

BiofilmX



Biofilm Disrupting Formula | VA-139

Key Features:

BiofilmX combines multiple fibrinolytic & mucolytic enzymes to help breakdown biofilms and augment the efficacy of anti-microbial agents when taken together.

- **Serrapeptase** - a potent mucolytic enzyme that help reduce the inhibitory effects of bacterial biofilms, enhance anti-microbial effect, and decrease chronic inflammation.
- **Systemic fibrinolytic proteases** and **polysaccharide-digesting enzymes** to help breakdown the integrity of biofilms and their adhesion to target tissues.
- **Alpha lipoic acid** - a sulfurhydryl-containing compound known to disrupt biofilm formation and provide antioxidant protection to the host.
- **Enteric-release encapsulation (FREE of phthalates)** that are commonly found in enteric coating) to bypass stomach acid.

Clinical Applications:

- Decrease inflammatory edema.
- Accelerates the elimination of sputum, pus and hematoma.
- Enhance pathogen eradication of antibiotics/ antimicrobials.

Description:

Antibiotic resistance has become increasingly prevalent in the past decade, and is now a global pandemic. Each year in the United States, more than 2,000,000 people acquire serious infections with bacteria that are resistant to one or more of the antibiotics designed to treat those infections. At least 23,000 people die each year as a direct result of these antibiotic-resistant infections, and many more die from other conditions that were complicated by an antibiotic-resistant infection.^[1]

The mechanisms of antibiotic-resistance include gene mutation, plasmid transfer, depletion of beneficial bacteria by antibiotics, allowing drug-resistant bacteria to take over, and **BIOFILM formation**, which is one of the most important mechanisms for chronic infectious diseases.

What are Biofilms?

Biofilms are a biopolymer matrix produced by microbes. The

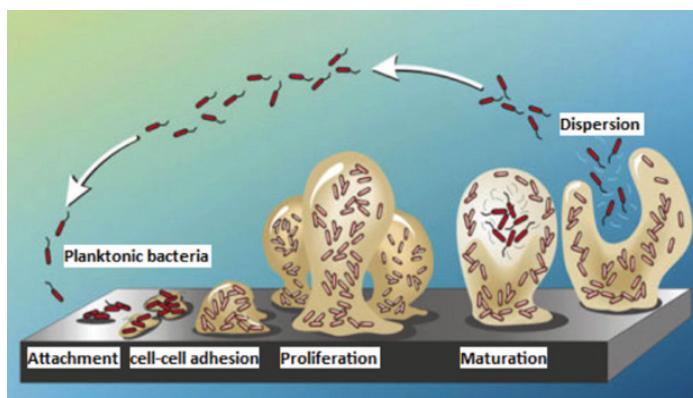


Figure 1. Development of Biofilms
[Source: https://microbewiki.kenyon.edu/index.php/Biofilms_and_Human_Implants]

Quantity: 84 Vegetarian Capsules

Ingredients (per capsule):

Serrapeptase (from <i>Serratia marcescens</i> E-15).....	30,000 SU
Protease (from <i>Aspergillus oryzae</i>).....	15,000 HUT
Alkaline Protease (*Nattozimes®).....	4,225 HUT (1,500 FU) (from <i>Aspergillus oryzae</i> & <i>Aspergillus melleus</i>)
Xylanase (from <i>Trichoderma longibrachiatum</i>).....	1,100 XU
Pectinase (from <i>Aspergillus niger</i>).....	50 endo-P
Beta-Glucanase (from <i>Trichoderma longibrachiatum</i>).....	30 BGU
Glucoamylase (from <i>Aspergillus niger</i>).....	25 AGU
Hemicellulase (from <i>Aspergillus niger</i>).....	4,000 HCU
Cellulase (from <i>Aspergillus niger</i>).....	500 CU
Alpha Lipoic Acid.....	200 mg

*Nattozimes® is a registered trademark of National Enzyme Company®

Non-medicinal Ingredients: Silicon dioxide, L-Leucine, pullulan/ hypromellose (capsule)

Suggested Use: Adults - Take 1 capsule with meal, 3 times a day, or as directed by a health care practitioner. Consult a health care practitioner for use beyond 4 months.

matrix is mainly made of **polysaccharides and proteins** providing structural stability and protection to the microbes.

Within biofilms, the microbes can replicate, share nutrients, and exchange genomic information (i.e. antibiotic resistance genes), making biofilms a sociomicrobiological “paradise” for microbes to thrive. ^[2]

Infectious microbes commonly known to produce biofilms include *Staphylococcus* sp., *Pseudomonas aeruginosa*, *Streptococcus* sp., *Listeria monocytogenes*, *Clostridium* sp., *N. gonorrhoea*, and *Candida albicans*.

Development of a biofilm starts with planktonic (free-moving) bacteria reversibly attaching to a surface [Figure 1]. Bacteria will then irreversibly bind to the surface within the next few hours or days while they replicate and begin to produce a polymer matrix to surround the microcolonies - forming biofilm. The biofilm can continue to grow and eventually possess tolerance to antibiotics, as well as chemical disinfectants.

Evidence has shown that the minimal inhibitory concentration (MIC) and minimal bactericidal concentration (MBC) of antibiotics to biofilm-growing bacteria may be up to 100-1000 times higher compared with free-moving bacteria. ^{[3],[4],[5]}

Biofilms can also help bacteria grow in vitro on abiotic surfaces, making biofilm-growing bacteria a serious



potential hazard in the food industry (eg. Listeria) and hospital / surgical settings (eg. MRSA).^[6]

Illnesses caused by biofilm-forming microbes include:

- Chronic sinusitis and UTI's
- *S. aureus* skin infection
- Antibiotic-associated enteritis caused by *Clostridium difficile*
- Candidiasis
- Autistic behaviors caused by neurotoxins from *Clostridium* overgrowth
- Lyme disease

Fibrin & Biofilms

Fibrin is an important part of our body's defense mechanism to protect tissues from infections and the inflammatory response caused by pathogens. However, many types of bacteria have evolved to exploit this mechanism to their own benefits.

To these bacteria, fibrin is like an adhesive matrix.^[8] These molecules help bacteria establish and colonize more easily on plasma-coated surfaces of the host where fibrin/fibrinogen molecules are abundant.

Moreover, many bacteria, such as *Staphylococcal sp.*, are able to secrete the enzyme - **coagulase** - to thicken blood by converting fibrinogen to fibrin; **they then deposit the fibrin on their own surfaces to form scaffolds of biofilms and shield against opsonophagocytosis** (ie. antibody-mediated phagocytosis).^[5] Such a protective mechanism can even extend to other microbes co-infecting the area, such as *Candida albicans*.^[9]

"Fibrinolytic Proteases" Disrupt Biofilms

Enzymes that possess both **fibrinolytic and proteolytic activities** may play a pivotal role in enhancing the effectiveness of antimicrobials because they are not only able to disperse the biofilms but also break the adhesion of biofilms to targeted tissues. Evidence has shown that breaking the integrity of biofilms not only allows more antimicrobial molecules to enter the infected tissue, but also exposes the microbes to the body's immune system.

Serrapeptase and Nattozimes® are both potent systemic proteases that can help break down the biofilms of bacteria, such as *S. aureus* and *Listeria*,^[11] attenuating their invasion abilities.

Serrapeptase is commonly used to alleviate post-operation swelling and pain due in parts to its anti-inflammatory & anti-edemic effects.^[12] It's also demonstrated beneficial effects in people with chronic airway disease^[13] and acute/chronic ear-nose-throat inflammations.^[14]

In Japan, serrapeptase is a widely used 'pharmaceutical' adjunctive medicine to various antibiotics to treat and prevent implant-related infections.^{[15],[16]}

Polysaccharide-Digesting Enzymes

Due to the fact that biofilms are also consisted of various sugar polymers, polysaccharide-digesting enzymes have been shown to help break down bacterial biofilms and enhance the

effectiveness of antiseptic agents.^{[17],[18]} **BiofilmX** includes **various polysaccharidases, especially ones not produced by the body**, to combat a wider spectrum of microbial biofilms internally.

Mucolytic Thiol Group in Alpha Lipoic Acid (ALA)

Thiol - or sulphhydryl group (R-SH) - is known to exert mucolytic effect. The most well-known mucolytic thiol-agent is N-acetylcysteine (NAC), which has only one R-SH group. While it has demonstrated its ability to help antibiotics like penicillins break biofilm to increase their efficacy, NAC has also been shown to reduce the effectiveness of antibiotics, such as aminocyclitols.^[19]

ALA, in its reduced form, has 2 sulphhydryl groups to provide comparable if not greater anti-biofilm benefits^[20], and without being shown to reduce the efficacy of any antibiotics.

Reference:

1. Centers for Disease Control and Prevention. U.S. Department of Health and Human Services. 2013.
2. Costerton W, Veeh R, Shirtliff M, Pasmore M, Post C, Ehrlich G. The application of biofilm science to the study and control of chronic bacterial infections. *J Clin Invest* 2003;112:1466-77.
3. Anwar H, Costerton JW. Enhanced activity of combination of tobramycin and piperacillin for eradication of sessile biofilm cells of *Pseudomonas aeruginosa*. *Antimicrob Agents Chemother* 1990;34:1666-71.
4. Moskowitz SM, Foster JM, Emerson J, Burns JL. Clinically feasible biofilm susceptibility assay for isolates of *Pseudomonas aeruginosa* from patients with cystic fibrosis. *J Clin Microbiol* 2004;42:1915-22.
5. Bjarnsholt T, Kirketerp-Müller K, Kristiansen S, Phipps R, Nielsen AK, Jensen PO, et al. Silver against *Pseudomonas aeruginosa* biofilms. *APMIS* 2007;115:921-8.
6. Hoiby N, Bjarnsholt T, Givskov M, Molin S, Ciofu O. Antibiotic resistance of bacterial biofilms. *IJAA* 2010; 35(4): 322-332.
7. Johnson LL, Berggren KN, Szaba FM, Chen WX, Smiley ST. Fibrin-mediated protection against infection-stimulated immunopathology. *J Exp Med*. 2003; 197(6): 801-806.
8. Foster TJ, Geoghegan JA, Ganesh VK, Hook M. Adhesion, invasion and evasion: the many functions of the surface proteins of *Staphylococcus aureus*. *Nat Rev Microbiol* 2014; 12:49-62.
9. Fehrmann C, Jurk K, Bertling A, Seidel G, Fegeler W, Kehrel BE, Peters G, Becker K, Heilmann C. *Intrn J Med Microbio* (2013); 303:230-238.
10. Zapotoczna M, McCarthy H, Rudkin JK, O'Gara JP, O'Neill E. An essential role for coagulase in *Staphylococcus aureus* biofilm development reveals new therapeutic possibilities for device-related infections. *JID* 2015; 212: 1883-1893.
11. Longhi C, Scoarughi GL, Poggiali F, Cellini A, Carpenteri A, Seganti L, Pucci P, Amoresano A, Cocconcelli PS, Artini M, Costerton JW, Selan L. Protease treatment affects both invasion ability and biofilm formation in *Listeria monocytogenes*. *Microb Pathog*. 2008; 45(1):45-52.
12. Tachibana M, Mizukoshi O, Harada Y, Kawamoto K, Nakai Y. A multi-centre, double-blind study of serrapeptase versus placebo in post-antrotomy buccal swelling. *Pharamatherapeutica*. 1984; 3(8):526-30.
13. Nakamura S, Hashimoto Y, Mikami M, Yamanaka E, Soma T, Hino M, Azuma A, Kudo S. Effect of the proteolytic enzyme serrapeptase in patients with chronic airway disease. *Respirology*. 2003; 8(3):316-20.
14. Mazzone A, Catalani M, Costanzo M, Drusiani A, Mandoli A, Russo S, Guarini E, Vesperini G. Evaluation of *Serratia peptidase* in acute or chronic inflammation of otorhinolaryngology pathology: a multicenter, double-blind, randomized trial versus placebo. *J Int Med Res*. 1990; 18(5):379-88.
15. Sannino G, Gigola P, Puttini M, Pera F, Passariello C. Combination therapy including serratiopeptidase improves outcomes of mechanical-antibiotic treatment of periimplantitis. *Int J Immunopathol Pharmcol*. (2013). 26(3): 825-31.
16. Mecikoglu M, Saygi B, Yildirim Y, Karadaq-Sayqi E, Ramadan SS, Esemenli T. The effect of proteolytic enzyme serratiopeptidase in the treatment of experimental implant-related infection. *J Bone Joint Surg Am*. 2006; 88(6):1208-14.
17. Craigen B, Dashiff A, Kadouri DE. The use of commercially available alpha-amylase compounds to inhibit and remove *Staphylococcus aureus* biofilms. *The Open Microbiology J* (2011). 5:21-31.
18. Chaignon P, Sadovskaya I, Ragunah C, Ramasubbu N, Kaplan JB, Jabbouri S. Susceptibility of staphylococcal biofilms to enzymatic treatments depends on their chemical composition. *Appl Microbiol Biotechnol* (2017). 75:125-132.
19. Parry MF, Neu HC. Effect of N-acetylcysteine on antibiotic activity and bacterial growth in vitro. *J Clin Microbiol*. (1977). 5(1):58-61.
20. Cevik K, Ulusoy S. Inhibition of *Pseudomonas aeruginosa* biofilm formation by 2,2'-bipyridyl, lipoic, kojic and picolinic acids. *Iran J Basic Med Sci* (2015). 18(8):758-763.

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