ANZ-A
ACTIVATED NATURAL ZEOLITES - AWKE

Food Supplement
100% natural
High antioxidant power

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ZEOLITAS MICRONIZADAS

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Free radicals, degenerative diseases, antioxidant and activated natural zeolites.

Food supplements, especially those 100% of natural origin, are increasingly popular in the western world. In 2011, in the United States, more than thirty billion dollars in food supplements were purchased by consumers and in Brazil one thousand and forty million dollars in 2008. In 2014, more than two hundred thousand dollars were sold worldwide. The need for alternative and non-chemical solutions is growing in the world population, especially regarding to cancer. Throughout the world, investments in scientific research on alternative medicine products, especially natural products, are growing steadily.

Organized and scientific research in *alternative medicine* (i) has grown exponentially in recent years, and there, is already, a lot of concrete evidence about the mechanisms of action and benefits of some natural products.

Natural zeolites have been used since the 1960s as additives in animal feed, for the control of toxins and to improve the profits of the animal production business, since they improve the feed conversion efficiency and significantly reduce the mortality in the industry. The producers and researchers in animal production began to notice that, when natural ground zeolites were added to the feed, there was also an increase in the general health status of the animals (very few diseases) and, when measurements were made, it was found an increase in the immune system of animals. It was also noted that degenerative diseases in animals did not appear or diminish markedly. This was the beginning of the idea of using natural zeolites in human food, although clinoptilolite has been used for more than 800 years in traditional medicine to improve general health in India, China, Russia and in almost all parts of Asia. The experiences began at the end of the 80s in the former socialist area (mainly Croatia and Russia) and Cuba.

By the way, the product to be used in humans must be a much more active product, that is, purer and finer, that is what we call "*Activated Zeolites*", when micronized they are ready to act on the human body. This is how today one of the most promising products, and that already has strong scientific support in the fight against cancer and other degenerative diseases, is the natural micronized zeolites.

(i) **Alternative medical** practices are generally not recognized by the **medical** community as standard or conventional **medical** approaches. **Alternative medicine** includes dietary supplements, vitamins, herbal preparations, among others.

Regarding to cancer, micronized natural zeolites, through special grinding, have demonstrated an anticancer and anti-metastasis ability in 'in vitro' and 'in vivo' tests, both in animals (dogs, rats, etc.) and humans. There are thousands of experiences throughout Europe, but mainly in Croatia and the United States. There are several publications in specialized journals that show conclusive results in this matter.

The scientific research carried out so far, mainly in Croatia, Russia, the United States, Cuba and England has demonstrated the strong antioxidant power possessed by natural activated zeolites. The antioxidant capacity of micronized natural zeolites far exceeds other antioxidant products of recognized capacity, such as chocolate, grape seeds, red wine, most vegetables and fruits (containing vitamins E and C) and selenium elements, calcium, magnesium, etc. The role played by free radicals in degenerative diseases is only surpassed by the discovery of DNA, this is considered as the second most important finding in the history of Medicine. Free radicals are one of the more significant causes of aging, as well as some 60 chronic degenerative diseases, which include all heart diseases, arthritis, osteoarthritis, all types of cancer, multiple sclerosis, Alzheimer, Parkinson, diabetes, high pressure, cholesterol diseases, varicose veins, rheumatism, stress, phlebitis, hemorrhoids and senility.

In the *Annals of Epidemiology*[39] magazine, of the year 2014, the article "The causes of cancer, revisited" was published, where an investigation was made to determine the main causes of cancer worldwide. The results are shown in the following table:

Factor or class of factors	Percent of all cancer deaths	
	Best estimate	Range of acceptable estimates
Tobacco	30	25-40
Alcohol	3	2-4
Diet	35	10-70
Food additives	<1	-5, -2
Reproductive and sexual behavior	7	1-13
Occupation	4	2-8
Pollution	2	<1-5
Industrial Products	<1	<1-2
Medicines and medical procedures	1	0,5-3
Geophysical factors	3	2-4
Infection	10?	1-?
Unknown	?	?

In conclusion, tobacco is, by far, individually the main factor responsible for deaths from cancer worldwide.

Respiration, in the presence of oxygen, is essential in the cellular life of our organism, but as a consequence of it, is where the most of the free radicals are produced, which cause negative effects in our health due to its great ability to alter, mutate or degenerate our DNA (genes). Our body renew between fifty thousand and seventy thousand million cells continuously (skin, intestine, liver, some neurons, etc.). Over the years, free radicals can produce a high genetic alteration on renewed cells, increasing the risk of degenerative diseases, and reduce the functionality of cells that are not renewed, which is a characteristic of aging. Habits as common as intense or exaggerated physical exercise, smoking, alcoholism, the consumption of diets rich in fats and overexposure to solar radiation, as well as environmental pollution (toxins and heavy metals, mainly), increase the production of free radicals and, therefore, increase the possibility of developing a degenerative disease.

In recent decades, the role played by antioxidants in cardiovascular pathologies, in numerous types of cancer, in AIDS and even others diseases directly associated with the aging process, such as cataracts or alterations of the nervous system, has been researched scientifically. The studies focus mainly on vitamin C, vitamin E, beta-carotenes, flavonoids, selenium and zinc. The relationship between these antioxidants and cardiovascular and even cerebrovascular diseases is now sufficiently demonstrated. It is known that the modification of "bad cholesterol" (LDL-c) plays a fundamental role both in the initiation and in the development of arteriosclerosis (thickening and abnormal hardness of the internal covers of the blood vessels due to a deposit of fatty material, which prevents or hinders the passage of blood). Antioxidants can block free radicals that modify bad cholesterol, thus reducing cardiovascular risk. On the other hand, low levels of antioxidants can be a risk factor for certain types of cancer.

Most important oxygen-free radicals (ROS – Reactive Oxygen Species)

1) $^{\bullet}OH$ Hydroxyl radical
2) $^{1}O_2^{\bullet}$ Singlet oxygen
3) $HO_2^{\bullet}$ Hydroperoxyl radical
4) $O_2^{-\bullet}$ Superoxide radical
5) R–O $^{\bullet}$ Alkoxy radicals
6) LOPs Lipid peroxides
7) H_2O_2 Hydrogen peroxide

The hydroxyl radical is the most powerful oxidant and indiscriminately attacks most biological compounds. The extremely reactive nature of the hydroxyl radical suggests that it will have immediate effects in the surroundings of where it formed (it does not reach to spread over great distances), that is, once it is formed, the hydroxyl radical damages the first organic molecule found in his short path. The

reactivity of the superoxide radical depends on the cellular environment. Oxygenated water (Hydrogen peroxide, as stated above) is not a free radical, since it does not have unpaired electrons, but it is an aggressive oxidant. Per se, oxygenated water is not very reactive. Its reactivity in biological systems depends on two properties: first, that it can diffuse large distances, crossing membranes, and second, that it reacts with transition metals to form the highly reactive hydroxyl radical (IUPAC, *International Union of Pure and Applied Chemistry*, defines a transition metal as "**an element whose atom has an incomplete sub layer or that can give rise to cations**." They are a total of 40 chemical elements, among them the metals zinc, cadmium and mercury). Finally, the oxygen singlet reacts efficiently with several molecules of biological importance: vitamin E or α-tocopherol, vitamin C or ascorbic acid, bilirubin, DNA, cholesterol, β-carotene, tryptophan, methionine, cysteine, NADPH and polyunsaturated fatty acids.

The chain of chemical reactions at a mitochondrial level, which are involved in the conversion of food into energy (by reacting with air) so that we can function, constitutes the main intracellular source of free radical production, both ROS (Reactive oxygen species) and RNS (Reactive nitrogen species). The steady-state concentration of these oxidants is maintained at non-toxic levels by a variety of antioxidant defenses and enzymes produced by the body that repair the damage. The delicate balance between antioxidant defenses and production of free radicals can be broken either by a deficient antioxidant defense, an inhibition of electron flow or exposure to xenobiotics. This imbalance appears as a common denominator in several pathological processes, in which the resulting oxidative stress produces tissue damage and, eventually, cell death.

Thus, in summary, the human body produces free radicals during metabolic processes (it has been determined that the production of radicals varies between 1,000 and 1,000,000 a day, depending mainly on food and our environment). Free radicals are basically atoms or molecules that have one or more unpaired electrons in their outermost orbit. They can have any charge or even be neutral (although in this case we are talking about oxidants, like oxygenated water). They are highly reactive, as they seek to achieve the lost balance of their outermost electronic orbit by either donating or "stealing" electrons from atoms or molecules. When they do this, they convert the atom or molecule attacked into a free radical, which can lead to a chain reaction, with disastrous results for the cell (death or onset of tumor formation). As we said before, the best known are the free oxygen radical or oxygen singlet and the hydroxyl radical, which lacks an electron in its outermost orbit and then has a high oxidizing power. By "stealing" an electron from an atom belonging to a cell, it "oxidizes" it. It has also been proven that, searching for the missing electron, it can damage RNA and DNA, as mentioned above.

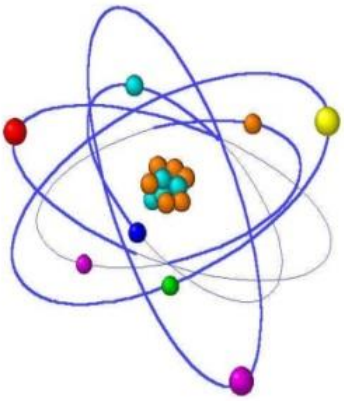


Figure 1. Complete oxygen atom, with 2 electrons in the internal orbit and 6 electrons in the outer orbit

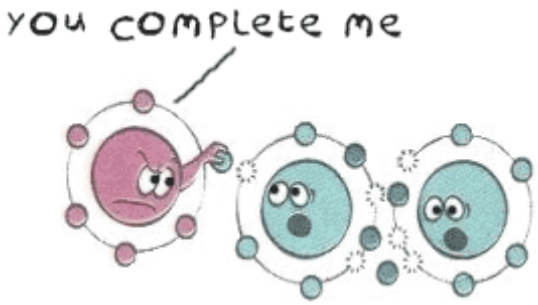


Figure 2. A free radical "stealing" an electron and, therefore, generating another free radical and its chain reaction

Every day in our body millions of cells die and they are replaced by new cells, which are "build" by the body according to the "blueprint" established in the DNA. If the DNA is damaged, the new cell is different from the old one. This is the main cause of the aging of the human body. Also the "bad" copy of the cell can induce a degenerative disease or other diseases (see Figures 4 and 5).

As explained above, the body produces antioxidants and repair enzymes, which are a strong defense against these highly aggressive free radicals. These antioxidants become much more efficient if they are "activated" by minerals, such as selenium, magnesium, calcium and zeolite. An antioxidant delivers, shares or transfers one or more electrons with the free radical without transforming it into a free radical, that is, antioxidants are electronically highly stable molecules.

If in a human organism the production of free radicals exceeds the production of antioxidants, the balance is lost and the free radical chain reaction begins on the cells of the body. The balance can be lost for several reasons: environmental pollution (cigarette smoke, dust, smog, etc.), ultraviolet light, contaminants in foods (for example arsenic, cadmium, quartz, mycotoxins, pesticides,

herbicides, dioxins, carragenina, etc.), excess of food, stress, etc., which are catalysts for chemical reactions that produce free radicals. Endogenous antioxidant compounds, including glutathione and lysozyme, can limit the effects of oxidative stress; However, these systems can be quickly monopolized by high amounts of free radicals[32]. Hence the importance of increasing the concentration of antioxidants in the cell, to prevent possible adverse agents that could lead to a cancerous process. A good diet, as well as knowing and using food and food supplements with antioxidant properties (including the natural zeolites clinoptilolite and mordenite) can be of great help for the prevention of cancer[32, 38].

On the other hand, a normal cell in all vertebrate animals has an internal or intracellular pH between 7.1 and 7.2 (in the blood this value is in the range between 7.35 to 7.45)[25]. Let's remember that the intracellular environment or intracellular environment is formed by a liquid solution called cytosol. A cancer cell is more acidic: it has a pH of around 7 or even lower. A change of 0.1 in the internal pH of a cell is very detrimental to its functioning. A superior change is usually deadly for a cell.

Recent experiments[36] have shown that solid tumors have an intracellular pH (pHi) neutral to alkaline (7.0–7.4) while the extracellular (pHe) of the same tumors is acid (6.0–6.9), giving a guide for anticancer therapies. The microenvironment in solid human tumors is characterized by great heterogeneity in oxygenation and it is known that hypoxia occurs at a very early stage in the formation of a tumor, producing a tumor microenvironment that is hypoxic, acid and very low in nutrients.

To get an idea of the pH scale, which indicates the acidity, neutrality or alkalinity of a solution, see figure 3. If the pH = 7 the solution is neutral, if the pH <7 the solution is acid and if pH> 7 The solution is alkaline. Figures 4 and 5 indicate the difference between a normal cell and a cancer cell. The acidified extracellular pH and the strong DNA damage are the main differences between a normal and a cancerous cell, although there are many more differences.

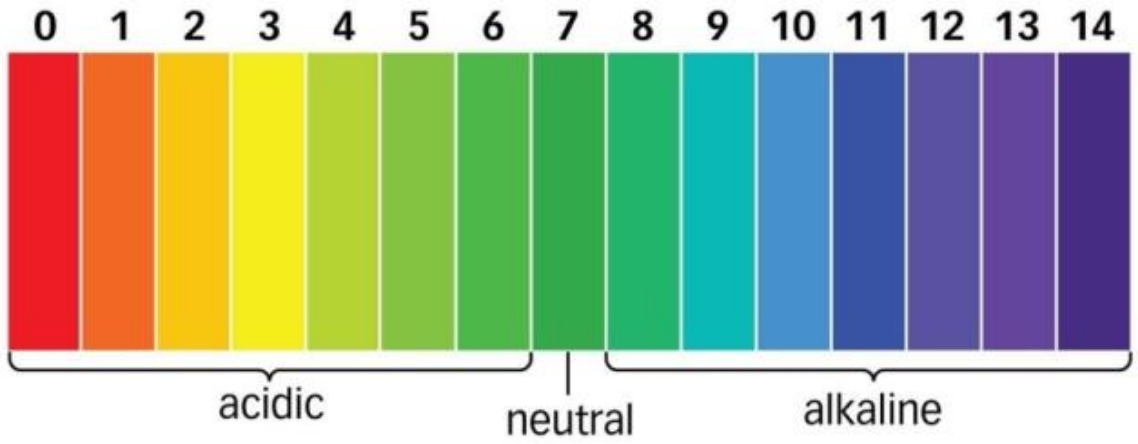


Figure 3. pH scale.

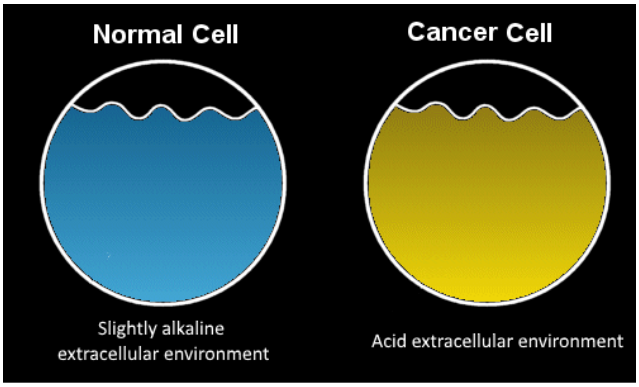


Figure 4. Difference between a normal and a cancerous cell: pH.

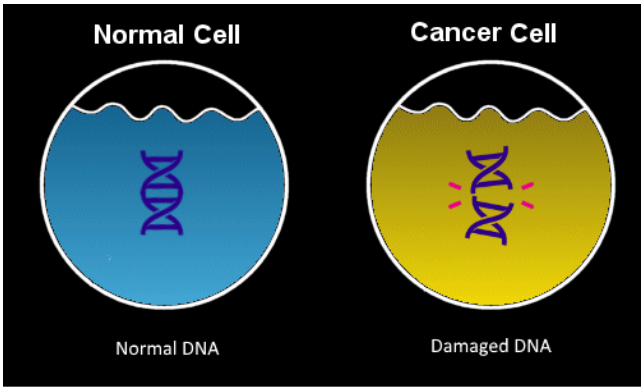


Figure 5. Differences between a normal and a cancerous cell: DNA.

We must say that the latest studies in molecular medicine definitely show that free radicals affect not only DNA, but also RNA (ribonucleic acid)[26,27], being in most cases the initial cause of degenerative diseases.

It is important to reaffirm that the human body consists of around 100 trillion cells (10^{15} cells) and that between 1,000 and 1,000,000 free radicals are produced every day. Therefore, the danger of oxidative damage to our cells is high. As stated earlier, that is how we get older and acquire degenerative diseases.

It is also remarkable to indicate that the probability of acquiring cancer is proportional to the age of a person elevated to the fourth power[26] (for example, a person who at the age of 10 had a certain probability of developing a cancer, usually very low, at 30 years this probability increases by 81 times). Also the world statistics show that 1 in 3 people will develop cancer of some kind. In some studies, it is mentioned that in Europe 1 out of every two men has developed or will develop cancer during their life and that in the case of women, this proportion changes to 1 out of every 3 women[38].

The replication of a cancer cell is much faster than a normal cell, which as we explained above, is programmed for each cell type. Thus tumors or aggregations of cancer cells are formed relatively quickly. As general knowledge, a tumor with a 1 cm diameter, contains about 1 billion clumped cancer cells[38], all of which are descendants of a first cell whose genes that control their capacity to divide were altered.

In oncology, the denomination of Warburg effect refers to the fact that most cancer cells produce energy mainly in the cytosol, by a process of anaerobic glycolysis, that is, thanks to high rates of glycolysis followed by process of lactic fermentation instead of producing energy through the aerobic oxidation pathway of pyruvate in the mitochondria, like in most normal cells[41]. This last process makes use of oxygen as the final electron acceptor in the respiratory chain. The damaged cells typically have glucose consumption rates about 200 times higher than those of the normal cells that gave them origin; and this happens even with a full supply of oxygen. Otto Warburg postulated that this change in metabolism is the fundamental cause of cancer, a hypothesis that is currently known as the Warburg hypothesis. Paradoxically, however, anaerobic cells cannot develop cancer because they do not have mitochondria and are dependent only on glycolysis. For example, the crystalline, the cornea, some parts of the retina and red blood cells.

It is well established that these minerals, activated natural zeolites, can control free radicals and reduce the probability of acquiring degenerative diseases. Zeolites, once they trap the free radicals, remove them from the body, mainly through feces and urine. A micronized natural zeolite forms covalent bonds with free radicals, literally sweeping them. A particle of micronized natural zeolite has a very high number of electrons to share on its surface, so its antioxidant power is extremely high. In fact, according to the International

Society for Research on Free Radicals (http://www.sfrr.org/), zeolites, properly activated, are the most potent antioxidant substances in nature.

The crystalline structure of the zeolites, which has millions of negatively charged micropores, as shown in Figure 7 (this electronegativity is balanced by the interchangeable cations housed in these micropores), allow the entrapment of toxins, as shown in figure 6

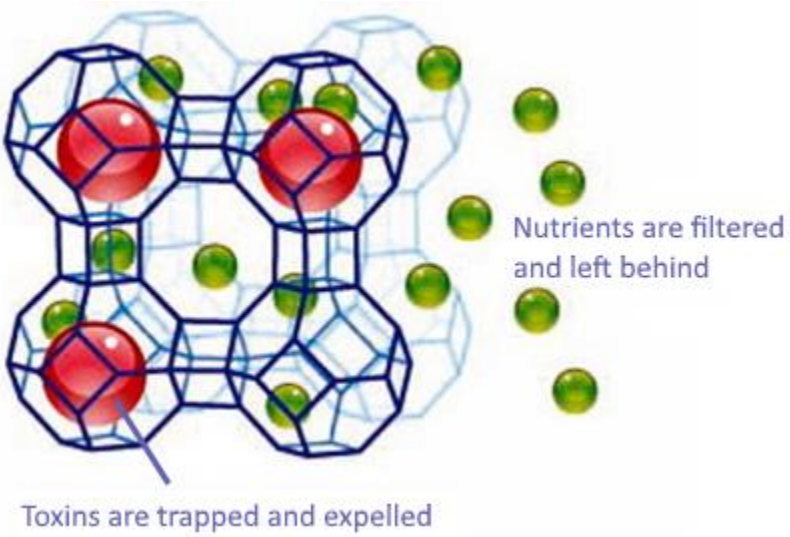


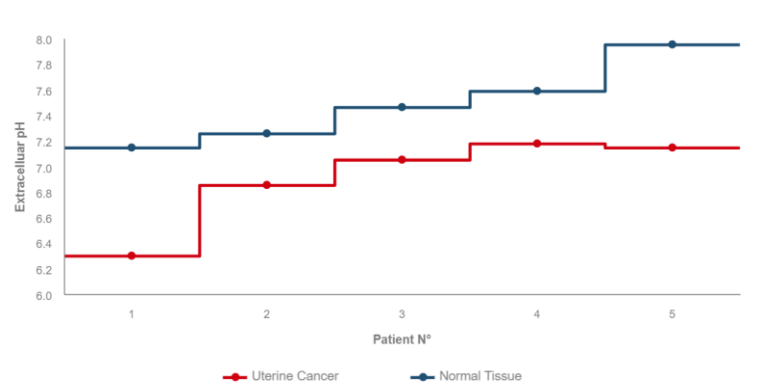
Figure 6. Trapping of toxins in the crystalline structure of a zeolite.

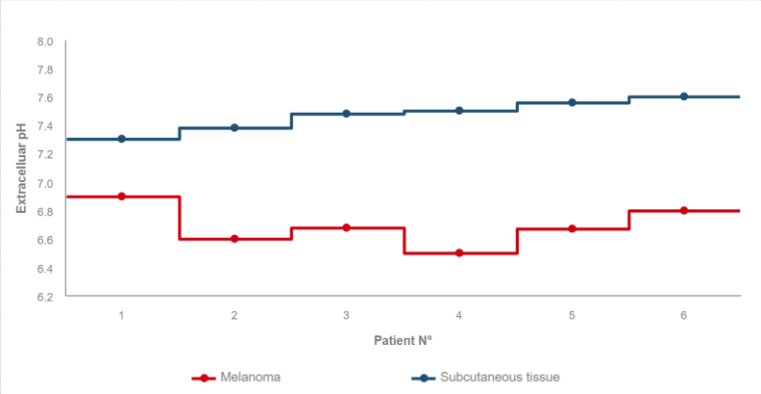
Additional comments about the cellular pH

Different measures made in cancer research centers have shown that the pH values of human tumors and adjacent tissues, which are obtained simultaneously by the same investigator in the same patient, consistently show that the pH of the extracellular tissue is substantially and consistently inferior in tumor tissue than in normal tissue[42]. The extracellular environment *immediately* becomes acid when a cell begins to become cancerous.

Thus, the manipulation of extracellular pH (and also of intracellular pH[43]) is a powerful tool in therapies for cancer treatment.

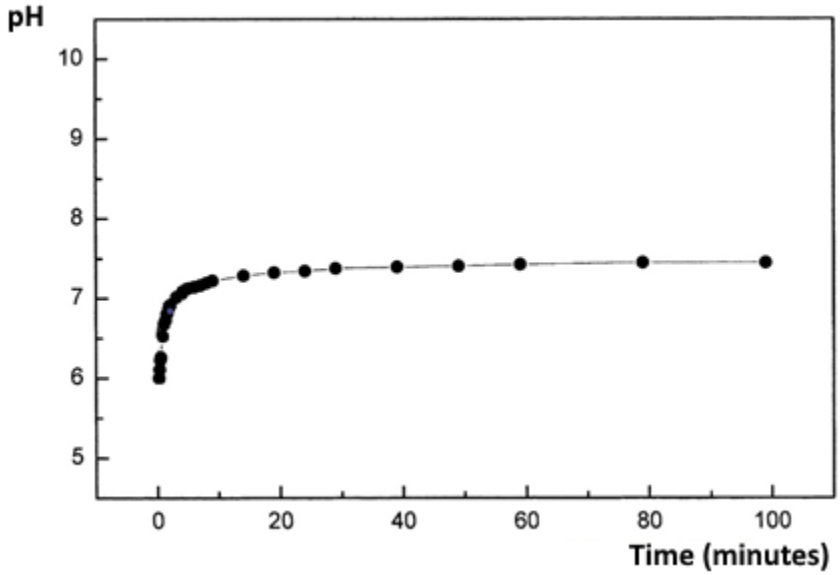
The following figures show a comparison of the pH of the extracellular fluid of a normal tissue with a cancerous one, for two cases of cancer,





Zeolites, when they touch a cancer cell, change the pH to the extracellular fluid, raising it and, therefore, killing the cancer cell, which needs an acid environment to live. Since zeolites are in balance with a normal cell, at pH level, they do not destroy normal cells.

The following figure shows a laboratory test that shows the typical evolution of a solution by adding zeolites in the appropriate dose. In the experience, it starts with a solution of pH = 6, evolving in a few minutes at pH = 7.3.



This effect, of alkalinization of the extracellular environment, means to "kill" cancer cells has been tested "in vitro" and "in vivo". With regard to the elimination of tumors "in vivo", 100% successful conclusive results are shown in this link, where a clinical trial is described with 19 patients suffering from cancerous tumors on the skin. The micronized zeolites were injected directly into the tumors or into the blood, through an intravenous injection. In all 19 cases, the tumors completely disappeared in at most 72 hours after the application of the zeolites.

What are natural zeolites?

Scientifically speaking, zeolites are natural minerals of volcanic genesis. When the volcanoes released their ashes over rising lakes, millions of years ago, the resulting chemical reactions between the ashes and the alkaline water altered the ashes in several crystalline forms of zeolites. Zeolites have a unique structure in nature and are classified as hydrated aluminosilicates (they contain crystalline water). This means that the crystals are formed mainly by hydrogen, oxygen, silicon and aluminum. The main characteristic of zeolites is that they are three-dimensional and microporous crystalline solids. The microporous structure is exactly defined, since the size of the pores is practically uniform and is a fundamental characteristic of each species of natural zeolite.

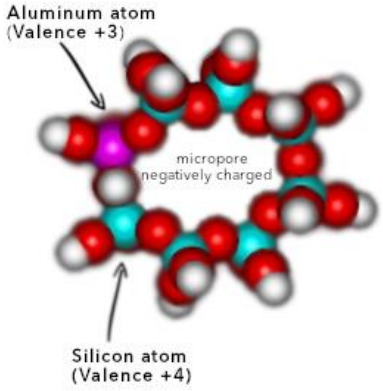


Figure 7. Representation of a molecule of a variety of zeolite, showing an electrically decomposed micropore

Natural zeolites were discovered in 1756 by the Swedish Geologist Axel Fredick Cronstedt, who named them zeolites, since he observed that they lost water when heated. "Zeo" and "Lite" are Greek words that mean "boiling" and "stone". The natural zeolites used in medicine are clinoptilolite, heulandite and mordenite.

Micronized natural zeolites have a great capacity to absorb polar molecules, of great importance in the toxins capture, which in general are polar molecules (mycotoxins, alcohols, neurotoxins, pesticides, herbicides, etc.).

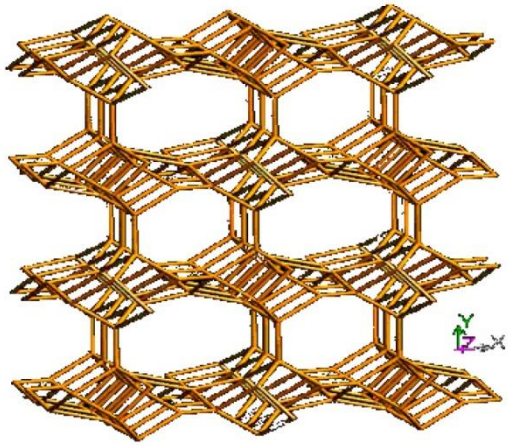


Figure 9. Clinoptilolite – Heulandite

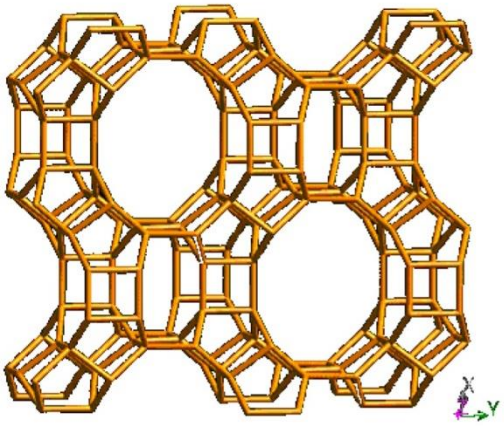


Figura 9. Mordenite

Another important property that gives the microporous crystalline structure to zeolites, is the ability to exchange cations. This process means the exchange of one cation for another. A cation leaves the microporous structure and another replaces it. This is of great importance in the anticancer capacity of zeolites, since this property involves the possibility of raising the pH to a cancer cell, causing it to die.

The mineral that contains our deposit of natural zeolites is formed by the three species of chemical composition shown below:

- **Clinoptilolite**: $(Na,K,Ca)_{2-3}\ Al_3\ (Al,Si)_2Si_{13}O_{36} \bullet 12H_2O$
- **Heulandite**: $(Na,Ca)_{2-3}\ Al_3\ (Al,Si)_2Si_{13}O_{36} \bullet 12H_2O$
- **Mordenite**: $(Na,K2,Ca_2)_{2-3}\ Al_2\ Si_{10}O_{24} \bullet 7H_2O$

We remark that our zeolites are predominantly calcic, since their main exchangeable cation is calcium.

Physicochemical properties of zeolites

- **Stability pH**: between 0.5 & 13
- **Thermal stability**: 650 ˚C (min)
- **Apparent Density**: 900 to 1300 (kg/m^3)
- **Real Density**: 1200 to 1500 (kg/m^3)
- **Cationic Exchange Capacity (CEC)**: 160 to 220 (meq/100gr) (High CEC)
- **Color**: White to white cream
- **Diameter of micropores**: 4 to 5.5 A˚
- **Solubility in water**: insoluble
- **Odor**: Odorless
- **Granulometry**: 100% <20 microns, 99.7% <10 microns. More than 25% <0.3 microns.