



15th Water-Rock Interaction International Symposium, WRI-15

## From water-rock interactions to the DNA: a review of selenium issues

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### Abstract

The increase of the world population in the very near future with 9 billion individuals by 2050 that need to be fed, and soaring urbanization, leads to increasing pressure on water resources, both in terms of quantity and quality. Health and environmental concerns cross society as well as research; water-quality questions are important issues, and those related to selenium are increasingly so. Many discussions focus on the permissible quantities and value of the standard for drinking water of 10  $\mu\text{g}\cdot\text{L}^{-1}$ , because the safety margin between nutritional requirements and toxic effects is complex to establish. Transdisciplinary approaches integrating current scientific issues to provide consistent answers to the multiple questions arising on Se origins, mechanisms and toxicity are needed. New approaches involve multi-scales studies of Se dynamics and transfer processes from host rock to groundwater and, through the soil and drinking water, to the human population and an evaluation of its effects from deficiency to excess. Finally, the measures required to achieve water standards or recover quality in water bodies should also be assessed to evaluate the solutions from the indirect human health, economic and environmental aspects.

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Peer-review under responsibility of the organizing committee of WRI-15.

**Keywords:** Selenium; rock; groundwater; speciation; human health; DNA; Life Cycle Thinking

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## 1. Introduction

Selenium (Se) is a non-metal element of nutritional and toxicological importance. Increasing research is being carried out on its potential applications in public medicine both as a preventive, especially in cancerology, and as a curative, such as for neurodegenerative diseases. Se, over the last decade, has been one of the most studied elements in terms of biological effects, notably because of its janus-faced properties (e.g. toxicity vs. antioxidant, mutagenic vs. anti-mutagenic) that are highly dependent on its concentration. Among essential elements, Se has one of the narrowest range between dietary deficiency ( $< 40 \mu\text{g}$  per day) and toxic levels ( $> 400 \mu\text{g}$  per day). Moreover, the safety margin between potential toxic intake and nutritional requirement is complex to establish, and much has been written about the optimal intake<sup>1,2</sup>, as well as about its effects in terms of health<sup>3-6</sup>. Although appropriate standards are needed in terms of the Se intake levels, there is no consensus on this issue. A reassessment of the safe upper limit of Se in drinking water is expected<sup>7,8</sup>; for the purpose of health control, the Water Framework Directive WFD (2000/60/EC) defines a Se threshold value of  $10 \mu\text{g}\cdot\text{L}^{-1}$  for human consumption, which is also the maximum Se content of tap water recommended by WHO in 1984 with the provision that this should be adapted according to the geographic area, that is, depending on the natural Se intake of each population. In this context, the question of the norm being adapted to the local geochemical context should be pointed out.

Solutions to control high Se levels in groundwater, which can be evaluated to minimize financial investment and divide charges on stronger actors by preserving the human environment, would contribute indirectly to the quality of life and water exploitation sustainability. Water resource management for the drinking water supply in areas of high Se geochemical background is a major economic challenge. Exceeding the drinking water standards requires demands for exemption and, if the excess is frequent, then the use of the involved wells should be stopped. Nonetheless, the WFD requires a good qualitative and quantitative status of all water bodies based on a determination of the ecosystem impact of toxic elements like Se. Not achieving a good status with respect to Se will require an action program. A major challenge is to integrate all the activities described in this article, to provide new and additional information on Se issues for human health, and to contribute to revision of the Se standards in water.

## 2. From the rock to the soil and drinking water

Areas low in natural Se are more widespread than areas with excess Se-levels e.g. in most parts of Europe and in Central China<sup>3</sup>. Se occurs naturally as a trace constituent in geologic formations (e.g. Permian marine black shale of the Phosphoria Formation<sup>9</sup> or Cretaceous black shale in USA<sup>10,11</sup>, Palaeozoic shales in Wales<sup>12</sup> or conglomerates derived from metamorphic rocks of Himalaya in Penjab<sup>13</sup>) and associated soils. In the Paris basin in France, Se is mainly found in Eocene formations<sup>14,15</sup>. Coal also contains important amounts of Se as observed within the central Appalachian region of the United States in which coal exploitation affects the quality of watersheds<sup>16,17</sup> or in the Huainan Coalfield in China<sup>18</sup>. Sediments may be also contaminated<sup>19-22</sup>. Se contamination affects surface and groundwater in irrigated alluvial valleys<sup>10,13,23,24</sup>. In Se-depleted regions, cereals are also depleted and systematic soil fertilization with 5g per ha of selenite (mixed with N fertilizers) is applied (e.g. in Finland, Belgium), while other countries (e.g. UK, France) still debate on the relevance of such fertilization. On the opposite, the seleniferous region of northwest India displays a total Se concentration in soils ranging from 0.32 to 4.55  $\text{mg}\cdot\text{kg}^{-1}$ <sup>13</sup>. The Mancos Shale in Colorado (USA) presents Se contents which increase with weathering (from 1.1  $\text{mg}\cdot\text{kg}^{-1}$  in the unweathered shale to 1.4 to 2.3  $\text{mg}\cdot\text{kg}^{-1}$  in the associated soil<sup>10</sup>). Se mobility, bioavailability, bioaccumulation and toxicity are linked to Se speciation and are controlled by sorption and redox reactions. The most common Se species within surface water, groundwater and soil are selenite [ $\text{SeO}_3^{2-}$ ], SeIV, and the more soluble and poorly adsorbed selenate [ $\text{SeO}_4^{2-}$ ], SeVI. Selenite is found in less oxic conditions than selenate and is adsorbed on iron hydroxides and clays to form poorly soluble stable surface complexes<sup>25</sup>. Microorganisms can catalyze SeIV reduction to Se0 with organic matter and can produce volatile Se methylated forms and Se-II organic compounds. Nitrates in groundwater inhibit reductive Se processes, thus inducing higher Se mobility. SeIV reduction to Se(0) can also occur abiotically through interaction with FeII-minerals<sup>26-28</sup>. Sulfide minerals, pyrite and chalcopyrite, significantly adsorb anionic Se species under acidic conditions<sup>29</sup>. The main chemical equilibria are acid–base, oxidation–reduction, precipitation, and complexation reactions<sup>30</sup>. There are very few data on water chemistry monitoring that takes Se speciation into account in water or in solids<sup>15,31,32</sup>.

### 3. Se intakes: from deficiency to excess

Se intake through drinking water occurs mainly in its inorganic form, whereas dietary Se is organic<sup>33</sup>. The toxicological and nutritional effects of Se greatly differ depending on the chemical form, with inorganic species being generally more toxic and of less nutritional importance than organic compounds. The amounts of different Se forms is of importance where human health is concerned, rather than the overall Se intake. The intake of inorganic Se has little effect on biomarkers of exposure (i.e. blood, urine, toenails), but does have a strong toxicological effect, whereas the opposite is true for the common organic Se forms introduced through food<sup>34</sup>. In France, the main human Se input comes from drinking water in regions where the groundwater has a high Se level<sup>8,33</sup>. The effects of Se compounds on cells are compositional and concentration-dependent. At supranutritional dietary levels, Se can prevent the development of many types of cancer. At higher concentrations, Se compounds can be either cytotoxic or possibly carcinogenic<sup>35</sup>. Therefore, it is critical to understand the interaction between Se intake and molecular events at the cellular and genetic level.

On a global scale it is estimated that 0.5 to 1 billion people are directly affected by Se deficiency. Insufficient Se intake is linked to serious health effects such as chronic, degenerative osteoarthritis Kashin Beck disease (KBD), an endemic ailment that has crippled and stunted the growth of a lot of young people in China with cartilage growth retardation and impaired metabolism. The discovery that Se is a pathogenic factor in KBD has increased interest in specific classes of selenoproteins, glutathione peroxidases, thioredoxin reductases, selenoprotein P, all involved in antioxidative defense. Low levels of Se in combination with mycotoxins, found in high levels in poorly stored cereals, exacerbate cartilage degradation. The benefit of Se to reverse cartilage degeneration is still debated and Se incorporation and the effects of different chemical forms of Se on cartilage maturation are unknown. In order to prevent human health impacts of Se deficiency, supplementation of Se is increasingly provided with a variety of Se compounds (salts, aminoacids, nanoparticles and «fortified» food) in which Se is present in its 4 major oxidation states. Several applications of SeO nanoparticles are reported in medical applications as anti-tumor effects, anti-leukemia agents or anti-oxidants. The Se supplementation is a problem of public health throughout two major features: toxicity and cancer risk, the molecular and cellular bases of which remain misunderstood despite considerable number of data. In areas with high and toxic environmental Se levels, the Se transfer from drinking water to human body and its health effects have deleterious effects. The toxicity of Se has been known since 1930, notably through acute selenosis known as “blind staggers” syndrome and chronic Se poisoning called “alkali” disease which is observed in animals that have consumed plants growing in highly seleniferous soils in China, Western USA and Canada. At high concentrations, different chemical forms of Se have produced not only genotoxic but also carcinogenic effects. Nevertheless, IARC has not classified this element as carcinogenic for humans, and its genotoxic status is still controversial<sup>36</sup>. Some Se compounds have the potential to induce DNA damage<sup>35, 37</sup> and genomic stability. An important biochemical consequence of exposure to Se is oxidative stress and DNA synthesis and cell growth inhibition by modifying gene expression and cell cycle progression. Despite a considerable amount of data, very few authors have investigated the Se exposure effects on the formation and repair of DNA double-strand breaks (DSBs) and its impact on end joining or recombination pathways. Unrepaired DSBs produced by genotoxic stress are considered as the key-lesions for cell death induction and misrepaired DSBs may be a source of genomic instability leading to cancer.

### 4. Conclusions and perspectives

On one hand, high Se intake from dietary or pharmacological supplements could expose the body tissues to toxic levels with negative consequences on DNA integrity and repair. On the other hand, Se compounds play important role in cancer prevention. Finally, the measures required to achieve water standards or recover quality in water bodies should also be assessed using the Life Cycle Thinking approach to evaluate the solutions from the indirect human health and the economic and environmental aspects. It would enable decision makers to choose between the available alternatives. Therefore, there is a need for projects carrying out a transdisciplinary approach of the physical, biological, and chemical processes that influence Se dynamics and impacts and of the assessment of the relevance of the identified solutions to improve the drinking water quality.

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