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Estimation of Diazepam adsorbed on Glass Surfaces and Silicone-coated Surfaces as Models of Surfaces of Containers[1)]

TAKAHARU MIZUTANI,* KAORUKO WAGI, and YOSHIE TERAI

Faculty of Pharmaceutical Sciences, Nagoya City University, Tanabe-dori, Mizuho-ku, Nagoya 467, Japan

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The amounts of diazepam adsorbed on silicone-coated glass surfaces (100 m^2) were 0.39 mg in 5% dextrose in water, 0.37 mg in lactated Ringer's solution, and 0.46 mg in Ringer's solution. The amounts of diazepam bound on non-coated glass surfaces were much lower (4—23 $\mu g/100\ m^2$) in the same solutions.

Keywords——diazepam; adsorption; container; glass surfaces; silicone-coated surfaces

Diazepam is a most useful minor tranquilizer and has been administered as an intravenous infusion in the treatment of eclampsia, convulsion, and tetanus. However, a potency loss due to adsorption on plastic *i.v.* bags has been reported.[2)] We have already investigated the adsorption of drugs on porous glass surfaces as a model of surfaces of glass containers.[3,4)] We have also reported the decreased activity of proteins adsorbed onto glass surfaces.[5)] Recently, glass containers coated with silicone have been used[6)] and the adsorption of secretin on silicone-coated glass surfaces has been reported.[7)] We also studied the adsorption of some drugs on silicone-coated porous glass.[8)] In this work, we determined the amounts of diazepam adsorbed on glass surfaces and silicone-coated surfaces.

Experimental

Meterials——Controlled-pore glass was used as a reference standard for surfaces of glass containers. The pore glass used was CPG-10 (pore diameter 240 Å; 100 μm particles) obtained from Electro-Nucleonics (Fairfield, NJ); it had a surface area of 97 m^2. After being washed with chromic acid mixture and then thoroughly with distilled water to neutrality in a column, the glass was dried at 180°. The silicone oil used was KF 96 (dimethyl polysiloxane), obtained from Shin-Etsu Chemicals. The pore glass was coated with silicone oil, precipitated in a water medium, and packed in a column according to the method described previously.[9)] The surface area of silicone-coated glass was determined to be 51.7 m^2/g with an Orr surface-area-pore volume analyzer, model 2100D. Diazepam was obtained from Maruco Pharmaceutical Co., Nagoya.

Methods——The amount of diazepam adsorbed on surfaces was estimated by frontal analysis. Coated and non-coated porous glasses (0.5 g) were packed in columns of 0.65×3.8 cm. Diazepam was dissolved at a concentration of 0.02 mg/ml in 5% dextrose in water (pH 6.5), Ringer's solution (pH 5.4), or lactated Ringer's solution (pH 5.9). These solutions were applied to columns at a flow-rate of 3 $ml/cm^2 \cdot min$ and at room temperature under normal lighting. The fraction volumes were 1 ml. The concentration of diazepam was determined by measurement of the adsorbance at 285 nm.

Results and Discussion

Figure 1 shows the adsorption patterns of diazepam in Ringer's solution. The amount of diazepam adsorbed on non-coated glass surfaces was about 4 $\mu g/100\ m^2$ and that on silicone-coated glass surfaces was 0.46 $mg/100\ m^2$. Similar adsorption patterns were obtained on both surfaces in lactated Ringer's solution and 5% dextrose in water. The amounts on non-coated surfaces were 23 μg in 5% dextrose solution and about 4 $\mu g/100\ m^2$ in lactated Ringer's solution and those on silicone-coated surfaces were 0.39 $mg/100\ m^2$ and 0.37 $mg/100\ m^2$, respectively.

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We have previously shown that the amounts of atropine (0.81 mg/100 m^2) and physostigmine (3.88 mg/100 m^2) adsorbed on silicone-coated glass surfaces in saline[8] are greater than those of atropine (0.05 mg/100 m^2) and physostigmine (0.08 mg/100 m^2) adsorbed on non-coated surfaces.[3] It has been shown that the adsorption of proteins on silicone-coated surfaces is caused by hydrophobic interaction,[8] so the adsorption of drugs on silicone-coated surfaces should also be due to hydrophobic bonding.

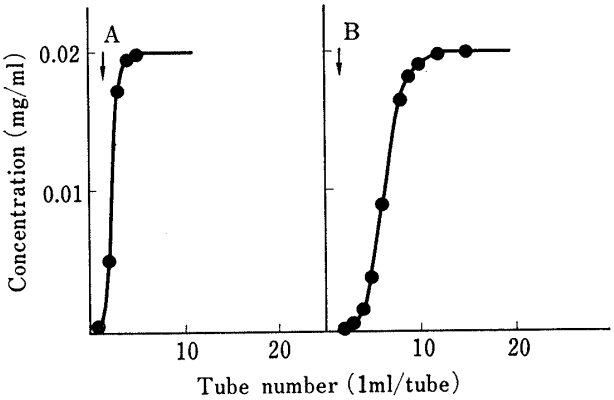

Fig. 1. Adsorption Patterns of Diazepam on Surfaces

Solutions containing diazepam at a concentration of 0.02 mg/ml in Ringer's solution were loaded on columns (0.65×3.8 cm, 0.5 g) of non-coated porous glass (A) and silicone-coated glass (B) at a flow-rate fo 3 ml/cm^2 min at room temperature. The fraction volumes were 1 ml. Arrows indicated the position of the column volume.

Parker and MacCara recently reported that diazepam injections were incompatible with plastic *i.v.* bags,[2] in which solutions showed greater than 24% loss of potency. It was shown that the loss was due to adsorption on a burette chamber (Venoset-78, Abbott Lab.) made of cellulose propionate. In this work, we showed that silicone-coated glassware or other apparatus is also incompatible with precise administration of diazepam, even though the amount of diazepam adsorbed on siliconized surfaces is low.

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References and Notes

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