daily injections with spiperone exactly as in control rats. Since this pretreatment with spiperone did not alter the acute response to pergolide, it became possible to do an experiment to see if spiperone given along with daily injections of pergolide would prevent the diminished response to acute pergolide injection. Fig. 2 shows the results of such a study. In control rats, the acute injection of pergolide caused a nine-fold increase in serum corticosterone. In rats pretreated with four daily injections of pergolide, the acute response to pergolide was greatly diminished. A statistically significant increase in corticosterone was produced by pergolide acutely in these rats, but the increase was only two-fold. In rats that had received spiperone along with daily injections of pergolide for four days, the acute injection of pergolide on day 5 again caused a nine-fold increase in serum corticosterone concentration. The decreased responsiveness that had occurred after daily administration of pergolide was totally prevented by daily co-administration of spiperone.

Discussion

These results strengthen the idea that the tolerance to the acute elevation of serum corticosterone by pergolide occurring after repeated treatment with pergolide is in fact related to adaptive changes in dopamine receptors. Previously, we had found that rats given daily injections of pergolide responded to quipazine with a normal rise in serum corticosterone concentration, indicating that corticosterone elevation by an agent acting other than through dopaminergic mechanisms occurred normally (Fuller & Snoddy 1981b). We had also shown that certain other effects of pergolide, e.g. decrease in dopamine turnover and decrease in serum prolactin concentration, showed a normal acute response to pergolide in rats pretreated with daily injections of pergolide (Fuller & Snoddy 1981b). The current finding that a dopamine antagonist, spiperone, prevents the altered responsiveness of the pituitary-adrenocortical system to acute administration of pergolide can most easily be explained by postulating that the diminished responsiveness occurred as a result of continued activation of dopamine receptors. The dopamine receptors that mediate corticosterone elevation by pergolide are believed to be central, since domperidone, which blocks dopamine receptors in the periphery (Laduron & Leysen 1979), is incapable of antagonizing the effect of pergolide (Fuller & Snoddy 1981a). Spiperone blocks the pergolide-induced elevation of corticosterone acutely (Fuller & Snoddy 1981a) and the development of tolerance after repeated pergolide injection, but does not itself cause supersensitivity to the pergolide effect, at least in the experimental conditions used.

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Adsorption of some antibiotics and other drugs on silicone-coated glass surfaces

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Drug adsorption on silicone-coated surfaces and non-coated glass surfaces was studied using porous glass as a reference standard for glass containers. Since glass surfaces coated with silicone can repulse a water layer, it is supposed that silicone-coated surfaces of pharmaceutical glass containers decrease adsorption of drugs. However, in practice, silicone-coated surfaces adsorb more secretin (Ogino et al 1979), insulin, atropine, physostigmine (Mizutani 1981a) and diazepam (Mizutani et al 1981) than non-coated glass surfaces (Mizutani & Mizutani 1978). A loss of potency of diazepam due to its adsorption on plastic i.v. bags has been reported (Parker & MacCara 1980). The purpose of this investigation was to confirm with some widely used antibiotics whether adsorption on silicone-coated glass surfaces as a general phenomenon was greater than that on non-coated glass surfaces. The amounts of drugs adsorbed on silicone-coated glass surfaces and non-coated porous glass surface (CPG-10 240Å, Electro-Nucleonics, Fairfield, N.J., U.S.A.) were estimated by elution of drug solution on columns according to Mizutani & Mizutani (1978). The column size of the non-coated pore glass column was 0·8 cm internal diameter × 4·5 cm length (2·25 ml, 1·12 g of pore glass, surface area 109 m^2) and that of silicone-coated pore glass, which was prepared by the previous method (Mizutani 1980), was 0·68 cm × 3·5 cm (1·26 ml, 0·63 g, surface area 25 m^2).

Drugs were dissolved in pH 7·2 phosphate-buffered saline. Streptomycin sulphate was used at 1 mg ml^{-1} and measured by absorbance at 215 nm. Potassium benzylpenicillin was used at 100 U ml^{-1} and measured

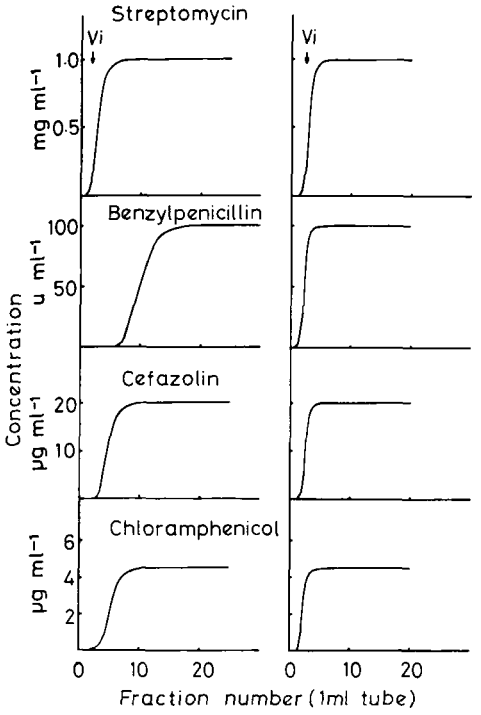

FIG. 1. Adsorption patterns of antibiotics onto the silicone-coated glass column (0·68 cm × 3·5 cm, surface area 25 m²) (left) and onto the non-coated glass column (0·8 cm × 4·5 cm, surface area 109 m²) (right) in phosphate-buffered saline at pH 7·2. Antibiotics are the same in both sides of the figure. Vi, inner volume of the column.

by absorbance at 230 nm. Cefazolin sodium (Fujisawa Pharm. Co., Japan) was used at 0·02 mg ml^{-1} and measured by absorbance at 270 nm. Chloramphenicol was used at 5 μg ml^{-1} and measured by absorbance at 278 nm.

Fig. 1 shows the patterns of drug adsorption onto silicone-coated glass columns. In phosphate-buffered saline at pH 7·2, the amount of streptomycin, benzylpenicillin, cefazolin, and chloramphenicol adsorbed onto silicone-coated glass surfaces (100 m²) were 3·96 mg, 3300 U (2·07 mg), 0·22 mg, and 0·064 mg, respectively. The amounts were higher than those onto non-coated glass surfaces (Fig. 1). The antibiotics adsorbed weakly or not at all onto non-coated glass surfaces and passed through the non-coated porous glass column.

Proteins will adsorb onto silicone-coated glass surfaces by hydrophobic interaction in saline solution and

Table 1. Amounts of drugs adsorbed onto surfaces in saline.*

Drugs and proteins	Amounts adsorbed (mg/100 m²) Glass surfaces	Siliconized surfaces
Streptomycin sulphate	0·3	3·96
Benzylpenicillin	0	2·07 (3300 U)
Cefazolin	0	0·22
Chloramphenicol	0	0·064
Atropine sulphate	0·05	0·81
Physostigmine salicylate	0·08	3·88
Diazepam	0·004	0·46
Adrenaline	0·03	0·025
Insulin	6·14	71
Albumin	136	107
Globulin	83	135
Lysozyme	84	97
Haemoglobin	—	119
Peroxidase	—	84
Chymotrypsin	233	—

* Data of four kinds of antibiotics are in this study and other data were cited from references (Mizutani & Mizutani 1978; Mizutani 1981a; Mizutani et al 1981).

the amounts of proteins adsorbed on silicone-coated surfaces were similar to those on non-coated glass surfaces (Mizutani 1981b) as shown in Table 1. Insulin adsorbed (71 mg/100 m²) onto silicone-coated surfaces in pH 2·6 isotonic glycerol solution to a much greater extent than on non-coated glass surfaces (6·14 mg/100 m²). Also, in phosphate-buffered saline, the values on coated surfaces for atropine sulphate, physostigmine salicylate, and diazepam were 0·81, 3·88, and 0·46 mg/100 m², respectively, and are greater than on non-coated glass 50, 80 and 4 μg/100 m² respectively. Thus drugs of a wide range of physical characteristics adsorb to a greater extent adsorb onto silicone-coated surfaces than onto non-coated glass surfaces.

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