

Effects of Ethanol on the Absorption and

Secretion of Mn^{54} , Zn^{65} , and Fe^{59}

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Introduction—Apparently little investigation has dealt with absorption and secretion of trace elements when a high concentration of ethanol is present in the blood. Some work has been done in the area of stimulation of gastric secretion by alcohol.

Chillenden, Mendell, and Jackson (1898) showed that alcohol stimulates gastric secretion. Orbell (1906) found that alcohol stimulates the vagus nerve but does not directly affect the gastric cells. Newman and Mehitens (1932) stated that alcohol *does* directly affect the gastric cells. Dragstedt, Gray, Lawton, and de Ramirez Arellano (1940) found that alcohol stimulates gastric secretion through release of a histamine. Hirschowitz, Pollard, Hartwell, and London (1956) concluded that alcohol stimulates gastric secretion by stimulating both gastric cells and the vagus nerve.

There are many different and conflicting opinions on the effect of alcohol but very little quantitative information. Experiments were done to ascertain the effects of elevated blood ethanol levels on some major organs and organ systems. The *absorption* study was designed to investigate the effects of ethanol on the ability of kidneys, liver, spleen, heart, and intestine to accumulate the isotopes Mn^{54} , Zn^{65} , and Fe^{59} after they had passed across the gastric mucosa. The *secretion* study was designed to investigate the effects of ethanol on ability of gastric mucosa to secrete isotopes into the stomach in the form of gastric juices.

Materials and Methods—A. Absorption Study—Eighteen Holtzman Albino rats, each weighing 250 ± 15 g were used. Rats were fasted 48 hr and dehydrated 12 hr prior to experiment. Rats were then divided randomly into control and experimental groups. Three control and three experimental animals were used for each of three trace elements. Experimental rats received intraperitoneal (I.P.) injections of absolute ethanol (4 cc/kg). A preliminary study had been made to determine an intoxicating dose ($LD_{50} = 7.00$ cc/kg).

After one hour, all rats were anesthetized with ether and placed on a dissecting board in a supine position. A midline abdominal incision approximately 4 cm in length was made. A 20-cm piece of polyethylene tubing (PE-50) was passed into the stomach through the mouth, and the stomach was tied off at the pylorus. A known quantity of isotope was passed down the tube, the tube was removed, and the stomach tied off at the esophageal junction. Peritoneum and fascia were closed with suture and clamps and the incision coated with collodion.

Four hours after injection with isotope, the rats were killed, and blood was taken from the inferior vena cava. A gross examination of the organs was made to determine changes produced by the experiment. Small sections of tissues showing changes and some control tissues were frozen, later sectioned on a cryostat, and stained with hematoxylin-eosin for histological study. The stomach, kidney, liver, spleen, heart, intestine, and gastric juice were then removed. The intestine was divided into three sections, two equal lengths of the upper tract and the colon. Each organ was rinsed in distilled water and dried. Samples were then counted for isotope content several times in a gamma counter (*Tracer-Lab Gamma Guard*).

B. Secretion Study—Operative procedure differed in the secretion study in that the stomach was tied off at the pylorus and esophageal junction without the isotope being placed in the stomach. Rats were then injected, subcutaneously in the back, with a known quantity of isotope. Post-operative procedure was the same as in the absorption study.

Results—No evidence of gross tissue alterations effected by the experiment were noted except in the liver of animals injected with ethanol. Small white nodules, ranging in size from less than 1 to 2 mm, were located in the superficial regions of the liver. A histological study showed necrosis of the liver cells.

A. Absorption Study (Table 1)— Mn^{4+} —Accumulations of manganese by the heart and spleen were not affected by ethanol while accumulation of manganese by the liver was only slightly affected. The kidney had 74% and the intestine 83% less manganese accumulation in experimental animals than in control animals.

Zn^{65} — In the zinc group, the liver and spleen were only slightly affected by ethanol. The accumulation of zinc by the intestine increased 583%, by the heart 1677%, and by the kidneys 323% when compared to that in control animals.

Fe^{59} — Accumulation of iron by the heart was depressed 76%, by the kidneys 59%, and by the intestine 42% in experimental animals. The liver and spleen were not affected by ethanol.

B. Secretion Study— Mn^{54} — The stomach showed 39% less manganese and the gastric juice 91% less manganese accumulation than in control animals. Accumulations of manganese by the kidney, liver, spleen, heart and intestine were *higher* in experimental animals.

Zn^{65} — In the zinc group, the liver and heart were not affected by ethanol. Spleen, kidney, and intestine accumulations of zinc were depressed in experimental animals. Accumulation of zinc by the gastric juice was elevated 1206% and that of the stomach lowered 69%.

Fe^{59} — Liver accumulation of iron was not affected by administration of ethanol. The spleen, kidney, and heart accumulations of iron were augmented, and the accumulation of iron by the intestine was depressed. Gastric juice accumulations of iron were the same in both experimental and control animals, while accumulation of iron by the stomach increased 32%.

Discussion—In all groups, isotope accumulation by blood was the same in both experimental and control animals. This suggests that any changes in isotope accumulation in the organs was not a result of amounts of isotope available to each organ but rather a result of effects of ethanol on that organ or organ system.

A. Absorption Group—One observation is that ethanol did not markedly affect the amount of isotope accumulated by the liver in any of the isotope groups. The fact that cross sections of liver showed extensive necrosis while the amount of isotope accumulation was not affected suggests the following possible explanations: 1) the undamaged cells were able to accumulate a larger amount of isotope, 2) dead cells absorbed some isotope, 3) some isotope was pooled in vacant areas left by dead cells, 4) a combination of any or all of the former propositions. With present data no choice of the possible explanations can be made.

The accumulation of zinc and iron by the heart was affected by ethanol while that of manganese by the heart was not. The decrease in iron accumulation is not easy to explain, since specific uses of accumulated isotopes were not determined. However the decrease in the heart is es-

pecially interesting, since a major role of iron in the heart is that of oxygen transport in the form of myoglobin (Theorell, 1934).

Ethanol depressed manganese and iron and augmented zinc accumulation. This is of interest in that zinc is the metal cofactor for alcohol dehydrogenase (ADH), the primary enzyme in oxidation of ethanol (Valee and Hoch, 1955).

B. Secretion Group—The main object of this group was to study secretion of the isotopes into the stomach and any changes produced by ethanol. The measurement that was used to demonstrate this effect was the amount of isotope in gastric secretions and gastric mucosa. These results, though significant, are not comparable with results of the absorption study. A comparison of absorption controls and secretion controls shows a difference in distribution of isotopes among organs, while no difference is shown in the accumulation of the isotopes by the blood. This difference is attributed to the different sites of injection of the two groups. Though not hypothesized in this experiment, the concept of differences in isotope absorption depending on site of injection is very significant. Further work will be needed to substantiate this concept.

Conclusions—In general, ethanol augmented zinc accumulation and depressed that of manganese and iron. Accumulation by the liver was not affected. It was also found that, depending upon the site of injection (I.P. vs subcutaneous), isotope distribution among the organs varied while blood concentrations did not vary.

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