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Herbs and Heavy Metal Detoxification

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What is a Heavy Metal?

Heavy metals are metallic elements which have a high atomic weight and a density much greater (at least 5 times) than water. There are more than 20 heavy metals, but four are of particular concern to human health: lead (Pb), cadmium (Cd), mercury (Hg) and inorganic arsenic (As).[1] According to the US Agency for Toxic Substances and Disease Registry, these four heavy metals are four of the top six hazards present in toxic waste sites. They are highly toxic and can cause damaging effects even at very low concentrations. They tend to accumulate in the food chain and in the body and can be stored in soft (eg kidney) and hard tissues (eg bone). Being metals, they often exist in a positively charged form and can bind on to negatively charged organic molecules to form complexes. Chelates are a special type of complex where the organic molecule binds to the metal at two or more points (and hence quite strongly). (The term chelation comes from the Greek *chēlē* meaning crab or lobster claw, suggested by the way in which the metal is gripped in at least two places by the organic groups.) Chelating agents are used to produce stable compounds with relatively low toxicity and also to enhance the excretion of metals.[2,3] Heavy metals can also exist covalently bound to organic molecules. In the case of As this substantially reduces its toxicity. For Hg it substantially increases toxicity, eg methyl mercury. Aluminium is not a heavy metal and considerations related to aluminium exposure, health effects and its detoxification are not always the same as for heavy metals.

Sources of Heavy Metals

The following table (Table 1) lists for the four major heavy metals the main types and sources of exposure, together with specific details of absorption and elimination.

Lead	
types	• elemental lead, inorganic lead compounds, organic lead
sources	• industrial and household products: paints, cans, plumbing fixtures, leaded petrol/gasoline, lead crystal • contaminated food: leafy vegetables grown in lead-contaminated soil, via improperly glazed ceramics • occupational/environmental exposure (eg living near industry): battery manufacturing, demolition, painting and paint removal, ceramics
absorption	• ingestion or inhalation • skin (organic lead in additives to gasoline) • children absorb up to 50% of lead ingested, adults absorb 10–20% • gastrointestinal absorption is enhanced by fasting and by dietary deficiencies in calcium, iron and zinc • absorbed into blood plasma and extracellular fluid, crosses membranes (eg blood-brain barrier, placenta), accumulates in soft and hard tissues • largest proportion of absorbed lead is incorporated into the skeleton (90% of the body's total burden)
elimination	• mainly in urine (depends on glomerular filtration and tubular secretion) and feces • can appear in hair, nails, sweat, saliva, breast milk • half-life of lead in blood is approx. 25 days, in soft tissue about 40 days, in the nonlabile portion of bone more than 25 years – so blood lead levels may decline significantly while the body's total burden remains heavy
Mercury	
types	• metallic mercury (Hg^0) • mercurous mercury (Hg^+) (a form of inorganic mercury) • mercuric mercury (Hg^{2+}) (the other form of inorganic mercury) • organic mercury compounds such as methyl mercury (slowly broken down to form inorganic compounds) • inorganic mercury can be converted by microorganisms in soil and water into methyl mercury

sources	• metallic mercury (Hg^0): thermometers, dental amalgams (typically containing about 50%), some batteries • inorganic mercury compounds: occupational exposure in some chemical, metal-processing, electrical-equipment, automotive and building industries; medical and dental services • methyl mercury: contaminated fish especially tuna and swordfish • other possible environmental exposure (controversial): contaminated drinking water, inhalation of fumes from incinerators burning mercury-contaminated waste products • estimates of daily intake (for people in the USA and Canada) of elemental mercury form amalgam restorations ranges from 1 to 27 µg/day; the majority of dental amalgam holders being exposed to less than 5 µg/day • the precise exposure from amalgam may not only be a function of amalgam-filled teeth, but may also be a function of the size and location of these fillings • ethyl mercury: in the form of thimerosal added as an antiseptic to widely used vaccines; has been assumed that the toxicology of ethyl mercury is similar to methyl mercury
absorption	elemental mercury • not well absorbed by GIT • when volatilized (eg upon standing at room temperature, or from dental amalgam) the vapour is well absorbed by inhalation, is then lipid soluble and crosses blood-brain barrier and placenta, oxidized into mercuric chloride which is retained in kidney and brain for years • half-life of elemental mercury as such: approx. 60 days inorganic mercury • GIT and dermal • large overdoses disrupt GIT barriers, further enhancing absorption • breaks down into metallic and mercuric forms • half-life: approx. 40 days organic mercury (especially methyl mercury) • when evaporates, can be absorbed by inhalation • well absorbed when ingested (eg contaminated fish) • only small amount absorbed via skin • when absorbed is lipid soluble, crosses the blood-brain barrier and placenta, appears in breast milk, concentrates in the kidneys and CNS • half-life of organic mercury compounds: approx. 70 days
elimination	• elemental mercury: mainly in urine and feces • inorganic mercury: mainly in urine and feces, some retained in kidney as mercuric mercury • organic mercury (especially methyl mercury): detoxified by the liver and excreted in urine (only 1% is excreted unchanged)
Cadmium	
sources	• contaminated food: especially grains, cereals and leafy vegetables which readily absorb cadmium occurring naturally or in soil contaminated by sewage sludge, fertilizers and polluted groundwater • contaminated water eg by mining effluents • environmental exposure: airborne cadmium from smelting or incineration of waste containing plastics and nickel-cadmium batteries or from wear on car tires • cigarette smoke • occupation exposure: metal-plating, pigment, battery and plastics industries
absorption	• ingestion or inhalation, only 5-10% absorbed • concentrates in liver and kidneys • half-life of 10–30 years • GI absorption may be influenced by nutritional factors, such as iron status
elimination	• lack of effective elimination pathway: reabsorbed in kidney
Arsenic	
sources	• natural processes (eg volcanoes, deep-water wells), industrial processes, contaminated food and tobacco
absorption	• ingestion: inorganic form (more toxic) accumulates in organs
elimination	• organic form: in urine (rapidly excreted) • inorganic form: somewhat metabolised in liver but leaves residue in skin, hair, nails

Table 1. Types, Sources, Absorption and Elimination for Lead, Cadmium, Mercury and Arsenic.[1,2,4,5,6]

Signs and Symptoms of Heavy Metal Exposure[7]

The typical signs and symptoms of heavy metal exposure are listed below:

Arsenic - Fatigue, headaches, dermatitis, increased salivation, muscular weakness, loss of hair and nails, hypopigmentation of skin, anemia, skin rashes, skin cancer.

Cadmium - Loss of sense of smell, anemia, dried scaly skin, hair loss, hypertension, kidney problems, skeletal damage, cancer.

Lead - In children: delayed mental development, hyperactivity, delayed learning, behavioral problems. Children and adults: fatigue, anemia, metallic taste, loss of appetite, weight loss and headaches, insomnia, nervousness, decreased nerve conduction, possibly motor neuron disorders.

Mercury - Reduced sensory abilities (taste, touch, vision and hearing), metallic taste with increased salivation, fatigue, anorexia, irritability and excitability, psychoses, mania, anemia, paresthesias, tremors, incoordination, cardiovascular disease, hypertension with renal dysfunction.

There is a general consensus that high level exposure to heavy metals can cause the symptoms described above. What is more controversial is whether these same toxic effects and symptoms can result from chronic, low level exposure in sensitive individuals. In addition other more subtle effects might result from such low level exposure.

Effects of Chronic Low Level Exposure

A selection of these issues in the mainstream peer review literature is presented in the following paragraphs. These studies are confirming what has long been suspected: that heavy metal exposure can cause subtle endocrine, neurological and immunological dysfunctions, even at low exposure levels.

It is well documented that low level exposure to Pb in children can lead to intellectual deficit.[8] On this topic, and the more general issue of lead exposure in children, one researcher suggested the following:

"Children differ from adults in the relative importance of lead sources and pathways, lead metabolism, and the toxicities expressed. The central nervous system effects of lead on children seem not to be reversible. Periods of enhanced vulnerability within childhood have not consistently been identified. The period of greatest vulnerability might be endpoint specific, perhaps accounting for the failure to identify a coherent "behavioral signature" for lead toxicity. The bases for the substantial individual variability in vulnerability to lead are uncertain, although they might include genetic polymorphisms and contextual factors. The current Centers for Disease Control and Prevention screening guideline of 10 µg/dL is a risk management tool and should not be interpreted as a threshold for toxicity. No threshold has been identified, and some data are consistent with effects well below 10. Historically, most studies have concentrated on neurocognitive effects of lead, but higher exposures have recently been associated with morbidities such as antisocial behavior and delinquency."[9]

A study in Poland found that increased average levels of lead in the hair of children suffering from "rheumatic" disease as compared with controls. The difference in the magnesium/lead ratio between the controls and rheumatic volunteers was statistically significant.[10] Traffic policemen in Egypt had higher lead levels in blood, urine, hair and nails compared to healthy (non-exposed) controls. Lead levels in blood, hair and nails showed significant and positive correlations with the duration of exposure to lead which was measured as the duration of employment. Urinary excretion of NAG (a marker of tubular damage) was positively correlated with duration of employment, blood lead and nail lead. Urinary albumin (a marker of glomerular injury) was positively correlated with duration of employment, blood lead and hair lead.[11]

The latest WHO evaluation concludes that As (inorganic) exposure via drinking water is causally related to cancer in the lungs, kidney, bladder and skin (for drinking water levels >50 µg/L). There is also relatively strong evidence between As exposure and risk for hypertension and cardiovascular disease.[1]

A link between Cd and skeletal damage was first reported from Japan in the 1950s due to Cd-contaminated water used for irrigation of rice fields (itai-itai disease). However, during recent years new data have emerged suggesting that relatively low Cd exposure may give rise to osteoporosis and fractures.[1] The levels of Cd in organs increase with age because of the lack of an active biochemical process for its elimination coupled with renal reabsorption. Cd-linked bone and kidney toxicities were observed in people whose intake was well within the provisional tolerable weekly intake (PTWI) set by FAO/WHO (see later). Also evidence for the carcinogenic risk of chronic Cd exposure is accumulating and effects on reproduction have begun to emerge.[12]

111 women with repeated miscarriages had their urinary excretion of heavy metals evaluated after challenge (with a chelating drug). Heavy metal excretion was significantly correlated to different immune and hormonal phenomena. The authors concluded that heavy metals appear to have a negative impact on ovarian and pituitary function and that

the induced immunological changes may lead to miscarriages.[13]

A high dietary intake of methyl mercury from consumption of fish has been shown to increase the risk of coronary artery disease. This has been confirmed in one study but challenged in another.[1]

A case-controlled study involving multiple sclerosis patients conducted between 1991 and 1994 found a suggestive elevated risk for those individuals with a large number of dental amalgams and for a long period of time. However the difference between cases and controls was not statistically significant.[14] A larger and more recent epidemiological study found some evidence of an association between dental amalgam and disease. (Disorders of the nervous system and kidney were examined in particular.) Multiple sclerosis had an adjusted hazard ratio of 1.24, but there was no association with chronic fatigue syndrome or kidney disease.[15]

One US study examined the effect of Hg and high-end fish intake. 89 patients with high-end fish intake or showing symptoms suggestive of Hg toxicity were assessed for Hg exposure (in San Francisco). 89% had whole blood Hg levels exceeding the recent US EPA and NAS recommended maximum of 5.0 µg/L. Swordfish intake was significantly and positively correlated with Hg blood levels, red snapper was negatively correlated. A significant decline in Hg levels was shown when fish intake was stopped. Some children were >40 times the national average.[16] This study also provided details of average methyl mercury levels in fish which are provided in Table 2.

High	
Shark	1.33
Swordfish	0.95
Ahi	0.38
Snapper	0.25
Halibut	0.25
Lobster	0.23
Tuna	0.21
Medium	
Sea bass	0.16
Crab	0.12
Flounder	0.09
Low	
Shrimp	0.047
Scallops	0.042
Salmon	0.035

Table 2. Average Methyl Mercury Levels in Fish.[16]

Note: All units in µg/g

Assessing Heavy Metal Exposure

Heavy metal exposure can be assessed by measuring levels in body tissues or excretions. Hair analysis is commonly used because it has some distinct advantages, it is easier and safer to collect, ship and store and is less expensive. It also can represent a record of long-term exposure. Whole blood is a good measure of current exposure and some examples of reference levels are provided in Table 3. Urine can be unreliable, but after provocation with a chelating agent such as EDTA or DMSA, 24-hour urine levels can give an indication of body stores.

Lead	
Reporting limit	1.0 µg/dL
Normal	<10 µg/dL
Exposed	
• Children (0-6 years)	>10 µg/dL
• Adults (OSHA action level)	40 µg/dL
Toxic	
• Children (0-6 years)	>70 µg/dL
• Adults (OSHA action level)	>80 µg/dL
Arsenic	
Reporting limit	10 ng/mL
Reference range	up to 10 ng/mL

Table 3. Example of Reference Levels for Heavy Metals in Blood.[17]

Hair analysis can be interfered with by some shampoos, hair dyes and dust exposure. There can be considerable variability in heavy metal levels from sample to sample of the same person's hair. Heavy metal analysis is tricky and the lab needs to have expert chemists using validated methods in a certified lab. As a consequence results can vary considerably. Reference ranges are different from lab to lab which can make interpretation of results difficult.[18,19] Hair analysis for Hg is, however, a very good indication of methyl mercury exposure (reference limit 1.0 µg/g).

A Strategy of Using Herbs for Heavy Metal Exposure

As outlined previously, we are exposed to heavy metal intake mainly through the environment, via the air, water and food. Occupational exposure can also be an issue in some instances, for example lead smelter workers. In terms of minimizing these exposures one can drink only purified water and choose to live in an area with less air pollution, but there is less that can be done from an avoidance perspective about dietary exposure. Also for individuals who unavoidably have a higher intake via the air they breathe, their daily heavy metal load can be managed by reducing their gastrointestinal intake. Both these considerations argue for an approach which is capable of minimizing heavy metal exposure via the inhibition of absorption from the gastrointestinal tract (GIT).

Hence any herbs which are capable of binding to heavy metals, but not making them more soluble as a result, are

likely to have a key role in reducing the GIT absorption of these elements. This will help to free up the body's excretion mechanisms (which can be overloaded if there is a high intake). In addition, any herbs which can actively encourage mobilization and excretion of heavy metals will also further assist in reducing an individual's overall exposure. Both the FAO and WHO have set provisional tolerable weekly intake (PTWI) values for lead, cadmium and mercury. These are as follows:[20] lead 50 µg/kg/week; cadmium 7 µg/kg/week; mercury 5 µg/kg/week. Assuming a 70 kg (154 lb) person, these values translate to: lead 3.5 mg/week; cadmium 490 µg/week; mercury 350 µg/week (EPA 49 µg/week).

These are small quantities and it is quite feasible that an herbal product taken regularly with each meal could selectively inhibit a substantial amount of this weekly intake. Hence the rationale behind using herbs is as follows:

- reduce gastrointestinal uptake of heavy metals (when the herbs are taken with meals)
- thereby help to free up the body's excretion mechanisms (which can be overloaded if there is a high intake or high stores)
- as an added factor, actively facilitate excretion of heavy metals from the body

Two key herbs which can act in this way are discussed in detail below, namely garlic and milk thistle. In addition cilantro is briefly discussed since it seems so popular for this application (perhaps undeservedly).

Garlic

Allium sativum contains alliin as the main sulfur-containing amino acid. In the presence of the enzyme alliinase (for example, when the bulb is crushed), alliin is converted to allicin (an odorous compound), which then produces a range of other constituents including ajoenes, vinyldithiines and polysulfides.[21] The sulfur-containing constituents are responsible for the characteristic smell of garlic.

Garlic demonstrated a protective effect against heavy metal poisoning in rats. Oral co-administration of garlic with cadmium or organic mercury compounds for 12 weeks resulted in a decrease in the accumulation of heavy metals in liver, kidneys, bone and testes. (These are the target organs of cadmium poisoning.) Histopathological damage and the inhibition of serum alkaline phosphatase were also decreased. The effective doses of fresh garlic were 3.35% and 6.7% of the diet, which provided 100 and 200 ppm of allicin, respectively. (The protective effect began to appear in the 3.35% group, and the heavy metal accumulation decreased more than 40% in the 6.7% group compared to the group exposed only to the metal.) Garlic at the higher dosage produced a decrease in mercury accumulation in the brain for animals treated with methyl mercury (but not for those treated with phenyl mercury). This protective effect is due to a smaller amount of mercury absorbed into the brain as a result of the enhanced excretion of mercury from the body by garlic. In another series of tests, administration of garlic (6.4% of the diet) enhanced the excretion of cadmium, more through feces than urine. In this test, administration of diallyl disulfide (30 mg/kg), a sulfur constituent of garlic, was inferior to whole garlic treatment. (In these tests, cadmium was administered by injection.) The protective effect of garlic is probably caused by the sulfur compounds combining with the heavy metals in the body and promoting excretion through bile to the feces.[22] Several other studies have confirmed a protective effect for garlic against cadmium and mercury poisoning in rats.[23]

Garlic juice almost doubled the survival of rabbits exposed to severe lead poisoning.[24] Concomitant use of garlic juice (100–400 mg/kg) prevented the accumulation of lead in liver, kidneys, brain, bone and blood in rats. The protective effect may be due to the combined effects of reduced absorption of the metal from the gastrointestinal tract and increased excretion.[25]

The oral feeding of fresh garlic to rats during the intraperitoneal injection of lead or cadmium reduced the accumulation of these metals and the biochemical alterations in the blood, liver and kidney. The antioxidant property of garlic may also protect against oxidative damage by these metals.[26] Lead concentrations were reduced in muscle and liver tissues of chickens given lead and garlic simultaneously, and also when given lead followed by garlic treatment. The reduction was in fact greater in birds given garlic as a post-treatment.[27]

Oral administration of aqueous extract of fresh garlic reduced the clastogenic (gene damaging) effect caused by exposure to inorganic arsenic in mice. At the lowest dosage of 25 mg/kg of garlic, at least 30 days of treatment was required.[28,29]

Clinical Study

The effect of a garlic supplement on workers in a lead smelter endangered by chronic lead poisoning was investigated in the 1960s in Europe. Clinical and pharmacological tests showed that under the influence of the garlic preparation the number of workers already exhibiting signs of early lead toxicity (such as damaged red blood cells) fell by 83% after one to three months. The amount of porphyrin still remaining in the urine was much decreased, and there was a statistically significant increase in the number of erythrocytes and in the amount of haemoglobin. Of the workers who were not showing signs of early lead toxicity at the beginning of the trial, 28% of these developed signs after three months compared to only 3% in the group given garlic. The authors suggested that some of the lead in the gastrointestinal tract may

have reacted with the sulfur compounds in garlic and was excreted via the feces in the form of insoluble sulfides. They also proposed that the removal of some of the garlic sulfides via the respiratory air may also restrict the absorption of lead powder in the respiratory tract.[24]

Milk Thistle

Silybum marianum fruit contains flavanolignans: silybin, silychristin, silydianin and 2,3-dehydro derivatives.[30] This flavanolignan mixture is commonly referred to as silymarin.

Oral administration of silybin (100 mg/kg/day, administered as silybin-β-cyclodestrin complex) protected against iron-induced hepatic toxicity in rats. Simultaneous treatment with silybin decreased the accumulation of malondialdehyde-protein adducts into iron-filled periportal hepatocytes (ie it reduced oxidative damage/lipid peroxidation). It also reduced the hepatic function impairment (mitochondrial energy wasting). In addition to the prominent antioxidant activity of silybin, this protective effect may be due to its strong ability to chelate iron.[31]

A group of Italian scientists investigated the iron-binding capacity of silybin, a component of the complex of flavanolignans known as silymarin found in milk thistle (Silybum marianum). Their motivation in doing so was to find an orally-active, non-toxic alternative to the iron-binding synthetic drug desferrioxamine, which causes side effects such as bone deformities, sensory abnormalities and cerebral toxicity[32] The scientists found that silybin strongly binds the ferric ion (Fe(III)), even at acidic pH. The complex of this molecule with iron demonstrated remarkable stability. Our lab results have shown that silymarin can also strongly bind heavy metals.[33] Given the bioavailability of silybin, it is probable that like garlic it can also mobilize the excretion of heavy metals. One important caveat is that iron-compromised individuals would need to take an iron supplement at a different time to this product. A combination of ascorbic acid (10 mg/kg) and silymarin (10 mg/kg) ameliorated the Pb toxicity on the liver of rats.[34] In Pb and Cd poisoning in an experimental model the structural and histochemical hepatic changes were significantly prevented by silymarin.[35]

Clinical Studies

The flavanolignans of *Silybum marianum* have demonstrated antioxidant activity and protection against drug-induced liver damage in clinical studies. The antioxidant activity was shown for example, in patients with cirrhosis or alcoholic liver damage by the increase in superoxide dismutase activity of lymphocytes and erythrocytes, and the increase in patient serum levels of glutathione and glutathione peroxidase. Silymarin (280 or 420 mg/day) was prescribed. Antioxidant activity was also demonstrated in granulocytes taken from healthy volunteers who had taken 240 mg of silybin. Silymarin (240 mg/day) also improved liver function in patients with liver disease caused by exposure to toxic levels of toluene or xylene.[36]

Cilantro

The reputation of cilantro (*Coriandrum sativum*) is based on two published studies which purport to establish that it helped to eliminate mercury from patients in a number of cases.[37,38] However, when these case studies are carefully analysed it becomes clear that at no stage were mercury or other heavy metal levels measured by normal conventional means. Instead the authors used some kind of subjective resonance methodology described as the Bi-Digital O'Ring Test, which has not been adequately described in this publication nor validated for heavy metal assessment.* This fact, combined with an unpublished study which found that cilantro possessed relatively weak heavy metal binding capacity[33] makes it a poor choice in our view, compared to garlic and milk thistle. There is one study that found that cilantro prevented localized lead deposition in mice, but the data is weak because results were only significant for bone and not for soft tissues and a dose-response relationship was not observed.[39]

* The Bi-Digital O-Ring Test is based on applied kinesiology, and is similar to muscle testing. The theory is that if there is a dysfunction in a certain organ, when a point on the body representing that organ is stimulated the force of the muscle tested (in this case an 'o-ring' formed by touching the thumb and index finger of one hand) is weakened through a brain response and the muscle tone decreases.[40] In the above study this test was used to examine the presence of heavy metals in the body, but it has not been validated by scientifically proven methods of analysis. It cannot be credibly applied to the quantification of heavy metals in tissues.

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