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Drug Interactions of Gliclazide and Other Sulfonylureas in Protein Binding in vitro and in Hypoglycemic Effect in Rats*

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Possible drug interaction in clinical use of a hypoglycemic sulfonylurea, gliclazide, was examined by two measures : its binding to protein in vitro and its hypoglycemic effect in vivo in the presence of other therapeutic agents. Binding of radiolabeled sulfonylureas to human serum albumin at its physiological concentration was determined by ultrafiltration in the presence of other agents. The concentrations of all agents examined were at their therapeutic (i.e., clinically observable) levels in the blood. Protein binding of [^{3}H]gliclazide and [^{14}C]tolbutamide was modified by salicylic acid and phenylbutazone but not by tolmetin, warfarin and propranolol. Binding of [^{3}H]-glibenclamide was not influenced by these agents under conditions employed.

Blood glucose lowering effect of sulfonylureas was studied in rats to which other agents were given. The hypoglycemic effect of gliclazide and chlorpropamide was enhances by concomitant administration of acetylsalicylic acid and phenylbutazone but not by dicumarol and warfarin. The enhancement of hypoglycemic effect is likely to result from the interaction of protein binding between the drugs.

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