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New Perspectives

Enzymes and Microbiome Health

Julia Craven

VP of Education and Innovation

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Julia Craven

VP of Education and Innovation for Enzymedica

- **2007**: Joined the Enzymedica team
- **1989:** Began working in independent health food stores
- **Areas of Specialty:** Digestive health, enzymes, gut/brain connection, traditional herbalism, dietary interventions, medical aromatherapy, flower essences, yoga, breathwork

New Perspective: Biofilms, Enzymes, and the Microbiome

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What's a Biofilm?

Biofilms are structured microbial communities that attach to surfaces in the body, such as: gut, respiratory tract, vaginal tract, and teeth.

They consists of microbial cells (bacteria, fungi, viruses, parasites) embedded in a sticky self-produced matrix of polysaccharides.

- **The Good:** They are the body's initial adaptation to capturing pathogens and parasites.
- **The Bad:** When biofilms are not kept in check, they can become self perpetuating and lead to dysbiosis and damage of the gut tissue. They become resilient to treatment due to the nature of the matrix.
- **The Ugly:** Certain amyloids that are created in biofilm communities are very similar to other amyloid plaques that contribute to Alzheimer's and Parkinson's.

Donlan RM. Biofilms: microbial life on surfaces. Emerging Infect Dis. 2002 Sep;8(9):881-90. doi: 10.3201/eid0809.020063.
PMID: 12194761; PMCID: PMC2732559.
Miller AL, Bessho S, Grando K, Tükel . Microbiome or Infections: Amyloid-Containing Biofilms as a Trigger for Complex Human Diseases. Front Immunol. 2021 Feb 26;12:638867. doi: 10.3389/fimmu.2021.638867. PMID: 33717189; PMCID: PMC7952436.

Dysbiosis

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Definition of Dysbiosis:

Dysbiosis is defined by an imbalance in bacterial composition, changes in bacterial metabolic activities, or changes in bacterial distribution within the gut. The three types of dysbiosis are:

1. Loss of beneficial bacteria
2. Overgrowth of potentially pathogenic bacteria
3. Loss of overall bacterial diversity

Biofilm Lifecycle:

DeGruttola AK, Low D, Mizoguchi A, Mizoguchi E. Current Understanding of Dysbiosis in Disease in Human and Animal Models. Inflammatory Bowel Dis. 2016 May;22(5):1137-50. doi: 10.1097/MIB.0000000000000750. PMID: 27070911; PMCID: PMC4838534.

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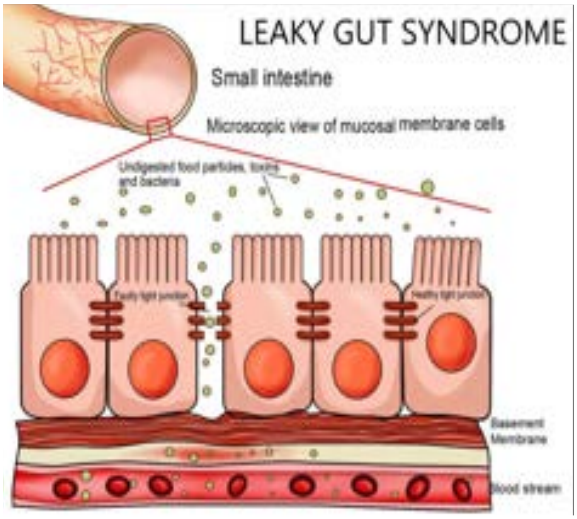

When out of balance, biofilms excrete cytokines.

- TNF-a,IL-2, INF-y

These cytokines can exacerbate growth of harmful bacteria and trigger chronic sub-clinical inflammation.

This can contribute to dysbiosis and gut cell permeability; eventually leading to leaky gut.

Leaky Gut can lead to inflammatory bowel disease, celiac disease, autoimmune hepatitis, type 1 diabetes (T1D), multiple sclerosis, autism spectrum disorder, subclinical hypo-thyroid, mental health issues, and learning disabilities- to name a few!

Miller AL, Bessho S, Grando K, Tükel Ç. Microbiome or Infections: Amyloid-Containing Biofilms as a Trigger for Complex Human Diseases. Front Immunol. 2021 Feb 26;12:638867. doi: 10.3389/fimmu.2021.638867. PMID: 33717189; PMCID: PMC7952436.

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Conventional Biofilm Disruptors

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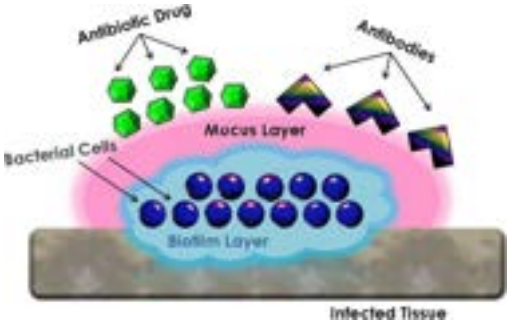
- Current conventional therapies, such as antibiotics, bacteriophages and quorum sensing inhibitors, are used to combat biofilms.
- Due to the sticky matrix that biofilms create, antibiotics and other chemical agents can't cleave the matrix effectively enough for eradication.
- By their self-perpetuating and self-protective nature, biofilms are apt to cause persistent infection and aggravate the occurrence of antibiotic resistance.
- For the same reason, our own antibodies and subsequent macrophages are unable to carry out phagocytosis on the biofilms.
- Some believe that biofilms START with antibiotic overuse.



Akkermansia muciniphila strains on chronic colitis in mice. Front Cell Infect Microbiol. 2019 July 5
Høiby N, Bjarnsholt T, Givskov M, Molin S, Ciofu O. Antibiotic resistance of bacterial biofilms. Int J Antimicrob Agents. 2010 Apr;35(4):322-32. doi: 10.1016/j.ijantimicag.2009.12.011. Epub 2010 Feb 10. PMID: 20149602.
Joural of Nanobiotechnology 2023/05/21
Role of bioactive magnetic nanoparticles in the prevention of wound pathogenic biofilm formation using smart nanocomposites
DO - 10.1186/s12951-023-01905-3

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Natural Biofilm Disrupters

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- Oregano, clove, cinnamon, garlic, rosemary, ginger
  - Plant derived aromatic compounds have been shown to have the capacity to degrade biofilms.
- Berberine
  - Berberine can disrupt the cycle of reproduction of biofilms.
- NAC
  - Helps to inhibit the formation of biofilms and reduces bacterial viability.
- Serrapeptidase
  - Enzymes, especially proteases can degrade the protective coating enhancing efficacy for other agents.

Blasi F, Page C, Rossolini GM, Pallecchi L, Matera MG, Rogliani P, Cazzola M. The effect of N-acetylcysteine on biofilms: Implications for the treatment of respiratory tract infections. Respir Med. 2016 Aug;117:190-7. doi: 10.1016/j.rmed.2016.06.015. Epub 2016 Jun 16. PMID: 27492531
Swati B. Jadhav, Neha Shah, Ankit Rathi, Vic Rathi, Abhijit Rathi,Serratiopeptidase: Insights into the therapeutic applications,Biotechnology Reports,Volume 28

Serrapeptidase

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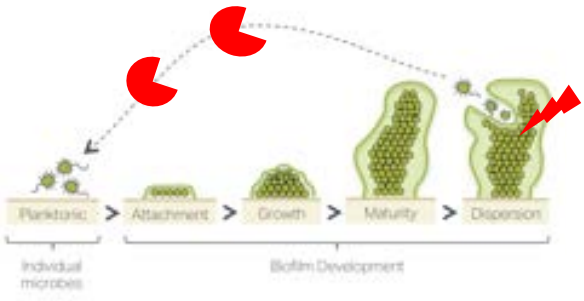
- Serrapeptidase is a bacterial derived protease with special analgesic, anti-edema, fibrinolytic and biofilm busting qualities.
- Myths:
  - Modern production does not use silkworm derived SPT.
  - It does not have to be enteric coated if it is the high quality Serratia E-15.
- SPT is thought to work like a biological "nanodrill" and disrupt the bacterial biofilm membrane, thus paving the way for antibiotics or other natural agents to act.
- SPT does double duty by supporting the macrophages to be able to better carry out phagocytosis.
- SPT has been shown to be more effective than other proteases regarding biofilms.

Biofilm Lifecycle Interruption:



Swati B. Jadhav, Neha Shah, Ankit Rathi, Vic Rathi, Abhijit Rathi,
Serratiopeptidase: Insights into the therapeutic applications,
Biotechnology Reports,
Volume 28,2020,

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Mastering the Market

How is understanding biofilms relevant to Mastering the Market?

- 40% of Americans suffer from digestive disorders.
- We meet consumers every day that are doing all the right things, but still not getting the right results.
- Could it be that their inner terrain isn't able to accept the beneficial bacteria, nutrients, and plant compounds that could cause a positive shift?
- Could biofilms and gut permeability be blocking their progress?

American Gastroenterological Association

Paths to Recovery

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Biofilms

- Diet
  - Low sugar and refined carbohydrates
  - Are food intolerances an issue?
  - Whole foods
- Digestive Enzyme
- Biofilm busters
  - Serrapeptidase + any of the 'killer herbs' + NAC

Leaky Gut

- Diet
  - Low sugar and refined carbohydrates
  - Are food intolerances an issue?
  - Whole foods
- Digestive Enzyme
- Gut healers:
  - L-Glutamine, slippery elm, zinc carnosine, aloe, whole oats

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Why Digestive Enzymes?

- **Prevention of 'sludge'** due to slow digestion of food and subsequent slow motility.
  - A 'cleaner' microbiome means better chances for positive bacteria to proliferate.
- **Enhancement of nutrient absorption.**
  - Many individuals with ongoing issues end up nutrient deficient.
  - Enzymes make more nutrients available.
- **Beneficial byproducts of enzyme activity.**
  - Short chain fatty acids are produced due to the activity of certain digestive enzymes.
- **Support hydrolyzation of pathogenic invaders.**

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Enzyme Superstar: Lipase

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Think about all the people taking Omega-3 that don't have enough endogenous lipase!

- Lipases are the family of enzymes that break down fats into fatty acids and glycerol so they may be utilized.
- Lipases are produced in the mouth, stomach and pancreas.
  - As we age, our pancreas naturally declines in enzyme production.
  - Think about all those people taking PPIs and what that does to gastric secretions.
- Supplemental lipases are available through pancreatic enzymes and fermented fungal enzymes.
  - Animal based enzymes degrade in stomach acid.
  - Fermented enzymes can be produced to be stable and have activity in various pH ranges. Acid stable lipases are very important!
- Gallbladder removal is consistently in the top 10 procedures in the US.
  - Without a gallbladder pancreatic lipases are not secreted at the proper time.

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www.healthgrades.com/right-care/tests-and-procedures/the-10-most-common-surgeries-in-the-u-s

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Darling of Microbiome Research

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- Akkermansia muciniphila is a native gut bacteria that should make up 3-5% of the human microflora.
  - Numerous studies have shown a positive correlation between robust Akkermansia populations and decreases in metabolic syndrome, obesity, and age associated mental decline.
- Akkermansia feeds on our gut's intestinal mucosal layer. As a byproduct of munching on mucin, short-chain fatty acids (SCFAs) including butyrate are created.
  - Butyrate is vital energy source for mucus-secreting cells and intestinal epithelial cells.
- SCFAs also strengthen tight junctions in the intestines.
  - This is why Akkermansia is effective as a preventative for many conditions. As a result of strengthened junctions, unwanted materials are not passing trough the intestines and the normal inflammation responses which can eventually run amok are curtailed.
  - Downregulates pro-inflammatory cytokines TNF-α, IFN-γ
- Omega-3 fatty acids can also enhance Akkermansia production.

N. Floch,Chapter 31 - The Influence of Microbiota on Mechanisms of Bariatric Surgery,Editor(s): Martin H. Floch, Yehuda Ringel, W. Allan Walker, The Microbiota in Gastrointestinal Pathophysiology,Academic Press,2017,Pages 267-281,

New Lipase Research

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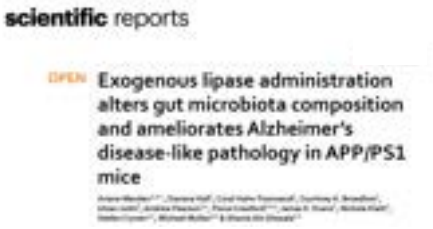
Enzymedica's team of PhD Enzymologists have executed studies proving the correlation of Lipase (Candida rugosa lipase) administration and positive outcomes on microbiome health.

"In a recent study we demonstrated that orally delivered CRL altered gut microbial β-diversity and promoted growth of bacterial species in Wt mice such as A. muciniphila and Anaerostipes, which have been associated with anti-inflammatory and anti-diabetic properties. CRL has a broad specificity range for triglyceride and cholesterol ester hydrolysis, which result in the release of fatty acids, cholesterol, and glycerol into the gut lumen. The lipase hydrolysis products can be absorbed by the host or gut microbiota to enhance their growth and metabolite production. The microbial associated metabolites can exert anti-inflammatory and anti-bacterial properties potentially ameliorating Alzheimer's Disease like pathology."



Process Overview

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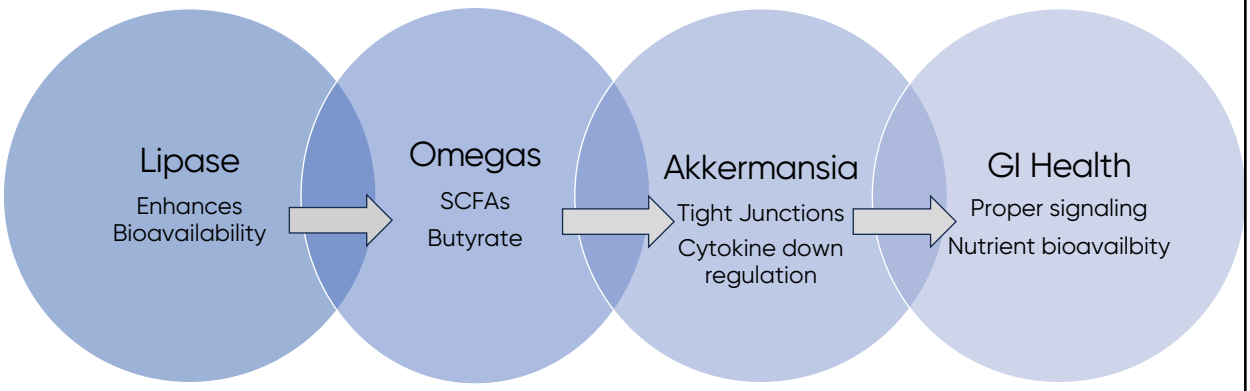

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Review + Q&A:

- What are biofilms and why they're a threat
- What is dysbiosis
- The prevalence and outcomes of leaky Gut
- Biofilm disrupters
- Enzymes-digestive and systemic
- Akkermansia muciniphila
- New lipase research

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