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Interaction of arsenic and selenium on the metabolism of these elements in hamsters

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The interaction of arsenic and selenium compounds on the metabolism of these elements in golden hamsters was studied. Golden hamsters were divided into three groups and administered sodium selenite (Na_2SeO_3), sodium arsenite ($NaAsO_2$) and Na_2SeO_3 with $NaAsO_2$, respectively, by a single subcutaneous injection of 25 μmol kg^{-1} body weight as As or Se (arsenic and selenium were calculated as weight of elemental arsenic and selenium). Selenium and arsenic metabolites were determined by high-performance liquid chromatography–graphite furnace atomic absorption spectrometry (HPLC–GFA AA) and gas chromatography (GC). The results show (1): About 10% by weight of the given dose of selenium was excreted in expiration air as dimethylselenide (Me_2Se) during 12 h after administration of Na_2SeO_3. Excretion of dimethylselenide with the respiratory air was inhibited by administration of Na_2SeO_3 simultaneously with $NaAsO_2$. (2) Giving Na_2SeO_3 plus $NaAsO_2$ had no appreciable effect on the excretion of the trimethylselenonium ion (Me_3Se^+) into the urine and the feces. (3) Giving Na_2SeO_3 plus $NaAsO_2$ increaed the excretion into the feces of an insoluble unknown-structure selenium compound, the proportion of which was 10.9% by weight of the given dose of selenium. (4) Giving $NaAsO_2$ plus Na_2SeO_3 decreased the excretion of dimethylarsinic acid (Me_2AsOOH) and inorganic arsenic into the urine during 120 h after the administration of the reagents, the decreased amount being 5.3% (dimethylarsinic acid) and 7.7% (inorganic arsenic) of the given dose of arsenic, respectively. (5) Giving $NaAsO_2$ plus Na_2SeO_3 increased the excretion into feces of insoluble unknown-structure arsenic compound and inorganic arsenic, the increased amounts being 10.6% and 7.0% of the given dose of arsenic, respectively. (6) Giving $NaAsO_2$ plus Na_2SeO_3 decreased the excretion into feces of extractable unknown-structure arsenic compound, and the decreased amount was 4.9% of the given dose of arsenic. (7) It made little difference to the excretion of monomethylarsonic acid [$MeAsO(OH)_2$] into urine and feces and of dimethylarsinic acid (Me_2AsOOH) into feces whether $NaAsO_2$ was administered alone or with Na_2SeO_3.

Keywords: Interaction, arsenic, selenium, monomethylarsonic acid, dimethylarsinic acid, dimethylselenide, trimethylselenonium ion, metabolites

INTRODUCTION

In a number of papers the metabolic interrelationships between arsenic and selenium compounds have been reported.[1–4] For example, Levander[5] reported that arsenic inhibited the excretion of volatile dimethylselenide (Me_2Se) via respiration, and stimulated the excretion of selenium into bile, and that likewise selenium stimulated the excretion of arsenic into bile when both elements were administered to animals at the same time. However, the metabolic interaction of arsenic and selenium had as yet been left unstudied. Various authors have reported methods for the determination of trace amounts of total arsenic,[6,7] total selenium[8] and trimethylselenonium ion (Me_3Se^+)[9] in biological materials by atomic absorption spectrometry (AA) with a graphite furnace atomizer (GFA), and measured Me_2Se in breath by gas chromatography (GC)[10] respectively. On the other hand, Inamasu[11] reported a separation and quantification method for arsenic metabolites in urine and feces using a high-performance liquid chromatography (HPLC) and GFA AA system.

Using these methods and a modified Inamasu's method, we studied to clarify the correlation behaviour between arsenic and selenium on the metabolism of

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these elements when both elements were simultaneously administered to golden hamsters.

EXPERIMENTAL

Apparatus

A Hitachi Model 655 liquid chromatograph equipped with a guard column (Wescan 269-003), miniguard column (4 mm × 10 mm) and separatory column (4 mm × 200 mm). Miniguard and separatory column were packed with Hitachi gel #3013-N (Hitachi Co., Japan).

The other apparatus used and measurement conditions were similar to those of previous publications.[6–10]

Reagents

All solutions were prepared from deionized water.

Sodium arsenite ($NaAsO_2$, purity 95% or greater; impurities were CO_2, Na_2AsO_3, Na_3AsO_3 and Na_2HAsO_3; Tokyo, Japan)[11] was freshly dissolved in water (3.4 mg $NaAsO_2$ cm^{-3}) just before administration to hamsters. Sodium selenite (Na_2SeO_3, purity 99%; obtained from Nakarai Chemical Ltd, Kyoto, Japan) was freshly dissolved in water (4.4 mg Na_2SeO_3 cm^{-3}) just before administration to hamsters. Sodium monomethylarsonic acid (MMA, purity 95%) was obtained from Alfa Co., Danvers, USA. Sodium dimethylarsinic acid (DMA, purity 98%) was obtained from Katayama Chemical Co., Osaka, Japan.

A 1.25% Mg^{2+} solution was prepared by dissolving 132 g of $Mg(NO_3)_2 \cdot 6H_2O$ into 1 dm^3 of water and a 0.025% Mg^{2+} solution was obtained by diluting 1.25% Mg^{2+} solution 50 times with water.

The other reagents or chemicals used were similar to those previously described.[6–10]

Treatment of animals

Male golden hamsters weighing 95–110 g at 8–9 weeks of age, obtained from the Gunma Animal Laboratory, Gunma, Japan, were used. The animals were maintained on laboratory pellet food, CE-2 (Clea–Japan Inc., Tokyo) for at least one week before the experiments and animals had free access to food and water. The hamsters were divided into three groups, i.e. (1) arsenic; (2) selenium; (3) selenium and arsenic. The animals of each group were administered respectively $NaAsO_2$, Na_2SeO_3 or $NaAsO_2$ with Na_2SeO_3 simultaneously by subcutaneous injection in a single dose of 25 μmol (1.87 mg) As kg^{-1} body weight, 25 μmol (1.97 mg) Se kg^{-1} body weight or equal amounts of 25 μmol kg^{-1} body weight of each simultaneously.

Then the animals were housed three hamsters in a metabolic cage, MC-Ap type (Sugiyama-gen Co., Tokyo, Japan). Their breath, urine and feces were collected, and selenium and arsenic metabolites were determined.

Preparation of samples

Respired air

After the administration of selenium alone or with arsenic to hamsters, Me_2Se in respired air was collected with a charcoal column every 3, 6, 12 and 15 h.

Urine

Urine was collected every 12 h and 24 h until 120 h after the administration of selenium, arsenic or selenium plus arsenic. Urine samples were centrifuged at 3000 rpm for 15 min. The supernatant aliquot was used as the test solution.

Feces

Feces were collected every 24 h until 120 h after the administration of agents, and the feces were frozen at −20°C until examination.[11] The frozen samples were thawed at room temperature and ground in a mortar before examination.

Analysis of selenium metabolites

Me_2Se in the respired air

Me_2Se was trapped on a charcoal column and measured by gas chromatography according to a previous report.[10]

Total selenium and Me_3Se^+ in urine

Total selenium and Me_3Se^+ in urine test solution were determined by GFA AA according to previous reports.[8,9]

Total selenium in feces

Samples (0.1 g) of the homogenized feces were put into a decomposition vessel, then digested and determined by a similar process to that used for urine.

Me_3Se^+ and total selenium in the water-soluble fraction

Samples (0.5–1.0 g) of the homogenized feces were put into a centrifuge tube, to which 5 cm^3 of water

was added. The mixture was shaken for 5 min and centrifuged at 1800 rpm for 20 min. Then the supernatant was transferred into 10 cm^3 of mesflask; this process was repeated once more. The combined supernatant was adjusted to 10 cm^3 with water. This combined supernatant was used as the test solution for measurements of Me_3Se^+ and total selenium in the water-soluble fraction. Then Me_3Se^+ and total selenium in this water-soluble fraction of feces were determined in the same manner as in urine.

Extractable unknown-structure selenium (EUSe)

EUSe was calculated by taking the amounts of Me_3Se^+ from the amounts of total selenium in the water-extractable fraction of feces.

Insoluble unknown-structure selenium (IUSe)

IUSe was calculated by taking the amounts of total selenium in the water-extractable fraction of feces from the amounts of total selenium in feces.

Analysis of arsenic metabolites in the urine and feces

Arsenic metabolites in urine

To the supernatant aliquot of centrifuged urine was added four times its volume of 0.25% ammonium carbonate solution. The urine mixture was passed through a membrane filter (pore size 0.45 μm, Millipore). A 1 cm^3 aliquot of filtrate was transferred to a test-tube to which 1/100 of this volume of 30% H_2O_2 was added to oxidize the arsenite to arsenate. The mixture was shaken for about 5 s and allowed to stand for 30 min at room temperature to complete the oxidation.[11] A 50 μL aliquot of the oxidized mixture was applied to HPLC. DMA, MMA and inorganic arsenic (In-As = arsenite plus arsenate) can be separated by employing a programmed gradient elution system. The initial percentage of the elution solvent was increased from 0.2% to 1.0% ammonium carbonate solution as shown in Fig. 1 and the flow rate was 1.0 cm^3 min^{-1}. Each 0.5 cm^3 fraction of the column effluent corresponding to each arsenic metabolite was analyzed for arsenic content by GFA AA after addition of 10 μL of 1.25% Mg^{2+} solution into each 0.5 cm^3 fraction.

Total arsenic in feces

Samples (0.2–0.5 g) of homogenized feces were determined according to a previous report.[7]

Total arsenic in feces extracted with 0.2% ammonium carbonate solution

Samples (0.5–1.0 g) of homogenized feces were placed in a centrifuge tube. Ammonium carbonate solution (0.2%, 5.0–10.0 cm^3) was added and heated to 50°C for 10 min in a water bath. Then it was shaken for 15 min and then centrifuged at 3000 rpm for 15 min. A 1 cm^3 aliquot of supernatant was passed through a membrane filter similar to that used for the urine samples. A 0.5 cm^3 aliquot was then taken into

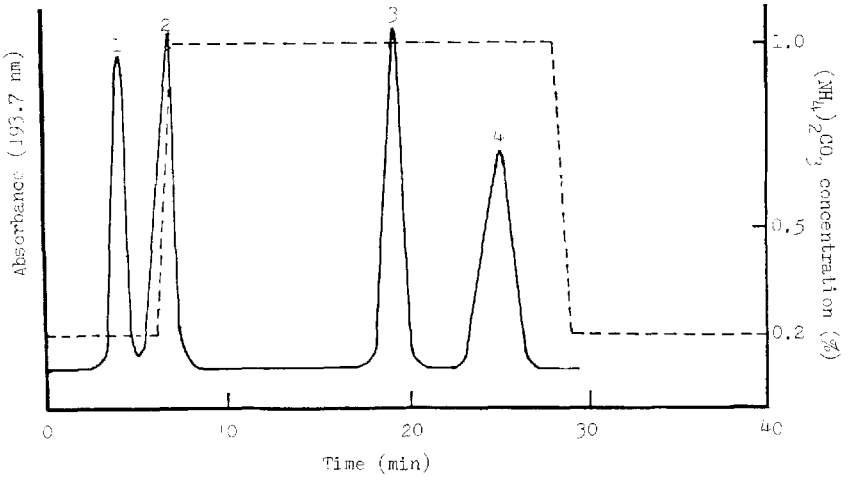

Figure 1 HPLC separation of mixture of arsenobetaine (1), dimethylarsinic acid (2), monomethylarsenic acid (3) and arsenate plus arsenite after oxidation with H_2O_2 (4). Chromatographic conditions: column, Hitachi gel #3013-N; the elution was with a gradient of ammonium carbonate solution from 0.2% to 1.0%; flow rate, 1.0 cm^3 min^{-1}. Each peak was detected with GFA AA.

a porcelain crucible together with 2 cm^3 of 25% magnesium nitrate. Then the total arsenic in the extracted feces fraction was determined by the same process as described above for total arsenic in feces.

Arsenic metabolites in water-extractable feces fraction

The arsenic metabolites (DMA, MMA and In-As) in the filtrate were analyzed by HPLC and GFA AA in the same manner as described for the urine sample.

Extractable unknown-structure arsenic (EUAs)

EUAs was calculated by taking the amounts of DMA, MMA and In-As from the amounts of total arsenic in the fraction extracted from feces with 0.2% ammonium carbonate solution.

Insoluble unknown-structure arsenic (IUAs)

IUAs was calculated by taking the amount of total arsenic in the feces fraction extracted with 0.2% ammonium carbonate solution from the amount of total arsenic in feces.

The measured values (percentages of selenium and arsenic metabolites) were calculated as selenium or arsenic values for the element rather than the compound.

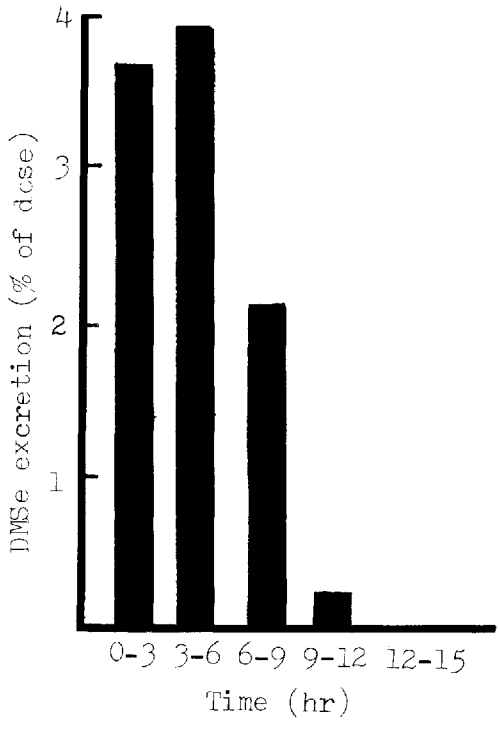

Figure 2 Changes of exhaled dimethylselenide (Me_2Se; DMSe) of hamsters after administration of Na_2SeO_3. Each value represents the mean of the percentage of the given dose of selenium from three experiments each combined for three hamsters

RESULTS AND DISCUSSION

Respiratory excretion of Me_2S and effects of arsenic on Me_2Se excretion

McConnell and Portman[3] reported that Me_2Se appeared in respiratory gases following the administration of inorganic selenium. Ganther and Baumann[4] reported that arsenic prevented the formation of Me_2Se in animals injected with selenite. Figure 2 shows the change in the amount of Me_2Se respired with the passage of time after subcutaneous administration of Na_2SeO_3: 9.7% of a given dose of selenium was excreted in the respiratory air as Me_2Se within 12 h after administration of Na_2SeO_3 to hamsters and we could not detect any Me_2Se after 12 h; the excretion of Me_2Se reached maximum levels by 3 to 6 h and diminished thereafter. On the other hand, no Me_2Se appeared in respiratory air when Na_2SeO_3 was given with $NaAsO_2$. Evidently arsenic showed the same behaviour to inhibit the formation of Me_2Se in hamsters as well as in rats, as reported by Ganther and Baumann.[4]

Urinary excretion of total selenium and Me_3Se^+

Table 1 shows the changes in the total selenium and Me_3Se^+ excreted into urine with time. In the case of administration of Na_2SeO_3 to hamsters, the amount of total selenium excreted was 37.4% of the given dose during 120 h, reaching maximum levels within 12 h and sharply decreasing thereafter. In the case of Na_2SeO_3 given with $NaAsO_2$, the excretion of total selenium was 34.7% of the given dose within 120 h, reaching maximum levels within 24 h and gradually decreasing thereafter. From these results, it seems that at early stages arsenic has a tendency to delay the urinary excretion time of total selenium by about 12 h when given with Na_2SeO_3. However, the cumulative excretion of total selenium recovered from urine during 120 h was similar for the administration of Na_2SeO_3 alone and with $NaAsO_2$. The daily urinary excretion pattern of Me_3Se^+ during 120 h was similar in the administration of Na_2SeO_3 alone and with $NaAsO_2$, and both the excretion ratios had the same value of

Table 1 Excretion of selenium metabolites[a] into the urine of hamsters during 120 h following a single subcutaneous administration of Na_2SeO_3 with or without $NaAsO_2$

Selenium metabolite	Group	Duration of experiment (h)					
		12	24	48	72	96	120
Total selenium	Na_2SeO_3 alone	19.6	4.9	8.0	1.9	1.8	1.1
		(19.6)	(24.5)	(32.5)	(34.3)	(36.2)	(37.3)
	Na_2SeO_3 + $NaAsO_2$	10.3	10.9	8.0	3.0	1.4	1.1
		(10.3)	(21.2)	(29.2)	(32.2)	(33.6)	(34.7)
Trimethylselenonium ion (Me_3Se^+)	Na_2SeO_3 alone	0.6	0.4	1.1	0.4	0.6	0.2
		(0.6)	(1.0)	(2.1)	(2.5)	(3.1)	(3.3)
	Na_2SeO_3 + $NaAsO_2$	0.7	0.8	0.7	0.7	0.2	0.2
		(0.7)	(1.5)	(2.2)	(2.9)	(3.1)	(3.3)

[a] Each value represents the mean of the percentage of the given dose from three experiments each combined for three hamsters. Each value in parentheses represents the mean for the cumulative percentage of the given dose.

3.3% of the given dose, respectively. So it does not appear that the urinary excretion of Me_3Se^+ is affected by arsenic. In these results, most of the selenium excreted into urine during 120 h after the administration of Na_2SeO_3 with and without $NaAsO_2$ were unknown-structure selenium compounds.

Fecal excretion of total selenium

Table 2 shows the time course for the excretion of total selenium into feces. In the case of administration of Na_2SeO_3 to hamsters, total selenium recovered from feces during 120 h was 4.2% of the given dose, the amount excreted by 24 h was 1.8% of the given dose, then between 24 and 48 h this decreased to 0.9% and gradually decreased thereafter. On the other hand, after the administration of Na_2SeO_3 with $NaAsO_2$, total selenium recovered from feces during 120 h was 15.9% of the given dose; the amount excreted by 24 h was 4.4% of the given dose, then between 24 and 48 h this reached maximum levels of 8.2% of the given dose, decreased to 1.5% between 48 and 72 h and gradually decreased thereafter.

Table 2 Excretion of selenium metabolites[a] into the feces of hamsters during 120 h following a single subcutaneous administration of Na_2SeO_3 with or without $NaAsO_2$

Selenium metabolite[b]	Group	Duration of experiment (h)				
		24	48	72	96	120
Total selenium	Na_2SeO_3 alone	1.8	0.9	0.7	0.5	0.3
		(1.8)	(2.7)	(3.4)	(3.9)	(4.2)
	Na_2SeO_3 + $NaAsO_2$	4.4	8.2	1.5	1.0	0.8
		(4.4)	(12.6)	(14.1)	(15.1)	(15.9)
Trimethylselenonium ion	Na_2SeO_3 alone	0.7	0.2	0.1	0.1	0.04
		(0.7)	(0.9)	(1.0)	(1.1)	(1.1)
	Na_2SeO_3 + $NaAsO_2$	0.4	0.2	0.1	0.1	0.1
		(0.4)	(0.6)	(0.7)	(0.8)	(0.9)
IUSe	Na_2SeO_3 alone	0.8	0.4	0.4	0.3	0.3
		(0.8)	(1.2)	(1.6)	(1.9)	(2.2)
	Na_2SeO_3 + $NaAsO_2$	3.4	7.6	1.1	0.6	0.5
		(3.4)	(11.0)	(12.1)	(12.7)	(13.2)
EUSe	Na_2SeO_3 alone	0.3	0.3	0.2	0.1	0.02
		(0.3)	(0.6)	(0.8)	(0.9)	(0.9)
	Na_2SeO_3 + $NaAsO_2$	0.6	0.4	0.3	0.4	0.2
		(0.6)	(1.0)	(1.3)	(1.7)	(1.9)

[a] Each value represents the mean of the percentage of the given dose from three experiments each combined for three hamsters. Each value in parentheses represents the mean for the cumulative percentage of the given dose. [b] Abbreviations. IUSe, insoluble unknown-structure selenium; EUSe, extractable unknown-structure selenium.

Fecal excretion of Me_3Se^+

The patterns of fecal excretion of Me_3Se^+ during 120 h after administration of Na_2SeO_3 alone and with $NaAsO_2$ to hamsters were very similar, and cumulative excretions of Me_3Se^+ during 120 h were 1.1% and 0.9%, respectively. It does not appear that arsenic affects the excretion of Me_3Se^+ into feces.

Fecal excretion of extractable unknown-structure selenium (EUSe)

The proportions of EUSe in feces during 120 h after the administration of Na_2SeO_3 alone and with $NaAsO_2$ were 0.9% and 1.9% of the given dose respectively. It does not appear that arsenic given with selenium to hamsters has an appreciable effect on the excretion of EUSe into feces.

Fecal excretion of insoluble unknown-structure selenium (IUSe)

When Na_2SeO_3 was administered to hamsters, the amount of excretion of IUSe into feces was 2.2% of the given dose during 120 h, reaching maximum levels of 0.8% of the given dose within 24 h and gradually decreasing thereafter. When Na_2SeO_3 was given with $NaAsO_2$, the amount of excretion of IUSe into feces was 13.2% of the given dose during 120 h, reaching maximum levels of 7.6% of the given dose between 24 and 48 h, then sharply decreasing to 1.1% between 48 and 72 h and finally decreasing to 0.5% of the given dose by 96–120 h. So the IUSe recovered from feces of hamsters given Na_2SeO_3 with $NaAsO_2$ increased by 6.0-fold compared with those given Na_2SeO_3 alone, and the increased IUSe was estimated to be 11.0% of the given dose. In these results, it seems that arsenic may antagonize the toxicity of selenium by accelerating the fecal excretion of IUSe when selenium was given simultaneously with arsenic to hamsters.

Urinary excretion of arsenic metabolites

Odanaka *et al.*[12] reported that the major urinary metabolites of arsenic in hamsters following intravenous and oral administration of arsenic acid were DMA and In-As, and MMA was excreted as a minor metabolite. Inamasu[11] reported similar results to Odanaka *et al.* using administration of $NaAsO_2$ following stomach intubation. In the present report, hamsters were administered $NaAsO_2$ with and without Na_2SeO_3 by subcutaneous injection. Only DMA, MMA and In-As in the urine were found. Table 3 shows the analytical determination of arsenic metabolites in the urine during 120 h after the administration of the agents.

Urinary excretion of DMA

The amount of DMA recovered from urine during 120 h after the administration of $NaAsO_2$ alone was 25.5% of the given dose, reaching maximum levels of 11.8% of the given dose between 12 and 24 h and gradually decreasing thereafter. The excretion of DMA during 120 h decreased to 20.2% of the given dose

Table 3 Excretion of arsenic metabolites[a,d] into the urine of hamsters during 120 h following a single subcutaneous administration of $NaAsO_2$ with or without Na_2SeO_3

Arsenic metabolite[b]	Group	Duration of experiment (h)					
		12	24	48	72	96	120
DMA	$NaAsO_2$ alone	5.9	11.8	5.1	1.5	0.7	0.5
		(5.9)	(17.7)	(22.8)	(24.3)	(25.0)	(25.5)
	$NaAsO_2$ + Na_2SeO_3	1.7	6.5	9.3	2.0	0.5	0.2
		(1.7)	(8.2)	(17.5)	(19.5)	(20.0)	(20.2)
MMA	$NaAsO_2$ alone	0.7	0.5	0.1	N.D.[c]	N.D.	N.D.
		(0.7)	(1.2)	(1.3)	(1.3)	(1.3)	(1.3)
	$NaAsO_2$ + $NaSeO_3$	N.D.	1.2	0.4	0.3	N.D.	N.D.
			(1.2)	(1.6)	(1.9)	(1.9)	(1.9)
In-As	$NaAsO_2$ alone	17.5	1.1	0.2	N.D.	N.D.	N.D.
		(17.5)	(18.6)	(18.8)	(18.8)	(18.8)	(18.8)
	$NaAsO_2$ + Na_2SeO_3	6.5	3.2	1.4	0.03	N.D.	N.D.
		(6.5)	(9.7)	(11.1)	(11.1)	(11.1)	(11.1)

[a] Each value represents the mean of the percentage of the given dose from three experiments each combined for three hamsters. Each value in parentheses represents the mean for the cumulative percentage of the given dose. [b] Abbreviations: DMA, dimethylarsinic acid; MMA, monomethylarsonic acid; In-As, arsenite + arsinate. [c] N.D., not detected. [d] Only DMA, MMA and In-As were detected in the urine.

following administration of $NaAsO_2$ simultaneously with Na_2SeO_3, reached maximum levels of 9.3% of the given dose between 24 and 48 h and sharply decreased thereafter. So it seems that selenium has a tendency to delay and decrease the excretion of DMA into urine.

Urinary excretion of MMA

The amount of urinary excretion of MMA during 120 h after the administration of $NaAsO_2$ alone and with Na_2SeO_3 were only 1.3% and 1.9% of the given dose, respectively. So it does not seem that selenium has an appreciable effect on the excretion of MMA into urine.

Urinary excretion of In-As

The excretion of In-As after administration of $NaAsO_2$ was 18.8% of the given dose during 120 h, reached maximum levels of 17.5% of the given dose by 12 h and sharply decreased to 1.1% between 12 and 24 h. On the other hand, the excretion of In-As after administration of $NaAsO_2$ simultaneously with Na_2SeO_3 was 11.1% of the given dose during 120 h, and reached maximum levels of 6.5% of the given dose by 12 h; however, the tendency to decrease was gradual. So it seems that selenium has a tendency to decrease the excretion of In-As as well as DMA into urine.

Total arsenic in the urine

Only DMA, MMA and In-As in urine were determined, so the total amount of DMA, MMA and In-As in urine was regarded as total arsenic. The excretion of total arsenic into urine during 120 h after the administration of $NaAsO_2$ alone and with Na_2SeO_3 were 45.6% and 33.2% of the given dose, respectively. Therefore it was estimated that the decrease in total arsenic in urine was 12.4% of the given dose following administration of $NaAsO_2$ simultaneously with Na_2SeO_3.

In these results, the major metabolites of arsenic were DMA and In-As, and the minor metabolite was MMA; the proportions of each metabolite were 55.9%, 41.2% and 2.9% of excreted cumulative arsenic during 120 h. These results were very similar to the reports of Odanaka *et al.*[12] and Inamasu.[11]

Fecal excretion of arsenic metabolites

Odanaka *et al.*[12] reported that the major fecal excretion product of arsenic metabolized in male hamsters following intravenous administration of arsenic acid was MMA. However, Inamasu[11] reported that the major fecal arsenic metabolites excreted were In-As and MMA (studied by stomach intubation for hamsters) and that MMA was the major methylated metabolite of arsenic in feces. Table 4 shows the analytical results of arsenic metabolites in feces during 120 h after the administration of $NaAsO_2$ with and without Na_2SeO_3.

Excretion of total arsenic into feces

Excretion of total arsenic into feces after the administration of $NaAsO_2$ was 24.5% of the given dose during 120 h, reaching maximum levels of 18.0% by 24 h and sharply decreasing thereafter. On the other hand, the excretion of total arsenic into feces after administration of $NaAsO_2$ simultaneously with Na_2SeO_3 was 38.2% of the given dose during 120 h, reaching maximum levels of 24.5% of the given dose by 24–48 h.

Excretion of insoluble unknown-structure arsenic (IUAs) into feces

IUAs recovered from feces after the administration of $NaAsO_2$ alone was 8.5% of the given dose during 120 h, reaching maximum levels of 6.3% of the given dose by 24 h. On the other hand, IUAs recovered from feces after the administration of $NaAsO_2$ with Na_2SeO_3 was 19.1% of the given dose, reaching maximum levels of 13.4% of the given dose by 24–48 h. Therefore it was estimated that the increase of IUAs in feces was 10.6% of the given dose following administration of $NaAsO_2$ simultaneously with Na_2SeO_3.

Fecal excretion of DMA and MMA

DMA and MMA were recovered from feces during 120 h after the administration of $NaAsO_2$ alone and with Na_2SeO_3; the amounts of DMA were 1.7% and 2.8% of the given dose, and those of MMA were 2.3% and 2.1%, respectively. In these results, it does not seem that selenium may affect the excretion of DMA and MMA into feces.

Fecal excretion of extractable unknown-structure arsenic (EUAs)

The amount of EUAs recovered from feces after the administration of $NaAsO_2$ was 10.8% of the given dose during 120 h, reaching maximum levels of 7.6% by 24 h and then sharply decreasing thereafter. On the other hand, the amount of EUAs recovered from feces

Table 4 Excretion of arsenic metabolites[a] into the feces of hamsters during 120 h following a single subcutaneous administration of $NaAsO_2$ with or without Na_2SeO_3

Arsenic metabolite[b]	Group	Duration of experiment (h)				
		24	48	72	96	120
Total arsenic	$NaAsO_2$ alone	18.0	3.7	1.2	0.9	0.7
		(18.0)	(21.7)	(22.9)	(23.8)	(24.5)
	$NaAsO_2$ + Na_2SeO_3	8.1	24.5	3.4	1.4	0.8
		(8.1)	(32.6)	(36.0)	(37.4)	(38.2)
DMA	$NaAsO_2$ alone	1.3	0.3	0.1	N.D.[c]	N.D.
		(1.3)	(1.6)	(1.7)	(1.7)	(1.7)
	$NaAsO_2$ + Na_2SeO_3	0.7	1.4	0.6	0.1	N.D.
		(0.7)	(2.1)	(2.7)	(2.8)	(2.8)
MMA	$NaAsO_2$ alone	1.9	0.4	0.04	N.D.	N.D.
		(1.9)	(2.3)	(2.3)	(2.3)	(2.3)
	$NaAsO_2$ + Na_2SeO_3	0.7	1.1	0.3	N.D.	N.D.
		(0.7)	(1.8)	(2.1)	(2.1)	(2.1)
In-As	$NaAsO_2$ alone	1.0	0.3	N.D.	N.D.	N.D.
		(1.0)	(1.3)	(1.3)	(1.3)	(1.3)
	$NaAsO_2$ + Na_2SeO_3	3.3	4.3	0.7	N.D.	N.D.
		(3.3)	(7.6)	(8.3)	(8.3)	(8.3)
EUAs[d]	$NaAsO_2$ alone	7.6	1.3	0.7	0.7	0.5
		(7.6)	(8.9)	(9.6)	(10.3)	(10.8)
	$NaAsO_2$ + Na_2SeO_3	0.3	4.3	0.2	0.7	0.4
		(0.3)	(4.6)	(4.8)	(5.5)	(5.9)
IUAs[e]	$NaAsO_2$ alone	6.3	1.5	0.3	0.2	0.2
		(6.3)	(7.8)	(8.1)	(8.3)	(8.5)
	$NaAsO_2$ + Na_2SeO_3	3.2	13.4	1.5	0.6	0.4
		(3.2)	(16.6)	(18.1)	(18.7)	(19.1)

[a] Each value represents the mean of the percentage of the given dose from three experiments each combined for three hamsters. Each value in parentheses represents the mean for the cumulative percentage of the given dose. [b] Abbreviations: DMA, dimethylarsinic acid; MMA, monomethylarsonic acid; In-As, arsenite + arsenate; EUAs, extractable unknown-structure arsenic: IUAs, insoluble unkown-structure arsenic. [c] N.D., not detected. [d] EUAs was calculated by taking the amounts of DMA, MMA and In-As from the amounts of total arsenic in the feces fraction extracted with 0.2% ammonium carbonate solution. [e] IUAs was calculated by taking the amounts of total arsenic in the feces fraction extracted with 0.2% ammonium carbonate solution from the amount of total arsenic in the feces.

after the administration of $NaAsO_2$ with Na_2SeO_3 was 5.9% of the given dose, reaching maximum levels of 4.3% of the given dose by 24–48 h and then sharply decreasing thereafter. So it seems that selenium has a tendency to decrease the excretion of EUAs into feces.

Fecal excretion of In-As

Excretion of In-As into feces after the administration of $NaAsO_2$ was 1.3% of the given dose during 120 h, reaching maximum levels of 1.0% of the given dose by 24 h; In-As could not be determined at 72 h. On the other hand, excretion of In-As into feces after the administration of $NaAsO_2$ simultaneously with Na_2SeO_3 was 8.3% of the given dose during 120 h, and reached maximum levels of 4.3% by 24–48 h, then decreased to 0.7% of the given dose by 48–72 h, and In-As could not be detected at 96 h. So it seems that selenium has a tendency to increase the excretion of In-As into feces, and it was estimated that the increase in In-As in feces was 7.0% of the given dose following administration of $NaAsO_2$ simultaneously with Na_2SeO_3.

In these results, it seems that the decrease of urinary excretion of DMA and In-As and acceleration of fecal excretion of IUAs and In-As by giving arsenic with selenium may be one of the factors in the detoxication of arsenic.

CONCLUSIONS

The results of our experiments can be stated as follows.

(1) About 10% of a given dose of selenium was

excreted into respired air as Me_2Se during 12 h after subcutaneous administration of Na_2SeO_3. Excretion of Me_2Se into the respiratory air was inhibited by administration of Na_2SeO_3 simultaneously with $NaAsO_2$.

(2) Giving Na_2SeO_3 with $NaAsO_2$ had no appreciable effect on the excretion of Me_3Se^+ into urine and feces.

(3) Giving Na_2SeO_3 with $NaAsO_2$ increased the excretion of IUSe into feces, and the amount of increase of IUSe was 10.9% of a given dose of selenium.

(4) Giving $NaAsO_2$ with Na_2SeO_3 decreased the excretion of DMA and In-As into urine during 120 h after the administration of their agents and the amounts of decrease were 5.3% and 7.7% of a given dose of arsenic, respectively.

(5) Selenium increased the excretion of IUAs and In-As into feces, and the amounts of increase were 10.6% and 7.0% of a given dose of arsenic, respectively.

(6) Selenium decreased the excretion of EUAs into feces, and the amount of decrease was 4.9% of a given dose of arsenic.

(7) It made little difference to the excretion of MMA into urine and feces and of DMA into feces whether $NaAsO_2$ alone or with Na_2SeO_3 was administered.

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