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Possibility of Application of Natural Zeolites for Medicinal Purposes

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ABSTRACT. **This paper discusses the effects of natural zeolites (particularly clinoptilolite-containing tuffs from various deposits) on the living organism, both animal and human.**

It is shown that natural zeolites are harmless, have metabolism-normalising, bactericidal, immunostimulatory and antioxidative effects. They diminish mortality and morbidity with regard to many diseases and disorders affecting cattle, sheep and goats, swine and poultry. Hence it is rational to utilize zeolites in animal husbandry. They are used successfully in the treatment of different human diseases. Zeolite efficacy in gastroenterology merits particular attention.

It is established that zeolites can be used both in human and veterinary medicine as biological active food additives (dietic additives), drugs, drug carriers, adjuvants in anticancer therapy and antimicrobial agents as well.

The data fully substantiate the expediency of further research in terms of studying natural zeolites and their biological and medicinal effects. *© 2009 Bull. Georg. Natl. Acad. Sci.*

***Key words**: natural zeolites, medicine, veterinary science, treatment, prophylaxis.*

Natural zeolites of sedimentary origin, which are present on all the continents of our planet as minable deposits, find extremely wide application in the solution of pressing problems in various areas of industry and agriculture due to their unique adsorptive, ion-exchange, catalytic, molecular-sieve properties as well as the recently discovered detoxication capacities [1,2].

Several symposiums and conferences were held in the second half of the past century, devoted to the use of natural zeolites in animal husbandry: in Rochester (USA) in 1982, in Sokhumi in 1978, in Tbilisi in 1981 and in Sokhumi in 1982 (Georgia, former Soviet Union) [3-5]. Later on, some presentations and reports with regard to the expediency of introducing this mineral into the diet designed for feeding swine, cattle and poultry were made at a number of scientific forums held in various countries of the world and devoted to the study and application of natural zeolites. But the majority of these works concentrated on the increase in the live weight of the livestock, on the nutrition efficiency, and on egg production in the case of the laying hens; this means that emphasis was made on the increase in productivity. Only single works highlighted the significance of the zeolites' role in veterinary medicine: in the prophylaxis and treatment of various non-infectious diseases. However, Japanese scientists have established the successfulness of applying natural zeolites (clinoptilolite-containing tuffs) in veterinary medicine for the prophylaxis

and treatment of various diseases already in the 70s of the past century [6]. Thus, inclusion of crushed clinoptilolite-containing tuffs in calves' fodder significantly diminishes the threat of developing severe or mild diarrhea. The production tests were carried out with 4 thousand livestock population at a pig farm in one of the prefectures of Japan. The experiment lasted for two years. In the first year of the experiment (February 1972 – January 1973) animals were given conventional fodder without the zeolite additive, while in the second year (February 1973 – January 1974) the diet was expanded by 6% inclusion of the clinoptilolite-containing tuffs.

It was found that in the second year of the experiment the animals developed stomach ulcer 3.5 times less frequently, pneumonia 2.5 times less frequently and cardiac dilatation 1.5 times less frequently, as compared to the control – the first year of the experiment. Mortality constituted 4% in the control group and 2.6% in the trial group. Moreover, it was noted, that newborn piglets from sows which had been on diet comprising the dietary additive (several percent of clinoptilolite) were virtually unsusceptible to the disease, like diarrhea.

Japanese specialists also established that natural zeolites had not just prophylactic but medicinal qualities as well [7]. Adding zeolite to the mixed fodder intended for piglets suffering from severe diarrhea appreciably suppressed this disease within several days and the animals recovered completely by the end of the seventh day, having appetite and cheerfulness restored.

In recent years, according to experts' assessments, morbidity among swine, sheep and goats and cattle as well as poultry averages about 40%, and in some cases the disease has a fatal outcome, which in the final analysis inflicts tangible losses upon modern poultry farming and animal husbandry [8].

These are predominantly the gastrointestinal tract diseases and a number of other diseases frequently caused by alimentary factors.

In swine these are as follows: diarrhea, gastroenteritis, helminthism, microelement deficit, cirrhosis, hepatitis, hepatosis, liver dystrophy, bronchopneumonia, salmonellosis, heart failure, prolapse of various organs (specifically, of uterus).

In cattle: gastrointestinal tract diseases, endometritis, prolapse of the uterus, pneumonia, diseases of the extremities, etc.

In poultry: pullorosis, colibaccilosis, coccidiosis, gastroenteritis, vitelline peritonitis, intoxication, metabolic derangements, avitaminosis, encephomalacia, pneumonia, dystrophy, asphyxia.

The research conducted recently, has highlighted the good prospects and expedience of employing natural zeolites for the prophylaxis and treatment of some of the above mentioned diseases [1,2,8,9].

At present, there is no consensus regarding the mechanism that would account for the positive impact of natural zeolites within the framework of treating as well as preventing various diseases in swine, cattle and poultry.

Some suppositions have been made, which could be formulated as follows:

1. Zeolites do not substitute nutrients, but are suppliers of a number of macro- and microchemical elements which are necessary for the vital activity of living organisms.

2. Zeolites, being the adsorbents, eliminate a number of toxic substances (heavy metal salts, nitrates, nitrites, mycotoxins, radionuclides, metabolism products) from the organism. Zeolites adhere to pathogenic bacteria; their use in the capacity of the matrix of pharmaceutical compositions inhibits the antibiotic (tetracycline, neomycin, framicoin) activity, therefore they act as detoxicants.

3. Zeolites, being ion-exchangers, participate in certain biochemical transformations, including the transport, activation and prolongation of enzyme and hormone action, maintain ion balance in terms of calcium and sodium, stabilize and regulate the soda-and-acid reserves in the gastrointestinal tract, normalize the homeostasis (inner medium) of animals, increase the nutrient conversion. High selectivity of natural zeolites, particularly that of the clinoptilolite and phillipsite with regard to the ammonium ion, provides the possibility to increase the non-protein nitrogen (carbamide, urea, ammonium sulphate and other synthetic nitrous substances) content in the fodder, hence averting its toxicity.

4. Zeolites, being catalysts, facilitate the improvement in the uptake of the nutrients incoming with the fodder within the diet of swine, cattle and poultry.

All these factors taken together facilitate the organism's resistance and tolerance with regard to poor quality fodder and unfavorable ambient conditions [8,9].

About 70 chemical elements were detected in living organisms, 47 being present permanently [10]. They are contained in animal tissues and are actively involved in metabolism reactions, being part of enzymes, hormones, vitamins, proteins, being indispensable and, as one frequently calls them, bioactive (biophilic) elements. The content of some of them is estimated at g/tons and even by the millionth of percent. Specialists distinguish up to thirty diseases associated with the deficit or excess of

mineral substances in animal fodder. For instance, application of unbalanced mixed fodder results in mineral metabolism disorder in cattle and poultry, in lesion of skeleton, etc.

Thus, it is pointed out [11] that fodder produced in the former Soviet Union was characterized by significant deficit of calcium, phosphorus, copper, cobalt, manganese, zinc, iodine etc., this being the cause of animal microelement deficit morbidity. The authors consider the natural zeolites of sedimentary origin, which are widely present on the territory of the former Soviet Union, particularly in Siberia, in the form of large-scale deposits, to be an additional reserve for enriching animals' dietary intake [8].

The microelements, present in zeolite-containing rocks of some of the mine deposits of the former Soviet Union are presented in Table 1. It has been shown [8] that the principal cations of these minerals, like calcium, potassium, sodium, as well as the majority of microelements are to some extent assimilated by living organisms, thus replenishing the deficiency of the former in mixed feed. As to the toxic cations like lead, iron and mercury, they are adsorbed by zeolites (by ion exchange) and egested from the esophagus.

Thus, by including natural zeolites into mixed feed, mineral metabolism in animals becomes augmented, the content of macro- (Ca, K, Na) and microelements in the tissues and the organs goes up. Due to the presence of these elements, which are capable of getting involved in the exchange, the ion composition of the chyme changes, which normalizes the pH and optimizes the activity of digestive enzymes.

Poor quality fodder is a source of many animal diseases. According to a number of researchers, vegetable fodder in the former Soviet Union was affected by microscopic fungi by up to 30-40% in some years; these fungi contaminate fodder, particularly grain with mycotoxicoses. This leads to alimentary mycotoxicoses in animals, taking a chronic course and impoverishing the organism resistance as well as creating conditions favorable to the initiation of many infectious diseases.

The work [8] showed the possibility of utilizing natural zeolites for decontaminating the contaminated fodder. Thus, there were no diarrhea cases in the experiment group (55 head) of shoats when adding 3% pegasin (heulandite-containing tuffs from the Pegas deposit, Siberia) to mixed feed of the 1st degree toxicity, whereas the shoats of the control group did suffer from this illness. An analogous effect was established when detoxicating the mycotoxins of the fungi of the genus Fusarium by adding to poor quality fodder 4% of pegasin.

In experiments with broiler poults, when they were fed with fodder contaminated with aflotoxin and T-2 toxin, enrichment of that fodder with pegasin also favored its detoxication and pointed to the efficiency of utilizing mixed feed of this kind. An identical result was obtained when utilizing yet another natural zeolite – khongurin (clinoptilolite tuff from the Khonguru deposit, Yakutia) as a detoxication agent for fodder infected with mycotoxins [12].

An experiment was performed with young cattle. It was found that when feeding livestock with poor quality hay which was contaminated with mold fungi of the genus Aspergillus, Mucor, Penicillium, Rhizopus, Fusarium, Alternaria, Stachybotrus and Trichoderma, it was advisable to utilize a special complex anti-toxin preparation, developed by the authors, or the zeolite khongurin, having an identical action in terms of effect, in order to provide for the prophylaxis and neutralization of the unfavorable effect of that fodder. However, khongurin adsorbed by that preparation is 2.2 times more efficient in terms of bactericidal action as compared to straight preparation. The proposed method for prophylaxis of mycotoxicoses favors the augmentation of immunobiological activity, readjusts the micro ecology of the intestine and prevents animal poisoning. It was also shown that the aforesaid preparation on the basis of khongurin decreases the strangles morbidity 4.7-fold.

The multiple data provided in [8] indicate that the addition of pegasin and khongurin to the diet of pregnant and suckling sows, sucker piglets and shoats, as well as fattening swines, favors the prophylaxis and treatment of a disease like diarrhea, which is so characteristic of these animals. Thus, the results of the test involving piglets intended for growing indicated that addition of this mineral to the mixed feed, 2.5% in quantity, decreased two-fold the morbidity for this disease as compared to the control group on a conventional diet.

Field experiments at one of the major swine-breeding farms in Siberia indicated that the addition of 2% of pegasin to the fodder "CK-5" and "CK-6" provided 2.7-fold improvement in the prophylaxis of gastric diseases, 11.9-fold improvement for liver diseases and 1.46-fold improvement for pulmonary diseases, as compared to the control group. The results of these tests fully conform with the data provided in the work of the Japanese specialists [6]. In connection with the aforesaid, one should, in our opinion, also mention quite an interesting experimental utilization of khongurin for the treatment of respiratory diseases carried out in Yakutia [13].

The experiment was performed involving two groups of rats affected by pneumonia. The first (trial) group

Table 1

Qualitative composition of the microelements in the zeolite-comprising rocks of some deposits on the territories of the former Soviet Union

Deposites	Khonguru (Yakutia, Russia)	Pegas deposit (Siberia, Russia)	Trans-Carpathia (Ukraine)	Eastern Georgia
Silver	+		+	+
Vanadium	+	+		+
Barium	+		+	+
Beryllium	+		+	+
Bismuth			+	
Cerium	+			+
Caesium			+	
Cobalt	+	+		+
Cadmium	+			
Copper	+	+	+	+
Gallium	+		+	
Germanium	+		+	+
Lanthanum	+		+	
Lithium			+	
Chromium	+			+
Molybdenum	+	+	+	+
Manganese			+	+
Arsenic		+		
Niobium		+		
Nickel	+	+	+	+
Lead	+	+		+
Antimony	+	+		
Scandium	+			+
Strontium	+		+	
Tin		+	+	+
Rubidium			+	
Titanium	+	+		+
Thallium				+
Yttrium	+		+	
Ytterbium	+			
Zinc	+	+	+	+
Zirconium	+		+	+

Note: The content of the microelements (+) in the rock is insignificant and is estimated at g/tons or at ppm %.

was put into the cage coated with zeolite layer, whereas the second (control) group was put into a conventional cage. By the 30th day of the experiment the animals of the first group had no signs of bronchial pneumonia, whereas the pathological process still continued in the pulmonary and cardial tissues of the rats in the second group. On this basis one may conjecture that the positive curative effect is exhibited not only at the zeolite-mixed feed-animal (living organism) level but at the zeolite-air-animal level as well.

Pegasin displays a positive effect with regard to the treatment of diarrhea in swine. Thus, in one of the pig farms of Siberia the sucker piglets were treated with conventional medicines and a decoction of flax and khongurin. In the former case the mortality was 5%, and 3.3% in the latter case, when the medication related expenditures were much lower as well. In another experiment, utilization of the khongurin mixture in kissel also had a favorable effect: the mortality was 17.65% in this group and 33.43% in the group treated with conventional medicines. This shows that utilization of zeolite is 1.88 times more efficient as compared to drug therapy.

The pegasin dose increase by 20-25% when treating diarrhea in piglets provided the same recovery effect as zeolite doses within the range of several percent (2-6%) but significantly decreased the treatment cost.

An epidemic of one of the swine-specific diseases was registered at one of the Poltava pig-breeding farms (Ukraine) in the 90s of the past century. Addition of clinoptilolite-containing tuff (from the Sokirnitsa deposit, Ukraine) to fodder at the amount of about 3% resulted in the preservation of the total livestock.

Utilization of natural zeolites is effective for maintaining the health of cattle as well. Thus, farm-scale experiments carried out at the fattening farm in the Altay region (Russian Federation) indicated the following [8]. Crushed pegasin was added to the fodder of the trial group (680 bull-calves) on the basis of 0.5 g per 1 kg of live weight. No zeolite was added to the fodder of the control group (520 bull-calves). Over the course of 10 months of the farm-scale experiment the bull-calves of the study group showed the gastrointestinal, respiratory organs' and the extremities' morbidity decrease respectively by 23%, 17% and 19% as compared to the control group.

Cuban scientists [15] managed to liquidate diarrhea in cows caused by dysentery outbreak by employing natural zeolites from Cuban deposits over the course of 48 hours.

Pegasin contained in the diet of heifers exerts some effect on the fetus formation. This is proved by the fact that there were 2 times less stillbirths, 1.5 times less calf morbidity, halved frequency of endometritis diag-

nosis, uterus prolapse and diseases of the extremities.

We consider it to be particularly important that fortification of fodder with zeolite, as indicated above, provides an opportunity to utilize fodder rich with non-protein nitrogen in order to increase the nutrition efficiency at no special risk [8].

Analogous favorable results were obtained while utilizing natural zeolites as a dietary additive to fodder in poultry farming as well.

A field trial, carried out at one of the poultry farms in Siberia, helped to study the effect of khongurin in the feeding ration on the survival rate of broilers. All the aforesaid diseases characteristic of poultry caused mortality rate equal to 14% in the control group comprising chickens which were receiving common fodder without zeolites, whereas in the trial group where zeolite was added to fodder the mortality rate constituted 6-10%. Most trustworthy results were obtained with regard to gastroenteritis. The mortality rate was 4% in the control group as opposed to 1.1% in the trial group [8]. The effect of yet another zeolite, pegasin on the survival rate of broilers was studied in the other work of this author [16]. While identifying the reasons for mortality, it was noted that the death rate caused by metabolism disorders, coccidiosis and colibaccilosis decreased by respectively 1.4, 3.3 and 0.7%. As a whole, the mortality caused by coccidiosis, colibaccilosis, gastroenteritis and metabolism disorder fell by 3-6% in the trial group as compared to control group.

Results, roughly such as these, were obtained by utilizing natural zeolites from Sakhalin [17]. Clinoptilolite-containing tuff (granulation 1-3 mm, 3% of the total ration weight) was added to the principal ration of broilers in the trial group during the trial period (58 days). The mortality rate in this group constituted 9% as opposed to 12% of the control group. Mass utilization of clinoptilolite-containing tuff from the Tedzami deposit (Georgia) as a dietary additive to the principal ration of poultry (3% for egg-laying chickens and 5% for broilers and ducklings) at the poultry farms of the former Soviet Union in 1984-1985 showed that addition of clinoptilolite to the mixed feed increased the livestock population survival rate by 0.6-2.9% as compared to the control group [18]. The author of the monograph [8] and other researchers active in the area of the utilization of natural zeolites in veterinary medicine have noted that these minerals diminish the morbidity rate of the animals 3-5 fold, the mortality rate 1.5-3 fold and drug-related expenditures by 20-40%, provided they constitute over 60-70% of the rock. Simultaneously, the survival rate in the cattle and swine breeding and poultry farming increases by respectively 5-7, 4-9 and 3-5%. One more interesting quality of natural zeolites, i.e. the anti-stress effect was discovered recently, in the last decade of the 20^{th} c.

Stress, particularly the alimentary one, is one of the reasons for the wide spread of non-contagious diseases. Stress factors like this are as follows: prolonged fasting, occasional underfeeding as well as the contrary, i.e. overfeeding, abrupt change of the diet contents and feeding rate, unbalanced diet, etc. As shown by practical experience, these as well as some other factors, like overheating and super-cooling affect animal organisms day by day. A series of experiments was carried out in Ukraine in 1985-1990 involving livestock in order to establish the efficiency of zeolite utilization in the capacity of anti-stress additives.

Zeolites from the Sokornitsk deposit – clinoptilolite-containing tuff – were added to the fodder of fattening swine and young cattle (on the basis of 3-7% of the dry solid matter of the ration). The swines and bull-calves which had been given the zeolite additive were less aggressive and rested for the major part of twenty-four hours [19]. It was shown in another work [20] that the behavior of hens from the control group was marked by more expressed excitability and aggressiveness after they had been transferred from production building into laboratory conditions, so that several ones died of pecking. In the trial group the hens were given the zeolite additive (20% of zeolite-containing tuff within the mixed feed mass) and there was no cannibalism there, the birds were quiet and quickly adapted to the new housing conditions.

Inclusion of natural zeolites in mixed feed contents augmented the animals' resistance against the exposure to cold, i.e. the antistress capacity with regard to cold increased. There were sows (who had zeolite–pegasin – added to their diet following copulation and till the end of the suckling period) and sucker piglets in the study group. Another group of the sows with piglets (control group) was put in the same conditions, except for the absence of the zeolite additive in their diet. Night frosts of +1 - 0^0 C were observed for several days, the piglets being 7-12 days old by that time. The effect of the low temperature resulted in the super-cooling and death of some piglets in the control group. All the piglets in the trial group tolerated the frosts well [21].

It is established that feeding the zeolite-containing tuff from the Pegas deposit to white nonpedigree rats in laboratory conditions decreased mortality among the animals in the case of overheating, the exposure in the thermostat being 42.5^0 C [22].

Thus, all the animals consuming fodder containing natural zeolite additives acquire stress-tolerance with regard to super-cooling and overheating.

Cuban specialists recorded one more medicinal property of natural zeolites – the handling of the abrasions and scratches in horses and cattle with zeolite dust accelerated the healing process [2].

However, despite the research carried out all over the world in the field of the application of natural zeolites in animal husbandry, no exact mechanism of zeolites' prophylactic and curative effect in living organisms was established. Some conjectures and hypotheses were made with regard to their positive action, albeit quite frequently contradicting each other. Therefore one needs to conduct serious physiological and biochemical researches to explain the nature of their effects on living organism, provided general statements are negated and explanation for their prophylactic and curative effect is provided individually, as zeolite is not a "balsam" for treating all diseases en masse and is characterized by selective action in the case of specific diseases, for instance, gastrointestinal diseases, appearing in the most of the studies. One can mention also the antistress effect of natural zeolites, which is virtually less studied. The author of the monograph [8] has very carefully expressed the idea about the possible use of this mineral in the prophylaxis and treatment of "non-contagious" diseases.

As a whole, application of natural zeolites in the prophylaxis and treatment of some diseases is reasonable and promising, and according to some scientists [2,10,23], may be successfully employed not only in animals, but in humans as well, taking into consideration zeolites' harmlessness, pronounced metabolism-normalizing and bactericidal effects and considerable cheapness. Zeolites can be used as drug carriers, and as adjuvants in anticancer therapy, dietetic supplements or antimicrobial agents as well [24,25, 26].

Some relatively isolated publications deal with the utilization of zeolites for medical purposes in humans, particularly in the capacity of food additives. It was pointed out that biostimulant food additives which were created on the basis of natural minerals (zeolite-clinoptilolite) with a proper ratio of vegetable constituents like rye, wheat, oats, devil's apron etc. and were represented by variable forms like powder, granules and pressed forms (dragée), alleviate the activity of a number of diseases of the gastrointestinal tract, immune, endocrinological, nervous and cardiovascular systems [10, 27].

The majority of patients with various forms of gastrointestinal diseases (ulcer disease, chronic colitis due to disbacteriosis, some chronic persistent hepatitis), encephalomyelitis, neurosis, chronic fatigue syndrome and dystrophic arthritis, which had been treated with zeolite-containing food additive "Litovit" presented with the general amelioration of the status as judged by subjective self-assessment. In particular, the patients had a better mood, their stool normalized, edema dropped, life activity rose, sleep and weight normalized as well. The patients considered all this to be a result of certain "purgation of the organism"[27]. Thus, it was concluded that "Litovit" had properties of detoxicant, hepatoprotector and immunostimulating agent.

It is recommended to employ zeolite additives, particularly to add them to bakery foods within the framework of safety precautions in the initial period of the morbidity rise in the areas where increase in the intestinal infections rate is forecast [28].

It is shown that Litovit can be successfully used in the overall treatment of functional constipation and accompanying colon disbacteriosis of degree I and II. It helps to improve the clinical symptomatics and the functional state of the gastrointestinal tract [29]. It is mentioned that in Cuba inexpensive indigenous natural zeolites have been studied as buffers to reduce stomach acidity and to treat stomach ulcers [30], there was elaborated a new antidiarrheal drug based on purified natural clinoptilite – Enterex – as well [31]. The severity of the clinical and laboratory parameters was significantly less in patients with acute viral hepatitis who were given the basic therapy in combination with a novel pathogenetic drug Litovit [32]. One may also conclude that Litovit is substantially effective within the framework of complex treatment of a patient with nonspecific ulcerative colitis. Since the beginning of the Litovit intake defecation became regular with the homogenous porridge-like dejection. The abdominal pains ceased as well. There is a solid basis for conjecturing the positive effect of Litovit in preventing the relapses of the disease as well: 6 patients taking Litovit regularly had no usual exacerbation of this chronic process in the autumn [27]

Litovit also causes general decrease in the blood level of the total cholesterol and the triglycerides, as well as significant decrease of the body mass. The utilization of Litovit within the framework of complex treatment of adults with bronchopulmonary pathology did not show any positive effect [27].

Peroral utilization of Litovit in the case of external intestinal fistulae facilitates accelerated and complete restoration of the crude protein content in the serum; stabilization of the liver function tests; normalization of the WBC count, urea; compensation of magnesium, zinc,

phosphorus, cadmium, titanium and manganese deficit; excretion of lead and mercury excess; accelerated restoration of iron and potassium-sodium balance. [27]. The first clinical results of Litovit utilization in patients with injuries and diseases of the thoraco-lumbar segment of the spine allow us to infer its indubitable efficacy in preventing and correcting gastrointestinal paresis which accompanies the aforesaid pathology. Patients with burn trauma, who had taken Litovit, showed earlier normalization of the blood concentration of trace elements and of the indices of neutrophil functional activity as compared to patients who had undergone no such treatment. Litovit facilitated early regression of clinic manifestations [34].

It was shown that Litovit may be efficiently utilized in expectant mothers as well as in patients with fibrous myoma of the uterine body at the critical gestation age for the sake of prophylaxis and treatment of extragenital diseases like gastrointestinal and cardiovascular ones, obesity, anemia, etc [27].

Utilization of Litovit in pediatrics resulted in the amelioration of the general condition of the patient, decrease in fatigability, normalization of blood pressure, extinction of dyspeptic manifestations, amelioration or arrest of headaches.

Litovit intake in obese children resulted in body mass reduction. Children with cutaneous allergic manifestations showed appreciable abatement or complete extinction of the rush [27]. Utilization of biologically active food additive Litovit in children with various diseases (predominantly of the gastrointestinal tract and various allergopathies) facilitated the intensity of the positive dynamics of the clinical signs as well as normalization of the biochemical indices of the liver function (AST, ALT, LDH).

It is recommended to utilize aggregate comprising zeolites and methyluracil for the treatment of chronic periodontitis [33]. Patients with odontogenic cyst had the bone cavity filled with natural zeolites during the operation following cystectomy. The results of the recent study of the treatment of odontogenic cyst reveal that the application of zeolites accelerated the bone formation process; this was confirmed by the positive effect of topical zeolite application for the treatment of the lower jaw in rabbits. The analysis of the obtained results showed that on the seventh day from the beginning of the experiment acceleration of osteogenous cell proliferation and differentiation were observed in the animals in the experimental group as opposed to the control group. Thus, topical application of natural zeolites stimulated reparative osteogenesis.

Utilization of Litovit facilitated substantial alleviation of the clinical manifestations of various dermatopathies (psoriasis, atopic dermatitis, eczema, neurodermatosis), possibly due to the positive effect exerted by this drug on the functional disorders of the gastrointestinal tract, particularly constipation [27].

Some promising data were obtained with regard to the efficiency of external application of montmorillonite for the treatment of pyoinflammatory diseases of the skin and the hypodermic tissue. [27]. External application of zeolite powder has been found to be effective in the treatment of athlete's foot and decreasing the healing time of wounds and surgical incisions [2]. "Litovit M" exerts a positive effect in the case of ulcerative stomatitis and streptoderma, as well as in the case of insect bites (arresting the edema, pruritus and pain) and posttraumatic haematomas, when applied topically.

However, one should note that the majority of the publications reflect the results of the open, often non-randomised clinical trials; therefore, the obtained data are of the preliminary nature only.

Utilization of zeolites for medical purposes has its substantiation in the results of experimental research.

Experimental study involving volunteers showed that after a single administration of zeolite-containing preparation Enterex Diabetic the glucose and insulin concentrations decreased without any modification of the triglyceride levels [35].

A number of changes in terms of the immune system were detected when feeding outbred white mice with briquetted feed containing natural zeolite (clinoptilolite, Khekordzula deposit, Kaspi district, Georgia) for 30 days, namely the following: *in vitro* production of the alpha- and gamma-interferon by the white cells of the peripheral blood, phagocyte activity of the blood neutrophils – the phagocytic number (%), index and the completeness of the process [36].

Immune (gamma) interferon displayed the greatest sensitivity towards zeolites; its rise was significant already by the 3^{rd} day of feeding (36.8 U/ml, $p<0.05$). The maximum indices were registered by the 10^{th} day (51.2 U/ml, $p<0.05$), persisting for one month. An analogous effect and dynamics were recorded when studying the alpha-interferon: Significant stimulation of the activity fell on the 7^{th} day of the diet (60.8 U/ml, $p<0.05$) with the maximum by the 15^{th} day and the subsequent descendent trend.

The effect of a zeolite diet on the phagocytosis system proved to be varied. The absorbing function of the phagocytes remained nearly intact against the background of a short-term (on the 10^{th}-25^{th} days) increase

in the phagocytic index, whereas the digestive capacity of the phagocytes increased noticeably and lasted for all the observation time [36].

Similar effects were obtained in rats as well; the latter were given the food additive "Litovit". This favored the normalization of the phagocytic index and the phagocytic number as well as the functional adequacy of the phagocytes, assessed by the kinetics of the chemiluminescent response of the whole blood to the staphylococcal reagent. The data were compared with those from the animals on the so called "refined" diet, distinguished from the standard one by the exclusion of bran [27].

When intravenously infecting the outbred white mice with the influenza A0 virus (PR8 strain), which was highly pathogenic for them, a significant mortality (of up to 50%) was observed in the animals already by the 2^{nd} day, even before the initiation of the active reproduction of the virus in the lungs. But the lethality among the animals decreased almost twofold when they were on the zeolite "diet", i.e. a trustworthy protective effect was obtained. It was concluded that zeolites were capable of neutralizing the immunosuppressive effect of the viral infection on the mouse organism [36].

Peroral intake of the "Litovit" preparation in Wistar rats with endotoxicosis simulated by the one-time intraperitoneal introduction of CCl_4 normalized the content of the lipid peroxidation products in the liver, the lymph nodes (hepatic and mesenteric), the small intestine and the peripheral blood, with the exception of the hepatic lymph node. Free fatty acids were detected by the method of high-performance capillary gas liquid chromatography. It was also revealed that the hepatocytes became hypertrophic at the expense of the increase in the volume of their nuclei and cytoplasm, and thus predetermined the diminished damaging effect of the hepatotropic toxin like tetrachloromethane. The cell-protector effect upon the mast cells was also exhibited; it was detected by means of azure-dyed native specimens of the intestinal mesentery. The experimental studies showed that Litovit constituted the complexing agent and the sorbent, which facilitated the excretion of toxic substances of both exogenous and endogenous origin from the organism, reinforcing the immune system, and having a good anti-inflammatory and regenerating effect [27].

Litovit utilization normalizes the granulocytopoiesis and the erythropoiesis, possibly due to the termination of endotoxemia, and activates the reticuloendothelial and the plasmocytic and lymphatic system.

It is considered that Litovit exerts a protective effect upon the cell texture structure of the liver, as proved by the absence of reliable difference in the specific electric conductivity when compared with intact animals. The affected animals presented a significant change in indices. Prophylactic utilization of Litovit provided a stabilizing effect on the *zona fasciculata* of the adrenal cortex as well [27].

There are several publications [37,38] on the possible immunostimulatory and antitumoral effects of natural clinoptilolites. Particularly, it was shown that micronized zeolite (MZ) administered by gastric intubation to mice injected with melanoma cells significantly reduced the number of melanoma metastases. In mice which had been fed MZ for 28 days, concentration of the lipid-bound sialic acid (LSA) in serum increased, but the lipid peroxidation in the liver decreased. Lymphocytes from the lymph nodes of these mice provoked a significantly more expressed allogenic graft-versus-host (GVH) reaction than the cells of the control mice. After intraperitoneal application of the MZ, the number of peritoneal macrophages, as well as their production of superoxide anion, increased. However, the generation of NO was totally abolished. At the same time, translocation of p65 (NF3B subunit) to the nucleus of the splenic cells was observed.

Immunohistochemistry was used to analyze whether the MZ could interfere with Doxorubicin-induced lipid peroxidation and the consequential production of the 4-hydroxynonenal (HNE). This study involved various tumor cell cultures and tumor-bearing animals and showed that the MZ reduced the metabolic rate of cancer cells and increased the binding of the HNE to the albumin *in vitro*. It also selectively reduced the generation of the HNE *in vivo* in the tumor stroma following Doxorubicin treatment without affecting the onset of lipid peroxidation in the malignant cells. Combined treatment with Doxorubicin and MZ resulted in a strong reduction of the metastatic dissemination. It was concluded that the interference of MZ with lipid peroxidation might explain some of the beneficial effects of this particular zeolite in combined cancer therapy.

Clinoptilolite treatment of mice and dogs suffering from a variety of tumor types led to the improvement in the overall health status, prolongation of the life-span, and decrease in tumor size. Local application of clinoptilolite to skin cancers in the dog effectively reduced tumor formation and growth. In vitro culture studies showed that finely ground clinoptilolite inhibited protein kinase B (c-Akt), induced the expression of $p21^{WAF1/CIP1}$ and $p27^{KIP1}$ tumor suppressor proteins, and blocked cell growth in several cancer lines [39].

However, the mechanism of the effect exerted by the drug on the organism is insufficiently known. De-

spite some very interesting experimental data, the mechanisms of zeolite action in terms of its effect on the living organism still remain uncertain.

On the basis of the foregoing, it should be acknowledged that zeolites have a substantial potential for the treatment and prophylaxis of various diseases in humans and in animals. Further research targeted at defining the medicinal mechanisms of their action, employing the principles of the evidence-based medicine shall be deemed as valid and indispensable.

სამედიცინო მეცნიერებანი

ბუნებრივი ცეოლითების გამოყენება სამკურნალო მიზნებისთვის

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სტატიაში განხილულია ბუნებრივი ცეოლითების (კერძოდ, კლინოპტილოლითის შემცველი სხვადასხვა წარმოშობის ტუფების) ზეგავლენა ცოცხალ ორგანიზმზე, როგორც ადამიანზე, ასევე სხვადასხვა ცხოველზე.

ნაჩვენებია, რომ ბუნებრივი ცეოლითები უვნებელია, მათ აქვთ მეტაბოლიზმის მანორმალიზებელი, ბაქტერიციდული, იმუნომასტიმულირებელი და ანტიოქსიდაციური თვისებები. ისინი ხელს უწყობენ მრავალი დაავადებისა და დარღვევით განპირობებული ავადობისა და სიკვდილიანობის შემცირებას მსხვილფეხა და წვრილფეხა ცხოველებში, აგრეთვე ფრინველებში, რაც მეცხოველეობაში მათი ფართო გამოყენების სასარგებლოდ მეტყველებს. ცეოლითები წარმატებით გამოიყენება ადამიანთა სამკურნალოდაც, განსაკუთრებით საჭმლის მომნელებელი სისტემის პათოლოგიის შემთხვევაში.

დადგენილია, რომ ცეოლითები შეიძლება გამოყენებულ იქნას მედიცინასა და ვეტერინარიაში როგორც კვების ბიოლოგიურად აქტიური დანამატები, წამლები, წამლის შემცველები, დამხმარე საშუალებები კიბოს საწინააღმდეგო მკურნალობისას, და ანტიმიკრობული აგენტები.

მონაცემები ადასტურებენ შემდგომი კვლევის მიზანშეწონილობას ბუნებრივი ცეოლითების ბიოლოგიური და სამკურნალო ეფექტების დასადგენად.

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