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Creatinine Formation and Inorg-As Biotransformation: Influence of Trace Elements

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ABSTRACT

Recently, a study showed that urinary creatinine concentrations (mg/L) were positively and significantly correlated with As concentrations, expressed as µg/L in urine (UAs) for both females and males[1]. The urinary creatinine concentrations were also positively correlated with As concentrations expressed as µg/L in blood[1].

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Recently, a study showed that urinary creatinine concentrations (mg/L) were positively and significantly correlated with As concentrations, expressed as µg/L in urine (UAs) for both females and males[1]. The urinary creatinine concentrations were also positively correlated with As concentrations expressed as µg/L in blood[1]. Other researchers also reported that urinary creatinine concentrations were positively correlated with UAs concentrations expressed as µg/L[2,3]. These results suggest that creatinine may influence the release of arsenic from the body with unknown mechanisms or maybe there is a correlation between the formation of creatinine and arsenic metabolism. Chowdhury UK (2021)[4] found the important results that adjusted urinary Se, Mn, and Hg concentrations expressed as ug/g cre were significantly and negatively correlated with urinary creatinine for both sexes. He also found a statistically significant and positive correlation between Mn and Hg in urine for both females and males (data not shown). Other studies reported that the combination of Mn and Hg might be more injurious to the brain, perhaps due to their synergistic effect[5]. The effect of Hg administered or exposed on renal dysfunction has been reported[6-8]. Selenium intoxication with selenite broth resulting in acute renal failure has also been reported[9]. Therefore, Se, Mn, and/ or Hg may have inhibitory effects in renal function and forming less creatinine when increasing Se, Mn, and/or Hg concentrations.

In Boeniger et al. (1993)[10] reported that 15-20% of the creatinine in urine could occur by active secretion from the blood through the renal tubules, i.e., urinary creatinine is influenced by renal function, which could have some unclear function for arsenic methylation process. Researcher[1] reported that urinary creatinine concentrations were strongly and positively correlated with % DMA in urines. Therefore, DMA formation could be decreased when creatinine formation will be decreased. On the other hand, creatinine formation/concentrations could be decreased when Se, Mn, and/or Hg concentrations will be increased, i.e., DMA concentrations might be decreased. The results also confirmed the other findings that % DMA and the ratio of % DMA to % MMA were decreased with increasing Se, Mn, or Hg concentrations expressed as ug/g cre in urine[1,4]. The correlation was stronger for males compared to females[1,4]. These results suggest that maybe Mn and Hg are more potent inhibitor for MMA methyltransferase in males compared to females and producing less % DMA in males compared to females. Due to that more MMA (highly toxic) accumulated in tissues of males compared to females. Other researchers have been reported that Se and Hg decreased As methylation[11-14]. They also suggested that the synthesis of DMA from MMA might be more susceptible to inhibition by Se(IV)[14] as well as by Hg(II)[11,13] compared to the production of MMA from inorg- As(III). A possible molecular link between As, Se, and Hg has been proposed by Korbas et al. (2008)[15]. The identifying complexes between the interaction of As and Se, Se and Hg as well as As, Se, and Hg in blood of rabbit has been reported[15,16](Table 1).

Table 1. The identifying complexes between the interaction of As and Se, Se and Hg as well as As, Se, and Hg.

	Complex identified
A. Interaction between As(III) and Se(IV) in erythrocytes [22]	$[(GS)_2AsSe]^-$
B. Interaction between Hg^{+2} and Se(IV) In the blood plasma [22]	$(Hg\text{-}Se)_{100}(GS)_5$
C. Interaction between $[(GS)_2AsSe]^-$ and CH_3HgOH in erythrocyte lysate [24]	$[(GS)_2AsSeHgCH_3]$

Some studies have also reported that Se supplementation decreased the As induced toxicity[17,18].

The concentrations of urinary Se expressed as ug/L were negatively correlated with urinary % Inorg-As and positively correlated with % DMA[19]. These studies did not address the urinary creatinine adjustment. Other researchers suggested that Se and Hg decreased As methylation[11-14](Table 2). They also suggested that the synthesis of DMA from MMA might be more susceptible to inhibition by Se (IV)[14] as well as by Hg (II)[11,13] compared to the production of MMA from Inorg-As (III). The inhibitory effects of Se and Hg were concentration dependent[11-14].

Table 2. The impact of Se as well as Hg for As-induced toxicity and metabolism.

		Results/impact
A.	Se supplementation in humans [25; 26]	Arsenic-induced toxicity decreased ↓
B.	The concentration of urinary Se expressed as µg/L [27]	Negatively (-) correlated with % Inorg-As and positively (+) correlated with % DMA i.e., arsenic methylation increased ↑
C.	Mice on the Se-excess diet [28]	Urinary % Inorg-As increased and the ratio of organic arsenic to Inorg-As decreased i.e., arsenic methylation decreased ↓
D.	Rat hepatocytes treated with As (III) and Se (IV) [29]	Significantly increased cellular Inorg-As(III) and the ratios of DMA to MMA decreased ↓
E.	In liver cytosol treated with As (III) & Se (IV) as well as As (III) & Hg (II) [30; 31]	Arsenite methyltransferase, and MMA(III) methyltransferase activities were inhibited, and arsenic methylation decreased ↓

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