

**OPTIMISING  
GUT HEALTH  
BY NEUTRALIZING  
 $\beta$ -MANNANS  
IN FEED INGREDIENTS**



**HEMICELL™ XT  
PRODUCT ENCYCLOPEDIA**



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# 1

## ENZYME BASICS



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#### What are enzymes?

Enzymes act as catalysts for many biochemical processes in the body, from digestion to tissue regeneration. They allow reactions to take place that would otherwise be too slow to be metabolically useful. Enzymes are proteins; organic compounds that are sensitive to temperature and pH.

Once they have done their job, enzymes are broken down into amino acids and peptides and either metabolised or excreted from the body.

Enzymes can be made by an animal itself (endogenous) or supplied to the animal, usually via the diet (exogenous).

#### How do enzymes work?

The molecules each enzyme can react with are referred to as substrates. Only substrates with exactly the right shape (chemical bonds) can bind to an enzyme and react. This means that enzymes are very selective and each catalyses one specific reaction.

That reaction could be joining substrates together to make new molecules, or breaking down the substrate into component parts, which the animal can then absorb or use.

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## β-MANNANS AND FIIR



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### What is FIIR?

FIIR is an acronym for Feed-Induced Immune Response. It's a name for the innate immune response that is triggered when a substance is recognized by the innate immune system as being pathogen-like. This recognition is due to specific molecular patterns called Pathogen Associated Molecular Patterns (PAMPs). Some non-pathogen compounds found in feed have similar molecular patterns to actual pathogens, that act as PAMPs. The result is that the innate immune system recognizes these non-pathogen compounds as a potential danger and initiates a counter-response that requires diversion of nutrients from productive purposes to fuel this response.<sup>6, 11-14, 31</sup>

### What is a β-mannan?

β-mannans are anti-nutritive non-starch polysaccharide fibres, commonly found in vegetable feed ingredients. They are high molecular weight molecules formed of a long chain of mannose sugar units with galactose side chains.

β-Mannans are unable to be naturally broken down in the bird or pig's digestive system.<sup>6</sup>

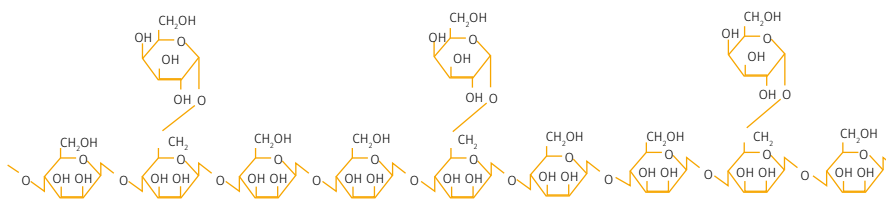


Figure 1. Legume galactomannan

### What feedstuffs contain β-mannans and how much do they contain?

Most vegetable feed ingredients contain β-mannans. Soybean meal, sunflower meal, rapeseed and copra meal are common β-mannan sources in poultry and swine diets across the globe.

Table 1: Estimated β-mannan content\*<sup>20, 30</sup>

Ingredients	β-mannans, Pct., as is <sup>1</sup>	Minimum	Maximum
Corn gluten meal	0.17	0.10	0.24
DDGS	0.57	0.23	1.09
Oats	0.31	–	–
Oats, dehulled	0.16	0.09	0.22
Palm kernel meal	7.24	5.34	10.90
Peas	0.11	0.09	0.12
Rapeseed meal	0.18	0.13	0.37
Rapeseed expeller	0.13	–	–
Rapeseed, whole	0.08	0.07	0.09
Soya hulls	6.67	6.43	6.91
Soybean meal 44% CP	0.79	0.38	1.30
Soybean meal 48% CP	0.59	0.28	1.00
Soybean meal, fermented	0.59	0.58	0.59
Soybean meal, Full Fat	0.71	0.42	1.05
Sunflower meal, ≤32% CP, w/ hulls	0.62	0.53	0.69
Sunflower meal, >32% CP, w/o hulls	0.57	0.42	0.75
Wheat	0.27	0.11	0.42
Wheat bran	0.25	0.21	0.34

<sup>1</sup> Estimated Soluble β-mannan, % = Soluble mannose % x 1.5



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### Do β-mannans affect Intestinal Integrity?

Yes, they may reduce Intestinal Integrity, decrease the absorptive capacity of the gut and increase the impact of infections.<sup>29,32</sup>

### Why do β-mannans affect performance?

Long mannose structures (found in the backbone of β-mannans) are also found in many pathogens.<sup>6,11</sup> This likely explains why mannose is one of the important PAMP (Pathogen Associated Molecular Patterns) molecules that triggers an innate immune response whenever they come into contact with immune receptors. Simply put, the immune system mistakes β-mannans as an invading pathogen.<sup>6,11,17,18</sup> β-mannan fibres “look like” a pathogen to the immune system, and will therefore trigger the cascade of events designed to protect the animal against infections. This type of immune response can have a negative impact on animal health and performance, as it typically consumes energy and other valuable nutrients.<sup>1-4, 6, 28</sup>

### Recognition of β-mannans by the innate immune system triggers a cascade of events:

- > Critical resources (energy and nutrients) that otherwise would be used for production, growth or health are diverted in favour of immune defence mechanisms. This unnecessary diversion leads to reduced efficiency, higher production costs and decreased sustainability, as more feed is required by the animal.<sup>1-5</sup>
- > Lowers plasma glucose and insulin secretion<sup>7,8,16</sup>
- > Reduces water absorption<sup>9,10</sup>
- > Reduces nitrogen retention<sup>4,17</sup>

### Does the effect of soluble β-mannans depend on the source?

The source of the soluble β-mannans is unlikely to affect their influence on FIIR or animal performance because it is the mannose sugar molecules that are recognized by the innate immune system.<sup>3,11,14</sup>

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### What is Hemicell™ XT?

Hemicell™ XT is a patented enzyme produced by fermentation of *Paenibacillus lentus*, (formerly known as *Bacillus lentus*), and the active ingredient is **endo-1,4- $\beta$ -D-mannanase**. The  $\beta$ -mannanase enzyme degrades soluble  $\beta$ -mannan fibres, mainly  $\beta$ -galactomannan and  $\beta$ -glucomannan.

### What's different about Hemicell™ XT compared to other enzymes?

Most feed enzyme products are nutrient releasing enzymes, which break down substrate in the feed to make more nutrients and energy available for growth and production. Hemicell™ XT is a nutrient-sparing enzyme that optimizes gut health by neutralizing (hydrolysing)  $\beta$ -mannans found in most vegetable feedstuffs (see Table 1) that trigger a Feed-Induced Immune Response (FIIR). By degrading these fibres, Hemicell™ XT reduces the nutrient waste and performance losses from the natural, but unnecessary innate immune response to  $\beta$ -mannans.<sup>6-11, 31</sup>

### How much substrate does Hemicell™ XT need to be effective?

Use of Hemicell™ XT to reduce unnecessary immune activity from  $\beta$ -mannans is expected to be cost effective in diets with at least 0.20% soluble  $\beta$ -mannans.

### If the $\beta$ -mannan content is so low, why should I use an enzyme?

Very little  $\beta$ -mannan is actually needed (0.20%) to trigger the innate immune response and because  $\beta$ -mannans are found in all vegetable feed ingredients.

The mannan oligosaccharide fragments that are produced when Hemicell™ XT hydrolyses  $\beta$ -mannans are too small to be recognized by the innate immune system. Reducing the Feed-Induced Immune Response (FIIR) from  $\beta$ -mannans helps spare valuable energy nutrients, which can be re-directed toward growth and performance.

### Does the value of Hemicell™ XT increase in diets with high $\beta$ -mannan content?

Yes, there are titration data to demonstrate this.<sup>6, 18</sup>

### What differentiates Hemicell™ XT from cocktail enzymes with $\beta$ -mannanase on the label?

Hemicell™ XT is a patented enzyme product with a guaranteed minimum  $\beta$ -mannanase activity. This ensures sufficient  $\beta$ -mannanase activity in the final feed to prevent FIIR from  $\beta$ -mannans, when used as recommended. When evaluating a cocktail enzyme product, you should only consider enzyme activities with a minimum guaranteed potency.

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### How fast does Hemicell™ XT work?

Hemicell™ XT, which is only effective against soluble  $\beta$ -mannans, begins to work after ingestion, as soon as enough moisture has been introduced to the feed.

### Does the response to Hemicell™ XT depend on the dietary energy level?

While Hemicell™ XT is effective at all energy levels and the benefits realistic in all diets, the expression of the benefits may depend on the dietary energy level. For example, broilers gradually lose their ability to respond to increasing nutrient density in high energy diets.<sup>36</sup> The best way to use Hemicell™ XT in high energy diets is usually to formulate it into the diets with all or part of its recommended energy matrix. Contact an Elanco Enzyme Specialist for further details.

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### What are the typical benefits from Hemicell™ XT?

Whenever we speak about typical benefits for Hemicell™ XT, we refer to animals reared in modern, well managed commercial production facilities.

The actual benefits from Hemicell™ XT are mainly influenced by:

- > The β-mannan content of the diet – We recommend using Hemicell™ XT in diets containing at least 0.2% soluble β-mannan content.<sup>4, 6, 18</sup>
- > The level of stress. More stress typically increases the response to Hemicell™ XT. The stress may come from any source, like the temperature, environment, population density, infections, management, etc. As such, to ensure variability in these factors don't affect results, pen trials are not recommended to assess the benefits of Hemicell™ XT.

The typical response to Hemicell™ XT on gain and feed efficiency in poultry is a consequence of the unnecessary immune response and inflammation that it prevents. This response is:

- > A saving in nutrients, typically equivalent to a metabolizable energy saving of up to 90 kcal ME/kg complete feed for broilers and 63 kg NE/kg for pigs.
- > Optimized Intestinal Integrity, which translates into drier litter and broilers with fewer foot pad lesions
- > Improvement in faecal scores

In order to maximise the value from the use of Hemicell™ XT, we recommend to always formulate it into the diets with a matrix value up to 90 kcal ME/kg (0.375 MJ/kg) for broilers or 63kcal NE/kg (0.264 MJ/kg) for pigs (or at least enough to make the inclusion cost neutral).

<sup>22-24, 29, 31-33, 35</sup>

### Typical benefits in broilers

	Hemicell™ XT formulated with full matrix
Feed Cost saving	Equal to the value of 90 Kcal ME/kg
Body Weight Gain	±0
Feed Conversion	±0
Uniformity	+6-10%
Health	Improved
Culling rate & mortality	Improved

### Typical benefits in pigs

	Hemicell™ XT formulated with full matrix
Feed Cost saving	Equal to the value of 63 kcal NE/kg
Health	Improved

### Can Hemicell™ XT be added when other enzymes are already present in the feed?

Yes. Hemicell™ XT is safe to use with other enzyme products. The specific mode of action of Hemicell™ XT has not been shown to interact with other enzymes mode of action. Many trials have shown that the benefits from Hemicell™ XT are additive to the benefits of other enzymes products.<sup>22, 23, 25</sup> Please contact an Elanco enzyme specialist for further information.

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### Could there be an interaction between Hemicell™ XT and immune stimulating additives (e.g. vit C and vit E)?

Elanco is not aware of any interaction between Hemicell™ XT and immune stimulating additives.  $\alpha$ -mannans, a component of mannan-oligosaccharide products and yeast based immune stimulants, are not degraded by Hemicell™ XT ( $\beta$ -mannanase) because it is only able to cleave  $\beta$ -mannans and therefore has no effect on  $\alpha$ -mannans.

### What about using Hemicell™ XT in combination with vet products and feed additives?

The use of Hemicell™ XT together with vet products, antibiotics, anticoccidials, and other feed additives is usually safe. The only known contraindications for Hemicell™ XT are with formaldehyde based products, which may denature Hemicell™ XT and other enzymes when they are added to the feed at the same time.<sup>27</sup> Ask an Elanco representative for guidance and analyse the final feed for  $\beta$ -mannanase activity if in doubt.

### Should I expect an improvement in the health of my animals from Hemicell™ XT?

Hemicell™ XT is not a medicine or an antibiotic. Hemicell™ XT spares nutrients by preventing the innate immune response triggered by  $\beta$ -mannans.<sup>1, 2, 15, 21-26</sup> Prevention of this unnecessary immune response may produce health benefits and optimize gut health.<sup>6, 29, 33</sup>

### What effect does the form of soybeans (hulls and meals with different protein content) have on Hemicell™ XT use recommendations?

The form of soybeans does not affect Hemicell™ XT use recommendations. However, the  $\beta$ -mannan content is typically highest in non-dehulled soybean meal ( $\approx$ 1.45%) intermediate in dehulled soybean meal ( $\approx$ 1.1%) and lowest in full-fat soybeans ( $\approx$ 0.7%). The  $\beta$ -mannan content in specialty soy products, like soy protein concentrate and -isolate, is usually much lower.<sup>30</sup>

### Why do the benefits from Hemicell™ XT increase with increasing challenge or stress in the production environment?

The primary reason for this is that the immune system prioritizes the nutrient supply to the more important defence mechanisms. The prioritization is managed via a negative feedback system that inhibits growth related processes, like feed intake, digestion, absorption, nutrient deposition etc. Loss of appetite often explains most of the performance losses during an immune challenge. The strength of this negative feedback increases with the level of challenge.<sup>6</sup> For example, Hemicell™ XT is expected to prevent a performance loss of about 3% under good commercial production conditions. In challenge trials with Hemicell™ XT, we have observed performance improvements equivalent to energy savings of at least 15-20% during the acute phase of the challenge.<sup>29</sup>

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### When should I use Hemicell™ XT in the diet? At what weight or age?

There are no age or weight restrictions for Hemicell™ XT. You should use Hemicell™ XT in all diets with soluble β-mannan levels equivalent to or higher than that of corn based diets with 12% soybean meal, rapeseed meal, sunflower meal, palm kernel meal and/or guar meal.<sup>3</sup>

### If I use Hemicell™ XT, can I reduce energy in my rations?

Yes, you can reduce dietary energy in most diets when you add Hemicell™ XT and still expect similar performance results. We recommend to formulate Hemicell™ XT into the diets with an energy value equivalent up to 90 Kcal/kg (0.375 MJ/kg) for broilers<sup>36</sup> or 63 kcal NE/kg (0.264 MJ/kg) for pigs. Ask an Elanco Enzyme Specialist for guidance.

### How can I be sure Hemicell™ XT is working?

Elanco provides assay services to identify activity and recovery capabilities. This service provides actual assay values using a secure, online reporting system.

### What are the recommended periods of Hemicell™ XT use?

Use Hemicell™ XT in all diets with at least 0.2% soluble β-mannan content. The potential periods of use are in the UK:

Broilers, turkeys and other meat producing birds	Day 1 to market
Layers and Breeders	Before production cycle starts
Pigs for fattening (not licensed in breeding sows)	From weaning

(Note: Hemicell™ XT is not approved for each species in all markets. The label contains complete use information, including cautions and warnings. Always read, understand and follow the label and use directions.)

### What are the typical Hemicell™ XT inclusion levels for all Species?

(Note: The approved dosage may vary between markets. The label contains complete use information, including cautions and warnings. Always read, understand and follow the label and use directions.)

PRODUCT (form)	MINIMUM INCLUSION PER TONNE OF COMPLETE FEED*			
	Broilers	Turkeys	Weaned Pigs	Pigs for Fattening
Hemicell™ XT dry	147 g*	147 g*	133 g*	133 g*

\* Product labels vary by country. The label contains complete use information, including cautions and warnings. Always read, follow and understand the label and use directions.

### What is the best way to test Hemicell™ XT in the field?

It is very difficult to conduct good field trials. The main challenge is usually to manage the natural variation between houses, farms or cycles, which typically exceeds the response to any feed additive. Consult with your Elanco representative to identify the best option(s).



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Date of preparation APRIL 2023. PM-UK-21-0757

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