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Original Article

The Role of ß-Mannanase (Hemicell) in Improving Poultry Productivity, Health and Environment

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ABSTRACT

The poultry nutritionists constantly attempt to identify and alleviate the factors responsible for adverse effects on nutrient utilization and production performance in avian species, which are necessary for successful productivity of poultry. Enhanced feed utilization can reduce levels of some nutrients in the diet with concomitant mitigation in nutrient excretion into the environment, reduction of eutrophication and acidification potentials of excreta. Commercial enzymes have been used to improve feed efficiency and utilization in poultry. Among many anti-nutritional factors, the existence of ß-mannans in poultry feed ingredients including soybean and other leguminous seeds has been associated with negative effects on nutrient digestibility and high intestinal viscosity that adversely affects innate immunity and microbial proliferation in poultry gut. The ß-mannanase (a commercial product named as Hemicell) can hydrolyze ß-mannan, an anti-nutritional fiber present in many poultry feed ingredients. Supplement of ß-mannanase to ß-mannan-rich diets may boost the population of intestinal beneficial bacteria, increase the digestibility of mannans, enhance the immunity, suppresses the growth of harmful intestinal bacteria, enhance the digestion and absorption of nutrients in intestinal tracts and reduce the environmental pollution due to poultry excreta. Supplementation of β-mannanase at the level of 200 and 400 mg/kg in poultry diets has positively improved blood glucose and anabolic hormone homeostasis, FCR, digestible energy, and digestible amino acids. This review describes the promising beneficial effects of β-mannanase, which may be used in the poultry feed industry for economic benefits. Another objective of this review is to explore the underlying mechanisms of ß-mannanase that can influence growth, digestion coefficients of nutrients, health and metabolism of nutrients in poultry birds and also the knowledge regarding the useful application of this feed enzyme in the commercial poultry feed industry.

INTRODUCTION

It is imperative to identify factors that inhibit the digestibility of nutrients for successful commercial poultry production. The non-starch polysaccharides (NSP) like substances of hemicellulose, cellulose, and pectin can reduce nutrient digestibility in poultry (Choct, 1999). Among the NSP, β-mannans are a group of hemicelluloses, which are present in many ingredients used for poultry feeds like soybean and other leguminous seeds. It occurs in the forms of galactomannans and glucomannans in the cell walls of the plant. The β-mannan is found in many feedstuffs including palm kernel meal, soybean meal, copra meal, and sesame meal and other leguminous feeds (Dierick, 1989). The soybean meal and full-fat soybean as protein sources are most important feed ingredients in poultry diets, and β-mannan is present in most of the poultry feed. On the other hand, β-mannan was found to have harmful impacts on performance and health of the animal, compromising feed conversion and weight gain (Anderson & Warnick, 1964), as well as water and glucose absorption (Rainbird *et al*., 1984) and insulin secretion (Sambrook & Rainbird, 1985). The negative impacts of B- mannans on poultry performance were attributed to low digestibility of nutrients and high intestinal viscosity that adversely affects the immune response and microbial proliferation in the gut as well as growth and carcass traits. To solve this problem, some exogenous enzymes such as protease, phytase, avizyme, ß-mannanase and β-gluconase could be added to poultry diets to help in the digestion of fibers and to decline their negative impact on poultry productivity and health (Alagawany *et al*., 2015, 2017). In an early study, Patel & McGinnis (1985) found that egg weight, egg production and feed intake significantly decreased with β-mannan in laying hen diets. Previously published literature demonstrated that β-mannan enzyme is capable of improving the innate immunity and promoting a non-productive energy draining response of the innate immune system (Zhang & Tizzard, 1996; Duncan *et al*., 2002). This resulted in an increase in monocytes and macrophages proliferation and increased the production of cytokine. On the other side, many researchers found the positive impact of enzymatic degradation of β-mannan via supplementation of β-mannanase to diets of broiler chickens (Lee *et al*., 2003; Jackson *et al*., 2004), laying hens (Wu *et al*., 2005) and turkey birds (Odetallah *et al*., 2002). Jackson *et al*., (2003) reported that performance of birds experimentally inoculated with *Clostridium perfringins* and *Eimeria* spp. improved with the supplementation of β-mannanase. Despite the popularity of soybean meal in poultry feed, the content of β-mannan of this feedstuff has gained scant attention. This review paper compiles the updated information about β-mannanase, sheds light on the useful application as a feed additive on a commercial level in the poultry feed industry and explores the underlying mechanisms of action of Hemicell® (ß-mannanase) on growth performance, metabolism, nutrient digestibility and health of poultry birds. Furthermore, research in depth on a molecular level is needed to expand the knowledge regarding the application of this important enzyme on a commercial level in the poultry feed industry.

The anti-nutritive factors (ß-mannan) and its content in different feedstuffs

Several anti-nutritive factors are used to prevent the nutrient utilization in avian species such as hemicelluloses, xylan, arabinan, galactan and mannan (Dhawan & Kaur, 2007). Among them, mannan as a hemicellulosic polysaccharide is most abundant in nature after xylan (McCleary, 1986). The mannanases are being considered the second most important enzyme after xylanases, for hemicelluloses hydrolysis as described by Chauhan *et al*. (2012). The ß-mannan is a highly anti-nutritional agent in poultry feeds (Odetallah *et al*., 2002). The contents of ß-mannan in common feed ingredients for poultry are illustrated in Fig. 1. The ß-mannan is always found in palm kernel meal, soybean meal, sesame meal, guar meal and copra meal (Dhawan & Kaur, 2007). Guar meal and guar gum also have high concentrations of β-mannan (Rogel & Vohra, 1983). The β-mannan content in soybean meal has an average galactose: mannose ratio between 1 and 1.8 which is similar to the guar gum i.e. 1 and 1.7 (Whistler & Saarnio, 1957). Whistler & Saarnio, (1957) demonstrated the galactomannan of soybean hulls in the 1950s. Another study confirmed that maximum mannan content was found in the NSP fractions (Dierick, 1989). The certain minor mixed linked mannans are also present in the fraction of soy protein as the major N-linked carbohydrate of β-conglycinin (7S), a glycoprotein (Koshiyama, 1966; Kimura *et al*., 1997).

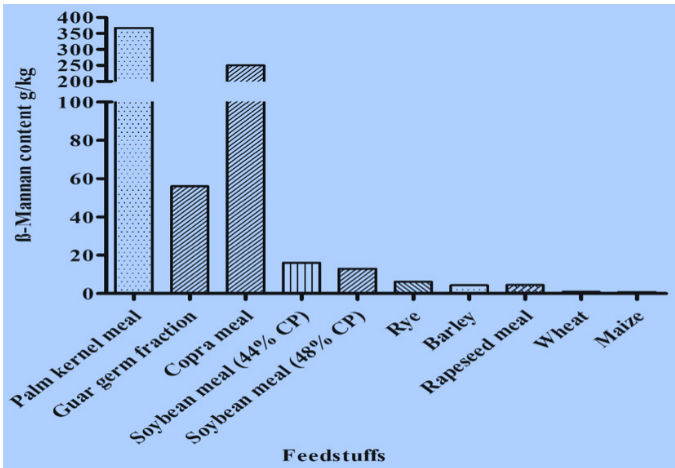

Figure 1 – The β-mannan contents g/kg in different feedstuffs used for poultry nutrition.

Different modes of action of β-mannanase

The enzyme supplementation to diets reduces the viscosity of the intestinal ingesta and causes harmful impacts accompanied by elevated viscosity in the contents of the intestine (Almirall *et al*., 1995). The β-mannans naturally occurring in guar meal at 60 to 80 g/kg bind large water amounts, which in turn increases the fluid viscosity of digestive tracts of animals (Danicke *et al*., 2000). The increases in viscosity can decrease water and glucose absorption as illustrated by Rainbird *et al*., (1984), consequently depressing growth performance and feed conversion ratio. The inclusion of endo-β-D-mannanase into guar meal diets lowered viscosity of intestinal digesta and improved feed efficiency and growth performance (Lee *et al*., 2003). Moreover, Karimi & Zhandi (2014) stated that feeding of β-glucanase and β-mannanase enzyme-supplemented diet in graded levels of energy can modify some morphological traits of the gastrointestinal tract. The diet supplemented with β-mannanase may lead to improve the resistance against pathogenic bacteria such as *Salmonella enteritidis* (Gutierrez *et al*., 2008). β-mannanase´s mechanism of action is by the hydrolysis of β-1, 4-glycosidic linkages in β-mannans Fig. 2, (Ooi & Kikuchi, 1995). The enzyme cleaves at random inside the 1, 4-β-D-mannan key chains of galactoglucomannan, galactomannan, and mannan (McCleary, 1986).

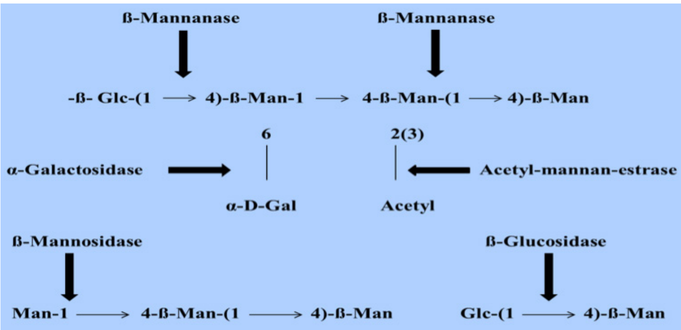

Figure 2 – Flow diagram about the enzymatic hydrolysis of galactoglucomannan (Glc=glucose; Man=mannose; Gal=galactose) (Puls & Schuseil, 1993).

Another essential β-mannanase´s mode of action is to reduce β-mannan levels in the gut, which may lead to a depression in the stimulation of innate immunity Fig. 3, (Jackson *et al*., 2004). Stimulation of the innate immunity occurs due to the absorption of β-mannan from the intestinal content and thereby improves the proliferation of monocytes and macrophages as well as resultant cytokine production. There are many other mechanisms which can explain the beneficial impacts of ß-mannanase regarding nutrient digestibility and performance in poultry birds. These modes of action could be categorized as given below: (Shastak *et al.*, 2015)

1) Impact on the viscosity of intestinal digesta
2) Release of some sugars such as D-mannose as a source of energy
3) Inhibition of pathogenic bacteria proliferation in the gut
4) Impact on immune response and release of bound nutrients.

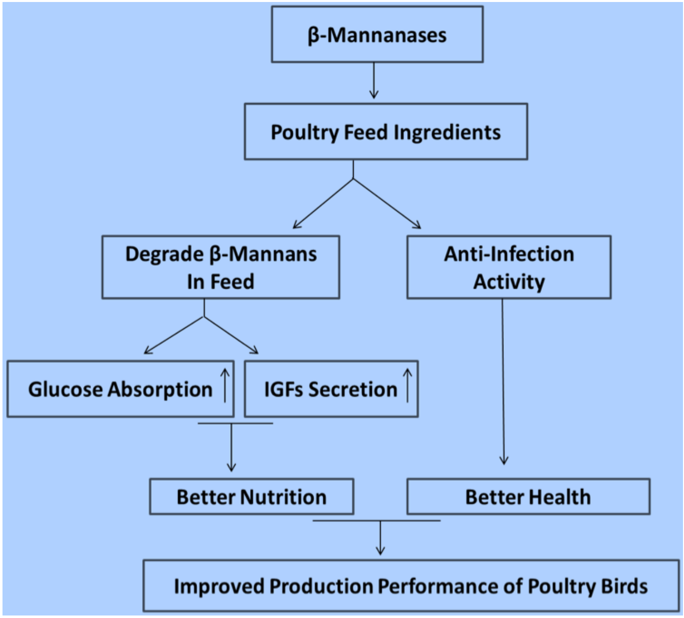

Figure 3 – Mode of action of β-mannanases.

Impact on the viscosity of intestinal digesta

The leguminous plants can be used as imbibing substances during the early period of germination, taking up water at high levels for spreading around the embryo as reported by Buckeridge *et al*., (2000). High molecular weight soluble copra and guar galactomannans could be dissolved in the gut forming high viscosity of intestinal digesta like other soluble ß-glucans and arabinoxylans. Because of the high viscosity of intestinal digesta, galactomannans can have deleterious impacts on digestibility. This undesirable effect could be eliminated by using dietary supplementation of ß-mannanase (Jackson *et al*., 2004). The supplementation of feed ingredients having a high amount of copra meal or guar meal (water-soluble galactomannan) may increase the viscosity of intestinal digesta in birds. Normally birds need a large amount of drinking water to keep the best mixing of intestinal substrates with enzymes. In research by Daskiran *et al*., (2004), supplementation of ß-mannanase reduced the consumption of water per feed unit consumed in broiler chickens. In another study, chickens fed diets (corn soybean and copra meal) enriched with ß-mannanase statistically enhanced protein, lipid and metabolizable energy utilization (Sundu *et al*., 2006, 2007). Results indicated that ß-mannanase supplementation enhances the hydrolysis of copra meal which leads to upregulate the nutrient utilization and flow of intestinal digesta. Therefore, using ß-mannanase to reduce the viscosity of the diets containing copra meal is similar to using xylanases in the diets containing wheat as mentioned by Dhawan & Kaur (2007).

Release of some sugars such as D-mannose as a source of energy

Enzymes like ß-mannosidase, α-galactosidase and ß-mannanase are needed for ß-mannans complete decomposition. The ß-mannanase alone liberates short ß-1,4-manno-oligomers like mannotriose, mannotetraose, and mannobiose which can be hydrolyzed by ß-mannosidases to mannose (Chauhan *et al*., 2012). Jackson *et al.* (2004) stated that positive impact of ß-mannanase on the production of birds fed corn-soya meal diets could not be simply explained via making ß-mannan available as a source of energy because the content of ß-mannan in this diet is only 0.4% to 0.7%. In addition, only a part of the absorbed D-mannose can be metabolized in birds (Duran *et al*., 2004). This means that the mode of action of ß-mannanase could not itself provide extra energy to the poultry birds.

Inhibition of pathogenic bacteria proliferation in the gut

It is possible that ß-1-4-mannan-rich feeds are pre-treated enzymatically and enriched with ß-1-4-MOS (manno-oligosaccharides) before fed to the poultry birds. In *in vivo* study by Agunos *et al*. (2007), MOS supplemented chicken feeds reduced caecal colonization *Salmonella enteric* in layer and broiler chickens (Shastak *et al*., 2015). In another study, regarding broilers, the addition of 20% ß-mannanase to treated copra meal diets reduced the population of *Salmonella* and *Escherichia coli* in excreta in comparison with non-enzymatic treated copra meal group (Khanongnuch *et al*., 2006). As reported by Jackson *et al*. (2003) and Latorre *et al*., (2015), ß-mannanase found microbial modulating action in broiler chickens fed on corn-soya diets and challenged with *Clostridium perfringens* and *Eimeria*. ß-mannanase reduced the severity of *Eimeria* and *Clostridium* infection verified by significant boost body weight gain and depression in some lesions in the intestine in comparison with the enzyme-free diet (Table 1).

Table 1 – Effect of infection, ß-mannanase and medication on production performance of broilers from 8 to 21 d of age.

Treatment	Infection[1]	ß-annanase	Medication[2]	BWG (g)	FCR (g/g)	Lesion score upper[3]	Lesion score (d 14) Lower[4]
1	-	-	+	540^{a}	1.45^{c}	0.0^{c}	0.0^{c}
2	-	+	+	548^{a}	1.42^{c}	0.0^{c}	0.0^{c}
3	+	-	-	429^{d}	1.70^{a}	1.38^{a}	1.56^{a}
4	+	+	-	490^{c}	1.54^{b}	1.16^{b}	1.44^{a}
5	+	-	+	522^{b}	1.45^{c}	1.03^{b}	0.88^{b}
SEM				5.9	0.025	0.069	0.09

a-d: Means within columns without common superscripts are significantly different (p<0.05). 1: Orally inoculated with E. acervulina and E. maxima on day 7. On days 11, 12 and 13, birds were given broth cultures of C. perfingens. 2: Salinomycin (60g/ton) and bacitracin methylene disalicilate (50g/ton). 3: Area most affected by E. acervulina. 4: Area most affected by E. maxima. BWG: body weight gain. FCR: Feed conversion ratio. SEM: standard error of mean. Source: (Jackson et al., 2003).

Impact on immune response and release of bound nutrients

ß-mannan has a molecular structure similar to some pathogens, which may trigger immune stimulation. Acemannan (ß-1,4-acetylated mannan) induced the activation of macrophages via increasing the nitric oxide synthase level at transcription level as reported by Ramamoorthy *et al.* (1996). Karaca *et al*. (1995) reported that nitric oxide acts as a cytostatic effector in the removal of viral replication and is proposed to be toxic for tumor cells (Karupiah *et al*., 1993). The response of this complex to ß-mannan containing compounds could lead to losses in dietary energy utilization. Supplementation of ß-mannanase improved the utilization of dietary energy in corn-soya diet in broiler chickens (Li *et al*., 2010) as well as layers (Wu *et al*., 2005). Impacts of Hemicell® (ß-mannanase) on the utilization of energy was partial because of the declined immune challenge which caused by ß-mannan in rations, allowing more energy for production purposes (Li *et al*., 2010). The authors also found that ß-mannanase mitigates the inhibitory impacts on digestive enzymes and thereby enhances the nutrient digestibility and reduces nutrient excretions. The aforementioned impact was assured by lower weights of the immune organs like bursa, thymus, and spleen; in addition to a lower concentration of serum IgG and IgM due to ß-mannanase supplementation to broiler diets. Dale *et al*., (2008) stated reduced plasma concentrations of the acute phase protein indicating less immune function through removing soybean or through adding ß-mannanase to broiler rations. Ferreira *et al*., (2016) studied the impact of β-mannanase addition to broiler diets on the growth, feed utilization, metabolizable energy, amino acid digestibility, and immune parameters and they found that immune response, energy values and growth were improved with β-mannanase-supplemented diets.

The importance of enzymes especially ß-mannanase in poultry feeds

Poultry nutritionists are constantly attempting to enhance production performance of avian species, which are necessary for successful farming. In the last two decades several strategies were applied to uplift the commercial poultry production such as introduce environmentally control forming, improve feed formulation (Saeed *et al*., 2019; Saeed *et al*., 2018 a, b; Yatao *et al*., 2018), application of probiotics (Sun *et al*., 2016) and the use of herbal medicinal plants as an alternative source of antibiotics. The dietary enzymes are biologically active proteins that facilitate the breakdown of complicated nutrients into smaller molecules for further digestion and absorption (Thacker, 2013). There are large numbers of enzymes that are derived from microbes like fungi and bacteria via fermentation and have been used in poultry and their benefits in improving feed efficiency and growth. There are different classes of enzymes that are commonly employed in poultry diets including phytase, carbohydrases (β-mannanase, xylanase, α-galactosidase, cellulase, pectinase, and α-amylase), and proteases as well. The biological activities of various in-feed enzymes in promoting the growth and improving the feed efficiency in poultry are well reported (Bedford & Schulze, 1998; Choct, 2007).

It is now accepted that commercial enzymes play an important role in reducing anti-nutritional factors that exist in plant-based feed ingredients like phytic acid, NSP and cell-wall complex. The improved growth of poultry due to enzyme supplementation thus has been linked to an increase in the digestibility and absorption of nutrients (Verstegen & Williams, 2002; Rebolé *et al*., 2010). The feed enzymes are considered as good potential as antibiotic alternatives to improve performance in poultry. Various meta-analyses studies conducted corroborate these benefits in birds upon supplementation of the enzyme (Rebolé *et al*., 2010).

The Hemicell enzyme is well known as a fermentation product of *Bacillus lentus*. It contains high contents of ß-mannanase that degrade -mannan in poultry ration. The ß-mannanase has been shown to enhance feed efficiency of broiler chickens (Ward & Fodge, 1996). The guar and copra meals have also been reported to improve utilization with bacterial mannanase treatment (Patel & McGinnis, 1985). Low-energy broiler chicken diets supplemented with ß-mannanase revealed a better performance than broilers fed high-energy diets without enzyme (McNaughton *et al*., 1998). Supplementation of β-mannanase at the level of 200 and 400 ppm in poultry diet has positively improved blood glucose and anabolic hormone homeostasis, FCR, digestible energy, and digestible amino acids (Caldas *et al*., 2018). Recently, the published study demonstrated that β-mannanase supplemented at the level of (200 or 400/ton) improved the ileal digestible energy (IDE), reduced intestinal viscosity, and improved growth performance of broiler chicken (Latham *et al*., 2017).

The findings from several researchers have shown increased utilization of nutrients in low β-mannans corn-soybean diets and other feed ingredients like copra and guar meal which are rich in mannan as a response to Hemicell supplementation. According to (Torki & Chegeni, 2007), Hemicell supplementation to diets enriched with canola meal enhanced feed consumption, weight gain, and feed conversion ratio; however, the only improvement in body weight in comparison with canola meal diet with no Hemicell was statistically significant. The broiler chickens offered diets with Hemicell statistically increased the serum level of IgM of broilers at 3 and 6 wk-old. It was shown that Hemicell may improve immune functions and growth performance of broilers (Zou *et al*., 2006; Table 2 and 3). Rehman *et al*. (2013) found that β-mannanase supplementation in a low energy diet had a beneficial effect on the body weight, feed conversion ratio. Furthermore, Mussini *et al*. (2011) conducted a dosage response study with different levels of βmannanase (CTCzyme) 0, 0.025%, 0.05% (recommended level) and 0.1% and observed that gross energy of excreta decreased with increasing enzyme level, demonstrating better nitrogen utilization by the birds. β-mannanase improves morphological status in the gut and immunological status in plasma in broiler chicks (Christine *et al*., 2002 and Mehri *et*

Table 2 – Results of different trials that represent the effect of β-mannanase on performance parameters.

Treatments	Feed consumption	Weight gain	FCR
Enzyme Hemicell , %			
0	74.60	74.60[a]	1.720[a]
0.025	74.61	44.30[b]	1.684[b]
0.05	73.80	45.07[b]	1.637[c]
0.075	75.91	44.44[b]	1.710[a]

[a, b, c]: means in the same column sharing different superscripts differ significantly ($p<0.05$), FCR: Feed conversion ratio. Source: (Zou et al., 2006).

Table 3 – β-Mannanase enzyme for hemicellulose and their various sources and functions.

Organism	Substrate	Function	Probable results
Aspergillus niger, var. Bacillus lentus *Bacillus subtitis* *Trichoderma longibrachiatum*	Cereals and legumes (e.g. Guar meal)	Hydrolyzes b - mannans, a component of hemicellulose	Decreased anti-nutritive effects of β-mannans by reducing digesta viscosity; increased β-mannans digestibility in feed, production of oligosaccharides and ultimately improved value of feed (energy). Also decreased problem of sticky dropping.

al., 2010), this may lead to the improved health status of birds. In another study, the supplementation of endo- β-D-mannanase (known as Hemicell®), which is commercially available to guar meal based diets, promoted the growth of broilers (Daskiran *et al*., 2004). Broilers supplemented with ß-mannanase in corn-soybean meal-based diets also increased daily weight gain of broiler chickens (Jackson *et al*., 2005; Zou *et al*., 2006). The better production performance may be associated with more energy availability by enzyme addition, since it minimizes the viscosity of the intestine by acting on the NSPs, allowing for better absorption of nutrient, thereby favoring higher body weight gain. In the study of Zangiabadi *et al.* (2010) broiler chickens fed on soybean or whole soy bean diets and added with β-mannanase at 350 g/kg revealed beneficial effects on performance and immunity. El-Masry *et al*. (2017) pointed out that guar meal could be used in broiler diets at 5% with β-mannanase enzyme without negative impacts on the growth rate, feed efficiency and blood parameters.

CONCLUSION

The Hemicell commercial enzyme products with ß-mannanase activity is a unique enzyme that can hydrolyze β-mannan, an anti-nutritional fiber in avian diets. Diet supplemented with β-mannanase may increase the population of intestinal beneficial bacteria, increase the digestibility of mannan, enhance the immunity, suppresses the growth of harmful bacteria, enhance the digestion and absorption of nutrients in the intestinal tract and reduce the environmental pollution by reducing ammonia emission. The promising effects of β-mannanase should be applied on a commercial level in the poultry feed industry. In addition, understanding the mechanisms which ß-mannanase supplementation uses to affect growth performance, metabolism, digestibility and birds' health is essential for broadening and optimizing the use of this enzyme on a commercial scale in the poultry feed industry.

CONFLICT OF INTERESTS

The authors declare they have no conflict of interest.

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