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Absorption, Distribution and Excretion of Orally Administered Cadmium in Rat

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Cadmium is commonly used in electroplating, in batteries and as a stabilizer in plastic industry. Emission of this metal from zinc refineries is another source of cadmium pollution. Exposure of man to cadmium may occur either by inhalation or by consuming cadmium contaminated food. Even heavy cigarette smoking could result in an intake of 5 ug Cd/day (FRIBERG et. al. 1971, LEWIS et al. 1972). Further, the cadmium content increases in the human tissues with age (ANKE AND SCHNEIDER 1971). Liver and kidneys reportedly retain cadmium selectively (HAMILTON et al. 1972/73). Despite the fact that cadmium is one of the serious environmental pollutants, data with respect to absorption, distribution and excretion of orally ingested cadmium is scanty.

MATERIALS AND METHODS

Male albino rats, each weighing 240-290 g, were employed in the present studies. The animals were housed individually in metabolic cages. ^{115m}Cd as $Cd(NO_3)_2$ (Spec. act, 9 μCi/mg of 'Cd') was obtained from Bhabha Atomic Research Center, Trombay (Bombay) India.

The rats were divided into thirteen groups, each group comprised five animals. A single dose of 50 uCi of ^{115m}Cd was fed orally to each rat employing the procedure of Burn (1952). The isotope- fed rats were sacrificed at varied intervals ranging from 30 min to 28 days following nembutal (5 mg/100g body weight) anaesthesia. The blood was drawn from the hearts of anaesthetized animals whereafter the heart was removed so as to cut off blood supply to the other organs. The different organs to be analysed were then dissected out in a particular sequance; viz testes, epididymes, seminal vesicles, prostate, adrenals, spleen, kidneys, liver, ileum 5 cm long piece (adjacent to caecum) along with luminal contents and the duodenum 5 cm long piece(next to the stomach). Faeces were also collected and analysed for determining faecal excretion of ^{115m} Cd. The tissues were carefully weighed and digested in 30% KOH at 90°C for 10 min. The digested samples were then monitored for ^{115m}Cd counts, employing a solid scintillation counter.

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RESULTS AND DISCUSSIONS

The distribution patterns of ^{115m}Cd varied widely in the different tissues of rat following a single oral dose of the radioisotope (cf. Table). The maximum uptake of ^{115m}Cd by any individual tissue never exceeded ~2% of the ingested dose. There was recorded an overall poor absorption of ^{115m}Cd inasmuch as more than 70% of the ingested isotope passed out in faeces in the first five days.

Highest levels of ^{115m}Cd in liver, spleen, adrenals duodenum and ileum were touched well before the second day, whereas in the kidneys the peak was attained after the sixth day. ^{115m}Cd incorporation retention in the circulating blood was rather poor suggesting slow absorption of the isotope. Highest level of ^{115m}Cd in the blood was recorded 12 h after oral administration. In comparison, cadmium levels rise quickly in blood and attain a peak value within 5-10 min following parenteral administration of the metal (JOHNSON and MILLER 1970). Further cadmium absorbed through gastro-intestinal tract is directly transported to liver where it is trapped and hence very high cadmium level in blood does not ever reach as is characteristic following parenteral administration.

The liver accumulated maximum ^{115m}Cd 12 h after administration. Further, sufficiently high levels of ^{115m}Cd in the liver were retained even on 7th day following administration and the rate of fall in radioactivity in the liver was gradual. Recent studies by many authors conclusively demonstrate the participation of a unique low molecular weight protein, metallothionein, in the long time retention of cadmium in the liver of animals subjected to cadmium treatment (cf. NORDBERG 1978). Our observations on the accumulation of ^{115m}Cd in the rat kidney show that the cadmium levels in kidney rise gradually and a peak is attained 7 days post administration of the isotope. There is also seen a marked retention of cadmium by the kidney in contrast to the other tissues which tend to get rid of the metal much faster. Extremely prolonged retention of cadmium in kidney is again related to its complexing with low molecular weight protein-metallothionein in this tissue (cf. CHERIAN and GOYER 1978).

The levels of ^{115m}Cd in the spleen following oral administration rise rather slowly; uptill 2h, there was hardly any incorporation. After 4 days, spleen lost only 15% of the peak activity recorded 12h post-administration . ^{115m}Cd content left in the spleen 7 days

TABLE

^{115m}Cd distribution in rats (0.2 uCi/g body weight)
% age uptake of the administered dose ± S.D.

Organ	1/2 h	1 h	2 h	4 h	8 h	12 h	1 d	2d	4 d	7 d	14 d	21 d	28 d
Blood	.002 ±.0001	.0023 ±.0002	.0027 ±.0002	.0055 ± .0003	.0072 ±.0004	.0080* ±.0004	.0066 ±.0004	.0057 ±.0003	.0053 ±.0003	.001 ±.0001	-	-	-
Liver	.014 ±.001	.066 ±.004	.084 ±.005	.222 ±.029	.302 ±.042	.422* ±.035	.394 ±.031	.383 ±.029	.353 ±.027	.323 ±.006	.095 ±.003	.049 ±.003	.024 ±.002
Kidney	-	-	-	.046 ±.003	.100 ±.006	.170 ±.009	.180 ±.009	.200 ±.017	.234 ±.021	.300* ±.019	.260 ±.019	.186 ±.014	.166 ±.019
Spleen	-	-	.018 ±.001	.022 ±.002	.041 ±.002	.076* ±.004	.070 ±.004	.072 ±.004	.068 ±.003	.036 ±.002	.016 ±.001	.006 ±.0003	-
Adrenals	-	-	-	.001 ±.0001	.003 ±.0002	.004* ±.0003	.0033 ±.0002	.003 ±.0002	.002 ±.0001	.0015 ±.0001	-	-	-
Duoden-um	.364 ±.021	.910 ±.054	1.30 ±.075	1.469 ±.096	2.145* ±.133	2.064 ±.130	1.859 ±.108	1.846 ±.106	1.781 ±.103	.494 ±.032	.182 ±.017	.039 ±.002	-
Illeum	-	.056 ±.014	.247 ±.022	.741 ±.047	1.57 ±.095	1.794 ±.106	1.91* ±.108	1.885 ±.107	1.729 ±.104	.273 ±.026	.013 ±.004	- ±	--
Total fecal excretion	-	-	-	-	-	-	6.5 ±2.4	26.25 ±5.4	65.0 ±7.4	70.5 ±3.5	70.9 ±6.8	71.1 ±6.9	71.0 ±6.4

* Indicates time period in which the highest ^{115m}Cd level was recorded.

± S.D. was calculated from the data on 5 animals at each time interval.

post administration was only 21% of the peak value and the activity further fell; lowest levels i.e. 7% of the peak value were recorded after 28 days. The appearance and disappearance patterns of ^{115m}Cd in the rat spleen studied by us are in conformity with the findings of GUNN and GOULD (1957) and COTZIAS et al. (1961). As also observed by GUNN and GOULD (1957), the adrenals in the present material also recorded peak ^{115m}Cd activity 12h post administration.

Sufficiently high levels of ^{115m}Cd in rat duodenum could be detected 1/2h post administration. Significantly high level declined after the fourth day; the peak was observed 8h post administration. Detectable amounts of ^{115m}Cd persisted in rat duodenum even 21 day after administration. ^{115m}Cd activity in the ileum of orally dosed rats followed a pattern identical to that of duodenum, though the peak was touched 1 day post administration. Our observations on the retention of ^{115m}Cd by rat duodenum and ileum are supported by work of MILLER et. al. (1968). Recent observations also suggest the involvement of metallothionein in the cadmium uptake by the intestine (cf. CHERIANand GOYER 1978)

The radiocadmium uptake by the testes and other accessory organs was too poor to be detected. This observation is not unexpected keeping in view the fact that orally given cadmium is very poorly absorbed and consequently only low levels of the metal are detected in the circulating blood. The selective heavy and abrupt accumulation of ^{115m}Cd by rat liver and kidney keep the level of radiocadmium in the circulating blood rather too low to affect the reproductive organs. However, parenteral administration of cadmium does provide a sufficiently good amount of metal to the reproductive organs leading to the selective damage (GUNN et al. 1968).

The present studies on the fecal excretion of ^{115m}Cd further strengthen the idea that over-all absorption of orally ingested ^{115m}Cd from the digestive tract is markedly low. More than 70% of the total isotope administration passed out within the first five days. However, there occurred a sharp decrease in the rate of faecal excretion till the 7th day, whereafter it levelled off. The rate of excretion was the highest on the second day. The rapid decline in the faecal excretion after 2nd day suggests that bulk of ^{115m}Cd is absorbed and distributed to the tissues of the body by 2nd day. Poor absorption of orally ingested cadmium have been observed by others too (FRIBERG et al. 1972).

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