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Review on Rabbit Feeding Options Other Than Antibiotics to Encourage Growth

Layla Abd-Al-Sattar Sadiq Laylani
Northern Technical University Kirkuk technical institute, Musul, Iraq

Corresponding Author: **Layla Abd-Al-Sattar Sadiq Laylani**

Abstract
For the purposes of this study, rabbit feeds specifically, the emphasis is on the most well-known compounds that have been explored and produced as alternatives to dietary antibiotics. The article begins with a brief review of the history and achievements of antibiotic growth promoters, before moving on to discuss probiotics, prebiotics, enzymes, and organic acids in that order. It should come as no surprise that when compared to animals like pigs and poultry, data on rabbits is quite limited. Nonetheless, the existing performance outcomes and their potential underlying causes are addressed. The effects of these compounds on digestibility and catcall activity are discussed in detail.

Keywords: Rabbits, Organic acids, Enzymes, Prebiotics, Probiotics

1. Introduction

When Stansted and Jukes mixed leftovers from chlortetracycline manufacturing into chicken feed fifty years ago, they started using antibiotic growth promoters (AGPs) in animal agriculture. Though their addition was motivated by a desire to supplement vitamin B12 levels, they ended up stimulating development in a way that cannot be attributed to the vitamin alone. The residues' antibacterial properties were the most likely culprit. Following this discovery, AGP was rapidly included into diets for a broad variety of animal species and antibiotics [1, 2].

Antibiotics have been widely employed in animal production in recent decades for both medicinal and growth-promoting purposes. Antibiotics are often used in large doses for a short period of time in the context of therapeutic use; they may be injected or given orally or via the animal's food or water. Instead, tiny doses given repeatedly, such as would be the case with feed, are the norm when trying to stimulate growth. It is obvious that there is some crossover between the two meanings. Despite its therapeutic intentions, prophylactic uses might seem a lot like growth-promoting uses, and vice versa. Growth promotion, on the other hand, can only be temporary in animals with short lifespans. Former EU law made a clear distinction between the two contexts. Antibacterial glycoproteins (AGPs) were a niche class of antibiotics that have been rapidly disappearing in recent years. Nonetheless, they generally maintained higher production performance, with most of the economic gains going to customers in the form of cheaper meat, eggs, and other animal products. Secondary benefits of AGPs are typically overlooked. Reduced feed consumption per unit of output means less land is required for feedstuff production, less feedstuffs are imported by many nations, and less manure is produced (manures are a liability in many modern production systems). In addition to lowering methane emissions, most AGPs used in cow production may improve animal health [3, 4].

Not as much is understood about the effects of AGPs as about their mechanisms of action, despite the fact that the latter have been the subject of extensive study. Over the years, several different processes have been hypothesized, some of which are unique to ruminants; it is possible that many of them may contribute to the final outcome. The fact that germ-free animals seldom react to AGPs implies that the majority of their effects take place in the gut microbiome. Molecular methods of microbiological identification have only just been widely used, therefore it is understandable that there is still no consensus on the mechanisms of action of AGPs. However, this is not surprising given the enormously complicated system in which AGPs function. In addition, the already complicated and imperfectly understood interactions between bacteria and the gut immune system may only add to the difficulty of the topic.

Many of the effects of AGPs are summarized in Table 1, which draws primarily from the [5] Commission on Antimicrobial Feed Additives report [6] but also from Barton [7, 8]. These effects include a degree of inhibition of pathogenic microorganisms, a reduction in microbial toxic metabolites, a lowering of epithelium turnover, a nutrient-sparing effect, and a reduction in intestinal motility. One further mechanism that gets a lot of attention is the suppression of bile salt deconjugation by bacteria [9, 10].

Increases in feed efficiency, growth rate, and egg output may all be attributed to the usage of AGPs on farms. Feed efficiency is increased in a particular way, likely associated with nitrogen metabolism, as seen by the fact that growth rate and feed conversion rate (FCR) both improve despite a constant intake [11, 12].

Table 1: Antimicrobial feed additives have been linked to a number of adverse impacts on animal physiology, nutrition, and metabolism

Implication for physiology		Consequences for nutrition		Resulting metabolic consequences	
Gut wall weight	R	Limiting amino acid supply	I	Fatty acid oxidation	R
Gut wall length	R	Nitrogen retention	I	Alfa- toxin production	R
Gut wall diameter	R	Gut energy loss	R	Toxic amine production	R
Gut food transit	R	Energy retention	I	Ammonia production	R
Stress	R	Fatty acid absorption	I	Gut urease	R
Gut absorptive capacity	I	Vitamin absorption	I	Faecal fat excretion	R
Faecal moisture	R	Vitamin synthesis	R	Liver protein synthesis	I
Mucosal cell turnover	R	Trace element absorption	I	Gut alkaline phosphatase	I
Feed intake	R=I	Ga	I		
		Ca	I		
		Plasma nutrients	I		

R: a reduction; =: no effect; I: an increase

That juvenile animals respond more strongly to AGPs than older ones may be explained in part by this mechanism.

2. Antibiotics in the Rabbit Diet

The Aldrich chemical Company in Milwaukee, Wisconsin, AGPs are antibacterial, hence it was assumed they would be counterproductive in animal species where microorganisms perform a large portion of the digestive process. This line of thinking is most at home with ruminants, but it may be extrapolated to include other herbivores that ferment their food in the hindgut, such the rabbit. Science and practice combined to prove that this was not always the case. Certain AGPs enhance the productivity of ruminants and rabbits. The most common anti-parasitic medication (AGP) found in rabbit food was zinc bacitracin [13, 14].

3. The ban on Antibiotics

European consumers opposed the use of AGPs in animal feeds despite the fact that they are often ineffective due to rising concerns about food safety. Antibiotic residues in foods including beef, milk, and eggs were a concern because of the AGPs. In reality, the antibiotics approved for use as AGPs in the European Union were little absorbed in the intestines. It was necessary for AGPs to have little absorption, a narrow antibacterial range, and no particularly important therapeutic uses in Europe before they could be approved for use in humans or animals. Milk residual issues are been linked to local udder treatments rather than in-feed AGPs, although they do occur [15, 16].

Others in the consumer community and the medical community have voiced concerns that AGPs, which are essentially antibiotics given in very small dosages over extended periods of time, may only increase the prevalence of microbial resistance in livestock. This is a major critique, and it has backed up by science (Wegener, 2006). The fact that bacteria of various species may exchange genetic material only makes the problem of AGP-selection for resistant strains worse. However, there is still debate over the real-world implications of these resistances, and how much of a role they play in the growing and concerning issue of antibiotic resistance in pathogenic organisms. Compared to the vast but mostly inevitable antibiotic use in hospitals, as well as the insufficient and partially avoidable antibiotic use by consumers, general practitioners, and field veterinarians, its contribution may be little. However, the conditions were ideal for AGP blocking.

The nations of Scandinavia were among the first to outlaw AGPs. Their limited performance in lowering resistance rates undoubtedly led to the EU's blanket ban on AGPs beginning in [19], and to the reason that a similar restriction is now a theoretical possibility in the United States. However, it is imperative that we do not lose sight of the fact that the Scandinavian ban was only one tool among a much larger arsenal of measures used to combat antibiotic-resistant germs throughout the world.

The Scandinavian region served as a kind of proving ground for the AGP prohibition. Farmers and technicians acclimated to the new reality after an early time when the withdrawal of AGPs was partially balanced by rising therapeutic use of antibiotics on farms, resulting in a reduction in worldwide antibiotic usage as envisaged. Several antibiotic substitutes used in animal feed have been useful in smoothing over this changeover.

Simultaneously, the quest for nonantibiotic compounds that could have comparable effects on food-producing animals was fueled by increased criticism of AGP usage in animal production. Antibiotic bans were a major impetus for their research and development, and as a result, they are often grouped together and referred to as alternatives to antibiotics, despite the fact that there is little overlap between them and that many of them are fascinating even when not used in place of antibiotics. Of all the options out there, probiotics, prebiotics, symbiotics, enzymes, and organic acids have gotten the most attention and research. It is possible that the first three be taken together, have also received a lot of attention from the fields of human nutrition and health. Immune system boosters and plant or herbal extracts are two examples of the alternative items that might be discussed.

In the '80s, consumers showed a lot of enthusiasm for these other options. It is understandable that performance studies were conducted at a higher rate initially than mode of action studies; yet, much study has already been conducted on the latter. Animal nutritionists and veterinarians initially had doubts about these products, and they had good reason to be skeptical. However, as time went on, they gained widespread acceptance, and the EU eventually amended its feed additive regulations to accommodate them.

Most, if not all, of these alternatives to antibiotics may also affect the gut macrobiotic and the gut immune system, making their mechanism of action as difficult to decipher as that of AGPs. Another apparent similarity is that they are most effective and efficient at certain crucial times (like weaning) and/or under less-than-ideal environmental settings [17, 18].

Antibiotic alternatives were explored most extensively in swine and chickens, as predicted by the monogastric group. The rabbit has a very specific digestive system, making it risky to extrapolate results from experiments done on other species. Where it is necessary, we will highlight certain distinctions.

4. Probiotics

Elie Metchnikoff's work on the possible health advantages of fermented milks for human nutrition around the turn of the twentieth century is universally credited as the impetus for the modern interest in probiotics. Even the term "probiotic" is rather recent. While the precise definition of probiotics (e.g., which types of microorganisms count, and whether or not they must be alive) remains contentious, the definition that a probiotic is a preparation of live microorganisms that, when given in sufficient doses, is beneficial to human or animal health is widely accepted.

Probiotic microorganisms have been shown to produce a variety of antibacterial compounds, according to many studies. Organic acids, hydrogen peroxide, and bacteriocins are all examples of compounds that may kill microorganisms, modify their metabolism, and/or decrease their toxin output. Although some of these pathways have been confirmed *in vitro*, they still need *in vivo* confirmation before being considered anything more than conjecture.

Some research has been done on the impact of probiotics on the gut microbiota, particularly pathogenic species, and on the gut's shape and physiology, but in general, *in vivo* studies with farm animals have focused on performance and health. Some studies have even utilized animals as a stand-in for humans (Thomke and Elwinger, 1998).

Probiotics often include strains of Gram-positive bacteria, including those from the genera Bacillus (B. cereus, var. toyoi, B. licheniformis, B. subtilis), Enterococcus (E. faecium), Lactobacillus (L. acidophilus, L. casei, L. farciminis, L. plantarum, L. rhamnosus), Pedicoccus (P. acidilactici (S. infantarius). Yeasts and fungi, especially Saccharomyces cerevisiae, are also used.

Probiotics have been shown to be effective in a variety of studies, particularly for use with chicks and piglets grown under less than optimum circumstances (reviewed by Thomke and Elwinger, 1998, and Simon *et al*., 2003). However, there have also been published a number that have no impact at all, or even have unintended consequences.

There are a variety of potential explanations for the inconsistent findings; some of them are animal-specific, while others are probiotic-specific. Among the former are all the variables that may impact the animal gut microbiota, including nutrition, stress, and/or illness. This is in addition to inherent individual variances (Simon *et al*., 2003). These include, but are not limited to, issues related to the selection of species and strains, the technical preparation of the probiotic, the production of the feed, the administration dosage, and the interactions between the probiotic and medications.

The probiotic's live bacteria and/or yeasts need to be able to survive the feeds' manufacturing and storage processes. Particularly important for bacteria that do not produce spores [21]. There is at least one commercial product on the market aimed towards ruminants that is based on clearly dead microorganisms and hence meets none of these criteria. It is debatable if scientifically speaking it qualifies as a probiotic.

Probiotics, too, ought to be able to withstand the digestive secretions of animals without posing any kind of hazardous danger to them. Specifically, probiotic organisms need to reach concentrations in the range of 106-107 per g in the intestinal material to have any detectable impact, as stated by Guillot (2001).

Symbiotics % preparations having a combination of a probiotic and a prebiotic are based, in part, on the fact that the composition of the feed may be modified so as to enhance the action of a probiotic [22] shown in pigs that probiotics in the small intestine may be enhanced by maltodextrins and polyunsaturated fatty acids, and in the large intestine by fructo-oligosaccharides (FOS).

Probiotics for rabbits

Naturally, there are fewer probiotic research using rabbits than there are with other monogastric farm animals. Still, there are a few studies that evaluate the impact on growth, feed conversion, reproduction, and mortality; sometimes, caecal activity and digestibility are also examined.

Tabulated in Table 2 is a condensed summary of a respectable sample size of experimental experiments using probiotics in maturing and fattening rabbits. Using data from these Experiments, Fig 1 depicts average daily gain (ADG), feed conversion ratio (FCR), and mortality. There is a direct correlation between ADG and FCR, and mortality is given as the absolute difference, in percentage points, between a therapy and the matching control. While changes were often not statistically significant, 15 of 20 studies did find improvements in ADG, thus this finding is nonetheless worth highlighting. One of the two studies that did not turn out well had a diet low in fiber (just 10% of ADF), which may have contributed to the disappointing results. For the most part, the same holds true for FCR. In several of the studies when mortality was evaluated, it was also lowered (7 positive, 6 null, and 3 negative results).

A lower sample size of studies examined reproductive outcomes. You can see a summary of the findings in Table 3, which suggests that the major impact may be an increase in litter weight at weaning. However, not all of the changes were statistically significant [20].

Histopathology sectioning and prepping

The tissues from the rat testicles were removed and promptly preserved in 10% formaldehyde saline. Paraffin blocks were made from tissue sections that had been treated (paraffin method). Rotatory microtome sections were placed on glass slides for examination. Hematoxylin and eosin (H&E) stain was used to examine the tissue slices. Light microscopy was used to analyze the tissue sections.

Table 2: A review of the methods employed in probiotic trials involving rabbits at various stages of development and fattening

Reference	A period of testing lasting days	Probiotic	No. trial	Degrees of probiotics	Unit Rabbits/ cages	Soluble fiber in the diet	Parameters of the test
De Blas *et al*., 1991	30 d-2 kg LW	Paciflor (Bacillus CIP 5832)	1	0.01% (10^6 spores/g)	45	36.5% NDF	Between 23-28°C and 18-22°C
Luick *et al*., 1992	36 d	Lacto- sacc (2)	2	0.2%	15	23.1% ADF	Experimental
Luick *et al*., 1992	36 d	Lacto- sacc (2)	3	0.2%	14	9.9% ADF	Experimental/low fibre
Gippert *et al*., 1992	28-84 d	Lacto-sacc (2)	4	0.1%	172	10.6% CF	Commercial
Gippert *et al*., 1992	42-77 d	Lacto-sacc(2)	5	0.1%	100	10.6% CF	Experimental
Maertens and De Groote, 1992	28-70 d	Biosaf S. cerevisae	6	0.15%	60	15.5% CF	Optimal housing conditions
Yamani *et al*., 1992	28-84 d	Lacto-sacc(2)	7	0.1%	24	16.7% CF	Commercial
Jerome *et al*., 1996	30-79 d	Saccharomyces cerevisae	8	10^6 spores/g	18 cages with 6 rabbits	16.5% CF	Experimental
Maertens *et al*., 1994	28-70 d	Paciflor (Bacillus CIP 5832)	9	0.01% (106 spores/g)	90	16% CF	Optimal housing Conditions
Amber *et al*., 2004	35-126 d	Lact-A-Bac (L.acidophilus)	10	0.05% (8 H 1011 cfu/g)	27	12.5% CF	Experimental
Kustos *et al*., 2004	35-77 d	Bioplus 2B (B. licheniformis, B. subtilis)	11	0.04% (1.28 H 106cfu/g)	60	15.5% CF	Experimental 18-23ºC - Thermal stress
Esteve-García *et al*.,2005	28 d	Toyocerin (B. cereus var. toyoi)	12	0.02%	15 H 5 cages	14.9% CF	Experimental
Trocino *et al*., 2005	35-70 d	Toyocerin (B. cereus var. toyoi)	13	0.02% (2 H 105spores/g)	63 cages	41% NDF	Commercial

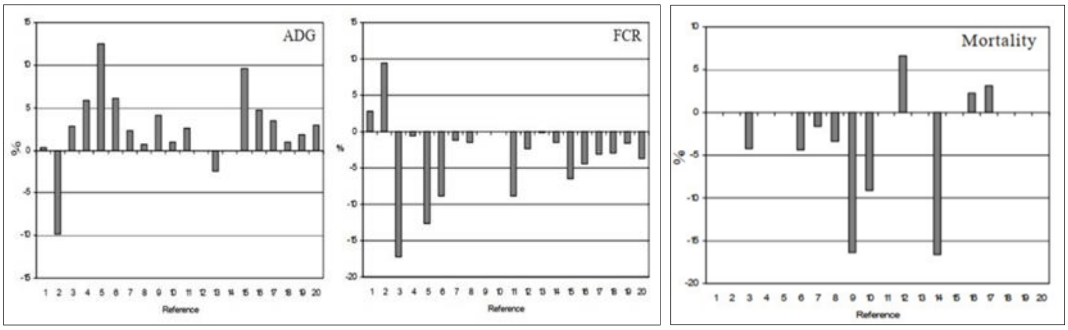

Fig 1

Table 2 summarizes data on the average daily gain (ADG), feed conversion ratio (FCR), and mortality of growing rabbits across all trials. Each reference number corresponds to a unique trial number in Table 2. The difference between the treatment and the control group in terms of mortality is stated as an absolute number (percentage) and the average daily gain (ADG) is reported as a percentage of the control group.

Many studies have investigated how adding probiotics may improve digestion. Although Gippert *et al*. (1992) and Luick *et al*. (1992) did not, other researchers did find a correlation. Crude fiber digestibility was enhanced at 8 and 12 weeks in a study conducted including crude fiber.

Either several authors have investigated the impact of probiotics on the catcall macrobiotic, by quantifying, the microbes present (Amber *et al*., 2004) or by analyzing the products they produce, notably volatile fatty acids (VFA) (Maertens *et al*., 1994). The probiotic considerably raised cellulolytic bacteria counts (cfu/ml) while simultaneously decreased ureolytic bacteria counts in the research by Amber *et al*. (2004). The caecal pH was not altered by the probiotic in this trial. Maertens *et al*. (1994) found that the probiotic Paciflor had no effect on caecal pH or volatile fatty acid levels.

It will be important to apply the sort of research that are now prevalent the effects on the gut immune system, as well as the shape, absorption capacity, and barrier impact of the epithelium, are all areas that Klis and Jansman (2002) highlight as needing further investigation. In the next part, we will apply this line of thinking to the topic of prebiotics and symbiotics.

Number crunching

The data are presented as the mean standard deviation of ten independent measurements. One-way analysis of variance (ANOVA) was used for statistical analysis to see whether there were statistically significant differences between the various treatment groups. Post hoc Tukey's test comparisons were performed for each treatment effect that was statistically significant. P values of 0.05 or 0.01 were chosen as the threshold for statistical significance. The SPSS 8 statistical software program was used for all analyses.

Table 3: Variations in reproductive outcomes because of probiotic use (expressed as a percentage of the baseline)

Reference	Probiotic	Parturition interval	Litter weight at weaning	Litter size at weaning
Pinheiro *et al*., 2006	Bacillus cereus var. toyoi		+5.4	!3.3
Nicodemus *et al*., 2004	Bacillus cereus var. toyoi	-10.2*	+7.6	+9.9
Maertens *et al*., 1994	Paciflor Bacillus cip 5832		+6.4*	-1.3
Maertens and De Groote, 1992	Biosaf		+3.5	+1.3

Only two probiotics are now recognized as safe and effective for rabbits in the European Union. Bacillus cereus var. toyoi is the bacterial strain, while Saccharomyces cerevisiae NCYC Sc 47 is the yeast strain.

5. Prebiotics

Prebiotics are another drug class that might be used instead of antibiotics. Prebiotic is a relatively new word that often refers to oligosaccharides that are indigestible by animal enzymes but may selectively activate particular gut bacteria species, which may have favorable impacts on the host's health. Prebiotics may be synthesized by partial acid or enzymatic hydrolysis of polysaccharides or transglycosylation processes, or it can be isolated directly from natural sources (plants, yeasts, milk). Fructo-oligosaccharides (FOS), α-galacto-oligosaccharides (GOS), transgalacto-oligosaccharides (TOS), and mannan-oligosaccharides (MOS) are the most common types of oligosaccharides sold on the marketplace today xilo-oligosaccharides (also known as MOS) and other similar sugars (XOS).

Oligosaccharides are aimed to selectively boost the good microorganisms that are already present in the gut, as opposed to

probiotics, which are meant to introduce beneficial microbes to the gut. They outperform probiotics in two distinct ways: technologically, as there are no major issues with the thermal feed processing and the acid conditions of the stomach, and they are safer since they do not introduce alien bacteria species into the gut. Beneficial microorganisms will be more able to compete with harmful ones if they are encouraged to thrive. But prebiotics may also have additional positive benefits, independent of activating that component of the gut microbiota (Forchielli and Walker, 2005): first, they can limit the adherence of pathogens to the mucosa, by competing with its sugar receptors.

Most of the published papers deal with human diets, and the majority of the research on prebiotics' method of action has been conducted *in vitro* and on laboratory animals. Positive benefits have been discovered in farm animals, such as increases in daily growth, feed conversion ratio and/or health condition, however the impact tends to differ depending on the oligosaccharide and the circumstances of use (Patterson and Burkholder, 2003; Lan *et al*., 2005).

The Role of Prebiotics in Rabbit Health

In the past, rabbits have been used to assess the effectiveness of some prebiotics. Most of the literature to far has focused on how they affect production rates and/or the caecal microbiota; only lately has there been research into how they affect gut architecture.

The impact of prebiotics on rabbit performances have been at best inconsistent. As far as FOS are concerned (Table 4), Aguilar *et al*. (1996) received a favorable impact on growth rate, without influence on FCR; Mourão *et al*. (2004) discovered the reverse, i.e., no effect on growth rate but a propensity for an improvement in FCR; conversely, Lebas (1996) did not receive any impact at all. While Peeters *et al*. (1992) found no deleterious impact of GOS on mortality or morbidity, Gidenne (1995) found the opposite.

Table 4: Trial results on the impact of FOS supplementation on growth-related performance and mortality in rabbits are presented

References	Mortality (% control -% xperim.)	Profit on average per day	Feedback alteration
Lebas, 1996	-1	NS (35.5 vs 35.6 g/d)	NS (3.30 vs 3.30)
Aguilar *et al*., 1996	NS (6.3 vs 5.9)	P<0.001 (32.3 vs 35.9 g/d)	NS (3.16 vs 3.10)
Mourão *et al*., 2004	NS (19.4 vs 16.7)	NS (40.1 vs 40.6 g/d)	P<0,01 (3.6 vs 3.3)

The caecum of rabbits fed prebiotics should become an unfavorable environment for pathogenic micrорganisms. With this goal in mind, a few research experiments were designed. The findings of Morisse *et al*. (1992) lend credence to the idea that FOS acts as a barrier in the caecum, protecting the resident population of saprophytic Escherichia coli. VFA production went up, while caecal ammonia went down. Despite this, Maertens *et al*. (2004) found that FOS and inulin had no influence on the absolute amounts of VFA. GOS (Peeters *et al*., 1992) and MOS (Mouro *et al*., 2006) are two more prebiotics that have been studied. resulted in a rise in caecal VFA concentrations. However, Gidenne (1995) found no change in the cecal VFA pattern when GOS was added.

The bacteria in the rabbit's upper intestine, particularly when the rabbit is actively engaging in caecotrophy, may hydrolyze the fructans with a reduced degree of polymerization (Carabao *et al*., 2001). To the contrary, they will do most of their work in the caecum, which might happen in very young animals. Maertens *et al*. (2004) found that the ileal digestibilities of FOS and inulin are about equal to 50% when rabbits are not permitted to engage in caecotrophy.

The MOS are potential prebiotics since their major action is expected to be to avoid colonization rather than to stimulate beneficial microbes (Kocher, 2006). A large number of pathogens contain fimbriae that bind to the mannose residues of intestinal cell receptors; if these fimbriae bind to MOS, they are unable to adhere to the mucosa. Performances with MOS were equivalent to those with AGPs in a number of studies (Fonseca *et al*., 2004; Pinheiro *et al*., 2004; Mouro *et al*., 2006). Regarding changes in gut shape, Mouro *et al*. (2006) found that MOS decreased microbial numbers and lengthened ileal villi.

Variations in experimental techniques, including the number of animals used, the cleanliness of the environment, the kind of prebiotic used, and the quantity of prebiotic given to the meal, may account for the inconsistent findings when testing the effects of prebiotics. Several scholars have placed an emphasis on this latter component (for instance, Mouro *et* *al*., 2006). The economic viability of using prebiotics is diminished if excessive quantities need to be added. It's also conceivable that prebiotics with shown advantages in long-lived animals, including humans, may not exhibit the same benefits in short-lived species, like the rabbit.

Finally, it is important to remember that rabbits need a diet high in fibrous feedstuffs, some of which include notably high concentrations of oligosaccharides. Selecting the feedstuffs having the most desired oligosaccharides for each point of the rabbit life might be an alternative to using commercial prebiotics.

6. Enzymes

Addition of enzymes to feeds is not a novel concept, although it did not become widespread until the late 1980s (Choct, 2006). Prior to this, enzymes were both too expensive and inadequate to be useful in the feed industry since they had been created for other functions (such as cleaning and cooking). In addition, most of these microorganisms lacked the thermostability to endure the feed pelleting process. It's not hard to see why they usually failed in the beginning; after all, many individuals just can't handle the acid of the stomach, and/or the digestive proteases.

Beta-glucanases and xylanases, enzymes that partly hydrolyze the NSP in wheat, rye, triticale, oats, and barley, were the first to be successfully introduced to diets. The advantages of using these enzymes in poultry feeding are well-documented, and their commercial usage is common at this point. Improvements in nutritional absorption, litter quality, and egg cleanliness result from their ability to decrease intestinal viscosity brought on by beta-glucans and arabinoxylans, respectively. In addition, the oligosaccharides and/or sugars they release may limit the growth substrates for pathogenic microbes in the ileum and caecum while encouraging the growth of benign ones (Bedford, 2000). In addition, the use of these enzymes allows for more adaptability and, ultimately, cost savings in feed formulation, which is particularly helpful in situations when maize is in short supply and/or relatively costly compared to other cereals. While full hydrolysis of glucans is often desired because it yields glucose, partial hydrolysis of arabinoxylans is likely sufficient, provided that viscosity is decreased enough.

Phytases were the second set of effective enzymes, but on a lesser scale. Phytases may increase the availability of other nutrients in the diet in addition to making previously inaccessible portions of the feed's phosphorus available. When phosphates are hard to come by and costly, and/or when phosphorus levels in manures are subject to taxation, phytases may become economically attractive.

Soybean and other legume grain flatus-causing oligosaccharides may be hydrolyzed utilizing enzymes such as a-1, 6 galactosidases and b-1,4- mananases, the activities of which have previously been examined. In a recent meta-analysis of 14 studies, Kim and Baker (2003) found that the addition of a-1, 6 galactosidases, b-1,4-mananases, or enzyme complexes to diets fed to pigs made from soybeans improved growth performances and digestibility in 70% of the trials.

Although glucose-liberating cellulases have shown promising results in the past, they remain the proverbial Holy Grail of feed enzymes. The limited reaction may be attributed in part to the enormous intricacy and interconnectedness of the plant cell wall structure. Silages, which are also used as animal feeds, have been studied extensively with cellulases, and their usage is not uncommon. However, silage enzymes are a niche issue that will not be covered here.

This means that all feed enzymes are hydrolases. They need to be resistant to the animal's own proteases, as well as heat, to withstand pelleting, acid, to withstand gastric transit, and the general environment of the animal's digestive tract. It is important to keep in mind, while attempting to make sense of results, that the vast majority of commercial enzymes are in fact crude extracts containing a wide range of enzyme activity beyond the primary and reported one.

Rabbit digestive enzymes

There was no discernible influence of enzymes on rabbit performance in the majority of studies conducted over the last decade (Remóis *et al*., 1996; Fernandez *et al*., 1996; Pinheiro and Almeida, 2000; Falco-e-Cunha *et al*., 2004; Garcia *et al*., 2005). Only with proteases and proteases + xylanases did Garca *et al*. (2005) find a reduction in mortality (probably reducing protein flow to the caecum). Other studies also found promising outcomes; Eiben *et al*. (2004) tested cellulases and found reductions in FCR and mortality in rabbits weaned at 23 days of age, although ADG was unaltered.

In other experiments, the addition of enzymes increased how well fiber was digested. As seen in the work of Fernandez *et al*. (1996) and Bolis *et al*. Cellulase and an enzyme pool (xylanase, b-glucanase, b-glucosidase, pentosanase, myloglucosidase, acid and neutral protease) significantly increased the digestibilities of NDF (+5%) and ADF (+13%) for the latter authors, while simultaneously decreasing digestible and metabolizable energies, and nitrogen balance, in comparison to the control diets.

Several studies examined how enzymes affected the digestive tract of rabbits. The enzyme combination comprising amylase, xylanase, b-glucanase, and pectinase had no influence on the digestive parameters assessed by Sequeira *et al*., 2000, save for a little decrease in stomach pH. Even in the time after an early weaning, exogenous enzymes often have little effect on enzyme activities in the stomach, intestines, and bowels (Sequeira *et al*., 2000; Falco-e-Cunha *et al*., 2004).

Rabbits have a higher phytic phosphorus digestion capacity than poultry and swine, but they still can't compete with ruminants. Nitrogen digestibility was also boosted by 7% when exogenous phytases were used in the research conducted by Gutiérrez *et al*. (2000). These authors argue that phytases are helpful in rabbit diets.

Because of their unique digestive physiology, and in particular the fact that caecotrophy casts microbial enzymes over the whole length of the gut (Marouneck *et al*., 1995), it is possible that rabbits might respond less favorably to exogenous enzyme supplementation than other species. This does not completely exclude the possibility of supplementing, but it likely limits it to certain stages of the bunnies' lives.

7. Natural Substances

The use of organic acids and salts as preservatives has a long history in the food and feed sectors. For this reason, they have been hailed by some writers as a potential replacement for antibiotics in animal diets, particularly pig

feeds, where they have shown to be rather effective. Formic, acetic, propionic, butyric, lactic, sorbic, fumaric, tartaric, and citric acids are the most promising in this respect, as stated by Partanen and Mroz (1999).
stomachs' naturally weak acid production, especially when they were weaned too soon. Later on, it was shown that they might have a benefit in the later stages of development as well, when they improved the apparent digestibility of energy and protein and the absorption and retention of several minerals (Partanen and Mroz, 1999; Diebold and Eidelsburger, 2006). The beneficial benefits of acidity have been the subject of several theories. For the traditionalists, the acid serves as a substitute for stomach HCl, facilitating the activation of proteolytic enzymes, denaturing and unfolding feed proteins, and creating a barrier against feed-borne germs. Although these are not alternatives, additional hypotheses may be given as well, such as a lingering antibacterial impact in the lower intestine, a particular trophic effect on the intestinal mucosa, and an activity as nutrients.

Organic acids have the same fundamental antibacterial action whether they are active in food, feed, or the gut lumen (Diebold and Eidelsburger, 2006). When they reach the neutral pH of the microbial cytoplasm, indissociable organic acids tend to dissociate. The freed protons may interfere with microbial metabolism by inhibiting enzymes and/or transport mechanisms. The pKa of an acid indicates the pH at which half of its hydrogen ions are dissociated, and therefore its effectiveness. Acids with a higher pKa tend to have a greater impact. But the antibacterial efficacy of organic acids tends to increase with both chain length and degree of unsaturation (as reviewed by Partanen and Mroz, 1999).

Table 5: The results of the trials on the performance (differences in % of the control group) and mortality (% of the control group minus the percentage of the experimental group) of developing rabbits with and without organic acid addition

Reference	Mortality	Profit on average per day	Feedback alteration
Michelan *et al*., 2002	-1	+22.0% (27.5 vs 33.6 g/d)	-14% (4.13 vs 3.55)
Scapinello *et al*., 2001	-1	+10.7% (28 vs 31 g/d)	-3.9% (3.34 vs 3.21)
Hollister *et al*., 1990	-7.2% (17.9 vs 10.7)	-4.0% (40.1 vs 38.5 g/d)	+3.77% (3.77 vs 3.91)

The MICs of organic acids against pathogenic bacteria have been determined *in vitro* (Strauss and Hayler, 2001 cited by Diebold and Eidelsburger, 2006; Mroz, 2005). These results demonstrate that the extent to which an acid inhibits a given bacterial species varies both with the acid and with the bacteria used in the experiment.

Nonetheless, reactions to organic acids might vary. The inherent acid activity and buffering capability of the diets may contribute to the variations observed.

Medium-chain fatty acids, which exhibit antibacterial properties as well, have also been studied (Decuypere and Dierick, 2003). Both the free form and the esterified form in triglycerides were put through their paces. Both endogenous and exogenous lipases are capable of deesterifying fatty acids. This may occur in the gut, in which case the stomach's processes may not be necessary.

Rabbit-safe organic acid

The research on organic acids in rabbits is limited, and the findings are inconsistent (Maertens *et al*., 2006). Inclusion of 1.5% fumaric acid in the feeds of developing rabbits was recently reported to boost daily gain and feed efficiency, although the effects were not statistically significant (Scapinello *et al*., 2001; Michelan *et al*., 2002). Hollister *et al*. (1990) found comparable outcomes (Table 5).

The effects of medium-chain fatty acids have been researched in depth by a team of Czech experts. Skivanová and Marounek (2002) found that lowering post-weaning mortality by 5% by adding 0.5% caprylic acid had no effect on any other performance traits. Later research by Skivanová and Marounek (2006) found the same thing with triglyceride-esterified medium-chain fatty acids: a decrease in post-weaning mortality with no impact on feed consumption, daily growth, or carcass output.

Although one experiment showed a substantial decrease in mortality when fumaric acid was mixed with Lacto-Sacc (Hollister *et al*., 1990), combining organic acids with prebiotics (Scapinello *et al*., 2001) or probiotics (Michelan *et al*., 2002) did not significantly enhance performances.

8. Conclusion

When compared to other farm animals, rabbits have not been the subject of nearly as much investigation into non-antibiotic growth promoter (AGP) options. There are likely many studies that have not been published due to confidentiality, either because of positive (protected for use with a license) or negative (no license required) results. Fewer works have focused on reproduction and mechanisms of action, in contrast to those that examine growth performances. A number of studies suggest it will be possible to develop alternatives for this species as well, despite often contradictory results. A lot of the work that needs to be done will have to be figured out through trial and error due to the complexity of its digestive system, but progress in the fundamental modes of action must lead to alternatives that are specifically tailored to the species' needs. There is still room for investigation into symbiotics, which combine two or more of these kinds of products.

9. References

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