acids in vitro, using a rat liver mitochondrial suspension prepared by the same method as that used for the in vivo experiment, 0, 0.2, 0.4 or 0.8 mg Co Q_{10} (10 mg/ml solution) or 0.1 mg α-tocopherol (10 mg/ml solution) was added to the mitochondrial suspension. Then, the lipoperoxide content of each sample was measured by the same procedure as in the in vivo experiment.

Results. In vivo study: Table 1 shows the lipoperoxide content of mitochondria isolated from liver. Lipoperoxides decreased significantly with the administration of Co Q_{10} and α-tocopherol. α-Tocopherol was more effective than Co Q_{10} in the prevention of an increase in lipoperoxides under these conditions. In mitochondria isolated from heart, the quantity of lipoperoxides was significantly decreased with the administration of Co Q_{10}, or with that of α-tocopherol, compared with the control group. There was no difference between the anti-oxidative capacities of the 2 drugs administered.

In vitro study: Table 2 shows the efficiency of Co Q_{10} and α-tocopherol in the prevention of an increase in lipoperoxides in vitro. The quantity of lipoperoxides decreased significantly in proportion to the administered dosage of Co Q_{10}. In the group which received α-tocopherol, there was a significant decrease in the quantity of lipoperoxides. The administration of α-tocopherol at this dose (0.1 mg) had almost the same efficiency as the administration of 0.2 mg of Co Q_{10}.

Discussion. We studied the anti-oxidant effect of Co Q_{10} both in vivo and in vitro in comparison with α-tocopherol. Co Q_{10} was revealed to have anti-oxidative activity. It was also demonstrated that administration of relatively small doses of Co Q_{10} (2 mg/kg) had the same anti-oxidant effect as that of α-tocopherol (10 mg/kg) on heart mitochondria, though α-tocopherol was more effective than Co Q_{10} in reducing lipoperoxides in liver mitochondria. These results indicate that Co Q_{10} has anti-oxidative capacity, and that the anti-oxidative activity of Co Q_{10} and that of α-tocopherol differ from organ to organ. The data suggest that an anti-oxidant which has a different hydrophobicity from others will show differences in anti-oxidative capacity from organ to organ. As the lipid composition of cell membranes differs from organ to organ, each organ may have a different permeability to anti-oxidants.

In conclusion, Co Q_{10} is a suitable anti-oxidant for the prevention of lipo-peroxidation in vivo. Selective usage of anti-oxidants such as Co Q_{10} or α-tocopherol for patients will open a new era in their linical application.

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Ethanol-induced changes in plasma glucose, insulin and glucagon in fed and fasted rats[1]

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Summary. Orally administered ethanol produced dose-related suppression of IRI levels and elevation of IRG levels in fed and fasting rats. Plasma glucose levels were unaffected in the fasting rats, but a moderate hyperglycemic response accompanied the decline in IRI and the rise in IRG observed in the fed rats.

Ethanol can produce effects on glucose homeostasis which are dependent upon dose and state of nourishment of the subject[2]. For example, the glycemic response to moderate or large doses of ethanol is hypoglycemia in fasting subjects but hyperglycemia in fed subjects. It has been stated that the decline in insulin and the compensatory increase in glucagon in ethanol-treated fasting subjects are indirect and that they are the consequence of the fall in blood glucose. The present study reports the dose-related effects of orally administered ethanol on plasma immunoreactive insulin (IRI) and glucagon (IRG) levels taken 1 h after gavage in fed and fasting rats.

Methods. Fully nourished or fasting (18 h) male Sprague-Dawley rats weighing between 350 and 450 g were administered saline or ethanol (150, 450 or 750 ml/100 g) by orogastric intubation. 45 min after gavage each animal was anesthetized with pentobarbital i.p., the dose of pentobarbital determined by the dose of ethanol: saline, 5 mg pentobarbital/100 g; 150 mg ethanol/100 g, 3.75 mg pentobarbital/100 g; 450 mg ethanol/100 g, 2 mg pentobarbital/100 g; 750 mg ethanol/100 g, 0.8 mg pentobarbital/100 g. The level of anesthesia produced by these combinations of drugs produced sufficient anesthesia to allow cardiac puncture without discomfort to the rat. Blood samples (1 ml) were taken by cardiac puncture 1 h after gavage (15 min after pentobarbital injection) and placed in iced test tubes containing 100 µl benzamidine (0.5 M) and 100 µl EDTA (12 mg/ml) to prevent proteolysis and coagulation, respectively. Plasma samples were subsequently analyzed in duplicate for IRI[3], IRG[4] and glucose[5] levels. Antiserum 30K (Roger Unger, Dallas, Texas), which reacts with no more than 2% of plasma gut GLI, was used for IRG determinations. Statistical analysis consisted of Students t-test for unpaired (group) data.

Results and discussion. As shown in figure 1, ethanol p.o. produced a decline in plasma IRI levels in fasted rats at 1 h after each dose of ethanol. Plasma IRG levels were not changed from control (saline-treated) levels by 150 mg ethanol/100 g but IRG levels after the intermediate (450 mg/100 g) and high (750 mg/100 g) doses of ethanol were elevated significantly ($p < 0.05$; $p < 0.01$). Plasma glucose levels were not different among the 4 groups of fasted rats.

Fed rats (saline-treated) had basal levels of IRI (4-fold higher) and IRG (3-fold lower) that were significantly different from those of fasted rats (figure 2) and are appropriate for their different state of nourishment. Administration of 150 mg ethanol/100 g p.o. produced no changes in glucose, IRI or IRG levels in fed rats. An oral dose of 450 mg ethanol/100 g produced significant eleva-

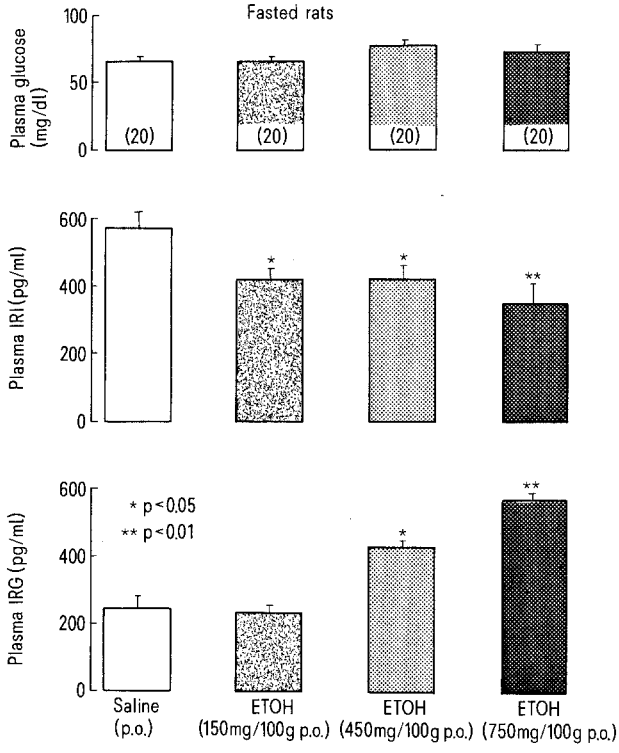

Fig. 1. Alterations in plasma levels of glucose, insulin (IRI) and glucagon (IRG) induced by ethanol in fasting rats. Values plotted represent the mean ± SE calculated from the number of rats shown in parentheses.

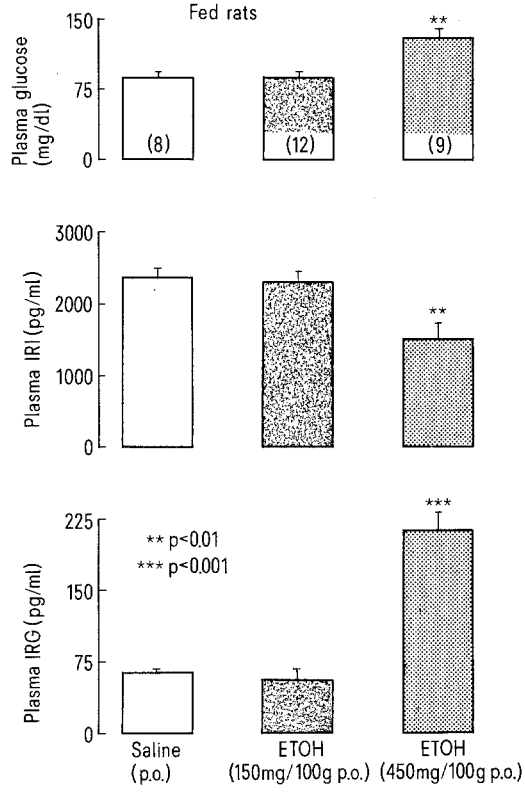

Fig. 2. Influence of orally administered ethanol on plasma glucose, IRI and IRG levels in fed rats. Numbers of rats are shown in parentheses. Values represent mean ± SE.

tions of plasma glucose and IRG levels ($p < 0.01$) and a significant depression of plasma IRI level ($p < 0.001$).

These findings demonstrate that orally administered ethanol can produce dose-related changes in plasma levels of IRI and IRG in fed and fasting rats at 1 h after gavage, but that these hormonal changes are accompanied by significant changes in plasma glucose levels only in fed rats. Thus, the magnitude and/or direction of ethanol-induced changes in IRI and IRG levels were dependent upon the dose of ethanol and the state of nourishment of the rats but were not always accompanied by significant changes in plasma glucose levels.

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Clearance of orally administered ^{115m}Cd from rat tissues

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Summary. Peak ^{115m}Cd levels in the liver, kidneys, spleen and duodenum of the rat, following a single oral dose, fell exponentially. Half-clearance time for ^{115m}Cd is highest in the kidney (30 days) followed by the liver (6.8 days), the spleen (5.5 days) and the duodenum (3.5 days).

The selective accumulation of cadmium in the liver and kidneys is well known[1]. This element is tenaciously retained in the tissues of the body; the biological half-life of cadmium in the human renal cortex is estimated to be more than 30 years[2]. Though there is strong evidence that metallothionein[3,4] is involved in the storage of cadmium, no systematic analysis of the clearance of orally ingested cadmium from the tissues of the body seems to have been carried out.

Material and methods. Male albino rats, each weighing between 240 and 290 g, were employed in the present studies. ^{115m}Cd as $^{115m}Cd(NO_3)_2$ (sp. act. 9 μCi/mg of Cd)