Technical Report

Significance of *Hemicellulase* in CanXida Restore (Formula RST)

"*In CanXida Restore (Formula RST),* ***Hemicellulase*** *disrupts Candida cell wall integrity, aiding immune responses and antifungal treatments.*

Contents

Executive Summary

Hemicellulases are enzymes crucial for breaking down hemicellulose, a prevalent plant polysaccharide, into smaller, more digestible components. Derived from various microorganisms, Hemicellulases target different bonds within hemicellulose molecules, aiding in their hydrolysis. These enzymes have diverse functional properties, including improved digestibility of plant-based foods, prebiotic effects, nutritional enhancement, and relief from digestive discomfort. They also potentially play a role in maintaining gut barrier function, supporting gut health, weight management, alleviating gastrointestinal conditions, and aiding individuals with gluten sensitivity.

Hemicellulases can target fungi and bacteria by degrading hemicellulose in their cell walls or extracellular matrices. In the context of probiotic supplementation, Hemicellulases contribute to a balanced gut microbiome and may hold promise in addressing Candida overgrowth*.

1. Introduction

Hemicellulose molecules are commonly found plant polysaccharides that exist as chains of pentoses and/or hexoses. These chains are connected through covalent hydrogen bonds (Houfani et al., 2020).

Hemicelluloses, which are found in plant cell walls, are polysaccharides featuring equatorial beta-(1-->4)-linked backbones.

Hemicelluloses consist of various types such as xyloglucans, xylans, mannans, glucomannans, and beta-(1-->3,1-->4)-glucans (Scheller & Ulvskov, 2010).

Hemicelluloses are found in the cell walls of most land plants, with the exception of beta-(1-->3,1-->4)-glucans, which are limited to Poales and a few other plant groups. The structure and abundance of hemicelluloses vary significantly across different species and cell types. Hemicelluloses play a crucial role in reinforcing the cell wall through their interactions with cellulose and, in certain cases, lignin (Scheller & Ulvskov, 2010).

2. Hemicellulases sources & mechanism

Hemicellulases are derived from a diverse range of microorganisms found in nature, with the most commonly used ones being those from fungus and thermophilic bacteria. Their primary role is to break down the polysaccharides found in hemicellulose through hydrolysis (Miranda-Lopez, 2022).

Hemicellulase typically denotes a set of enzymes capable of synergistically breaking down hemicellulose. The hemicellulolytic system primarily consists of the following (Bajpai, 2021; Dekker & Richards, 1976; Tian et al., 2021).

2.1. Endo- and Exo-1,4-β-Xylanase:

These enzymes target the β-1,4 glycosidic bonds within the xylan backbone of hemicellulose. Endo-xylanases cleave internal bonds within the xylan chain, while exo-xylanases act on the ends of the chain, releasing xylose monomers.

2.2. β-Arabinofuranosidases:

β-Arabinofuranosidases are responsible for cleaving arabinose side chains from xylan,

which are commonly found in hemicellulose structures. This enzyme hydrolyzes the glycosidic bonds between arabinofuranose units and the main xylan backbone.

2.3. α- and β-Galactosidases:

These enzymes catalyze the hydrolysis of galactose residues linked to hemicellulose, such as those found in galactoglucomannans and arabinogalactans. α-Galactosidases act on α-galactosidic linkages, while β-galactosidases target β-galactosidic bonds.

2.4. β-Xylosidases:

β-Xylosidases function to cleave off xylose residues from the non-reducing ends of xylo-oligosaccharides generated by the action of endo- and exo-xylanases. This enzyme plays a crucial role in the complete degradation of xylan into xylose monomers.

2.5. Endo-1,4-β-Mannanase:

Endo-1,4-β-Mannanase is responsible for breaking down β-1,4 glycosidic bonds in mannan polysaccharides, which are another type of hemicellulose commonly found in plant cell walls. This enzyme cleaves internal bonds within the mannan chain.

2.6. β-Mannosidases:

β-Mannosidases catalyze the hydrolysis of terminal mannose residues from mannooligosaccharides or mannan polysaccharides. They act on the non-reducing end of the molecule, releasing mannose monomers.

3. Functional and Health Properties of Hemicellulases:

These enzymes have various functional and health properties, which are significant in several industries and biological processes*:

3.1. Improved digestibility of plant-based foods:

Hemicellulases can enhance the digestibility of plant-based foods by breaking down the complex carbohydrates present in cell walls (Saeed et al., 2019).

This can be particularly beneficial for individuals with digestive issues or those following a plant-based diet.

3.2. Prebiotic properties:

Hemicellulases can produce prebiotic oligosaccharides during the breakdown of

hemicellulose. These oligosaccharides can serve as food for beneficial gut bacteria, promoting gut health and potentially enhancing overall immunity(Jana et al., 2021).

3.3. Nutritional enhancement:

By breaking down hemicellulose, Hemicellulases release nutrients trapped within plant cell walls, increasing the nutritional value of plant-based foods (Tharifkhan et al., 2021).

3.4. Digestive Aid:

Hemicellulase can break down hemicellulose into smaller, more digestible molecules such as xylose, arabinose, and mannose (Houfani et al., 2020). This digestive activity can aid in the breakdown of dietary fibers, potentially improving overall digestive function and reducing gastrointestinal discomfort.

3.5. Potential Role in Gut Barrier Function:

Hemicellulase may play a role in maintaining gut barrier function by modulating the composition of the gut microbiota and reducing inflammation (Saeed et al., 2019). A healthy gut barrier is essential for preventing the translocation of harmful substances from the gut into the bloodstream, which can contribute to systemic inflammation and various health issues.

3.6. Relief from Digestive Discomfort:

Supplementing with hemicellulase can alleviate symptoms associated with digestive discomfort, such as bloating, gas, and indigestion **(Table 1)**. By aiding in the breakdown of complex plant fibers, hemicellulase reduces the burden on the digestive system, leading to smoother digestion (Saeed et al., 2019).

3.7. Support for Gut Health:

Hemicellulase promotes a healthy balance of gut bacteria by fermenting hemicellulose in the colon. This fermentation process produces short-chain fatty acids, which nourish the cells lining the colon and support a healthy gut microbiome (Jana et al., 2021; Saeed et al., 2019). A balanced gut microbiome is linked to numerous health benefits, including improved immune function and reduced risk of digestive disorders.

3.8. Support for Weight Management:

Hemicellulase may aid in weight management by promoting satiety and reducing food cravings. The increased breakdown of dietary fibers can help regulate blood sugar levels and prevent spikes in insulin, which may contribute to more stable energy levels and reduced appetite (Lattimer & Haub, 2010) .

3.9. Alleviation of Gastrointestinal Conditions:

In individuals with conditions such as irritable bowel syndrome (IBS), hemicellulase supplementation may help alleviate symptoms such as abdominal pain, diarrhea, and constipation (Graham et al., 2018; Saeed et al., 2019). By assisting in the digestion of dietary fibers, hemicellulase can ease the strain on the digestive system and promote gut health.

3.10. Support for Gluten Sensitivity:

Hemicellulase supplementation may benefit individuals with gluten sensitivity or celiac disease (Gallagher, 2009) by assisting in the breakdown of gluten-containing grains. While not a substitute for a gluten-free diet, hemicellulase can help reduce the digestive discomfort associated with accidental gluten exposure

Table 1: *Clinical trials that have used Hemicellulases for either treatment or prevention are detailed here. Source: clinicaltrials.gov*

Clinical trial ID	Health Condition	Status
NCT05520411	• Bloating • Stomach Distended	*Completed*
NCT00881322	• Abdominal Cramps • Abdominal Pain • Flatulence	*Completed*

3.11. May reduce Candida

Several studies indicate that elevating this particular enzyme could potentially aid in the prevention and reduction of yeast infestations, such as Candida. It is possible that the presence of hemicellulose in the cell wall of Candida is a contributing factor. Furthermore, the digestion of hemicellulose by hemicellulase could potentially contribute to the reduction of Candida. (Dutta et al., 2021).

4. Biosafety Profile of Hemicellulases*:*

It is important for individuals to be aware of potential side effects associated with hemicellulase, a dietary supplement commonly used to assist in the digestion of carbohydrates, proteins, and fats. Although it can aid digestion, certain individuals may encounter negative side effects like nausea, vomiting, diarrhea, and abdominal pain*.

Therefore, individuals who have weak immune system or on some medications should exercise caution. In some cases, individuals may experience allergic reactions to hemicellulase*.

However, it is also experimented in **DRUG BANK** to be used for therapeutics purposes under the accession ID of DB15820

It is crucial to seek guidance from a healthcare professional before adding hemicellulase or any dietary supplement to your routine, particularly if you have underlying medical conditions or are taking medications that may interact with the supplement. Implementing proactive measures can effectively reduce potential risks and promote safe practices for supplementation*.

5. Effective Targets of *Hemicellulases*

Species that may be affected by the action of Hemicellulases could include*:

Fungi:

Certain fungi utilize hemicellulose as part of their cell walls. Species like *Aspergillus*, *Trichoderma*, *Penicillium*, *Candida* and others may be susceptible to degradation by Hemicellulases under certain conditions.

Bacteria:

Some bacteria produce extracellular matrices or biofilms containing polysaccharides like hemicellulose. Genera like *Bacillus*, *Clostridium*, and *Xanthomonas* may have components of their structure that could be degraded by Hemicellulases.

6. Significance of *Hemicellulases* in CanXida Restore Formula

When integrated into probiotic supplementation, hemicellulases can create a more favorable environment in the gut by breaking down complex plant fibers, facilitating the colonization and activity of beneficial probiotic bacteria*.

This synergistic effect between hemicellulases and probiotics may further enhance digestive function and contribute to a balanced gut microbiome*.

The inclusion of hemicellulase in the Candida Restore formula holds significant promise in addressing Candida overgrowth and associated complications.

Hemicellulases, possess the enzymatic capability to break down hemicellulose, a component of the cell wall of Candida. By targeting the hemicellulose within the cell wall, hemicellulases could potentially disrupt the structural integrity of Candida, rendering it more susceptible to immune system responses and other antifungal treatments*.

The production of prebiotic oligosaccharides during hemicellulose breakdown could promote the growth of beneficial gut bacteria, which may help restore microbial balance disrupted by Candida overgrowth*

Additionally, the relief of digestive discomfort associated with Candida infections, such as bloating and abdominal pain, could be facilitated by hemicellulase supplementation*.

Furthermore, individuals considering the use of hemicellulase or any dietary supplement for Candida management should consult with their healthcare provider to ensure safety and efficacy, particularly if they have underlying medical conditions or are taking medications that may interact with the supplement.

References

Bajpai, P. (2021). Lignocellulosic Biomass in Biotechnology. In *Lignocellulosic Biomass in Biotechnology*. Elsevier. https://doi.org/10.1016/B978-0-12-821889-1.00031-X

Dekker, R. F. H., & Richards, G. N. (1976). Hemicellulases: Their occurrence, purification, properties, and mode of action. *Advances in Carbohydrate Chemistry and Biochemistry*, *32*(C), 277–352. https://doi.org/10.1016/S0065-2318(08)60339-X

Dutta, P., Lu, Y. J., Hsieh, H. Y., Lee, T. Y., Lee, Y. T., Cheng, C. M., & Fan, Y. J. (2021). Detection of Candida albicans Using a Manufactured Electrochemical Sensor. *Micromachines*, *12*(2). https://doi.org/10.3390/MI12020166

Gallagher, E. (2009). Gluten-Free Food Science and Technology. *Gluten-Free Food Science and Technology*, 1–246. https://doi.org/10.1002/9781444316209

Graham, D. Y., Ketwaroo, G. A., Money, M. E., & Opekun, A. R. (2018). Enzyme therapy for functional bowel disease-like post-prandial distress. *Journal of Digestive Diseases*, *19*(11), 650. https://doi.org/10.1111/1751-2980.12655

Houfani, A. A., Anders, N., Spiess, A. C., Baldrian, P., & Benallaoua, S. (2020). Insights from enzymatic degradation of cellulose and hemicellulose to fermentable sugars– a review. *Biomass and Bioenergy*, *134*, 105481. https://doi.org/10.1016/J.BIOMBIOE.2020.105481

Jana, U. K., Kango, N., & Pletschke, B. (2021). Hemicellulose-Derived Oligosaccharides: Emerging Prebiotics in Disease Alleviation. *Frontiers in Nutrition*, *8*, 670817. https://doi.org/10.3389/FNUT.2021.670817/BIBTEX

Lattimer, J. M., & Haub, M. D. (2010). Effects of Dietary Fiber and Its Components on Metabolic Health. *Nutrients*, *2*(12), 1266. https://doi.org/10.3390/NU2121266

Miranda-Lopez, R. (2022). *Cellulases, Hemicellulases and ligninolytic enzymes: mechanism of action, optimal processing conditions and obtaining value-added compounds in plant matrices;* https://doi.org/10.15406/mojfpt.2022.10.00270

Saeed, M., Ayaşan, T., Alagawany, M., El-Hack, M. E. A., Abdel-Latif, M. A., & Patra, A. K. (2019). The Role of ß-Mannanase (Hemicell) in Improving Poultry Productivity, Health and Environment. *Brazilian Journal of Poultry Science*, *21*(3), eRBCA-2019-1001. https://doi.org/10.1590/1806-9061-2019-1001

Scheller, H. V., & Ulvskov, P. (2010). Hemicelluloses. *Annual Review of Plant Biology*, *61*, 263–289. https://doi.org/10.1146/ANNUREV-ARPLANT-042809-112315

Tharifkhan, S. A., Perumal, A. B., Elumalai, A., Moses, J. A., & Anandharamakrishnan, C. (2021). Improvement of nutrient bioavailability in millets: Emphasis on the application of enzymes. *Journal of the Science of Food and Agriculture*, *101*(12), 4869–4878. https://doi.org/10.1002/JSFA.11228

Tian, B., Zhou, C., Li, D., Pei, J., Guo, A., Liu, S., & Li, H. (2021). Monitoring the effects of hemicellulase on the different proofing stages of wheat aleurone-rich bread dough and bread quality. *Foods*, *10*(10), 2427. https://doi.org/10.3390/FOODS10102427/S1