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# Acute Effect of Orally Administered Gallium Arsenide, Gallium Nitrate and Disodium Arsenate on Heme Synthesis in Male and Female Mice

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**Gallium arsenide (GaAs), gallium nitrate and disodium arsenate were each administered orally to mice of both sexes (Jcl:ICR strain) at varying dosage levels and examined for their effects on the heme biosynthetic enzyme system in the spleen, liver, kidney and peripheral blood.**

**The results indicate that the areas most affected by administration of gallium nitrate or disodium arsenate were enzymes in the hematogenous cells of mouse spleen. In mice of the disodium arsenate-treated groups δ-aminolevulinic acid synthase (ALAS, EC 2.3.1.37), the first enzyme in the heme biosynthetic pathway and the rate-limiting enzyme for heme synthesis, δ-aminolevulinic acid dehydratase (ALAD, EC 4.2.1.24) and porphobilinogen deaminase (PBGD, EC 4.3.1.8) activities in the spleen were markedly depressed in a dose-dependent fashion. A similar, but apparently less marked, reduction in these enzyme activities in the spleen was also observed in the gallium nitrate-treated groups. The effects of these treatments were more conspicuous in female than in male mice. An *in vitro* experiment demonstrated that activities of purified ALAS, ALAD and PBGD were not inhibited to any noticeable extent by arsenic compounds.**

**These results suggest that disodium arsenate may strongly inhibit heme biosynthesis in mouse spleen.**

**Keywords: gallium arsenide; arsenic compounds; heme synthesis; δ-aminolevulinic acid synthase; mouse; spleen**

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## ABBREVIATIONS

| | |
|---|---|
| ALA | δ-aminolevulinic acid |
| ALAS | ALA synthase |
| ALAD | ALA dehydratase |
| PBGD | porphobilinogen deaminase |
| PROTO | protoporphyrin |
| Zn–PROTO | zinc–protoporphyrin |
| DTT | dithiothreitol |
| RBC | red blood cell |

## INTRODUCTION

While gallium arsenide (GaAs) is currently in widespread use in advanced microelectronic industries as an intermetallic semiconductor,[1,2] few reports have been made so far on the influence of GaAs, gallium or arsenic upon activities of the porphyrin metabolic enzymes.[3–5] Webb *et al.*[3] demonstrated an increased uroporphyrin/coproporphyrin ratio in urine after the exposure of rats to GaAs; Woods and Fowler[6] and Martinez *et al.*[7] observed that administration of trivalent and pentavalent arsenic resulted in an increase in the urinary ratio of uroporphyrin relative to coproporphyrin in rats. In our previous experiments on female Wistar rats, we found that GaAs and arsenic compounds, when each was administered in a single intratracheal or intragastric dose, gave rise to a significant elevation of ALAS activity in bone marrow cells as

compared with untreated controls, with a concurrent reduction in ALAD and PBGD activities in blood and kidney.[8] Moreover, in a subsequent experiment on female mice, we also recognized that the same compounds administered in the same way cause ALAS, ALAD and PBGD activities in spleen to decrease to a marked extent.[9] On the other hand, Goering *et al.*[10] found that intratracheal administration of GaAs to male CD rats resulted in an increase in urinary δ-aminolevulinic acid (ALA) and a marked decrease in erythrocyte ALAD activity. They reported later that gallium was identified as the causative agent of GaAs-induced decrease in ALAD activity, stating that determination of the enzymes and metabolic products of the porphyrin metabolic pathway would be useful as biological indicators of intoxication by gallium compounds.[11] From these reports one can surmise that the influence of GaAs on porphyrin metabolic enzymes is not due to GaAs itself but to gallium or arsenic isolated therefrom and varies in magnitude from one animal species to another and also between the sexes within a given species.

In the present study the effects of GaAs, disodium arsenate and gallium nitrate on the porphyrin metabolic enzyme were investigated in mice of both sexes.

## MATERIALS AND METHODS

### Chemicals

GaAs (purity 99.999%) was obtained from Alfa Products (Danvers, MA, USA) and was prepared by the method of Yamauchi *et al.*[12] ALA was obtained from Daiichi Pure Chemicals Company (Tokyo). Porphobilinogen (PBG), protoporphyrin (PROTO), and zinc–protoporphyrin (Zn–PROTO) were obtained from Porphyrin Products (Logan, UT, USA). Other chemicals used were of reagent grade as available.

### Animals and treatment

Male and female Jcl:ICR mice at 5 weeks of age were used. These animals were allocated to three treatment groups each consisting of five or six animals and received three oral doses of GaAs (0.5, 1.0 and 2 g/ml/kg body weight), sodium arsenate ($Na_2HAsO_4 \cdot 7H_2O$) (27, 54 and 82 mg/ml/kg body weight) or gallium nitrate ($Ga(NO_3)_3 \cdot nH_2O$) (0.64, 1.28 and 2.55 g/ml/kg body weight). The injection volume was used in order to average body weight of mice in each group: male mice 28.6±1.94 g and female mice 25.0±0.75 g. Control mice received the same volume of 5% glucose solution without the metals. These animals were sacrificed under anesthesia with ether 18 h after the administration, heparinized whole blood was collected, and the livers were perfused with cold saline. The hematocrit was determined by capillary tube methods. Kidney and spleen were carefully removed and weighed.

### Enzyme preparation from liver, kidney, spleen and blood

Liver, kidney and spleen were homogenized in 0.25 M sucrose solution (pH 8.0). The supernatant and precipitation fractions were prepared from the homogenates by centrifugation at 48 800*g* for 30 min. The precipitation fraction was further washed twice with 0.25 M sucrose, resuspended in the same solution and used for the assay of ALAS. The supernatant fraction was used for the assay of ALAD and PBGD. Whole-blood lysates were also used for the assay of ALAD and PBGD.

### Enzyme assay

ALAS,[13] ALAD[14] and PBGD[13] were assayed according to the method described previously.

### Other procedures

Protein was determined by the method of Lowry *et al.*[15] with a modification.[16] Erythrocyte porphyrins were determined by the method reported previously.[17] Purified ALAS and ALAD were taken from rabbit liver according to the method previously reported[16, 18] and used in the *in vitro* study.

The statistical significance of the differences between the treated and the control groups was determined using Student's *t*-test.

**Table 1** Effects of arsenate and/or gallium compounds on body weight; spleen, liver and kidney weights; and hematocrit and hemoglobin values in whole blood of male mice

| Dose (g/kg body wt) | Weight[a] (g) | | | | Hematocrit (%) | Hemoglobin (g/dl) |
|---|---|---|---|---|---|---|
| | Body | Liver | Spleen | Kidney | | |
| Control | 31.3±0.95 | 2.80±0.13 | 0.13±0.04 | 0.51±0.02 | 42.6±1.75 | 13.9±0.52 |
| GaAs | | | | | | |
| 0.5 | 31.1±0.80 | 2.46±0.12** | 0.13±0.03 | 0.54±0.05 | 41.0±0.64 | 14.1±0.18 |
| 1.0 | 31.1±0.80 | 2.58±0.22 | 0.12±0.03 | 0.54±0.03 | 40.6±0.58* | 13.8±0.44 |
| 2.0 | 31.4±0.49 | 2.18±0.11** | 0.13±0.01 | 0.53±0.03 | 39.7±1.60* | 13.4±1.09 |
| $Ga(NO_3)_2 \cdot nH_2O$ | | | | | | |
| 0.64 | 31.0±0.86 | 2.12±0.32** | 0.10±0.02 | 0.47±0.04 | 40.6±2.13 | 13.4±0.77 |
| 1.28 | 30.9±0.69 | 2.30±0.33** | 0.11±0.01 | 0.50±0.02 | 42.4±0.96 | 14.4±0.64 |
| 2.55 | 30.8±0.97 | 2.03±0.24** | 0.11±0.00 | 0.52±0.02 | 41.4±0.58 | 14.1±0.76 |
| $Na_2HAsO_4 \cdot 7H_2O$ | | | | | | |
| 0.027 | 30.9±1.28 | 2.08±0.30** | 0.10±0.01 | 0.51±0.05 | 41.2±1.03 | 13.5±0.22 |
| 0.054 | 29.8±0.98* | 2.00±0.22** | 0.09±0.01* | 0.49±0.04 | 41.4±1.45 | 13.5±0.10 |
| 0.108 | 29.3±1.08** | 2.02±0.36** | 0.08±0.02* | 0.49±0.06 | 41.1±0.62 | 13.4±0.21 |

[a] Values represent means±SD for 5–6 mice. Statistically significant from control at $*P<0.05$ and $**P<0.01$.

## RESULTS

### Body weight, liver and spleen weights, hematocrit and hemoglobin values

Body weight and liver and spleen weights of male and female mice in the $Na_2HasO_4$-treated group were found to decrease in a dose-dependent manner to a significant extent as compared with the control group. No significant changes in kidney weight and hematocrit and hemoglobin values were noted in any of the treated groups (Tables 1, 2).

### Porphyrin metabolic enzyme activities in spleen

ALAS activity in spleen was significantly decreased in both the $Ga(NO_3)_3$- and the $Na_2HAsO_4$-treated groups, the decrease being greater in females than in males and in the

**Table 2** Effects of arsenate and/or gallium compounds on body weight; spleen, liver and kidney weights; and hematocrit and hemoglobin values in whole blood of female mice

| Dose (g/kg body wt) | Weight[a] (g) | | | | Hematocrit (%) | Hemoglobin (g/dl) |
|---|---|---|---|---|---|---|
| | Body | Liver | Spleen | Kidney | | |
| Control | 26.3±1.28 | 2.02±0.21 | 0.13±0.04 | 0.33±0.07 | 44.7±1.49 | 14.8±1.50 |
| GaAs | | | | | | |
| 0. 5 | 26.0±0.55 | 1.89±0.20 | 0.11±0.02 | 0.33±0.04 | 44.0±2.68 | 14.3±0.85 |
| 1.0 | 25.6±0.86 | 1.61±0.22* | 0.07±0.02* | 0.34±0.03 | 45.8±1.72 | 15.0±1.14 |
| 2.0 | 26.2±1.29 | 2.02±0.17 | 0.09±0.01 | 0.37±0.04 | 44.2±3.05 | 14.4±1.22 |
| $Ga(NO_3)_2 \cdot nH_2O$ | | | | | | |
| 0.64 | 25.7±1.21 | 1.76±0.37 | 0.08±0.01* | 0.32±0.04 | 45.4±1.36 | 15.0±0.91 |
| 1.28 | 24.2±1.69* | 1.64±0.26* | 0.08±0.02* | 0.31±0.04 | 47.9±3.81 | 15.4±0.94 |
| 2.55 | 25.7±1.69 | 1.64±0.26 | 0.10±0.03 | 0.32±0.03 | 47.5±2.57* | 16.2±1.39 |
| $Na_2HAsO_4 \cdot 7H_2O$ | | | | | | |
| 0.027 | 26.0±0.84 | 2.05±0.18 | 0.08±0.01* | 0.33±0.03 | 43.1±1.20 | 15.1±1.03 |
| 0.054 | 23.5±0.63** | 1.67±0.12** | 0.07±0.01* | 0.30±0.03 | 44.1±1.69 | 14.9±0.56 |
| 0.108 | 22.8±0.74** | 1.64±0.24* | 0.07±0.02* | 0.33±0.03 | 44.1±2.46 | 15.6±0.67 |

[a] Values represent means±SD for 5–6 mice. Statistically significant from control at $*P<0.05$ and $**P<0.01$.

**Table 3** Effects of arsenate and/or gallium compounds on porphyrin metabolic enzymes in spleen of male mice

| Dose (g/kg body wt) | Activity[a] (nmol/mg h) | | | |
|---|---|---|---|---|
| | | ALAD | | |
| | ALAS | −DTT | +DTT | PBGD |
| Control | 0.77±0.24 | 15.41±3.58 | 25.6±5.71 | 0.96±0.16 |
| GaAs | | | | |
| 0.5 | 0.79±0.21 | 11.94±2.70 | 21.8±3.63 | 0.93±0.12 |
| 1.0 | 0.61±0.14 | 9.60±2.97* | 19.4±5.81 | 0.80±0.17 |
| 2.0 | 0.59±0.07 | 9.86±1.38** | 20.9±1.89 | 0.86±0.17 |
| $Ga(NO_3)_2 \cdot nH_2O$ | | | | |
| 0.64 | 0.45±0.22* | 9.28±3.33* | 13.6±4.09** | 0.66±0.11** |
| 1.28 | 0.38±0.07** | 8.88±2.72** | 13.3±3.66** | 0.47±0.08** |
| 2.55 | 0.71±0.11 | 13.91±1.26 | 19.4±2.23* | 0.95±0.12 |
| $Na_2HAsO_4 \cdot 7H_2O$ | | | | |
| 0.027 | 0.66±0.25 | 8.27±1.88** | 12.6±2.71** | 0.54±0.17** |
| 0.054 | 0.39±0.22* | 5.01±1.39** | 8.3±2.79** | 0.37±0.14** |
| 0.108 | 0.23±0.11** | 4.84±1.56** | 7.9±2.62** | 0.28±0.05** |

[a] Values represent means±SD for 5–6 mice. Statistically significant from control at *$P<0.05$ and ** $P<0.01$.

$Na_2HAsO_4$-treated group than in the $Ga(NO_3)_3$-treated group. ALAD and PBGD activities, too, were more markedly decreased in the $Na_2HAsO_4$-treated than in the GaAs- or $Ga(NO_3)_3$-treated groups, the decreases being again greater in female mice (Tables 3, 4).

## ALAD and PBGD activities and porphyrin content of peripheral blood

ALAD and PBGD activities did not undergo any conspicuous dose-dependent changes in the

**Table 4** Effects of arsenate and/or gallium compounds on porphyrin metabolic enzymes in spleen of female mice

| Dose (g/kg body wt) | Activity[a] (nmol/mg h) | | | |
|---|---|---|---|---|
| | | ALAD | | |
| | ALAS | −DTT | +DTT | PBGD |
| Control | 0.68±0.20 | 9.67±3.80 | 18.8±5.84 | 0.56±0.10 |
| GaAs | | | | |
| 0.5 | 0.57±0.07 | 9.26±2.45 | 16.8±3.82 | 0.58±0.08 |
| 1.0 | 0.57±0.43 | 6.73±4.55 | 12.1±8.80 | 0.34±0.19* |
| 2.0 | 0.60±0.27 | 6.30±2.02 | 13.1±4.37 | 0.43±0.13 |
| $Ga(NO_3)_2 \cdot nH_2O$ | | | | |
| 0.64 | 0.37±0.16* | 5.68±2.99 | 11.0±5.82 | 0.39±0.20 |
| 1.28 | 0.40±0.16* | 10.02±3.98 | 16.1±5.35 | 0.65±0.17 |
| 2.55 | 0.29±0.11** | 10.36±4.31 | 16.1±5.83 | 0.60±0.24 |
| $Na_2HAsO_4 \cdot 7H_2O$ | | | | |
| 0.027 | 0.27±0.08** | 5.07±0.83* | 9.8±2.43* | 0.32±0.14** |
| 0.054 | 0.19±0.09** | 3.68±1.19** | 7.7±2.41** | 0.24±0.09** |
| 0.108 | 0.16±0.13** | 2.58±0.78** | 5.1±1.04** | 0.11±0.10** |

[a] Values represent means±SD for 5–6 mice. Statistically significant from control at *$P<0.05$ and ** $P<0.01$.

$Ga(NO_3)_3$- and $Na_2HAsO_4$-treated groups though they were consistently lower than the respective control levels, with the decrease being greater for PBGD than for ALAD and in females than males. Although there were no gross changes in the porphyrin content of erythrocytes, the zinc–protoporphyrin (Zn–PROTO) content of erythrocytes varied with the sexes, being higher in females (Tables 5, 6).

## Porphyrin metabolic enzyme activities in liver

ALAS activity in liver showed a tendency to be higher in $Na_2HAsO_4$-treated males than the control group, the difference failing to achieve statistical significance. This enzyme activity was not determined in female mice. On the other hand, ALAD activity was decreased to a significant dose-dependent extent in females of the $Na_2HAsO_4$-treated group. PBGD activity was found to be significantly decreased in females receiving 0.65 mg $Ga(NO_3)_3$/kg body weight, while, conversely, it was higher than the control level in males treated with $Na_2HAsO_4$ at 108 mg/kg (Tables 7, 8).

## ALAD and PBGD activities in kidney

ALAD activity was significantly decreased in males of the $Ga(NO_3)_3$-treated group. Changes in PBGD activity were observed to occur in $Ga(NO_3)_3$-treated females and in $Na_2HAsO_4$-treated males, but no distinct dose–response relationship was observed for the activity level of either of these enzymes (Tables 7, 8).

# DISCUSSION

Administration of $Na_2HAsO_4$ gave rise to a marked dose-dependent decrease in ALAS, ALAD and PBGD activities in spleen in male and female mice, the decreases being greater in females than in males invariably for all the enzymes. In view, however, of the previous findings that $Na_2HAsO_4$ had little influence on these enzyme activities in rat spleen and that an approximately two-fold, significant increase in ALAS activity in bone marrow cells as compared with the control level occurred without concomitant inhibition of ALAD and PBGD activities following treatment with $Na_2HAsO_4$ in rats,[8] it was presumed that the effect of GaAs or of arsenic compounds on the porphyrin metabolic

**Table 5** Effects of arsenate and/or gallium compounds on porphyrin metabolic enzymes and porphyrin in peripheral blood of male mice

| Dose (g/kg body wt) | Enzyme activity[a] ALAD (μmol/m RBC h) −DTT | ALAD (μmol/m RBC h) +DTT | PBGD (nmol/ml RBC h) | Porphyrin contents[a] (μg/ml RBC) PROTO | Porphyrin contents[a] (μg/ml RBC) Zn–PROTO |
|---|---|---|---|---|---|
| Control | 1.32±0.32 | 1.48±0.34 | 40.5±0.88 | 28.8±9.89 | 104.9±15.3 |
| GaAs | | | | | |
| 0.5 | 1.26±0.26 | 1.36±0.22 | 42.6±4.37 | 30.8±6.69 | 119.8±29.7 |
| 1.0 | 1.29±0.15 | 1.54±0.16 | 38.5±2.68 | 21.7±9.31 | 105.7±18.2 |
| 2.0 | 0.80±0.10** | 1.04±0.20* | 39.9±4.10 | 27.3±6.44 | 129.1±17.5* |
| $Ga(NO_3)_2 \cdot nH_2O$ | | | | | |
| 0.64 | 0.93±0.24 | 1.06±0.21* | 33.3±4.20** | 20.7±6.48 | 86.8±10.1 |
| 1.28 | 1.07±0.42 | 1.33±0.48 | 34.2±4.84* | 16.9±2.48* | 96.7±8.1 |
| 2.55 | 1.13±0.21 | 1.32±0.25 | 44.1±5.48 | 28.3±5.61 | 128.6±22.8 |
| $Na_2HAsO_4 \cdot 7H_2O$ | | | | | |
| 0.027 | 0.92±0.22* | 1.03±0.22* | 31.3±3.49** | 23.5±2.87 | 104.9±6.2 |
| 0.054 | 0.96±0.22 | 1.11±0.27 | 31.7±3.54** | 17.6±4.80* | 88.4±14.2 |
| 0.108 | 1.36±0.18 | 1.54±0.34 | 34.5±3.88** | 19.7±2.51 | 89.1±4.9 |

[a] Values represent means±SD for 5–6 mice. Statistically significant from control at * $P<0.05$ and ** $P<0.01$.

**Table 6** Effects of arsenate and/or gallium compounds on porphyrin metabolic enzymes and porphyrin in peripheral blood of female mice

| Dose (g/kg body wt) | Enzyme activity[a] ALAD (μmol/m RBC h) −DTT | ALAD (μmol/m RBC h) +DTT | PBGD (nmol/ml RBC h) | Porphyrin contents[a] (μg/ml RBC) PROTO | Porphyrin contents[a] (μg/ml RBC) Zn–PROTO |
|---|---|---|---|---|---|
| Control | 1.01±0.06 | 1.21±0.09 | 39.4±4.45 | 22.6±8.14 | 84.8±13.3 |
| GaAs | | | | | |
| 0.5 | 0.99±0.16 | 1.17±0.19 | 37.9±3.82 | 19.8±6.71 | 88.0±8.3 |
| 1.0 | 0.73±0.27 | 0.90±0.33 | 31.7±6.06 | 17.7±6.42 | 112.6±25.7* |
| 2.0 | 0.84±0.16 | 1.05±0.23 | 35.1±4.71 | 25.8±6.94 | 115.9±24.2* |
| $Ga(NO_3)_2 \cdot nH_2O$ | | | | | |
| 0.64 | 0.80±0.22 | 0.98±0.27 | 32.4±1.65* | 22.4±4.10 | 116.4±22.2* |
| 1.28 | 0.77±0.17* | 0.95±0.19* | 32.1±4.11* | 26.4±9.04 | 104.5±22.1 |
| 2.55 | 0.79±0.10** | 0.97±0.11** | 35.2±1.56 | 25.1±7.49 | 101.2±28.1 |
| $Na_2HAsO_4 \cdot 7H_2O$ | | | | | |
| 0.027 | 0.80±0.18* | 0.95±0.16* | 33.0±4.39 | 22.2±7.82 | 131.9±29.6** |
| 0.054 | 0.79±0.25 | 1.01±0.28 | 29.3±4.30** | 22.9±7.32 | 102.0±10.4* |
| 0.108 | 0.58±0.07** | 0.82±0.10** | 28.7±4.46** | 20.6±6.42 | 120.2±27.4* |

[a] Values represent means±SD for 5–6 mice. Statistically significant from control at * $P<0.05$ and ** $P<0.01$.

enzymes in hematopoietic tissue varies in nature and magnitude from the rat to the mouse.

It is known that, in the mouse, 50% of hematopoiesis occurs in the spleen (the remaining 50% is in the bone marrow erythroblast).[19] Decreased spleen ALAS, ALAD and PBGD activities in this particular animal species may therefore be interpreted as directly animal species may therefore be interpreted as directly indicating inhibited biosynthesis, although a decreased hemoglobin content of the spleen was not observed in the present experiment. Further studies to assess the time course of the hemoglobin content of spleen following administration of arsenic compounds in mice thus seems indicated.

**Table 7** Effects of arsenate and/or gallium compounds on porphyrin metabolic enzymes in liver and kidney of male mice

| Dose (g/kg B.W.) | Liver ALAS activity (pmol/mg/h) | Liver ALAD activity (nmol/mg/h) | Liver PBGD activity (nmol/mg/h) | Kidney ALAD activity (nmol/mg/h) | Kidney PBGD activity (pmol/mg/h) |
|---|---|---|---|---|---|
| Control | 95.2±28.3 | 19.6±3.73 | 0.15±0.02 | 10.08±2.99 | 86.9±5.39 |
| GaAs | | | | | |
| 0.5 | 68.9±25.1 | 18.7±1.98 | 0.15±0.00 | 8.53±0.68 | 91.6±2.01 |
| 1.0 | 84.8±34.2 | 18.2±3.25 | 0.15±0.01 | 9.34±1.32 | 94.9±7.81 |
| 2.0 | 75.1±35.0 | 17.3±1.42 | 0.15±0.01 | 8.35±1.34 | 95.4±7.19 |
| $Ga(NO_3)_2 \cdot nH_2O$ | | | | | |
| 0.64 | 88.6±31.9 | 15.7±2.83 | 0.14±0.01 | 6.71±0.55* | 83.9±5.46 |
| 1.28 | 93.2±14.8 | 21.5±2.30 | 0.16±0.01 | 7.52±1.04 | 78.8±10.07 |
| 2.55 | 113.6±50.6 | 19.3±3.34 | 0.14±0.02 | 8.09±0.47 | 92.6±4.25 |
| $Na_2HAsO_4 \cdot 7H_2O$ | | | | | |
| 0.027 | 83.7±15.6 | 17.0±2.97 | 0.14±0.02 | 7.87±1.36 | 88.9±11.09 |
| 0.054 | 109.6±17.4 | 17.9±1.49 | 0.16±0.01 | 7.46±0.56 | 88.5±4.50 |
| 0.108 | 133.3±31.8 | 16.5±1.98 | 0.18±0.01* | 9.25±1.18 | 107.1±5.97** |

Values represent means±SD. for 5–6 mice. Statistically significant from control at: * $P<0.05$ and ** $P<0.01$.

**Table 8** Effects of arsenate and/or gallium compounds on porphyrin metabolic enzymes in liver and kidney of female mice

| | Liver | | Kidney | |
|---|---|---|---|---|
| Dose (g/kg body wt) | ALAD activity[a] (nmol/mg h) | PBGD activity[a] (nmol/mg h) | ALAD activity[a] (nmol/mg h) | PBGD activity[a] (pmol/mg h) |
| Control | 30.6±3.59 | 0.16±0.02 | 9.60±0.90 | 88.6±5.13 |
| GaAs | | | | |
| 0.5 | 27.8±2.33 | 0.14±0.01 | 9.18±0.86 | 86.5±7.78 |
| 1.0 | 29.3±4.74 | 0.15±0.02 | 9.48±1.15 | 85.8±8.56 |
| 2.0 | 29.5±4.10 | 0.16±0.02 | 9.24±0.80 | 91.2±5.94 |
| $Ga(NO_3)_2 \cdot nH_2O$ | | | | |
| 0.64 | 28.2±6.56 | 0.12±0.01** | 8.50±1.22 | 77.0±6.99* |
| 1.28 | 23.8±6.78 | 0.14±0.02 | 8.64±1.23 | 84.7±10.1 |
| 2.55 | 25.6±2.54* | 0.14±0.02 | 9.03±0.88 | 86.3±9.78 |
| $Na_2HAsO_4 \cdot 7H_2O$ | | | | |
| 0.027 | 29.3±5.77 | 0.15±0.01 | 10.18±1.40 | 92.5±9.34 |
| 0.054 | 24.1±4.27* | 0.18±0.01 | 10.07±1.08 | 92.1±11.0 |
| 0.108 | 16.1±2.57** | 0.14±0.02 | 8.48±0.72 | 91.4±9.23 |

[a] Values represent means±SD for 5–6 mice. Statistically significant from control at * $P<0.05$ and ** $P<0.01$.

Under the influence of arsenic compounds, ALAS, ALAD and PBGD activities in the liver showed virtually the same pattern of change in mice as in rats.[8]

In contrast, a considerable difference was deserved to exist between the two animal species in the effects of the arsenic compounds on ALAD and PBGD activities in the kidney. Thus, the toxicants caused the activity of both enzymes to be reduced in rats,[8] whereas they had little influence on the enzymes in mice.

These results suggest that the influence of administration of arsenic compounds on porphyrin metabolism may vary with different animal species, depending upon tissue type and also according to the sex of the recipient animals. Notably, the rat and mouse were suggested as differing in their regulatory mechanism for heme biosynthesis in hematopoietic cells. The reason for this dissimilarity is obscure, but one can at least surmise that it stems from a difference between the two animal species in ALAS, ALAD and PBGD activity content of hematopoietic cells. The other five heme biosynthetic enzymes, it would seem, need to be quantified. Furthermore, arsenic compounds did not inhibit ALAS, ALAD and PBGD to any noticeable extent *in vitro* (data not shown). In this context, it seems justifiable to presume that decreased activities of these enzymes in the spleen following arsenic compound administration are consequent on either decreased specific content of, or impaired protein biosynthesis in, these tissue cells of mouse. On the other hand, it would be interesting to know whether ALAD activity in peripheral blood will prove to be useful as a biological indicator of exposure to GaAs and other gallium or arsenic compounds.

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