between the amount of diquat adsorbed and the equilibrium concentration was plotted on log-log graph paper. Linearity was expressed in the Freundlich equation as below:

\[
\log V = \frac{1}{n} \log C + \log k,
\]

where \( V \) is the amount adsorbed, \( C \) the equilibrium concentration, and \( 1/n \) and \( k \) the constants. The equilibrium amounts of diquat adsorbed at each equilibrium concentration were estimated by the Freundlich equation.

The time course of adsorption was also examined at 37\°C in distilled water and physiological saline solution. Five grams of activated charcoal was added to 1,000 ml of stirred diquat solution (300 rpm, \textit{ca.} 2000 mg/l). Each diquat concentration in the suspension was measured at regular intervals.

The surface area and pore size of each activated charcoal products were measured with a Brunauer, Emett and Teller (B. E. T.) apparatus using nitrogen gas for its boiling temperature (—196\°C). Pore volume was calculated by the Dollimor-e Heal method.

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{figure1.png}
\caption{Adsorption Isotherm of Diquat by Activated Charcoal at 37\°C.}
\end{figure}

\begin{table}[h]
\centering
\caption{Physical Properties of Activated Charcoal}
\begin{tabular}{|c|c|c|c|c|}
\hline
Activated Charcoal & Surface Area (m\(^2\)/g) & Pore Volume (ml/g) & \\
& \(r<20 \\AA\) & 20<\(r<100 \\AA\) & \(r<100 \\AA\) \\
\hline
No. 1 & 849.98 & 0.455 & 0.046 & 0.501 \\
No. 2 & 1081.08 & 0.507 & 0.088 & 0.595 \\
No. 3 & 1268.06 & 0.596 & 0.099 & 0.695 \\
\hline
\end{tabular}
\end{table}

\begin{table}[h]
\centering
\caption{Equilibrium Amount of Diquat Adsorbed by Activated Charcoal}
\begin{tabular}{|c|c|c|c|c|c|}
\hline
Activated Charcoal & \multicolumn{5}{c|}{Amount Adsorbed (mg/g)} \\
& \(V\) at 1 mg/l & \(V\) at 10 mg/l & \(V\) at 100 mg/l & \(V\) at 1000 mg/l \\
& \(\text{H}_2\text{O}: \text{NaCl}\) & \(\text{H}_2\text{O}: \text{NaCl}\) & \(\text{H}_2\text{O}: \text{NaCl}\) & \(\text{H}_2\text{O}: \text{NaCl}\) \\
\hline
No. 1 & 4.7 & 5.4 & 12.3 & 15.3 & 32.3 & 43.4 & 84.4 & 123.2 \\
No. 2 & 1.5 & 15.0 & 5.8 & 32.9 & 22.5 & 72.2 & 87.7 & 158.3 \\
No. 3 & 0.7 & 3.0 & 2.8 & 9.2 & 11.2 & 27.9 & 44.3 & 84.6 \\
\hline
\end{tabular}
\end{table}

* \text{H}_2\text{O}: in distilled water, \text{NaCl}: in physiological saline solution.
Results

Figure 1 shows the adsorption isotherms of diquat onto activated charcoal in distilled water and physiological saline solution at 37°C. The logarithm of the amount adsorbed was plotted linearly against the logarithm of equilibrium concentration. The adsorption isotherm of diquat onto activated charcoal was of the Freundlich type. For each activated charcoal, the amount of diquat adsorbed in physiological saline solution was larger than that in distilled water.

Table 2 represents the amounts of diquat adsorbed at each equilibrium concentration. The difference between the amount adsorbed in distilled water and that in physiological saline solution was observed. The amount of diquat adsorbed by activated charcoal in physiological saline solution was more than that in distilled water at each equilibrium concentration.

Figure 2 shows the time courses of the amount of diquat adsorbed by activated charcoal at 37°C in distilled water and physiological saline solution. Adsorption in physiological saline solution was more than that in distilled water. This order was the same as that for equilibrium adsorption. The adsorption rate of diquat in physiological saline solution was faster than that in distilled water. Table 3 shows the amount of diquat adsorbed at each elapsed time and the kinetic constant of diquat adsorption by activated charcoal in the solutions. The kinetic constant was calculated by using the formula of a zero-order reaction. All activated charcoal had larger kinetic constant values in physiological saline solution. Compared with that in distilled water the kinetic constant value increments in physiological saline solution were 70% (No. 1), 195% (No. 2) and 206% (No. 3). In conclusion, diquat was effectively adsorbed by activated charcoal in physiological saline solution.

To determine which properties of adsorbents were important in diquat removal, the adsorption characteristics of diquat and physical properties of activated charcoal were investigated, but no significant correlations were found.

Discussion

The nature of acute poisoning by diquat is little known because cases are rarely reported. Considering the high diquat concentrations in commercial preparations, diquat poisoning must be as lethal as paraquat poisoning and therefore, deserves appropriate medical care.

In the primary treatment of acute poisoning, activated charcoal is commonly used as an effective adsorbent for removing diquat from the body. The adsorption rate and the kinetic constant of diquat adsorption were found to be significantly higher in physiological saline solution compared to distilled water.

Table 3. Amount of Diquat Adsorbed at Elapsed Time and Kinetic Constant

<table>
<thead>
<tr>
<th>Activated Charcoal</th>
<th>Amount Adsorbed (mg/g)</th>
<th>Kinetic Constant (mg/g/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5 min.</td>
<td>30 min.</td>
</tr>
<tr>
<td>No. 1</td>
<td>52.2*</td>
<td>79.4</td>
</tr>
<tr>
<td></td>
<td>(72.4)**</td>
<td>(110.0)</td>
</tr>
<tr>
<td>No. 2</td>
<td>31.7</td>
<td>62.3</td>
</tr>
<tr>
<td></td>
<td>(56.9)</td>
<td>(111.0)</td>
</tr>
<tr>
<td>No. 3</td>
<td>30.5</td>
<td>33.0</td>
</tr>
<tr>
<td></td>
<td>(60.0)</td>
<td>(74.4)</td>
</tr>
</tbody>
</table>

*: in distilled water,**: in physiological saline solution.
antidote\textsuperscript{18,11}. The adsorption capacity of activated charcoal for toxic substances is largely dependent on its pore structure\textsuperscript{14,10}. This study, however, revealed no correlations between the adsorptivity for diquat and physical properties, like surface area and pore volume. Activated charcoal presumably adsorbs more easily non-ionized molecules rather than ionized ones, and diquat is perfectly ionized in the liquid phase.

It is believed that anions in a saline solution are first adsorbed by activated charcoal. After an electrical double layer is formed on the surface of the activated charcoal, then the cations are adsorbed\textsuperscript{16}.

The adsorptivity for diquat in physiological saline solution was greater than in distilled water. Diquat removal by activated charcoal was enhanced in saline solution. The effects of saline addition on the adsorptivity of activated charcoal for toxic substance have previously been reported\textsuperscript{17,18}. Ryan \textit{et al}\textsuperscript{17} found that more sodium salicylate was adsorbed by activated charcoal in the presence of magnesium citrate, a purgative, than in distilled water. Lapierre \textit{et al}\textsuperscript{18} also reported that magnesium citrate actually enhanced the adsorptivity for aspirin in simulated intestinal solution and made the salicylate ionized. They concluded that the enhancement was due to the pH change in the simulated intestinal solution brought about by the addition of magnesium citrate.

In our experiments, the adsorptivity of activated charcoal for diquat was enhanced in the presence of sodium chloride. Honda \textit{et al}\textsuperscript{19} reported the enhanced adsorption of paraquat by activated charcoal in saline solution. They suggested that salting out resulted from saline addition. However, since the crystalline structure of paraquat is as ionic as diquat, salting out could not have taken place in the solution.

We have reported that the amount of paraquat adsorbed by activated charcoal was successively greater in the order of physiological saline solution > artificial gastric juice > distilled water\textsuperscript{20}. We concluded that the change in the amount of diquat adsorbed by activated charcoal was due to the saline concentration and not the pH in the solutions.

The enhancing effect on diquat removal by activated charcoal in physiological saline solution could be attributed to the increase in electrostatic interaction between the surface on which an electrical double layer is formed by saline and diquat.

**Conclusion**

To find out an antidote for diquat, a herbicide, its adsorptivity on activated charcoal was investigated in distilled water and physiological saline solution.

There was no significant relationship between the adsorptivity for diquat and the physical properties of activated charcoal.

The amount of diquat adsorbed and the rate of removal was greater and faster in physiological saline solution than in distilled water.

**References**

12) Yuen SH, Bagness JE, and Myles D: Spectrophotometric

急性農業中毒における初期処置を指向した活性炭に対するジクワットの吸着特性に関する研究

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急性ジクワット中毒の初期処置における経口解毒剤としての活性炭の評価に関し、水中および生理食塩水中でのジクワットの吸着特性について検討した。
生理食塩水中からの活性炭へのジクワット吸着量は、水中からの吸着量よりも高値であり、活性炭によるジクワット除去に対し、塩化ナトリウム共存による促進効果が認められた。また活性炭へのジクワットの吸着速度についても、生理食塩水中での値が高く、塩化ナトリウム添加による促進効果を認めた。ジクワット吸着量と活性炭の著性物との間には有意な相関性は認められなかった。
活性炭へのジクワット吸着量が増大した理由は、塩化ナトリウム共存により活性炭表面に形成された電気二重層とジクワットとの静電気的相互作用の増大に基づくことが推察された。

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