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**Sodium selenite may be not the optimal speciation as an effective therapy for arsenic-induced anxiety-/depression-like behavior**

Ren XH *et al*. SS may be not optimal speciation

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**Abstract**

Major depressive disorder is a serious and prevalent neuropsychiatric disorder, affecting more than 350 million people worldwide. Here, sodium selenite (SS) was selected as the selenite supplement to improve the behavior in a mouse model of depression induced by As. SS may be not the optimal speciation for selenite supplementation and the source of the SS used in the study was not disclosed. There are many mouse models of depression and anxiety; however, in the current study, a classical mouse model of depression was not used. Thus, several questions still need to be further discussed. Taken together, the results indicate that SS may be not the optimal speciation as an effective therapy for As-induced anxiety-/depression-like behavior.

**Key Words:** Depression; Arsenic; Major depressive disorder; Sodium selenite; Optimal speciation

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**Core Tip:** Sodium selenite (SS) may be not the optimal speciation for selenite supplementation and the source of the SS used in the study was not disclosed. There are many mouse models of depression and anxiety; however, in the current study, a classical mouse model of depression was not used.

**TO THE EDITOR**

Major depressive disorder is a highly disabling psychiatric syndrome associated with deficits of specific subpopulations of cortical GABA-ergic interneurons[1,2]. We were pleased to read the article by Samad *et al*[3]. Their work highlights that Se, as a dietary source and/or supplement, is an effective therapy for As poisoning and its associated disorders. Furthermore, this study provides important findings regarding the prevention and treatment of anxiety disorders and depression. However, we believe there are several issues with the research design that need to be addressed. First, the use of sodium selenite (SS) as the Se supplement to improve the behavior of depression-like behavior in mice induced by As. Second, the use of the mouse model of depression. There are many mouse models of depression and anxiety; however, the authors chose not to use a classical mouse model of depression. As a result, questions remain regarding the validity of the study.

The main weakness of the study is SS as a means of Se supplementation. In particular, Se biological activity is dependent on its metabolic disposition; for example, absorption and excretion. It was observed that selenomethionine (SeMet) in organic form is more rapidly and completely (98%) absorbed than SS (84%) in inorganic form, and that liver uptake occurs faster after intake of organically bound Se than that of inorganic Se (SS)[4,5]. Moreover, various excretion indices confirm that SeMet has lower excretion (4%) than SS (18%)[4]. SS was also reported to induce DNA damage, particularly DNA strand breaks and base damage[6]. Se nanoparticles can also be used as a means to supplement Se. A recent study found Se nanoparticles to be a Se species with novel biological activities, bioavailability, and low toxicity[7]. Therefore, SS may not be the optimal speciation for selenite supplementation and as the source of the SS used in the study was not disclosed, questions remain.

The failure to select a suitable mouse model for depression was another issue with the study. A chronic unpredictable mild stress (CUMS) mouse model of depression is widely used[8]. As-induced depressive-like behavior cannot be used as a model of depression. Whether dietary Se can alleviate symptoms of the CUMS mouse model of depression needs to be further determined. In addition, dietary Se supplementation for depression in large-scale clinical trials is also necessary. As-induced depression-like behavior in mice may be associated with a large number of inflammatory factors and neurotransmitter changes that were not explored in this study.

***Conclusion***

Overall, SS may be not the optimal speciation for selenite supplementation and the source of the SS used in the study was not disclosed. The failure to select a suitable mouse model for depression was another issue, which the authors need to address.

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