Peer reviewed

Practice tip

Feed additives for swine: Fact sheets – carcass modifiers, carbohydrate-degrading enzymes and proteases, and anthelmintics

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This is the second in a series of peer-reviewed practice tip articles, each including two or three fact sheets on feed additives for swine. The previous practice tip, published in the September-October issue of the *Journal of Swine Health and Production*, included fact sheets on acidifiers and antibiotics (*J Swine Health Prod*. 2009;17:270-275.)

Future fact-sheet topics will include flavors; high dietary levels of copper and zinc for growing pigs; mold inhibitors, mycotoxin binders, and antioxidants; phytase; phytogenic feed additives (phytobiotics-botanicals); and probiotics and prebiotics.

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FACT Sheet: Carcass modifiers

There is increasing consumer demand for leaner and healthier pork products. Improvements in genetics, new technologies, and increased understanding of nutrition have become instrumental in helping producers meet this demand. Continued research also has led to the development of products that can be included in swine diets as carcass modifiers. A dietary carcass modifier is broadly defined as any component of the diet that alters the resulting carcass composition of pigs. Generally, the mechanism of action of carcass modifiers is aimed at increasing protein and muscle deposition while reducing fat deposition. These products vary in the mechanisms by which they modify carcass quality. In addition, not all carcass modifiers are approved for use in pig diets, for public-health reasons. Understanding the modes of action and differences between these products is important for safe and effective use.

Fast facts

Carcass modifiers, which are feed additives included in swine diets to improve carcass quality, include chromium, betaine, carnitine, conjugated linoleic acid, and ractopamine HCl.

Ractopamine HCl, which has shown the most consistent results among the carcass modifiers, acts as a repartitioning agent by redirecting nutrients away from adipose tissue and towards muscle growth.

Amino-acid levels need to be adjusted to meet the increased requirement for protein deposition with ractopamine supplementation.

Growth response to ractopamine HCl decreases over time.

More research is needed to validate the beneficial effects of the other carcass modifiers

What compounds are commonly used as carcass modifiers?

Carcass modifiers available for use in swine include chromium, betaine, carnitine, conjugated linoleic acid, and ractopamine.

Chromium. Chromium is an element essential for growth and development in animals. It plays an important function in metabolic processes involved in the regulation of glucose, proteins, lipids, and cholesterol. Chromium from organic complexes like chromium picolinate and chromium nicotinate is more readily absorbed than other inorganic forms, such as chromium chloride. A number of studies,[1-3] mostly utilizing chromium picolinate, have shown that adding chromium to pig diets during the growing-finishing period can improve growth performance or lean meat yield. However, the responses have not been consistently observed in all studies.[4-7] The exact physiological action of chromium that results in increased carcass leanness is not clear. One possible mechanism of action is improved insulin sensitivity of tissue, causing enhanced deposition of dietary protein and carbohydrate in the muscle cells.

Betaine. Betaine is a byproduct of molasses production from the sugar beet and plays a role in metabolic processes as a methyl donor. Interest in this product increased after studies[8,9] indicated that it can increase carcass leanness and improve feed efficiency when added to finishing diets. However, results were not consistently repeated in other studies,[10,11] indicating unreliability of the responses.

Carnitine. Carnitine is a vitamin-like compound essential for fatty-acid transport across the mitochondrial membrane. While results from earlier research[12] were inconsistent, more recent studies[13-15] have provided further evidence that the addition of carnitine in finishing diets results in a leaner carcass and thinner backfat. This has been attributed to the increased ability of the pig to more efficiently use fat for energy, divert carbon toward amino-acid synthesis, and spare branched-chain amino acids for protein synthesis.

Conjugated linoleic acid. Conjugated linoleic acid is a feed additive that has been shown[16-17] to reduce whole-body fat accretion by repartitioning fat and lean tissue. The use of conjugated linoleic acid in pig diets also influences fat quality by lowering its iodine value. Lower iodine value is an indication of a more saturated (firm) fat. However, the high cost of conjugated linoleic acid limits its practical use in swine diets.

Ractopamine HCl. Among the substances categorized as carcass modifiers, ractopamine HCl has received the greatest amount of attention. Ractopamine HCl belongs to a group of compounds called ß-agonists, that include zilpaterol, cimaterol, clenbuterol, and salbutamol. However, only ractopamine HCl is approved for use in pigs in the United States. It is also legal for use in swine diets in more than 20 countries, but not in some other parts of the world. It is recommended that this product be fed at concentrations of 5 to 10 ppm in the diet.

How does ractopamine improve carcass quality?

Ractopamine HCl, like the other β-agonists, acts as a repartitioning agent by redirecting nutrients away from adipose tissue and towards muscle growth. It modifies the metabolic signals within muscle and fat cells to direct more nutrients to lean growth. Pigs fed diets supplemented with ractopamine HCl also exhibit an increase in daily gain, accompanied, in many instances, by a slight decrease in feed intake. Efficiency of gain also is improved, because it takes less energy to deposit lean than fat. These improvements in growth performance have been consistently demonstrated in many experiments.[18] However, it should be noted that the use of ractopamine in pig diets can also have potentially negative consequences. Ractopamine HCl affects behavior and stress-hormone profiles of finishing pigs, which makes them more difficult to handle.[19] This potentially could lead to difficulty in handling and increasing susceptibility to transport stress at the time of marketing.

Do diet formulations need to be modified when ractopamine HCl is added?

Appropriate nutritional adjustments in finishing-diet formulations need to be made to capture the maximum benefits of ractopamine HCl. This is due to the increased requirement for nutrients to support the higher rate of muscle deposition that results with dietary ractopamine HCl use. According to the product label, diets should contain ≥ 16% crude protein when ractopamine HCl is added. However, because swine do not have a requirement for crude protein, but

rather requirements for amino acids, it is important that the appropriate amino-acid levels be fed. The lysine requirement, in particular, is increased in pigs fed ractopamine HCl. It is recommended that diets supplemented with ractopamine HCl should have a standardized ileal digestible-lysine level that is 0.3% higher than that required by a pig of equal weight fed an unsupplemented diet.

At what stage of production should ractopamine be fed to pigs and for how long?

Ractopamine HCl is labeled for continuous feeding up to the last 90 lb before marketing. It is important to note that the response to the growth-promoting ability of ractopamine HCl is greatest during the first 2 weeks of feeding and progressively decreases over time. This is due to the down-regulation or desensitization of ß-receptors that results from chronic administration of ß-agonists. Therefore, feeding ractopamine HCl-supplemented diets longer than recommended will not translate to further improvement in performance. Also, pigs must be continuously fed ractopamine HCl-supplemented diets until market. Beneficial effects on performance will be lost once ractopamine HCl is removed from the diet. This beneficial effect can be lost with removal for as little as 7 days prior to market.

Is pork from a pig that was fed a diet containing ractopamine HCl safe for human consumption?

The use of ractopamine HCl as a feed additive in swine diets has been extensively studied for many years prior to its Food and Drug Administration approval in 1999. These studies[20] have shown that pork from pigs fed diets containing ractopamine HCl is safe for human consumption. There is no withdrawal time required. A major limitation to the acceptance of ß-agonists such as ractopamine HCl in animal production in other countries is the risk associated with drug residues in the meat products. This is especially true for clenbuterol, which has a rather long elimination time from the animal body (> 21 days),[21] and thus may cause unsafe drug residues in meat and meat products.[22] Consumption of pork containing clenbuterol residues can have adverse effects in humans.[20] For this reason, clenbuterol and other related products have been banned for use as repartitioning agents in many parts of the world, including the United States.

Summary

Carcass modifiers are feed additives that can be used to increase lean-growth rates and improve efficiency. Among these, ractopamine HCl has shown the most consistent results. However, optimal results for ractopamine HCl use depend on the dose, duration of treatment, and nutrient levels in the diet.

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FACT Sheet: Carbohydrate-degrading enzymes and proteases

Swine diets are composed mostly of plant-based ingredients. Nutrients contained in these feedstuffs need to be broken down by the pig into simpler forms that will be used to support maintenance, growth, and reproduction. This poses a problem, because, unlike ruminants, pigs do not have the ability to efficiently digest plant components that have relatively high fiber content. Pigs lack specific enzymes needed to break down fiber. Supplementing swine diets with exogenous carbohydrate-degrading enzymes that break down fiber has become increasingly popular to potentially improve availability of nutrients from ingredients with high fiber content.

Fast facts

Carbohydrases and proteases can increase the nutrient digestibility in plant-derived feedstuffs.

Enhanced nutrient digestibility does not necessarily translate to improvement in performance.

More research is needed to support the claimed effects of enzyme supplementation on growth performance.

What are enzymes?

Enzymes are proteins that accelerate chemical reactions that would proceed at a very slow rate under normal conditions. Enzymes are used as feed additives in swine nutrition to improve digestion and utilization of nutrients. On the basis of this premise, enzyme supplementation may potentially result in better growth performance and less nutrients being excreted as waste. Most enzymes, especially those used as feed additives, are characterized by names with the suffix "ase" (eg, xylanase). Carbohydrate-degrading enzymes or carbohydrases act on starches and indigestible cell-wall components. Carbohydrases commonly used in swine diets include ß-glucanase and xylanase, as well as α-amylase and cellulase. Proteases are enzymes that break down protein molecules into simpler forms that can be absorbed in the gut. They can also act on protein-based anti-nutritional factors (ANFs) to neutralize their effects.

What are the enzyme modes of action?

Plant-based ingredients contain varying amounts of ANFs, such as non-starch polysaccharides in cereal grains and trypsin inhibitors in soybean meal. Their anti-nutritive effect, caused by their resistance to the pig's digestive enzymes, may interfere with digestion and negatively affect performance. The proposed modes of action and roles of exogenous enzymes[1] include the following:

- Degrading feed components resistant to endogenous enzymes;
- Inactivating ANFs to increase the efficacy of endogenous enzymes;
- Supplementing endogenous enzymes that are otherwise present in insufficient amounts within the animal (eg, proteases in young pigs).

Enzymes are highly specific and therefore must match the specific substrates present in feedstuffs included in the diets. It is, therefore, necessary to carefully evaluate the active enzymes present in a product and the level of enzyme activity present. If possible, feedstuffs must be analyzed for the types of substrates present to better match the enzyme product.

What are the expected benefits from using enzymes?

While carbohydrases and proteases have been used in poultry quite successfully, this has not been the case in pigs. A number of studies[2-5] have shown that exogenous enzymes can improve the digestibility of nutrients in feedstuffs commonly used in pig diets, though the positive increases in digestibility have not consistently translated into improvements in growth performance, especially in diets based on corn and soybean meal.[6-9] One of the supposed effects of enzymes is the increased availability of energy from fibrous plant materials. Increasing the availability of energy from feed ingredients should improve feed efficiency. Published scientific data,[6,7,10-13] on the other hand, show mixed results and are inconclusive. One theory accounting for the differences in digestibility data and production responses is that the enzymes increase the digestibility of feed ingredients in the large intestine, while most of the absorption of nutrients occurs in the small intestine. Thus, the absence of a beneficial effect of enzyme supplementation in pigs, or a limited beneficial effect, may be the result of increases in digestibility occurring at a location in the gastrointestinal tract where the pigs are unable to use the increased energy to influence growth rate or feed efficiency.

Use of enzymes in diets containing dried distillers grains with solubles

Dried distillers grains with solubles (DDGS) have relatively higher fiber content than do traditional feed ingredients like corn and soybean meal. As more DDGS are used in swine diets, there also has been an increasing interest in adding enzymes in such diets to improve their energy value. However, data from recent studies [5,8,14] have not shown significant improvements in growth performance of pigs fed enzyme-supplemented diets. Even at very high levels of DDGS (60%), addition of commercial enzymes did not result in performance improvements.

How should I choose the enzyme product appropriate for my diets?

Choosing the appropriate enzyme product depends on the chemical composition of the diet, which is determined by the feedstuffs included in the diet. For example, diets based on wheat will probably respond more to added xylanase, while barley will respond more to β-glucanase. It is very important to ask suppliers for published data on the enzymes actually present in the commercial product, and not just their research data. This will be helpful in evaluating the cost benefit of using the product. In other parts of the world, enzyme products may be available from unreliable traders. Procure products only from companies with proven track records and that are well-known in the industry.

Do multi-enzyme combinations (cocktails) work better than single-enzyme preparations?

As enzymes are highly specific, a combination of different enzymes may work better than a single enzyme. However, several studies[4,6,14,15] have not been able to support this assumption. Still, the use of multi-enzyme products is widely practiced in other countries, where a variety of byproducts can be found in a single diet and where, theoretically, more significant response to enzymes may be seen.

Withdrawal period

Like other proteins, enzymes are broken down in the digestive tract. No metabolites are absorbed or residues excreted through the feces, so no withdrawal period is required.

Summary

Carbohydrate-degrading enzymes, proteases, and their combination have been shown to improve nutrient digestibility of feedstuffs in pigs.[2,10,16] However, there is still a lack of scientific data that would support commercial enzyme use in pig diets, as research data have failed to consistently show benefits in performance.[5-7,12,14] Therefore, enzyme cost relative to the benefits achieved is not justifiable at this time for regular inclusion in swine diets.

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FACT Sheet: Anthelmintics

Parasite control, in addition to control of viruses and bacteria, must be part of a comprehensive herd-health program in every swine production system. Gastrointestinal worm infections may result in significant economic losses. Signs of infection are general and not readily apparent, since worm infections rarely cause elevated mortality levels. Some worms commonly found in pigs are roundworms (*Ascaris suum*), nodular worms (*Oesophagostomum* species), intestinal threadworms (*Strongyloides ransomi*), whipworms (*Trichuris suis*), kidney worms (*Stephanurus dentatus*), and lungworms (*Metastrongylus* species). Anthelmintics or "dewormers" are chemical substances that can be added to pig diets to control parasitic worms.

Fast facts

Worm infections can negatively affect growth performance and decrease carcass value.

In-feed anthelmintics can be used for a successful deworming program.

Anthelmintics vary in efficacy and spectrum of activity.

An effective control program depends on the specific worm problem, stage of production, and type of production system.

Anthelmintics are classified as drugs and their use is regulated by the Food and Drug Administration.

What are the consequences of worm infection?

Worms are parasites that deprive the pig of nutrients, negatively affecting pig growth and feed efficiency. Heavy infestation in some cases can lead to condemnation and loss of carcass value. An example is liver condemnation due to larval migration of *A suum*. During their development, the larval forms of this worm pass through the liver and create white scars known as "milk spots."

What products are available for use as anthelmintics in swine feed?

Dichlorvos. Dichlorvos is indicated to remove and control mature and immature forms of the most common pig worms. However, it is relatively ineffective in controlling early larval forms of roundworms. Two consecutive days of feeding is recommended when dichlorvos is added to pig diets. No withdrawal time is required when this product is used at the approved dose.

Fenbendazole. Fenbendazole has a relatively broad spectrum of activity. It is effective against mature and immature forms of common worms that infect pigs. However, fenbendazole has a higher activity when given at low doses for several days (9 mg per kg body weight with the dose divided over 3 to 12 days) than when single-dosed. No withdrawal time is required when this product is used at the recommended dose.

Ivermectin. Ivermectin is highly effective against immature and adult forms of most gastrointestinal roundworms, as well as against pig external parasites such as lice and mange mites. Ivermectin is available in an injectable preparation as well as in the premix form. The premix product is labeled to be fed for 7 consecutive days. A withdrawal time of 5 days is required when this product is administered in feed.

Levamisole. Levamisole is effective against mature roundworms, but only moderately effective against nodular worms. This anthelmintic has a negative effect on diet palatability. Thus, it is more commonly administered through drinking water to insure intake. When levamisole is administered in pig diets, withdrawal of regular feed overnight is recommended prior to feeding the medicated diet the following morning. Treated pigs should be fed the regular diet once the medicated diet is completely consumed. A withdrawal time of 3 days is required.

Piperazine. Piperazine has a relatively narrow spectrum of activity. It has good efficacy against roundworms and moderate efficacy against nodular worms, but is ineffective against other types of pig worms. This drug is more commonly available commercially as a water-soluble product, but it is also approved by the Food and Drug Administration for use as a feed additive. The main advantage of piperazine is that it is relatively inexpensive and is administered as a 1-day single treatment. However, a withdrawal period of 21 days is required.

Pyrantel tartrate. Pyrantel tartrate is fed for 3 consecutive days to remove large roundworms or continuously to prevent migration and establishment of roundworms and nodular worms. This drug is photodegradable and, hence, must be used immediately upon opening the package. It also should not be mixed in diets containing bentonite. A withdrawal time of 24 hours is required.

Additional detailed information on dewormers approved for swine can be found in the Feed Additive Compendium[1] or on the Food and Drug Administration (FDA) Web site.[2]

When is it necessary to treat pigs with anthelmintics to control worms?

Worm infections occur more frequently in pigs raised in outdoor lots than in conventional confinement facilities. Therefore, production design is one consideration in terms of determining how frequently pigs should be fed anthelmintics. Breeding stock should be given anthelmintics after arrival at the farm and before introduction to the herd. Sows are a common source of worm eggs for piglets and should be dewormed several days before farrowing and before moving to the farrowing room. Scrubbing the sow to remove the worm eggs attached to her body before transfer to the farrowing barn also can reduce exposure of baby pigs.

Knowledge of the specific parasites present in the herd and their life cycle is helpful in establishing an effective control program. Prepatent period (Table 1) refers to the period between the time when the infection occurs and when the adult worms begin shedding eggs. Some worms produce eggs several days after infection, while others take months to begin producing eggs. Most anthelmintics are not able to destroy the egg and larval forms that develop into adults after several days. The interval for repeating

Table 1: Prepatent periods of common pig worms*

Type of worm	Prepatent period (days)
Kidney worm (*Stephanurus dentatus*)	180-270
Lungworm (*Metastrongylus* species)	30
Nodular worm (*Oesophagostomum* species)	23-60
Red stomach worm (*Hyostrongylus rubidus*)	20
Roundworm (*Ascaris suum*)	42-56
Threadworm (*Strongyloides ransomi*)	3-8
Whipworm (*Trichuris suis*)	40

* Adapted from Myers, 1988.[3]

deworming can be determined on the basis of the prepatent periods. Deworming must be repeated before the minimum prepatent period to kill the adult forms and prevent them from laying eggs.

Choosing the appropriate anthelmintic

Anthelmintics have different modes of action and vary in their effectiveness against different species of pig worms. Therefore, choosing the proper anthelmintic to be used in the feed will depend on the specific worm problem. The relative effectiveness and spectrum of activity of common anthelmintics are listed in Table 2. Brand names of products available in the United States are enumerated in Table 3. It should be noted that anthelmintics, like antibiotics, may require specific withdrawal periods (Table 4).

Summary

Worm control is an important component of every herd-health program. Many anthelmintics are effective against different types

Table 2: Effectiveness (% of adult worms killed) and relative costs of in-feed anthelmintics against common pig worms*

Anthelmintic	Roundworm	Nodular worm	Whipworm	Lungworm	Threadworm	Kidney worm	Relative cost
Dichlorvos	99-100	95-100	90-100	0	60-80	0	++
Fenbendazole	92-100	99-100	94-100	97-99	Variable	100	++++
Ivermectin†	90-100	86-100	Variable	99-100	99-100	100	+++++
Levamisole	99-100	80-100	60-80	90-100	80-95	80-100	+++
Piperazine	75-100	50	0	0	0	0	+
Pyrantel tartrate	96-100	88-100	0	0	0	0	+

* Adapted from Myer and Brendemuhl, 2009.[4]

† Also highly effective against external parasites (mange and lice).

Table 3: Registered brand names of FDA-approved anthelmintic products*

Anthelmintic	Brand name	Manufacturer	Address
Dichlorvos	Atgard C Swine Wormer	Boehringer Ingelheim Vetmedica, Inc	St Joseph, Missouri
Fenbendazole	Safe-Guard	Intervet, Inc	Millsboro, Delaware
Ivermectin	Ivomec	Merial	Duluth, Georgia
Levamisole	Tramisol	Fort Dodge Animal Health	Fort Dodge, Iowa
Piperazine	Wazine Pig Wormer	Fleming Laboratories, Inc	Charlotte, North Carolina
Pyrantel tartrate	Banminth 48	Phibro Animal Health	Ridgefield Park, New Jersey
	Worm-Ban	North American Nutrition Co, Inc	Lewisburg, Ohio
	Purina Ban Worm	Virbac AH, Inc	Ft Worth, Texas

Source: Food and Drug Administration Center for Veterinary Medicine.[2]

Table 4: Withdrawal periods of FDA-approved in-feed anthelmintics*

Anthelmintic	Withdrawal period (days)
Dichlorvos	0
Fenbendazole	0
Ivermectin	5
Levamisole	3
Piperazine	21
Pyrantel tartrate	1 (24 hours)

* Source: 2008 Feed Additive Compendium.[1]

of worms. Therefore, selection of an appropriate anthelmintic will depend on the type of worm to be controlled. Also, use of anthelmintics must not be relied on as the sole approach in controlling worms, but must be combined with good sanitation and production practices to be successful.

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