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Tissue Distribution of Cadmium-109 after Tracheal and Gastric Administration in Rats

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Cadmium is known to be a toxic trace element and its ingestion into the human body via dietary, inhalation, occupational, or non-occupational sources can induce a variety of pulmonary, renal, or reproductive dysfunction (Smith et al. 1976; Hietanen 1981). Many acute and chronic studies with cadmium have been conducted in experimental animals to determine its mechanism of action, and it has been reported that cadmium may enhance or deactivate several enzyme systems *in vitro* or *in vivo*, and it may act as a potent calcium blocker, and can inhibit calmodulin activity (Suzuki et al. 1985). In addition, cadmium is distributed and retained in organ systems such as liver, kidney and lung (Shaikh and Smith 1977; Squibb and Cousins 1974). We have previously shown that a significant amount of cadmium is accumulated in lung, kidney, liver and gastrointestinal tract following intravenous or intraperitoneal injection (Chowdhury et al. 1983a; Chowdhury et al. 1983b). This study was conducted to delineate the tissue distribution of cadmium in animals following more physiologic route of exposure, such as tracheal and gastric administration of cadmium.

MATERIALS AND METHODS

Cadmium chloride was purchased from Sigma Chemicals (St. Louis, MO), and cadmium-109 was purchased from New England Nuclear (Boston, MA).

Twelve male Sprague-Dawley rats, approximately 450 g of body weight (Charles River, NJ), were housed in a screen bottomed cage at 22°C on a 12-hr light-dark cycle with free access to water and standard laboratory diet (Purina Mills Inc., St. Louis, MO). Rats were maintained at least for two weeks prior to the studies.

Seven rats were used for tracheal exposure, five rats were used for gast-

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ric exposure. Rats were deprived of food, but free access to water, for 24 h before experiments.

Tracheal exposure of cadmium-109: Rats were anesthetized with a mixture of ketamine hydrochloride (50 mg/kg of body weight) plus acepromazine maleate (1 mg/kg). Through a small midline cervical incision, trachea was exposed. A 26-gauge needle was inserted into just proximal to the bifurcation, and cadmium chloride (0.25 mg/kg of body weight) and a tracer amount of cadmium-109 (2.5 μCi) dissolved in 0.2 ml saline was placed in the tracheal lumen. After the procedure, the needle was removed carefully, and the skin incision was closed with silk sutures.

Gastric exposure of cadmium-109: Rats were anesthetized as described above. A gastric tube was inserted orally till the tip of the tube passed over the cardiac ring, and cadmium chloride (0.25 mg/kg of body weight) and a tracer amount of cadmium-109 (2.5 μCi) dissolved in 1 ml saline was placed in the stomach.

Following recovery from anesthesia, each rat was housed in separate cages without food, but free access to water. Twenty four hours after the exposure, rats were anesthetized with ketamine chloride (50 mg/kg of body weight), and blood samples were collected by cardiac puncture in chilled glass tubes containing 100 KIU/mL of aprotinin (Trasylol, Nova Industries Institute, Bagsvaerd, Denmark) and 15 U/mL of heparin (Sarstedt, Princeton, NJ). The animals were then sacrificed, tissue samples were collected, washed with ice-cold saline, blotted and weighed. The radioactivity associated with the whole blood and tissue samples was counted with a Packard 5650 auto gamma counter (Packard Instrument, Downers Grove, IL). All counts were corrected for the background. The distribution of the cadmium-109 was calculated from the total radioactivity associated in individual tissues over the total radioactivity administered to rats, and expressed as percent per gram tissue. All results are expressed as the mean ± SEM.

RESULTS AND DISCUSSION

The distribution of cadmium-109 in a variety of organs following tracheal or gastric administration was presented in Figures 1 and 2. Trachea, lung and liver retained a great amount of cadmium following tracheal exposure. Heart, spleen, kidney and muscle were also target organs for cadmium retention following tracheal exposure. Following gastric exposure, heart, kidney, liver and gastrointestinal tract retained a significant amount of radioactivity (Figures 1 and 2). These findings agree with the previous studies in rats that were exposed to cadmium by intravenous or intra-peritoneal injection (Chowdhury et al. 1983a; Chowdhury et al. 1983b).

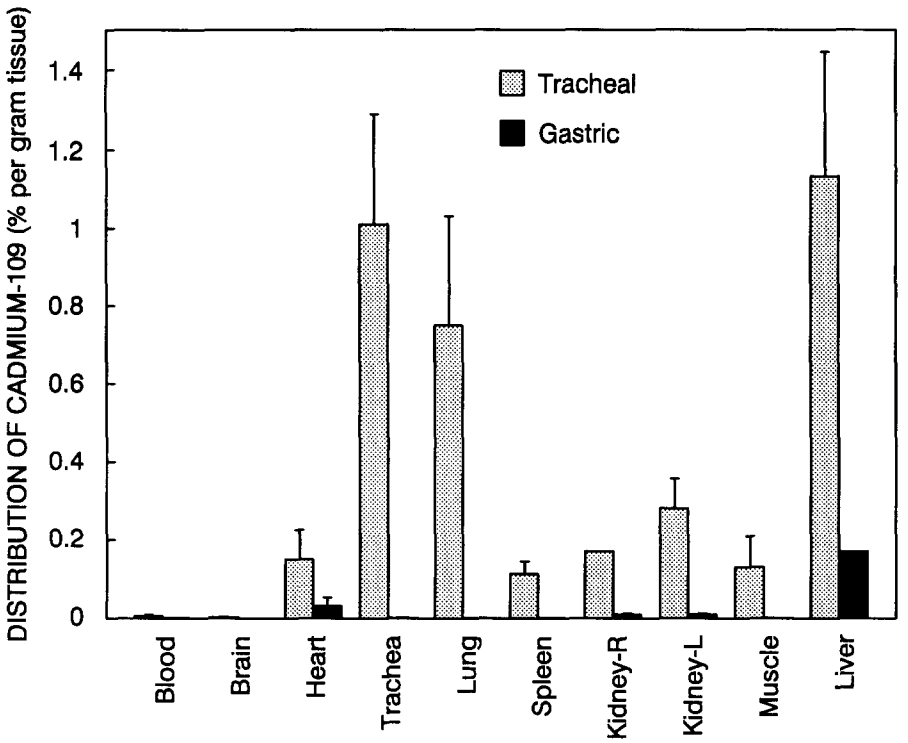

Figure 1. Tissue distribution of cadmium-109 in a variety of organs following tracheal and gastric exposures.

The current results further showed that, among digestive organs, liver and esophagus retained a great amount of cadmium following tracheal exposure (Figure 2). Pancreas and gastrointestinal tracts were also associated with a significant amount of radioactivity. After gastric exposure, esophagus and cecum retained a great amount of cadmium. Pancreas and gastrointestinal tracts were associated with a significant amount of radioactivity. Liver retained a radioactivity after gastric exposure, however, it was significantly smaller when compared with that after tracheal exposure.

Cadmium retention by various organs occurs due to industrial and environmental air pollution, and presents a potential health problem as cadmium is known to induce a variety of pathological conditions (Hietanen 1981). In addition, cadmium is known to be ingested through various dietary sources (Hietanen 1981) and cigarette smoking (Shuman et al. 1974). Therefore, the current results in rats may implicate a simulation of the events after acute exposures via physiological routes like respiratory or digestive tracts.

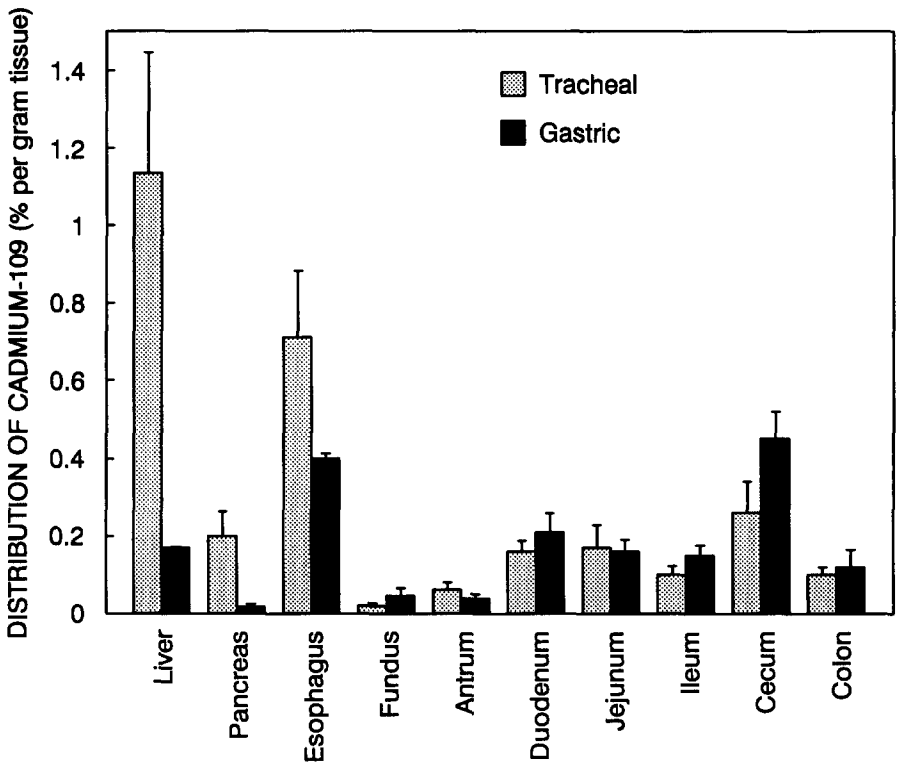

Figure 2. Tissue distribution of cadmium-109 in digestive organs following tracheal and gastric exposures.

Twenty four hours after the administration of cadmium-109, no significant radioactivity was detected from blood samples (Figure 1). This finding is consistent with the previous study in rats that were exposed to cadmium by intravenous or intraperitoneal injection (Chowdhury et al. 1983a; Chowdhury et al. 1983b). This is probably due to the rapid catabolism of cadmium in blood. Cadmium-109, when injected intravenously as either a bolus or as a constant infusion, was quickly eliminated from blood (Chowdhury et al. 1983a). It has been shown that in rats, an initial disappearance half-time of cadmium was 3.4 min after a bolus injection and 6.3 min after a constant infusion (Chowdhury et al. 1983a). Further, we have shown that no significant radioactivity was detected from urine samples at 24 hr to 72 hr after cadmium-109 exposure (Chowdhury et al. 1983b). Taken together, the results indicate that cadmium-109, after it was administered to rats, may be absorbed, distributed and retained by certain organs.

It should be noted that in the current study, a significant amount of cadmium was retained by digestive organs following either respiratory or

gastric exposure. Gastrointestinal organs, in addition to kidney, have been shown to be a primary target site for accumulation of cadmium when cadmium is given through various routes of administration (Hietanen 1981; Chowdhury et al. 1983a; Chowdhury et al. 1983b). We have previously reported the effect of cadmium on bombesin-stimulated release of gastrointestinal hormones such as gastrin and cholecystokinin, which are released from stomach or small intestine (Chowdhury et al. 1984; Chowdhury et al. 1986). In addition, acute studies on the effect of cadmium in rats indicated that cadmium increases bombesin-stimulated pancreatic exocrine secretions (Chowdhury et al. 1986). Further, intravenous administration of cadmium in dogs potentiated bombesin-stimulated releases of pancreatic polypeptide (Chowdhury et al. 1984).

Cadmium and zinc have been shown to influence the release of calcium from its intracellular storage (Plishker 1984), and the released calcium may act as an important mediator for both endocrine and exocrine functions. The results from the current study and the previous results in *in vitro* studies (Andrews et al. 1990; Suzuki et al. 1990) implicate that cadmium may have diverse physiological functions in both exocrine and endocrine pancreatic cells. The current results indicate that cadmium ingested via physiological routes can be distributed and retained by gastrointestinal organs, therefore, it is possible that cadmium may affect their physiologic functions.

Recent studies have shown that cadmium can enhance metallothionein messenger RNA and synthesis of metallothionein (Andrews et al. 1990; Suzuki et al. 1990), and bind to cytosolic metallothionein in pancreatic exocrine cells (Suzuki et al. 1990). Further, it has been reported that cadmium induced a transformation of rat pancreatic cells to hepatocytes (Konishi et al. 1990). These reports suggest that cadmium may have potential physiological functions on both exocrine and endocrine pancreatic cells.

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