Available online at www.sciencedirect.com
SCIENCE DIRECT®
ELSEVIER
Microporous and Mesoporous Materials 84 (2005) 161–170
MICROPOROUS AND MESOPOROUS MATERIALS
www.elsevier.com/locate/micromeso

The role of natural and synthetic zeolites as feed additives on the prevention and/or the treatment of certain farm animal diseases: A review

D. Papaioannou, P.D. Katsoulos, N. Panousis *, H. Karatzias

Clinic of Productive Animal Medicine, School of Veterinary Medicine, Aristotle University of Thessaloniki, 541 24 Thessaloniki, Greece

Received 4 April 2005; received in revised form 12 May 2005; accepted 12 May 2005
Available online 28 June 2005

Abstract

The present review comments on the role of the use of zeolites as feed additives on the prevention and/or the treatment of certain farm animal diseases. Both natural and synthetic zeolites have been used in animal nutrition mainly to improve performance traits and, based on their fundamental physicochemical properties, they were also tested and found to be efficacious in the prevention of ammonia and heavy metal toxicities, poisonings as well as radioactive elements uptake and metabolic skeletal defects. During the last decade, their utilization as mycotoxin-binding adsorbents has been a topic of considerable interest and many published research data indicate their potential efficacy against different types of mycotoxins either as a primary material or after specific modifications related to their surface properties. Ingested zeolites are involved in many biochemical processes through ion exchange, adsorption and catalysis. Recent findings support their role in the prevention of certain metabolic diseases in dairy cows, as well as their shifting effect on nitrogen excretion from urine to faeces in monogastric animals, which results in lower aerial ammonia concentration in the confinement facilities. Moreover, new evidence provide insights into potential mechanisms involved in zeolites supporting effect on animals suffered from gastrointestinal disturbances, including intestinal parasite infections. All the proposed mechanisms of zeolites' effects are summarized in the present review and possible focus topics for further research in selected areas are suggested.

Keywords: Zeolites; Animal health; Prevention; Treatment

1. Introduction

Zeolites are crystalline, hydrated aluminosilicates of alkali and alkaline earth cations, consisting of three-dimensional frameworks of SiO_4^{4-} and AlO_4^{5-} tetrahedra linked through the shared oxygen atoms. Both natural and synthetic zeolites are porous materials, characterized by the ability to lose and gain water reversibly, to adsorb molecules of appropriate cross-sectional diameter (adsorption property, or acting as molecular sieves) and to exchange their constituent cations without major change of their structure (ion-exchange property) [1,2]. The exploitation of these properties underlies the use of zeolites in a wide range of industrial and agricultural applications and particularly in animal nutrition since mid-1960s [3].

Many researchers have proved that the dietary inclusion of zeolites improves average daily gain and/or feed conversion in pigs [1,4–13], calves [1,7], sheep [7,14–16], and broilers [17–19]. Zeolites also enhance the reproductive performance of sows [1,20,21], increase the milk yield of dairy cows [22,23] and the egg production of laying hens [24,25] and have beneficial effects on egg weight and the interior egg characteristics [24–26]. However, the extent of performance enhancement effects is related to the type of the used zeolite, its purity and

* Corresponding author. Tel.: +30 2310 994501; fax: +30 2310 994550.
E-mail address: panousis@vet.auth.gr (N. Panousis).

1387-1811/$ - see front matter © 2005 Elsevier Inc. All rights reserved.
doi:10.1016/j.micromeso.2005.05.030

Table 1
Proposed mechanisms involved in animals' performance promoting properties of the dietary use of zeolites

	Mechanisms
Ammonia binding effect	Elimination of toxic effects of NH_4^+ produced by intestinal microbial activity [8,10]
Fecal elimination of *p*-cresol	Reduction of the absorption of toxic products of intestinal microbial degradation, such as *p*-cresol [27]
Retarding effect on digesta transit	Slower passage rate of digesta through the intestines and more efficient use of nutrients [1,25,28]
Enhanced pancreatic enzymes activity	Favorable effect on feed components hydrolysis over a wider range of pH, improved energy and protein retention [29,30]
Aflatoxin sequestering effect	Elimination of mycotoxin growth inhibitory effects [31–37]

physicochemical properties, as well as to the supplementation level used in the diets. Besides, the particle size of the zeolitic material, crystallite size and the degree of aggregation, as well as the porosity of individual particles determine the access of ingesta fluids to the zeolitic surface during passage across gastrointestinal tract and strongly affect its ion exchange, adsorption and catalytic properties. Table 1 summarizes the possible mechanisms by which zeolites may exert their performance promoting properties in farm animals.

Apart from the positive effects on animals' performance, dietary supplementation of zeolites appears to represent an efficacious, complementary, supportive strategy in the prevention of certain diseases and the improvement of animals' health status. The aim of the present review article is to address the data concerning the influence of the in-feed inclusion of natural and synthetic zeolites on certain diseases of farm animals, to summarize the proposed mechanisms of zeolites' effects and to suggest possible focus topics for further research in selected areas.

2. Ameliorative effect on the consequences of mycotoxicoses

In the recent years, high incidence rates of contamination of cereal grains and animal feed with mycotoxins are reported worldwide [38]. One of the latest approaches to this global concern has been the use of nutritionally inert adsorbents in the diet that sequester mycotoxins, thus reducing intestinal absorption and, additionally, avoiding toxic effects for livestock and the carry-over of toxin compounds to animal products. For this purpose, phyllosilicates such as hydrated sodium calcium aluminosilicates (HSCAS) and bentonite—which consist of layered crystalline structures and possess similar physicochemical properties with zeolites—have been first used successfully in poultry, pig, sheep, cattle and laboratory animals [33,34,39–47].

Apart from phyllosilicates, the use of zeolites has shown, lately, very promising results as well. In general, adsorption process on binders is strongly related to charge distribution, pore dimensions and accessible surface area of the adsorbent, as well as to polarity, solubility and molecular dimensions of the certain mycotoxin which is to be adsorbed [46]. Molecular sizes of aflatoxins range from 5.18 Å (B_1 and B_2) to 6.50 Å (G_1 and G_2) and only zeolites with entry channels wide enough to permit the diffusion of aflatoxin molecules to the intracrystalline structure are capable of demonstrating a clear sequestering effect. Clinoptilolite, a natural zeolite, has high adsorption indexes in vitro, more than 80%, for aflatoxins B_1 [48,49] and G_2 [48] and the adsorption process begins with a fast reaction whereby most of the toxin is adsorbed within the first few minutes [48]. On the contrary, Lemke et al. [50] conducted a variety of in vitro adsorption studies and reported a limited degree of clinoptilolite ability to bind aflatoxin B_1 effectively. According to them, adsorbent materials should be checked through a multi-tiered system of in vitro tests in order potential interactive factors, such as intestinal physicochemical variables and feed components, to be precluded. Indeed, a previous in vitro study had demonstrated average aflatoxin retention in natural zeolites of 60%, but also a nitrogen compound-related adsorbent effectiveness, when liquid media quality parameters had been taken into account [51]. The in vivo efficacy of zeolites to ameliorate the consequences of aflatoxicosis, mainly in poultry, has also been verified in many cases (Table 2).

In the case of phyllosilicates, the results of in vitro mycotoxin–clay interaction tests suggest the existence of areas of heterogenous adsorption affinities onto surface, the presence of different adsorption mechanisms or both [57]. Nevertheless, the formation of strong bonds by chemisorption and the interaction of β-carbonyl group of aflatoxin B_1 with the uncoordinated edge site aluminum ions in these adsorbents have been suggested as the binding mechanism which interprets their well-established high affinity for aflatoxin B_1 [39,58,59]. Although the exact binding mechanisms of zeolites on aflatoxins have not been determined the possibility to act through similar with phyllosilicates mechanism cannot be precluded and should be investigated.

As far as other mycotoxins are concerned, mineral adsorbents exert a lower efficacy against mycotoxins containing less polar functional groups, which are required for efficient chemisorption on hydrophilic negatively charged mineral surfaces to occur. This limitation can be overcome by the use of chemically modified clays. Modifications consist of alterations of

Table 2
In vivo studies concerning the effect of the dietary use of zeolites during aflatoxicoses

Type of zeolite	Dietary inclusion rate (%)	Animal model	Observations
Clinoptilolite	1	Broilers	Growth depression caused by 2.5 ppm aflatoxin (afl) was alleviated by 15% [31]
Clinoptilolite	5	Geese	Prophylactic effect on growth rate and liver enzymatic activity [32]
Mordenite	0.5	Broilers	Reducing effect on toxicity of afl (3.5 mg kg^{-1} diet) as indicated by weight gain and changes in uric acid and albumin concentrations [33]
Clinoptilolite	0.5	Weaned piglets	Growth inhibitory effects and alterations of liver enzyme activity induced by 500 ppb afl were prevented [34]
Synthetic zeolite	0.5	Broilers	No significant effect on biochemical or haematological indexes when administered simultaneously with 2.5 mg afl kg^{-1} diet [52]
Clinoptilolite	0.5	Pregnant rats	No effect on maternal and developmental toxicities of afl (2 mg kg^{-1} body weight) [53]
Clinoptilolite	5	Quail chicks	Growth inhibitory effects of 2 mg kg^{-1} diet diminished by 70% [35]
Clinoptilolite	1.5	Broilers	Growth inhibitory effects of 100 ppb afl diminished over a study period of 42 days [36]
Clinoptilolite	1.5–2.5	Broilers	Adverse effects of 2.5 mg kg^{-1} diet on biochemical and haematological profiles were reduced [54]
Zeolite NaA	1	Broilers	Protection against growth inhibitory effects of 2.5 mg kg^{-1} diet [37]
Clinoptilolite	1.5–2.5	Broilers	Moderate to significant decrease of incidence and severity of certain target-organs degenerative changes induced by 2.5 mg afl kg^{-1} diet [55]
Clinoptilolite	2	Laying hens	Significant decrease in liver mycotoxin concentration and liver weight during aflatoxicosis caused by 2.5 mg kg^{-1} diet [56]

surface properties resulting in an increased hydrophobicity, by exchange of structural charge-balance cations with high molecular weight quaternary amines. In vitro results have verified the binding efficacy of modified montmorilonite and clinoptilolite against zearalenone and ochratoxin A [60,61]. However, naturally occurring clays also exert a moderate binding efficacy against mycotoxins, other than aflatoxins, as evidenced for zearalenone and ochratoxin A by in vitro [57] and field trials [62,63], as well as for cyclopiazonic acid in experiments with broilers [45].

Remarkable conclusions related to zeolites' efficacy against zearalenone toxicosis have also been drawn by in vivo studies. Feeding zearalenone to rats, Smith [64] demonstrated that the dietary use of a synthetic anion exchange zeolite could alter the faecal and urinary excretory patterns of zearalenone due to the elimination of its intestinal absorption. Recently, the dietary use of a clinoptilolite-rich tuff was also effective in decreasing zearalenone and α-zearalenole excretion in pigs fed diets contaminated with 500 ppb zearalenone [65]. Additionally, in a field-case of zearalenone toxicosis with mean concentrations of 660 ppb, Papaioannou et al. [20] reported that the supplementation of a clinoptilolite rich tuff at the rate of 2% in the ration of pregnant sows implied a rather protective role against the consequences of zearalenone ingestion, as evidenced by the improvement of indicative performance traits. Similar results were also obtained in swine with the dietary use of a modified clinoptilolite–healandite rich tuff at 0.2% and with zearalenone concentration exceeding 3.5 ppm [66].

Apart from surface interactions, the in vivo efficacy of mineral adsorbents against zearalenone could also result from other implicating mechanisms. The entero-hepatic circulation of zearalenone and its derivatives in pigs retards their elimination and enhances the duration of adverse effects [67]. Whether certain types of zeolites are able to affect the entero-hepatic cycling of zearalenone, thus counteracting the toxic effects of its biological action, is a hypothesis that awaits further research, although there is evidence of Ca-enriched clinoptilolite's high affinity to the bile acids in the intestinal tract [68].

3. Supportive effect on diarrhoea syndrome

There is an abundance of published data which indicate that the dietary use of natural zeolites reduces the incidence and decreases the severity and the duration of diarrhoea in calves [1,69–72] and pigs [1,5,13,72–75]. The exact mechanism of zeolites' effect is not quite clear so far, although there is evidence that the use of zeolites may eliminate various predisposing and/or causative factors which are associated in the culmination of intestinal disturbances in an interactive way. Apart from zeolites' retarding effect on intestinal passage rate [1] and their water adsorption property, which leads to the appearance of drier and more compact faeces, as in the case of phillipsite [75] or clinoptilolite [76], Vrzgula et al. [71] also proposed that the ameliorative effect on diarrhoea syndrome of calves might result from either the alteration of metabolic acidosis, through effects on osmotic pressure in the intestinal lumen, or the increased retention of the enteropathogenic *Escherichia coli*. As far as we know, there is no evidence in the available literature for retention of enteropathogenic *E. coli* on the outer surface of zeolite particles. However, clinoptilolite and mordenite are capable to adsorb and partially inactivate the thermo-labile (LT) *E. coli* enterotoxin in vitro, thus constricting its attachment to the intestinal cell-membrane receptors [77]. Furthermore, the adsorption capacity of clinoptilolite and mordenite has been proved to be higher than 94% for virions of bovine rotavirus and coronavirus, although infectivity level of zeolite–virus complex seems to remain unchanged [78]. Interactions among virions and the outer surface of adsorbent particles have been proposed, since the former have dimensions considerably larger (60–80 nm and 60–220 nm for rota- and coronavirus particles, respectively) than the entry channels of the aforementioned zeolites.

In a more recent study of Rodrigues-Fuentes et al. [68], dealing with the development and the properties of an anti-diarrhoeic drug for humans based on clinoptilolite, zeolite had no effect on rate of passage of ingesta, neither acted as a water adsorbent. Instead, they proposed that the anti-diarrhoeic effect of clinoptilolite is due to the adsorption of (i) bile acids, "one of the endogenic causes of diarrhoea", (ii) aflatoxin B_1, "a mycotoxin that produces severe toxicity in animals and humans" and (iii) glucose, "whose high content in intestinal fluid acts as an irritant factor and whose transport through the intestinal cells is reversed during diarrhoea".

Concerning the newborn animals, the administration of zeolites appears to reduce the incidence of diarrhoea through the enhancement of passive immunity, as they increase the net absorption of colostrum immunoglobulins in calves [71,79,80] and pigs [81].

Intestinal hypersensitivity to feed antigens or the malabsorption syndrome, induced by a low enzyme activity, can both predispose to post-weaning infectious enteritis in pigs. According to Papaioannou et al. [13], clinoptilolite has the ability to adsorb dietary substances, which may result in intestinal hypersensitivity phenomena [82], or to support the maintenance and even the restoration of the digestive enzyme activity in newly weaned piglets. This should also be evaluated in future studies as an additional explanation for clinoptilolites' minimising effect on diarrhoea syndrome.

4. Prevention of metabolic diseases in dairy cows

Milk fever and ketosis are of the most common metabolic diseases in high producing dairy cows. In the recent years, a number of experiments have been conducted in order to control these diseases using zeolites as feed additives. The results of these experiments are very promising but further investigation is required to define the exact mechanisms of zeolites' action.

4.1. Milk fever

Initially, a series of experiments has been conducted in order to study the potential use of synthetic zeolite A for the prevention of milk fever in dairy cows. The objective of these experiments was to reduce the bioavailability of dietary Ca in the gastrointestinal tract by the administration of synthetic zeolite A, based on the evidence that one of the best ways to prevent milk fever is to feed cows with low calcium diets during the dry period [83–87]. The results obtained were satisfactory as the administration of synthetic zeolite A, either as an oral drench or supplemented to the total mixed ration, during the dry period reduced the bioavailability of dietary Ca and efficiently protected against milk fever, by stimulating Ca-homeostatic mechanisms prior to parturition [88–93]. Furthermore, Thilsing-Hansen et al. [92] proposed that the best ratio zeolite/Ca for the prevention of milk fever was 10–20 and that zeolite had the same efficiency either administrated for the last 4 or 2 weeks of the dry period.

More recently, Katsoulos et al. [94] showed that clinoptilolite was effective in the prevention of milk fever as well. The incidence of milk fever was significantly lower in cows that were receiving a concentrate supplemented with clinoptilolite at the level of 2.5% (5.9%) during the last month of the dry period and the onset of lactation compared to the animals in the control group (38.9%), which were not receiving clinoptilolite, whereas was not significantly different than those that were receiving 1.25% clinoptilolite (17.6%) with the concentrates at the same period. The authors suggested that clinoptilolite might have had similar effect with zeolite A in activating Ca homeostatic mechanisms prior to parturition. As a consequence, the animals receiving 2.5% clinoptilolite responded faster and more efficiently in the drop of serum Ca observed at the day of calving and did not show any clinical signs of milk fever the following days. However, the exact mechanism for this positive effect of clinoptilolite is currently unknown and should be further investigated.

4.2. Ketosis

The best strategy to prevent ketosis in dairy cows is to improve the energy uptake both in the dry period and the onset of lactation [95]. According to Katsoulos et al. [23], the use of clinoptilolite has been shown to be effective in improving the energy balance at this critical period as they observed that feeding dairy cows on a diet supplemented with clinoptilolite at the level of 2.5% of the concentrate feed, resulted in significantly lower incidence of ketosis (5.9%) during the first month after parturition, compared to the control group (38.9%) and the group of the animals receiving a concentrate supplemented with 1.25% clinoptilolite (35.3%). These researchers suggested that clinoptilolite improved the energy status of the cows, either via prepartum enhancement of propionate production in rumen or through the improvement of the post-ruminal digestion of starch.

5. Protective role in intoxications and poisonings

5.1. Ammonia toxicity

White and Ohlrogge [96] first stated that ammonium ions formed by the enzyme decomposition of non-protein nitrogen were immediately ion exchanged into the zeolite structure and held there for several hours until released by the regenerative action of Na^+, entering the rumen in saliva during the after-feeding fermentation period. From both in vitro and in vivo experiments they found that up to 15% of the NH_4^+ in the rumen could be taken up by the zeolite. These observations were the causation for the conduction of many experiments in order to determine the influence of zeolites on rumen NH_4^+ concentration and their potential use for the counteraction of the toxic effects of urea inclusion in ruminants' rations.

Hemken et al. [97] showed that supplementation of 6% clinoptilolite, in the ration of dairy cows containing urea, significantly reduced rumen NH_3 concentration. The same trend was observed by the dietary addition of 5% clinoptilolite in steers [98] and lambs [99]. Furthermore, clinoptilolite was effective in reducing rumen ammonia concentration even when no urea was present in the ration of steers receiving a high concentrate diet, and that this reduction was linearly associated to the percentage of clinoptilolite inclusion [100]. Nestorov [101] referred that simultaneous administration of clinoptilolite and urea in sheep protects rumen flora from toxic effects of ammonia by inhibiting the reduction of microbiota population.

In contrast to the former observations, Bergero et al. [102] and Bosi et al. [103] found that daily administration of 250 g or 200 g of clinoptilolite, respectively, in dairy cows did not affect rumen NH_4^+ concentration. The same result had the dietary inclusion of 2% synthetic zeolite A in dairy cows ration [104] and 5% clinoptilolite in steers receiving a high roughage diet [98].

The binding of NH_4^+ to zeolites has been noted in pigs as well, and many researchers suggested this action as the possible mechanism for the observed improved performance of the animals receiving zeolites. There are evidences that clinoptilolite elevates nitrogen excretion in feces [8,105] and reduces the ammonia concentration in blood serum [8,10,106], when supplemented to the basal diets of pigs. Furthermore, Pond et al. [10] and Yannakopoulos et al. [12] found that clinoptilolite reduced the weight of the organs involved in the metabolism of ammonia (liver and kidneys), as the consequence of the reduced ammonia concentration in the gastrointestinal tract. Such observations result from the direct binding of NH_4^+ to zeolites, as clinoptilolite has no adverse effect on the ureolytic bacteria of the large intestine and urease activity [107].

5.2. Organophosphate poisoning

The dietary use of clinoptilolite appears to be effective in the prevention of organophosphates poisoning. Experiments in sheep have shown that the oral administration of clinoptilolite at the dose of 2 g/kg of body weight, earlier or simultaneously with an organophosphate (VX), partially protects from poisoning by inhibiting the decrease in cholinesterase activity [108] and by protecting rumen flora [109]. The protective effect of clinoptilolite on cholinesterase activity has been observed in mice receiving higher doses of organophosphates as well [110,111].

5.3. Heavy metal toxicity and adsorption of radioactive elements

Zeolites, due to their high ion-exchange capacity, have been used effectively for the prevention of heavy metal toxicity in animals. Pond et al. [112] found that clinoptilolite protects growing mice from lead (Pb) toxicity when added to their ration in such quantities that the ratio clinoptilolite/Pb to be 10/1. According to Pond et al. [113], similar protection is provided in swine as well. The selectivity of clinoptilolite for cadmium (Cd) and Pb has been studied in vitro in order to be investigated whether its use reduces the levels of these elements in rumen and abomasal fluid. The experiments showed that clinoptilolite bent the 91% of Pb and the 99% of Cd in rumen fluid within 24 h, and in the abomasal fluid the 94% of Pb within less than 1 h [114]. The toxic effects of long-term ingestion of Cd (100 ppm $CdCl_2$) on female rats and their progeny were not diminished by the simultaneous feeding of a clinoptilolite-rich tuff at 5% in the diet [115]. Adversely, the efficacy of clinoptilolite against Cd toxicity has been proved in pigs by the same authors who observed that 3% clinoptilolite supplementation prevented the cadmium-induced iron deficient anemia in growing swine that were receiving 150 ppm $CdCl_2$ [116]. The results of these experiments suggest the feasibility of using zeolites and mainly clinoptilolite as a feed additive in the prevention of certain types of heavy metal intoxications in farm animals or in aquatic biological systems, as is the case in the study of Jain [117], where is ascertained the capacity of zeolite to enhance the removal of Pb from water, thus decreasing its availability to the teleost fish Heteropneustes fossilis.

Apart from heavy metals, zeolites can also bind radioactive elements, thus being suggested as a means of altering their uptake and excretion from the body. Zeolitic matrix exchanges radio-nuclides in the gastrointestinal tract and is excreted by normal processes, thereby eliminating radioactive elements' assimilation into the body. Arnek and Forsberg [118] proved the selectivity of some natural zeolites such as clinoptilolite, chabazite and modernite for cesium and Gomonaj et al. [119] the selectivity of clinoptilolite for strodium and zirconium. Phillippo et al. [120] showed that the dietary use of clinoptilolite may constitute a simple and cost-effective method for minimizing the adsorption of radioactive cesium by sheep grazing contaminated pastures, although there might be no effect on cesium already been built-up in the body due to a previous exposure. Furthermore, Forsberg et al. [121] observed that the administration of mordenite in sheep and goats increased the excretion of cesium with feces and reduced its accumulation in tissues. On the other hand, Rachubik and Kowalski [122] demonstrated that synthetic zeolite-enriched diets exerted an inconsistent pattern of radiostrontium assimilation in the bone tissue and liver or kidneys of rats intragastrically dosed with an aqueous solution of $^{90}SrCl_2$.

5.4. Copper toxicity

Ivan et al. [123] observed that the inclusion of bentonite, a phyllosilicate, in the ration of sheep at the rate of 0.5% significantly reduced the Cu concentration in liver and suggested the use of this material in order to prevent copper poisoning. In contrast, clinoptilolite does not seem to be effective, as Pond [124] found that the addition of 2% clinoptilolite to the basal diet of sheep containing 10 or 20 ppm Cu did not protect against the toxic signs of Cu and increased the mortality in lambs fed the diet with 20 ppm Cu. A lack of any effect on liver Cu accumulation was also found in growing pigs which were on diets supplemented with 0.5% synthetic zeolite A and 250 ppm Cu [125]. Clinoptilolite was expected to exchange Cu in the lumen of the intestine, thereby decreasing the toxicity of excess Cu for sheep, whose tolerance for Cu is low compared with that of other food animals. However, such action was not observed probably due to a shift in ion-exchange relative to Cu and NH_4^+ or to some other complex interaction, which resulted in a net increase in Cu available for absorption from the intestinal tract [124]. The optimum ratio of clinoptilolite to Cu in the diet for reducing the intestinal absorption of the latter has not been determined, but such information, according to Pond [126], is needed in order to establish appropriate levels of dietary clinoptilolite supplementation.

6. Impact on parasite infections

Considering the potential efficacy of zeolites against parasite infections, the results of the experiments first conducted in rats were encouraging for their use in other animal species as well. According to Wells and McHugh [127], the administration of clinoptilolite at the rate of 10% of a conventional diet facilitated the removal of parasites from the intestinal lumen of rats infected with the nematode *Nippostrongylus brasiliensis*. Furthermore, Wells and Kilduff [128] observed a more accelerated intestinal α-D-glucosidase and aminopeptidase activity restitution in rats fed a commercial diet supplemented with clinoptilolite (5%) and recovering from *N. brasiliensis* infection. Confirming the observations in rats, Deligiannis et al. [129] recently proved the efficacy of clinoptilolite against parasite infections in growing lambs. They showed that feeding lambs, primarily infected with a single dose of gastrointestinal (GI) nematodes, with a concentrate mixture containing 3% clinoptilolite significantly decreased their total worm burden and faecal egg counts per capita fecundity and demonstrated that clinoptilolite supplementation reduced the establishment of GI nematodes and resulted in a good performance of the animals.

Interestingly, zeolites have also been tested as anthelmintic loaded carriers, through retarding drug release and prolonging its therapeutic action. Sustained-release mechanism implies a slow desorption of the drug molecules from the external surface and the internal zeolitic cavities, as they are progressively replaced by host proteins and water molecules, respectively, during the intestinal transport of the drug-zeolite compound. Promising results were obtained, at first, as regards tetramisole-loaded synthetic zeolite Y [130] and recently, pyrantel- and fenbendazole-loaded synthetic zeolite Y in rats infested with *N. brasiliensis* and dichlorvos-loaded zeolite Y in pigs infected with *Ascaris suum* [131]. In the case of tetramisole and dichlorvos, anthelmintic molecules are small enough to fit through the entry channels of zeolite Y (windows of 7.4 Å), while fenbendazole loading requires an initial partial dealumination of the zeolitic carrier and large pyrantel molecules allow only outer surface loading to occur.

7. Prevention of metabolic skeletal defects

The dietary inclusion of synthetic zeolite A (at the rates of 0.75% or 1.5%) in broilers which are on a diet with inadequate or marginal levels of calcium results in an increase of bone ash content along with a reduction of rachitic lesions [132]. Accordingly, the incorporation of zeolite A in the same diets at 1% exerts a clear beneficial effect in reducing the incidence of tibial dyschondroplasia [132–134]. Although tibial dyschondroplasia is a metabolic cartilage disease which represents the endpoint of several mechanisms, the incidence is increased when high dietary levels of phosphorus are used [135] or when dietary calcium is lower than 0.85% [136]. Similarly, the beneficial effect of zeolite A is inconsistent and largely depends on the dietary level of calcium. According to Watkins and Southern [137], the dietary use of 0.75% zeolite A in broilers is accompanied by alterations in mineral absorption and tissue distribution, resulting in increased tibia ash and density and improved fresh tibia shearing force scoring, but only when dietary calcium ranges from 0.6% to 0.8%. In the same direction, the reduction in the incidence and severity of dyschondroplastic lesions in the research of Edwards [134] in broilers was associated with a zeolite-induced decrease in calcium, total phosphorus and, in particular, phytate phosphorus retention.

8. Potential interaction with drugs

One of the major concerns that arise from the dietary use of zeolites is whether they have any adverse influence on the effectiveness of various medicaments when they are simultaneously administrated to the animals via feed and many experiments have been conducted lately in this area. Indeed, zeolites' non-specific adsorption property and cation exchange capacity could raise potential risks concerning the availability of medicaments used in on-farm strategic medication programmes for performance enhancement and health status preservation. Even if the cross-sectional diameter of a drug molecule is incompatible with the entry channels of the zeolitic structure—in this case being unable to pass through and being adsorbed on inner surfaces of the zeolitic matrix—the aforementioned consideration cannot be precluded since the external surface of the zeolitic particles is also offered for potential drug–zeolite interactions [138,139].

Rodriguez-Fuentes et al. [68] tested the potential interference of a natural zeolite with the bacteriostatic effect of tetracycline and chloramphenicol used in minimum inhibitory doses. The simultaneous presence of clinoptilolite–heulandite enriched zeolite and antimicrobials in Vibrio cholerae serotype 01 cultivations did not ameliorate the total inhibition of bacteria growth. Adversely, in vitro studies conducted by the same authors indicated that the zeolitic material slightly adsorbs theophyline, propanolole and phenobarbital. Interestingly, Lam et al. [139] demonstrated, through quantum mechanical calculations, the possibility of the adsorption of metronidazole on clinoptilolite and suggested that the principal interaction stands at the formation of hydrogen bonds and coulombic forces among groups of the metronidazole molecule and the external surface of the zeolitic matrix. However, in experiments which were carried out in aqueous medium simulating pH and temperature conditions of human gastrointestinal tract, the adsorptive behaviour was basically related to the zeolite's level of purification, as in the case of metronidazole, and moreover to the polarity of the molecules, since no interference with sulfamethazole was confirmed [140]. Both antimicrobials have molecule dimensions which are too large to enter the channels of the natural clinoptilolite used in these experiments, implying that potential interactions concern the outer surface of the zeolite, including the mesoporosity. However, the amphoteric character shown by natural zeolites as a consequence of their bufferant behaviour in an aqueous solution, suggests that they could attenuate the side effects derived from gastrointestinal sharp pH changes, favouring the absorption of some simultaneously administered drugs.

Furthermore, the potential interaction of clinoptilolite and antimicrobials was also tested in field studies. From a clinical point of view, the study of Papaioannou et al. [13] established the absence of any interactive effect of clinoptilolite on the availability of chlortetracycline in sows which were on a diet supplemented with both additives, since the beneficial effect of chlortetracycline (800 mg/kg feed) on the sow's health status during lactation was not inhibited by the concurrent use of clinoptilolite (2% inclusion rate). Similar results, concerning health status and performance evaluation, were also obtained in weaned, growing and finishing pigs fed diets supplemented with a clinoptilolite-rich tuff (at a rate of 2%) along with enrofloxacin (50 mg/kg of starter feed) or salinomycin (60 and 30 mg/kg of growers' and fatteners' feed, respectively) [20]. An additive net effect or an "enhanced-by-clinoptilolite" enrofloxacin efficacy was also proved in the case of post-weaning diarrhoea syndrome, supporting the results of a previous research [141], in which the concurrent use of a clay and lincomycine in the starter diet resulted in an additive net effect on the improvement of feed efficiency.

9. Elimination of gas pollutants in confinement facilities

Natural zeolites have been used as an effective tool in several wastewater treatment technologies. Laboratory studies verified that the addition of clinoptilolite- and phillipsite-rich tuffs in pig and cattle fresh slurry mixtures, respectively, could offer an effective mean of trapping the ammoniac nitrogen during composting and consequently reducing ammonia emissions [142,143]. Given the high ammonium and ammonia adsorption capacities of the zeolites, some researchers focused their studies at the evaluation of the effect of the dietary use of zeolites on environmental stressors, such as aerial ammonia, recognized to contribute to persistent health problems under intensive rearing conditions.

Ma et al. [144] reported that the incorporation of a zeolitic-tuff in the basal diet of finishing pigs at the inclusion rate of 5% had a favorable deodorizing effect and resulted in a lower aerial ammonia concentration by 28.5%. Furthermore, studies in growing pigs by Barrington and El Moueddeb [145] established the effectiveness of the same dietary scheme in reducing nitrogen volatilization and ammonia emission by 21%, while Saoulidis et al. [146] demonstrated that the dietary use of a clinoptilolite-rich tuff at the supplementation rate of 2% was accompanied by a reduction of 27.1% and 21.3% in aerial ammonia level of growing and finishing pig facilities, respectively. According to them, a possible mode of action by which zeolites exert their beneficial effect on aerial ammonia level, could be the shifting of the nitrogen excretion from urine to faeces and the consequent reduction of urea excretion, the main organic source of ammonia. Previous published data [105] are also confirmatory to this hypothesis.

10. Conclusions

Natural and synthetic zeolites have been extensively used in animal nutrition as performance promoters and, since early-1980s, several works have been published demonstrating that their use additionally exerts various favorable effects on the prevention and/or treatment of certain farm animal diseases. In the case of mycotoxicoses, their applicability as binders against polar toxins, such as aflatoxins, has been verified by in vitro and consequently in vivo studies, though the results obtained were characterized by inconsistency in many cases. Latest trends are directed to the in vitro prescreening of candidate zeolitic sorbent materials through a multi-tiered analysis system which will reassure the selection of the most potentially efficacious sorbent for further in vivo evaluation and will elucidate several gastrointestinal and feed factors which may interact with chemisorption process. As regards less polar mycotoxins such as zearalenone and ochratoxin A, innovative derivative zeolitic adsorbents with high binding capacity have been developed, according to chemical modifications related to increased surface hydrophobicity.

The physicochemical properties of ingested zeolites may result in intestinal lumen or even systemic effects affecting the biochemical processes, many of which are related to ion exchange, adsorption and catalysis. From this standpoint of view, recent research efforts provide insights into theoretical mechanisms interpreting the supportive effect of the dietary use of zeolites on animal diarrhoea syndromes, such as sequestration and lack of cytotoxicity of enterotoxins, binding of endogenous substances implicated in gastrointestinal disturbances, earlier restoration of impaired digestive enzyme activity in animals suffered from diarrhoeas or reduction of nematodes' establishment in the gastrointestinal tract. Furthermore, zeolite-enriched diets exert a clear beneficial effect on the prevention of certain metabolic diseases in dairy cows, as recently evidenced by researchers who underlined the restrictive role of zeolites in the bioavailability of dietary Ca as the interpreting mechanism in the case of milk fever and the improved dietary energy uptake as the one in the case of ketosis.

From a pharmaceutical and a clinical point of view, in vitro and latest field studies respectively, confirmed the lack of any obvious interaction among zeolites and certain drugs, which are used for animal health status preservation, when administered in parallel with the formers. On the contrary, recent works suggest that zeolites could also be ascribed as supportive means for more pronounced drug availability, due to their buffering capacity of the lumen contents across the different parts of the gastrointestinal tract.

In conclusion, a broad base of scientific data verifies that the proliferation of zeolites' dietary use will contribute to the improvement of animals' health status, additionally implying a potential improvement in final meat and dairy products quality.

References

[1] F.A. Mumpton, P.H. Fishman, J. Anim. Sci. 45 (1977) 1188.
[2] A. Filippidis, A. Godelitsas, D. Charistos, P. Misaelides, A. Kassoli-Fournaraki, Appl. Clay Sci. 11 (1996) 199.
[3] F.A. Mumpton, Proc. Natl. Acad. Sci. USA 96 (1999) 3463.
[4] E. Petkova, T. Venkov, P. Chushkov, T.S. Stefanov, E. Poshchakov, Vet. Med. Nauki. 19 (1982) 45 (abstract).
[5] L. Vrzgula, P. Bartko, J. Blazovsky, J. Kozac, Vet. Med.-Czech. 27 (1982) 267 (abstract).
[6] P. Bartko, J. Chabada, L. Vrzgula, I. Solar, J. Blazovsky, Vet. Med. (Praha) 28 (1983) 429 (abstract).
[7] N. Nestorov, in: W.G. Pond, F.A. Mumpton (Eds.), Zeo-agriculture: Use of Natural Zeolites in Agriculture and Aquaculture, Westview Press Inc., Boulder, Colorado, 1984, p. 167.
[8] G.C. Shurson, P.K. Ku, E.R. Miller, M.T. Yokohama, J. Anim. Sci. 59 (1984) 1536.
[9] W.G. Pond, J.T. Yen, Nutr. Rep. Int. 35 (1987) 801.
[10] W.G. Pond, J.T. Yen, V.H. Varel, Nutr. Rep. Int. 37 (1988) 795.
[11] M. Castro, M. Pastrana, in: D. Kallo, H.S. Sherry (Eds.), Occurrence, Properties and Utilization of Natural Zeolites, Academiai Kiado, Budapest, 1988, p. 721.
[12] A. Yannakopoulos, A. Tserveni-Gousi, A. Kassoli-Fournaraki, A. Tsirabides, K. Michailidis, A. Filippidis, U. Lutat, in: C. Colella, F.A. Mumpton (Eds.), Natural Zeolites for the Third Millennium, De Frede Editore, Napoli, 2000, p. 471.
[13] D.S. Papaioannou, C.S. Kyriakis, C. Alexopoulos, E.D. Tzika, Z.S. Polizopoulou, S.C. Kyriakis, Res. Vet. Sci. 76 (2004) 19.
[14] E. Petkova, T. Ventkov, K. Stanchev, Vet. Med. Nauki 20 (1983) 36 (abstract).
[15] W.G. Pond, J. Anim. Sci. 59 (1984) 1320.
[16] W.G. Pond, J. Lee, in: W.G. Pond, F.A. Mumpton (Eds.), Zeo-agriculture: Use of Natural Zeolites in Agriculture and Aquaculture, Westview Press Inc., Boulder, Colorado, 1984, pp. 129–145, 167.
[17] R. Fethiere, R.D. Milles, R.H. Harms, Poult. Sci. 73 (1994) 118.
[18] J. Mirabdolbaghi, D.K. Lotfolahian, in: P. Misaelides (Ed.), Zeolite '02, Int. Conf. Occurrence, Properties and Utilization of Natural Zeolites, Thessaloniki, Greece, 2002, p. 234.
[19] E. Christaki, P. Florou-Paneri, P. Fortomaris, A. Tserveni-Gousi, A. Yannakopoulos, in: P. Misaelides (Ed.), Zeolite '02, Int. Conf. Occurrence, Properties and Utilization of Natural Zeolites, Thessaloniki, Greece, 2002, p. 61.
[20] D.S. Papaioannou, S.C. Kyriakis, A. Papasteriadis, N. Roubies, A. Yannakopoulos, C. Alexopoulos, Res. Vet. Sci. 72 (2002) 1.

[21] A. Yannakopoulos, A. Tserveni-Gousi, P. Fortomaris, G. Arsenos, A. Filippidis, A.Kassoli-Fournaraki, in: P. Misaelides (Ed.), Zeolite '02, Int. Conf. Occurrence, Properties and Utilization of Natural Zeolites, Thessaloniki, Greece, 2002, p. 393.
[22] R. Garcia Lopez, A. Elias, M.A. Menchaca, Cuban J. Agric. Sci. 26 (1992) 131.
[23] P.D. Katsoulos, N. Panousis, N. Roubies, E. Christaki, G. Arsenos, H. Karatzias, Vet. Rec., in press.
[24] A.L. Yannakopoulos, A.S. Tserveni-Gousi, N.K. Katsaounis, A. Kassoli-Fournaraki, A. Filippidis, A. Tsolakidou, in: International Symposium and Exhibition of Natural Zeolites, Sofia, Bulgaria, 1995, p. 120.
[25] M.D. Olver, Brit. Poultry Sci. 38 (1997) 220.
[26] A.S. Tserveni-Gousi, A.L. Yannakopoulos, N.K. Katsaounis, A. Filippidis, A. Kassoli-Fournaraki, Arch. Geflugelk. 61 (1997) 291.
[27] G.C. Shurson, I.G. Lumanta, P.K. Ku, M.T. Yokohama, E.R. Miller, in: W.G. Pond, F.A. Mumpton (Eds.), Zeo-agriculture. Use of Natural Zeolites in Agriculture and Aquaculture, Westview Press Inc., Boulder, Colorado, 1984, p. 147.
[28] M. Evans, D.J. Farrell, in: D.J. Farrell (Ed.), Recent Advances in Animal Nutrition in Australia, University of New England, Armidale, 1993, p. 303.
[29] M.J. Cabezas, D. Salvador, J.V. Sinistera, J. Chem. Technol. Biotechnol. 52 (1991) 265.
[30] P. Parisini, G. Martelli, L. Sardi, F. Escribano, Anim. Feed Sci. Technol. 79 (1999) 155.
[31] S.E. Scheideler, Poult. Sci. 72 (1993) 282.
[32] E. Lonwo, V. Zaldivar, E. Margolles, Cuban J. Agric. Sci. 27 (1993) 199.
[33] R.B. Harvey, L.F. Kubena, M.H. Elissable, T.D. Phillips, Avian Dis. 37 (1993) 67.
[34] T.C. Schell, M.D. Lindemann, E.T. Kornegay, D.J. Blodgett, J.A. Doer, J. Anim. Sci. 71 (1993) 1226.
[35] S.S. Parlat, A.O. Yildiz, H. Oguz, Br. Poult. Sci. 40 (1999) 495.
[36] H. Oguz, V. Kurtoglu, B. Coscun, Res. Vet. Sci. 69 (2000) 197.
[37] R. Miazzo, C.A. Rosa, E.C. De Queiroz Carvalho, C. Magnoli, S.M. Chiacchiera, G. Palacio, M. Saenz, A. Kikot, E. Basaldella, A. Dalcero, Poult. Sci. 79 (2000) 1.
[38] C.M. Placinta, J.P.F. D'Mello, A.M.C. Macdonald, Anim. Feed. Sci. Technol. 78 (1999) 21.
[39] T.D. Phillips, A.B. Sarr, B.A. Clement, L.F. Kubena, R.B. Harvey, in: Pennington Centre Nutrition Series (Ed.), Mycotoxins, Cancer and Health, Louisiana State University Press, Baton Rouge, LA, 1990, p. 223.
[40] L.F. Kubena, R.B. Harvey, W.E. Huff, D.E. Corrier, T.D. Phillips, Poult. Sci. 69 (1990) 1078.
[41] R.B. Harvey, T.D. Phillips, J.A. Ellis, L.F. Kubena, W.E. Huff, H.D. Petersen, Am. J. Vet. Res. 52 (1991) 1556.
[42] R.B. Harvey, L.F. Kubena, T.D. Phillips, D.E. Corrier, M.H. Elissalbe, W.E. Huff, Am. J. Vet. Res. 52 (1991) 152.
[43] L.F. Kubena, R.B. Harvey, T.D. Phillips, W.E. Huff, Poult. Sci. 72 (1993) 651.
[44] M.D. Lindemann, D.J. Blodget, E.T. Kornegay, G.G. Schuring, J. Anim. Sci. 71 (1993) 171.
[45] M.R. Dwyer, L.F. Kubena, R.B. Harvey, K. Mayura, A.B. Sarr, S. Buckley, R.H. Bailey, T.D. Phillips, Poult. Sci. 76 (1997) 1141.
[46] A. Huwing, S. Friemund, O. Kappeli, H. Dutler, Toxicol. Lett. 122 (2001) 179.
[47] M.A. Abdel-Wahhab, S.A. Nada, F.A. Khalil, Anim. Feed Sci. Technol. 97 (2002) 209.
[48] A. Dacovic, M. Tomacevic-Canovic, V. Dondur, A. Vujakovic, P. Radosevic, J. Serb. Chem. Soc. 65 (2000) 715.
[49] M. Tomacevic-Canovic, A. Dacovic, V. Markovic, D. Stojcic, J. Serb. Chem. Soc. 66 (2001) 555.
[50] S.L. Lemke, S.E. Ottinger, K. Mayura, C.L. Ake, K. Pimpukdee, N. Wang, T.D. Phillips, Anim. Feed Sci. Technol. 93 (2001) 17.
[51] M. Dvorak, Vet. Med. (Praha) 34 (1989) 307.
[52] T. Kececi, H. Oguz, V. Kurtoglu, O. Demet, Brit. Poult. Sci. 39 (1998) 452.
[53] K. Mayura, M.A. Abdel-Wahhab, K.S. McKenzie, A.B. Sarr, J.F. Edwards, K. Naguib, T.D. Phillips, Toxicol. Sci. 41 (1998) 175.
[54] H. Oguz, T. Kececi, Y.O. Birdane, F. Onder, V. Kurtoglu, Res. Vet. Sci. 69 (2000) 89.
[55] M. Ortatatli, H. Oguz, Res. Vet. Sci. 71 (2001) 59.
[56] L. Rizzi, M. Simioli, P. Rocanda, A. Zaghini, J. Food Protect. 66 (2003) 860.
[57] A.J. Ramos, E. Hernández, J.M. Plá-Delfina, M. Merino, Int. J. Pharmaceut. 128 (1996) 129.
[58] A.B. Sarr, B.A. Clement, T.D. Phillips, Toxicologist 10 (1990) 163.
[59] A.B. Sarr, B.A. Clement, T.D. Phillips, Toxicologist 11 (1991) 97.
[60] S.L. Lemke, P.G. Grant, T.D. Phillips, J. Agric. Food Chem. 46 (1998) 3789.
[61] M. Tomasevic-Canovic, A. Dakovic, G. Rottinghaus, S. Matijasevic, in: P. Misaelidis (Ed.), Zeolite '02, Occurrence, Properties and Utilization of Natural Zeolites, 6th Int. Conf., Thessaloniki, Greece, 2002, p. 353.
[62] S.J. Bursian, R.J. Aulerich, J.K. Cameron, N.K. Ames, B.A. Steficek, J. Appl. Toxicol. 12 (1992) 85.
[63] W.E. Huff, L.F. Kubena, R.B. Harvey, T.D. Phillips, Poult. Sci. 71 (1992) 64.
[64] T.K. Smith, Can. J. Physiol. Pharmacol. 58 (1980) 1251.
[65] B. Boyens, Inaugural-Disseration, Tierarztlichen Hochschule, Hannover, 2001.
[66] D. Avacumovic, I. Rajic, V. Vidovic, A. Dacovic, M. Tomasevic-Canovic, in: P. Misaelidis (Ed.) Zeolite '02, Occurrence, Properties and Utilization of Natural Zeolites, 6th Int. Conf., Thessaloniki, Greece, 2002, p. 31.
[67] M.L. Biehl, D.B. Prelusky, G.D. Koritz, Toxicol. Appl. Pharmacol. 121 (1993) 152.
[68] G. Rodrigues-Fuentes, M.A. Barrios, A. Irainoz, I. Perdomo, B. Cedré, Zeolites 19 (1997) 441.
[69] E. Petkova, T. Ventkov, P. Chushkov, A. Dzhurov, T.S. Stefanov, Vet. Med. Nauki 19 (1982) 55.
[70] F.A. Mumpton, in: W.G. Pond, F.A. Mumpton (Eds.), Zeo-agriculture. Use of Natural Zeolites in Agriculture and Aquaculture, Westview Press Inc., Boulder, Colorado, 1984, p. 3.
[71] L. Vrzgula, M. Prosbova, J. Blazovsky, U. Jacobi, T. Schubert, G. Kovac, in: D. Kallo, H.S. Sherry (Eds.), Occurrence, Properties and Utilization of Natural Zeolites, Academiai Kiado, Budapest, 1988, p. 747.
[72] P. Bartko, H. Seidel, G. Kovac, in: D.W. Ming, F.A. Mumpton (Eds.), Natural Zeolites '93, Int. Comm. Natural Zeolites, Brockport, New York, 1995, p. 467.
[73] L. Vrzgula, P. Bartko, in: W.G. Pond, F.A. Mumpton (Eds.), Zeo-agriculture: Use of Natural Zeolites in Agriculture and Aquaculture, Westview Press Inc., Boulder, Colorado, 1984, p. 161.
[74] K.D. Gunther, Zeolite minerals in pig and poultry feeding, Schweinewelt 15 (1990) 15.
[75] G. Benatti, D. Bergero, G. Ladeto, C. Sarra, Zootec. Nutr. Anim. 20 (1994) 153.
[76] P.G. Monetti, M. Tassinari, G. Vignola, J.L. Gonzales-Valdez, Zootec. Nutr. Anim. 22 (1996) 159.
[77] J. Ramu, K. Clark, G.N. Woode, A.B. Sarr, T.D. Phillips, J. Food Protect. 60 (1997) 358–362.
[78] K.J. Clark, A.B. Sarr, P.G. Grant, T.D. Phillips, G.N. Woode, Vet. Microbiol. 63 (1998) 137.
[79] V. Stojic, H. Samanc, N. Fratric, Acta Vet. (Beograd) 45 (1995) 67.

[80] A. Nik-Khah, A.A. Sadeghi, in: P. Misaelidis (Ed.) Zeolite '02, Occurrence, Properties and Utilization of Natural Zeolites, 6th Int. Conf., Thessaloniki, Greece, 2002, p. 253.
[81] V. Stojic, M. Garcin, N. Fratric, M. Tomacevic-Canovic, D. Kirovski, Acta Vet. (Beograd) 48 (1998) 19.
[82] G. Marastoni, G. Belladelli, M. Curti, E. Gozzi, G. Panciroli, C. Spreafico, in: Proceedings of the 14th International Pig Veterinary Society Congress, Bologna, Italy, 1996, p. 454.
[83] R.L. Goings, N.L. Jacobson, D.C. Beitz, E.T. Littledike, K.D. Wiggers, J. Dairy Sci. 57 (1974) 1184.
[84] K.D. Wiggers, D.K. Nelson, N.L. Jakobsen, J. Dairy Sci. 58 (1975) 430.
[85] J.F. Yarrington, C.C. Cappen, H.E. Black, R. Re, J. Nutr. 107 (1977) 2244.
[86] H.B. Green, R.L. Horst, D.C. Beitz, E.T. Littledike, J. Dairy Sci. 64 (1981) 217.
[87] T.S. Kichura, R.L. Horst, D.C. Beitz, E.T. Littledike, J. Dairy Sci. 65 (1982) 480.
[88] R.J. Jorgensen, T. Hansen, M.L. Jersen, T. Thilsing-Hansen, J. Dairy Sci. 84 (2001) 609.
[89] T. Thilsing-Hansen, R.J. Jorgensen, J. Dairy Sci. 84 (2001) 691.
[90] T. Thilsing-Hansen, R.J. Jorgensen, J.M.D. Enemark, T. Larsen, J. Dairy Sci. 85 (2002) 1855.
[91] R.J. Jorgensen, M.J. Bjerrum, H. Classen, T. Thilsing-Hansen, Acta Vet. Scand. Suppl. 97 (2003) 83.
[92] T. Thilsing-Hansen, R.J. Jorgensen, J.M. Enemark, R. Zelvyte, A. Sederevicius, Acta Vet. Scand. Suppl. 97 (2003) 87.
[93] J.M. Enemark, A.M. Frandsen, T. Thilsing-Hansen, R.J. Jorgensen, Acta Vet. Scand. Suppl. 97 (2003) 97.
[94] P.D. Katsoulos, N. Roubies, N. Panousis, G. Arsenos, E. Christaki, H. Karatzias, Am. J. Vet. Res., accepted for publication.
[95] J.P. Goff, R.L. Horst, J. Dairy Sci. 80 (1997) 1260.
[96] J.L. White, A.J. Ohlrogge, Can. Patent 939186, January 2, 1974.
[97] R.W. Hemken, R.J. Harmon, L.M. Mann, in: W.G. Pond, F.A. Mumpton (Eds.), Zeo-agriculture. Use of Natural Zeolites in Agriculture and Aquaculture, Westview Press Inc., Boulder, Colorado, 1984, p. 175.
[98] T.F. Sweeney, A. Cervantes, L.S. Bull, R.W. Hemken, in: W.G. Pond, F.A. Mumpton (Eds.), Zeo-agriculture. Use of Natural Zeolites in Agriculture and Aquaculture, Westview Press Inc., Boulder, Colorado, 1984, p. 183.
[99] N. Nestorov, N. Stantschef, D. Katzarov, N. Popov, in: Program 2nd Bulgarian–Soviet Symposium on Natural Zeolites, Kardjali, Bulgaria, 1979, p. 59.
[100] F.T. McCollum, M.L. Galyean, J. Anim. Sci. 56 (1983) 517.
[101] N. Nestorov, in: W.G. Pond, F.A. Mumpton (Eds.), Zeo-agriculture. Use of Natural Zeolites in Agriculture and Aquaculture, Westview Press Inc., Boulder, Colorado, 1984, p. 167.
[102] D. Bergero, G. Rumello, C. Sara, A. D' Angelo, in: G. Kirov, L. Filizova, O. Petrov (Eds.), Natural Zeolites Sofia '95, Pensoft Publishers, Sofia-Moscow, 1997, pp. 67–72.
[103] P. Bosi, D. Creston, L. Casini, Ital. J. Anim. Sci. 1 (2002) 187.
[104] M.A. Johnson, T.F. Sweeney, L.D. Muller, J. Dairy Sci 71 (1988) 946.
[105] H.D. Poulsen, N. Oksbjerg, Anim. Feed Sci. Technol. 53 (1995) 297.
[106] S.C. Kyriakis, K. Alexopoulos, K. Saoulidis, D. Papaioannou, G.C. Balkamos in: Proceedings of the 16th International Pig Society Congress, Melbourne, Australia, 2000, p. 382.
[107] V.A. Varel, I.M. Robinson, W.G. Pond, Appl. Envir. Microbiol. 53 (1987) 2009.
[108] G. Kovac, P. Bartko, L. Vrzgula, P. Reichel, F. Nistiar, J. Mojzis, H. Seidel, in: D.W. Ming, F.A. Mumpton (Eds.), Natural Zeolites '93, Int. Comm. Natural Zeolites, Brockport, New York, 1995, p. 459.
[109] F. Nistiar, J. Mojzis, G. Kovac, H. Seidel, O. Racz, Folia Microbiol. 45 (2000) 567.
[110] J. Mojzis, F. Nistiar, G. Kovac, G. Mojziosova, Vet. Med. (Praha) 39 (1994) 443.
[111] J. Mojzis, F. Nistiar, G. Kovac, Vet. Hum. Toxicol. 36 (1994) 533.
[112] W.G. Pond, J.T. Yen, L. Krook, Nutr. Rep. Int. 32 (1983) 815.
[113] W.G. Pond, K.J. Ellis, L.P. Krook, P.A. Schoknecht, in: Program and Abstracts, Zeolite '93, 4th Int. Conf. Occurrence, Properties and Use of Natural Zeolites, Boise, Idaho, Int. Comm. Natural Zeolites. Brockport, New York, 1993, p. 170.
[114] L. Vrzgula, H. Seidel, Vet. Med. (Prague) 34 (1989) 537.
[115] W.G. Pond, J.T. Yen, Bull. Environ. Contam. Toxicol. 31 (1983) 666.
[116] W.G. Pond, J.T. Yen, Proc. Soc. Exp. Biol. Med. 173 (1983) 332.
[117] S.K. Jain, Chemosphere 39 (1999) 247.
[118] R. Arnek, S. Forsberg in: National Council for Radioactive Waste, Fack, S-102 40, Stockholm, Sweden, Prav 3.19, 1979.
[119] V. Gomonaj, P. Gomonaj, N. Golub, K. Szekeresh, B. Charmas, R. Leboda, Adsorp. Sci. Technol. 18 (2000) 195.
[120] M. Phillipo, S. Gvozdanovic, D. Gvozdanovic, J.K. Chesters, E. Paterson, C.F. Mills, Vet. Rec. 122 (1988) 560.
[121] S. Forsberg, B. Jones, T. Westermark, Sci. Total Environ. 79 (1989) 37.
[122] J.W. Rachubik, B. Kowalski, Bull. Vet. Inst. Pulawy 45 (2001) 341.
[123] M. Ivan, M.S. Dayrell, M. Hidiroglou, J. Dairy Sci. 75 (1992) 201.
[124] W.G. Pond, J. Anim. Sci. 67 (1989) 2772.
[125] T.L. Ward, K.L. Watkins, L.L. Southern, P.G. Hoyt, D.D. French, J. Anim. Sci. 69 (1991) 726.
[126] W.G. Pond, in: D.W. Ming, F.A. Mumpton (Eds.), Natural Zeolites '93, Int. Comm. Natural Zeolites, Brockport, New York, 1995, p. 449.
[127] P.D. Wells, M. McHugh, Zeolites 4 (1983) 353.
[128] P.D. Wells, P. Kilduff, Zeolites 5 (1985) 145.
[129] K. Deligiannis, T. Lainas, G. Arsenos, E. Papadopoulos, P. Fortomaris, D. Kufidis, C. Stamataris, D. Zygogiannis, Livestock Prod. Sci., in press.
[130] S.K. Shaker, A. Dyer, D.M. Storey, J. Helminthol. 66 (1992) 288.
[131] A. Dyer, S. Morgan, P. Wells, C. Williams, J. Helminthol. 74 (2000) 137.
[132] R.M. Leach Jr., S. Brenda, S. Heinrichs, J. Burdette, Poult. Sci. 69 (1990) 1539.
[133] R. Ballard, H.M. Edwards Jr., Poult. Sci. 67 (1988) 113.
[134] H.M. Edwards Jr., Poult. Sci. 67 (1988) 1436.
[135] H.M. Edwards Jr., J. Nutr. 114 (1984) 1001.
[136] M.F. Ledwaba, K.D. Roberson, Poult. Sci. 82 (2003) 1769.
[137] K.L. Watkins, L.L. Southern, Poult. Sci. 70 (1991) 2295.
[138] A. Lam, L.R. Sierra, G. Rojas, A. Rivera, G. Rodriguez-Fuentes, L.A. Montero, Micropor. Mesopor. Mater. 23 (1998) 247.
[139] A. Lam, A. Rivera, G. Rodriguez-Fuentes, Micropor. Mesopor. Mater. 29 (2001) 157.
[140] T. Farias, A.R. Ruiz-Salvador, A. Rivera, Micropor. Mesopor. Mater. 61 (2003) 117.
[141] G.F. Collings, S.A. Thomasson, P.K. Ku, E.R. Miller, J. Anim. Sci. 50 (1980) 272.
[142] M.P. Bernal, J.M. Lopez-Real, K.M. Scott, Biores. Technol. 43 (1993) 35.
[143] I.M. Dwairi, Bull. Envir. Contam. Toxicol. 60 (1998) 126.
[144] M.D. Ma, W.Y. Huang, J.F. Wu, C.M. Fu, J. Chin. Soc. Anim. Sci. 22 (1993) 229.
[145] S. Barrington, K. El Moueddeb, in: Proceedings of International Livestock Odor Conference, Iowa State University, Ames, 1995, p. 65.
[146] K. Saoulidis, C. Alexopoulos, D.S. Papaioannou, S.K. Kritas, S.C. Kyriakis, J. Hell. Vet. Med. Soc. 52 (2001) 292.