Microalgae Chlorella - effective mechanisms of action in support of a natural detoxification.

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Chlorella is a microscopic green alga (Chlorophyta), not much larger than a red blood cell. The name of this unicellular aquatic plant is derived from the Greek *chloros* (green, yellow-green) and -*ella* (small). The microalgae is spherical in shape and occurs worldwide. It has long been known that due to the complex interplay of its unique ingredients, Chlorella is able to bind various metals such as copper, cadmium, nickel, gold, chromium, lead, mercury and arsenic. In recent years, research in this area has been massively intensified and the mechanisms of detoxification further decrypted. The following article portrays the multifaceted microalgae for their potential for elimination and detoxification.

Keywords: Chlorella; Heavy Metals; Lead; Mercury; Detoxification ; Drainage; Biosorption; Antioxidants; Research; Quality

Chlorella is one of the most extensively studied plants. It owes this success above all to its nutritional properties and its role as a model organism in biology. In PubMed alone, there are now well over 5,000 entries for the search term Chlorella (1). The microalgae have been cultivated in Asia since the middle of the last century, and later also in Europe and the USA. Different cultivation methods are used: open concrete ponds or foil tanks, fermenters or photo bioreactors.

1. CHLORELLA SPECIES

The determination of the Chlorella species is not trivial and is carried out today mainly with the help of molecular markers. In the past, more than 100 Chlorella species were differentiated, most of which had to be revised. Today, only three species are counted to the genus Chlorella: C. *vulgaris*, C. *lobophora* and C. *sorokiniana*. C. *pyrenoidosa* is still available as a product. However, this is an obsolete term. As early as 1992, it was stated (and later confirmed in several studies) that such a species does not exist. On the contrary, quite different algae species and genera were used under the term (2,3).

Chlorella consists of about 50% of proteins with a very good AAS (Amino Acid Score) and up to 50% of chlorophyll, which makes them the chlorophyll-richest plant ever. Chlorella also contains dietary fibers, carotenoids (-carotene, lutein), alpha-linolenic acid (an essential omega-3 fatty acid), bioavailable vitamin B_12 (depending on the cultivation method, chlorella is the richest vitamin B_12 plant), - 1,3-glucan (an active immune stimulator and radical scavenger, lowers lipid levels in the blood), salicylic acid, caffeic acid and e-cinnamic acid (antioxidants, analgesics, anti-inflammatory drugs).(4,5)

2. POTENTIAL EFFECTS OF CHLORELLA

Chlorella is traditionally used for the drainage or detoxification of various pollutants such as heavy metals or dioxin. In addition, a large number of studies show an immunomodulatory effect, a reduction in susceptibility to infection, improved wound healing, a positive effect on the intestinal flora, an increase in insulin sensitivity, anti-inflammatory and anti-oxidative effects and a reduction in the consequences of (stress-influenced) metabolic disorders (positive influence on blood sugar and cholesterol levels, blood pressure reduction). (4,6,7)

2.1. Drainage and detoxification.

The theme of drainage, detoxification or detox is a constant theme that has now reached the general public and is sometimes controversial. While emeritus Professor Edzard Ernst in *The Guardian* speaks "You can not detoxify your body, it's a myth (8), *Vogue* writes, with a focus on algae the same year and just a few months earlier: "Detoxifying with algae. Detox without giving up [...] The wellness detox wonder, the Chlorella alga, is currently experiencing a hype (9) Who is right now? The fact is, our body is actually a perfect detoxification machine, with all its detoxification organs

such as the skin, lungs, kidneys, liver, intestines and bile. However, it is also a fact that our bodies are confronted with ever new toxins and in some cases ever larger quantities. This pollution of the body by various environmental toxins is today seen as the cause of a variety of diseases.(10,11)

2.2. Example Lead.

Lead in particular accumulates in our bones. Today, we have a 10-100 times higher lead content in the bones than the original human (12), and in the blood alone the lead content in the last 100 years has increased to 300-500 times (13). Lead damages the organism in low doses, as the *Pharmazeutische Zeitung* put it together in their article "Lead in the blood - Even little is poisonous".(14)

2.3. Example Mercury.

Mercury is ubiquitous in the environment and has a high human toxicity in concentration ranges that are critically close to the nutritional underground load (11). Additional sources of intake are amalgam fillings (3-17 g / d), occupational exposure and above all the consumption of fish and fish other sea animals (11,15). Mercury primarily accumulates in the nervous system.

2.4. Biosorption of (heavy) metals by Chlorella.

In the case of Chlorella, biosorption describes, on one hand, the adsorption of the positively charged metal ions on extracellular, cell-associated materials (e.g.polysaccharides) or negatively charged groups of the cell surface (e.g. carboxy, hydroxy, sulfate or phosphate groups) and their accumulation in the cytoplasm (only in living cells)(16).

The ability of chlorella to bind or to accumulate various metals, such as copper, cadmium, nickel, gold, chromium, lead, mercury, and arsenic, has long been known (16-18). Thus, the potential of Chlorella in the range Biomining is researching to win valuable resources such as gold (19) or rare earths such as neodymium (20).

In wastewater treatment, the biosorption of lead on Chlorella was investigated. In particular, amino, carboxy, hydroxy, and carbonyl groups were found to be responsible for binding (21, 22). In vitro studies showed that 1 g Chlorella powder can bind up to 90 mg lead, that is, at least 9% their own weight! Within the first 15 minutes, 80-90% of the available lead (concentration range 0.5-500 mg / l) was bound (Table 1). In the test, Chlorella powder with broken cell walls bound slightly less lead (66.97 mg Pb / g) than Chlorella with intact cell walls (90.28 mg Pb / g) (23).

In other studies, the rapid biosorption of uranium (VI) to Chlorella was demonstrated (living Chlorella: 14.3 mg U / g, dried: 28.3 mg U / g, both within 5 minutes, at 0.1 mM uranium in solution). Here too, carboxyl groups as well as phosphate groups involved in the complexation were identified (24). In comparison to strontium, a maximum sorption capacity of Chlorella of 9.06 mg / g was shown (25).

3. QUALITY CONCERNS IN SOME CHLORELLA PRODUCTS

The ability of Chlorella to bioabsorb heavy metals can also affect the heavy metal content of Chlorella products (an important quality criterion). Thus, in some Chlorella products, lead variation ranges from 0.1 - 1.1 mg / kg, for arsenic 0.1-1.3 mg / kg, for cadmium 0.02-0 11 mg / kg and mercury of 0,01-0,07 mg / kg were found (2). In addition, the *European Rapid Alert System for Food and Feed* (RASSF) website reports analysis which contain abnormalities in the heavy metal content of some Chlorella products. For example, in 2013 a sample of Chlorella from the Czech Republic (country of origin: Spain) was found to contain 5.5 mg / kg lead (26). But other potential pollutants in Chlorella should also be investigated. For example, the polycyclic aromatic hydrocarbons (PAHs), formed during the incomplete combustion of organic material, are known to be carcinogenic and teratogenic. In the RASSF portal, a Bio-Chlorella (origin: China) was analyzed on April 24, 2015 in which 3,189 g / kg total PAH were detected (26). Since April 2016, a limit value of 50 g / kg PAH has been set in food supplements (VO (EU) 2015/1933). *the inspection offices for food control and animal health* in Baden-Wrttemberg reported increased PAH levels in some Spirulina microalgae between 2010 and 2012, and identified diesel-powered drying machines as a possible source of the increased levels (27).

4. RESEARCH STATUS ON DETOXIFICATION PERFORMANCE.

Kanno et al. investigated the effect of Chlorella on patients with chronic cadmium, mercury and arsenic intoxication. Positive results were achieved with doses of between 4.5 and 6 g Chlorella per day (28,29).

4.1. Cadmium

increased excretion of cadmium via urine and faeces, reduction in the incidence of arthritis, improvement in subjective symptoms.

4.2. Mercury

Reduction of the toxicity of mercury, alleviation of malnutrition in patients with chronic organic mercury poisoning, reduction of uncomfortable drowsiness, increased levels of hemoglobin, red blood cells and serum protein.

4.3. Arsenic

Reduction of concentration in the blood, increased excretion via the urine after chronic intoxication, significant improvement in the appearance of the skin.

A number of tests have also been conducted on animals exposed to various heavy metals to study the effect of different Chlorella strains at different doses. These studies showed that gastrointestinal absorption of heavy metals was prevented and faecal excretion of lead in mice was increased (30). Chlorella increased urinary excretion of mercury and faecal excertion in mice (31, 32) exposed to methyl mercury (MeHg). In addition, Chlorella reduced the accumulation of MeHg in tissues, including brain, and suppressed the transfer of MeHg in pregnant mice from mother to foetus (33). In rats exposed to cadmium, Chlorella prevented the absorption and accumulation of cadmium by increased excretion via urine and faeces (34).

5. ANTIOXIDANTS PROPERTIES.

Heavy metals can induce oxidative stress even in low concentrations. In rats exposed to low levels of cadmium, administration of Chlorella was able to prevent oxidative stress by reducing the activity of free radical enzymes and the formation of lipid peroxides.(3) Heavy metals can induce oxidative stress even in low concentrations. In rats exposed to low levels of cadmium, administration of Chlorella was able to prevent oxidative stress by reducing the activity of free radical enzymes and the formation of lipid peroxides(35). In mice with mercury poisoning (HgCl2) Chlorella administration could prevent oxidative stress and renal cell damage(36). An ethanolic extract of Chlorella (0.5 g / kg bw / d) effectively protected rats exposed to toxic tetrachloromethane from oxidative stress. The hepatoprotective effect was comparable to the effect of the drug Sylimarin (0.2 g / kg bw / d), which is used in clinical practice in the treatment of chronic inflammatory liver diseases (37). A comparable detoxification effect of a Chlorella extract was observed by Hwang et al. The group noted an increase in certain biomarkers that occur in the body during phase I and II (38). Chlorella also protects the barrier of the intestinal mucosa, reducing the penetration of bacteria and endotoxins (39).

6. CHLORELLA AND THE RELEASE OF DIOXINS, PESTICIDES AND OTHER ENVIRONMENTAL TOXINS.

Studies in humans have shown that Chlorella reduces the transfer of dioxins from mother to fetus across the placenta during pregnancy by about 30% compared to the control group (40). In addition, the concentration of dioxin in breast milk was reduced as well increase the amount of immunoglobulin A (41). Morita et al. could demonstrate that in rats exposed to dioxin, Chlorella and a chlorophyll extract from Chlorella prevented the gastrointestinal absorption of dioxin and accelerated the excretion of dioxin (42, 43). Chlordecone is a harmful insecticide that can not be detoxified or eliminated by the body. Although it is excreted in the intestinal lumen with bile, it is later reabsorbed. In rats exposed to chlordecone, administration of Chlorella accelerated detoxification and reduced the half-life of the toxin from 40 to 19 days (44). In 2015, Zenker describes case studies on how patients suffering from Borreliosis could be helped by adding Chlorella. He justified this with the ability of Chlorella to bind the neurotoxins produced by the Borrelia (45). However, there are no scientifically sound studies on this.

7. CHLORELLA AND THE MOBILIZATION OF HEAVY METALS IN THE BODY.

Klinghardt postulated the possible mobilization of heavy metals in the body through Chlorella supplements. According to him, amino acids of Chlorella are reponsible for it. Symptoms such as headache, discomfort, flatulence, and nausea may then accompany the mobilization. The reason he reckons is that more heavy metals are mobilized as they can be bound in the intestine by Chlorella. He recommends an increased dose of Chlorella in such a case (46).

8. EXECUTIVE SUMMARY

Chlorella can support a natural detoxification through a complex interaction of very different mechanisms:

1. Reduction of the absorption of heavy metals during food intake
2. Prevention of reabsorption of heavy metals in the intestinal lumen by biosorption
3. Complex formation (e.g. chlorophyll with dioxin) prevents absorption.
4. The mineral components of Chlorella can competitively inhibit the uptake of heavy metals in the gut
5. Increasing intestinal activity and stimulating excretion (47).
6. Antioxidants (chlorophyll, carotenoids, lutein, some vitamins) prevent the formation of radicals and thus cell damage
7. A suppressed immune system can be stabilized and re-strengthened by immunomodulation.
8. Stimulation of Phase II and Phase III elimination processes, e.g. by increased formation of conjugating enzymes such as glutathione S-transferases (48).

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