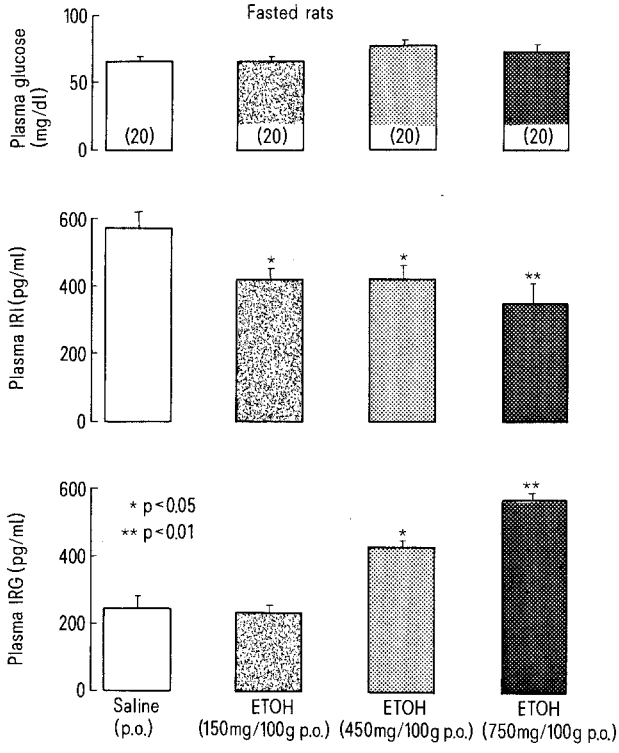

Fig. 1. Alterations in plasma levels of glucose, insulin (IRI) and glucagon (IRG) induced by ethanol in fasting rats. Values plotted represent the mean ± SE calculated from the number of rats shown in parentheses.

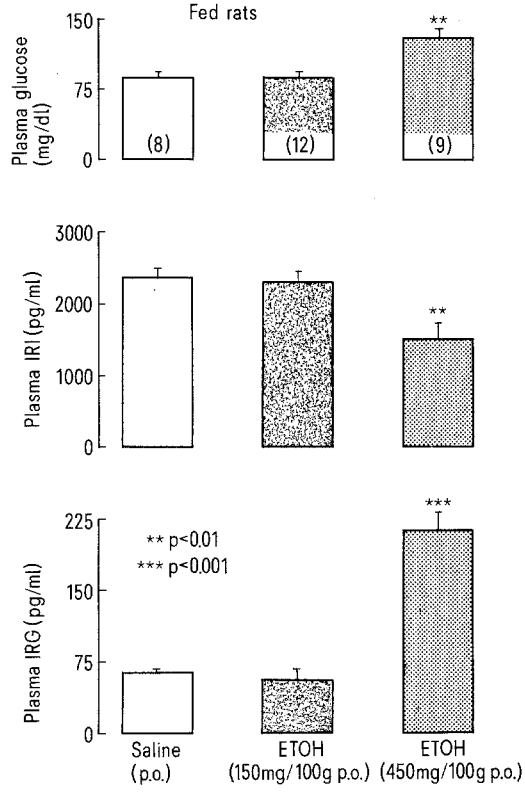

Fig. 2. Influence of orally administered ethanol on plasma glucose, IRI and IRG levels in fed rats. Numbers of rats are shown in parentheses. Values represent mean ± SE.

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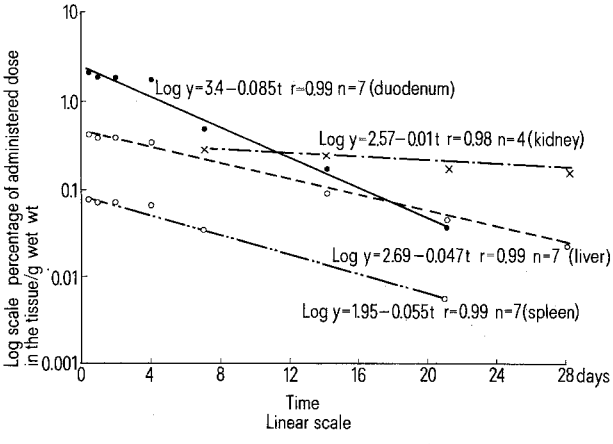
Summary. Peak ^{115m}Cd levels in the liver, kidneys, spleen and duodenum of the rat, following a single oral dose, fell exponentially. Half-clearance time for ^{115m}Cd is highest in the kidney (30 days) followed by the liver (6.8 days), the spleen (5.5 days) and the duodenum (3.5 days).

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)

was obtained from Bhabha Atomic Research Center, Trombay, Bombay, India. The rats were divided into 13 groups, each group consisting of 5 animals. A single oral dose of 50 μCi (0.5 ml) of ^{115m}Cd was administered to each rat. The isotope-fed rats were sacrified at various intervals ranging from 30 min to 28 days, and the different tissues, viz the spleen, kidney, liver and a 5-cm long piece of duodenum next to the stomach were then dissected out. The tissues were carefully weighed and digested in 30% KOH at 90 °C for 10 min. The digested samples were monitored for ^{115m}Cd counts employing a solid scintillation counter. ^{115m}Cd counts so obtained were then expressed as the percentage of the administered dose and the latter values were plotted against time (figure). The experimental points were analyzed by the method of least squares to obtain the best-fit curves described by the equation log $Y = mt + C$, Y = percentage of the administered dose per g of wet tissue at a time = t. Half clearance time (HCT) of ^{115m}Cd in the tissues was then calculated from these equations employing the formula $HCT = -\log 2/m$.



Percentage values of administered doses of ^{115m}Cd plotted against time.

Results and discussion. The observations clearly suggest that the peak ^{115m}Cd level, attained following a single oral administration, falls exponentially with time in all the tissues studied, viz the spleen, kidney, liver and duodenum. A highly significant negative correlation is obtained between log (percentage of the administered dose per g of wet tissue) and the time in all the 4 tissues. The striking feature of the present observations is that the duodenum, which attains a peak ^{115m}Cd activity just 8 h post-administration, is also the quickest in clearing cadmium (HCT = 3.5 days). The kidney, though it shows maximum ^{115m}Cd activity 7 days post-administration, retains ^{115m}Cd the longest (HCT = 30 days). The spleen (HCT = 5.5 days) and the liver (HCT = 6.8 days) show intermediate clearance of cadmium, although the liver incorporates much more ^{115m}Cd than the spleen (figure). It is known that the tissues studied in the present report contain metallothionein[4], and this protein plays a significant role in cadmium retention. The biological half-life of cadmium metallothionein has been variously estimated as being between 3 and 5 days[5-7]. The comparatively long HCT of cadmium from both the liver and kidney thus suggests that the degradation of cadmium metallothionein does not lead to the removal of cadmium. Probably the cadmium complexes from the degraded metallothionein are reutilized for the synthesis of new metallothionein molecules[5-7]. There is evidence that liver cadmium is transported to the kidneys by metallothioneins[3] and this may explain the much longer HCT of ^{115m}Cd in the kidneys compared with that of the liver.

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Synaptic development in brains of rats exposed perinatally to ethanol[1]

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Summary. Development of brain synaptosomal uptakes of ^{3}H-norepinephrine and ^{3}H-dopamine in pups whose mothers received ethanol were nearly normal. However, development of synaptosomal uptake of ^{3}H-serotonin was significantly lower than in controls, while uptake of ^{3}H-norepinephrine into synaptic storage vesicles was increased.

The fetal alcohol syndrome is associated with retardation of general growth and decreased mental capacity[2]. In the adrenal medulla of the rat, maternal ethanol administration produces a developmental deficit in adrenal catecholamines which results from an apparent lag in development of adrenal storage vesicles[3]. Alterations also have been reported in brain tyrosine hydroxylase activity (the rate-limiting step in catecholamine biosynthesis) and in synaptosomal uptake of tyramine and subsequent conversion to octopamine in rats born to ethanol-treated mothers[4-6]. It is not certain, however, whether the biochemical changes in the brain represent effects on synaptic dynamics (transmitter synthesis, storage, release) or whether synaptogenesis itself is affected by ethanol exposure. In the present study, synaptosomal uptakes of norepinephrine, dopamine and serotonin have been used as indices of synaptic development, as previous studies have shown that this procedure provides an estimate of the numbers of synaptic terminals for each neurotransmitter[5,7-9]. In addition, storage capabilities for catecholamines were assessed by measurement of norepinephrine uptake into isolated storage vesicles[8,9].

Timed pregnant Sprague-Dawley rats (Zivic-Miller) were housed individually in breeding cages without access to water and were fed a nutritionally complete liquid diet (Sustacal) from the 11th day of gestation. On the 13th day of gestation and thereafter, the experimental group received ethanol (6.8% v/v) in Sustacal while controls received Sustacal made isocaloric and isonutritional to the