Proc. Indian natn. Sci. Acad. **B 46** No. 5 pp 615-620 (1980)

Uptake Of Selenium-75 and its Interaction with Arsenic, Cadmium and Mercury in the Rat

P C MANGAL and GURMAIL SINGH
Department of Biophysics Panjab University Chandigarh 160 014

(Received 11 March 1980)

Tissue uptake, distribution and retention of Selenium-75 in the rat has been studied. Maximum activity of ^{75}Se is found, in most of the rat organs, within 1-3 hr, except in the brain and the colon where the maxima are reached within 6-8 hr post-administration. Graphical analysis of the biological decay of ^{75}Se in the rat organs indicates that the decay is a sum of two exponentials except in the brain and the spleen. In the brain the level of ^{75}Se stays constant, once maximum is reached and in the spleen the decay is single exponential in character. The biological half-lives of ^{75}Se in various rat organs have been worked out.

The effect of Cd and Hg is more or less similar but opposite to that of As, suggesting that the uptake of Se, an essential trace element, is dependent to a great extent on the level of As, Cd or Hg present concurrently in the biological systems at the time.

Key Words: ^{75}Se uptake, Biological half-life, Interaction with Cd, Hg & As

Introduction

During the last two decades the effect of Se on the uptake, tissue-distribution and retention of As, Cd and Hg has been extensively studied. Kowsta-Szumska et al. (1976) reported that the uptake of Hg by kidney and liver of the rat exposed to Se is changed from 42% to 7% and 6% to 33% respectively. Potter and Matrone (1974), Hill (1974) and Parizek et al. (1976) noted the protective effects of Se in Hg toxicity. Parizek et al. (1968) and Hill et al. (1970) also observed a protective effect of Se against the known specific effects of Cd in reproductive and other organs of the rat. Hill et al. (1970), Levander (1977) and Parker (1976) have demonstrated the effect of As on selenium metabolism. Most of the previous investigations are concerned with the role of Se to combat the toxicity of heavy elements such as Cd, Hg and As. The effect of As, Cd and Hg on the uptake, distribution and retention of Se is not yet well understood. Se is an essential trace element and its deficiency or excess can impair several biological functions. Heavy elements such as Cd, Hg or As enter the biological systems as pollutants. It is therefore, of paramount interest to investigate the effect of As, Cd and Hg

on the uptake, distribution and retention of Se.

Materials and Methods

Sexually mature female albino rats, each weighing 145-170g, were kept on standard (Hindustan Lever) rat and mice feed. The feed and water were provided *ad libitum*. Twenty-four animals were divided in eight groups of three animals each. Each animal was given intraperitoneally a dose of 0.1 ml of seleniate in NaOH solution having a radioactivity of 2.4 μci of ^{75}Se. The specific activity of the original solution was 50 mci/g of Se. By dilution with normal saline solution the dose was made to contain 0.3 mg of Se/kg of body-weight. The animals were sacrificed in groups of three each at 1, 2, 4, 6 and 12 hr and 2, 3, 6 and 7 days post-administration. Three groups of animals were independently given subcutaneous injections of isotonic solutions of $CdCl_2$, $HgCl_2$ and Na_2HAsO_4 in doses of 2.5, 3 0 and 2.5 mg of Cd, Hg and As per kg body-weight respectively. After 15 min these animals were administered intraperitoneally equal doses of ^{75}Se similar to those animals having no exposure of Cd, Hg or As. The latter groups of animals were sacrificed 24 hr after the administration of ^{75}Se. From all the rats a part or whole of the 15 tissues, viz., liver, kidney, spleen, pancreas, heart, lung, ovary, small and large intestines, duodenum, caecum, colon, trachea, brain and blood were taken out of the animals, weighed and digested in 20% KOH. In each case the solution was made to 3 ml, transferred to the counting tube and counted in a well-type scintillation spectrometer. The mean value from the three animals and the corresponding statistical error were worked out. It was ensured by adjusting the counting time that in each case the statistical error is less than 2%.

Results and Discussion

The retention of ^{75}Se in the various organs of the rat not exposed to As, Cd or Hg is plotted as a function of time on the semi-log scale (figure 1, curves a to d). Maximum uptake of Se in all the organs except in the brain and the colon is reached within 1-3 hr post-administration. In the brain and the colon the maxima are reached within 6-8 hr of dose administration. The uptake of ^{75}Se is maximum in the kidney — 43% of the administered dose—and minimum in the brain viz. 2.5% of the dose.

The retention curves of figure 1 (a to d) have been analysed graphically. It is found that except for the brain and the spleen all the curves consist of two components each having exponential decay; one component has a slow decay while the other has a relatively fast decay. The equation for these curves is, therefore, written as

$$C = A_1 e^{-\lambda_1 t} + A_2 e^{-\lambda_2 t}$$

where C = concentration of Se in the organ at time 't'

λ_1 and λ_2 = decay constants for the fast and slow decaying components respectively,

A_1 and A_2 = constants

The values of A_1, λ_1 and A_2, λ_2 as found from the graphical analysis are given in table 1. The biological half-lives (T_{b1}, T_{b2}) for the two components and the fractions decaying via each channel expressed as percent of the administered dose are also given in this table.

The retention of ^{75}Se in the spleen follows a straight line on the semi-log scale and therefore its decay is single exponential in character. In the brain,

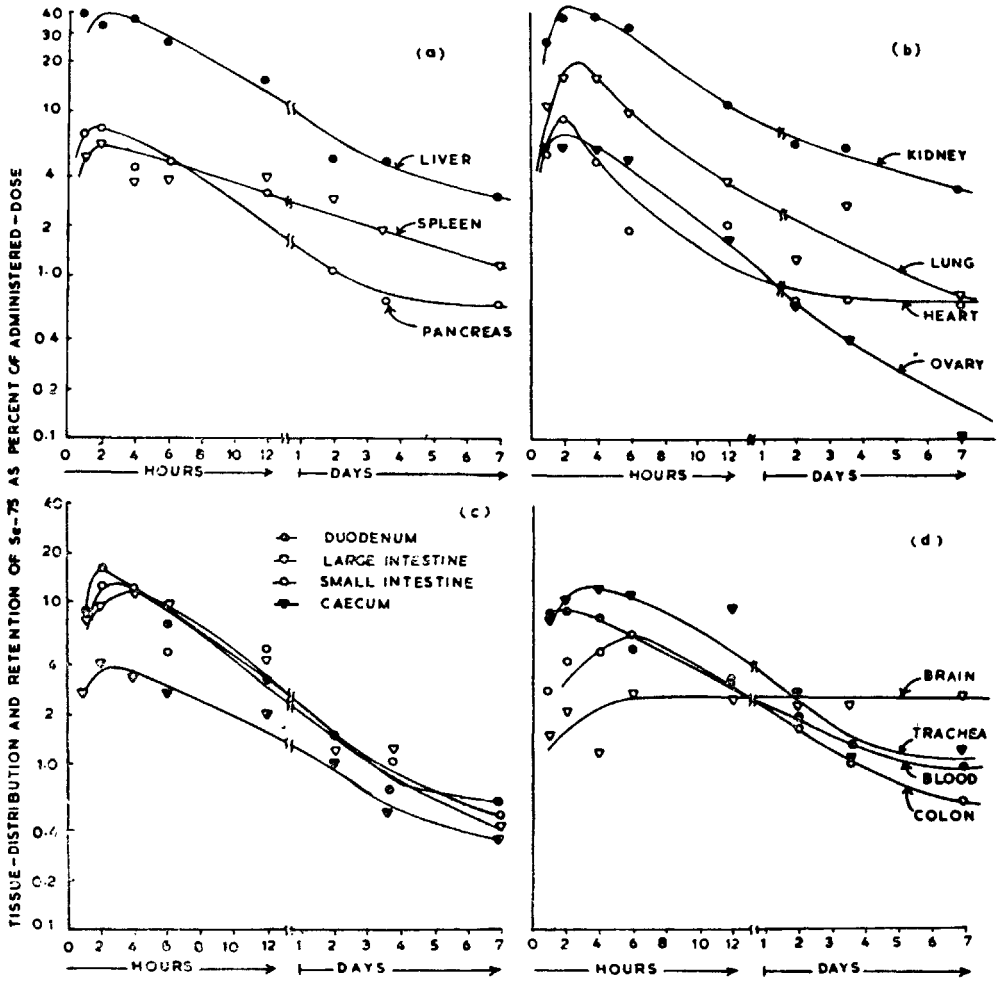

Figure 1 Distribution and retention of ^{75} Se administered as sodium Selenite in the rat Organs/tissues not exposed to As, Cd or Hg (*a*) Liver, spleen and pancreas, (*b*) Kidney, Lung, Heart and Ovary, (*c*) Duodenum, Large and Small intestine and caecum, (*d*) Brain, Trachea, blood and colon

once maximum is reached, the level of Se stays almost constant, at least for the period of the present experiment.

In the rats exposed to As the retention of Se is diminished in all the animal organs except in the kidney and the parts of g.i. tract (table 2). Maximum decrease is in the brain (81%). In the kidney and the parts of g.i. tract there is increase in the retention, maximum being in the kidney (31%).

The increased retention of Se in the kindey and the g.i. tract and corresponding decrease in all the other organs indicate that Se is eliminated at a faster rate from the system in the presence of As as compared to the unexposed ones.

Present results for the effect of As on the retention of Se in the liver, kidney and blood agree with those reported by Ganther et al. (1972).

Table 1 *Decay constants of the two components of the retention curves for ^{75}Se in the various rat organs/tissues*

Organ/Tissue	Fast component				Slow component			
	λ_1	A_1	T_{b1} (hr)	% dose/g of wet tissue*	λ_2	A_2	T_{b2} (Days)	% g of wet tissue*
Liver	0.110	42.0	6.3	33.0	0.0045	6.3	6.4	5.0
Kidney	0.228	62.5	3.0	37.0	0.0071	10.0	4.1	6.0
Spleen	—	—	—	—	0.0082	4.3	3.5	5.3
Pancreas	0 093	6.4	7.5	6.8	0.0031	1.1	9.3	1.2
Heart	0.127	6.0	5.4	7.9	0.0010	0.8	29.5	1.1
Lung	0.316	15.8	2.2	12.6	0.0105	4.2	2.8	3.4
Ovary	0.029	4.8	23.6	5.1	0.0128	1.2	2.3	1.3
Duodenum	0.246	24.0	2.6	15.3	0.0048	1.4	6.0	0.9
Small intestine	0.196	20.0	3.7	10.0	0.0110	2.5	2.6	1.3
Large intestine	0.076	9.0	9.1	11.5	0.0083	2.4	3.5	3.1
Caecum	0.128	3.0	5.4	2.8	0.0078	1.3	3.7	1.2
Colon	0 098	5.8	7.0	6.1	0.0022	1.6	13.3	1.7
Trachea	0.044	13.0	15.6	8.2	0.0013	2.0	22.4	1.3
Blood	0.139	9.0	5.0	7.2	0.0050	2.2	5.8	1.7

* Values given at the maximum uptake of selenium in the tissue/organ

Table 2 *Effect of As, Cd and Hg on the retention of Se in the various rat organs/tissues*

Organ/Tissue	Retention of Se as percent of administered dose						
	Without As, Cd or Hg	With As[1]	% change	With Cd[2]	% change	With Hg[3]	% change
Liver	16.0	9.5	−41	20.0	+25	18.0	+ 13
Kidney	11.5	15.1	+31	5.1	−57	64.4	+ 43
Spleen	3.2	0.9	−72	4.6	+44	24.0	+650
Pancreas	2.5	1.7	−32	1.4	−44	1.8	− 28
Heart	1.4	0.6	−57	2.1	+50	5.0	+186
Lung	3.4	2.2	−35	2.1	−38	8.1	+138
Ovary	3.5	0.7	−80	1.3	−63	2.8	− 20
Duodenum	3.0	2.8	− 7	0.9	−70	2.4	− 20
Small intestine	4.1	3.9	− 5	0.9	−78	2.6	− 37
Large intestine	3.0	3.5	+17	1.1	−63	2.6	− 13
Caecum	1.4	1.8	+29	1.3	− 7	1.8	+ 29
Colon	2.5	2.7	+ 8	1.4	−44	1.8	− 28
Trachea	6.8	1.6	−77	1.5	−78	2.8	− 58
Brain	2.6	0.5	−81	0.4	−85	0.5	− 81
Blood	2.8	2.1	−25	4.5	+61	11.6	+314

Note: The comparison has been made 24 hr after the administration of ^{75}Se (dose of Se=0.3 mg/per kg of Body weight, injected intraperitoneally)

[1] Dose of As=2.5 mg/kg body weight; injected subcutaneously as Na_2HASO_4 (0.05M)

[2] Dose of Cd=3.0 mg/kg body weight; injected subcutaneously as $CdCl_2$ (0.018M)

[3] ose of Hg=2.5 mg/kg body weight; injected subcutaneously as $HgCl_2$ (0.025M)

The exposure of animals to Cd leads to the increased retention of Se in the liver (25%), spleen (44%), heart (50%) and blood (61%), maximum being in the blood. In other organs, namely, kidney, pancreas, lung, ovary, trachea, brain and all parts of g.i. tract there is decrease in the retention of Se. Maximum decrease is in the brain (85%). It is seen that the effect of Cd on the retention of Se in the liver, kidney, spleen, heart, parts of g.i. tract and blood is in the opposite direction from that of As.

In the animals exposed to Hg the retention of Se is enhanced appreciably in the liver, kidney, spleen, heart, lung, caecum and blood. Maximum increase is observed in the spleen where the retention of Se is increased by a factor of about eight in the rats exposed to Hg as compared to unexposed ones. In the other organs the retention of Se is decreased but the decrease is relatively small except in the brain and trachea where the decrease is 81% and 59% respectively.

The mechanism of interaction of Cd and Hg with Se seems to be similar, but opposite to that of As. Both, Cd and Hg tend to promote the retention of Se in most of the rat organs whereas As reduces it in all except the excretory organs.

Se is lost from the body mainly as volatile dimethyl selenide (Challenger 1955)—methylation of Se takes place in the body. Possibly, Cd and Hg make complexes with Se in the body and the selenides so formed are not easily excreted from the body but keep floating in the blood stream, or finally deposited in the spleen. This may account for the prominent increase in retention of Se in the spleen and the blood, particularly in the presence of Hg. The other possibility is that Cd or Hg may remove sulphur from the sulphur containing proteins which permits Se to get into the vacancy of sulphur, leading to the enhanced retention of Se in the presence of Hg or Cd. As seems to compete with Se from the binding sites leading to the observed decrease in the retention of Se in the animals exposed to As.

It is apparent from the study that the exposure of the rats to the sub-toxic doses of As, Cd or Hg results in the altered uptake, distribution and retention of Se in the various rat organs. Therefore, it is essential that the tissue uptake, distribution and retention of Se is assessed, keeping in view the concentration of As, Cd and Hg in the system.

References

Challenger F 1955 Biological methylation; *Qurat. Rev. Chem Soc.* **9** 255-286

Ganther H E and Baumann C A 1962 Selenium metabolism I — effect of diet, Arsenic and Cadmium; J. *Nutr.* **77** 210-216.

——Levander O A and Baumann C A 1966 Dietary control of selenium volatisation in the rat; *J. Nutr.* **88** 55-60

——Gouide G, Sunde M L, Kopecky M J, Wanger P, Oh S H and Hoekstra W G 1972 Selenium: relation to decreased toxicity of methyl-mercury added to diets containing tuna; *Science.* **175** 1122-1124

Hill C H 1974 Reversal of selenium toxicity in chicks by mercury, copper and cadmium; *J. Nutr.* **104** 593-598

——and Matrone C 1970 Chemical parameters in the study of in vivo and in vitro interactions of transaction elements; *Fed. Proc. Amer. Soc. exp. Biol.* **29** 1474-1481

Kowsta-Szumska E, Chmielnicka J and Protsowski J K 1976 The influence of selenium

on binding of inorganic mercury by metallothionein in the kidney and liver of rat; *Biochem. Pharmacol.* **25** 2539-2540

Levander O A 1977 Metabolic interrelationships between arsenic and selenium; *Environ. Health Perspects* **19** 159-164

Parizek J, Ostadalova I, Benes I and Basicky A 1968 Pregnancy and trace elements — The protective effect of compounds of an essential trace element—selenium against the peculiar toxic effect of cadmium during pregnancy; *J. Reprod. Fert.* **16** 507-513

Parizek J, Ostadalova I, Kalouskova J and Babicky A 1976 Effect of mercuric and cadmium compounds on the transmission of selenium in rat; *Arch. Toxicol.* **36** 120-126

Parker J 1976 Arsenilic acid and its relationship to selenium and vitamin E in the nutrition of the pig; *Proc. Nutr. Soc.* **35** 83-84

Potter S and Matrone G 1974 Effect of selenite on the toxicity of dietary methylmercury and mercuric chloride in the rats; *J. Nutr.* **104** 638-647