Managing Heavy Metals and Detoxification with Herbs

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What Is a Heavy Metal?

- Heavy metals are metallic elements which have a high atomic weight and a density at least 5 times than water
- There are more than 20 heavy metals, but three are of particular concern to human health: lead (Pb), cadmium (Cd), mercury (Hg) and we can also include inorganic arsenic (As)[1]
- In addition, according to the US Agency for Toxic Substances and Disease Registry, these heavy metals are 4 of the top 6 hazards present in toxic waste sites

1. Järup L. Hazards of heavy metal contamination. *Br Med Bull* 2003; **68**: 167-182

What Is a Heavy Metal?

- These four heavy metals are highly toxic and can cause damaging effects even at very low concentrations
- They can 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

What Is a Heavy Metal?

- Chelates are a special type of complex where an organic molecule binds to a metal at two or more points (and hence quite strongly)
- Heavy metals can also exist covalently bound to organic molecules:
  - Arsenic in a covalently bound form has substantially reduced toxicity
  - Covalently bound Hg has substantially increases toxicity, eg methyl mercury

Effects of Chronic Low Level Exposure

- There is a general consensus that high level exposure to heavy metals can cause the symptoms described in the appendix slide
- 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 eg, endocrine, neurological and immunological dysfunctions, might result from low level exposure

Lead and Children

- Children differ from adults in the relative importance of lead sources, lead metabolism, and the toxicities expressed
- The central nervous system effects of lead on children are not reversible
- 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

Bellinger DC. Lead. *Pediatrics* 2004; **113**(4): 1016-1022

Lead and Children

- No level of lead exposure is 'safe'
- Adverse outcomes, such as reduced intelligence quotient and academic deficits, occur at levels below 10 µg/dL
- Some studies even suggest that the rate of decline in performance is greater at levels below 10 µg/dL than above 10 µg/dL
- Increased exposure is also associated with attention deficit hyperactivity disorder and antisocial behavior
- Current protocols for chelation therapy appear ineffective in preventing such effects

Bellinger DC, 2008, *Very low lead exposures and children's neurodevelopment*, Curr Opin Pediatr;20(2):172-7

Heavy Metal Exposure and Repeated Miscarriages

- 111 women with repeated miscarriages had their urinary excretion of heavy metals evaluated after challenge (with a chelating drug)

	Basal Levels	180 min Challenge
Arsenic	4.80 µ/dL	15.3 µ/dL
Cadmium	0.52	0.84
Mercury	5.40	97.14
Lead	3.90	41.73

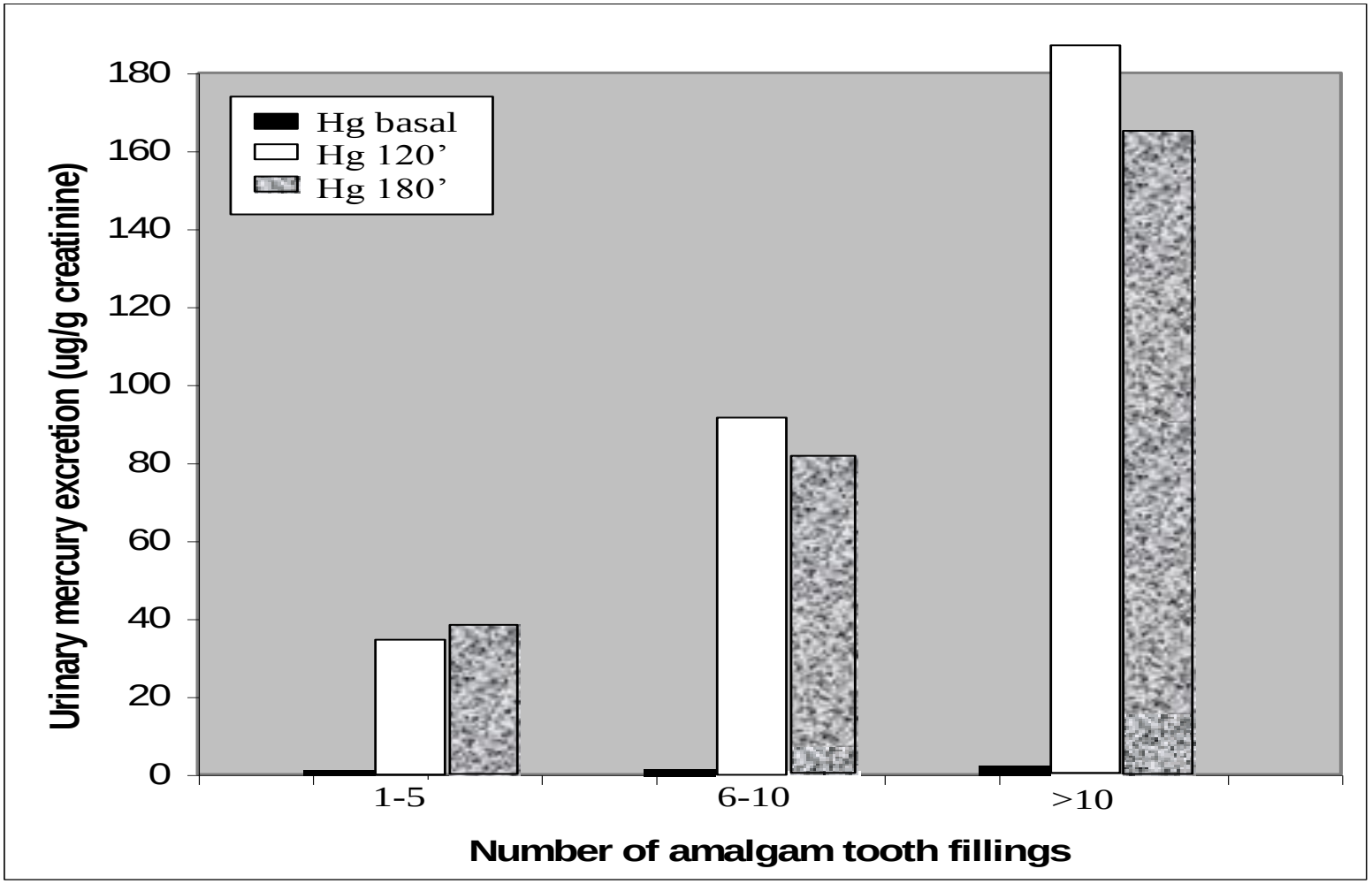
Gerhard I, Waibel S, Daniel V et al. Impact of heavy metals on hormonal and immunological factors in women with repeated miscarriages. *Hum Repro Update* 1998; **4**(3): 301-309

Heavy Metal Exposure and Repeated Miscarriages

- 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

Gerhard I, Waibel S, Daniel V et al. Impact of heavy metals on hormonal and immunological factors in women with repeated miscarriages. *Hum Repro Update* 1998; **4**(3): 301-309

Mercury Excretion and Amalgam



Gerhard I, Waibel S, Daniel V et al. Impact of heavy metals on hormonal and immunological factors in women with repeated miscarriages. *Hum Repro Update* 1998; **4**(3): 301-309

Heavy Metal in Living Kidney Cortex

- Most current knowledge on kidney concentrations of nephrotoxic metals, cadmium, mercury and lead, comes from autopsy studies
- Metal concentrations were determined in 109 living Swedish kidney donors aged 24-70 years
- Median kidney concentrations were
  - 12.9 µ/g (wet weight) for cadmium
  - 0.21 µ/g for mercury
  - 0.08 µ/g for lead

Heavy Metal in Living Kidney Cortex

- Kidney cadmium increased by 3.9 μ/g for a 10 year increase in age, and by 3.7 μ/g for an extra 10 pack-years of smoking
- Low iron stores (low serum ferritin) in women increased kidney cadmium by 4.5 μ/g
- Kidney mercury increased by 6% for every additional amalgam surface
- Dental amalgam is the main determinant of kidney mercury

Barregard L, etal, *Cadmium, mercury, and lead in kidney cortex of living kidney donors: Impact of different exposure sources*. Environ Res. 2010 Jan;110(1):47-54

Mercury and High-End Fish Intake

- 89 patients with high-end fish intake or showing symptoms suggestive of Hg toxicity were assessed
- Whole blood Hg levels were 2.0 to 89.5 µg/L
- 89% had Hg levels exceeding the 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
- Women were 10 times and some children were >40 times the national average

Hightower JM, Moore D. *Mercury Levels in High-End Consumers of Fish*. Environ Health Persp 2003; **111**(4) 604-608

Cadmium

- Cadmium accumulates in the body, particularly the kidney. Half-life 10-30 years
- Women generally accumulate more than men
- Urinary Cd (U-Cd) is a biomarker for lifetime Cd body burden in people with lower exposures
- In the absence of episodes of high-level exposure, Cd-binding sites are not saturated, and the urine Cd level increases in proportion to the amount of Cd stored in the body

Centers for Disease Control and Prevention (CDC) 2005; IPCS 1992

Agency for Toxic Substances and Disease Registry (ATSDR) 1999

Cadmium

- FDA total Diet Study showed Cd exposure in the US increased 21% from 1990 to 2003 or 8.81 to 11.06 µg/person/day
- 11.06 µg/person/day exposure constitutes ~17% of the WHOs PTWI of 7 µg/kg/week
- OSHA minimum safety standard for Cd is:
  - < 3 µg/g in urine (as creatinine)
  - < 5 µg/L in blood

Egan SK, Bolger PM, Carrington CD, *Update of US FDA's Total Diet Study food list and diet,* I. 2007 Sep;17(6):573-82. Epub 2007 Apr 4

Cadmium Health Effects

- Cd is a potent xenoestrogen or metalloestrogen
- At a dose similar to the WHO PTWI, Cd mimics the *in vivo* effects of estrogen in target organs in animal studies
- Strong evidence exposure to environmentally relevant doses of cadmium may increase the risk of breast and endometrial cancer due to its ability to activate ERα
- Also prostate cancer (metalloandrogen)
- And adversely effects the lung, liver, immune system and bone

Bryne C, etal, Cadmium - A metallohormone?, *Toxicol Appl Pharmacol*. 2009 Aug 1;238(3):266-71. Epub 2009 Apr 9

Cadmium Population Study

- NHANES data, 4,258 U.S. women > 50 Yrs from MA
- Risk of having hip-BMD-defined osteoporosis (OP) was correlated with urinary Cd levels
- Women with U-Cd b/w 0.50 & 1.0 µg/g creatinine had 43% increased risk compared to women with levels < 0.50 µg/g
- Smokers did not show a statistically increased risk

Gallagher CM, John S. Kovach JS, and Meliker JR, Urinary Cadmium and Osteoporosis in U.S. Women ≥ 50 Years of Age*: NHANES 1988–1994 and 1999–2004, Environmental Health Perspectives*, Vol 116, 10, Oct 2008 pp. 1338-43

Cadmium Population Study

- U.S. women are at risk of developing OP at U-Cd levels 3 to 6 times less than the OSHA minimum safety standard of 3 µg/g and even at levels < 1 µg/g, a concentration not previously associated with renal tubular damage.
- Study concluded that 21% of OP prevalence among women > 50 years of age may be attributable to Cd body burden

Gallagher CM, John S. Kovach JS, and Meliker JR, Urinary Cadmium and Osteoporosis in U.S. Women ≥ 50 Years of Age*: NHANES 1988–1994 and 1999–2004, Environmental Health Perspectives*, Vol 116, 10, Oct 2008 pp. 1338-43

Cadmium Swedish Study

- Cd related effects on bone in 820 women (53-64 years of age)
- U-Cd was 0.67 µg/g creatinine
- Bone mineral density, parathyroid hormone, and urinary deoxypyridinoline (U-DPD) were adversely associated with U-Cd ($p < 0.05$) in all subjects.
- Smokers did not show a statistically increased risk

Akesson A, etal, Cadmium-induced effects on bone in a population-based study of women. *Environ Health Perspect*. 2006 Jun;114(6):830-4.

Cadmium Swedish Study

- For U-DPD, there was a significant interaction between cadmium and menopause (p = 0.022)

Results

  - Low-level cadmium exposure:
    - Has negative effects of on bone
    - Increases bone resorption
    - Intensifies bone loss after menopause

Akesson A, etal, Cadmium-induced effects on bone in a population-based study of women. *Environ Health Perspect*. 2006 Jun;114(6):830-4.

Cadmium Swedish Study

- Also looked at Lead (Pb)
- Pb accumulates in bone by replacement of Ca
- The skeleton contains as much as 90% of the lead body burden
- Bone markers showed clear associations with blood lead
- ↑ blood lead levels = ↑ bone resorpton

Akesson A, etal, Cadmium-induced effects on bone in a population-based study of women. *Environ Health Perspect*. 2006 Jun;114(6):830-4.

Lead

- Pb adversely affects osteoblast, osteoclast, and chondrocyte function and has been associated with osteoporosis
- Pb delays fracture healing at environmentally relevant doses and induces fibrous nonunions at higher doses by inhibiting the progression of endochondral ossification

Carmouche JJ, Lead exposure inhibits fracture healing and is associated with increased chondrogenesis, delay in cartilage mineralization, and a decrease in osteoprogenitor frequency, Environ Health Perspect. 2005 Jun;113(6):749-55

Metallothionein Protection of Cadmium Toxicity

- Metallothioneins (MTs) are proteins with a high cysteine content (high in sulfur)
- Responsible for metal transport within the body
- Zinc is able to upregulate MT significantly
- MTs are critical for protecting human health from Cd toxicity

Klaassen CD. Metallothionein protection of cadmium toxicity. Toxicol Appl Pharmacol. 2009 Aug 1;238(3):215-20. Epub 2009 Apr 9

Alscher DM, etal. Induction of metallothionein in mesothelial cells by zinc, *Artif Organs*. 2007 Jun;31(6):488-91

Transport Pathways for Cd and the Interaction with Essential Metals

- There is still uncertainty about how cadmium gains entry into the proximal tubule cells of the kidney to induce toxicity
- Transport proteins/channels used by essential metals (iron, zinc, calcium) are thought to be responsible
- When these dietary essential metals are in short supply and deficiencies develop, Cd absorption and toxicity are enhanced

Vesey DA, *Transport pathways for cadmium in the intestine and kidney proximal tubule: focus on the interaction with essential metals.* Toxicol Lett. 2010 Sep 15;198(1):13-9. Epub 2010 May 13

Herbs for Heavy Metal Exposure

- 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

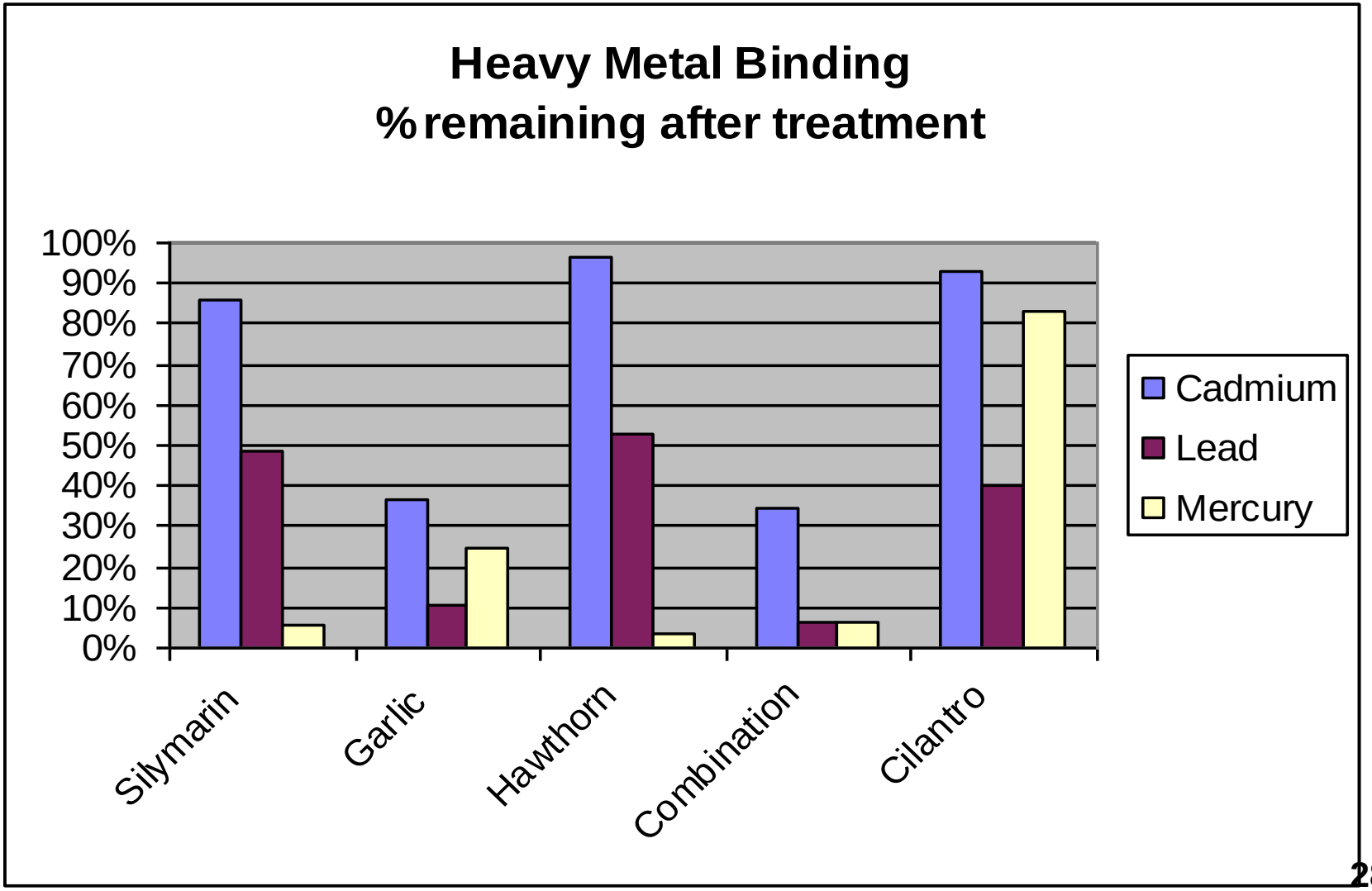
Herbs for Heavy Metal Exposure

- 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)

Herbs for Heavy Metal Exposure

- 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

Heavy Metal Binding Capacity of Herbs



Herbs for Heavy Metal Clearance

Garlic

- Garlic is well-known to antagonize lead and other heavy metal toxins, Cd, Hg, Cu
- It protected against poisoning by cadmium and organic mercury in a rat model.
- The protective effect of Garlic was comparable or superior to those of conventional drugs used to treat heavy metal toxicity such as D-penicillamine and DMSA

Cha CW. *J Korean Med Sci* 1987; **2**(4): 213-224

Herbs for Heavy Metal Clearance

Garlic

- Workers endangered by chronic lead poisoning received Garlic tablets
- Signs of chronic lead toxicity ↓ by 83% after one to three months treatment
  - Punctured red blood cells
  - Porphyrin in the urine
  - Statistically significant ↑ in red blood cell numbers and their hemoglobin content
- Garlic was preventative in another cohort of workers

Petkov V. *J Ethnopharmacol* 1986; **15**: 121-132

Herbs for Heavy Metal Clearance

Milk Thistle

- Italian scientists investigated the iron-binding capacity of silybin from Milk Thistle
- 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
- They discovered that Silybin strongly binds the ferric ion (Fe(III)), even at acidic pH. The complex of this molecule with iron demonstrated remarkable stability

Borsari M, Gabbi C, Ghelfi F et al. *J Inorg Biochem* 2001; **85**: 123-129

Herbs for Heavy Metal Clearance

Milk Thistle

- MediHerb lab results show silymarin can also strongly bind heavy metals
- 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

Herbs for Heavy Metal Clearance

Hawthorn

- Hawthorn leaf and flower contain flavonoids and procyanidins (a type of polyphenol)
- The chemical structure of polyphenols makes them excellent chelators of metal ions, a property used for the recovery of heavy metals from waste water
- The ability of procyanidins to chelate metals was confirmed *in vitro* and in oral studies in rats
- Chelation of metals is one of the ways polyphenols exert their antioxidant activiy.

ChelaCo

- Garlic bulb powder 100 mg
  from *Allium sativum* bulb 100 mg
  Containing alliin 2.0 mg

Hawthorn flowering tops extract 3:1 100 mg
from *Crataegus monogyna*
flowering tops 300 mg

Milk Thistle seed extract 70:1 100 mg
from *Silybum marianum* seed dry 7.0 g
Containing flavanolignans as silybin 80 mg

Dose: 1 enteric coated tablet, 3 times daily with meals

Primary Indication

- Environmental exposure to heavy metals

Suggested Use

- Preventing / minimizing the gastrointestinal absorption of environmental metals
- Promoting the excretion of metals from the body
- Antioxidant
- In anemia and cases where iron supplementation is required, do not take simultaneously with meals to iron supplements

Heavy Metal Support

Core Support

- ChelaCo, 1 tablet 3 times daily

or

- Garlic 5000mg, 1 tablet 2 to 3 times daily
- And
- Parotid PMG, 2 tablets 3 times daily
- Zinc Liver Chelate, 1 tablet 3 times daily

Heavy Metal Support

Additional support

- Support liver, kidney, adrenal and bone function
- Traditional herbal approaches with depurative or alterative herbs
- Bowel cleansing
- In severe cases extra Milk Thistle because of its anti-toxic effects

Menopausal Osteoporosis

- Bone Complex, 1 tablet 3 times daily
- Ostrophin, 2 tablets 3 times daily
- Calcifood Powder, 1 to 2 tablespoons per day
- Cataplex D, 1 tablet 3 times daily
- Zinc Liver Chelate, 1 tablet 3 times daily
- Whey Pro Complete
- Garlic 5000mg, 1 tablet 2 to 3 times daily
- Bowel Flora Protocol yearly
- Exercise