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Natural zeolites as detoxifiers and modifiers of the biological effects of lead and cadmium in small rodents: A review

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Abstract
The present investigation analyzes the literature about the toxicity of Cd and Pb in small rodents' organisms and the role of natural zeolites as modifiers of the biological effects. An array of ecotoxicological, morpho-physiological, hematological, genetic and biochemical methods as most representative are under discussion as a basic point for further exploration of biological effects in laboratory mice. The review of existing results demonstrated that there is abundant data on the sorption of lead and cadmium by modified natural zeolites in water and soils. Nevertheless, there is insufficient data on the ion exchange capacity and biological effects of this sorbent in living organisms, especially regarding Cd detoxification. On the basis of the current review, it is possible to conclude that future investigations in this field will elucidate the potential of the use of zeolites as successful detoxifiers against heavy metals and other toxic elements in living organisms.

Keywords
Cadmium, lead, natural zeolites, small mammals

Introduction

Pollution of the environment by different xenobiotics is a problem that still raises major concerns about the resilience of ecosystems. Despite serious measures having been taken, there is still the problem of removing toxicants already accumulated in the soil and water. Their slow elimination and high rate of accumulation at higher levels of the food chains is expected to create problems in the next decades. Discovering suitable sorbents with detoxifying properties that reduce the content of heavy metals in nature will help to solve a number of problems related to the environment and the risk to public health. In recent years, natural zeolites are increasingly used in this field. There is a growing discussion of a direct positive effect of these exceptional crystalline minerals on improving the state of ecosystems and the quality of life.

Sorption properties of natural and modified zeolites and their application

Natural zeolites form one of the most unique groups among minerals, some of which, for example clinoptilolite, mordenite, and chabazite, have good potential due to their high sorption capacity and the presence of deposits with huge reserves in many countries. Bulgaria is one of the first countries in the world for the presence of quality clinoptilolites (Aleksiev and Djourova 1976; Aleksiev et al. 1997). They have a specific microporous crystal structure, permeated by channels and voids, which are formed by different numbers of SiO_4^{4-} and AlO_4^{5-}- tetrahedral rings. Skeletal charge-compensating cations (Na^+, K^+, Ca^{2+}, Mg^{2+} and Ba^{2+}) and coordinating water molecules are located in the channels and gaps. The structural configuration of the mineral predetermines its unique properties related to ion exchange and selective sorption (Mumpton 1999). It is possible to modify zeolite surfaces by adding specific surfactants, and thus to improve the ion exchange capacity to remove cations, anions, and different organic compounds (Apreutesei et al. 2008). This procedure is very important for enlarging the sorption capacity of these minerals.

The establishment of significant reserves of clinoptilolite in Bulgaria (Eastern Rhodopes) and their growing importance as an effective sorbent of heavy metals, determines the interest in their use as suitable detoxifiers of living organisms. Zeolitized tuffs are found in large areas in the Eastern Rhodopes and contain the largest deposits of zeolites in Bulgaria, formed during the Oligocene (Aleksiev and Djourova 1976; Jurova and Alexiev 1984; Jurova and Alexiev 1989; Djourova and Aleksiev 1990, 1995; Aleksiev et al. 1997; Raynov et al. 1997; Yanev and Ivanova 2010) (Fig. 1).

The study on zeolites' properties began in the 18th century, but they remained a curiosity for scientists and collectors until the middle of the past century, when their unique physicochemical features attracted the attention of many researchers. The absorption capacity of natural zeolites was first developed by Ames (1967) and Mercer et al. (1970), who demonstrated the effectiveness of clinoptilolite for extracting from municipal and agricultural waste streams and when materials with enhanced sorption capacity were necessary for nuclear waste management. In the past 60 years there has been an extraordinary development in zeolite science. Many investigations have been published on these promising silicate minerals, but none has been devoted specifically to natural zeolites, even though this theme may be of interest not only to earth

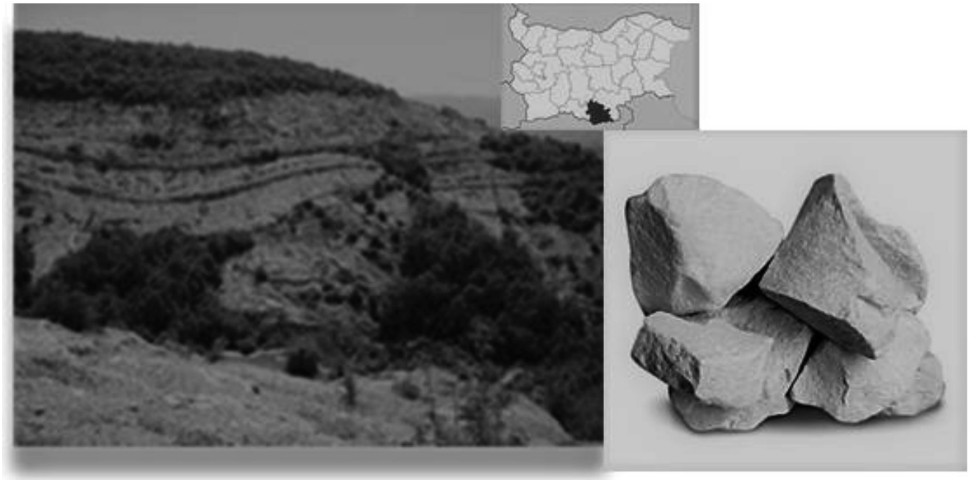

Figure 1. The largest deposits of zeolites in Bulgaria (Eastern Rhodopes).

scientists, but also to chemists and biologists, as the information obtained from natural samples complete and integrate the characterization of many zeolites.

Other areas of applications of natural zeolites are the purification of waters and the industrial and urban wastewaters (Boulinguez 2005). Natural zeolites were mainly investigated and applied as sorbents for ammonium ions from urban pollution, as well as for heavy metals (Pitcher et al. 2004) and dyes from industrial wastewaters. The removal of nutrient species (e.g. NH_4^+, $H_2PO_4^{2-}/HPO_4$), quantitative precipitation and recovery in slow-release fertilizer was also reported in the literature (Filippidis et al. 2008).

Nowadays natural zeolites have wide applications to limit the consequences of pollution and for purifying Cs- and Sr-isotopes from the nuclear industry and eventual accidents (Borai et al. 2009). Very effective zeolite pills have been prepared for humans to counteract Chernobyl fallout in Bulgaria (Filizova 1993), as well as for the workers in the nuclear power plant. The mechanism of action of zeolite is that the ion exchanges of ^{137}Cs and ^{90}Sr are carried out in the gastrointestinal tract and is eliminated by the excrements, thus minimizing assimilation into the blood system. The removal of heavy metals (e.g. Fe, Pb, Cd, Zn) from acidic mine drainage is another field of potential environmental applications of natural zeolitic materials (Xu et al. 2010).

Moreover, natural zeolites are used in agriculture to increase soil fertility through their useful adsorption and sorption, and cation-substituting catalytic properties. The most effective of the natural zeolites, is clinoptilolite. A lot of tests have been performed on rocks containing clinoptilolite on different types of soils, in different climatic conditions and geographical regions, in clear form or modified with mineral and organic fertilizers. The action of rocks containing clinoptilolite is diverse and affects both the characteristics of the soil and the growth, development and productivity of plants, as well as the quality of production. The use of clinoptilolite as a principal ingredient of artificial soil was developed in Bulgaria in the late 1970s. A nutrient-treated substrate used for growing crops and the rooting of saplings in greenhouses produced greater development of root systems and larger yields of vegetables and fruits (Petrov et al. 1982).

Detoxification properties of natural zeolites and biological response of the organism

The use of natural clinoptilolites for animal nutrition began in Japan in the middle of the past century. Tests were initially made in Japan offering zeolite as a food additive to swine and poultry, and later to other animals. The experiments were successful. Researchers obtained good or excellent results with significant increases in productivity (Torii 1974, 1978; Mumpton 1978). Using clinoptilolite as a food additive could increase not only the animal production. Pigs fed with clinoptilolite gain significant weight and are more resistant to disease than pigs fed on a normal diet. Crucially they show regular digestion, increase in appetite, and the meat content increases due to the absence of needless fat (Veldman and Vanderaar 1997).

More of the biological applications of zeolites include ammonium removal from wastewaters and animal manure (Bernal and Lopez-Real 1993) air filtration, deodorants (Miner 1980) and soil fertilization (Mumpton 1999).

Clinoptilolite has incredible healing properties and has the power as mentioned above to remove from the body all kinds of toxins and poisonous substances, including radioactive particles, locking them in itself, so they can no longer be released.

Zeolite addition to cattle's fodder improves the caloric intake, digestion, appetite and the animal's body mass. Using clinoptilolite as a food additive to the diet of pigs and poultry also improves their body weight and leads to gains in the feed conversion ratios. Clinoptilolite binds some mycotoxins, absorbing toxins dangerous to animals' health. It also is useful for controlling toxins in animal food. This way the mineral decreases the mortality from digestive stress and alleviates the antibiotic needs. It is also able to absorb toxins produced by molds and microscopic parasites and thus improve the absorption of food by animals (Cooney et al. 1999).

One of the important questions is whether zeolites are able to adsorb vitamins and microelements which can potentially disturb physiological balance in organisms. By the way, Tomasevic-Canovic et al. (2000) found that amino acids and fat-soluble vitamins such as A, D and E do not get absorbed by clinoptilolite. Nevertheless, natural zeolites have some low affinity for binding vitamin B6 in vitro. This process closely depends on the crystalline and mineralogical structure of the zeolites. Investigations have demonstrated that, compared to all minerals with similar crystalline structure and functions, clinoptololite associates least with them.

Martin-Kleiner et al. (2001) report the effects of the natural clinoptilolite on hematopoiesis, serum electrolytes and other essential biochemical indicators of kidney and liver function in mice. The authors found a small increase in potassium levels in mice reared on a zeolite-rich diet but without any other changes in serum chemistry. Erythrocyte, hemoglobin and thrombocyte levels in peripheral blood were not affected. There are studies that demonstrated that a natural clinoptilolite maintained the good condition of the mouse organism and prevented negative effects from the iron overload. When zeolites are given with iron in the form of intraperitoneal injections, mice showed near normal histology in comparison to mice injected with iron only. Such a pilot study examined potential possibilities to current treatments, and the results show positives in using zeolites in iron excess conditions (Fan et al. 2018).

Zeolite use in ecotoxicology and medicine is relatively recent, but its application in these areas has reached significant importance in the last few decades. Antioxidant and immunostimulatory properties of natural zeolites have been reported in different tumor types, and prove that zeolite acts as a serious immune system modulator (Pavelic et al. 2001, 2002). Montinaro at al. (2013) investigates the antioxidant properties of natural zeolites against oxidative stress, which is one of the main causes leading to the aging and degeneration process. The authors suggest zeolites as a novel potential adjuvant in counteracting oxidative stress and plaque accumulation in the context of neurodegenerative diseases.

Zeolite application as a food supplement in animal feeding is based on effects as a drug or detoxifier. These effects have been demonstrated in preliminary longtime investigations and critical assessments of its toxicological effects. Many studies demonstrate that zeolite, especially clinoptilolite addition in the feeding process, even for several months, showed no evidence of negative reactions or any pathological changes of animals' biochemical and hematological profiles. Topashka-Antcheva et al. (2012) tested the modified natural clinoptilolite KLS-10-MA to establish the LD_{50} of the used sorbent. The results show that all test group animals survived successfully up to the end of the experiment, with significant increases in body weight compared to the control group, and demonstrated a good activity and physiological condition. No symptoms of increased toxicity were recorded during the experiment. Any pharmacological effects were not established. Also, unusual behavior was not observed. The results on the toxicity of natural modified and nonmodified zeolites, and especially clinoptilolites, on the basis of their ion exchange capacity, have allowed research groups to investigate the detoxification possibilities of the mineral on animals and humans. Studies have been conducted in contaminated areas to eliminate some of the accumulated Pb in the body of hyperactive children. Clinoptilolite nanoparticles in the form of injection were applied. The idea was to minimize the effect of the lead on their central nervous system. It is important to note that these treatments have not been clinically approved yet (Delavarian et al. 2013). It was established that consumption of alcohol in parallel with clinoptilolite decreased the ethanol level in the blood in drinkers (Federico et al. 2015). Microencapsulated urease-zeolite sorbent was also investigated. The aim was to remove the urea from the organism during uremia (Cattaneo and Chang 1991). The established kinetic curves clearly showed the selective adsorption of zeolite for lead ions, as well as a significant removal of cadmium not only from wastewaters and soil but from the animal organism (Malion et al. 1992; Beltcheva et al. 2012).

On the basis of everything mentioned above, Beltcheva et al. (2012) and Topashka-Antcheva et al. (2012) provided a series of long term ecotoxicological experiments to test the levels of clinoptololite sorption capacity against Pb cations in the animal organism. Laboratory white mice were used in 90-day variant experiments. Animals were divided into four experimental settings: with and without zeolite supplement as food additive, and with and without lead supplementation. The results showed that the sorbent reduced Pb concentrations in the body and different tissues and organs as follows – 84% in carcass, 89% in liver, 91% in kidneys, 77% in bones and the adsorbed quantity of Pb was excreted via the feces. A mathematical model for the bioaccumulation of lead in bones has been developed and the trends in animals fed with and without zeolite in the diet are presented. The absorption coefficient of Pb from the gastrointestinal mucosa was derived and a difference of about 4.5 times was found. In mice with zeolite, it is $\eta_0$3.53% and in those without additives – $\eta_0$15%. The biological response of the organism was analyzed at the organ, tissue, cellular and subcellular levels. Changes in chromosome structure, mitotic index, erythrocyte shape and positive changes in animal body mass were recorded. The main results show that in animals fed with Pb and clinoptilolite as food additive, 2.3 times lower frequency of chromosomal aberrations, 2.5 times higher mitotic index and 1.5 times higher percentage of normal erythrocytes were observed, as well as 1.3 times increase in body weight compared to those exposed to Pb intoxication, but without the addition of a mineral sorbent.

It is well known that in regions with industries that seriously contaminate the environment with lead, high levels of cadmium in the environment are also reported. A future investigation aims to demonstrate that zeolite modifications in the direction of inset additional active sites of the inner mineral surface and adequate activation of the clinoptilolite sorbent will increase its sorption capacity compared to the natural material. This would increase the detoxification potential and reduce Cd and combinated Cd+Pb-induced oxidative stress and overall toxicity at the cellular and organism level.

Future prospects

The results of such types of investigations will have a significant theoretical contribution towards expanding our understanding of the ability of clinoptilolites to reduce the harmful biological effects of certain heavy metals, which are environmental pollutants. In the long run, such products may be used as low-cost detoxifiers in areas with a high level of anthropogenic pressure and contribute to solving important problems related to the environment, quality of life and health risk not only in nature but also in the human population.

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