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RESEARCH ARTICLE

Application of a β-mannanase enzyme in diets with a reduced net energy content in post-weaning piglets resulted in equal performance and an additional economic benefit

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Abstract:
β-Mannans are strongly anti-nutritive polysaccharide fibers found in most vegetable feed ingredients. The estimated content of soluble β-mannans in common swine diets range from 0.15 to 0.40%. *In vitro* studies have demonstrated that as little as 0.05% soluble β-mannan content in feed can elicit a strong innate immune response. Hemicell HT (Elanco Animal Health) is a β-mannanase enzyme for animal feed that breaks down β-mannans, thereby preventing economic losses from the wasteful immune response to β-mannans. The present study aimed to compare pig performance on a control diet and a reformulated diet with a lower energy content – 45 kcal/kg NE reduction – and the inclusion of a β-mannanase enzyme. A six-week feeding trial was conducted on a commercial post-weaning facility with DanBred x Belgian Piétrain pigs starting at 21 days of age. Standard three-phase control diets were compared to reformulated diets with an energy reduction of 45 kcal NE/kg and inclusion of a β-mannanase enzyme (Hemicell HT; Elanco) at 300 g/tonne. Standard production data were collected. The data were analyzed using JMP 15.0 statistical program. Overall, performance data did not differ significantly between trial groups in both Phase 1 and Phase 2, and overall, during the entire post-weaning period. Mortality was only numerically, but not significantly higher in the Control as compared to the Hemicell HT group. Hemicell HT had an overall benefit of € 1.69 per piglet and € 15.18 per tonne of feed due to the 45 kcal/kg NE reduction. The current trial demonstrated that the inclusion of Hemicell HT in reformulated diets with a lower energy content (45 kcal NE/kg) was able to retain production performance in post-weaned piglets with an economic benefit.

Keywords: β-mannanase, post-weaned pigs, net energy reduction, equal performance, economic benefit

Introduction

Polysaccharides, polymers of monosaccharides linked by glycosidic bonds, are major components of all vegetable feed ingredients used in common swine diets. Starch, a polymer of glucose units linked by α-(1-4) with a few α-(1-6) bonds, is digested in the small intestine of pigs through endogenous enzyme activity. Non-starch polysaccharides (NSPs) are fibrous materials found in the plant cell wall, including celluloses, hemicelluloses, pectins and oligosaccharides. Monogastric animals such as pigs do not produce endogenous enzymes needed to digest β-linked NSPs like β-mannans.[1] β-Mannan is an antinutritive factor found in many common feed ingredients[2], which has received increasing attention in recent years. β-Mannans are linear polysaccharides composed of repeating units of β-1,4-mannose and α-1,6-galactose and/or glucose units attached to the β-mannan backbone.[3,4] High concentrations of them are considered unsuitable in monogastric diets because of their antinutritive properties, mainly due to stimulation of the innate immune response. The innate immune cells identify pathogens using distinct molecules, called pathogen-associated molecular patterns (PAMP), expressed on the surface of the pathogen.[5] The binding of PAMP to pathogen recognition receptors (PRR) present on innate immune cells, result in the release of innate defense molecules such as reactive oxygen and nitrogen species, bacteriolytic enzymes, antimicrobial peptides and complement proteins.[6] These PAMPs include complex polysaccharides that resemble β-mannans.[5] Therefore, β-mannans in the feed can be mistaken by the immune system in the gastro-intestinal tract for an invading pathogen causing an unwarranted immune activation[7,8], also known as a feed-induced immune response (FIIR).[9] This misrecognition of β-mannans as an invading pathogen leads to a futile immune response that causes energy and nutrients to be wasted.[3] Hydrolysis of these β-mannans through inclusion of exogenous β-mannanase enzymes can reduce and potentially eliminate their ability to induce a FIIR.

In mice β-mannan selectively promotes beneficial gut bacteria, as demonstrated by the increased *Roseburia intestinalis* populations and the reduction of mucus-degraders.[10] *Roseburia intestinalis* is apparently a primary degrader of this dietary fiber, and this metabolic capacity could in the future be explored to selectively promote several key members of the healthy microbiota using β-mannan-based therapeutic interventions in humans.[10]

β-Mannans in swine diets have been suggested to hinder the utilization of nutrients[11], and therefore, positive effects of supplementing β-mannanase to maize-soybean meal (SBM)-based diets on nutrient digestibility and growth performance have been studied.[12] In poultry, the inclusion of dietary β-mannanase has been shown to improve daily gain and feed efficiency, while decreasing digesta viscosity[13], and to upregulate a broad range of metabolic functions related to digestion, metabolism, and immunity.[9] Moreover, the beneficial

effects of β-mannanase addition in chickens, challenged with *Eimeria* sp. and *Clostridium perfringens*, were observed with improved performance and reduced lesion scores in disease-challenged birds.[14]

Supplementation of β-mannanase to low- and high-mannan diets has the potential to improve the performance of growing pigs.[15] Others concluded that β-mannanase improved growth performance in both weanling and growing-finishing pigs on corn-SBM diets[12,16,17] with minimal effects on nutrient digestibility.[12] Additionally, β-mannanase supplementation to corn-SBM diets reduced the population of fecal coliforms and tended to reduce the NH_3 concentration of fecal slurry after 24 h fermentation.[18] The reduction of fecal coliforms might impact the environmental infection pressure from coliforms, related to clinical problems of post-weaning diarrhea (PWD). Another study demonstrated *in vivo* anti-inflammatory activity of mannanase-hydrolyzed copra meal in a porcine colitis model, with decreased expression of mRNA for ileal IL-1β, IL-6, IL-17 and TNF-α.[19] Innate immune activation is accompanied by downregulation of anabolic functions[20], which translates into a reduced performance capacity. Therefore, supplementation of a β-mannanase enzyme to post-weaning diets could reduce or eliminate the occurrence of FIIR and increase available energy and proteins for growth.

The objective of the current study was to evaluate the effects of β-mannanase supplementation of post-weaning diets with a reduced net energy content of 45 kcal/ kg of feed on piglet performance and economic parameters during the post-weaning phase.

Materials and Methods

Description of Experimental Farm

The field trial was performed on a conventional post-weaning unit in Belgium with 1 compartment containing 20 pens of which 10 Control and 10 Enzyme-treated pens. Each pen housed 16 post-weaned piglets. Compartments were ventilated through mechanical ventilation with an air inlet through the ceiling. All pens had partially slatted plastic floors. Water was distributed through a nipple in the feeder. Each pen was equipped with a dry feeder. Meal feed consumption was registered at group level. Both study groups were randomly distributed throughout the post-weaning compartment.

Experimental design

Treatment groups

At weaning, the piglets were assigned to one of both treatment groups, Control and Enzyme-treated, respectively. A three-phase diet was distributed with Phase 1 during week 1-2, Phase 2 during week 3, and Phase 3 during week 4-6 (Table 1). Groups were blinded to the farm personnel and only distinguished by color codes (red and blue). Piglets from each individual pen were considered one experimental unit and were weighed together.

Table 1. Feed composition of both Control and Enzyme-treated post-weaning diets in terms of feed cost per tonne of feed, net energy content, estimated β-mannan content and supplementation of a β-mannanase enzyme according to the three-phase schedule.

	Phase 1 (week 1-2)		Phase 2 (week 3)		Phase 3 (week 4-6)	
	Control	Enzyme	Control	Enzyme	Control	Enzyme
Feed cost (€/tonne)	735	710	610	595	534	526
Net energy content (kcal/kg)	2464	2419	2400	2353	2390	2349
Δ NE content		45		47		41
Estimated β-mannan content (%)	0.32	0.32	0.35	0.35	0.34	0.34
Hemicell HT inclusion	-	0.030	-	0.030	-	0.030

Experimental diets

The pigs were fed a three-phase mash diet consisting of phase 1 (0-14 d), phase 2 (15-21 d), and phase 3 (22-42 d) in each of the treatment groups. The main difference between the diets for the Control and the Enzyme-treated group was a reduction in net energy content of 45, 47, and 41 kcal/kg of feed in Phase 1, 2, and 3, respectively (Table 1). The Enzyme-treated group was supplemented with a β-mannanase enzyme (Hemicell HT; Elanco, Indianapolis; IN) at an inclusion rate of 300 g per tonne of feed, according to the manufacturer's instructions for use. All other enzymes (xylanase and phytase) in the diets remained at the same level in both study groups.

Experimental animals

DanBred * Belgian Piétrain piglets were obtained from the conventional commercial sow farm linked to the post-weaning facility. Piglets were vaccinated to protect against *Mycoplasma hyopneumoniae* and Porcine Circovirus type 2 (PCV-2) using a one-shot commercial vaccine (Ingelvac Combo-Flex; Boehringer Ingelheim). One batch of piglets (n = 640) was enrolled for the feed trial.

Performance data collection

Pig body weight (BW) per pen was measured at 0-, 14-, and 42-days post-weaning. Feed provision (*ad libitum*) was only recorded at the level of treatment group. Average daily weight gain (ADWG; expressed as g/d), average daily feed intake (ADFI; expressed as g/d) and feed conversion rate (FCR; expressed as kg feed per kg of weight gain) were calculated for Phase 1 (week 1-2) and the combined Phase 2-3 (week 3-6), respectively. Mortality was recorded with the date of death and the number of dead animals.

Veterinary treatments

Individual antibiotic treatments were performed as needed due to the critical clinical state of the piglet and in case of a broader health issue in the barn, group treatment could be performed. The same veterinary products and dosages (ml/kg) were used throughout the entire study period. Individual antibiotics treatments or group treatments were recorded daily by date, product, dose, ID number of treated piglets, presumed cause of treatment, and number of times the treatment was repeated.

Economic benefit per piglet and per tonne of feed

The economic benefit of β-mannanase supplementation combined with a reduction in net energy of approximately 45 kcal/kg feed was calculated both at piglet level and at feed cost level. For the calculation of economic benefit at piglet level, the following parameters were taken into account: feed cost reduction, piglet price correction (standard price for 25 kg piglet), and opportunity costs of mortality. For the calculation of economic benefit at feed cost level, the following parameters were considered: the total feed cost and the total amount of feed consumed.

Data management and statistical analysis

Data were hand-recorded by the farm personnel and stored in MS Excel on OneDrive at the end of each day. Following the end of the feed trial, data were extracted from Excel into JMP 15.0 and the blinded color-coded treatments were unblinded to reveal the respective treatment groups. Calculations, exploratory data analysis, quality review, and subsequent statistical analysis were all performed in JMP 15.0. All data are presented as means with their respective pooled standard error of the mean (SEM). All means were tested for significant differences ($P < 0.05$) using a T-test.

Results

Pig weight and average daily weight gain

Data on piglet weight are given in Table 2. The piglets arrived at the post-weaning facility at an average weight of 5,66 kg. No significant differences ($P > 0.05$) were present in the start weight (d0) between both treatment groups. At d14, piglets in the Enzyme-treated group were slightly, but non-significantly ($P > 0.05$) heavier with 8.90 kg (± 0.40 kg) as compared to the Control group (8.78 ± 0.33 kg). At d42, the end of the feed trial, the piglets in the Enzyme-treated group were again slightly, but not significantly ($P > 0.05$) heavier with 22.18 kg (± 0.84) as compared to the Control group (21.89 ± 0.60 kg). Data on ADWG are given in Table 2. In Phase 1 (0-14 d), piglets in the Enzyme-treated group had slightly, but not significantly higher ($P > 0.05$) ADWG (216 g/d ± 8) compared to the Control group (207 g/d ± 7). In the combined Phase 2-3, piglets in the Enzyme-treated group has a slightly, but not significantly higher ($P > 0.05$) ADWG (492 g/d ± 17) as compared to the Control group (486 g/d ± 10). Overall, ADWG was not significantly different between both study groups (393 g/d ± 13 *vs.* 386 g/d ± 9 in Enzyme-treated and Control group, respectively).

Table 2. Performance parameters for both Control and Enzyme-treated groups in Phase 1 and combined Phase 2-3. Weight, average daily weight gain (ADWG) and mortality are given as mean ± SEM. Average daily feed intake (ADFI) and feed conversion rate (FCR) are given as mean. *P*-values < 0.05 represent statistically significant differences.

Parameter	Control	Hemicell HT	*P*-value
Phase 1 – 0-14 d			
Weight d0 (kg)	5.67 ± 0.25	5.66 ± 0.29	0.983
Weight d14 (kg)	8.78 ± 0.33	8.90 ± 0.40	0.702
ADWG (g/d)	207.3 ± 6.6	215.8 ± 8.0	0.255
ADFI (g/d)	307	306	-
FCR (kg feed/kg growth)	1.48	1.42	-
Mortality (%)	1.85 ± 1.2	1.53 ± 0.6	0.866
Phase 2 – 15-42 d			
Weight d14 (kg)	8.78 ± 0.33	8.90 ± 0.40	0.702
Weight d42 (kg)	21.89 ± 0.60	22.18 ± 0.84	0.663
ADWG (g/d)	485.6 ± 10.2	491.8 ± 16.7	0.637
ADFI (g/d)	786	771	-
FCR (kg feed/kg growth)	1.62	1.57	-
Mortality (%)	0.9 ± 0.4	0.3 ± 0.3	0.347
Overall – 0-42 d			
Weight d0 (kg)	5.67 ± 0.25	5.66 ± 0.29	0.983
Weight d42 (kg)	21.89 ± 0.60	22.18 ± 0.84	0.663
ADWG (g/d)	386.2 ± 8.6	393.2 ± 13.4	0.506
ADFI (g/d)	615	605	-
FCR (kg feed/kg growth)	1.59	1.54	-
Mortality (%)	2.78 ± 1.2	1.84 ± 0.6	0.589

Table 3. Detailed calculation of economic benefit per piglet considering reduction in feed cost, piglet price corrections (standard price at 25 kg) and opportunity costs of mortality.

Parameter	Control	Hemicell HT
Feed cost per piglet (0-42 d)	€ 15.20	€ 14.57
Benefit feed cost reduction		+ € 0.63
Piglet price corrections (€ 50,- for 25 kg)	- € 6.22	- € 5.64
Benefit technical results		+ € 0.58
Mortality (#)	9	6
Total opportunity cost due to mortality (€)	€ 450	€ 300
Opportunity cost per marketed piglet (€/piglet)	€ 1.42	€ 0.94
Benefits mortality		+ € 0.48
Overall benefit per piglet		**+ € 1.69**

Average daily feed intake and feed conversion rate

Data on ADFI and FCR are given in Table 2. The ADFI was similar among the treatment groups in Phase 1. In the combined Phase 2-3, the ADFI was lower in the Enzyme-treated group (771 g/d) as compared to the Control group (786 g/d). Overall, ADFI was 10 g/d lower in the Enzyme-treated group as compared to the Control group.

The FCR was 0.06 lower in the Enzyme-treated group as compared to the Control group in Phase 1, and remained 0.05 lower in the combined Phase 2-3. Overall, FCR was 0.05 lower in the Enzyme-treated group as compared to the Control group.

Antimicrobial treatment

No significant differences were observed either at the level of individual treatment nor group treatment between both treatment groups during the entire feed trial.

Mortality

Data on mortality are given in Table 2. In Phase 1, mortality was slightly, but not significantly ($P > 0.05$) lower (1.53 % ± 0.6) in the Enzyme-treated group as compared to the Control group (1.85% ± 1.2). In the combined Phase 2-3, mortality was slightly, but not significantly ($P > 0.05$) lower (0.3 % ± 0.3) in the Enzyme-treated group as compared to the Control group (0.9 % ± 0.4). Overall, mortality was slightly, but not significantly ($P > 0.05$) lower (1.84 % ± 0.6) in the Enzyme-treated group as compared to the Control group (2.78 % ± 1.2).

Economic benefit per piglet and per tonne of feed

The detailed calculation of economic benefit per piglet is given in Table 3. Overall, supplementation of a β-mannanase enzyme combined with a reduction of net energy with 45, 47 and 41 kcal/kg feed over the three phases, respectively, resulted in an economic benefit per piglet of € 1.69.

The detailed calculation of economic benefit per tonne of feed is given in Table 4. Overall, supplementation of a β-mannanase enzyme combined with a reduction of net energy with 45, 47 and 41 kcal/kg feed over the three phases, respectively, resulted in a feed cost reduction of € 15.18 per tonne of feed.

Table 4. Detailed calculation of economic benefit of feed cost per tonne of feed considering total feed costs and total amount of feed consumed.

Parameter	Control	Hemicell HT
Total feed costs (0-42 d)	€ 1,880.00	€ 1,831.00
Total amount of feed consumed (tonne)	8,340.00	8,235.00
Feed cost per unit (€/tonne)	€ 588.52	€ 573.34
Overall benefit per tonne of feed		**- € 15.18**

Discussion

In the current study, the β-mannan content in all three phases, which ranged from 0.32 to 0.35%, was sufficiently high to preserve the standard feed composition without the need for additional substitutions of more expensive proteins to extruded SBM, as previously reported.[21] The relatively high level of β-mannans, a known antinutritive factor[2], which may stimulate an innate immune response through their resemblance with PAMPs[5], may induce FIIR (Feed Induced Immune Response)[9] and lead to an unnecessary immune activation, causing energy and nutrients to be wasted.[22] Therefore, 300 g/tonne of an exogenous β-mannanase enzyme (Hemicell HT; Elanco, Greenfield, IN) was added to hydrolyze these antinutritive β-mannans in the trial feed. The results in phase 1 and phases 2-3 demonstrated no significant differences in the measured (piglet weight, ADFI) or calculated (ADWG, FCR) performance parameters between both treatments. Although minor numerical differences were observed, the overall result confirmed that the addition of an exogenous β-mannanase to adapted formulations with a reduction in net energy content of 45 kcal/kg of feed, in the presence of a sufficient level of β-mannans, allowed them to perform equally to the standard post-weaning Control diets. These results are in accordance with other recent studies in low- and high-mannan diets.[15,21]

In addition to similar results in production performance, a substantial economic benefit of supplementation of a β-mannanase enzyme could be calculated. Based on the feed prices presented in Table 1 and the actual feed intake, we obtained a 4.1% reduction in the feed cost (€ 14.57 *vs.* € 15.20, in Enzyme-treated *vs.* Control group, respectively) per piglet produced and a 2.6% reduction in feed cost per tonne of feed (€ 573.34 *vs.* € 588.52, in Enzyme-treated *vs.* Control group, respectively). Considering all costs (feed cost,

basic piglet market price at 25 kg, and opportunity costs for mortality) the income per produced piglet was € 1.69 higher for the Enzyme-treated group. Others concluded that β-mannanase improved growth performance in both weanling and growing-finishing pigs on corn-SBM diets.[12,16,17] A diet with a 150 kcal/kg reduction in digestible energy supplemented with β-mannanase outperformed in weight gain and feed efficiency.[16] Others have also observed the energy sparing effect from the supplementation of β-mannanase. For example, the supplementation to a common nursery diet resulted in similar effects on performance of a comparable diet supplemented with 2% soya oil.[12] In poultry, beneficial effects of β-mannanase supplementation on the performance of chickens challenged with *Eimeria* sp. and *Clostridium perfringens* were observed together with reduced lesion scores in disease challenged birds.[14] This observation was confirmed by a recent study in post-weaned piglets, where antimicrobial use for the treatment of PWD due to *Escherichia coli* was significantly reduced in the Enzyme-treated group as compared to the Control group.[21] However, in the current study, disease challenge during the post-weaning period was relatively low, and therefore no differences in antimicrobial treatment could be observed between both treatment groups.

In a recent mice study, β-mannan-based interventions did not only contribute to the prevention of mucus barrier dysfunctions, but also maintained a gut environment that keeps pathogenic bacteria away.[10] These findings are in contrast with our observations that higher levels of β-mannans in swine diets induce a FIIR that provokes an activation of the innate immune response[9], which results in a reduced performance in both post-weaned and fattening pigs.[12,21]

Conclusions

The current trial demonstrated that the inclusion of Hemicell HT in reformulated diets with a lower energy content (45 kcal NE/kg of feed) was able to retain production performance in post-weaned piglets with an economic benefit. The inclusion of Hemicell HT had an overall benefit of € 1.69 per piglet and € 15.18 per tonne of feed due to the 45 kcal/kg NE reduction.

Abbreviations

ADFI	average daily feed intake
ADWG	average daily weight gain
FCR	feed conversion rate
FIIR	feed induced immune response
NE	net energy
NSP	non-starch polysaccharide
PAMP	pathogen associated molecular pattern
PRR	pathogen related receptor
PWD	post-weaning diarrhea
SBM	soybean meal

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Declarations

Ethics approval and consent to participate –
Field trial with an EFSA approved feed supplement for use in swine. No additional ethical approval needed. Consent to participate was obtained following full information of the farmer on the study protocol.

Consent for publication –
Not applicable.

Availability of data and material –
The datasets analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests –
The authors declare that they have no other competing interests.

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Author's contributions –
FV and AdB were both involved in study design, data collection, data analysis and manuscript preparation. SG and DVZ were both involved in study design, data collection and manuscript revision prior to submission. All authors read and approved the final manuscript.

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Author's information –
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