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Langmuir Isotherms of Diazepam on Glass Surfaces

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The adsorption of diazepam dissolved in distilled water, 5% dextrose solution, normal saline, Ringer's solution and lactate Ringer's solution on porous glasses with controlled surface area was investigated. The adsorption phenomena principally obeyed the Langmuir adsorption isotherm. The reciprocal plots of the amount of adsorption *vs.* concentration of diazepam suggested that the maximum amounts of diazepam adsorbed onto the glass surfaces were the same from four of the solutions, excluding the dextrose solution, but the adsorption strengths differed considerably. The decrease of the adsorption strength of diazepam in lactated Ringer's solution, Ringer's solution and normal saline compared with that in distilled water could be ascribed to the decrease of the activity coefficient of diazepam in these solvents.

Keywords——adsorption; diazepam; Langmuir adsorption isotherm; porous glass; adsorption strength; effective surface area

It is well known that potency loss of some drugs is often attributed to their adsorption on the inner surface of glass or plastic containers.[1] Recently, Mizutani *et al.* estimated the amounts of drugs adsorbed onto porous glasses and siliconized glasses with controlled surface area as a model of the container.[2,3] However, in their series of investigations, only one drug concentration was tested. As is well known, the amount of adsorption onto an adsorbent should be dependent on the solute concentration in the medium, if the adsorption is reversible. If the adsorption behavior were of the Langmuir type, the amount of adsorption would be expected to vary hyperbolically against the solute concentration in the medium at equiliblium. In this work, we studied the adsorption of diazepam, which is a typical minor tranquilizer, onto controlled-pore glasses and analyzed the results on the basis of the Langmuir adsorption isotherm.

Experimental

Materials——Diazepam (pure; from Takeda Chemical Industries, Ltd.) was used as an adsorbate. A controlled-pore glass (CPG-10, Electro-Nucleonics, Inc.) was used as an adsorbent. It had 94 m^2/g surface area and 226 Å mean pore diameter. As solvent, distilled water (Otsuka Pharmaceutical Co., Ltd.), 5% dextrose solution (Otsuka Pharm. Co.), normal saline (prepared in our laboratory), Ringer's solution (Termo Co.) and lactated Ringer's solution (Otsuka Pharm. Co.) were used. The pH range of all solutions were 5.4 to 6.5.

Methods——Experiments were performed according to the methods of Mizutani *et al.* as follows: 0.5 g portions of porous glass were packed in columns of 0.58×4.47 cm. Diazepam was dissolved at concentrations of 0.01, 0.02, 0.03, 0.05 and 0.1 mg/ml in each solvent. These solutions were applied to the columns at a flow-rate of 4.43 $ml/cm^2 \cdot min$ at room temperature 25 ± 1°C). Fractions of 1 ml were collected. The concentration of diazepam was determined by measuring the absorbance at 285 nm.

Results and Discussion

Typical adsorption patterns of diazepam in distilled water are shown in Fig. 1. The amount of diazepam adsorbed on glass surfaces was determined according to the method of Mizutani *et al.*[3] The experiments were performed three times for each solute concentration

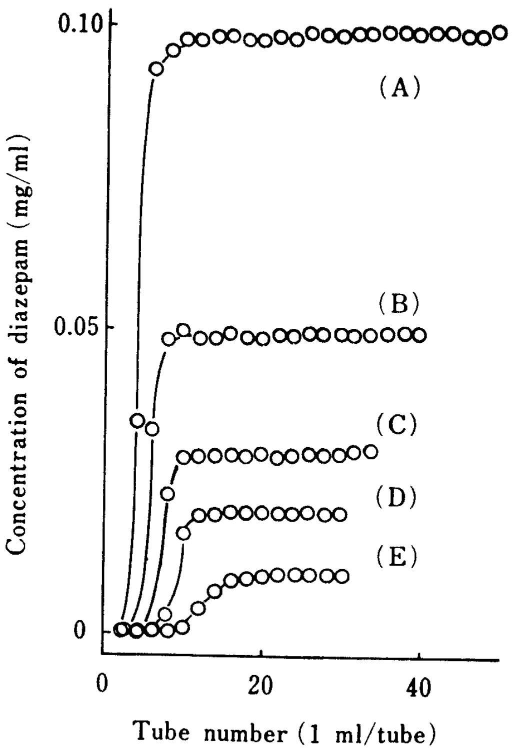

Fig. 1. Adsorption of Diazepam on Glass Surfaces Concentrations of the Solutions were 0.1 (A), 0.05 (B), 0.03 (C), 0.02 (D) and 0.01 (E) mg/ml

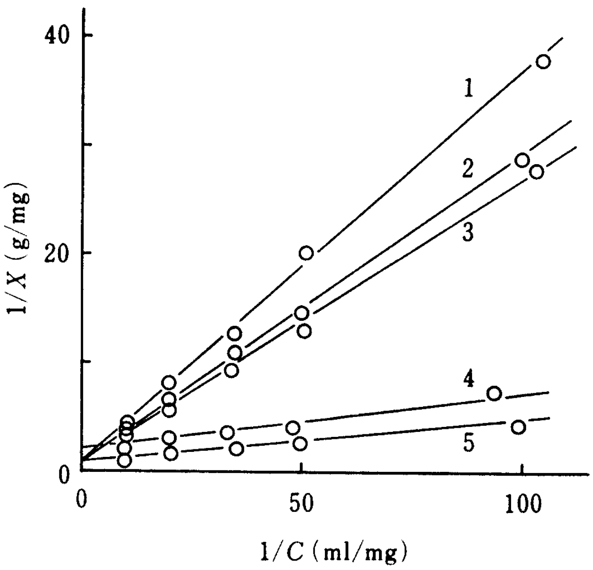

Fig. 2. Langmuir Plots of Diazepam Adsorbed on Glass Surfaces from Various Solutions

1, lactated Ringer's solution; 2, Ringer's solution; 3, normal saline; 4, 5% dextrose solution; 5, distilled water. X, amount of adsorption; C, concentration of diazepam.

in each solvent. The experimental data were reproducible within ±10% on the repeated runs. In Fig. 2, the reciprocal of the value of the adsorbed solute on glass surfaces is plotted against the reciprocal of the solute concentration in each solvent at equilibrium. The plots gave straight lines. This observation shows that the adsorption behavior of diazepam on glass surfaces essentially obeys the Langmuir adsorption isotherm (Eq. 1 or Eq. 2).

$$X = X_{\infty} \frac{KC}{1+KC} \quad (1)$$

$$\frac{1}{X} = \frac{1}{X_{\infty}} + \frac{1}{X_{\infty}K} \cdot \frac{1}{C} \quad (2)$$

where X is the amount of solute adsorbed on the surfaces of 1 g of the porous glass at a given solute concentration in the medium at equilibrium, X_{∞} is the maximum amount of solute adsorbed on the surfaces, C is the equilibrium concentration of unbound solute, and K is the parameter measuring adsorption strength. From the intercepts of the plots based on Eq. 2 on the ordinate in Fig. 2, and the slopes of the lines, we can obtain X_{∞} and K. Under the condition $KC \ll 1$, or $C \ll 1/K$, Eq. 1 can be reduced to the following equation:

$$X = X_{\infty}KC \quad (3)$$

Eq. 3 shows that the amount of adsorption should be proportional to solute concentration in the low concentration region. Under the condition $C \gg 1/K$, Eq. 3 can be reduced to the following equation:

$$X = X_\infty \tag{4}$$

Eq. 4 shows that at high concentration, the amount of adsorption should be constant, that is, independent of solute concentration.

It is interesting that in Fig. 2 the plots for all solvents except the dextrose solution had the same intercept on the ordinate but had different slopes. These observations suggested that the maximum amounts of solute adsorbed on the surfaces were the same in these solvents, except in the dextrose solution, but the adsorption strengths were considerably different from each other. The values of X_∞, K and $X_\infty KC$ obtained from Eq. 2 and Fig. 2 are summarized in Table I.

TABLE I. The Values of X_∞, K and $X_\infty KC$

	X_∞ (mg/g)	K (ml/mg)	$X_\infty KC$ (mg/g)[a]
Distilled water	1.05	23.8	25.2C
5% dextrose solution	0.45	55.6	25.0C
Normal saline	1.05	3.7	3.9C
Ringer's solution	1.05	3.5	3.7C
Lactated Ringer's solution	1.05	2.6	2.7C

a) Under the condition $C<<1/K$, $X=X_\infty KC$.

The fact that the values of X_∞ are the same among these solutions except for the dextrose solution means that the effective surface areas on which diazepam can be adsorbed are the same for these solutions; in other words, inorganic ions and lactate anion cannot be adsorbed on the negatively charged glass surfaces. On the other hand, dextrose molecules, which have no charge, may significantly reduce the effective surface area by so-called "sorption" into glass pores.[4]

The decrease of the adsorption strength of diazepam in lactated Ringer's solution, Ringer's solution and normal saline compared with that in distilled water can be ascribed to the decrease of the activity coefficient of diazepam in these solutions as a result of the interaction of positively charged diazepam[5] with negatively charged lactate anion or inorganic anions. The adsorption strength of diazepam in dextrose solution is almost the same as that in distilled water. This means that there is little interaction between diazepam and dextrose.

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