Supporting Documentation
Waiora USA, Inc
Zeolite Supplement

Natural Cellular Defense®

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Introduction

Natural Cellular Defense® (NCD) is a colloidal suspension of activated zeolite produced by Wellness Industries, Inc. and marketed and distributed by Waiora, Inc. NCD contains primarily clinoptilolite as the constituent zeolite, a naturally-occurring Sodium aluminosilicate. This product is classified as a dietary supplement under US-FDA guidelines. The following report will outline the history of use and safety of the zeolite, clinoptilolite, in both animals and humans. It will also include published data on the ingredient as well as unpublished clinical data on the NCD itself.

Background of clinoptilolite

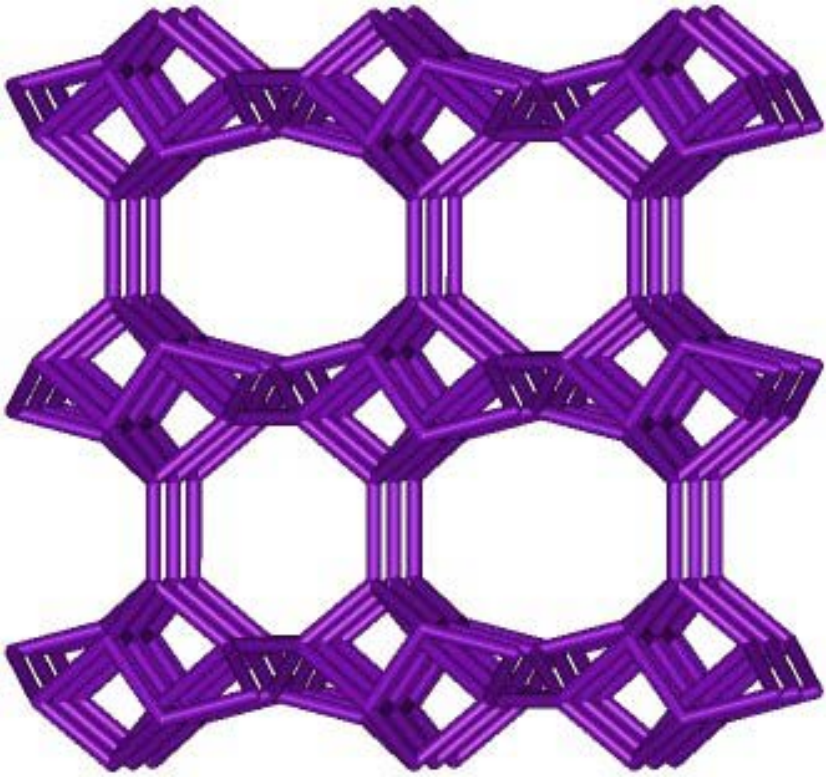
Zeolites are a family of crystalline aluminosilicate minerals. The first zeolite was described in 1756 by Cronstedt, a Swedish mineralogist who coined the name from two Greek words meaning 'boiling stones', referring to the evolution of steam when the rock is heated. About fifty different natural zeolites are now known and more than one hundred and fifty have been synthesized for specific applications such as industrial catalysis or as detergent builders.

Clinoptilolite is a naturally-occurring zeolite, formed by the devitrification (ie the conversion of glassy material to crystalline material) of volcanic ash in lake and marine waters millions of years ago. It is the most researched of all zeolites and is widely regarded as the most useful. In common with other zeolites, clinoptilolite has a cage-like structure consisting of SiO_4 and AlO_4 tetrahedra joined by shared oxygen atoms. The negative charges of the AlO_4 units are balanced by the presence of exchangeable cations - notably calcium, magnesium, sodium, potassium and iron. These ions can be readily displaced by other substances, for example heavy metals (mercury, lead, cadmium, etc..) and ammonium ions. This phenomenon is known as cationic exchange, and it is the very high cationic exchange capacity of clinoptilolite which provides many of its useful properties. Being a naturally occurring mineral, the precise composition of clinoptilolite is subject to a degree of variation. However, an approximate empirical formula is (Ca, Fe, K, Mg, Na)3-6Si30Al6O72.24H2O. The Chemical Abstracts Service (CAS) Number for clinoptilolite is **12173-10-3**.

Clinoptilolite is currently used in diverse applications such as drinking water purification, air filtration, plant fertilizer and as an animal feed additive. Many studies have shown that clinoptilolite absorbs toxins created by molds in animal feeds, as well as enhancing nutrient absorption by cattle, pigs, lambs and other animals. Clinoptilolite of volcanic origin has been approved by the EU for use in the category of "Binders, anti-caking agents and coagulants" in feeding stuffs for pigs, rabbits and poultry at levels of up to 20,000 mg/kg. In the United States, clinoptilolite falls under the category of sodium aluminosilicate and has GRAS (Generally Recognized as Safe) status used primarily as an anti-caking agent (Code of Federal Regulations, Title 21, Section 182.2727).

Clinoptilolite forms the basis of the anti-diarrhea drug 'Enterex', which was approved by the Cuban Drug Control Agency in 1995. The large majority of toxicology studies on zeolites have been performed on clinoptilolite, chabazite and Zeolite A – the latter because of its widespread

use in household detergents. No fatal case arising from the oral uptake of any of these zeolites has been identified.



Framework structure of clinoptilolite

Source of Clinoptilolite

Deposits of clinoptilolite exist in many countries around the world, including the USA, Cuba, Italy, Turkey, Greece, Ukraine and Japan. Wellness Industries, Inc. currently imports clinoptilolite only from a single mine in New Mexico, USA. This deposit is a very high purity clinoptilolite and, unlike many deposits, contains no radioactive materials and very low levels of heavy metals. In the event of alternative source(s) being utilized in the future, the mineral will of course be subjected to the same rigorous quality control procedures.

How does it work?

Clinoptilolite has a cage-like structure, with pores and channels running through the crystal. The cage carries a net negative charge, making it one of the few negatively-charged minerals found in nature. Because of its cage-like structure and negative charge, clinoptilolite has the ability to draw to itself and trap within itself positively charged heavy metals and other toxic substances. The zeolite in the Natural Cellular Defense attracts and traps small, highly-charged particles that fit into the pores and channels of the zeolite cage. The SiO_4 units are electrically neutral, but each AlO_4 unit carries a negative charge, creating fixed, negatively charged sites throughout the crystal structure. The negative charges of the AlO_4 units are balanced by the presence of

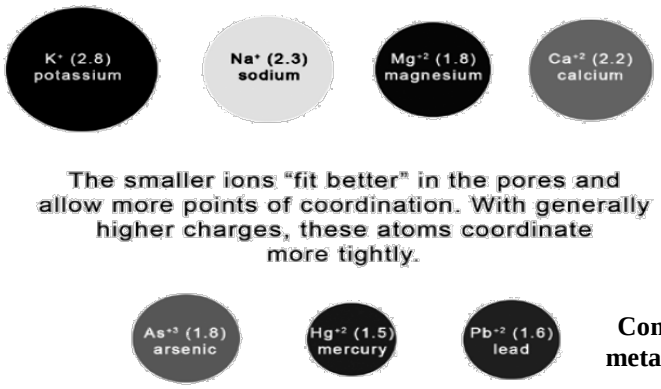
exchangeable, positively charged metals known as *cations* (pronounced “CAT- ions”). These cations usually consist of calcium, magnesium, sodium, potassium and iron. These ions are only loosely held and can be readily displaced by other substances, such as toxic heavy metals. This phenomenon is known as cationic exchange, and it is the very high cationic exchange capacity of zeolites which provides for many of their useful properties. In their chemical makeup, zeolites are a lot like clay, in that they are both made up of aluminum, silica and oxygen. However, there is an important difference in their structure. Many types of clay have a layered crystalline structure (similar to a deck of cards) and are subject to shrinking and swelling as water is absorbed and removed between the layers. In contrast, zeolites have a rigid, 3-dimensional crystalline structure (similar to a honeycomb) consisting of a network of interconnected tunnels and cages. Water moves freely in and out of these pores but the zeolite’s framework remains rigid. Another special aspect of this structure is that the pore and channel sizes are nearly uniform, allowing the crystal to act as a molecular sieve.

Whereas most chelating agents used for detoxification are non-specific, only relying on charge for binding potential, the clinoptilolite seems to be highly specific for the toxic heavy metals. Research has shown that the smaller the diameter of the metal and the higher the charge of the metal, the greater the affinity it has for the activated liquid zeolite. Higher charges simply increase the strength of binding with higher binding characteristics. The small size allows for deeper access into the zeolite pores with more points of coordination (attachment). Larger atoms do not fit into the zeolite cage as well and so are more easily exchanged for higher-affinity metals. As an example of this phenomenon, arsenic has a charge of +3 and an atomic radius of approximately 1.8 angstroms, while potassium has a charge of only +1 and an atomic radius of approximately 2.8 angstroms. The arsenic binds with very high affinity for the zeolite while the potassium has no affinity whatsoever.

The metals that are toxic to humans are toxic *because* they are smaller atoms that carry a higher positive charge and can easily displace the essential electrolytes, which tend to be larger and have less charge density. These essential ions are not essential *because* they are larger or “weaker”, they are essential because nature integrated them into human biochemistry - the size and charge of the essential metals integrate with the peptides, proteins and enzymes they are components of, allowing the biomolecules to fold properly and take on the form and function necessary to support life. The smaller, higher charged ions insert into these precisely folded peptides, proteins and enzymes, displace the essential metals and, simply because they are the wrong size and charge, change the 3-dimensional structure of the biomolecule which alters both form and function. Size and charge, in this case, are simply circumstantial to activity. The zeolite in NCD preferentially binds smaller, more charge-dense ions. That is the primary characteristic for which it was selected for use in the product. Metals with a smaller size and a higher charge will bind with greater affinity for the zeolite. The smaller size allows for deeper penetration into the zeolite cage. Additionally, the smaller size allows for more points of coordination with the zeolite. In other words, more of the surface of a small atom will be held directly by the zeolite. The higher charge allows for a tighter bond simply because of charge-to-charge interactions. Consider the example of refrigerator magnets to illustrate this point. A weak magnet will not stick well to the side of a refrigerator and will not even hold one piece of paper. This is like a metal with a low charge trying to be held by the high negative charge of the zeolite. A strong magnet can hold many pieces of paper to the refrigerator and is hard to remove because of its strong interaction. This is similar to a metal with a high positive charge that will bind very

strongly to the high negative charge of the zeolite cage. As we stated previously, all of the metals that are good for us (magnesium, calcium, potassium, etc..) tend to be large with lower charges. All of the metals that are toxic (mercury, lead, arsenic, etc..) tend to be smaller with higher positive charges.

The clinoptilolite binds a variety of toxins. This includes heavy metals (Lead, Cadmium, Mercury, etc..), nitrosamines and others. Cationic exchange is an entirely passive process – when the zeolite is in close proximity to these high-affinity compounds, they will be drawn to the zeolite and either absorbed into the cage or adsorbed onto the surface of the zeolite. There is no chemical activity in this process. The zeolite will not be drawn to compounds in an effort to 'rip' metals away from them. In other words, the zeolite will not pull metals that are sequestered inside tissue or bone. If, on the other hand, the tissue has already released free metals into the system, the zeolite will have the ability to trap and remove it.



Comparison of low-affinity metals to high-affinity metals

Literature

There are extensive reports in the chemical engineering, crystallographic and synthetic chemistry literature regarding the use of zeolites, including clinoptilolite (CLN), as molecular sieves and filtration agents. Nitrosamines, heavy metals, dichlorobenzene and mycotoxins, such as aflatoxin B-1 have been shown to coordinate with the structure of, or adsorb into the structure of, zeolites. In addition, the structure of this naturally occurring mineral is well documented and crystal structures have been grown which demonstrate coordination of CLN with many other compounds, natural and synthetic. The role of CLN as a chemical adsorbent is without question. For the purpose of this report, that literature will not be discussed except as references.

The first studies conducted in a complete toxicology profile usually consist of exposing cells in culture to the agents in question. This has been done with CLN and a summary of this *in vitro* data will be presented. However, this data is more useful in measuring comparative toxicities and is generally not considered to be as relevant as indicators of *in vivo* toxicity. The evaluation of dietary CLN supplementation through agricultural/animal science research makes up the bulk of the safety data used in this report. Reports of use in humans do exist in the medical literature and those data will also be outlined herein.

Cell Culture Data

CLN has been shown in the chemical engineering literature to be an effective adsorbent for metal ions that serve as serum electrolytes, like sodium, potassium, calcium, magnesium, as well as toxic heavy metals and environmental poisons. In cell culture experiments, CLN has been shown to cause cell death or a slowing of the growth of the cultured cells. In a culture of human embryonic lung cells, three zeolites were compared: CLN vs mordenite vs erionite[1]. Nikolova and colleagues observed an increasingly toxic effect of these zeolites on the cultures of lung cells, ordered CLN, MOR, and ERI. Suggestions as to particle size were discussed, however the ionosorbent properties of the individual zeolites, which correlated to their relative toxicities, is ultimately the cause. Cells in culture require calcium and magnesium, some in excess, for successful culture. The in vitro environment is defined and is limited in the amount of these electrolytes that are available. Loss of those, as well as other serum components, was ultimately the cause of the cell death. In other studies, the effect of CLN has been measured against tumor cells and mechanisms of antitumor activity proposed[2,3,4] including alteration of cell cycle genes like $p21^{cip1/waf1}$ and $p27^{kip1}$.

In these cell culture studies, the authors unsuccessfully argue specific influence of CLN on genes and growth regulation pathways. In all cases, the influence of CLN on cultured cells appears to be an artifact of sequestration of necessary nutrients, growth factors and serum components. The position that particle size played a role in toxicity would not come into consideration since the product in question contains micronized zeolite. The sheet-like structure of CLN also differs from more toxic species of zeolite, such as asbestos. Asbestos is described macroscopically as rod-like or needle-shaped. As such, these other minerals could be mechanically cytotoxic.

Use as a feed supplement in agriculture

Clinoptilolite (CLN) has been evaluated as a food additive in cows, pigs, rats, mice, dogs, sheep and hens and as a potential candidate for the experimental-induction of carcinogenesis agent in rats.

Cattle

Cattle awaiting parturition underwent long-term feed supplementation with CLN and were evaluated for changes in serum electrolyte levels (Ca, Mg, K, Na, PO_4)[5] and on serum beta-carotene, Vitamin A and Vitamin K levels[6]. In both studies, no changes in serum levels were detected with CLN feed supplementation. In addition, the cows were evaluated for the development of parturient paresis, also known as “milk fever”, a post-partum condition characterized by low serum calcium. Supplementation with CLN reduced the instance of this condition indicating it does not bind and sequester serum calcium. Katsoulos et. al. also evaluated the effect of long-term feed supplementation on the serum concentration of certain trace metals (Fe, Zn, and Cu)[7]. At a level of 1.25% of feed, CLN had no effect on these serum metals while 2.5% resulted in minimally detectable differences which held no clinical relevance. Other work demonstrates the ability of CLN feed-supplementation to reduce the transfer of radioactive cesium from lactating dairy cattle to the milk.[8]

No literature exists describing any adverse clinical events associated with feed supplementation in cattle. Rather, the published clinical experience associated with this species has described benefit and safety.

Swine

CLN has been extensively studied in this model. Animals were fed a diet of 5% CLN and monitored for general health status, blood composition, weight gain, feces production and odor and on the course of gastroenteritis of alimentary origin and diarrhea affecting these animals[9]. This study revealed that feeding swine CLN reduced overwhelming fecal odor, and hastened symptom resolution for animals affected by diarrhea and gastroenteritis. In addition, no hematological affects (reduction in red or white blood cell numbers or morphology) were observed in the test animals. Moreover, swine fed CLN gained an average of 23% more weight compared to controls. This weight gain is postulated to result not from CLN directly, but from the overall improved health and reduced incidence of gastrointestinal distress by the test animals compared to control animals. CLN adsorbs ammonia (as NH_4^+) from the gastric compartment of these animals.

In another series of experiments, swine were exposed to cadmium with or without 3% CLN feed-supplementation and the effects of Fe-deficiency anemia measured[10]. Adding CLN to the diet of these swine resulted in a reduction in the severity of anemia associated with cadmium poisoning and an overall reduction in the amount of Cd isolated from tissue procured from the poisoned pig, demonstrating the ability of CLN to effectively remove that toxin from the animal's body.

Similar to the cattle study described earlier, the effect of feed supplementation with CLN was evaluated in sows[11]. Vitamins, serum electrolytes and other trace elements were measured in animals with and without pre-treatment with CLN. The effects on serum and tissue levels were evaluated. Papaioannou found no changes in levels of K, Na, P, Ca, Mg, Zn or Cu, nor in Vitamin A or E, in the serum, liver or kidneys of the sows.

The effect of CLN feed supplementation has been compared to that of other zeolites. Zeolite A, a synthetic version of the mineral, and CLN were fed to growing pigs of varying developmental stages[12]. Weight gains, feed conversion ratios and serum electrolyte levels were measured, as well as the biological value of proteins synthesized (a marker of ammonia removal), plasma ammonia, digestibility of nitrogen, and urinary p-cresol levels were measured. Shurson and colleagues found, in contrast to the other studies, that no effect of weight gain or daily feed intake was observed with either zeolite. CLN supplementation, however, did result in an increased feed conversion ratio. The synthetic zeolite reduced each serum electrolyte measured (Ca, P, Mg, Na, and Fe) linearly with dose but CLN reduced only serum phosphates. Daily fecal nitrogen increased with both zeolites but net protein utilization was reduced in the CLN group. Urinary p-cresol and plasma ammonia were reduced by feeding CLN.

Papaioannou went on to evaluate the effect of combining oral antimicrobial medication with 2% CLN feed supplementation in weaned, growing and finished pigs[13] and in sows and their litters[14]. His group observed no adverse reaction to ingesting CLN. Antimicrobial drugs to prevent diarrhea given simultaneously with CLN did not result in adsorption of the antibiotic. In fact, the co-administration of the drug with the CLN resulted in a shorter clinical course of

diarrhea compared to antibiotics alone. In fact, CLN supplementation resulted in an overall reduction in the mortality of weanlings associated with administration of antimicrobial agents. Overall and average daily weight gains increased as well as the feed-conversion-ratio, the measure of how efficiently the piglets convert food to body weight. Finally, the overall well-being score of all animals improved. Since antibiotic exposure alone carries risk, the major conclusions drawn from this work are the lack of interactive effect of CLN on the systemic availability and efficacy of the antibiotics and the apparent protective effect the CLN provided over the toxicities associated with antibiotic use.

Though one study did show a net reduction in serum phosphates in swine supplemented with CLN, the reduction was described as "clinically insignificant" by the authors. The overall clinical experience with CLN in this species would be described as positive.

Rodents

There are many papers evaluating the effects of CLN in several species of rodent. Rats fed Cd along with CLN give birth to litters of normal size and the pups develop normally[15]. Rats fed CLN after being exposed to 2,2-dichlorovinyl dimethyl phosphate, known commercially as dichlorvos, a neurotoxic pesticide sprayed onto farm animals to eliminate parasites, showed reduced intoxication by the chemical and significantly reduced tissue-level reduction in cholinesterase (a tissue-level effect of dichlorvos poisoning) in all tissues evaluated[16]. Even more remarkable, tissue cholinesterase activity was maintained in rats exposed to the nerve agent, VX, after pre-treatment with CLN[17]. Rats fed CLN alone and in combination with Aflatoxin B-1, a carcinogen produced by the fungi, Aspergillus flavus and Aspergillus parasiticus, demonstrated some reduced aflatoxicosis, but an increase in maternal liver lesions, even above aflatoxin B-1 alone[18].

Because both are zeolites, references are made to the similarity between asbestos and CLN. However, they each possess unique structural and chemical properties. Studies have been conducted; questioning the wisdom and safety of zeolite treatment in general[19], but ultimately proves CLN is safe among zeolites. Diatomaceous earth, quartz, mordenite and CLN were introduced into the respiratory tract of rats by bronchial levage. With all minerals except CLN, this treatment resulted in cytotoxic effects in the tissues, attributed to the rod- or needle-like structure of the other minerals. Carcinogenicity of CLN was evaluated by direct intratracheal administrating of CLN in Wistar rats[20]. The authors found no transformation or carcinogenesis in the rat lung with up to 60 mg of CLN.

Tumor bearing mice were treated with micronized CLN and doxorubicin[21]. The lipid-peroxidation of doxorubicin to 4-hydroxynenal, and thus the cytotoxic effects of the drug, were reduced outside the tumor but left intact within. The combination with CLN also resulted in "a strong reduction of the pulmonary metastasis count, increasing the anticancer effects of Doxorubicin. Mice were injected with melanoma cells and fed micronized CLN for 28 days[22]. The authors reported a significant reduction in melanoma metastasis. In the same study, mice fed CLN for 28 days showed increased lipid-bound sialic acid but, interestingly, a decrease in liver lipid peroxidation. The lymphocytes isolated from these mice provoked a significantly higher graft-versus-host response in control mice. After intraperitoneal injection of micronized CLN, the number of peritoneal macrophages increased. The authors concluded CLN causes an

immunostimulatory effect, as evidenced by the hyperactivated lymphocytes and the increased macrophage count in the peritoneum.

Serum chemistry in mice treated with CLN was evaluated along with hematopoetic effects and biochemical indicators of kidney and liver function. The CLN used was either finely or coarsely ground[23]. Ingestion was well tolerated. Animals receiving the zeolite-rich diet were found to have a 20% increased serum potassium level compared to control. Erythrocyte, platelet and hemoglobin levels were also unaffected by the CLN treatment. The coarse material, however, causes a luekocytosis and concomitant reduction in GM-CFU in the bone marrow. The study demonstrated the absolute necessity of using micronized CLN particles.

Pavelic's group also showed significant antitumor effects of micronized CLN in CBA/HZgr mice with spontaneous mammary carcinoma and in C57BL/6 mice with melanoma tumors and mammary aplastic tumors implanted on the flank[3]. Interestingly, the antitumor effect was not increased with CLN supplementation prior to tumor induction but was similar to groups treated after tumor implantation. In both cases, growth delay continued until abolishment of the treatment, at which point the tumor grew out. Importantly, this study also evaluated the structure/effect of micronized CLN. Scanning electron microscopy revealed a lack of fibers and instead, a rough, roundish particles in contrast to asbestos, which was very needle like. They also found that asbestos, unlike CLN, catalyzed the production of hydroxyl radicals.

Other animal species

CLN feed supplementation was ineffective against copper poisoning in lambs fed a diet enriched with 20 ppm copper sulfate, but only at the dosing schedule used[24]. Furthermore, Bartko and colleagues showed no effect of CLN therapy on experimentally induced acidosis in sheep[25]. Sheep fed CLN were found to have no deleterious effects after feed supplementation but showed no evidence of health advantage either[26].

Hens fed CLN did benefit from the supplement. In laying hens, supplementation with CLN resulted in significantly lower liver mycotoxin levels after adding CLN and aflatoxin B-1 to the feed[27], but more importantly caused no gross histopathologic changes compared to control. Olver observed no significant effects (body weight, egg weight and age at first egg, rate of amino acid adsorption) of feeding hens up to 50 g/kg CLN[28].

Reviews

Many of the above-mentioned articles were reviewed in a single paper. The first study, an article by Elmore, et. al. is a review of what has been described in use of CLN and other zeolites[29]. Notably mentioned is the determination by the International Agency for Research on Cancer which describes zeolites with a size greater than 5 microns as being carcinogenic to humans. Oral administration of CLN is shown to be non-toxic in animals, but inhalation toxicity is readily demonstrated, especially with particle sizes greater than 5 microns. Along with particle size, fibrousness presents the greatest toxicity. In the rabbit skin sensitivity model, CLN caused no sensitivity reaction. CLN had no effect on reproductive capacity in rats. The basic conclusion was that CLN was safe, but respiration of the dust should be avoided.

Use in Humans

Only one published trial could be reviewed for the effect of CLN in humans[30]. This paper describes a prospective, open and controlled parallel-group study of 61 immunodeficient patients who received a CLN preparation for 6 to 8 weeks. During this course, there was no change in the primary medical care given to the individuals. The effects of CLN on the cellular immune system were evaluated. The therapy resulted in CD3+, CD4+, CD9+ and HLA-DR+ lymphocyte counts increasing and CD56+ counts decreasing. The interpretation was an overall stimulation of the immune system, with no adverse reactions to the treatments observed.

Wellness Industries has conducted six clinical studies in humans. These are all awaiting publication:

- NCD therapy in healthy individuals without chronic exposure to heavy metal toxins: A Short-term (7-day) trial in eleven individuals to evaluate changes in urinary excretion of heavy metals. Urinary excretion was measured with Atomic Absorption Spectroscopy (AAS). Participants noted an average fivefold increase in heavy metal excretion.
- NCD therapy in healthy individuals without chronic exposure to heavy metal toxins – An Intermediate-term (30-day) trial in twenty-two individuals to evaluate changes in urinary excretion of heavy metals. Urinary excretion was measure with Atomic Absorption Spectroscopy (AAS). All of the individuals noted an average 5-7 fold increase in heavy metal excretion.
- NCD therapy in otherwise healthy individuals with chronic, employment-related exposure to heavy metal toxins (West Virginia Coal Miners) – A Long-term (84-day) blinded clinical trial in fifty individuals to evaluate changes in urinary excretion of heavy metals and determine longevity of the effect. Urinary excretion was measure with Atomic Absorption Spectroscopy (AAS). Additionally, hair and saliva was collected at the beginning and the end of the trial and measured for heavy metal content. All 40 patients on the NCD noted a 12-15 fold increase in heavy metal excretion with subsequent improvement in general health.
- Electrolyte levels with the use of NCD – A trial to evaluate changes in vital serum electrolytes in healthy individuals following 30-day NCD therapy. There were no changes in serum electrolytes from baseline in these patients.
- Exercise recovery with NCD – A trial to evaluate the effect of NCD therapy on post-workout recovery-time in competitive athletes vs. non-competitive participants. The largest NCD trial to-date included 357 individuals. Approximately 80% of the participants on the NCD noted: less pain during exertion, the ability to workout longer and faster recovery time after physical activity.
- pH balancing with NCD – A trial to evaluate the effect of short- vs long-term NCD therapy on serum and salivary pH in healthy and compromised individuals. All of the patients noted more alkaline pH levels throughout the trial with the use of the NCD.

The following *in-vitro* analyses have been performed to provide rationale for further human trials:

- An *in vitro* analysis was conducted to measure the affinity of NCD for volatile-organic-compounds (VOCs). Sixty compounds were tested to provide information to support a future trial in humans focusing on benzene and dioxin derivatives. The zeolite in the NCD was found to have a high affinity for a variety of different VOCs
- An *in vitro* analysis was conducted to measure the affinity of NCD for uranium. This provides a rationale to study urinary excretion in patients using the NCD that have been exposed to depleted uranium sources. The NCD was found to have a high affinity for U^{6+}.

Uniqueness of Natural Cellular Defense

Research conducted in the development of the Natural Cellular Defense found that there were two major obstacles in using natural clinoptilolite as a dietary supplement and oral chelator.

- First, the average particle size of mined clinoptilolite is 40-250 microns. Particles in this size range are far too large to allow for absorption from the digestive tract into the bloodstream. Therefore, every zeolite that had been used previously would be primarily a digestive cleanser. In order to utilize the zeolite as a systemic detoxifier, the crystals would have to be reduced in size to less than 2 microns.
- The second issue is one of activity. Natural zeolites act as filters in nature, absorbing a variety of toxins that surround the minesite. Clinoptilolite analyzed from the minesite contains heavy metals, volatile organic compounds (VOCs) and other high-affinity toxins that, in essence, take up space in the crystal – thus limiting its potential to detoxify by reducing its available surface area.

To remedy these issues, the product is manufactured in two distinct steps: Micronization and Activation.

Micronization

The zeolite mineral used in NCD is reduced in size mechanically, prior to the activation process, to a size of 0.39 to 5 microns. This does not destroy the properties of the molecule. To the contrary, reducing the particle size increases access to the charged “cages” that would otherwise be unusable. For instance, a micron-sized particle has millions of “pores” available to bind heavy metals and other toxins. The small size of the particle permits diffusion deep within itself, allowing access to the inner “cages” that would be inaccessible in a larger particle due to limitations in diffusion distance. Most importantly, the structure of the individual “cages”, and therefore the ability to sequester heavy metals and other toxins, is unaffected. Consider this: If a five-carat diamond is broken into five one-carat diamonds, the structure of each one-carat diamond is exactly like that of the original five-carat diamond, only smaller. And if that one-carat diamond were pulverized into dust, each resulting, tiny piece of diamond would have the same structure and properties of the original five-carat diamond. The Silicon-Oxygen bonds in the zeolite are even more thermodynamically stable, i.e. are stronger, than the Carbon-Carbon bonds of the diamond. It would take a concerted effort and extreme amounts of energy to reduce the zeolite to particles that no longer possessed the characteristic “cage” structure and therefore the ability to sequester toxic metal ions. Nature required over 1000^{o}C and tremendous pressures

to create a zeolite. The conditions used to activate Clinoptilolite, the zeolite used in NCD, are insufficient to dehydrate the mineral or alter its physical characteristics.

Micronization of the zeolite also allows for uptake into the bloodstream from the digestive tract. Many compounds (minerals and pharmaceuticals/nutraceuticals) are absorbed in the gut that are in this size range. For example: sucrose molecules greater that 2 microns are absorbed through the gut; several sugar-coated proteins (biopharma oral preps designed to prevent digestion in the stomach prior to absorption) are in the 3-5 micron range and are easily absorbed; albuterol sulfate has an average particle size of 4 microns and is absorbed through the lung mucosa (which has similar permeability to the gut mucosa); pharmaceutical preparations of the immunosuppressant, cyclosporin, consist of particles 2-4 microns in size. In short, the concept of absorbing a particle that is sub-0.5 to 5 microns is generally well established. Additionally, preliminary studies done on human volunteers taking the Natural Cellular Defense chronically have demonstrated the presence of clinoptilolite in the serum at concentrations greater than 1ng/dL.

Activation

The Natural Cellular Defense is manufactured under a closely-guarded, proprietary process. The primary goal of this process is to remove the toxins naturally present in the mineral. Just as it does in the body, zeolite absorbs metal ions and other toxins that filter through it as it sits in the ground waiting to be mined. The toxins that the mineral absorbs prior to being mined do not make it dangerous, *per se*, as zeolite sequesters these toxins very well. The zeolite is simply less effective. For instance, if the particle has ten thousand “cages” and five thousand are already full before it is mined, the particle will not be as effective when introduced as a supplement as a particle with all ten thousand “cages” available. The Natural Cellular Defense undergoes an ‘activation process’ that forces the removal of all these toxins. This process removes all extraneous metals and empties out the zeolite cage - therefore removing any toxins that were found with the zeolite and 'activating' the molecule to be at its most effective. Understand that the zeolite molecule is, for all practical purposes, indestructible. Heat up to 900º Fahrenheit will not crack the molecule and it can be frozen in solution and defrosted without any change in activity. It is also amphoteric – meaning that it exists just as well in an acidic or a basic environment. The zeolite is activated in a very weak acid under high temperature conditions. This does not break the zeolite down; it simply forces the evacuation of stored toxins in the zeolite cage. For purposes of activation, heat is added to the system *only* to increase the bond resonance within the structure of the cage, effectively “loosening the grip” of the zeolite, promoting a more complete exchange of the naturally occurring toxic metal ions with more beneficial ones. Being positively charged and thus absorbed by the zeolite, Calcium and Magnesium are used to exchange for the toxins. The presence of these compounds result in a “milky” or cloudy appearance of the product. These healthy metals migrate back into the zeolite and help stabilize the molecule. After ingestion, they easily undergo cationic exchange with metals that are higher in the affinity scale of the zeolite (i.e. Mercury, Lead, Cadmium, etc..). Without this process, other zeolite products must contain toxins and heavy metals as part of the zeolite cage. Additionally, without a heat process or some preservative, they must contain bacterial and fungal contamination. **The Natural Cellular Defense is the only zeolite formulation that is micronized and activated.**

Analysis

Inductively coupled plasma optical emission spectroscopy (bulk elemental analysis of inorganic materials) revealed a composition of 92.47% clinoptilolite and 5.93% heulandite.

Gas Chromatography-Mass Spectroscopy, Thin Layer Chromatography and High Performance Liquid Chromatography and Elemental Analysis revealed no unexpected organic contaminants traceable to the manufacturing or bottling process.

Atomic Absorption Spectroscopy revealed no Al, Sb, As, Bi, Cd, Pb, Hg, Ni or Sn and confirmed the presence of Ca, N, K and H_20 with the CLN preparation as submitted.

Particle size analysis revealed over 99% of CLN particles are 5 microns or less in diameter. The smallest particles were 0.39 microns (390 nanometers).

pH of the solution tested was 6.13.

Addition of Natural Cellular Defense to a solution of 25% $PbCl_2$ resulted in a spontaneous removal of Pb (at least to a level below 1% by weight), as indicated by the immediate inability of the solution to convert a LeadCheck® swab to a pink color.

Product Claims and Benefits

Today, clinoptilolite is being used as a dietary supplement, primarily for human detoxification. Clinoptilolite has many well-documented benefits:

Removes heavy metals: This zeolite has the perfect molecular structure for capturing and removing heavy metals from the body, including; mercury, cadmium, lead, arsenic, aluminum, tin, and excess iron. It also removes radioactive metals like cesium and Strontium-90.[31,32]

Reduces absorption of nitrosamines: Nitrosamines (or nitrates) are most commonly found in processed meat, and have been linked to pancreatic, stomach and colon cancer, as well as Type II diabetes. The zeolite captures nitrosamines in the digestive tract before they can be absorbed.[33]

Helps to buffer blood sugar: The zeolite may help reduce blood sugar spikes by buffering excess glucose with its negative charge.[34]

Helps to buffer body pH to a healthy alkalinity: A slightly alkaline body pH (7.35 - 7.45) is essential for good health and optimal immune function. The zeolite attracts and then buffers excess protons which cause acidity. This can help many conditions from acid reflux to Candida and arthritis.[34]

Improves nutrient absorption: In the gastrointestinal tract, the presence of the zeolite increases nutrient absorption and helps promote healthy microorganisms, decreasing the likelihood of stomach flu and infections.[11]

Reduces symptoms of allergies: The zeolite captures some of the allergens and antigens that trigger allergies, migraines, and asthma. This can help to reduce symptoms.

Stabilizes immune system function: The zeolite does not stimulate the immune system, but allows it to function optimally by removing toxins, viruses, yeasts, bacteria, and fungi which can depress immune function and interfere with hormones. Many people report feeling increased energy, clarity, and vitality.[35]

Acts as a powerful antioxidant: The cage-like structure of the zeolite also traps free radical molecules, making it an effective antioxidant (this does not mean that cellular zeolite is a substitute for more conventional antioxidants such as Vitamins C, E and A, lutein and selenium, all of which have other vital roles to play in the body).[21]

Completely safe: The zeolite is considered to be completely safe and non-toxic for oral administration in humans and animals. This includes infants, children, pregnant women and nursing mothers. Studies have also been conducted in feed animals and companion animals, including: dogs, cats, horses and birds.[36+additional references]

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Clinical evidence supporting the use of an activated clinoptilolite suspension as an agent to increase urinary excretion of toxic heavy metals

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Effective treatment of chronic illness resulting from the long-term buildup of heavy metals in the body, such as chelation therapy, presents numerous clinical challenges, including undesirable side effects and unpredictable efficacy. Use of a naturally occurring zeolite, clinoptilolite, to remove these toxic substances may offer an efficacious and safe alternative to the traditional approaches. This study was designed to evaluate the ability of activated clinoptilolite suspended in water (ACS) to enhance excretion of heavy metals from the body without the undesirable removal of physiologically important electrolytes. The protocol utilized two treatment groups, each consisting of eleven healthy men, aged 36 to 70 years who were positive at baseline for at least four of the nine heavy metals in the screen. The screen measured aluminum, antimony, arsenic, bismuth, cadmium, lead, mercury, nickel and tin. Volunteers were given a commercially available version of the study substance for 7 days (Group 1) and 30 days (Group 2) and urine samples were collected at specified time points in the study. Changes in urinary concentration of the heavy metals were measured by inductively coupled plasma mass spectrometry (ICP-MS) and compared to the baseline. Also, serum samples were obtained from five individuals in each group and serum electrolytes were measured prior to and after taking the product. In Group 1, the participants had increased concentrations of heavy metals in the urine on days 1, 4 and 7, with the peak excretion at around seven days with the mean value trending towards baseline on day 7. Participants in the second group demonstrated mean peak excretion by 4 days and a return to near-baseline levels by 30 days. Three members of Group 2 continued to excrete higher mean levels of metals until the 7- or 14-day mark. All but one participant in Group 2 returned to levels at or below baseline by 30 days. No clinically significant alterations in serum electrolyte levels were seen at either 7 or 30 days on ACS. In conclusion, this study demonstrates that the daily use of an activated clinoptilolite suspension represents a potentially safe and effective way to remove toxic heavy metals from the body through increased urinary excretion without removing clinically detrimental amounts of vital electrolytes.

USE OF ACTIVATED, LIQUID ZEOLITE IN HEAVY METAL DETOXIFICATION

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ABSTRACT: Heavy metal toxicity is known to be a significant contributing factor in the aging process. Lead, cadmium, tin, nickel, mercury, aluminum, antimony, arsenic and bismuth are contaminants found in both rural and industrialized settings. These metals also pose some of the most significant hazards to human health. Oral chelating agents have been utilized for the removal of these metals with varying degrees of efficacy. This study evaluates a single oral chelating agent for its efficacy and will be compared against more common therapies. Zeolites such as clinoptilolite and heulandite, are able to coordinate with toxic metal ions due to their unique 3-dimensional structure and chemical composition, and transport them innocuously for excretion. This study was designed to evaluate the efficacy of an activated zeolite colloidal suspension (AZ) supplied as a dietary supplement, in removing these heavy metals from the human body. Two populations were used to this end. First, a relatively healthy cohort of men with no obvious chronic exposure to heavy metals, aged 50 to 70 years. The second cohort consisted of 50 otherwise healthy men, employed as coal miners and chronically exposed to heavy metals, and aged 30 to 60 years. For all subjects, AZ was administered as 15 drops p.o. b.i.d., an hour before meals. In the first cohort, urine from the first morning elimination was collected from each subject before initiating AZ therapy, and after 1, 3, 7 days or 1, 3, 7, 15 and 30 days following the first treatment. The timing of urine collection in the second cohort was extended to 90 days post-therapy due to the chronic nature of the metals exposure. Subjects in all groups experienced a significant increase in urinary excretion of heavy metals, as determined by atomic absorption spectroscopy, following treatment with AZ. Subjects continue to be evaluated for effects of longer-term therapy with AZ on urinary excretion of heavy metals. In summary, AZ has proven to be an efficacious tool in the detoxification through removal of heavy metal ions, which in turn may aid in the reduction of age-related deterioration of the human body.

SUPPLEMENTATION WITH ACTIVATED ZEOLITE SUSPENSION IMPROVES POST-WORKOUT RECOVERY AND PERCIEVED PAIN LEVELS IN COMPETITIVE AND NON-COMPETITIVE ATHLETES.

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Individuals who exercise regularly are familiar with the need for post-workout time to recover from the fatigue of effort as well as the pain or discomfort associated with a rigorous workout. During this time of recovery, the body is actively washing out the build-up of waste products from cellular respiration as well as repairing microscopic muscle tears caused by the exertion. The wise athlete knows that "tomorrow's workout is only as good as today's recovery," but time spent recovering is time that is not spent training. Thus, athletes looking for an edge in extremely competitive sports often go without adequate post-workout recovery time (PWOR).

Lactic acid is a common metabolic waste product generated during intense muscle activity and frequently the cause of the discomfort experienced after workout. (An acid is defined as a compound that donates a proton (H+, or hydrogen ion) to a system.) Activated zeolite suspension (AZS) is a relatively new class of nutritional supplement designed to aid the body in excretion of toxins, particularly heavy metal ions with a positive charge (cations). Through this mechanism, AZS also helps balance the pH of body fluids.

The other major cause of post-workout muscle pain, muscle fiber damage, is repaired over time through complex cellular mechanisms. Some of the repair machinery used by the body for this function use cations like manganese and zinc to perform their function. This activity can be inhibited by small, highly charged heavy metal cations like mercury, lead, bismuth and antimony. A small slow-down in this process, perhaps caused by one or more of these toxic heavy metals, could significantly lengthen recovery time.

The purpose of this study was to determine if supplementation with AZS could reduce the time needed to recover after a workout by eliminating these contributory ions. To this end, questionnaires were sent to 500 volunteer athletes, including 250 individuals who identified themselves as "competitive" and 250 who were "recreational" participants. Each athlete received a 30-day supply of Natural Cellular Defense® (Waiora, LLC, Boca Raton, FL) and a 30-day journal. Volunteers were asked to evaluate the effect of the supplement on athletic performance, PWOR time and perceived pain daily. After 30 days, the forms and journals were returned and evaluated.

The 357 respondents were grouped by sport (power-lifting/bodybuilding, running and bicycling) and then by competition level (competitive vs. recreational). Through the questionnaire, we sought to determine improvement in perceived pain and reduction in PWOR time, rated as: no change, minor reduction, moderate reduction, and significant reduction. We also sought to identify any improvement in athletic performance, rated as: no improvement, minor improvement, moderate improvement, and significant improvement. After cataloging the responses of each participant, data were analyzed and evaluated.

Participants in all sports at all levels reported improvements in both perceived pain and PWOR time. 82.8% of competitive athletes reported moderate to significant reduction in PWOR time and perceived pain while 47% reported an improvement in athletic performance. 76.5% of all recreational participants reported significant improvement while 85% of recreational bicyclists reported a performance boost. 70% of recreational runners got moderate to significant reduction in PWOR time.

We propose that AZS is directly acting on the muscular microenvironment to reduce the presence of both hydrogen and heavy metal ions that are responsible for the discomfort experienced following a rigorous workout. The pH regulation occurs when AZS sequesters this hydrogen ion and either redistributes it or facilitates excretion via the kidneys. Further, the AZS is also there to scavenge any stray heavy metal ions that might reduce the ability to conduct cellular and muscular repair.