History of Feed Additives

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Abstract

Feed additives have been used in animal nutrition for centuries, with the earliest recorded use dating back to ancient civilizations. Initially, farmers and nutritionists relied on natural products such as plants, minerals, and waste products to supplement animal diets. Over time, with advancements in technology and scientific understanding, the use of feed additives evolved to include synthesized vitamins, minerals, and growth promoters. The twentieth century saw significant growth in feed additive industry, driven by increased demand for animal protein as a source of food for a rapidly growing human population. In the latter part of the twentieth century, the industry continued to expand, with the introduction of new products such as antioxidants, antibiotics, and enzymes. The use of antibiotics as feed additives was especially popular, with farmers and nutritionists relying on them to prevent and treat bacterial infections in livestock and poultry. In recent decades, there has been increasing concern about the use of antibiotics as feed additives, with evidence suggesting that the widespread use of antibiotics has contributed to the development of antibiotic-resistant bacteria. This has led to stricter regulations, with many countries now limiting or banning, i.e., the EU, the use of antibiotics as feed additives. In response, the industry has shifted toward the use of alternative feed additives such as probiotics, prebiotics, and essential oils, which seem to have a positive impact on animal health and performance.

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1 Introduction

Feed additives are substances added to animal feeds to improve the nutritional value and confer health benefits to animals and further improve the quality of produced products of animal origin. The notion is that feed additives can enhance growth, improve feed efficiency, prevent disease, and improve overall animal performance. Marketing of feed additives is highly regulated subject to rigorous scientific evidence regarding their impact on animal health and the environment as well as the health of consumers of animal products. Hence, authorizations are for designated use in feed of certain animal species or groups, as well as under specified circumstances. Due to the large variety of additives, they are divided into the following groups:

- Technological additives (preservatives, antioxidants, emulsifiers, stabilizing agents, acidity regulators, silage additives)
- Sensory additives (flavorings, colorants)
- Nutritional additives (vitamins, minerals, amino acids, trace elements)
- Zootechnical additives (digestibility enhancers, gut flora stabilizers)
- Coccidiostats and histomonostats

These categories are further subdivided into functional groupings according to additive's primary functions. Antibiotics other than coccidiostats and histomonostats are not permitted as feed additives in Europe. Authorization of feed additives has become an important issue, especially in current century. In the previous era, and soon after the Second World War, growth rate of animal production was continuous and constantly positive. Simultaneously, development and usage of different feed additives was easy and easily applied. However, since the establishment of resistant strains of bacteria to antibiotics, the idea of using antimicrobial feed additives has been under thorough scientific scrutiny. Today, there are two kinds of licensing permitting the use of specific feed additives:

- Licenses issued to a holder of authorization. Those are granted for additives characterized as "zootechnical additives" and "coccidiostats and histomonostats," as well as those that consist of, contain, or are produced from genetically modified organisms (GMOs).
- Licenses not issued to a holder of authorization for substances characterized as "technological additives" and "sensory additives." The terms "additional ingredients" and "nutritional additives" are used interchangeably.

Both types of licensing authorizations are valid for ten years throughout the EU and the European Economic Area (EEA). Those authorizations are renewable for ten-year period. Generally, the Feed Additives Regulation (Regulation [EC] No 1831/2003 of September 2003) establishes a common procedure for authorizing feed additives and lays down rules for their marketing, labeling, and use. The regulation applies to all feed additives and premixtures except the following:

- Processing aids
- Veterinary medicinal products (VMPs) that are regulated by "Regulation (EU) 2019/6 on veterinary medicinal products that repeals Directive 2001/82/EC" (Regulation EU 2019, 2018)

The European Commission is now reassessing existing regulations on Feed Additives. The aim is to assess if the current legislation framework catered to the needs of citizens, businesses, and public authorities as expected and also to identify any gaps. The whole process is being carried out according to *Better Regulation Guidelines* (2021).

As stated above, there is a large variety of feed additives that are commonly used in animal nutrition. The major categories are the following (Fig. 1):

1. Antibiotics: Antibiotics are used to prevent and treat bacterial infections in animals. They are classified either as growth promoters, or as therapeutic agents to treat specific diseases. Their use in animal feeds has been a controversial issue, as there are concerns about the development of antibiotic-resistant bacteria.
2. Probiotics and Prebiotics: Probiotics are live microorganisms that are added to animal feed to improve the health of the digestive system and boost immune status. They can also reduce the risk of infection and improve feed efficiency. Some common probiotics used in animal nutrition include lactic acid bacteria, yeast, and bifidobacteria. Prebiotics on the other hand are compounds that promote the well-being of microflora of the gut. Common prebiotics are fructooligosaccharides, galactooligosaccharides, and xylooligosaccharides.
3. Enzymes: Enzymes are proteins contributing to breakdown of complex molecules into simpler components and hence facilitating their absorbance in the digestive tract. Their addition to animal feed improves digestibility, nutrient utilization, and feed efficiency.
4. Vitamins and Minerals: Vitamins and minerals are essential nutrients that are necessary for optimal animal health and performance. They are added to animal feed to ensure a balanced and complete diet, especially in cases where feedstuffs are deficient in certain nutrients.
5. Acidifiers: Acidifiers can lower pH of the digestive tract and hence reduce the risk of digestive problems and improve feed efficiency. Some common acidifiers used in animal nutrition include organic acids such as propionic acid and formic acid, as well as inorganic acids such as hydrochloric acid.
6. Antioxidants: Antioxidants protect against oxidative damage, which can occur because of normal metabolic processes. They improve overall health and

Fig. 1 Types of feed additives

performance of animals by reducing the risk of disease and improving feed efficiency. Some common antioxidants are vitamin E, selenium, and beta-carotene.

7. Essential Oils: Essential oils are highly concentrated liquids extracted from plants that contain volatile aromatic compounds. These compounds have various therapeutic and nutritional benefits, including antimicrobial and antioxidant properties. In animal nutrition, essential oils are often used as feed additives to enhance gut health, improve feed efficiency and growth performance, and promote overall health and wellness in livestock and poultry.
8. Amino Acids: Amino acids are the building blocks of proteins and are essential for growth and maintenance in animals. Their addition ensures that animals receive a balanced and complete diet, especially in cases where feedstuffs are deficient in certain amino acids (Kim and Kim 2017; D'Mello 2015).

The use of feed additives in animal nutrition can have a significant impact on animal performance and overall health. For example, the addition of antibiotics to animal feed has been shown to improve growth rates, feed efficiency, and overall health, while the addition of probiotics reduces the risk of digestive problems and improves gut health. However, it is important to use feed additives responsibly and only as directed by a veterinarian, as the overuse of certain additives can lead to the development of resistance, which can reduce their effectiveness over time (D'Mello 2015).

The history of feed additives in animal nutrition can be traced back to the early twentieth century, when the discovery of vitamins and minerals revolutionized the field of animal nutrition. Prior to this time, farmers relied on natural feed sources, such as grass and grain, to provide the necessary nutrients for their animals. However, the lack of knowledge about the specific nutritional requirements of different species of animals, as well as the variability in the quality of natural feed sources, led to poor performance and health outcomes for many animals (Grimble 1998). After the discovery of vitamins and minerals, farmers were able to supplement the diets of their animals with specific nutrients to improve their health and performance. This marked the beginning of the use of feed additives in animal nutrition. Over the following decades, advances in the field of animal nutrition, such as the discovery of antibiotics, probiotics, and enzymes, led to the development of a wide range of feed additives that could be used to improve the health and performance of animals.

One of the earliest uses of feed additives in animal nutrition was the addition of antibiotics to animal feed. Antibiotics were first introduced into animal feed in the 1950s, and quickly became a popular tool for improving growth and preventing disease in livestock. Antibiotics are still widely used in animal nutrition today, although their use has become controversial due to concerns about the development of antibiotic-resistant bacteria (Hornitzky and Rawnsley 2015). Another important development in the history of feed additives was the introduction of probiotics. Probiotics are live microorganisms that can improve digestive health and boost the immune system in animals. They were first introduced into animal feed in the 1980s and have since become a popular tool for improving gut health and preventing digestive problems in livestock (Gaur and Singh 2020). The use of enzymes in animal nutrition also has a long history, with the first commercial enzyme products being introduced into animal feed in the 1970s. Enzymes are proteins that help to break down complex molecules into simpler components that can be more easily absorbed by the animal, and they can be added to animal feed to improve digestibility and nutrient utilization (Zhou et al. 2021). The use of vitamins and minerals in animal nutrition has a similarly long history, with farmers having been supplementing the diets of their animals with these essential nutrients for over a century. Vitamins and minerals are still widely used in animal feed today, as they play a crucial role in maintaining the health and performance of animals (Bai et al. 2021).

Despite the long history of feed additives in animal nutrition, their use remains a subject of debate, with some experts arguing that the overuse of certain additives can lead to the development of resistance, reducing their effectiveness over time. However, there is also a growing body of research demonstrating the benefits of feed additives, such as improved growth, feed efficiency, and overall health in animals, leading many experts to conclude that their use is important for the sustainability of animal production.

2 History of Antibiotics as Feed Additives

Back in the 1930s, antibiotics' use, not only in human medicine but also in food and animal production, began to get established with the ultimate goal of effective disease prevention and rapid enhancement of animal growth. The first antibiotic for animal use was none other than synthetic sulfonamides that present antibacterial activity against Gram-positive and certain Gram-negative bacteria (White and Cooper 2005). The first sulfonamide drug was inaugurated by Bayer AG pharmaceutical company under the brand name Prontosil in 1935.

Thenceforth, because of World War II, drug manufacturing in Europe deteriorated in comparison to US pharmaceutical companies such as Merck and Pfizer that proceeded toward production of many synthetic and biological antibiotics. Meanwhile, researchers trialed mass-medication of entire herds and flocks. In 1948 Merck entered the animal health market with sulfaquinoxaline, the first antibiotic officially licensed to be used as a food or water additive in poultry. Sulfaquinoxaline in final concentration of 0.0125% in feed produces anticoccidiotic effects (Campbell 2008). After this, the use of antibiotics expanded to other animal species such as beehives, farmed fish, and cattle.

Vitamin B_{12} was then known as the main growth promoter in farm animal, but later studies revealed that dried mycelia of fungi caused better growth in chicks (Stokstad and Jukes 1949). Given the fact that antibiotics were growth-promoting substance in fungal mycelia, the idea of using antibiotics in animals' diets as growth-promoting factors prevailed, as, among others, they were also inexpensive in comparison to B_{12}. Moore et al. (1946) first proved that addition of antibiotics in chickens' diet contributed to weight gain. A few years later, many researchers found similar effects on pigs and chicks (Groschke and Evans 1950; Stokstad and Jukes 1951; Oleson et al. 1950).

The use of antibiotics in low doses as animal feed additives seemed very promising for both farmers and pharmaceutical companies. The benefits of prophylactic protection against bacterial diseases, growth promotion along with faster paces in weight gain, and therapeutic results of antibiotics were profound. Thereafter, in Midwest antibiotic growth promoters (AGP) feeds were officially licensed in 1951. After the prevalence of AGPs in the United States, European countries one after another began to adopt the idea and license AGPs without veterinary prescription in early 1950s (Thoms 2012; Kirchhelle 2018a, b). Penicillin, oxytetracycline, and chlortetracycline growth promoters were among the most commonly used AGPs in Europe during this decade. Contrary to US market situation, European farmers were only allowed to purchase premixed antibiotic solution and feeds (Jones 2003; Smith-

Howard 2017), thus avoiding the unrestrained use of antibiotics. According to researchers, some interesting facts are that in 1958 up to 50% of British pigs were fed antibiotics (Smith 1958) and by 1966 West Germany's Ministry of Agriculture's estimation was that 80% of mixed feeds for young pigs, veal calves, and poultry contained antibiotic additives (Kirchhelle 2016). Japan also licensed its own antimicrobial additives since 1953 (Morita 1997), both in livestock and fish production. In a need of modernization of their agriculture methods, Africa, South America, and Southeast Asia imported antibiotic additives for their livestock from the United States.

In the scenario of population increase and emerging economic development, there was intense need for a fast-paced agricultural production that resulted in a global outspread of the use of antibiotics as feed additives. However, concerns by experts about antimicrobial resistance (AMR) did not take long to arise. Thus, in late 1960s, national regulatory organizations and governments started to establish monitoring programs for antibiotics use and set certain limitations on their usage.

Scandinavian countries were the first to take precautions concerning AGPs. Sweden banned all AGPs' use in 1986. Norway started to adopt vaccinations instead of antibiotics in aquaculture since 1987. In Denmark, due to the association between the occurrence of resistance to vancomycin *Enterococcus faecium* (VREF) in healthy pigs and poultry (Bager et al. 1997) and use of avoparcin, the latter antibiotic was banned in 1995 and general AGP consumption decreased by 103,503 kg when producers decided to voluntarily give up on AGPs (Aarestrup and Engberg 2001; Kahn 2016).

Following Scandinavian countries' measures, EU's Scientific Committee on Animal Nutrition (SCAN) member states banned four AGPs and established the European Resistance Surveillance System (EARSS) in 1998 (Kirchhelle 2018a, b). Japan banned avoparcin and orienticin as feed additives in 1997 and South Korea restricted 45 different antimicrobial additives to only be administered after veterinary prescription.

However despite the partial restrictions, the use of AGPs still remains even in higher levels in most high-income countries than in 1960s (Kirchhelle 2018a, b). For example, there is significant difference in consumption of antibiotics between countries of Southwest Europe like Italy and Spain and Northern countries that have limited their use. In 2017, several Indian pharmaceutical businesses promoted colistin growth enhancers (Davies and Walsh 2018). By 2010, China surpassed the United States as the world's largest consumer of agricultural antimicrobials (about 23% of worldwide consumption) (Van Boeckel et al. 2015).

3 History of Probiotics

The use of probiotics in animal nutrition can be traced back to the early twentieth century, when scientists first began to study the role of microorganisms in the digestive system of animals. In the late nineteenth and early twentieth centuries, researchers such as Elie Metchnikoff began to study the role of microorganisms in the gut and their impact on health. Metchnikoff was particularly interested in the role of lactic acid bacteria, which he believed were responsible for the longevity of Bulgarian peasants. This early work laid the foundation for the development of probiotics as a tool for improving animal health and performance (Bengmark 1998). In the mid-twentieth century, scientists made significant advances in the production and formulation of probiotics. In 1958, the first probiotic product, *Lactobacillus acidophilus*, was commercialized by Yakult, a Japanese company (Fuller 1989). Over the following decades, the use of probiotics in animal nutrition grew rapidly, as researchers and farmers alike recognized the potential benefits of these beneficial bacteria. One of the first studies to demonstrate the efficacy of probiotics in animal nutrition was conducted by Fullers and Bradley in the 1980s. The study found that supplementing the diet of chickens with a mixture of *Lactobacillus* and *Bifidobacterium* species improved growth performance, feed efficiency, and overall health (Fuller and Bradley 1985). This work helped to establish the role of probiotics in animal nutrition and sparked a wave of research into the use of probiotics in livestock and aquaculture.

The use of probiotics in animal nutrition has continued to evolve and expand over the past few decades. Today, probiotics are widely used in the production of livestock and aquaculture species, including chickens, pigs, cows, fish, and shellfish (Bari and Roy 2016). The benefits of probiotics in animal nutrition are well-established, and include improved growth performance, feed efficiency, disease resistance, and gut health (Rao et al. 2018). In recent years, the use of probiotics in animal nutrition has become increasingly sophisticated, with the development of novel probiotic strains and delivery systems. For example, researchers have developed probiotic products that are specifically formulated for different species of animals, based on their unique digestive physiology (Kim et al. 2019). Additionally, advances in genomics and microbial ecology have allowed scientists to better understand the complex relationships between probiotics, the gut microbiota, and animal health (Rao et al. 2020).

In conclusion, the use of probiotics in animal nutrition has a long and rich history, dating back to the early twentieth century. Today, probiotics are widely used in the production of livestock and aquaculture species, and their benefits in animal health and performance are well-established. With continued advancements in our understanding of probiotics and their mechanisms of action, the use of probiotics in animal nutrition is poised to play an increasingly important role in sustainable and responsible animal production in the coming years.

4 History of Prebiotics

The concept of prebiotics is relatively new and has only been established in the last few decades. However, the history of prebiotics can be traced back to the early twentieth century when a Russian scientist named Élie Metchnikoff first proposed the idea that consuming fermented foods could promote longevity and improve health (Mackowiak 2013).

The term "prebiotics" was first used in the late 1990s and early 2000s to describe non-digestible food ingredients that selectively stimulate the growth and activity of beneficial bacteria in the gut (G. R. Gibson and Roberfroid 1995). This definition may correlate with the definition of dietary fiber (De Vrese 2001). Later on, prebiotics were defined as "selectively fermented ingredients that allow specific changes, both in composition and/or activity in the GI microflora that confer benefits upon host wellbeing and health" (Gibson et al. 2004, p. 269). Finally, Roberfroid et al. (2011) updated the definition of prebiotics based on International Life Sciences Institute (ILSI) Europe task force.

It is likely that prebiotics have been consumed in some form since prehistoric times, as they are naturally occurring in many foods. Archaeological evidence from dry cave deposits in the northern Chihuahuan Desert shows that desert plants high in inulin were extensively used (Slavin 2013). While the concept of prebiotics and their specific definition as non-digestible food ingredients is a relatively recent development, it is possible that our ancestors consumed prebiotic-rich foods as part of their diets. For example, fermented foods, such as yogurt, kefir, and sauerkraut, contain both prebiotics and probiotics, and have been consumed for thousands of years in various cultures (Jew et al. 2009). It is important to note, however, that the human gut microbiome has changed significantly over the course of human evolution, and our diets today are quite different from those of our prehistoric ancestors. Despite this, consuming prebiotic-rich foods is still considered important for maintaining gut health and promoting overall well-being (Moran et al. 2019).

Prebiotics have received increased scientific attention, and several studies have been conducted to determine the potential health benefits of consuming prebiotics. Today, prebiotics are considered an important component of a healthy diet and are often used in functional foods and dietary supplements to promote gut health (Roberfroid 2000). While research in this field is ongoing, there is growing evidence to suggest that consuming prebiotics can support the growth of beneficial bacteria in the gut, which can have a positive impact on overall health and well-being (Moran et al. 2019).

Prebiotics are commonly used as feed additives in human and animal nutrition. The use of prebiotics as feed additives is based on the idea that they can improve gut health by promoting the growth of beneficial bacteria in the gut and reducing the growth of harmful bacteria (Dahiya and Nigam 2022). The use of prebiotics as feed additives in animal nutrition is a relatively recent development, with the first commercial products appearing in the market in the late 1990s and early 2000s (Davani-Davari et al. 2019). Since then, the use of prebiotics in animal feed has grown rapidly, and they are now widely used in various livestock and poultry species (Alloui et al. 2013). Figure 2 shows a timeline of the use of prebiotics as feed additives. It is important to note that this timeline is a rough approximation and that the specific timeline of the use of prebiotics as feed additives may vary in different regions and countries. However, the overall trend has been one of steady growth in the use of prebiotics as feed additives in animal nutrition.

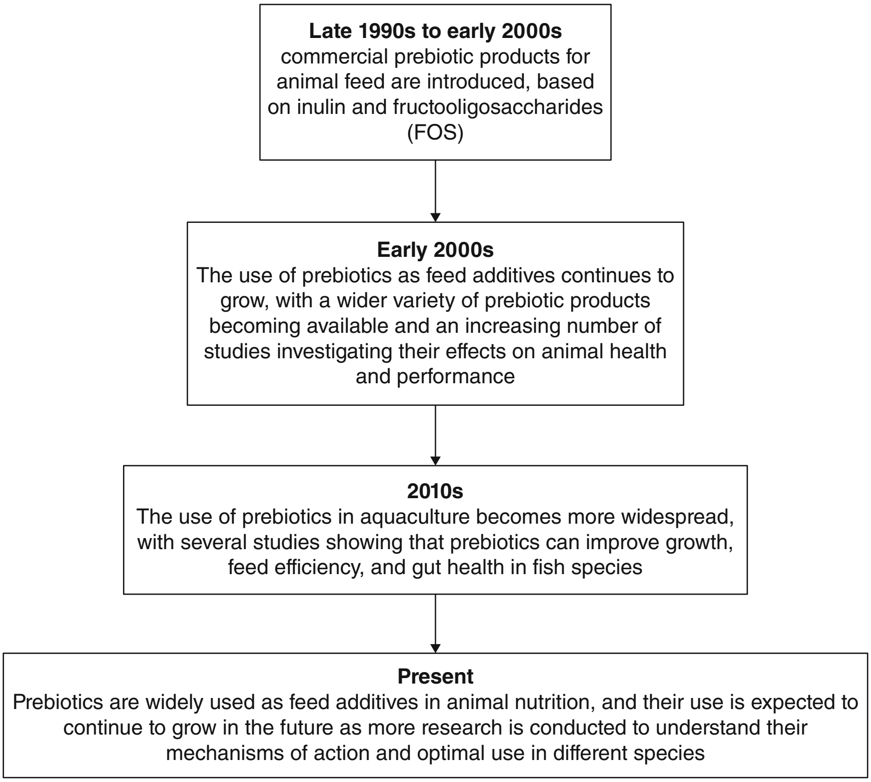

Fig. 2 The use of prebiotics in time

5 History of Essential Oils

The use of essential oils as feed additives in animal nutrition has a long history dating back to the early 1900s. Essential oils composed of a complex mixture of volatile compounds, including terpenoids, phenols, and aldehydes, which give essential oils their distinctive odor and flavor (Alfermann and Njardvik 1998). One of the earliest uses of essential oils in animal nutrition was for their antimicrobial properties, which were thought to improve animal health and growth by controlling gut pathogens. For example, the use of oregano and thyme essential oils as feed additives was shown to have potent antimicrobial effects against various bacteria and parasites, such as *Escherichia coli*, *Salmonella*, and *Ascaris suum* (Burt 2004). These findings paved the way for the widespread use of essential oils as feed additives in animal nutrition, especially in poultry and swine production. Over time, the use of essential oils as feed additives has expanded to include a wide range of applications, including improved growth performance, feed efficiency, and gut health. For example, the addition of peppermint oil to pig diets was shown to improve weight gain and feed efficiency, while also reducing the incidence of diarrhea (Wang et al. 2010). Similarly, the use of rosemary and eucalyptus essential oils in poultry diets was shown to improve growth performance, feed efficiency, and gut health by modulating the gut microbiota (Abdelqader et al. 2013). More recently, the use of essential oils as feed additives has expanded to include their potential as natural growth promoters, immunomodulators, and antioxidants. For example, the addition of clove and cinnamon essential oils to broiler chicken diets was shown to improve growth performance, feed efficiency, and immune function (Hossain et al. 2016). Additionally, the use of lemon and ginger essential oils was found to have potent antioxidant effects in pig diets, which could improve animal health and prevent oxidative stress (Sari et al. 2019).

Despite the long history and growing body of research on the use of essential oils in animal nutrition, there is still much to be learned about the mechanisms of action and optimal usage of these feed additives. For example, the complex composition of essential oils, including their volatile and highly reactive compounds, poses challenges for their safe and effective use in animal nutrition (Alfermann and Njardvik 1998). Additionally, there is a need for more research to determine the optimal dose and form of essential oils for different species and production systems.

In conclusion, the use of essential oils as feed additives in animal nutrition has a long history and a growing body of research to support its benefits for animal health and performance. While there are still challenges to overcome and much to be learned about their optimal usage, essential oils have the potential to be a valuable tool for improving animal nutrition and sustainability (Giannenas et al. 2013).

6 History of Minerals and Vitamins

The incorporation of supplemented minerals and vitamins in animal diets was a milestone for the increment in their productivity. Although they make up a small part of an animal's diet, vitamins and minerals are vital to maintaining their health, comfort, and performance. These nutrients perform crucial roles in metabolic process. The scarcity of vitamins and minerals in animal nutrition can negatively affect growth and performance yields (McDowell 1996).

The mineral content in animal tissues and feeds varies widely. Before the mid-nineteenth century, there was limited understanding of the mineral constituents in plant and animal tissues and their role. The first evidence of the importance of minerals in nutrition came from Fordyce (1791), who indicated the need of a supplement "calcareous earth" for canaries to stay healthy and produce eggs. References on the importance of salt in cattle nutrition were made in 1850 (Boussingault 1847) along with the consideration of iodine as significant for maintaining a healthy organism (Chatin 1854). Later on, during the second quarter of the twentieth century, several researchers focused on mineral investigation regarding deficiencies, imbalances, or toxicities, and basic studies with laboratory animals fed specialized diets were performed. Sodium, potassium, calcium, magnesium, phosphorus, chlorine, sulfur, iron, coper, cobalt, iodine, and zing were recognized as essential minerals and efforts took place to meet their requirements when formulating diets (Haag 1951). Great knowledge regarding mineral metabolism was provided by Underwood and Suttle (1999) in all livestock species. Changes in animal husbandry and immense intensification of livestock sector have led to the substantial need of balancing trace elements to maintain both production and health status. Currently, mineral supplementation in concentrate feed is an indispensable practice. New technological and biomedical applications, for example providing minerals in the form of nanoparticles, are adopted to increase bioavailability and absorption (Bhagat and Singh 2022).

Vitamins are a group of organic compounds, essential for normal growth and production processes. Dietary supplementation provides the small quantities of vitamins required, due to their inability of being directly synthesized through animal metabolic pathways. The term vitamin was first introduced by the biochemist Casimur Funk in 1912, originating from the Latin word vita (life) and amine, based on the original perception that vitamins contained an amino acid (Halver 2003). In the early 1900s, vitamins research began to rise in the effort to treat several disorders identified in humans, such as scurvy, night blindness, beriberi, and pellagra. Experiments with animals including rats, mice, chickens, pigeons, guinea pigs, and dogs contributed significantly to the advances made in vitamin research (McDowell 2006).

Monogastric animals depend solely on external sources to meet their vitamin requirements, while in the rumen symbiotic processes lead to the production of vitamin B complex (McDonald et al. 2011). Livestock animals' optimal performance is the ultimate goal under commercial conditions. Their requirements cannot be met only by providing raw materials such as forage and cereal grains, hence additional supplementation is needed (McDowell 2006).

7 History of Enzymes

Proteins called enzymes operate as biological catalysts by quickening chemical reactions. Enzyme catalysts are required for the majority of metabolic processes in the cell to proceed at speeds quick enough to maintain life (Stryer et al. 2002). Enzymes serve a plethora of an organism's functions including signal transduction, cell regulation, transportation of cargos, and of course metabolic activity.

Enzymes that are aftereffect of the metabolic activity of animal's system or of the microorganisms that constitute their natural microflora are so called endogenous enzymes. The main activity of endogenous enzymes is to promote the digestion of animal feed and therefore the weight gain and animal growth. However, despite their beneficial results, endogenous enzymes do not sufficiently contribute to their goal, thus rendering necessary their supplementation in animal's feed with exogenous enzymes (Velázquez-De Lucio et al. 2021).

The most significant and practical additives in the animal feed sector are enzymes (Ojha et al. 2019). Although its usage in the livestock feed business was modest a few years ago (Walsh et al. 1993), the poultry sector was the first to express interest in it in the 1980s, and, over time, their use in animal feed increased significantly, with an estimated commercial value of $1280 million in 2019 (Brufau 2014).

Exogenous enzymes are zootechnical additions that enhance the uniformity and nutritional value of animal feed, increase digestibility, especially of carbohydrates, and animal performance, decrease the effect of antinutrients, maintain intestinal health, and reduce the viscosity that would otherwise have a negative impact on energy intake by generating unstirred layers on the epithelium's surface (Rainbird et al. 1984). Celluloses, β-glucanases, xylanases, and associated enzymes phytases, proteases, lipases, and galactosidases are the most widely utilized exogenous enzymes in the animal feed business. Exogenous enzymes are largely used in monogastrics in the animal feed sector, like poultry and swine, to counteract the negative effects of cereals' viscous, non-starchy polysaccharides (NSPs). In the livestock feed industry, other enzyme products are being tested. These include proteases to enhance protein digestion, lipases to enhance fat digestion, galactosidases to mitigate certain antinutritional elements in non-cereal feedstuffs, and amylases to facilitate starch digestion in young animals (Adeola and Cowieson 2011).

In poultry supplementation, the most commonly used enzymes are xylanases, glucanases, pectinases, cellulases, proteases, amylases, phytases, and galactosidases. The use of enzymes has grown to the point where the majority of intensively raised poultry diets now include carbohydrases to improve nutrient bioavailability and assimilation and to alleviate digestive issues caused by viscosity issues (Ojha et al. 2019). Because phytases aid in the absorption of metals like Ca, Mg, and Zn as well as amino acids during the past few decades, they are now widely employed as broiler additives in Europe and the United States (Acosta 2006). Exogenous enzymes are utilized in swine feeding to shorten the maturation and fattening stage of piglets. Pigs need phytases because their endogenous counterparts have almost minimal action, which results in the complete excretion of phosphorus. Amylolytic enzymes are a necessary component of high-starch forages for ruminants, and using phytases has been shown to minimize phosphorus in feces from the perspective of the environment (Pariza and Cook 2010). Due to their capacity to hydrolyze the polysaccharides found in plant diet, phytases and carbohydrases are the enzymes most frequently used in aquaculture. Concerning the use of exogenous enzymes in companionship animals, it is far well known about the administration of amylases, lipases, and proteases in dogs with exocrine pancreatic insufficiency (EPI). Furthermore, some vets propose the use of exogenous enzymes in all pets for digestibility promotion and enhancement of immune system.

Traditionally, the enzymes were isolated from animals, plants, and microorganisms. Recombinant DNA technology facilitated enzyme production for industrial use with expression of single enzyme genes of certain microorganisms by bacterial expression systems in large volumes and with low cost. The search for alternate sources of enzymes, such as ruminal fluid from slaughterhouses, which is rich in cellulases and xylanases but also contains toxic ammonia and phosphorus, has also been prompted by the current environmental crisis (Sarteshnizi et al. 2018a, b). The design of thermostable enzymes with better, particular features and their incorporation in granulated meals are future issues regarding research and development in new enzyme systems (Ravindran 2013). This will enable the manufacturing of high-value products at cheaper costs.

8 History of Antioxidants

The use of antioxidants in animal nutrition, as the most of feed additives, dates back to the early twentieth century, when scientists first discovered the role of vitamins in maintaining animal health. Since then, the field of animal nutrition has made tremendous progress in understanding the specific nutritional requirements of different species of animals, and the role that antioxidants play in maintaining animal health.

One of the earliest uses of antioxidants in animal nutrition was the addition of vitamin E to animal feed. Vitamin E is a fat-soluble vitamin that plays an important role in maintaining the integrity of cell membranes and protecting against oxidative damage. In the 1950s, it was discovered that supplementing animal diets with vitamin E could improve growth, health, and fertility in livestock (Bogden et al. 1987). In addition to vitamin E, other antioxidants, such as vitamin C, carotenoids, and selenium, have also been shown to play important roles in animal nutrition. Carotenoids, for example, are pigments that are found in plant-based diets and have been shown to have antioxidant and immune-boosting properties. Selenium is an essential trace mineral that is required for proper immune function and has been shown to play a role in reducing oxidative stress in animals (Goff and Horst 1997).

In recent years, the use of antioxidants in animal nutrition has become increasingly important as the global demand for animal products continues to rise. The increased demand for animal products has led to increased production pressures and has resulted in animals being exposed to a variety of stressors, such as high-density housing, transportation, and disease challenges. These stressors can lead to oxidative stress and reduced performance and health outcomes for animals (Wang et al. 2018). In response to these challenges, the use of antioxidants in animal nutrition has become a major area of research and development. Scientists are working to develop new and innovative methods for delivering antioxidants to animals, such as encapsulated antioxidants, which can protect the antioxidants from degradation and improve their efficacy in the gut (Niu et al. 2017). Lately, extracts and essential oils of aromatic and so called medicinal plants have been largely exploited as excellent sources of food or diet antioxidants, among which oregano can be regarded as one of the most efficient (Giannenas et al. 2018).

In conclusion, the history of antioxidants in animal nutrition dates back to the early twentieth century, and the use of antioxidants has become increasingly important as the global demand for animal products continues to rise. Antioxidants play a critical role in maintaining animal health and protecting against oxidative stress, and the field of animal nutrition continues to make important advancements in the development of new and innovative methods for delivering antioxidants to animals.

9 History of Amino Acids

Amino acids are essential nutrients for animals, and their importance in animal nutrition has long been recognized. They are the building blocks of proteins and play a crucial role in many physiological processes, including growth, reproduction, and immune function. The use of amino acids as feed additives in animal nutrition has therefore become an important area of research and development, with scientists seeking to optimize their use to improve the health, performance, and efficiency of livestock and poultry.

The amino acids as feed additives in animal nutrition have a hundred-year history, when scientists first began to understand the role of amino acids in animal growth and development. Amino acids are the building blocks of proteins, and are essential for many physiological processes, including muscle growth, immune function, and tissue repair. The discovery of individual amino acids and their specific functions, combined with advances in feed technology, led to the development of amino-acid-based feed additives for animals.

One of the earliest uses of amino acids in animal nutrition was the addition of methionine to poultry diets. Methionine is an essential amino acid that is required for the synthesis of proteins but is often limiting in poultry diets due to its low availability in plant-based feed ingredients. The addition of methionine to poultry diets has been shown to improve growth performance, egg production, and feed efficiency (Wang et al. 2016). In addition to methionine, other essential and non-essential amino acids, such as lysine, threonine, and tryptophan, have been used as feed additives in animal nutrition. These amino acids are added to animal diets to address specific nutritional deficiencies, and to improve the balance of amino acids in the diet. For example, lysine supplementation has been shown to improve growth performance, feed efficiency, and meat quality in pigs (Yao et al. 2015). More recently, advances in animal nutrition research have led to the development of new and innovative amino-acid-based feed additives, such as peptides and nucleotides. Peptides are short chains of amino acids that are rapidly absorbed and utilized by animals, and have been shown to improve growth performance, immune function, and gut health in various species of animals (Geng et al. 2018). Nucleotides are the building blocks of DNA and RNA, and have been shown to improve immune function, tissue repair, and gut health in animals (Xie et al. 2019).

In conclusion, the use of amino acids as feed additives in animal nutrition has a long and rich history. Today, advances in animal nutrition research have led to the development of new and innovative amino-acid-based feed additives, such as peptides and nucleotides, which offer new opportunities for improving animal performance and health.

10 History of Acidifiers

Acidifiers have been used as feed additives in animal nutrition for several decades. Their primary function is to regulate the pH of the digestive system, which can have a profound impact on the health and performance of animals. Acidifiers work by lowering the pH in the digestive tract, creating a more acidic environment that is less hospitable to harmful bacteria and other pathogens. This can help to reduce the risk of disease, improve nutrient absorption, and enhance overall health and performance.

One of the earliest uses of acidifiers in animal nutrition was the addition of organic acids, such as formic and propionic acid, to animal feed (Kirsch et al. 2006). These organic acids have been shown to have a number of benefits for animal health and performance, including improved gut health, enhanced feed utilization, and increased weight gain. In addition to organic acids, other types of acidifiers have been developed and used in animal nutrition, such as mineral acids and feed-grade enzymes. Mineral acids, such as sulfuric and hydrochloric acids, have been shown to be effective in reducing the pH level of the digestive tract, which can help to control harmful bacteria and improve feed utilization (Flesner et al. 2011). Feed-grade enzymes, such as phytases, can also help to improve the efficiency of feed utilization by breaking down plant fibers and releasing the nutrients for absorption (Shan et al. 2016).

Despite the long history and widespread use of acidifiers in animal nutrition, their use is not without controversy. Some research has suggested that excessive use of acidifiers may lead to nutrient imbalances, digestive disorders, and reduced feed utilization (Kirsch et al. 2006). Therefore, it is important to use acidifiers in animal nutrition with caution and only under the guidance of a veterinarian or nutritionist.

In conclusion, acidifiers have played a significant role in the development of modern animal nutrition, providing a means to improve the health and performance of livestock through the manipulation of the digestive environment. However, the use of acidifiers should be approached with caution and only used under the guidance of a professional in order to ensure that their benefits are realized without any adverse effects (Fig. 3).

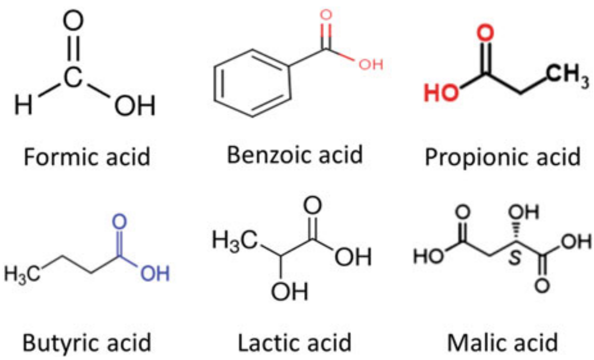

Fig. 3 Common type of acidifiers used in animal nutrition

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