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**Non-ruminants** Full-length research article

# Performance responses of broilers and pigs fed diets with β-mannanase

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ABSTRACT - This study was developed using meta-analysis to evaluate the effect of  $\beta$ -mannanase on both poultry and pig performance. Two databases were constructed using information from previous studies that evaluated the  $\beta$ -mannanase supplementation in diets for broilers (30 papers; 19,643 birds) and pigs (20 papers; 5,319 animals). The meta-analysis followed three sequential analyses: graphical, correlation, and variance-covariance. The effect of  $\beta$ -mannanase supplementation on performance considerably varied in both databases. Data analysis considering the study effect showed that  $\beta$ -mannanase supplementation did not influence feed intake. Diets supplemented with  $\beta$ -mannanase did not influence weight gain, but improved feed conversion (-1%) of broilers compared with the control group. Feeding pigs diets supplemented with  $\beta$ -mannanase improved weight gain (+5%) and feed conversion (-6%) compared with pigs fed non-supplemented diets.  $\beta$ -mannanase supplementation increased the digestibility coefficient of dry matter, crude protein, and energy in both species. The inclusion of  $\beta$ -mannanase also improved the metabolizable energy content in broiler diets and enhanced the digestibility of energy in pig feeds. Current results indicate that  $\beta$ -mannanase can be considered as an important tool for nutritionists who search for improved feed conversions and nutrient digestibility coefficients.

Keywords: enzyme, meta-analysis, nutrition, poultry, swine

# **1. Introduction**

 $\beta$ -mannans (BM) are commonly present in a wide variety of feedstuffs, including soybean meal, and have been described as one of the major anti-nutritional factors for non-ruminant animals (Bertechini, 2013). Dietary BM are associated with negative effects in pigs and broilers, such as increased intestinal viscosity and decreased nutrient digestibility (Shastak et al., 2015). Despite being naturally found in non-pathogenic substances, these compounds may activate the innate immune system (Aderem and Ulevitch, 2000; Gharaei et al., 2012). Thus, the response induced by BM may affect animal performance because energy is drained by the immune system activation (Sato et al., 2009).

The dietary supplementation with exogenous  $\beta$ -mannanase may be an alternative to deal with the adverse effects associated with BM. Positive mechanisms of  $\beta$ -mannanase supplementation include the effects on immunity, releasing energy sources, and the modification of substrate viscosity in the gut lumen, which may improve nutrient availability (Li et al., 2010; Mehri et al., 2010).

Although several studies have been conducted to assess the effects of  $\beta$ -mannanase on poultry and pig performance, more information is needed to better understand the variations in those findings. In this context, the current study was developed by using meta-analytic techniques to assess the effect of  $\beta$ -mannanase supplementation on broiler and pig performance.

# 2. Material and Methods

Digital databases (Google Scholar, HighWire, ScienceDirect, Scielo, and PubMed) were searched to identify studies published in scientific journals that reported the performance and metabolism of broilers and pigs fed diets supplemented with  $\beta$ -mannanase. The keyword " $\beta$ -mannanase" combined with "broiler" or "pig" was used in the search. The main criteria for paper selection were: experimental evaluation of  $\beta$ -mannanase supplementation in diets, broilers in different growth phases or pigs from nursery to finishing rearing phases, and performance responses. The literature search was performed in June 2017.

After paper selection, the information related to the proposed theoretical model and other additional variables were extracted from both Material and Methods and Results sections in the original publications and transferred to an electronic spreadsheet. Results collected in animals subjected to any health or environmental challenge were not included in the database.

The methodology applied to database construction and coding followed the proposals described in the literature (Lovatto et al., 2007; Sauvant et al., 2008). Codes were used with qualitative grouping criteria in the analytical models. In this item, the main codes were applied for supplementation (control or  $\beta$ -mannanase-supplemented diet) and dietary energy content [adequate levels according to the growth phase or lower levels than Rostagno et al. (2011) recommendations]. Other codes were used to consider the variability among all compiled experiments (e.g., the effect of study or trial).

Performance results were evaluated as raw data (as presented in the original papers) or as relativized information (responses of  $\beta$ -mannanase-supplemented treatments were relativized to the respective control treatment and expressed as a percentage of variation). This second procedure was adopted because it considerably reduced variations among experiments in the database.

Statistical analyses were performed using the Minitab software (Minitab for Windows, v. 17, Pine Hall Rd, Pennsylvania, USA). Meta-analyses were independently performed for poultry and pigs, following three sequential analyses: graphical (to control database quality and observe biological coherence of data), correlation (to identify related factors among variables), and variance-covariance (to compare treatments and obtain prediction equations). Variance analysis was performed considering the following statistical model:

$$Y_{ijk} = \beta_i + \delta_j + \alpha_k + \varepsilon_{ijk},$$

in which  $Y_{ijk}$  is the response,  $\beta_i$  is the fixed effect of treatment,  $\delta_j$  is the fixed effect of energy content,  $\alpha_k$  is the random effect of study, and  $\varepsilon_{ijk}$  is the residual variation.

Equations were used to predict the effect of  $\beta$ -mannanase supplementation on energy expenditure of the animal for growth, which was obtained estimating the metabolizable energy (ME) amount spent for each unit of body weight gain. These equations were independently fitted for control and supplemented treatments. This paper presents only equations in which all components were significant (P<0.05). Estimated values for both control and supplemented groups were simulated to assess potential energy savings due to dietary  $\beta$ -mannanase supplementation.

## 3. Results

The broiler database was composed of 30 scientific papers (Table 1) published from 2002 to 2016, which used 19,643 broilers in total. The genetic line was Cobb in 58% of the treatments, while the other 25% were Ross (other treatments used less representative genetic lines or the information was not available in the papers). Male broilers were used in 52% of the studies, while 34% of the trials used mixed sexes and 14% did not describe this trait.

The pig database was composed of 20 scientific papers (Table 2) published from 2002 to 2017, which used 5,319 pigs in total. On average, initial and final body weights were 32.5 kg and 56.2 kg, respectively. The growing and finishing phases were studied in most treatments, while nursery piglets were only

studied in 28% of the treatments of the database. Barrows and females were used mixed in 34% of the studies, while 29% of the trials used only barrows, 6% of the trials used only females, and 31% did not describe this trait.

Feeds based on corn and soybean meal were used in most treatments in both databases (57% in the broiler database and 45% in the pig database). Alternative ingredients were used in 39% of the treatments in the broiler database and in 44% of the treatments in the pig database. In addition, 4% of the treatments in the broiler database and 11% of the treatments in the pig database could not be classified for this trait due to the lack of information in the articles. Feed was provided in mash form in 31% of the treatments in the broiler database and in 78% of the treatments in the pig database, while the pelleted form was used in 36% of the treatments in the broiler database and in 5% of the treatments in the pig database. Feed form was not described for the other treatments, which comprised 33% of the broiler database and 17% of the pig database. In both databases, most of the treatments used feeds with a conventional (normal) energy level. Only a minor part of the treatments (5% of all treatments in the broiler database and 8% of treatments in the pig database) used feeds with energy levels lower than the nutritional recommendations.

Reference <sup>1</sup>	Dietary β-mannanase level <sup>2</sup>			
Ouhida et al., 2002	0, 0.35, and 0.875 g kg $^{-1}$ of a product (1,400,000 U g $^{-1}$ )			
Jackson et al., 2003	0 and 100 million U ton <sup>-1</sup>			
Lee et al., 2003	0 and $1.09 \times 10^5$ U kg <sup>-1</sup>			
Daskiran et al., 2004	Exp 1: 0 and 0.05% of a product (158 million U kg <sup>-1</sup> )			
	Exp 2: 0, 0.05, 0.1, and 0.15% of a product (158 million U kg $^{-1}$ )			
Jackson et al., 2004	0, 50, 80, and 110 million U ton <sup>-1</sup>			
Lee et al., 2005	0 and 1.09 $ imes$ 10 <sup>5</sup> U kg <sup>-1</sup>			
Saki et al., 2005	0 and 0.5 g kg <sup>-1</sup> of a product			
Khanongnuch et al., 2006				
Sundu et al., 2006	0, 0.02, and 0.05% of a product			
Zou et al., 2006	0, 0.025, 0.05, and 0.075% of a product (165 $\times$ 10 <sup>6</sup> U kg <sup>-1</sup> )			
Zakaria et al., 2008	0 and 0.05% of a product (14,000 U g <sup>-1</sup> )			
Li et al., 2010	0, 10, and 20 million U ton <sup>-1</sup>			
Mehri et al., 2010	0, 500, 700, and 900 g ton <sup><math>-1</math></sup> of a product			
Zangiabadi and Torki, 2010	0 and 0.4 g kg <sup>-1</sup> of a product (158 million U kg <sup>-1</sup> )			
Kong et al., 2011	0 and 400 U kg <sup>-1</sup>			
Mussini et al., 2011	0, 0.25, 0.5, and 1 g kg <sup><math>-1</math></sup> of a product			
Torki, 2011	0 and 0.4 g kg <sup>-1</sup> of a product (165 × $10^6$ U kg <sup>-1</sup> )			
Gharaei et al., 2012	0 and 0.5 g kg <sup>-1</sup> of a product			
Mohayayee and Kazem, 2012				
Azarfar, 2013	0, 0.5, and 1 g kg <sup>-1</sup> of a product			
Cho and Kim, 2013b	0 and 0.04% of a product (1.09 $\times$ 10 <sup>5</sup> U kg <sup>-1</sup> )			
Mishra et al., 2013	0 and 32 million U kg <sup>-1</sup>			
Sornlake et al., 2013	0, 200, 400, and 800 U kg <sup>-1</sup>			
Zou et al., 2013	0 and 140 × $10^6$ U kg <sup>-1</sup>			
Farahiyah et al., 2014				
Williams et al., 2014	0 and 363.2g t <sup>-1</sup> of a product (159.5 × 10 <sup>6</sup> U kg <sup>-1</sup> )			
Barros et al., 2015	0 and 0.500 kg ton <sup>-1</sup> of a product			
Klein et al., 2015	0 and 100 mL ton <sup>-1</sup> of a product (720 million U L <sup>-1</sup> )			
Ferreira et al., 2016	0 and 800 U g <sup>-1</sup>			
Latham et al., 2016	0 and 800,000 U kg <sup>-1</sup>			

#### Table 1 - Dietary β-mannanase levels in the studies of broilers database

<sup>1</sup>Chronological sequence, according to publication year.

<sup>2</sup> Levels are presented as in the original publication to highlight the lack of uniformity among studies.

Reference <sup>1</sup>	Dietary β-mannanase level <sup>2</sup>			
Pettey et al., 2002	0 and 103 mm U t <sup>-1</sup>			
Wang et al., 2009	0 and 0.5 g kg <sup>-1</sup> of a product (800,000 U kg <sup>-1</sup> )			
Jacela et al., 2010	0 and 0.5 g kg <sup>-1</sup> of a product			
Jones et al., 2010	0 and 0.5 g kg <sup>-1</sup> of a product			
Yoon et al., 2010	Exp 1: 0, 200, 400, and 600 U kg <sup>-1</sup>			
	Exp 2: 0, 200, 400, and 600 U kg <sup>-1</sup>			
	Exp 3: 0 and 400 U kg <sup>-1</sup>			
	Exp 4: 0 and 400 U kg <sup>-1</sup>			
Oluwafemi and Akpodiete, 2011	-			
Jo et al., 2012	Exp 1: 0 and 0.05% of a product (800,000 U kg <sup>-1</sup> )			
	Exp 2: 0 and 0.05% of a product (800,000 U kg <sup>-1</sup> )			
Oluwafemi et al., 2012	0 and 600 g ton <sup>-1</sup> of a product			
Cho and Kim, 2013a	0 and 0.5 g kg <sup>-1</sup> of a product (800 U g <sup>-1</sup> )			
Kerr and Shurson, 2013	0 and 500 mg kg <sup>-1</sup> of a product			
Kim et al., 2013	0 and 400 U kg <sup>-1</sup>			
Lv et al., 2013	0, 200, 400, and 600 U kg $^{-1}$			
Mok et al., 2013	0 and 1600 U kg <sup>-1</sup>			
Carr et al., 2014	0 and 0.25 g kg <sup>-1</sup> of a product			
Kwon and Kim, 2015	0 and 2400 U kg <sup>-1</sup>			
Kwon et al., 2015	0, 400, 800, 1600, 2400, and 3200 U kg <sup>-1</sup>			
Mok et al., 2015	0 and 800 U $kg^{-1}$			
Upadhaya et al., 2016	0 and 400 U kg $^{-1}$			
Kim et al., 2017	Exp 1: 0, 400, 800, and 1600 U kg <sup><math>-1</math></sup>			
	Exp 2: 0, 400, and 800 U kg <sup>-1</sup>			
Diarra, 2017	0 and 0.3 g kg <sup>-1</sup> of a product			

**Table 2** - Dietary β-mannanase levels in the studies of pig database

<sup>1</sup>Chronological sequence, according to publication year.

<sup>2</sup> Levels are presented as in the original publication to highlight the lack of uniformity among studies.

In both databases, most trials were developed using commercially available enzymes. However, the supplementation greatly varied among studies in terms of  $\beta$ -mannanase units contained in each product. In addition, the dietary inclusion of these products was expressed in different ways among studies. This is an important factor to be considered and should be better described in future publications. Due to the lack of standardization in the description of dietary enzyme concentration, it was not possible to access the effect of this factor on animal performance in the current meta-analytical study.

Improvements in weight gain were observed in 57% of the comparisons between supplemented and control treatments in the broiler database and in 81% of the comparisons in the pig database (Figures 1 and 2). In addition, 63 and 83% of all treatments containing  $\beta$ -mannanase reported improved feed conversion ratio compared with control treatments, respectively, in broilers and pigs (Figures 1 and 2). The magnitude of this performance change greatly varied in both databases. This is probably due to the large diversity of experimental conditions, such as BM source or enzyme supplementation. Meta-analysis is a useful tool to deal with experimental variability as it allows establishing systematic responses adjusted to the diversity of available publications. The meta-analysis also increases the sample number, thereby highlighting possible effects that would not be observed in conventional studies.

Diets supplemented with  $\beta$ -mannanase did not influence (P>0.05) feed intake and weight gain of broilers (Table 3). However,  $\beta$ -mannanase improved feed conversion (-1%; P = 0.04) compared with the control group. The inclusion of  $\beta$ -mannanase in broiler diets also improved the digestibility coefficient of dry matter (+6%; P<0.01) and crude protein (+5%; P<0.01). In addition, feeds supplemented with  $\beta$ -mannanase showed a 2% higher (P = 0.04) content of ME.

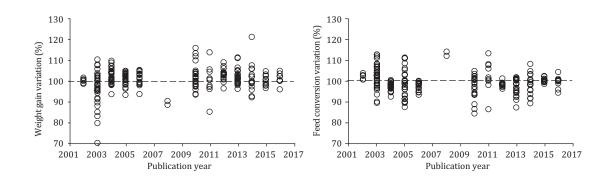


Figure 1 - Performance responses of  $\beta$ -mannanase-supplemented treatments relativized to the respective control treatment in the broiler database.

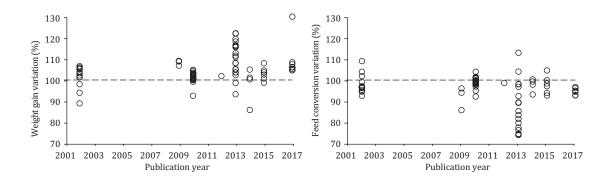


Figure 2 - Performance responses of  $\beta$ -mannanase-supplemented treatments relativized to the respective control treatment in the pig database.

	β-mannanase <sup>1</sup>		D2	DEC	<b>.</b> *
-	-	+	R <sup>2</sup>	RES	P-value*
Performance					
Mean body weight (g)	567.60	574.40	62.31	285.20	0.838
Daily feed intake (g day <sup>-1</sup> )	100.10	99.58	60.48	51.91	0.926
Daily weight gain (g day-1)	53.11	53.73	81.96	10.82	0.568
Feed conversion ratio (g g <sup>-1</sup> )	1.74	1.72	79.53	0.182	0.041
Digestibility coefficients					
Dry matter (%)	73.11	77.84	90.65	1.57	0.002
Crude protein (%)	69.54	72.91	93.14	2.05	< 0.001
Metabolizable energy (kcal kg <sup>-1</sup> )	2,710	2,768	97.42	85.91	0.044

Table 3 - Performance and digestibility coefficients in broilers fed diets supplemented or not with  $\beta$ -mannanase

 $R^2\mbox{-}$  coefficient of determination; RSE - residual standard error.

<sup>1</sup> Values adjusted by covariance to average live body weight.

\* P-value - probability of treatment effect. Statistical model also considered the study effect (P<0.01 in all performed analysis) and the energy level effect (P<0.01 in all performed analysis).

The relationship between weight gain and ME intake in broilers was studied in control treatments (y = 10.54 + 143.91x; R<sup>2</sup> = 0.95, in which y is weight gain, expressed in g, and x is energy intake, expressed in Mcal) and in broilers fed diets containing  $\beta$ -mannanase (y = 10.45 + 147.84x; R<sup>2</sup> = 0.95). According to the estimation,  $\beta$ -mannanase saved about 2.7% of ME expenditure for growth.

Feeding pigs diets supplemented with  $\beta$ -mannanase did not influence (P>0.05) feed intake (Table 4). However,  $\beta$ -mannanase improved weight gain (+5%; P = 0.04) and feed conversion (-6%; P<0.01) compared with non-supplemented pigs. Pigs fed diets containing  $\beta$ -mannanase also presented higher digestibility coefficients of dry matter (+2%; P<0.01), crude protein (+2%; P<0.01), phosphorus (+6%; P = 0.04), and energy (+1%; P = 0.03).

The relationship between weight gain and ME intake in pigs was studied in control treatments (y = 284.20 + 108.52x; R<sup>2</sup> = 0.84, in which y is weight gain, expressed in g, and x is energy intake, expressed in Mcal) and in animals fed diets containing  $\beta$ -mannanase (y = 284.69 + 113.72x; R<sup>2</sup> = 0.89). According to the estimation,  $\beta$ -mannanase saved about 4.6% of ME expenditure for growth.

Table 4 - Performance and digestibility coefficients in pigs fed diets suppl	lemented or not with β-mannanase
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	β-mannanase <sup>1</sup>		<b>P</b> <sup>2</sup>	DEC	א. ו. מ
	_	+	R <sup>2</sup>	RES	P-value*
Performance					
Mean body weight (kg)	59.17	58.26	84.30	11.84	0.784
Daily feed intake (kg day <sup>-1</sup> )	1.72	1.72	97.88	0.127	0.822
Daily weight gain (g day <sup>-1</sup> )	657.10	687.00	89.48	85.27	0.036
Feed conversion ratio (g g <sup>-1</sup> )	2.64	2.49	84.45	0.30	0.002
Digestibility coefficients					
Dry matter (%)	80.67	82.04	93.69	0.97	< 0.001
Crude protein (%)	77.13	78.75	90.69	1.69	0.001
Phosphorus (%)	42.58	45.07	74.20	3.38	0.041
Energy (%)	79.72	80.64	90.12	1.58	0.027

 $R^2$  - coefficient of determination; RSE - residual standard error.

<sup>1</sup> Values adjusted by covariance to average live body weight.
\* P-value - probability of treatment effect. Statistical model also considered the study effect (P<0.01 in all performed analysis) and the energy level effect (P<0.01 in all performed analysis).</li>

## 4. Discussion

The BM are water-soluble non-starch polysaccharides fibers, which are commonly present in various ingredients used in animal feeding, especially soybean meal (Choct, 2015). The BM are resistant to most chemical and physical processes commonly used in feed manufacture, even when exposed to high temperatures (Hsiao et al., 2006). Ruminants are little or not affected by dietary BM, as they are degraded by rumen microorganisms. However, BM are not digested by non-ruminant animals and represent a major anti-nutritional factor for both pigs and broilers (Choct, 2015; Shastak et al., 2015; Singh et al., 2018).

Even small amounts of BM crossing the intestinal mucosa can trigger an innate immune-system response in animals (Jackson et al., 2003). The activation of macrophages occurs either by phagocytosis or by contact with surface receptors (Duncan et al., 2002). Furthermore, BM showed bilateral synergism with some substances, such as interferon- $\gamma$ , leading to a stronger macrophage activation than other mechanisms (Hibbs et al., 1988). This feed-induced immune response consumes energy that, in a normal metabolic state, would be used for animal growth (Ferreira et al., 2016). This condition was observed in the current meta-analysis, in which the relation between weight gain and energy intake was studied in broilers and pigs. The relationship was studied using empirical equations, which means

that other influential factors may probably influence the data. One example was the animal age, as the simulations were performed considering a constant efficiency of weight gain in relation to energy intake over the growing period. Despite the empirical approach, the models clearly indicated changes in the energy metabolism of animals fed diets supplemented with  $\beta$ -mannanase.

The dietary BM fibers were associated with reduced nutrient absorption, hormonal changes, increasing viscosity, and intestinal transit time modifications in previous publications (Shastak et al., 2015). Changes in nutrient digestibility were observed in both broiler and pig databases used in the current study. This effect may also be due to the interaction between BM and glycocalyx, which leads to mucus layer thickening and physically prevents the absorption (Montanhini Neto et al., 2013). In addition, animals fed diets containing high BM levels have lower glucose uptake (El-Masry et al., 2017) and tend to reduce insulin secretion, leading to a lower amino acid absorption rate (Nunes et al., 1991). Increasing the availability of non-absorbed nutrients into the intestinal lumen creates a favorable environment for microorganism proliferations. Some of them are pathogenic and may suppress performance by reducing health status (Teirlynck et al., 2009). In summary, the combination of all these previously mentioned factors leads to a reduction in feed efficiency responses, a trend clearly observed in this meta-analysis for animals fed non-supplemented diets.

Previous research has addressed the beneficial effects of using  $\beta$ -mannanase in pigs and broilers. However, several experimental features may influence enzyme effectiveness. Dietary composition is one of the most important factors, considering that  $\beta$ -mannanase shows better results when supplemented in diets containing higher BM levels (Jacela et al., 2010; Mussini et al., 2011). This condition could not be quantified in the current study due to the lack of information concerning BM levels.

Although the enzyme action mechanism is well-known, its effect may differ on broilers and pigs (Fang et al., 2007). In birds,  $\beta$ -mannanase appears to act earlier in the digestive tract, which facilitates the absorption of BM catabolites and the reduction of excreta humidity (Oliveira and Moraes, 2007). Reduction in feces viscosity is also observed in pigs. However, the absorption of BM catabolites may not necessarily be enhanced as BM is degraded at the end of the ileal portion (Johansen et al., 1997).

The current meta-analytic study showed that  $\beta$ -mannanase supplementation improves feed conversion ratio in both broilers and pigs. Previous studies indicated that  $\beta$ -mannanase can stimulate the activity of other digestive enzymes, such as amylases and trypsin, which improves both nutrient digestion and absorption in non-ruminant species (Li et al., 2010). Positive effects of  $\beta$ -mannanase on nutrient digestibility were also reported in the current meta-analysis.

## **5.** Conclusions

The supplementation of  $\beta$ -mannanase in diets for broilers and pigs saves energy for animal growth, improving the feed conversion ratio. The  $\beta$ -mannanase enzyme is an important tool for nutritionists searching for improved nutrient digestibility coefficients.

## **Conflict of Interest**

The authors declare no conflict of interest.

## **Author Contributions**

Conceptualization: M. Kipper and V.R.Q. Quadros. Data curation: M. Kipper, I. Andretta, V.R.Q. Quadros, B. Schroeder, P.G.S. Pires, C.S. Franceschina, F.M.W. Hickmann and I. França. Formal analysis: M. Kipper, I. Andretta, B. Schroeder, P.G.S. Pires, C.S. Franceschina, F.M.W. Hickmann and I. França. Investigation: M. Kipper, I. Andretta, V.R.Q. Quadros, B. Schroeder, P.G.S. Pires, C.S. Franceschina, F.M.W. Hickmann and I. França. Investigation: M. Kipper, I. Andretta, V.R.Q. Quadros, B. Schroeder, P.G.S. Pires, C.S. Franceschina, F.M.W. Hickmann and I. França. Methodology: M. Kipper. Project administration: I. Andretta. Supervision: I. Andretta. Writing-original draft: M. Kipper and I. Andretta. Writing-review & editing: V.R.Q. Quadros, B. Schroeder, P.G.S. Pires, C.S. Franceschina, F.M.W. Hickmann and I. França.

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