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Chapter

Zeolites Applications in Veterinary Medicine

Marc Simona and Tulcan Camelia

Abstract

Zeolites have a wide range of use, from construction industries, aquaculture industries, agriculture, space research to human and veterinary medicine. This broad application of natural and synthetic zeolites is given by their main properties: adsorption, molecular sieving and cation exchange capacity. In this chapter the main use of zeolites in veterinary medicine is reviewed. The beneficial effects of zeolites in animal nutrition, on mycotoxins, as an adjuvant in anticancer treatment and in increasing passive immunity of newborn ruminants are reported. Furthermore, multiple advantageous immune effects of zeolites such as their antioxidant capacity or their non-specific superantigen-like immunoglobulin action are also reviewed. Finally, their main positive effect on passive immunity in newborn calves is discussed. Literature data reviewed confirms their beneficial role in newborn calves during colostral period.

Keywords: zeolites, feed additive, immunostimulation, ruminants

1. Introduction

The first group of zeolite minerals was discovered in 1765 by a Swedish mineralogist A.F. Cronstedt who described several species found in well-defined crystals. He noticed that some heated minerals began to lose their constituent water with a boiling-like appearance, hence the name of zeolite (from the Greek words "zeos" and "lithos" which translate as "boiling stone") [1].

Zeolites are natural, hydrated, crystalline aluminosilicates made up of three-dimensional networks extended by AlO_4 and SiO_4 linked together by oxygen atoms, which make up a rigid, open, honeycomb-like skeleton, generally including cations which neutralize the excess negative charge of aluminum tetrahedra and water molecules. Each AlO_4 tetrahedral network supports a net negative charge that is balanced by a cation, usually from the I-A or II-A group (Ca, Mg, Na, K, Fe). These ions are not part of the zeolite network and can be changed by other cations such as heavy metals (Hg, Pb, Cd) or ammonium ions [2–4].

There are 67 natural zeolite minerals accepted by the Natural Zeolites Commission of the International Zeolite Association (IZA) and all have a unique three-letter code [5].

Clinoptilolite of sedimentary origin, generally the most used natural zeolite, is authorized by the Commission Implementing Regulation (EU) no. 651/2013 as a feed additive for all animal species [6]. In the United States, clinoptilolite belongs to the sodium aluminosilicate category and has the status of Generally Recognized as Safe (GRAS) (Code of Federal Regulations CFR, Title 21, Section 182.2727) [7].

Due to their main properties: adsorption, molecular sieving and cation exchange, zeolites have a wide use in many areas. For example, in agriculture, natural zeolites are used to obtain fertilizers capable of better nitrogen retention and in a slow and controlled release of fertilizers, nitrogen use efficiency (NUE) increase [8, 9]. In aquaculture industry natural, synthetic or modified zeolites are used as adsorbents for ammonia removal from fish farming ponds and transportation tanks, as a cation-exchanger for removal of different toxic heavy metals from fresh water and sea water cultures and as a feed supplement to enhance fish growth [3]. Also, zeolites can increase the nutrient (by addition of micronutrients) and water use efficiency of drylands (by their water holding capacity) [9]. Natural zeolites are used in wastewater, surface waters, ground and underground water, drinking water treatment [10, 11], in decontamination of radioactive waste water [12] and in agro-industrial wastewater treatment due to their exceptional cationic exchange and adsorption properties [13]. In construction field through their excellent properties, mainly porosity, specific weight and adsorption, they can be used as a building stone [14], in zeoponic substrates—artificial soils developed by the National Aeronautics and Space Administration—for plant growth in space [15], and as potential slow-release carriers for herbicides, insecticides and other organic compounds, protecting in this way the environment from chemicals [16].

In animal production, alternative products as zeolites are a solution to ensure health, productive performance (yield and quality of carcass, milk yield), to reduce the effects of mycotoxins on animal health status, to remove selectively pathogens from the animal gut without reducing microbial richness and finally to increase farm profitability. All of these effects has been extensively studied in the last decade [17–28] and are schematic represented in **Figure 1**.

Clinoptilolite is also used as a biomedical feed ingredient due to its beneficial properties as a growth-promoter and immunostimulant and can constitute an alternative to antibiotic growth promoters [29], since European Union legislation has banned the use of antibiotics for growth promotion in 2006, because the overuse of antibiotics in animals can contribute to emergence of antibiotic resistance [30].

Zeolites can have a protective effect in intoxication and in reducing parasite infestations. These effects are evidenced by researchers who observed that clinoptilolite (2 g/kg) could have some protective effect in organophosphorus poisoning in sheep by protecting the rumen flora and by preventing the decrease of cholinesterase activity [31]; in lead intoxication in mice, clinoptilolite given in 10/1 ratio

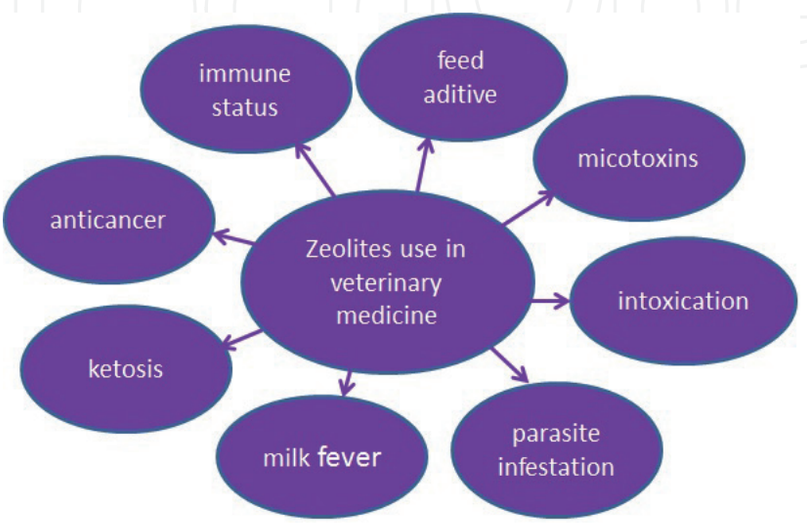


Figure 1.
The main applications of zeolites in veterinary medicine.

(clinoptilolite/Pb) adsorbed 91% of Pb, and when supplementing 3% clinoptilolite feed to pigs that received 150 ppm $CdCl_2$, clinoptilolite prevented Cd-induced anemia by adsorption of Cd [32]; and in reducing the excretion of cysts in goat kids with giardiasis [33]. It also had beneficial effects in infestations with nematode larvae in lambs, producing an increase in feed consumption and in body mass [34].

Some types of zeolites are studied for their adsorption properties in order to improve the life of people suffering from chronic kidney disease, who need to undergo weekly hemodialysis. Dialysis membranes made from zeolite and polymer are studied in order to improve the performance of hemodialysis. Nanofiber membranes made from zeolite and polyacrylonitrile (PAN) adsorb creatinine, with the best results for 940-HOA (beta) zeolites (25,423 μg/g in 625 μmol/L creatinine solution) [35] and P87 zeolite in combination with polyethersulfone, used because of their improved resistance to fouling, thermal stability, chemical resistance and due to their high adsorption level of indoxyl sulfate (550 μg/g membrane) [36]. When zeolite was used along polyethersulfone (PES) and dimethyl formamide (DMF) in proper concentration: 17:0.5:82.5 (PES:zeolit:DMF), creatinine concentration decreased by 91.99%, which suggests the possibility of using these membranes in haemodialysis [37].

2. As dietary supplements in animal nutrition

In animal husbandry, natural and synthetic zeolites have been mostly used to improve productive performance. The proposed mechanisms involved in achieving the increase in productive performance in animals are: ammonia binding, reducing toxic effects of ammonia produced by intestinal microbial activity; low passage rate of digesta through the intestines and more efficient use of nutrients; enhanced pancreatic enzymes activity-favorable effect on feed components hydrolysis over a wider range of pH, improved energy and protein retention; elimination of mycotoxin growth inhibitory effects [32].

Due to the beneficial effects of the gradual release of ammonia ions on microbial synthesis in the rumen, zeolites are used especially in high non-protein nitrogen feed ratio. *In vitro* and *in vivo* experimental studies have shown that 15% of ruminal NH_4^+ can be adsorbed by zeolites, thus reducing the toxic effects of urea (increased rumen pH and ammonia concentration in rumen and blood). Thus clinoptilolite (6%) in the feed of dairy cows receiving urea significantly reduced the concentration of NH_4^+ in the rumen [32]. Also, a decrease in ruminal pH in diets with 1% clinoptiloliten is reported [38].

Milk fever and ketosis are the most common metabolic diseases that occur in cows with high milk production. Cows that received zeolite (1 kg zeolite/day for 4 weeks before calving) did not experience subclinical hypocalcemia [39]. Also, the administration of zeolite A (sodium aluminosilicate) to pregnant cows during the dry period (1.4 kg zeolite A/day in the last 2 weeks of gestation) reduced the incidence of milk fever. The mode of action of synthetic zeolite A is to reduce the bioavailability of fodder calcium at the gastrointestinal level (calcium binding capacity of zeolite is 110 mg/g Ca at pH 11), stimulating Ca-homeostatic mechanisms before calving. At calving, the plasma level of calcium was significantly higher in the experimental group ($p < 0.0001$); with a slight drop of inorganic magnesium and phosphorus, that set up a week postpartum [40].

When clinoptilolite was administered (2.5%) in the last month of gestation, the incidence of milk fever was 5.9%, compared to 38.9% in the control group. Also, clinoptilolite (2.5%) administered during the dry period reduced the incidence of ketosis (5.9%) by improving the energy metabolism through increased production of propionate in the rumen and by better recovery of feed [32]. Katsoulos

et al. revealed that long-term clinoptilolite administration (from 4 weeks before calving to the next dry period) at different doses (1.25 and 2.5%) did not have adverse effects on the liver and serum glucose concentrations, ketone bodies, total protein and urea did not change, with a higher milk production and a lower ketosis incidence [41]. Moreover, other important minerals such as: Cu, Zn, Fe were not influenced by the long-term administration of clinoptilolite (1.25 and 2.5%), which highlights the safety of this natural compound [19].

Also, in combination with yeast, clinoptilolite (Rumencure: yeast 60% and clinoptilolite 40%) given to cows for a long period (30 days) had no apparent adverse effects on their liver function and on some biochemical parameters (glucose, ketone bodies, blood urea nitrogen and total proteins) [42].

3. Positive effects against mycotoxins

Due to the increased incidence of contamination with mycotoxins, it has been attempted to use inert feed adsorbents to bind mycotoxins, thus reducing their

Dietary rate	Species (N)	Effect	Ref.
20 g/kg clinoptilolite in feed contaminated with 1 mg/kg aflatoxins for 42 days	Broiler chickens N = 480	Decreased the severity of lesions and effectively diminished the detrimental effects of aflatoxins	[45]
1% synthetic zeolites NaA in feed contaminated with 2.5 mg/kg aflatoxin B1 from 21 to 42 days of age	Male broiler chicks N = 80	Zeolite NaA can counteract some of the toxic effects of aflatoxin A in growing broiler chicks	[46]
3 and 5% clinoptilolite in feed contaminated with 2 ppm aflatoxin from day 1 to 7 weeks of age	Male chicks N = 900	The level of 5% clinoptilolite was better in reduction the effects of alfatoxin than 3% clinoptilolite ratio	[47]
0.2% Minazel Plus/0.2% Mycosorb/0.2% Mycofix-plus in feed contaminated with 2 ppm T-2 toxin for 21 days	"Ross" broiler chicks N = 160	Pathohistological examination of liver, bursa of Fabricius and small intestine revealed better protective effects in groups fed with Mycofix-plus than in groups with Minazel Plus and Mycosorb were protective failure was noted	[48]
2% clinoptilolite in feed contaminated with 2.5 ppm aflatoxin B1 for 4 weeks	Laying hens N = 96	The livers of hens showed very low mycotoxin concentrations	[49]
0.2% Min-a-Zel Plus in feed contaminated with 3 mg/kg zearalenone for 14 days	Piglets N = 20	Agonistic effect due to oestrogen reduction	[22]
0.2% organozeolite 0.5% organozeolite in feed contaminated with 8.3 mg ZEN/kg for 53 days	Lambs N = 64	The organozeolite reduced the content of zearalenone in liver, kidneys and muscles Addition of 0.5% Min-a-Zel Plus eliminated zearalenone from all organs, totally	[17]
200 g clinoptilolite/animal/day for 7 day	Dairy cattle N = 15 farms	Significantly reduced aflatoxin M1 in milk at an average rate of 56.2%	[50]

Table 1.
The summarized effects of zeolites on mycotoxins as reported in literature data.

intestinal absorption and toxic effects on animals and animal products. Annually, it is estimated that about 25% of the world's harvested crops are contaminated by mycotoxins, leading to huge agricultural and industrial losses [43]. The first adsorbents successfully used in poultry, swine, sheep and bovine breeding were phyllosilicates, namely bentonite [32].

The adsorption process is strongly related to the pore size, the adsorbent contact surface, polarity, solubility, and the size of the mycotoxin molecules that are adsorbed (e.g., aflatoxins B1 and B2 have 5.18 Å and aflatoxins G1 and G2 are 6.50 Å). Clinoptilolite has the highest *in vitro* adsorption, over 80% for aflatoxins B1 and G2 [44], with effects demonstrated especially in the poultry industry [45–49], but also in piglets [22], lambs [17] and dairy cattle [50] as are presented in **Table 1**.

Studies performed by Serbian researchers have demonstrated *in vivo* and *in vitro* that clinoptilolite preparations adsorb ohratoxin A, zearalenone, aflatoxin B1, B2, G2, T-2 toxin, ergosine, ergocristine, ergocryptine and ergometrine in feed [51, 52]. The proportion of adsorption by clinoptilolite particles of the toxins enumerated *in vitro* varies depending on the concentration of these toxins and can range up to 99%. The main mycotoxins adsorbed by Min-a-Zel Plus, modified clinoptilolite, are: aflatoxin B1–99%, zearalenone—94%, ochratoxin A—96% and ergot alkaloids—97% [51, 52]. In another study, T2 toxin—a secondary metabolite of *Fusarium fungi*—was adsorbed on average in 30% by Min-a-zel Plus, Mycosorb (esterified glucomanane) and mixed binder Mycofix (inorganic binder, bacteria, enzymes and phytogenic material extracted from plants) in *in vitro* conditions at pH 3 [53].

4. Adjuvant in anticancer treatment

The first studies of anticancer effect of zeolites were performed at the beginning of 2001 when it was observed that the treatment with clinoptilolite of different tumors in mice and dogs have improved their life span and tumors have decreased in size [54]. *In vitro* studies using cancer cell cultures revealed the clinoptilolite inhibitory effect on protein kinase B (B-Akt), which reduced the growth of cancer cells and increased their apoptosis. Inhibition occurred only in the presence of serum. This finding suggests that adsorption of serum components may be a possible mode of action. Adsorption of molecules involved in transduction signals, such as inositol, phosphatides and Ca, can contribute to its therapeutic efficacy. It also induces expression of tumor suppressor proteins, p21 WAF1/CIP and p27 KIP1, blocking the growth of cancer cell lines. It is assumed that clinoptilolite reduces the exchange rate of intestinal epithelial cells, prolonging their activity, and that silicates and aluminosilicates can interact directly with some cells by modifying their intracellular pathways, and this leads to the alterations in the regulation of gene expression. Changing the order of interaction of other proteins with membrane proteins may be involved, since membrane transport is required to activate protein kinase B [54]. Studies in mice injected i.v. with melanoma cells but receiving a micronized zeolite through gastric intubation for 28 days, revealed an increase in allogeneic graft versus host (GVH) in lymphocytes in the lymph nodes and a reduction in pulmonary metastases. The researchers' hypothesis is that the local inflammation caused by zeolite application, attracts peritoneal macrophages, and these cells in turn produce TNFα that stimulates spleen T-cells, which amplify the local inflammatory response [55]. Also, a reduction in the metabolic rate of cancer cells and a reduced production of 4-hydroxyinonenal following an anti-cancer treatment (Doxorubicin) along with tribomechanically micronized clinoptilolite, having in this way a potentiator effect on anticancer drugs, were reported [56].

In another *in vitro* study done on mouse fibrosarcoma cells and other types of cells incubated for 24 h together with clinoptilolite researchers observed that the number of viable cells, DNA synthesis and activity of EGF-R, PKB/Akt and NFKB was reduced while apoptosis was enhanced maybe because clinoptilolite affects cellular microenvironment through mechanisms that are dependent on its characteristics [57].

5. Effects on health status and growth performance

Clinoptilolite is also used as feed ingredient due to its beneficial properties as immunostimulant. One explanation of beneficial immune effects of silica, silicates and aluminosilicates could be their action as non-specific superantigen-like immunoglobulins (SAg). SAg are viral and bacterial toxins that are capable of activating a large population of T-cells. Activation occurs as a result of the simultaneous interaction between SAg, the T cell receptor (TcR) variable region β and the major histocompatibility complex (MHC) class II molecules on the surface of antigen presenting cells (APC). Consequently, SAg stimulates 10–30% of T-cells, as opposed to 0.01–0.0001% as it stimulates common antigens. Proinflammatory macrophages belonging to APC cells, CMH class II are activated by the particles of silicates [58].

An indirect action of clinoptilolite on the immune system is also achieved by its antioxidant capacity. Sverko et al. showed that administration of tribomechanically-activated clinoptilolite (12.5%) alone or together with *Urtica dioica* extract in mice *per os* for 3 weeks significantly reduced lipid peroxidation processes in the liver and significantly increased the content of superoxide-dismutase, an antioxidant enzyme. The antioxidant role of clinoptilolite is probably given by positive electrons that neutralize free radicals [59].

In weaned piglets that received 0.5% clinoptilolite for 5 weeks, it was observed that clinoptilolite was effective as an immunomodulatory agent by promoting the recruitment of circulating and intestinal immune cell subsets, even though it did not improve growth in weaned pigs, and generally failed to improve their feed conversion efficiency [60]; in heifers vaccinated against *Escherichia coli* (day 210 and 240 of gestation) the potentiating effect of clinoptilolite on the immune response was highlighted, and it indirectly improved the protection of calves [61].

In newborns, adding clinoptilolite to colostrum improves intestinal absorption of colostrum globulin, creating a good protection against neonatal diseases [18, 62–64].

Colostral period represents an important moment for the newborn ruminants, because in these species acquiring passive immunity is achieved exclusively through ingestion and absorption of adequate amounts of colostral immunoglobulins (Ig) [65]. Obtaining a good protection against neonatal diseases depends on how well this period is managed.

Scientific evidence highlights positive effects of zeolite supplementation on passive immunity [18, 21, 62] and on biochemical parameters [20, 23, 66] in newborns calves.

When we analyzed the effects of clinoptilolite supplemented in colostrum on blood serum protein electrophoretic pattern of newborn calves that received colostrum supplemented with 0.5 and 2% clinoptilolite, at 30 h after birth, the concentrations of γ-globulins, β-globulin and total protein in the group of calves that received 0.5% clinoptilolite (E1) were higher than in the control group by 42.11% ($p < 0.05$), 28.48% ($p > 0.05$) and 18.52% ($p > 0.05$), respectively, and were higher, but not significantly, in the group that received 0.5% clinoptilolite (E2), and a significantly lower albumin/globulin ratio in groups E1 and E2 (29.35%, $p < 0.05$

and 35.87%, $p < 0.05$, respectively) was reported, compared with the control group at 30 h postpartum, which indicates an obvious increase in globulin fractions in experimental groups. Clinoptilolite was effective in improving passive transfer in newborn calves, better if added in colostrum in a dose of 0.5% than in a dose of 2% (**Figure 2**) [67].

A possible way of clinoptilolite action is explained, based on observation in Wistar rats that received zeolite for 34 days (6% of their weight) [68]. Some modifications of intestinal cells were observed, such as: the microvilli length was higher (1.2 vs. 2.0), the number of microvilli per 10 μm was higher (54.4 vs. 64.8) their diameter was smaller (0.17 vs. 0.13) compared to the control group, and also that the cellular organisms of the enterocytes, the density of mitochondrial membranes and the number of attached ribosomes were higher, which indicates a rise in the adaptation processes of the cells [68].

In an experiment carried out in 20 newborn calves in order to observe the clinical effects of clinoptilolite added in colostrum (20 ml clinoptilolite/L colostrum) during the first three meals, we concluded that administration of zeolites appears to reduce the incidence of diarrhea because only two calves from experimental group had health problems, one had bronchopneumonia and the other digestive transit difficulties with symptoms appearing after 28 days (not in neonatal period) in comparison with the control group where all calves had diarrhea in the first 11 days of life. The other parameter, growth performance measured on day 0, 45 and 90 revealed that during the first 45 days body weight of calves treated with clinoptilolite was significantly higher compared with the group of calves receiving only colostrum (C) ($p < 0.0058$) (E1/C = +16.96%). This statistical difference at 45 days may be explained by the high number of calves from the control group suffering from health problems and this affected the daily gain. At 90 days, the difference between groups was not significant ($p < 0.1035$) (E2/C = +7.19%) [69, 70]. Similar results were obtained by Step et al. who found that body weight and average daily gain did not differ between treatment groups (clinoptilolite dosage was 0.5 and 2%) [23]. More

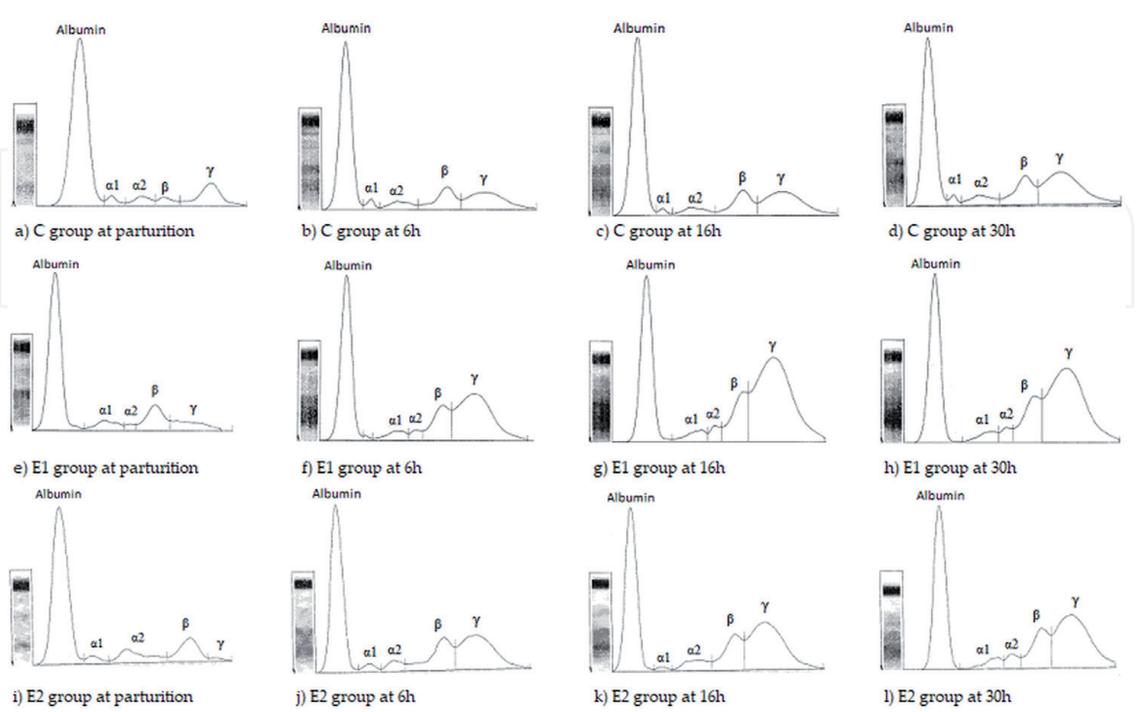


Figure 2.
Representative serum protein electrophoretograms observed in calves that received colostrum supplemented with 0.5% (e–h) and 2% clinoptilolite (i–l) compare with control group (a–d) at different time interval (0, 6, 16 and 30 h postpartum) [67].

recently, Ural et al. observed increased total weight and mean daily gain in calves that receive clinoptilolite (1 or 2 g/kg) in colostrum at calving, 12 and 24 h [71].

In another study, the addition of 0.5 g and 1 g/kg body weight per day in colostrum and milk for 45 days reduced fecal score and its severity, probably by retarding effect of clinoptilolite on intestinal passage rate [21]. The activity of clinoptilolite on reducing signs of diarrhea could be caused by: alteration of metabolic acidosis through effects on osmotic pressure in the intestinal lumen; or through retention of the enterotoxigenic *E. coli* thus limiting its attachment to the intestinal cell-membrane receptors); and also due to water adsorption property of zeolites, the feces appear drier and more compact [32].

In human medicine there are studies that support the beneficial properties of purified natural clinoptilolite as an anti-diarrheic treatment [72]. More recent studies performed on aerobically trained subjects, who received for 12 weeks zeolite-clinoptilolite supplementation, highlighted the positive effects of zeolites on intestinal wall integrity. The results were based on decreased concentrations of zonulin, an intercellular tight junction modulator, improving in this way intestinal barrier integrity [73].

Also, clinoptilolite improve antioxidant capacity in broilers [74]; it is used as a feed additive in fish diets [75] and in turkey diets [76].

Analyzing the effects of clinoptilolite on mineral parameters in newborn Romanian Black and White calves that received 5 g/l (group E1) and 20 g/l (group E2) at parturition, and 12 and 24 h postpartum, we observed that clinoptilolite supplementation increased serum Ca (with 37.34% in group E1, with 21.42% in group E2 in comparison with the control group and with 13.11% in E1/E2 at 30 h postpartum), P (with 37.34% in group E1, with 21.42% in group E2 in comparison with the control group and with 13.11% in E1/E2 at 30 h postpartum), Mg concentration (increased in groups E1 in comparison with the control group ($p < 0.003$) and E2 ($p < 0.009$) at 30 h postpartum in neonatal calves) with the most spectacular increase in iron concentration (with +144.70% in group E1 ($p < 0.0005$) and with +126.16% in group E2 ($p < 0.002$) at 30 h postpartum) [64].

When analyzing the same parameters in other breed (Holstein) and other colostrum quantity (3 L), we observed that the most significant effect ($p < 0.0006$) was on serum iron concentrations in experimental (27.64 ± 3.78 μmol/l) vs. control group (8.93 ± 1.26 μmol/l) and it did not have negative effects on other biochemical parameters (Ca, P, Mg, GGT, ALAT, ASAT, ALP) after 48 h postpartum, one more time proving that morpho-functional processes that take place in the newborns, necessary for adapting to the new environment, were not affected by clinoptilolite [63]. A possible explanation of increased iron level could be that in duodenum and in the anterior part of jejunum, where iron absorption takes place, clinoptilolite influences iron absorption due to the ion exchange properties, altering in this way the pH or reducing intestinal transit of digesta, which could lead to a better utilization of nutrients [32, 77]. It has been shown previously that low intestinal motility and acidic pH promote iron absorption and that in the bovine neonate, the pH of the whole intestinal content ranges from 5.5 to 6.5; also, the motility of the gastrointestinal tract becomes well organized only after 2–3 days of postnatal life [78, 79]. This feature could be important in preventing iron deficiency anemia (Fe < 14.32 μmol/l) especially in veal calves fed exclusively with milk.

Short term supplementation of clinoptilolite did not affect hepatic and renal function of newborn calves and that morpho-functional changes of the newborn organism in adapting to extrauterine environment were normal, without any influence of clinoptilolite, as observed after analyzing α-amylase, total bilirubin, creatinine, uric acid, urea, glucose, cholesterol and triglycerides. Biochemical values were measured in the first 48 h in the newborn calves. Values recorded were physiological

for the neonatal period and had no significant difference between groups, highlighting once more the safety of clinoptilolite in newborn nutrition [80].

The activity of the most important enzymes is changing very fast after the first feedings. We observed that adding clinoptilolite in the first three meals of colostrum influenced the enzymes as follows: GGT activity significantly increased in group E2 (20 g/L clinoptilolite) at 6 h after birth (E2/C: +64.83%, $p < 0.05$) and in group E1 (5 g/L clinoptilolite) at 16 h after birth (E1/C: +118.55%, $p < 0.05$) in comparison with the control group (C—received only mother colostrum); ALP increased after birth in all calves and adding clinoptilolite in colostrum influenced activity of ALP only in group E1 at 30 h postpartum; transaminases were low at birth in all calves but after feeding they increased, this coincided with the period when a morpho-functional condition of the liver is changing in a newborn calf; adding clinoptilolite (5 g/L colostrum) to colostrum determined increased ASAT (E1/C: +71.58%, $p < 0.01$) and ALAT (E1/C: +278.82%, $p < 0.006$) activity at 30 h postpartum [81]. As literature data suggests, serum GGT is the only enzyme to increase markedly as a result of its absorption from the colostrum; other serum enzymes, such as aspartate aminotransferase (ASAT) and alkaline phosphatase (ALP), are presumably released from the tissues of the calf [82]. A good interpretation of the serum enzyme activity in newborn calves must consider the physiological increase which occurs after feeding colostrum in the first days after parturition, a period very important for the calf but also for the cow [83].

6. Conclusion

Based on our research data and on continuously published literature data worldwide regarding the use of zeolites in veterinary medicine, we confirm that they can be used in animal nutrition as feed additives, mainly to reduce the gastrointestinal absorption of mycotoxins; in newborn calves, they can be used as enhancers of passive immunity during colostral period; also, to increase health status and growth performance of animals and as an adjuvant in anticancer treatment, with a promising perspective in this field.

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References

[1] Zimmermann NER, Haranczyk M. History and utility of zeolite framework-type discovery from data-science perspective. Crystal Growth and Design. 2016;**16**:3043-3048. DOI: 10.1021/acs.cgd.6b00272

[2] Georgiev D, Bogdanov B, Angelova K, Markovska I, Hristov Y. Synthetic zeolites—Structure, classification, current trends in zeolite synthesis review. In: International Science Conference "Economics and Society Development on the Base of Knowledge"; 4-5 June 2009; Stara Zagora, Bulgaria; Technical Studies; volume VII; pp. 1-5

[3] Mumpton FA. La roca magica: Uses of natural zeolites in agriculture and industry. Proceedings of the National Academy of Sciences. 1999;**96**:3463-3470

[4] Roth WJ, Nachtigall P, Morris RE, Cejka J. Two-dimensional zeolites: Current status and perspectives. Chemical Reviews. 2014;**114**:4807-4837. DOI: 10.1021/cr400600f

[5] International Zeolite Association [Internet]. Available from: http://www.iza-online.org/ [Accessed: 06 April 2019]

[6] European Union. Authorisation of Clinoptilolite Use as a Feed Additive [Internet]. Available from: https://www.ecolex.org/details/legislation/commission-implementing-regulation-eu-no-6512013-concerning-the-authorisation-of-clinoptilolite-of-sedimentary-origin-as-a-feed-additive-for-all-animal-species-and-amending-regulation-ec-no-18102005-lex-faoc125758/ [Accessed: 07 April 2019]

[7] FDA. U.S. Food and Drug Administration [Internet]. Available from: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=182.2727 [Accessed: 06 April 2019]

[8] Bernardi AC, Mota EP, SCH S, Cardoso RD, Peronti P, Oliviera A. Ammonia volatilization, dry matter and nitrogen levels of Italian ryegrass fertilized with urea and zeolite. In: 19th World Congress of Soil Science, Soil Solutions for a Changing World; 1-6 August. 2010. pp. 22-25

[9] Jakkula VS, Wani SP. Zeolites: Potential soil amendments for improving nutrient and water use efficiency and agriculture productivity. Scientific Reviews & Chemical Communications. 2018;**8**(1):119

[10] Karmen M, Natasa ZL, Siljeg M, Anamarija F. Natural Zeolites in Water Treatment—How Effective Is their Use. Intech; 2013. DOI: 10.5772/50738

[11] Wang S, Peng Y. Natural zeolites as effective adsorbents in water and wastewater treatment. Chemical Engineering Journal. 2010;**156**(1):11-24. DOI: 10.1016/j.cej.2009.10.029

[12] Yeritsyan H, Sahakyan A, Harutyunyan V, Nikoghosyan S, Hakhverdyan E, Grigoryan N, et al. Radiation-modified natural zeolites for cleaning liquid nuclear waste (irradiation against radioactivity). Scientific Reports. 2013;**3**:2900. DOI: 10.1038/srep02900

[13] Kotoulas A, Agathou D, Triantaphyllidou I, Tatoulis TI, Akratos CS, Tekerlekopoulou AG, et al. Zeolite as a potential medium for ammonium recovery and second cheese whey treatment. Water. 2019;**11**(1):13. DOI: 10.3390/w11010136

[14] Samardzioska T, Jovanovski M. Zeolites-sustainable building material. In: Proceedings of the 1st International Conference on

Construction Materials for Sustainable Future; Zadar, Croatia; 19-21 April. 2017. pp. 146-151

[15] Ming DW, Allen ER. Zeoponic substrates for space applications: Advances in the use of natural zeolites for plant growth. Natural Microporous Materials in Environmental Technology. 1999;**362**. DOI: 10.1007/978-94-011-4499-5_11

[16] Bish DL, Ming DW. Natural zeolites: Occurrence, properties, applications. Mineralogical Society of America, Reviews in Mineralogy. 2001;**45**:639. ISBN 1529-6466

[17] Dakovic A, Adamovic M, Tomasevic-Canovic M. Efficacy of organozeolite to ameliorate the toxic effects of zearalelone in lambs. Acta Veterinaria. 2004;**54**(1):53-62

[18] Fratric N, Stojic V, Jankovic D, Samanc H, Gvozdic D. The effect of a clinoptilolit based mineral adsorber on concentrations of immunoglobulin G in the serum of newborn calves fed different amounts of colostrum. Acta Veterinaria. 2005;**55**(1):11-21

[19] Katsoulos PD, Roubies N, Panousis N, Karatzias H. Effects of long-term feeding dairy cows on a diet supplemented with clinoptilolite on certain serum trace elements. Biological Trace Element Research. 2005;**108**(1-3):137-145. DOI: 10.1385/BTER:108:1-3:137

[20] Mohri M, Seifi HA, Maleki M. Effects of short-term supplementation of clinoptilolite in colostrum and milk on the concentration of some serum minerals in neonatal dairy calves. Biological Trace Element Research. 2008;**123**(1-3):116-123

[21] Sadeghi A, Shawrang P. Effects of natural zeolite clinoptilolite on passive immunity and diarrhea in newborn calves. Livestock Science. 2008;**113**(2-3):307-310. DOI: 10.1016/j.livsci.2007.08.010

[22] Speranda M, Liker B, Speranda T, Seric V, Antunovoc Z, Grabarevic Z, et al. Hematological and biochemical parameters of weaned piglets fed on fodder mixture contaminated by zearalenone with addition of clinoptilolite. Acta Veterinaria. 2006;**56**(2-3):121-136

[23] Step DS, Litherland NB, Burciaga-Roble O, Breshears M, Krehbiel CR, Confer AW, et al. Clinical observations, biochemical data and postmortem and histopathologic findings in young dairy calves fed zeolite clinoptilolite binder combined with milk replacer. American Journal of Veterinary Research. 2008;**69**(12):1587-1594

[24] Stojic V, Gvozdic D, Anna N, Samanc H, Jovanovic I, Magdalena T-C, et al. The serum levels of insulin and IGF-1 in newborn piglets treated with clinoptilolite. Acta Veterinaria. 2003;**53**(4):219-228

[25] Prasai TP, Walsh KB, Bhattarai SP, Milmore DJ, Van TTH, Moore RJ, et al. Biochar, bentonite and zeolite supplemented feeding of layer chickens alters intestinal microbiota and reduces Campylobacter load. PLoS One. 2016;**11**(4). DOI: 10.1371/journal.pone.0154061

[26] Schneider AF, Zimmermann OF, Gewehr CE. Zeolites in poultry and swine production. Animal Production. 2017;**47**(8). DOI: 10.1590/0103-8478cr20160344

[27] Burmańczuk A, Roliński Z, Kowalski C, Burmańczuk N, Markiewicz W. Possibilities of using the natural zeolites in animals production and environment protection. Journal of Elementology. 2014;**20**(4):803-811. DOI: 10.5601/jelem.2014.19.4.759

[28] Khachlouf K, Hamed H, Gdoura R, Gargouri A. Effects of zeolite supplement on dairy cow production and ruminal parameters—A review. Annals of Animal Science. 2018;**18**(4):857-877. DOI: 10.2478/aoas-2018-0025

[29] Valpotic H, Gracner D, Turk R, Duricic D, Vince S, Folnozic I, et al. Zeolite clinoptilolite nanoporous feed additive for animals of veterinary importance: Potentials and limitations. Periodicum Biologorum. 2017;**119**(3):159-172. DOI: 10.18054/pb.v119i3.5434

[30] World Health Organization [Internet]. Available from: https://www.who.int/news-room/detail/07-11-2017-stop-using-antibiotics-in-healthy-animals-to-prevent-the-spread-of-antibiotic-resistance [Accessed: 07 April 2019]

[31] Nistiar F, Mojžiš J, Kovac G, Seidel H, Rácz O. Influence of intoxication with organophosphates on rumen bacteria and rumen protozoa and protective effect of clinoptilolite-rich zeolite on bacterial and protozoan concentration in rumen. Folia Microbiologica. 2000;**45**:567-571

[32] Papaioannou D, Katsoulos PD, Karatzias H. The role of natural and synthetic zeolites as feed additives on the prevention and/or the treatament of certain farm animal diseases: A review. Microporous and Mesoporous Materials. 2005;**84**:161-170. DOI: 10.1016/j.micromeso.2005.05.030

[33] Ural DA, Erdoğan E, Toplu S, Ayan A. Application of oral clinoptilolite intended for prevention of giardiasis in goat kids. Kocatepe Veterinary Journal. 2017;**10**(3):158-163

[34] Deligiannis K, Lainas TH, Arsenos G, Papadopoulos E, Fortomaris P, Kufidis D, et al. The effect of feeding clinoptilolite on food intake and performance of growing lambs infected or not with gastrointestinal nematodes. Livestock Production Science. 2005;**96**(2-3):195-203

[35] Limin L, Champika S, Yeow JTW. Creatinine adsorption capacity of electrospun polyacrylonitrile (PAN)—Zeolite nanofiber membranes for potential artificial kidney applications. Journal of Applied Polymer Science. 2015;**132**:42418. DOI: 10.1002/app.42418

[36] Limin L, Yeow JTW. An adsorption study of indoxyl sulfate by zeolites and polyethersulfone-zeolite composite membranes. Materials & Design. 2017;**120**:328-335. DOI: 10.1016/j.matdes.2017.01.094

[37] Prelina B, Wardana J, Isyatir RA, Syukriyah Z, Wafiroh S, Raharjo Y, et al. Innovation of zeolite modified polyethersulfone hollow fibre membrane for haemodialysis of creatinine. Chemistry & Chemical Technology. 2018;**12**(3):331-336. DOI: 10.23939/chcht12.03.331

[38] Mumpton FA, Fishman PH. The application of natural zeolites in animal science and aquaculture. Journal of Animal Science. 1977;**45**:1188-1203

[39] Thilsing-Hansen T, Jorgensen RJ. Prevention of parturient paresis and subclinical hypocalcemia in dairy cows by zeolite A administration in the dry period. Journal of Dairy Science. 2001;**84**(3):691-693

[40] Thilsing-Hansen T, Jorgensen RJ, Enemark JMD, Larsen T. The effect of zeolite A supplementation in the dry period of periparturient calcium, phosphorus and magnesium homeostasis. Journal of Dairy Science. 2002;**85**(7):1855-1862

[41] Katsoulos PD, Panousis N, Roubies N, Christaki E, Arsenos G, Karatzias H. Effects of long-term feeding of a diet supplemented with

clinoptilolite to dairy cows on the incidence of ketosis, milk yield and liver function. The Veterinary Record. 2006;**159**(13):415-418

[42] Uyarlar C, Akkaya AB, Gultepe EE. Effects of yeast (*Saccharomyces cerevisiae*) and clinoptilolite administration on milk yield and some metabolic parameters in early lactation dairy cows. Journal of Turkish Veterinary Medical Society. 2018;**89**(1):3-10

[43] Alshannaq A, Yu JH. Occurrence, toxicity, and analysis of major mycotoxins in food. International Journal of Environmental Research and Public Health. 2017;**14**(6):632. DOI: 10.3390/ijerph14060632

[44] Aleksandra D, Magdalena T-C, Dondur V, Vujakovic A, Radosevic P. Kinetics of aflatoxin B1 and G2 adsorption on caclinoptilolite. Journal of the Serbian Chemical Society. 2000;**65**(10):715-723

[45] Safameher A. Effects of clinoptilolite on performance, biochemical parameters and hepatic lesions in broiler chickens during aflatoxosis. Journal of Animal and Veterinary Advances. 2008;**7**:4

[46] Miazzo R, Rosa CAR, De Queiroz Carvalho EC, Magnoli C, Chicchiera SM, Palacio G, et al. Efficacy of synthetic zeolite to reduce the toxicity of aflatoxin in broiler chicks. Poultry Science. 2000;**79**(1):1-6

[47] Goodarzi M, Modiri D. The use of clinoptilolite in broiler diet to decrease of aflatoxin effects. In: 2011 International Conference on Asia Agriculture and Animal; 13. 2011. pp. 38-43

[48] Nesic VD, Marinkovic DM, Nesic KD, Resanovic RD. Examination of the efficacy of various feed additives on the pathomorphologocal changes in broilers treated with T-2 toxin. Zbornnk Matice srpske za prirodne nauke. 2009;**116**:49-54. DOI: 10.2298/ZMSPN0916049N

[49] Rizzi L, Simioli M, Roncada P, Zaghini A. Aflatoxin B1 and clinoptilolite in feed for laying hens: Effects on egg quality, mycotoxin residues in livers, and hepatic mixed-function oxygenase activitites. Journal of Food Protection. 2003;**66**(5):860-865

[50] Katsoulos PD, Karatzi MA, Boscos C, Wolf P, Karatzias H. Field evaluation of clinoptilolite feeding efficacy on the reduction of milk aflatoxin M1 concentration in dairy cattle. Journal of Animal Science. 2016;**58**:24. DOI: 10.1186/s40781-016-0106-4

[51] Canovic MT, Dakovic A, Matijasevic S, Mihajlavic AR, Adamovic M, Stojsic D. Minazel plus—The efficient adsorbent for mycotoxins. Zbornik naucnih radova. 2003;**9**:343-351

[52] Minazel-plus [Internet]. Available from: www.patent-co.com [Accessed: 06 April 2019]

[53] Nesic VD, Ostojin MV, Nesic K, Resanovic RD. Evaluation of the efficacy of different feed additives to adsorbe T-2 toxin in vitro. Zbornnk Matice srpske za prirodne nauke. 2009;**116**:55-59. DOI: 10.2298/ZMSPN0916055N

[54] Pavelic K, Hadzija M, Bedrica L, Pavelic J, Dikic I, Katic M, et al. Natural zeolite clinoptilolite: New adjuvant in anticancer therapy. Journal of Molecular Medicine. 2001;**78**(12):708-720

[55] Pavelic K, Katic M, Sverko V, Marotti T, Bosnja B, Balog T, et al. Immunostimulatory effect of natural clinoptilolite as a possible mechanism ot its antimetastatic ability. Journal of Cancer Research and Clinical Oncology. 2002;**128**:37-44

[56] Zarkovic N, Zarcovik K, Kralj M, Borovic S, Sabolovic S, Blazi MP,

et al. Anticancer and antioxidative effects of micronized zeolite clinoptilolite. Anticancer Research. 2003;**23**(2B):1589-1595

[57] Katic M, Bosnjak B, Gall-Troselj K, Dikic I, Pavelic K. A clinoptiolite effect on cell media and the consequent effects on tumor cells in vitro. Frontiers in Bioscience. 2006;**1**(11):1722-1732

[58] Ivkovic S, Deutsch U, Silberbach A, Walraph E, Mannel M. Dietary supplementation with the tribomechanically activated zeolite clinoptilolite in immunodeficiency: Effects on the immune system. Advances in Therapy. 2004;**21**(2):135-147

[59] Sverko V, Sandra S, Balog T, Colic M, Tatjana M. Natural micronised clinoptilolite mixtures with *Urtica dioica* L extract as possible antioxidants. Food Technology and Biotechnology. 2004;**42**(3):189-192

[60] Valpotic H, Terzic S, Vince S, Samardzija M, Turk R, Lackovic G, et al. In feed supplementation of clinoptilolite favourably modulates intestinal and systemic immunity and some production parameters in weaned pigs. Veterinární Medicína. 2016;**61**(6):317-327. DOI: 10.17221/175/2015-VETMED

[61] Karatzia M. Effect of dietary inclusion of clinoptilolite on antibody production by dairy cows vaccinated against *Escherichia coli*. Livestock Science. 2010;**128**(1):149-153

[62] Fratrić N, Stojić V, Rajcić S, Radojičić B. The effect of mineral adsorbent in calf diet colostrum on the levels of serum immunoglobulin G, protein and glucose. Acta Veterinaria. 2007;**57**:169-180

[63] Marc Zarcula S, Mircu C, Bonca G, Kirovski D, Otava G, Ahmai-Khoie M, et al. Effects of clinoptilolite addition to colostrum on the concentration of serum proteins, minerals, enzyme activities in neonatal calves. Journal of Advances in Chemistry. 2014;**10**(2):2290-2296

[64] Zarcula S, Tulcan C, Cernescu H, Mircu C, Anca LN, Urian-Suesca RI, et al. Influence of clinoptilolite on some mineral parameters in neonatal calves. Lucrări Ştiinłifice Medicină Veterinară. 2011;**XLIV**(2):41-48

[65] Weaver DM, Tyler JW, Van Metre DC, Hostetler DE, Barrington GM. Passive transfer of colostral immunoglobulins in calves—Review. Journal of Veterinary Internal Medicine. 2000;**14**:569-577

[66] Samanc H, Danijela K, Adamovic M, Vujanac I, Natalija F, Prodanovic R. Effects of natural zeolite on body weight, weight gain, hematology and biochemical blood parameters in calves. Veterinarski Glasnik. 2008;**62**(3-4):153-166

[67] Marc S, Kirovski D, Mircu C, Hutu I, Otava G, Paul C, et al. Serum protein electrophoretic pattern in neonatal calves treated with clinoptilolite. Molecules. 2018;**23**(1278):1-9. DOI: 10.3390/molecules23061278

[68] Bgatova NP. Influence of long-term administration of naturally occuring sorbents on the ultrastructure of small intestine enterocyte in rats. Bulletin of Experimental Biology and Medicine. 1998;**6**:626-629

[69] Zarcula S. Research regarding immune status in newborn calves [thesis]. Romania: Banat's University of Agricultural Sciences and Veterinary Medicine "King Michael I of Romania" Timişoara; 2010

[70] Zarcula S, Cernescu H. Influence of clinoptilolite on health status in calf neonatal period. In: Proceedings of the XIth International Symposium "Young

People and Multidisciplinary Research"; 12-13 November 2009; Timişoara, România. 2009. pp. 195-200. ISSN: 1843-6609

[71] Ural DA, Ural K. Effects of short term clinoptilolite supplementation on weight gain in Holstein calves. Revista MVZ Córdoba. 2016;**22**(1):5631-5637. DOI: 10.21897/rmvz.923

[72] Rodriguez-Fluentes G, Barrios MA, Iraizoz A, Perdomo I, Cedre B. Enterex: Anti-diarrheic drug based on purified natural clinoptilolite. Zeolites. 1997;**19**(5-6):441-448

[73] Lamprecht M, Bogner S, Steinbauer K, Schuetz B, Breiberger JF, Leber B, et al. Effects of zeolite supplementation on parameters of intestinal barrier integrity, inflammation, redox biology and performance in aerobically trained subjects. Journal of the International Society of Sports Nutrition. 2015;**12**(40). DOI: 10.1186/s12970-015-0101-z

[74] Wu Y, Wu Q, Zhou Y, Ahmad H, Wang T. Effects of clinoptilolite on growth performance and antioxidant status in broilers. Biological Trace Element Research. 2013;**155**:228-235. DOI: 10.1007/s12011-013-9777-6

[75] Yildirim O, Turker A, Senel B. Effects of natural zeolite (clinoptilolite) levels in fish diet on water quality, growth performance and nutrient utilization of tilapia (*Tilapia zillii*) fry. Fresenius Environmental Bulletin. 2009;**18**(9):1567-1571

[76] Hcini E, Slima AB, Kallel I, Zormati S, Traore A, Gdoura R. Does supplemental zeolite (clinoptilolite) affect growth performance, meat texture, oxidative stress and production of polyunsaturated fatty acid of Turkey poults? Lipids in Health and Disease. 2018;**17**:177. DOI: 10.1186/s12944-018-0820-7

[77] Martin-Kleiner I, Flegar-Meštric Z, Zadro R, Breljak D, Stanović Janda S, Stojković R, et al. The effect of the zeolite clinoptilolite on serum chemistry and hematopoiesis in mice. Food and Chemical Toxicology. 2001;**39**:717-727

[78] Guilloteau P, Zabielski R, Blum JW. Gastrointestinal tract and digestion in the young ruminat: Ontogenesis, adaptations, consequences and manipulations. Journal of Physiology and Pharmacology. 2009;**60**:37-46

[79] Pârvu G. Animal Metabolic Surveillance. Bucharest, Romania: Ceres; 1992

[80] Marc Zarcula S, Tulcan C, Kirovski D, Samanc H, Mircu C, Bonca G, et al. Effects of short term addition of clinoptilolite to colostrum on some biochemical parameters in newborn calves. Lucrări Ştiinłifice Medicină Veterinară. 2013;**XLVI**(3):167-172

[81] Zarcula S, Tulcan C, Mircu C, Kirovski D, Samanc H, Cernescu C. Influence of clinoptilolite on some enyzmatic parameters in neonatal calves. In: Proceedings of the XIIth International Symposium "Young people and multidisciplinary research"; 11-12 November 2010; Timişoara, România. 2010. pp. 167-173. ISSN 1843-6609

[82] Boyd JW. Serum enzyme changes in newborn calves fed colostrum. Veterinary Clinical Pathology. 1989;**18**(2):47-51

[83] Andrei S, Groza IS, Pintea A, Ciupe S, Chirila F, Miclean M. Physiology and Pathology of the Mammary Gland in the Cow. Cluj: Academic Press; 2010. ISBN: 978-973-744-232-1