Mycotoxins as contributors to antibiotic resistance?

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Antibiotic resistance is a growing global health concern, making infections more complicated to treat and increasing the risk of disease spread, severe illness, and death. While overuse and misuse of antibiotics are the primary causes, recent research has uncovered another unexpected contributor: mycotoxins. Among these, deoxynivalenol (DON), a toxin commonly found in contaminated grains, has been shown to significantly alter gut microbiota and promote antibiotic resistance. This article examines how DON impacts gut bacteria, influences antibiotic resistance, and highlights why this issue warrants urgent attention.

Mycotoxins – originators of antimicrobial resistance?

Actually, it would be logical…

Alexander Fleming discovered Penicillin when he returned after the summer holidays and saw that a mold had grown on the agar plate he had prepared. Around the mold, Staphylococcus was unable to proliferate. The reason was a substance produced by the mold – penicillin, which, like other toxins produced by molds, is a mycotoxin. In his article about the origin of antibiotics and mycotoxins, Shier (2011)

stated that antibiotics and mycotoxins share considerable similarities in structure, metabolic roles, and biosynthesis.

A short excursus to antimicrobial resistance

In general, the primary mechanisms of resistance involve the prevention or limitation of the antimicrobial substance's uptake, modifying the drug target, inactivating the drug, or facilitating its discharge with efflux pumps.

There are two types of resistance: natural resistance, which is further divided into intrinsic and induced resistance, and acquired resistance.

Intrinsic resistance is a "characteristic" of a bacterial species and is not dependent on antibiotic exposure. An example is the reduced permeability of the outer membrane of gram-negative bacteria, which prevents certain antibiotics from entering.

Induced resistance, however, needs to be initiated by antibiotics. Here, multidrug-efflux pumps can be mentioned.

The third one, acquired resistance, refers to the process by which bacteria acquire genetic material, the resistance genes, from other bacteria that are resistant. The mechanisms include vertical transfer to daughter cells and horizontal transfer, such as the transfer from dead bacteria to living ones, by viruses, or the transfer of plasmids (Reygaert, 2018).

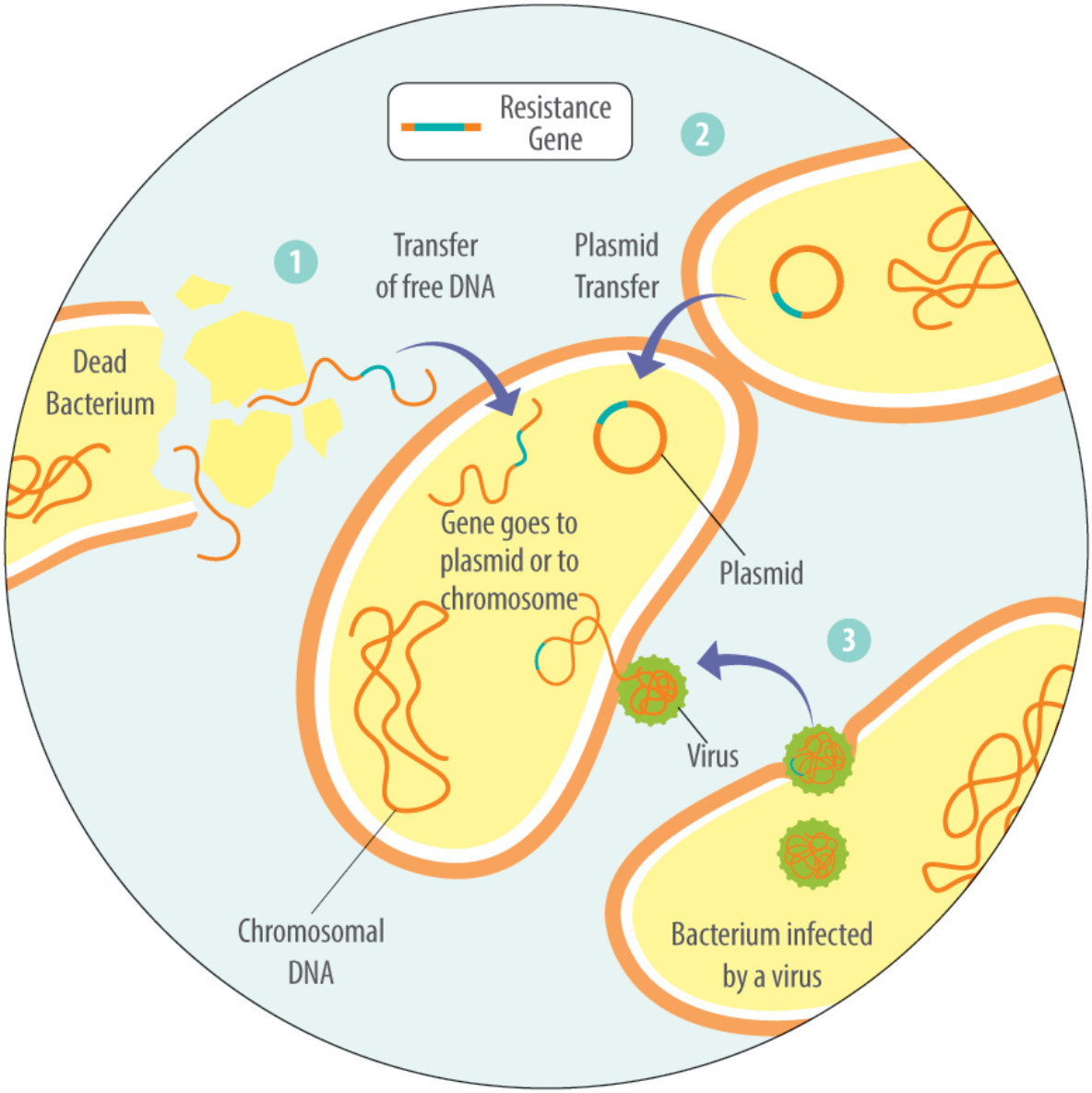

Figure 1: Different possibilities of transfer of resistance genes

Deoxynivalenol (DON) promotes resistance in gut microbiota

A Chinese group of researchers (Deng et al., 2025) examined for the first time the influence of DON on the intestinal microbiota of chickens. One of the most alarming findings is DON's ability to enhance antibiotic resistance. It contributes to this issue in several ways:

1. Encouraging resistant bacteria – By disrupting microbial balance, DON provides a survival advantage to bacteria that carry resistance genes.
2. Activating resistance genes – Studies suggest that DON can increase the expression of genes that help bacteria withstand antibiotics.
3. Enhancing gene transfer – Bacteria can share resistance genes through horizontal gene transfer. DON appears to promote this process, making antibiotic-resistant strains spread more rapidly.
4. Weakening antibiotic effectiveness – DON-induced changes in the gut environment can reduce the effectiveness of antibiotics, making treatments less successful.

A further indication that mycotoxins can enhance resistance is the significant overlap in the geographical distribution of antimicrobial-resistant bacteria and genes with that of mycotoxins, as noted by Deng et al.

Which protection mechanisms do bacteria have against mycotoxins?

In the case of mycotoxins, bacteria employ similar molecular mechanisms to those used against antibiotics. In an in vitro experiment, Hassan et al. (2019) challenged Devosia mutans, a gram-negative bacterium, with DON in the growth medium. DON inhibits protein synthesis, induces oxidative stress, and compromises cell membrane integrity in eucaryotic cells. Hassan et al. asserted three adaptive mechanisms as the response to the challenge:

1. Activation of cellular membrane proteins (adenosine 5'-triphosphate-binding cassette -ABC-transporters) responsible for the unidirectional transport of substrates, either outward or inward. These ABC transporters can work as drug efflux pumps.
2. Production of DON-specific deactivation enzymes, thereby engaging a toxin-specific pyrroloquinoline quinone-dependent detoxification pathway. This enables the bacterial isolate to transform DON to a non-toxic stereoisomer.
3. Upregulation of auxiliary coping proteins, such as porins (transmembrane proteins involved in metabolite exchange), glutathione S-transferases, and phosphotransferases, both of which are likely involved in the detoxification of xenobiotics.

Public health implications and preventive measures

Given the widespread presence of DON in food and animal feed, its potential role in antibiotic resistance poses a serious threat. The combination of increased bacterial resistance and weakened antibiotic efficacy could lead to more difficult-to-treat infections. This is particularly concerning in hospital settings, where antibiotic-resistant infections already cause high mortality rates.

To address the issue, several strategies can be implemented:

1. Reducing DON contamination: Implementing improved agricultural practices, such as crop rotation, the use of fungal-resistant crop varieties, and maintaining proper storage conditions, can help limit fungal growth and DON production.
2. Monitoring food and feed supply – Strict regulations and testing for DON contamination in grains and animal feed are essential to minimize human and animal exposure.
3. Effective mycotoxin risk management at feed mill and farm levels: Using tools such as MasterRisk and effective products combatting mycotoxins.
4. Maintaining gut health: A healthy diet rich in fiber, probiotics, and gut health-supporting feed supplements, such as Ventar D or products from the Activo line, may help counteract some of the adverse effects of DON on gut microbiota.
5. Developing new treatments: Research into alternative therapies and new antibiotics is crucial to combat the rise of antibiotic resistance.

Antimicrobial resistance: Be aware of the mycotoxins!

The connection between mycotoxins, such as DON, and antibiotic resistance underscores the need for a broader perspective on public health and food safety and once again brings the "One Health Concept" into focus. While antibiotic overuse remains the primary driver of resistance, environmental factors, such as

exposure to mycotoxins, should not be overlooked. By increasing awareness, enhancing food safety regulations, and investing in research, we can take steps to mitigate this emerging threat and safeguard the effectiveness of antibiotics for future generations.

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Enhancing Poultry Gut Health with Novel Xylanase: A Sustainable Path to Reduced Antimicrobial Use

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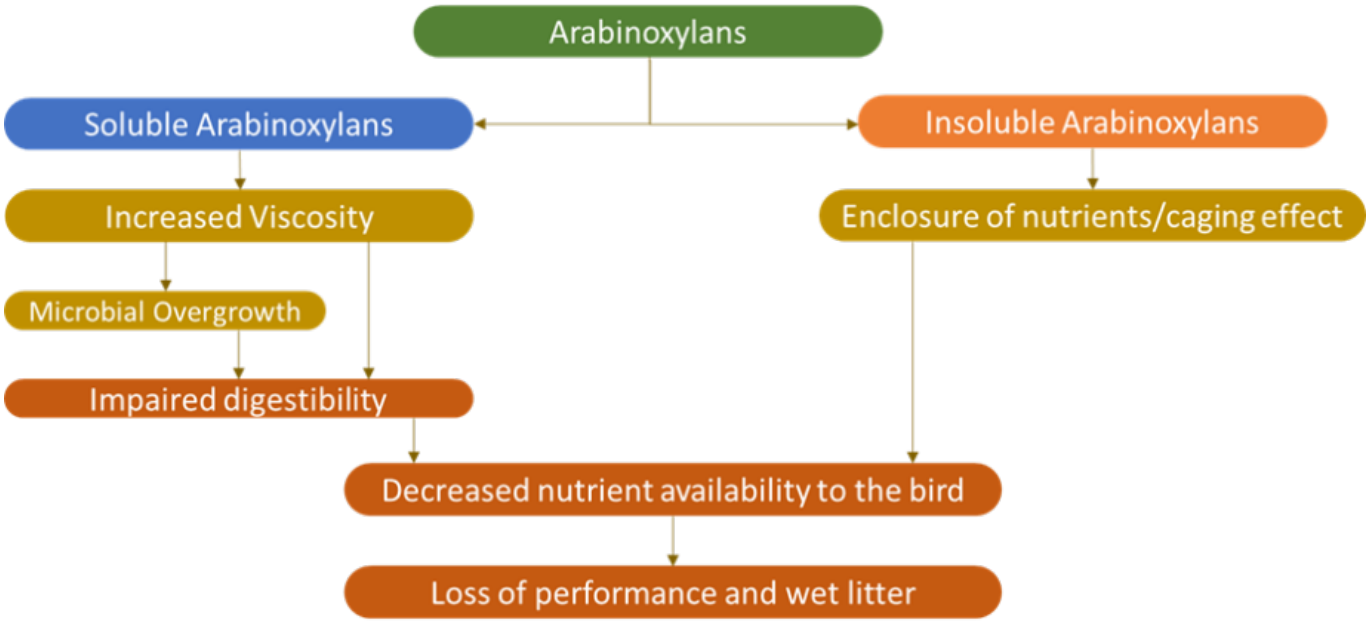
Gut health is pivotal to profitable poultry production, as the gastrointestinal tract (GIT) enables nutrient digestion and absorption while acting as a defense against pathogens. A healthy gut improves feed conversion, boosts immune resilience, and reduces reliance on antimicrobials—critical in the fight against antimicrobial resistance (AMR). With AMR posing significant threats to public health and animal agriculture, strategies like biosecurity, sustainable management, and effective dietary interventions are gaining traction. Feed enzymes have emerged as essential tools for managing feed costs, mitigating anti-nutritional factors, and improving nutrient utilization. Among these, feed enzymes like xylanase stand out. By breaking down xylan, a major component of non-starch polysaccharides (NSPs) in plant-based feed ingredients, xylanase reduces gut viscosity, enhances nutrient utilization, and supports optimal gut health and productivity. This article explores the innovative application of novel GH10 xylanases, such as Axxess XY, as a sustainable solution for improving feed efficiency and gut health in poultry production.

Xylanase in Poultry Nutrition

Xylanase plays a pivotal role in enhancing nutrient availability by addressing the limitations of endogenous enzyme synthesis in poultry. Xylanase enzymes belong to the carbohydrase class, catalyzing the breakdown of xylan, a major NSP in plant-based feed ingredients. They hydrolyze xylan into simple sugars like arabino-xylo-oligosaccharides (AXOs) and xylo-oligosaccharides (XOs), reducing the encapsulation of nutrients and digesta viscosity. These actions improve overall nutrient digestibility and bird performance.

Fig.1: Arabinoxylans – anti-nutrient mode of action in chicken



The primary benefit of feed xylanase lies in its ability to reduce digesta viscosity. By partially hydrolyzing NSPs in the upper digestive tract, xylanase ensures better nutrient absorption in the small intestine. Studies (Matthiesen et al., 2021; Choct & Annison, 1992) confirm that reduced viscosity enhances feed digestibility, leading to improved performance in poultry. Further, to realize the optimum benefits, it is crucial that xylanase efficiently degrades both soluble and insoluble arabinoxylans. The insoluble arabinoxylans are part of the cell wall structure of plant cells, resulting in a cage effect, entrapping nutrients like starch and protein. Effectively breaking down insoluble arabinoxylans ensures that the nutrients trapped in plant cell walls are released for growth and production.

Mechanisms Supporting Gut Health

Viscosity Reduction

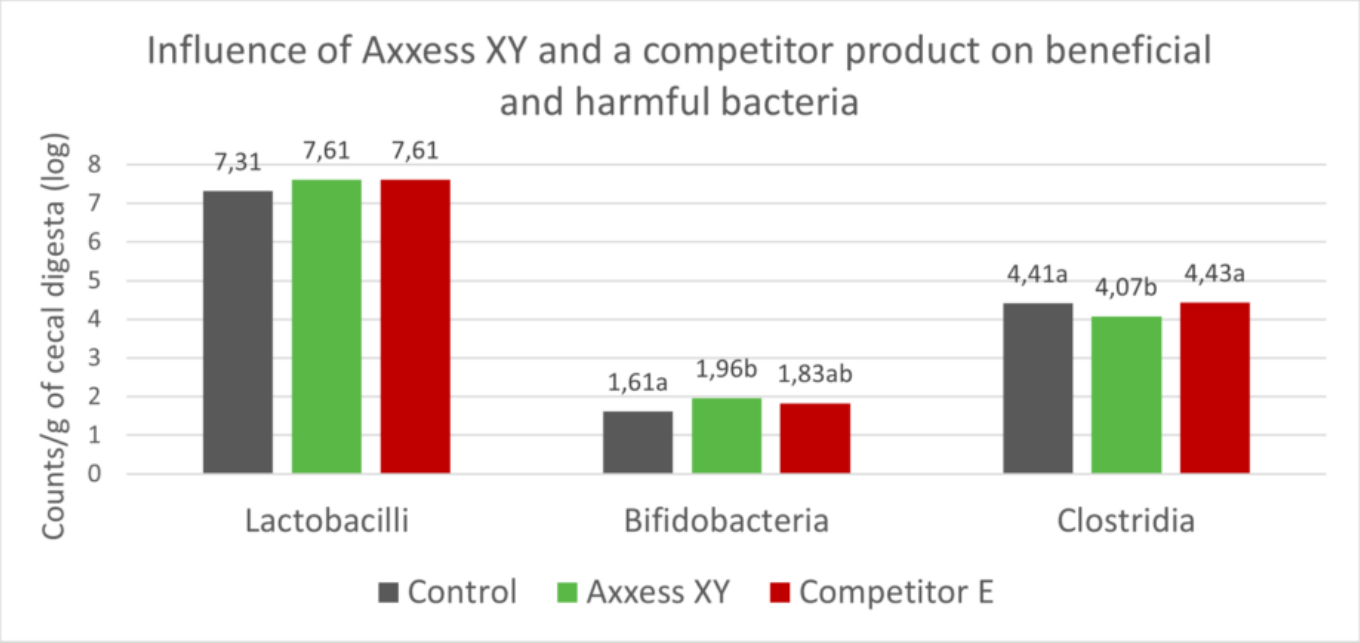
High NSP content increases digesta viscosity and slows digestion and nutrient absorption. Soluble arabinoxylan is not digested in the small intestine of broilers. It produces a viscous chime, leading to the proliferation of pathogenic bacteria, intestinal inflammation, impairment of barrier function in the intestine, and severe intestinal lesions (Teirlynck et al., 2009). Xylanase mitigates this by breaking down xylans, a major component of NSPs in common feed ingredients. This results in a better flow of digesta and reduced energy losses.

Microbial Metabolites

Xylo-oligosaccharides (XOS) can also be produced in the intestine of monogastric animals to some extent when exogenous enzymes, such as xylanase, are added to the feed (Baker et al., 2021).

The XOS generated by xylanase action on arabinoxylans can act as prebiotics, fostering beneficial bacteria like Lactobacillus and Bifidobacterium, which can outcompete harmful species. XOS can positively impact the gut microbiota, enhance short-chain fatty acid (SCFA) production, stimulate immune activity in the gastrointestinal tract, and improve energy utilization.

Fig. 2. Axxess XY improved beneficial microbes and reduced the clostridial population in broilers.



Barrier Function

By lowering inflammation and irritation in the intestine, xylanase helps maintain gut integrity, reducing the risk of pathogen translocation from the intestinal lumen. In a broiler study, xylanase decreases epithelial apoptosis index, up-regulates tight junction gene expression, and inhibits mucin synthesis in the small intestine, likewise alleviating the intestinal mucosal barrier impairment from *Clostridium perfringens* challenge (Liu et al., 2012).

Practical Considerations for Xylanase Use

Enzyme Stability

Enzymes are proteins that tend to lose their catalytic activity at high temperatures. When exposed to excessive heat, an enzyme's protein structure can irreversibly unfold, disrupting its active site and causing loss of function. Therefore, ensuring enzyme stability during feed processing is critical for maintaining its activity in the intestine. Intrinsically heat-stable enzymes have an inherent ability to withstand higher temperatures without the need for a protective coating and are immediately available for action upon ingestion.

Feed Composition

Xylanase efficacy is influenced by diet composition, particularly the NSP content and the presence of xylanase inhibitors in common feedstuffs. It is important to choose a xylanase that can resist the activity of xylanase inhibitors and is effective against both soluble and insoluble arabinoxylans.

The recommended energy matrix value for the xylanase enzyme should be used while formulating the feeds to create energy-deficient diets to reap the full benefits of xylanase use.

Optimal Dosage

Proper dosing is essential to maximizing the benefits of feed enzymes while avoiding unnecessary costs. It is important to follow manufacturers' recommendations and avoid underdosing an enzyme.

GH10 Xylanases: The Superior Choice for Animal Nutrition

Most feed xylanases are classified into glycoside hydrolase families 10 (GH10) and 11 (GH11) based on their substrate specificity, catalytic action, and structural features.

Why GH10 Xylanases Are More Effective

1. **Broader Substrate Specificity:**

   Unlike GH11 xylanases, GH10 xylanases can effectively hydrolyze both soluble and insoluble xylan substrates. This broader activity ensures an efficient breakdown of xylans in a wide range of feed ingredients.

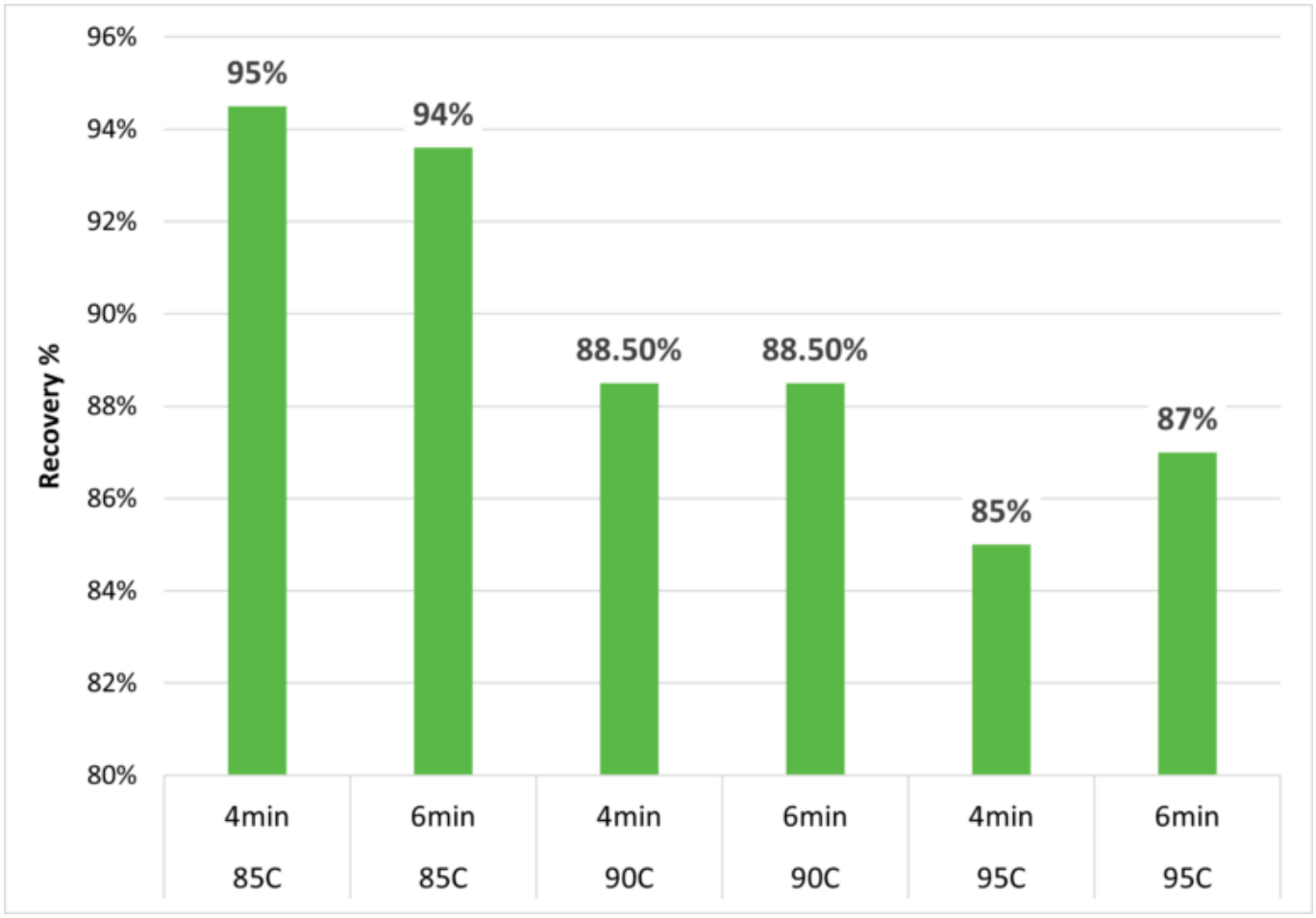
2. **Higher Catalytic Efficiency:**

   GH10 enzymes cleave xylan at substituted regions, yielding shorter xylo-oligosaccharides that can positively impact gut health and maximize nutrient availability.

3. **Thermostability:**

   Feed processing often involves high temperatures during pelleting. Axxess XY, a GH10 family xylanase, demonstrates remarkable thermostability, maintaining over 85% activity even at 95°C for extended conditioning times. This resilience ensures consistent enzyme performance during feed manufacturing and digestion.

Fig.3: Optimum recovery of Axxess XY at elevated conditioning time and temperatures



Novel Applications of Axxess XY: A GH10 Xylanase

Axxess XY exemplifies the advantages of GH10 xylanases in poultry nutrition. Its ability to efficiently act on both soluble and insoluble arabinoxylans makes it a versatile feed enzyme. The enzyme's high thermostability ensures efficient enzyme activity in the gut and subsequent optimum nutrient utilization under challenging processing conditions, promoting gut health and maximizing performance.

Key Benefits of Axxess XY

1. **Enhanced Nutrient Utilization:**

   By unlocking nutrients trapped in NSPs, Axxess XY promotes better feed conversion ratios (FCRs).

2. **Improved Gut Health:**

   Reducing the digest's viscosity reduces gut health challenges and predisposition to gut infections. Further, the short-chain oligosaccharides released by Axxess XY support beneficial gut microbiota, improving digestive health.

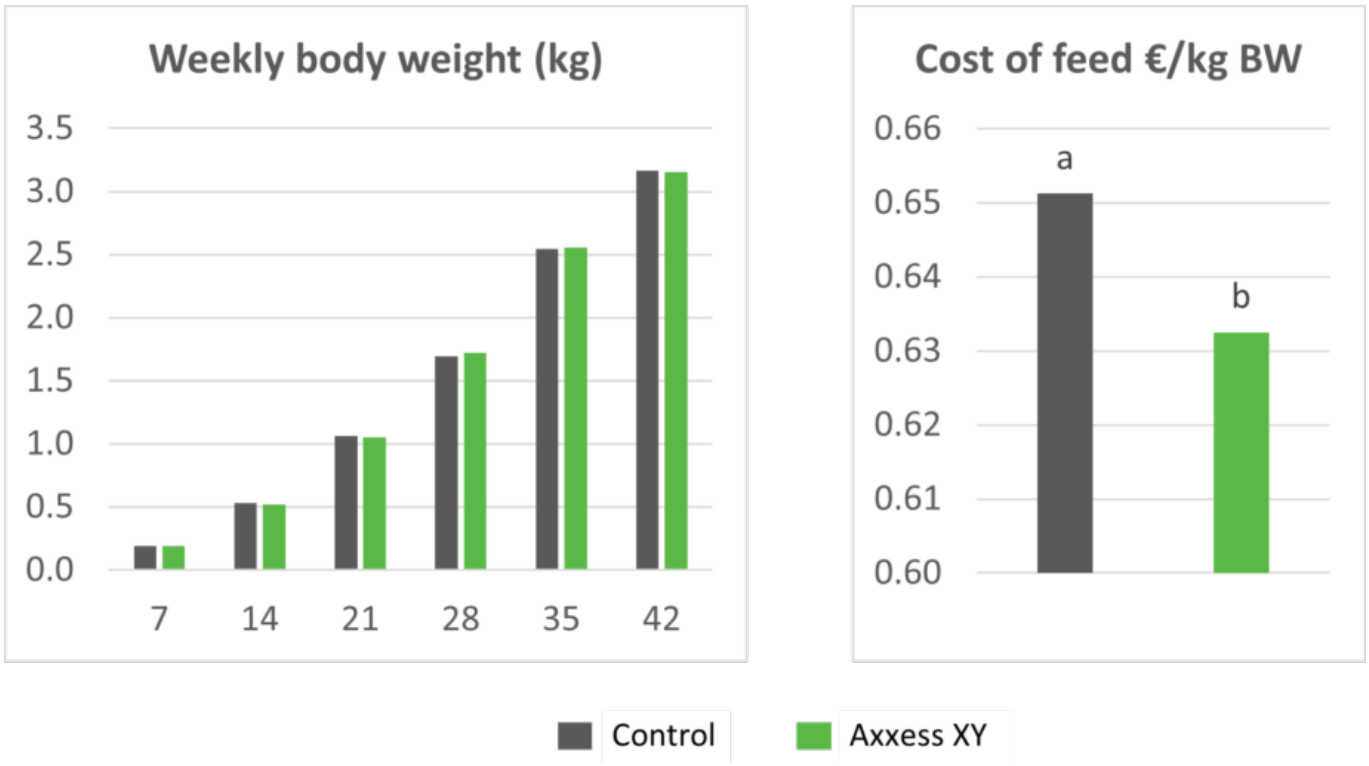
3. **Economic Efficiency:**

   Enabling the optimum use of high-fiber, cost-effective, locally available feed ingredients without

compromising performance makes Axxess XY an asset for profitability.

In a recently conducted 42-day trial at a commercial farm, Axxess XY maintained the average body weight of broilers with a 100 kcal/kg reduction in metabolizable energy while significantly reducing feed cost/kg body weight. The diets were based on corn, DDGS, and soybean meal.

Figures 4 and 5: Body weight and cost of feed in broilers fed a diet reduced by 100 kcal/kg in metabolizable energy compared to a standard diet without Axxess XY



Conclusion

Xylanase exemplifies how feed enzymes can transcend their traditional role in feed cost reduction to support enhanced gut health. Xylanase supports reduced antimicrobial use in poultry production by improving nutrient utilization, reducing digesta viscosity, and fostering healthy microbiota. Its integration into comprehensive gut health management strategies offers a sustainable pathway to combat AMR and ensure the long-term viability of poultry farming. By targeting NSPs, these enzymes enhance nutrient digestibility, reduce feed costs, and support sustainable production practices.

GH10 xylanases, particularly Axxess XY, stand out for their superior substrate specificity, catalytic efficiency, and thermostability. By incorporating **Axxess XY** into feed formulations, poultry producers can unlock the full nutritional potential of feed ingredients, ensuring optimal performance and profitability. As the poultry industry continues to evolve, adopting advanced enzyme technologies like Axxess XY represents a strategic step toward sustainable and efficient animal nutrition.

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