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CURRENT ASPECTS REGARDING THE USE OF ZEOLITES IN THE PROPHYLACTIC-THERAPEUTIC MANAGEMENT OF GASTROINTESTINAL DISORDERS IN POULTRY, SWINE, RUMINANTS AND DOGS (REVIEW)

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Abstract

Among the factors that cause gastrointestinal disorders in animals, along with microbial pathogens (bacteria, viruses), a major impact have the factors related to diet and stress. The use of effective alternative treatments of natural origin has really materialized. In recent decades, natural products have expanded and the overuse of synthetic drugs has been reduced because of their decreased therapeutic efficacy. Zeolites are volcanic compounds with a porous structure and a complex chemical composition. Their mineralogical, structural and physicochemical peculiarities underlie several applications in many fields, of which the biomedical one has a major impact on the prevention and therapy of gastric and intestinal pathologies. In gastrointestinal pathology, zeolites are used for their adsorbent and absorbent properties, which have been shown to be effective in the treatment of oral intoxications, diarrheal syndromes, and other digestive pathologies.. This review is intended to document and deepen the prophylactic-therapeutic actions of zeolites in gastrointestinal disorders in various animal species, their biomedical potential not being fully explored.

Key words: *gastrointestinal disorders, prevention, therapy, zeolites.*

INTRODUCTION

Gastrointestinal disorders in farm animals and small animals can have multiple aetiologies, including various pathogens (such as viruses, bacteria, fungi, parasites, protozoa), stress factors, microbiota dysbiosis, and unbalanced diets.
The high incidence of antibiotic resistance has led to the imperative development of new therapeutic and prophylactic alternatives of natural sources that can improve efficacy and at the same time reduce the pathologic repercussions. In this context, zeolites represent a veritable alternative because of their diverse structure and physicochemical properties.
Zeolites are compounds of volcanic origin that have been discovered in the XVIIIth century by the Swedish mineralogist Axel Fredrik Cronstedt (Mumpton & Fishman, 1977). Zeolites, that are also known as volcanic tuffs, are microporous aluminosilicate minerals that due to their unique structure have three important characteristics, which are the ability to exchange ions, the ability to perform absorption, and adsorption.
In 1977, Mumpton and Fishman describe the structure of zeolites as a three-dimensional network made up of SiO_4 and AlO_4 tetrahedra that are interconnected through oxygen molecules. Another structural feature is the presence of channels and cavities within the structure. Both natural and synthetic zeolites have a porous structure that allows them to dehydrate and rehydrate reversibly, and thus to adsorb molecules acting like true molecular sieves (Papaioannou et al., 2005). The size of the pores varies between 0.3-1 nm (Bogdanov et al., 2009). The inner network has a negative charge which is balanced by the positive charge of the cations within the pores. Each tetrahedral structure of AlO_4 has a negative charge that is balanced by additional cations such as sodium, potassium, and/or calcium (Bogdanov et al., 2009; Nadziakiewicza et al., 2019). These volcanic tuffs are of great medical interest in many parts of the world, most of the zeolites

that are commercially available being of synthetic origin.

Currently, there are over 50 types of known zeolites, such as phillipsite, chabazite, analcime, clinoptilolite, and so on. Among the characteristics that can vary between different types of zeolites, it is important to mention cationic selectivity, particle density, molecular pore size (https://www.lenntech.pl/zeolites-structure-types.htm).

The aim of this review is to create an overview of the studies that have been conducted in the biomedical field of the use of natural zeolites and provide an overall picture of the prophylactic and therapeutic use of these materials.

MATERIALS AND METHODS

The studies used in this review were taken from using databases such as Google Academics, Web of Science, and Science Direct. A set of eight international articles from the past 15 years, two for poultry, swine, ruminants, and dogs respectively, have been analysed and reviewed in order to exemplify the prophylactic and therapeutic potential of zeolite enriched feed to reduce gastrointestinal disorders. The articles featured a well-rounded experimental design with a large number of animals that participated in the studies.

RESULTS AND DISCUSSIONS

The analysed data has shown great improvement in the gastrointestinal health of the study subjects. The incidence of diarrheic episodes in young animals has been significantly reduced due to the in-feed administration of zeolites as can be seen for swine, ruminants, and poultry. The morphology of the intestinal tract of poultry that benefited from zeolite supplemented diets was improved, namely the duodenal, jejunal and ileal villi count. In poultry, zeolite administration has improved some enzymatic activity as well, for example, the maltase. The in-feed administration of zeolites also had a beneficial effect on the microbiome of the digestive tract in poultry, swine and dogs by reducing the population of harmful bacteria such as *Escherichia coli*, *Vibrio cholerae* and *Enterobacteriaceae* spp.

The bifidobacterial population *(Lactobacillus* spp., *Bifidobacterium* spp. etc.) colonies in dogs' intestinal tract were also shown to be improved by the administration of zeolites.

THE MECHANISM OF ACTION OF ZEOLITES IN THE DIGESTIVE TRACT

Zeolites are biomaterials that have been popularly used in animal husbandry technologies starting with the XXth century. In current times, zeolites have become known and preferred alternatives that still require research to further explore their biomedical potential and mechanism of action, which is yet to be fully understood.

There are some scientific hypotheses that state the fact that zeolites can remove some of the predisposing and causal factors of gastrointestinal disorders. It is already known the fact that zeolites such as phillipsite and clinoptilolite are capable of absorbing water from the intestinal contents, retaining it in its endogenous canalicular system, and thus aiding in the result of well-formed faeces (Papaioannou et al., 2005). This effect is due to the three-dimensional structure of aluminosilicate compounds that create a big internal surface of approximately 300 m^2/g of interconnected channels that can be occupied by ions and water molecules (Luz, 1995). Zeolites are also believed to reduce intestinal peristalsis (Papaioannou et al., 2005).

After conducting research, Vrzgula et al. (1988) have proposed a different mechanism of action of zeolites in the gastrointestinal tract in the case of post-weaning diarrheic syndrome in cattle which involves the shift in the osmotic pressure in the intestinal lumen, thus preventing the occurrence of metabolic acidosis.

It is also known that zeolites can adsorb enterotoxins produced by *Escherichia coli,* and like other inorganic adsorbents (such as silica and carbon), zeolites can also adsorb heat-labile toxins produced by *Escherichia coli* and *Vibrio cholerae.* Thus, the use of these inorganic adsorbents can have a beneficial role in the treatment of diarrheal syndromes by reducing the activity of the enterotoxins (Thomson et al., 2004).

THE USE OF ZEOLITES IN FARM ANIMALS (POULTRY, SWINE, RUMINANTS)

Zeolites in poultry

In 2017 Wawrzyniak et al. conducted a study to evaluate the effects of zeolites on the morphology and physiology of the gastro-intestinal tract in Broiler chicken from the Ross line. The experiment involved 90 chicks, randomly selected, that were divided into three groups: the first lot was the control group, the second one was given feed that contained zeolite 2% and the last group had 3% zeolite in the feed. The study was conducted over a 40-day period, and at the end of the experiment, 3 chicks from each group were randomly picked and slaughtered, and their digestive tract was collected to do morphometrical and histological analyses. During the morphometric analyses, the dimensions of both the villi and the intestinal crypts were evaluated from 5 different regions of the small intestine (duodenum, the proximal part of the jejunum, the middle part of the jejunum, the distal part of the jejunum, and the ileum). The results stated a drop in the width of the duodenal villi and an increase in the number of villi in the groups that were fed with basal diet and 2% and 3% zeolite addition. On the other hand, the same two groups presented an increase in the depth of the intestinal crypts all over the small intestine.

This study also revealed the fact that the supplementation of the feed with zeolites resulted in an increase in the activity of maltase in the duodenal sector and in the proximal and distal sections of the jejunum in the chicks which received 3% zeolites.

The experiment conducted by Wu et al. (2013) evaluated the effects of the administration of natural and synthetic clinoptilolite on growth performance, morphology, and gut microbiota in Broiler chicks has also proven to be of major interest. The study was conducted on 240 Broiler chicks over a 42-day period. The control group was fed a basal diet while the experimental groups were fed a basal diet that was enriched with natural clinoptilolite 2% respectively 2% modified clinoptilolite.

The experimental groups presented an increase in the production parameters and an increase in the height of the intestinal villi in the jejunum and ileum compared to the control group. The addition of clinoptilolite to the basal diet did not have any effects on the depth of the jejunal and ileal crypts. A decrease in the total viable counts of *Escherichia coli* was noticed on day 21 for both experimental groups and an increase in the total viable counts of *Lactobacillus acidophilus* on day 22 of the study. The pH levels in the cecum for the experimental groups have proven to be lower than the control group. This study ultimately proved the beneficial effects of the administration of both natural and modified clinoptilolite on gut microbiota in Broiler chicks.

Zeolites in swine

Valpotic et al. conducted a study in 2016 in which they evaluated the effects of clinoptilolite administration on growth parameters, gut microbiota, and lymphoid cellular populations in the ileum in weaned piglets. The study was conducted over five weeks and the experimental model included 46 pigs. The animals were divided into two groups, a control group, and an experimental group, the latter being fed a 0.5% clinoptilolite enriched basal diet. The study revealed that the experimental group showed an improvement in the daily weight gain on day 28 of the study, but eventually on day 35 it went down. The experimental group presented a significantly higher feed conversion ratio compared to the control group throughout the whole period of the study. The faecal elimination of *Escherichia coli* viable counts was also monitored, and it proved to be higher in the experimental lot but the severity of the diarrheic score was 12,96% lower than the control group (47 compared to 54).

Another study of great interest is the one conducted on 720 mixed pigs (Large White x Landrace x Belgian Landrace) by Papaioannou et al. (2004) which was centred on the effects of the administration of clinoptilolite by itself and in combination with antimicrobial substances such as enrofloxacin and salinomycin.

The results stated that the symptoms of the post-weaning diarrheal syndrome were lessened in the experimental group compared to the control group. Moreover, there was a 28,7%

decrease in the mortality rate in the experimental group. These results are in direct accordance with other studies conducted in the field by Benatti et al. (1994) and Gunther (1990).

Zeolites in ruminants

In 2010 Norouzian et al. published a study regarding the effects of clinoptilolite enriched diets on general health, growth performance and some haematological parameters in Baluchi lambs. Thirty 3-week-old lambs were randomly selected and divided into three groups, the C0 control group, which was fed a basal diet, the C1 group which was fed a basal diet plus 1.5% clinoptilolite and the C2 group which had a 2% clinoptilolite enriched basal diet. The study was conducted over a 6-week period. At the beginning of the study, the lambs weighed 6.5 ± 1.2 kg. The lambs were given free access to the feed and water. The results of the study stated that the lambs that were in the C1 and C2 groups had a lower diarrheic incidence than the lambs in the C0 group. Another finding of significance was regarding the daily weight gain of the lambs which was higher in the C1 (138.58 g/day) and C2 (170.56 g/day) as opposed to the control group (136.32 g/day).

Zarcula et al. (2010) conducted a study on the effects of the supplementation of clinoptilolite in the colostrum administered to calves. The study included 26 newborn Romanian Black and White calves which were divided into three groups, the control group, the experimental group E1 which received colostrum with 5 g/L of clinoptilolite and the E2 experimental group which was fed colostrum and clinoptilolite 20 g/L. The study was conducted over a 90-day period. The administration of colostrum enriched with clinoptilolite started immediately after parturition. The calves were fed twice a day every twelve hours. The early incidence of diarrhoea was observed, and the conclusions stated that the animals which were included in the experimental groups had a lower incidence compared to the control group.

ZEOLITES IN SMALL ANIMALS (DOGS)

Zeolites in dogs

To comprehend the gastrointestinal effects of zeolites in the digestive tract, it is important to mention the fact that both human and animal organisms alike have a neurohormonal system that is also known as the brain-gut axis that integrates the intestinal activity with the cerebral one (Superchi et al., 2017).

It is also important to mention that both physical activity and stress have an impact on the permeability, motility, the secretion of mucus, gut microbiota, and implicitly gastrointestinal digestion. The zeolite dietary supplementation can thus modulate the gut microbiota and generate a favourable environment in terms of pH levels and oxidative status (Superchi et al., 2017).

In 2017 Superchi et al. conducted a study in which the effects of the administration of chabazite and phillipsite on the gut microbiota and oxidative status were evaluated. The study was conducted on 40 English Setters over a 28-day period. The experimental groups were given a 5 g/animal/day dosage of zeolites. It is important to mention the fact that the bodyweight of the experimental group did not suffer any changes in the experimental groups. The faeces of the experimental groups were more compact compared to the control group. On day 29 the faecal *Lactobacilli* spp. and *Enterobacteriaceae* spp. faecal colonies were quantified for both control and experimental groups. The reports stated a rise of the number of lactobacilli colonies and a drop in the *Enterobacteriaceae* spp. colonies in the experimental groups compared to the control group. The rise in the number of lactobacilli colonies was associated with a decrease in bacteria with pathogenic potential in the faeces (Grieshop et al., 2002, Superchi et al., 2017). Moreover, it is a known fact that *Lactobacillus* spp. is categorized as probiotic bacteria that have been studied for their potential in the improvement of general health and their beneficial effect on neuronal activity in dogs (Grieshop et al., 2002; Superchi et al., 2017).

The analysis of the potential of chabazite to modulate the intestinal bifidobacterial population in dogs has been the object of an important study conducted by Sabbioni et al. in 2016. The study was conducted on 20 English Setters over 28 days. The conclusions of this study stated that chabazite has a favourable effect on the faecal microbial populations. In return, there were not any changes in the consistency of the faeces, which maintained a normal consistency throughout the study. The microbiological analysis of the faeces revealed a rise in the number of *Lactobacillus* spp. and *Bifidobacterium* spp. colonies and a drop in the *Enterobacteriaceae* spp. colonies. Chabazite also proved to have a good affinity towards the adsorption of *Escherichia coli* and *Clostridium perfringens.*

CONCLUSIONS

Even though there are a lot of studies that show promising results of zeolite administration in animal models, it is imperative that more research is conducted in this matter to fully investigate the biomedical potential of zeolites. The overall analysis of this review shows that the medical-veterinary research of zeolites is focused less on the implementation of prophylactic-therapeutic remedies than on the formulation of feed supplements that improve the living conditions of animals and facilitate the obtaining of effective combinations with other medicinal products. Out of the many biomedical applications of natural zeolites, the detoxifying potential of this compound involved in the elimination of many toxic metabolites and drug residues is of major importance.

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