Welcome



Enzymes and Intestinal Health

Leyla El Moudden



"It's not just what you eat. It's what you digest."

About Enzyme Science UK

ENZYME SCIENCE UK EXCEPTIONAL ENZYME FORMULAS

- Strict quality standard adherence for all ingredients in our finished product
- Ingredients are derived from natural sources produced under strict cGMP-controlled environments
- No artificial fillers and binders
- Enzyme Science continually verifies product quality including purity, efficacy, and safety by evaluating products via our on-site laboratory and through accredited thirdparty facilities



Therapeutic Enzyme Blends



Pure vegan enzymes are blended to address various conditions

Major categories include enzyme blends focused on:

- Overall Digestive Support / Digestive Health
- Multiple Food Intolerances
 - i.e. Gluten, Lactose, Casein, Phenols, etc.
- o Indigestion, Acid Reflux, GERD
- Many non-digestive / Therapeutic uses (away from food)
- o Absorption





Leyla El Moudden BA, Dip Herb, Dip Nat mANP

- Director of Education for Enzyme Science & Enzymedica UK
- Naturopath at Surrey Holistic, Godalming
- Metabolic Balance Coach
- Contributing Editor IHCAN



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Overview

- Food Sensitivity Reactions
- Candida
- SIBO
- LPS
- Leaky Gut
- Microbiome
- Histamine
- Q&A



Rapid impact





TUESDAY



• 10:39 PM

Hi Leyla, truly enjoyed your talk and I have been taking the Enzymes for 2nd day now and have noticed subtle positive changes. I have Fibromyalgia, Crohn's and Chronic Fatigue. I have been managing all 3 with a blend of probiotics, vitamins, Aroma therapy, Bowen Technique and Osteopthy among other holistic modalities

Systemic and Digestive

- Systemic enzymes enter the bloodstream intact, then travel to tissues and then onto available cells – these are often protease enzymes
- Most enzymes can reach the circulation where their benefits continue
- Protease enzymes trim and prune proteins such as those that contribute to and result from inflammation:
 - Fibrinolytic enzymes
 - Serrapeptase
 - Nattokinase

<u>Front Pharmacol.</u> 2021; 12: 603997. Published online 2021 Jun 24. doi: <u>10.3389/fphar.2021.603997</u> PMCID: PMC8265778 PMID: <u>34248612</u>

Go to: 🕨

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EXCEPTIONAL ENZYME FORMULAS

Serratiopeptidase, A Serine Protease Anti-Inflammatory, Fibrinolytic, and Mucolytic Drug, Can Be a Useful Adjuvant for Management in COVID-19

<u>Charu Sharma</u>, ¹ <u>Niraj Kumar Jha</u>, ² <u>M. F. Nagoor Meeran</u>, ³ <u>Chandragouda R. Patil</u>, ⁴ <u>Sameer N. Goyal</u>, ⁵ and <u>Shreesh Ojha</u> ³.*

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The COVID-19 pandemic, which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a public health emergency with high mortality and disability rates. Given its high mortality rate, there is a serious need for possible effective medications to eliminate the virus, limit the severity, and improve the prognosis (Altay et al., 2020). The management of COVID-19 has continued to rely on drugs repurposed based on their pharmacological effects, including antiviral, antibiotic, anti-inflammatory, and or immunomodulatory, along with availability of numerous vaccines against SARS-CoV-2 in past few months (Fan et al., 2020). Repurposing of drugs has gained enormous attention over identifying novel drug candidates, due to known safety, potency, and multitargeted pharmacological action as an immunomodulatory, anti-inflammatory, and antimicrobial agent. Studies report that after fever, cough is one of the major symptoms in about 76% patients and sputum production in 28% patients along with 55 and 44% of patients showing dyspnea and myalgia, respectively (Huang et al., 2020). In a study determined the prevalence of asymptomatic cases of COVID-19 and characterized the symptoms of patients with mild COVID-19 report that of the 213 individuals with COVID-19, 19.2% were asymptomatic until admission (Kim et al., 2020). Among the remaining patients with mild COVID-19, cough (40.1%) was the most common symptom followed by hyposmia (39.5%) and sputum (39.5%). In individuals with hyposmia, 90% had accompanying symptoms such as hypogeusia, nasal congestion or rhinorrhoea (Kim et al., 2020). Sputum or productive cough seem a significant symptom in asymptomatic as well as symptomatic (Kim et al., 2020). Cough was observed most common symptom followed by hyposmia and sputum, while fever (>37.5°C) was only observed in 11.6% (Kim et al., 2020). Another study reported that nasal congestion (62%) was the most common symptom in individuals with mild COVID-19 (Chang et al., 2020).



- The role of digestive enzymes in functional GI disorders, including:
 - GERD, IBS, SIBO, Intestinal Permeability (Leaky Gut), and Malabsorption
- How Digestive Enzymes influence the microbiome
- Understanding Biofilm & how Digestive Enzymes help
- Enzymes as a large part of the solution to multiple health conditions
- Identifying and addressing Enzyme Deficiencies
- The use of Digestive Enzymes for multiple food intolerances
- Practical guidance on selection and dosage of Digestive Enzymes



Foods as structures





Foods as structures

Mackerel

Salmon

- Red meat
- Liver
- Eggs
- Fish
- Dairy
- Fortified plant-based
- Nutritional yeast
- Fortified non-dairy milk and grains









Pathogens as structures





Quick Recap - Protein





intact protein, folded into quaternary structure

denatured protein, unfolded to reveal primary structure



denatured protein, unfolded to reveal primary structure

Enzymatic digestion by pepsin begins to break the protein into shorter polypeptides





Quick Recap-Intact protein effects





Antigen processing cells in the gastrointestinal mucosa and presented on the major histocompatibility complex (MHC), leading to immune reactions, dietary intolerances, or allergy. In the partially hydrolyzed diets (lower panel), the dietary protein has been partially degraded before consumption, with the proteins broken down into small peptides that are not processed and presented as effectively, thus reducing immune response against the diet.

Protein

The effects of protein on the GI tract are subtle and often less clinically obvious than that of fat or CHO, but they are crucially important to disease treatment because the amino acid glutamine is the primary source of respiratory fuel for enterocytes. <u>5</u> The presence of a protein meal in the GI tract increases lower esophageal sphincter pressure, is a potent stimulus for secretion of GI hormones, including gastrin and pancreatic hormones, and increases gastric emptying and intestinal transit. <u>1</u>,

However, intact protein reaching the distal small intestine and colon will increase bacterial ammonia production, alter bacterial numbers and species, and may contribute to colitis or colonic hypersensitivity.





Where is the vulnerability?





Intestinal Growths





- Candida
- Yeast
- Pseudo
- Hyphal
- Sporulation

- Small Intestinal Bacterial Overgrowth
- Hydrogen / Methane
- Hydrogen sulphide





- Biofilms
- Antimicrobial and antifungal resistance

Candida



- 1. Invasion of the intestinal lining by hyphal Candida causes "leaky gut"
- 2. Arabinose interferes with vitamin and amino acid metabolism – may affect behaviour, cause plaque build up and muscle weakness and mental health symptoms
- **3. Tartaric acid** interferes with energy production, leading to fatigue
- **4. Gliotoxin** from candida and other yeasts suppress immunity
- 5. Acetyl aldehyde –interferes with vitamin B6 metabolism, affecting hormones, brain chemistry and detoxification, leading to brain fog, poor skin health, and fatigue
- **6. Biofilms** make it hard to eradicate infections and perpetuate infections
- 7. High Oxalate production causes achy joins and muscle soreness

Urine

| 6 | Tartaric | ≤ | 4.5 | | 0.49 | | |
|---|----------------|---|------|---|------|------|----|
| 7 | Arabinose | ≤ | 29 | н | 108 | | 10 |
| 8 | Carboxycitric | ≤ | 29 | н | 35 | | |
| 9 | Tricarballylic | ≤ | 0.44 | | 0.22 | 0.22 | |

Blood

| CANDIDA ANTIBODIES | | | | | |
|--------------------|-----|-------------------------------|----|-------------|--|
| Candida Antibodies | s | 160 | | (< 160) | |
| Please note that t | the | e Candida albicans test range | is | as follows: | |
| Titre <160 : | : | non significant reaction. | | | |
| Titre =160 : | : | equivocal reaction. | | | |
| Titre >320 : | : | significant reaction. | | | |

Stool

| Fungi & Yeast | Result | Range | Units | | |
|------------------------|---|-------|-------------|---|--|
| Candida species. | 1.3 | < 5.0 | x10^3 org/g | • | |
| Candida albicans. | <i>97.9</i> *H | < 5.0 | x10^2 org/g | | |
| Geotrichum species. | <dl< td=""><td>< 3.0</td><td>x10^2 org/g</td><td>•</td><td></td></dl<> | < 3.0 | x10^2 org/g | • | |
| Microsporidium species | <dl< td=""><td>< 5.0</td><td>x10^3 org/g</td><td>•</td><td></td></dl<> | < 5.0 | x10^3 org/g | • | |
| Rhodotorula species. | <dl< td=""><td>< 1.0</td><td>x10^3 org/g</td><td>•</td><td></td></dl<> | < 1.0 | x10^3 org/g | • | |

Candida – typical intervention



- Low sugar diet
- Medium chain fatty acids like Caprylic acid show an inhibitory effect low concentrations, remain in gut for 3 hours reduces candida populations by up to 80%
- Berberis aquifolium, Berberis vulgaris, Berberis aristata, Hydrastis canadensis, Phellodendron amurense, Coptis chinensis, and Tinospora cordifolia (da Silva et al., 2016)
- Beneficial bacteria such as Saccharomyces boulardii inhibitory effects
- Pau D'Arco, Olive Leaf Extract, Oregano Extract, Grapefruit Seed Extract, coconut-based aplitic acid, Garlic, Uva ursi
- Antifungal resistance = biofilm formation **RELAPSE**



Candida Adhesion





- B-defensins are antimicrobial peptides produced by phagocytic cells, lymphocytes and the epithelial lining.
- SFCA are produced by bacterial metabolism from 'malabsorbed' carbohydrates entering the colon
- Hydrolytic enzymes penetrate the intestinal barrier
- SAPS secreted aspartic proteases

Candida Structures





Cellulase

Hemicellulase, Beta Glucanase, Lysozyme + antifungals

Candida Structure



- The cell wall makes up ~30 % of the dry weight of the cell.
- It is made of
- ~25% helical $\beta(1-3) \beta(1-6)$ -D-glucans (hemicellulose)
- ~ 25% oligo-mannans
- ~20 % protein
- ~10% lipids
- some chitin



Fungal Beta Glucan

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• Fungal β-1,3glucan is one of the key components of the matrix of *C. albicans-S. aureus* biofilms

• Inhibition of β-1,3glucan significantly alters fungal and bacterial resistance to antibiotics



Biofilm structure and matrix









Polymicrobial biofilm = coated S. aureus

C. albicans + S. aureus = increased biomass

β-1,3-glucan

β-1,6-glucan

🗖 a-mannan

Beta-Glucanases



• β-1,3-glucanases produced by plants are natural anti-fungals

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- Aspergillus niger
- β-1,3-Glucan hydrolysing enzymes
- Hydrolysis of polymers like cellulose, laminarin, and β-1,6-glucans produce glucose as the end product
- Cellulase, protease and chitinase also facilitate
 breakdown



 Lysozyme damages the cell walls of bacteria and fungi by hydrolysing the β1–4 glycosidic bonds between the components of fungal chitin

Hemicellulase



Hemicellulases are enzymes that break down material typically associated with or attached to cellulose

This category of enzyme includes xylanase, arabinoxylanase, beta-glucanase, betamannanase, pectinase, arabinase, pectin methylesterase, pectin lyase, and polygalacturonases

Antimicrobial Agents and Chemotherapy

Role of Matrix β -1,3 Glucan in Antifungal Resistance of Non-albicans Candida Biofilms

K. F. Mitchell, H. T. Taff, M. A. Cuevas, E. L. Reinicke, H. Sanchez and D. R. Andes Antimicrob. Agents Chemother. 2013, 57(4):1918. DOI: 10.1128/IAC.02378-12. Published Ahead of Print 14 January 2013. We utilized a 6-well plate format for assessment of antifungal drug biofilm penetration using [H³]fluconazole as described previously (13, 19). Briefly, mature biofilms (24 h of incubation) were washed twice with sterile water followed by exposure to a total of 8.48×10^5 cpm of [H³]fluconazole in RPMI-MOPS medium. Biofilms were incubated for 30 min at 37°C and then chased with 20 μ M unlabeled fluconazole in medium. The fluconazole content was measured in intact biofilms, isolated matrix, cell wall, and cell cytoplasm by scintillation counting. Assays were performed in triplicate for each *Candida* isolate. Consistent with previous findings in *C. albicans* (13, 19), the majority of [H³]fluconazole is present in the extracellular matrix for each of these species, with very little or no drug found intracellularly or in the cell wall (Fig. 1B).

We next determined the effect of matrix β -1,3 glucan hydrolysis on biofilm susceptibility to fluconazole. Using a 96-well plate format, biofilm cell metabolic activity was assayed following exposure to fluconazole and β -1,3 glucanase alone and in combination using a tetrazolium salt XTT reduction assay (20–23). Briefly, after 24 h of biofilm growth, medium was replaced by fresh RPMI-MOPS with dilutions of fluconazole at 1 mg/ml, β -1,3 glucanase (Zymolyase 20T; MP Biomedicals) at 0.7 U/ml, or a combination of the two. The β -1,3 glucanase concentration was chosen based upon our previous studies with *C. albicans* demonstrating synergy with fluconazole and no effect on cell viability for the enzyme alone (12, 19). Experiments were performed in triplicate. Drug effect is expressed at the percent biofilm reduction relative to growth of untreated controls. The statistical significance of differences among therapies was determined using analysis of variance (ANOVA). Similar to previous reports, fluconazole alone exhibited minimal activity against biofilms for each strain and species (12, 19). The low concentration of β -1,3 glucanase also produced little change in cell metabolic activity. However, fluconazole caused marked biofilm reduction in the presence of the β -1,3 glucanhydrolyzing enzyme. This effect was observed for all strains tested (Fig. 1C).

Mannan

Review > Appl Microbiol Biotechnol. 2008 May;79(2):165-78. doi: 10.1007/s00253-008-1423-4.

An overview of mannan structure and mannandegrading enzyme systems

L R S Moreira ¹, E X F Filho

Affiliations + expand PMID: 18385995 DOI: 10.1007/s00253-008-1423-4

Abstract

Hemicellulose is a complex group of heterogeneous polymers and represents one of the major sources of renewable organic matter. Mannan is one of the major constituent groups of hemicellulose in the wall of higher plants. It comprises linear or branched polymers derived from sugars such as Dmannose, D-galactose, and D-glucose. The principal component of softwood hemicellulose is glucomannan. Structural studies revealed that the galactosyl side chain hydrogen interacts to the mannan backbone intramolecularly and provides structural stability. Differences in the distribution of D-galactosyl units along the mannan structure are found in galactomannans from different sources. Acetyl groups were identified and distributed irregularly in glucomannan. Some of the mannosyl units of galactoglucomannan are partially substituted by O-acetyl groups. Some unusual structures are found in the mannan family from seaweed, showing a complex system of sulfated structure. Endohydrolases and exohydrolases are involved in the breakdown of the mannan backbone to oligosaccharides or fermentable sugars. The main-chain mannan-degrading enzymes include betamannanase, beta-glucosidase, and beta-mannosidase. Additional enzymes such as acetyl mannan esterase and alpha-galactosidase are required to remove side-chain substituents that are attached at various points on mannan, creating more sites for subsequent enzymatic hydrolysis. Mannandegrading enzymes have found applications in the pharmaceutical, food, feed, and pulp and paper industries. This review reports the structure of mannans and some biochemical properties and applications of mannan-degrading enzymes.



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Lysozyme

> Int J Biol Macromol. 2018 Mar;108:942-946. doi: 10.1016/j.ijbiomac.2017.11.003. Epub 2017 Nov 4.

β-1,3-glucanase disrupts biofilm formation and increases antifungal susceptibility of Candida albicans DAY185

Yulong Tan ¹, Su Ma ², Matthias Leonhard ³, Doris Moser ⁴, Berit Schneider-Stickler ³ Affiliations + expand PMID: 29104052 DOI: 10.1016/j.ijbiomac.2017.11.003

Abstract

 β -1,3-glucan plays a role in Candida biofilm formation and survival of biofilm-forming Candida to stresses. In this study, we evaluated the antibiofilm activity of β -1,3-glucanase, which can degrade poly- β (1 \rightarrow 3)-glucose of Candida albicans biofilms. Biofilm was dispersed by 55.96%. β -1,3-glucanase had no effect on Candida planktonic growth as well as adhesion. β -1,3-glucanase markedly enhanced the antifungal susceptibility of fluconazole and amphotericin B. The examination using confocal laser scanning microscopy and scanning electron microscope confirmed the antibiofilm activity of β -1,3-glucanase. Our findings demonstrate that β -1,3-glucanase may be useful as an antibiofilm agent.

Keywords: Antibiofilm; Antifungal; Enzyme.

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> Med Mycol J. 2017;58(3):J63-J69. doi: 10.3314/mmj.17-00005.

[Inhibition of Growth of Candida albicans by a Lysozyme-chitosan Conjugate, LYZOX and its Combination with Decanoic Acid]

[Article in Japanese]

Hiroki Kageshima ¹, Kazumi Hayama ², Miki Takahashi ², Miho Abe ², Tsuyoshi Yamada ², Akira Saito ¹, Shoichiro Hirano ¹, Yoichi Murakami ¹, Shigeru Abe ²

Affiliations + expand PMID: 28855481 DOI: 10.3314/mmj.17-00005 Free article

Abstract

A lysozyme-chitosan conjugate preparation (LYZOX), produced from egg white lysozyme and chitosan by Maillard reaction, is a commercial product developed as a cosmetic ingredient or food additive. Effects of LYZOX on in vitro growth of Candida albicans were examined. C. albicans cells were treated with LYZOX for 3 hrs, and then washed and cultured for an additional 16 hrs in modified RPMI1640 medium. Mycelial growth of C. albicans was clearly inhibited by more than 100 µg/ml of LYZOX in a concentration-dependent manner. On the other hand, corresponding concentration of chitosan or lysozyme or their mixture only scarcely showed clear inhibitory effect. Similarly, anti-Candida activity of the combination of LYZOX and decanoic acid, a middle-chain fatty acid, was also examined. Inhibitory activity of this combination against mycelial growth of C. albicans was very potent and appeared synergistic, since fractionated inhibitory concentration (FIC) index for 70% growth inhibition was calculated to be 0.20. Oral application of this combination improved the symptoms of Candidainfected-tongue in an experimental murine candidiasis model. On the basis of these results, the possible application of LYZOX as a new functional product with anti-candida activity was discussed.

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Experimental Dermatology

ADF Perspectives 🛛 🔂 Free Access

Alternative approaches to antifungal therapies

Tarun Mehra, Martin Köberle, Christina Braunsdorf, Daniela Mailänder-Sanchez, Claudia Borelli ... See all authors $\,\, \lor$

First published: 08 August 2012 | https://doi.org/10.1111/exd.12004 | Citations: 38

Lysozyme

Lysozyme is an enzyme classically known for its muramidase activity lysing bacterial peptidoglycan and killing bacteria. However, as early as 1970, it was shown that lysozyme was also active against *C. albicans*, its mechanism of antifungal action staying subject to speculation <u>5</u>. Subsequently, broad antifungal activity was also shown against numerous clinical isolates of all *Candida spp.*, with a significant variation of interstrain and intrastrain sensitivity and against *Aspergillus fumigatus* and *Penicillium spp.* <u>6</u>.

Lysozyme is found in virtually all human body fluids (e.g. saliva, respiratory secretions and liquor). Expression of lysozyme in the skin has been located in the cytoplasm of epidermal cells and throughout the pilosebaceous apparatus 6, in body secretions such as saliva and in neutrophils 7. Wu et al. investigated the effect of lysozyme on the viability and Sap activity of C. albicans. Saps are secreted aspartic proteases, and their main functions are probably to provide nutrition, aid penetration and invasion and evade immune responses 8. An incubation period of 24 h with sublethal concentrations of lysozyme resulted in a dosedependent reduction in Sap activity and secretion, measured by spectrophotometry and ELISA, respectively. This finding was paralleled by decreasing *Candida* viability at higher, lethal concentrations (15 and 20 µg/ml), with significant differences in various strains, quantified by colony-forming units yielded per ml cultivated medium. Electron microscopy showed ballooned cells, some appearing collapsed and deflated, after 24-h exposure to lysozyme at concentrations below 10 µg/ml, which did not affect the viability of *C. albicans*. The fungicidal activity at high concentrations therefore was suggested to result in membrane or cell wall damage leading to osmotic imbalance 9. Also, the negatively charged domain of lysozyme has been assumed to target the Candida surface 9. Very recently, it could be demonstrated that the digestion of human milk lysozyme by pepsin yields five different antimicrobial peptides that are also active against *C. albicans* 10.





Ingredients Serving Size: 1 Targeted Delivery Capsule Servings Per Container: 42

Amount Per Serving

| Botanical, enzyme and bacteria blend | 290 mg |
|--|-------------|
| Garlic Powder (Allium sativum) (Bulb) | |
| Grape seed extract (Vitis vinifera) | |
| Lysozyme (from egg) | |
| Oregano oil (<i>Origanum vulgare</i>) | |
| Thyme oil (<i>Thymus vulgaris</i>) | |
| Clove oil (Syzygium aromaticum) | |
| Peppermint extract (aerial) | |
| Bacillus subtilis | 1 x 109 CFU |
| 100% Vegetarian Capsule (gellan gum, cellulose, wa | ter) |
| Hemicellulase | 20,000 HCU |
| Protease Thera-blend™ | 10,000 HUT |
| Cellulase Thera-blend™ | 500 CU |



> Appl Microbiol Biotechnol. 2019 Jun;103(11):4377-4392. doi: 10.1007/s00253-019-09805-z. Epub 2019 Apr 17.

Capability of iturin from Bacillus subtilis to inhibit Candida albicans in vitro and in vivo

Shuzhen Lei¹, Haobin Zhao¹, Bing Pang¹, Rui Qu¹, Ziyang Lian¹, Chunmei Jiang¹, Dongyan Shao ¹, Qingsheng Huang ¹, Mingliang Jin ¹, Junling Shi ²

Affiliations + expand PMID: 30997554 DOI: 10.1007/s00253-019-09805-z





Microb Cell. 2020 May 4; 7(5): 129-138. Published online 2020 Mar 20. doi: 10.15698/mic2020.05.716 PMCID: PMC7199281 PMID: 32391394

Sulforaphane alters the acidification of the yeast vacuole

Alexander Wilcox, ^{1,#} Michael Murphy, ^{1,#} Douglass Tucker, ^{1,#} David Laprade, ¹ Breton Roussel, ¹ Christopher Chin,² Victoria Hallisey,¹ Noah Kozub,¹ Abraham Brass,² and Nicanor Austriaco^{1,*}

Author information Article notes Copyright and License information Disclaimer

This article has been cited by other articles in PMC.

Pharmacology

Original Paper

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Growth Inhibition of a Spectrum of Bacterial and Fungal Pathogens by Sulforaphane, an Isothiocyanate Product Found in **Broccoli and Other Cruciferous Vegetables**

Noelle L. Johansson¹ , Charles S. Pavia¹ , ² , Jen Wei Chiao²

¹Department of Biomedical Sciences, New York College of Osteopathic Medicine of New York Institute of Technology, Old Westbury, NY, USA ²Department of Medicine, New York Medical College, Valhalla, NY, USA

Further Information



Supplement Facts

Serving Size: 2 Capsules Servings Per Container: 42

| Amount Per Serving | | %DV |
|-------------------------------|--------------------|-------|
| Cellulase Thera-blend™ | 70,000 CU | ** |
| Protease <i>Thera-blend</i> ™ | 230,000 HUT | ** |
| Broccoli Seed Extract | 40 mg | ** |
| Probiotic Blend: | 1 Billion CFU | ** |
| L.acidophilus | DDS-1, L. rhamn | OSUS, |
| L.casei, L. gas | seri, L. plantarun | 7, |
| L. bulgaricus, | L. salivarius, | |
| L. paracasei | | |
| ** Daily Value not establis | shed | |



SIBO – Small Intestinal Bacterial Overgrowth



The relative sterility of the small intestine relies on:

- Gastric acid
- Pancreatic enzyme production
- Gut motility
- Systemic and local immunity
- An intact ileal valve

Clinical Manifestations of SIBO



| Weight loss Steatorrhea Vitamin/mineral deficiency – Fat-soluble vitamins (A, D, E, K) – Vitamin B12 | |
|--|--|
| - Iron Vitamin excess | Normal results: Adults - 2-20 ng/mL, 2-20 μg/L, or 4.5-45.3 nmol/L Children - 5-21 ng/mL, 5-21 μg/L, or 11.3-47.6 nmol/L |
| - Folate | Infants - 14-51 ng/mL, 14-51 μg/L, or 31.7-115.5 nmol/L |
| Hypoproteinaemia/hypoalbuminemia | |
| Decreased xylose absorption (test) | Normal results: |
| Diarrhoea | Serum xylose concentration at 1 hr in excess of 1.3 mM Urinary xylose excretion in excess of 7.0 mmol/5 hr |
| Constipation | |
| Abdominal pain or tenderness | |
| Flatulence | |
| Hydrogen / Methane Breath Test >20 | |

Gastric acid, pyloric valve





- Reduces bacterial content from millions to thousands
- Triggers release of digestive enzymes
- Protects the small intestine from overload



Moxon TE, Nimmegeers P, Telen D, Fryer PJ, Van Impe J, Bakalis S. Effect of chyme viscosity and nutrient feedback mechanism on gastric emptying. Chem Eng Sci. 2017 Nov 2;171:318–330. doi: 10.1016/j.ces.2017.05.048. PMID: 29104301; PMCID: PMC5569601.



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Sites of absorption of nutrients within the gastrointestinal tract. Adapted from: Mahan and Escott-Stump: Krause's Food, Nutrition and Diet Therapy, 9/e, p 13, ©1996, with permission from Elsevier

SIBO Method

- 1. Hydrochloric acid retore bacteriostatic effect of stomach
- 2. Digestive enzymes ensure uptake of nutrient, protection from food intolerance
- 3. Antimicrobials in rotation
- Bile diet, bile salts, lipase, pancreatic enzymes – remove additional burden of LPS
- 5. Motility & Migrating Motor Complex supplementation, stress relief, fasted states
- 6. The ileocecal valve chiropractic, 5HTP, enhance digestion (enzymes and HCL)
- 7. Immune system **restoration**



SIBO Structure



a Gram-negative bacteria



- SIBO bacteria are primarily gramnegative.
- LPS initiates reprogramming in both monocyte macrophages and neutrophils
- Suppresses host lipase in a variety of environments

Image credit: Detailed structure of gram positive bacterial, gram negative bacterial, mycobacterial, and fungal cell walls, Nature Reviews, Microbiology.

Ishaq, S. L. , Moses, P. L. , Wright, A. G. , 2016, 'The Pathology of Methanogenic Archaea in Human Gastrointestinal Tract Disease', in G. Mozsik (ed.), The Gut Microbiome - Implications for Human Disease, IntechOpen, London. 10.5772/64637.

Medvedev et al., 2006, Wysocka et al., 2001, Cross, 2002, Cavaillon et al., 2003, McCall and Yoza, 2007, Foster et al., 2007



Reference Module in Life Sciences Brenner's Encyclopedia of Genetics (Second Edition) 2013, Pages 292-293

Lysozyme

E.M. Kutter

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https://doi.org/10.1016/B978-0-12-374984-0.00893-7

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Life Sciences

Abstract

Bacterial cells are generally protected from lysis induced by factors such as osmotic shock by having a cell wall made of peptidoglycan, also called murein. The entire peptidoglycan sack around each bacterial cell is in fact one giant, covalently bonded bag-shaped molecule. Growth of the cell requires that links of this sack be opened up long enough to insert new links in between them; penicillin leads to the death of growing bacterial cells by interfering with the filling and resealing of these small gaps in the cell's armor. Lysozymes are a particular class of enzymes that are able to attack this murein structure and thus generally effect the destruction of the cell. In 1922, the Scottish physician Alexander Fleming showed that saliva, tears, and sweat all contained a substance that could destroy bacteria. What he was observing was in fact lysozyme - the first human secretion shown to have chemotherapeutic properties. From a genetic/molecular biology perspective, one of the most important lysozymes is that produced by <u>bacteriophage T4</u> to rupture the cell and release the phage. The early work of George Streisinger with mutants of this enzyme played a key role in exploring the nature of the genetic code, the generation, and study of a set of mutants with each of crystal structures.





Ingredients Serving Size: 1 Targeted Delivery Capsule Servings Per Container: 42

| Amount Per Serving | |
|---|-------------------------|
| Botanical, enzyme and bacteria blend | 290 mg |
| Garlic Powder (Allium sativum) (Bulb) | |
| Grape seed extract (Vitis vinifera) | |
| Lysozyme (from egg) | |
| Oregano oil (<i>Origanum vulgare</i>) | |
| Thyme oil (<i>Thymus vulgaris</i>) | |
| Clove oil (Syzygium aromaticum) | |
| Peppermint extract (aerial) | |
| Bacillus subtilis | 1 x 10 ⁹ CFU |
| 100% Vegetarian Capsule (gellan gum, cellulose, | , water) |
| Hemicellulase | 20,000 HCU |
| Protease Thera-blend™ | 10,000 HUT |
| Cellulase Thera-blend™ | 500 CU |



> Cardiovasc Toxicol. 2021 Jul;21(7):582-591. doi: 10.1007/s12012-021-09651-4. Epub 2021 Apr 15.

Bacterial Lipase Neutralized Toxicity of Lipopolysaccharide on Chicken Embryo Cardiac Tissue

Afsaneh Bagherzadeh ¹, Hamidreza Vaziri ¹, Fatemeh Sokouti Nasimi ², Shahin Ahmadian ², Adel Feyzi ³, Mehrdad Farhadi ⁴, Fariba Yahyavi ², Behnam Hashemi ², Reza Rahbarghazi ⁵, ⁶, Mahdi Mahdipour ^{7, 8}

Affiliations + expand PMID: 33856644 DOI: 10.1007/s12012-021-09651-4

> iScience. 2021 Aug 19;24(9):103004. doi: 10.1016/j.isci.2021.103004. eCollection 2021 Sep 24.

A host lipase prevents lipopolysaccharide-induced foam cell formation

Jintao Feng ¹, Wei Jiang ¹ ², Xiaofang Cheng ¹, Benkun Zou ¹, Alan W Varley ³, Ting Liu ¹, Guojun Qian ¹, Wenjiao Zeng ⁴, Jianguo Tang ², Qiang Zhao ⁵, Yiwei Chu ¹, Yuanyuan Wei ¹, Xiaobo Li ⁶, Robert S Munford ⁷, Mingfang Lu ¹ ²

Affiliations + expand PMID: 34522852 PMCID: PMC8426562 DOI: 10.1016/j.isci.2021.103004 Free PMC article

Published: 11 September 2005

Lipopolysaccharide deacylation by an endogenous lipase controls innate antibody responses to Gramnegative bacteria

Mingfang Lu, Mei Zhang, Akira Takashima, Jerrold Weiss, Michael A Apicella, Xiang-Hong Li, Dorothy Yuan & Robert S Munford 🖂

Nature Immunology 6, 989–994 (2005) Cite this article 787 Accesses 55 Citations 3 Altmetric Metrics





Antimicrobials

- 1. Berberine (extract of berberis vulgaris and other berberine containing herbs)
- 2. Wormwood (Artemisia absinthium)
- 3. Goldenseal (high berberine content)
- 4. Oregano (dried or tincture)
- 5. Allicin (extract of garlic)
- 6. Neem
- 7. Oregon grape root dried, tablet, tincture 6x per day
- 8. Neem leaf

Method

Choose 2 antimicrobials at a time. Dose as high as tolerable - 3-5g / 3000- 5000mg berberine 4- 6 weeks 2700 mg Allicin 4- 6x per day If SIBO still present – repeat with two different antimicrobials **Consider an elemental diet if SIBO is unresponsive** > Glob Adv Health Med. 2014 May;3(3):16-24. doi: 10.7453/gahmj.2014.019.

Herbal therapy is equivalent to rifaximin for the treatment of small intestinal bacterial overgrowth

Victor Chedid ¹, Sameer Dhalla ², John O Clarke ³, Bani Chander Roland ⁴, Kerry B Dunbar ⁵, Joyce Koh ⁶, Edmundo Justino ⁷, Eric Tomakin ⁸, Gerard E Mullin ⁹

Affiliations + expand PMID: 24891990 PMCID: PMC4030608 DOI: 10.7453/gahmj.2014.019 Free PMC article

ENZYME SCIENCE UK EXCEPTIONAL ENZYME FORMULAS

Biofilms





Biofilm formation can protect pathogens from many aspects of the innate immune system, including by inactivating neutrophils and monocytes. Altered immune recognition during this phase of growth is also evident by changes in the cytokine profiles of monocytes exposed to biofilm.

Serrapeptase

Biotechnol Rep (Amst). 2020 Dec; 28: e00544.

Published online 2020 Oct 17. doi: <u>10.1016/j.btre.2020.e00544</u>

Serratiopeptidase: Insights into the therapeutic applications

- Swati B. Jadhav, a,* Neha Shah,^b Ankit Rathi,^{a,c} Vic Rathi,^{a,c} and Abhijit Rathi^a
- ► Author information ► Article notes ► Copyright and License information <u>Disclaimer</u>

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Abstract

Therapeutic applications of enzymes have been widely accepted in clinical practices for decades. Proteolytic enzymes in particular, have been used for the treatment of diseases and disorders. Serratiopeptidase is a proteolytic enzyme having immense applications in therapeutic areas which have been validated by several *in vitro*, *in vivo*, and clinical studies as well as through anecdotal evidences. These applications are attributable to its versatile properties including antiinflammatory, anti-biofilm, analgesic, anti-edemic, and fibrinolytic effects. The significant impact of serratiopeptidase reported needs to be backed by more scientific data. This review encompasses the details of therapeutic applications of serratiopeptidase based on available *in vitro*, *in vivo*, and clinical studies. We found some strong evidences regarding the efficacy of serratiopeptidase. However data on safety, tolerability, and its mechanism of action need detailing. This review aims to further explore the available literature on serratiopeptidase as well as provide scientific details for existing applications.

- It can modify the virulent phenotype of bacteria in biofilms
 - It is effective against mature biofilms
 - It enhances the bactericidal effect of antibiotics against bacterial biofilms
- Anti-inflammatory, anti-biofilm, analgesic, anti-edemic, and fibrinolytic effects
- Serratiopeptidase is widely used in Japan and Europe as the anti-inflammatory and pain treatment of choice



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PMCID: PMC7585045

PMID: 33134103

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Serrapeptase

The role of serratiopeptidase in the resolution of inflammation

| Manju Tiwari 🖰 🖾 | |
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Abstract

Review

Inflammation remains a key event during most of the diseases and physiological imbalance. Acute inflammation is an essential physiological event by immune system for a protective measure to remove cause of inflammation and failure of resolution lead to <u>chronic inflammation</u>. Over a period of time, a number of drugs mostly chemical have been deployed to combat acute and chronic inflammation. Recently, enzyme based anti-inflammatory drugs became popular over conventional chemical <u>based drugs</u>. <u>Serratiopeptidase</u>, a <u>proteolytic enzyme</u> from <u>trypsin</u> family, possesses tremendous scope in combating inflammation. <u>Serine protease</u> possesses a higher affinity for <u>cyclooxygenase</u> (COX-I and COX-II), a key enzyme associated with production of different inflammatory mediators including <u>interleukins</u> (IL), <u>prostaglandins</u> (PGs) and <u>thromboxane</u> (TXs) etc. Currently, arthritis, <u>sinusitis</u>, <u>bronchitis</u>, <u>fibrocystic breast disease</u>, and <u>carpal tunnel syndrome</u>, etc. are the leading inflammatory disorders that affected the entire the globe. In order to conquer inflammation, both acute and chronic world, physician mostly relies on conventional drugs. The most common drugs to combat acute inflammation are A 2017 review established that serrapeptase was able to block the enzymes responsible for triggering painful inflammatory responses. It was observed that serrapeptase did this just as effectively as other commonly used COX-I inhibitor drugs, including naproxen



Low Grade Inflammation

<u>World J Gastroenterol.</u> 2010 Mar 7; 16(9): 1057–1062. Published online 2010 Mar 7. doi: <u>10.3748/wjg.v16.i9.1057</u> PMCID: PMC2835780 PMID: <u>20205274</u>

Even low-grade inflammation impacts on small intestinal function

Katri Peuhkuri, Heikki Vapaatalo, and Riitta Korpela

► Author information ► Article notes ► Copyright and License information Disclaimer

This article has been cited by other articles in PMC.

Abstract

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Independent of the cause and location, inflammation - even when minimal - has clear effects on gastrointestinal morphology and function. These result in altered digestion, absorption and barrier function. There is evidence of reduced villus height and crypt depth, increased permeability, as well as altered sugar and peptide absorption in the small intestine after induction of inflammation in experimental models, which is supported by some clinical data. Identification of inflammatory factors which may promote the process of gastrointestinal dysfunction as well as clinical research to verify experimental observations of inflammatory modulation of gastrointestinal function are required. Moreover, nutritional strategies to support functional restitution are needed.



Leaky Gut





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Relationship with enzymatic function

ENZYME SCIENCE^{UK} EXCEPTIONAL ENZYME FORMULAS



Popular digestive support



SUPPLEMENT FACTS

Amylase Thera-blend[™] Protease Thera-blend[™] ATPro[™] Blend

Glucoamylase DPP-IV

| nela-Dienu | 23,300 00 | |
|--------------------------|----------------------|---|
| hera-blend™ | 75,000 HUT | |
| end | 78 mg | |
| Magnesium Citrate, Col | Q10, Phytase, ATP | |
| lase | 50 AGU | |
| | 250 DPPU | |
| ra-blend™ | 4,000 FIP | |
| actosidase | 500 GalU | |
| | 150 Endo-PGU | |
| hera-blend™ | 1,500 CU | |
| | 900 ALU | |
| inase | 25 BGU | |
| | 1,000 XU | |
| | 200 DP° | |
| Blend | 1 Billion CFU | |
| L. acidophilus DDS-1, L. | bulgaricus 535 SU | |
| laca | 555 50 | NON-GMO ¹ |
| | | INTOLEI COMI © GLUTEN, DAIRY & PI |
| | | Targeted enzymes for ser |
| D9 | | |
| | | |

SUPPLEMENT FACTS

| DPP-IV | 2,000 DPPU | | |
|-------------------------------|-------------|--|--|
| Xylanase | 30,000 XU | | |
| Protease Thera-blend™ | 140,000 HUT | | |
| ATPro™ Blend | 156 mg | | |
| Magnesium Citrate, CoQ10, Phy | rtase, ATP | | |
| Amylase Thera-blend™ | 14,000 DU | | |
| Alpha Galactosidase | 1,200 GalU | | |
| Glucoamylase | 40 AGU | | |
| Lactase | 3,000 ALU | | |
| Pectinase | 50 Endo-PGU | | |
| Maltase | 200 DP° | | |
| Lipase Thera-blend™ | 800 FIP | | |
| Cellulase Thera-blend™ | 400 CU | | |
| Invertase | 150 SU | | |
| Hemicellulase | 50 HCU | | |



Any questions?



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Register for a practitioner account for our practitioner resource pack, training, information and discounts on products and to access recordings and clinical support

ENZYME DEFICIENCY TEST GUIDE

WHAT YOU DO: **RESULTS:**

1. Integrate this test

into your practice

Distribute the Enzyme Deficiency test during the check-up process in the waiting room. Then, consult with your client on the results.

2. Dispense products

when necessary

patient's enzyme deficiencies,

you can offer them a solution

by suggesting a corresponding

Enzyme Science product. Read

about which product is perfect for each enzyme deciency in the

Now that you know your

training guide.

Amylase

Breads, pastas or desserts are most likely one's favourite foods, although they may be taxing for the body to digest. Amylase is a family of enzymes that is responsible for breaking down sugars, carbohydrates and fibre.

Optimal Diet: Include protein in the first meal of the day. Focus on whole grains, vegetables and protein-based snacks. If your patient is a vegetarian, emphasise nuts, seeds, soy and beans to get the protein you need. Reduce white flour, white rice and white sugar and include whole, unrefined grains along with fruit and natural sweeteners like agave and stevia to help satisfy your sweet tooth. As they move toward a less refined, more whole foods diet they may crave sweets less and less.

High Amylase formulas include:

- ES Digest Gold: For Optimal Digestive Support 23,000 DU of Amylase Thera-blend Comprehensive digestive formula Ideal for those requiring a vegan and kosher product without probiotics Provides nutrient absorption and energy promotion
- Critical Digestion: Supports Maximum Nutrient Absorption 23,000 DU of Amylase Thera-blend Powerful support for moderate to intense digestive distress · Breaks down carbohydrates, dairy, fats and fibre Hardy probiotic blend at 1 billion CFU per dose Includes ATPro[™] for energy promotion
- Intolerance Complex: For Gluten, Dairy & Phenol Digestion 14,000 DU of Amylase Thera-blend Provides targeted enzymes for the most common food intolerance · High-potency digestive enzymes for entire meal digestion Includes ATPro[™] for energy promotion
- Complete Digestion: Comprehensive, Full-spectrum Enzyme Blend 11,500 DU of Amylase Thera-blend
 - Introductory enzyme formula for mild to moderate digestive discomforts Breaks down every category of food Hardy probiotic blend at 125 million CFU per dose
- 3. Track progress and Includes ATPro[™] for energy promotion