APPLICATIONS OF CLINOPTILOLITE IN VETERINARY MEDICINE AND ANIMAL HUSBANDRY

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Abstract: Zeolites are compounds of either natural or synthetic origin and have been employed successfully in a number of industries, including veterinary medicine and animal husbandry. Clinoptilolite is the form of naturally occurring zeolite that has undergone the most scientific study out of the 140 various varieties and is also used the most as a component in animal feed. Natural clay minerals and zeolites are administered with encouraging results due to their detoxifying, antioxidant, hemostatic, anti-diarrheal, and immunostimulant properties. In this paper, the characteristics and possible applications of clinoptilolite as an animal feed additive in order to prevent and/or treat particular diseases in dairy cows will be discussed. Natural and manufactured zeolites have been used as feed additives in cow nutrition, primarily to reduce the absorption of mycotoxins through the gastrointestinal tract, improve general health status, and increase overall animal performance. Clinoptilolite is marketed as a feed additive that helps maintain and improve the fertility, well-being, and productivity of cattle

Key words: clinoptilolite, dairy cow, feed additive, immunostimulant.

INTRODUCTION

According to the International Zeolite Association (IZA), there are 67 different types of natural zeolites, each of which has its own three-letter code. The Commission Implementing Regulation (EU) No. 651/2013 authorizes sedimentary-derived clinoptilolite, which is often the most popular natural zeolite, as a feed ingredient for all animal species.

Clinoptilolite is a sodium aluminosilicate that is classified and generally recognized as safe in the United States (Code of Federal Regulations CFR, Title 21, Section 182.2727). In the European Community is registered as a food additive with DIN code 53 770 (Marc S., Tulcan C., 2019).

Zeolites may be used in animal nutrition as feed additives, primarily to reduce the gastrointestinal absorption of mycotoxins. In newborn calves, they may be used as passive immunity enhancers during the colostrum period and also, to improve the health status and growth performance of animals.

In companion animals, zeolites have been used and as an adjuvant in anticancer treatment, with a promising potential outcome, according to published literature data worldwide (Marc S., Tulcan C., 2019).

Clinoptilolite is particularly significant since it might also reduce mastitis problems in dairy cattle, in addition to increasing milk yield and feed effectiveness. According to Deniz Alic Ural's 2014 study (Alic Ural D., 2014), milk production and somatic cell count were positively impacted in dairy cows receiving clinoptilolite supplementation at a rate of 3% (w/v) when it was added to the feed ratio (Benić M. *et al*, 2018).

Additionally, it has just been given EU authorization for use as a mycotoxin binder in veterinary medicine feed additives, specifically in the cattle industry (Benić M. *et al*, 2018; Valpotić H. *et al*. 2017; Valpotić H. *et al*. 2018).

This paper reviews the most important properties of clinoptilolite regarding their use in animal husbandry and veterinary medicine, as well as their potential in different areas, emphasizing the necessity of further involvement by scientists from various backgrounds for future studies regarding the applications of clinoptilolite.

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METHODS

Natural or artificial Zeolites are crystals composed of a microporous aluminosilicate skeleton containing alkaline and alkaline earth cations and a free, limitless, three-dimensional structure.

These materials have specific chemical and physical properties. They are distinguished by their ability to reversibly lose and gain water, to absorb substances with a sufficient cross-sectional diameter (adsorption property), and to remove their cations from their environment with cations such as $Ca2^{+}$, Mg^{2+}, K^{+}, and $NH4^{+}$ without significant structural changes.

Zeolite has recently been approved by the European Union as an ingredient in farm animal feed, with a maximum dry matter inclusion score of 2 percent (European Commission Order, 2005) (Khachlouf K. *et al*, 2018).

In veterinary medicine, it may act as a detoxifier, antioxidant, hepatic, antidiarrheal, antioxidant, growth stimulant, and immunostimulant agent (Valpotić H. *et al.* 2018). Zeolites may enhance animal health through several mechanisms, including direct positive effects on digestive tract morphology, function and microbial flora, delivery of metabolically active ions, improvement of nutritional status, enhancement of immunity, decontamination of food and drinking water from toxins (Bacakova L. *et al*, 2018). One of zeolites' best-known efficacy is detoxification, which is highly necessary for the removal of toxic substances from both the body and the environment.

Two zeolite properties are critical for detoxification: the exchange of ions and the capacity for adsorption. Because of this, zeolite is successful in adsorbing heavy metals like lead, silver, arsenic, cadmium, ammonia, and radioactive substances including phenols, pesticides, and mycotoxins (Eisenwagen S., Pavelić K., 2020; Pavelić S.K. *et al,* 2018).

Figure 1 shows the main properties of clinoptilolite:

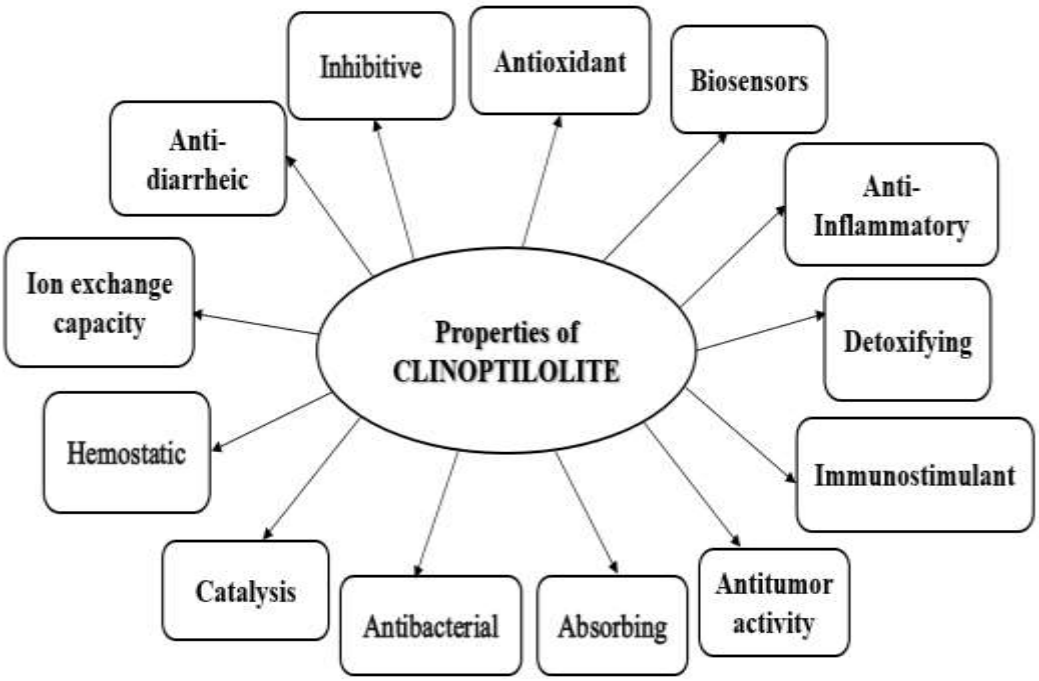

Figure 1 The main properties of clinoptilolite

DISCUSSIONS

Application of clinoptilolite

Clinoptilolite is recognized as a nanoporous material having a wide range of possible applications. Due to its excellent characteristics, particularly its porosity, specific weight, and adsorption (Samardzioska T., Jovanovski M., 2017), it can be used as a building stone in the construction industry and may also serve as a potential slow-release carrier for herbicides, insecticides and other organic compounds, protecting the environment from chemicals in the process (Marc S., Tulcan C., 2019). Figure 2 depicts the primary applications of clinoptilolite.

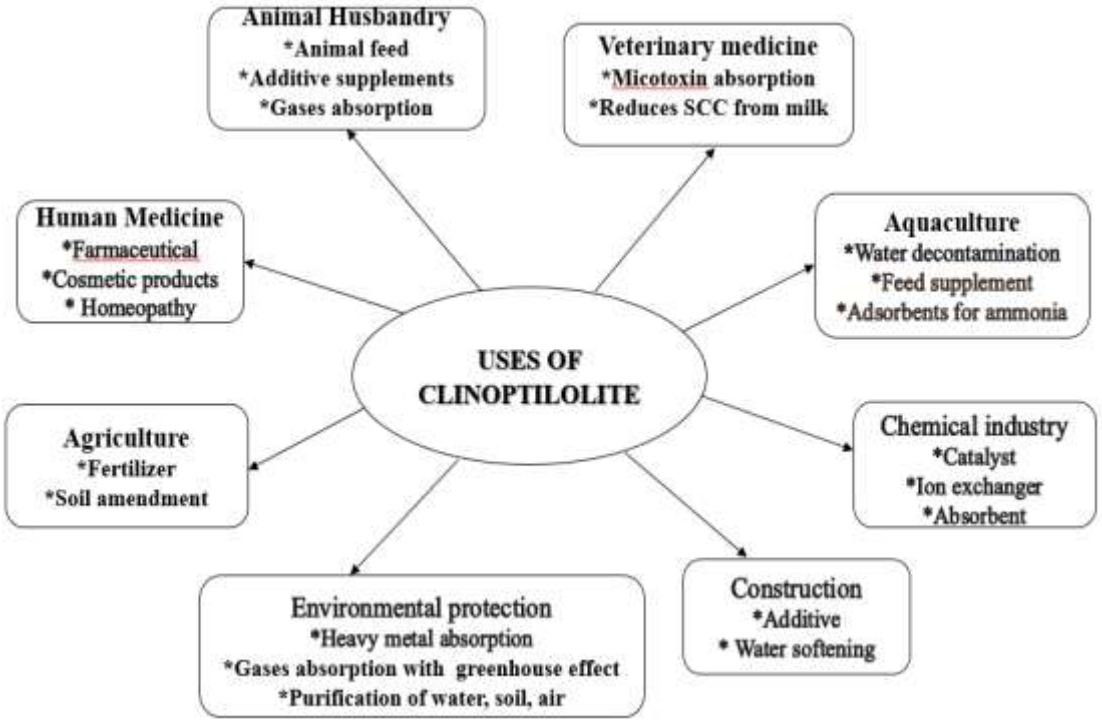

Figure 2 The main applications of clinoptilolite

Applications in veterinary medicine and animal husbandry

Clinoptilolite is considered a nano porous material with tremendous potential for use in veterinary medicine, especially in livestock production. Unsurprisingly, a large amount of work is underway to test novel approaches regarding the application of clinoptilolite in dairy cows (Valpotić H. *et al*, 2018). Clinoptilolite is the most commonly scientifically studied material among the 140 forms of natural zeolites and is best established as a zootechnical and biomedical feed ingredient commonly used as a candidate agent for replacing antibiotics in farm animal nutrition (Đuričić D. *et al*, 2017).

Natural and manufactured zeolites have mostly been employed in animal husbandry to increase production. Ammonia binding, decreasing the toxic effects of ammonia produced by intestinal microbial activity, reducing the passage rate of digesta through the intestines and improving nutrient utilization, increased pancreatic enzyme activity-favorable effect on feed components hydrolysis over a wider pH range, improved energy, and protein retention are some of the proposed applications.

Elimination of mycotoxin growth inhibitory factors is one of the mechanisms proposed for achieving the increase in productive performance in animals. Due to its detoxifying/decontaminating qualities and capacity to act as reducers of heavy metals, organic pollutants, radionuclides, and antibiotics, clinoptilolite is frequently used by livestock farmers as a feed additive for beef cattle, dairy cows, sheep, goats, pigs, poultry (broilers and egg production), rabbits, and turkeys. It is already known that adding clinoptilolite to the diet of pigs, poultry, and cattle improves their ability to acquire weight and raises feed conversion ratios.

Clinoptilolite functions as a binder of mycotoxins, blocking toxins that may be aggressive. It also helps to control aflatoxins in animal feed, thus lowering mortality from digestive stress and reducing the need for antibiotics. Clinoptilolite absorbs other toxins produced in the feed by molds and microscopic parasites and enhances food absorption by animals. The capacity of clinoptilolite to absorb aflatoxins that contaminate feed and improve the health of cattle has led to its use in this area.

There are countless reviews regarding mycotoxin binders, which present the advantages and the adsorption ability of the zeolites (Avantaggiato G. *et al*, 2005, Ariton A.M. *et al*, 2020). In the event of mycotoxicosis, zeolites may bind polar toxins such as aflatoxins, a feature confirmed in many types of research (Ariton A.M. *et al*, 2020).

Scientists have found that non-nutritional adsorbent zeolite has no harmful effect on lactating cows. Parameters are competitive when the degree

of inclusion does not go above 400 g /cow/ week. Studies carried out in the last decades have shown a high potency of clinoptilolite, *in vitro* and *in vivo* for various medical applications.

Clinoptilolite has been commonly used as an additive to animal feed or for the removal of ammonia in animal manure (Pavelić S.K. *et al*, 2018). The long-term dietary treatment of clinoptilolite to dairy calves increased milk production significantly (Katsoulos P.D. *et al*, 2005), without having any negative effects on serum concentrations of fat-soluble vitamins, specific trace minerals, or macro elements (Katsoulos P.D. *et al*, 2006). The animals' energy status was enhanced by the addition of clinoptilolite in feed during late pregnancy. Furthermore, the prevalence of metabolic disorders like ketosis was significantly decreased (Katsoulos P.D. *et al*, 2005; Katsoulos P.D. *et al*, 2006). Recently, Duričić and collaborators, (2017) evaluated the effects of dietary clinoptilolite, a novel vibro-activated and micronized modification of the natural mineral, in lactating dairy cows, on milk composition, somatic cells and the incidence of subclinical mastitis from the third to the seventh month of gestation (Đuričić D. *et al*, 2017).

The authors concluded that this predictive and beneficial consequence of clinoptilolite-supplementation may be due to its antibacterial, detoxifying, and immunostimulant impact on the incidence of subclinical mastitis and general udder health in dairy cows (Benić M. *et al*, 2018). An examination of the chemical composition and somatic cells count of milk from dairy cows, as well as a decline in the prevalence of milk fever in cows, allowed researchers to detect the favorable effects of dietary zeolites (Alic Ural D., 2014; Jorgensen R.J., Theilgaard P., 2014). Given the well-known chemical characteristics of zeolites (Pavelic K.M. et al, 2002) positive effects on health and dairy cow productivity are anticipated and demonstrated (Bosi P. *et al*, 2002). According to Valpoti and collaborators in 2017, clinoptilolite is believed to improve the health, fertility, and milk production of dairy cows by modulating their metabolic, endocrine, and antioxidant state (Valpotić H. *et al, 2018*).

In 2014, Alic Ural discovered that giving dairy cows feed containing 3% clinoptilolite enhanced milk yield and lowered the somatic cells count (Alic Ural D., 2014; Đuričić D. *et al, 2017*). The majority of research findings point to the possibility that adding clinoptilolite may increase milk production. In addition, various management techniques for clinoptilolite food supplements in dairy farms must be used with the utmost caution (Alic Ural D., 2014).

Since the content of milk fat was statistically different in the third and fourth samplings compared to the first sampling in the control group, whereas this difference was only seen between the first and third samplings in the clinoptilolite-fed cows, the chemical composition of milk was found to be more stable in this study (Đuričić D. *et al*, 2017).

Clinoptilolite shows properties, in particular, to reversible ion exchange and adsorption capacity of gases (Pavelić S.K. *et al., 2018*). Natural zeolites may absorb CO, CO_2, SO_2, H_2S, NH_3, HCHO, Ar, O_2, N_2, H_2O, He, H_2, Kr, Xe, CH_3OH, and many other gasses, and therefore can be used to capture or regulate odors. Such minerals are also used in intensive animal husbandry barns, substantially reducing the ammonia and H_2S content, which causes unwanted odors. The high absorption ability of ammonia makes it a very effective natural mean of controlling high levels of this gas, generated by animals, in farms.

This may be used in filtration systems or simply spread across the water surface, as it is absolutely harmless to aquatic life. Food crops that grow in soil containing high concentrations of Pb, Cd and Cu may also benefit by the zeolite absorption ability (Laurino C., Palmieri B., 2015). Such a result may be explained by the moderation of stressful events that occur during these times since cows are more susceptible to metabolic imbalance and environmental negative impacts during these times, which increases their vulnerability to intramammary infections and immunosuppression (Đuričić D. *et al*, 2017).

CONCLUSIONS

Zeolites can be used in animal nutrition as additives, primarily to reduce the gastrointestinal absorption of mycotoxins; In newborn calves, they can be used as enhancers of passive immunity during the colostral period. Studies have shown that the use of clinoptilolite as a feed additive in cattle can have a significant contribution to the prevention and treatment of certain diseases.

The use of natural zeolites in the feeding of dairy cows during the pre-calving, and post-calving periods and in the first part of lactation plays the role of promoter of productive performances. In this context, it is estimated that zeolites will play a more important role in food safety and agricultural practices in the near future.

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