

Biofilms Protocol

CREATED IN COLLABORATION WITH DR. PAUL ANDERSON

Antibiotic resistance is a growing and serious concern, causing more than 2.8 million infections and over 35,000 deaths each year in the U.S.¹ Biofilms are a primary mechanism of antibiotic resistance and allow bacteria to evade host defense systems and other external stressors (UV damage, mechanical force, temperature fluctuations).² In any patient with persistent, recurrent, or refractory illness, biofilm involvement should be suspected and addressed.

Biofilm bacteria can resist up to 5,000 times the antibiotic concentration that would typically be needed to resolve infection.³ Moreover, the National Institutes of Health (NIH) states that 80% of chronic infections are associated with biofilm formation,⁴ while other research suggests that ~65% of nosocomial infections, including major hospital-acquired infections such as those associated with indwelling catheters and prostheses, are due to biofilms.⁵

What are biofilms?

A biofilm is a living microbial community of organisms that adheres to one another and to surfaces. They can be composed of a single species of organism, but most often, they are polymicrobial (including bacterial, fungal, and/or viral species).

Planktonic (free-floating) microorganisms readily colonize new niches but have a lower chance of survival. Biofilms provide a more secure way for bacteria to reproduce and survive.⁶ Approximately 10% of bacteria are planktonic, whereas the remaining 90% form biofilm colonies that excrete a sticky matrix called extracellular polymeric substance (EPS).^{4,7} EPS creates a mechanical barrier protecting the internal organisms.

Additionally, the EPS biofilm matrix enables communities of bacteria to exist in close proximity, providing an ideal reservoir for the cellular exchange of resistance genes – one mechanism for spreading bacterial resistance. According to recent research, the horizontal transfer of resistance-conferring genes between bacterial cells within biofilms has been reported as being 700 times more efficient than among free-living, planktonic bacterial cells.⁵

Biofilm production is initiated in response to a hostile environmental shift and can form in less than an hour. Biofilms are everywhere, dominating all habitats on the Earth's surface and accounting for up to 80% of the approximate 1.2×10^{30} bacterial cell population.⁵

Questions?

For clinical questions, email clinical@biocidin.com
or call 800-775-4140, x3.

¹ <https://www.cdc.gov/drugresistance/biggest-threats.html#:~:text=More%20than%202.8%20million%20antibiotic,people%20die%20as%20a%20result.>

² <https://aricjournal.biomedcentral.com/articles/10.1186/s13756-019-0533-3>

³ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6312881>

⁴ Joo, H. S., & Otto, M. (2012). Molecular basis of in vivo biofilm formation by bacterial pathogens. *Chemistry & biology*, 19(12), 1503–1513. <https://doi.org/10.1016/j.chembiol.2012.10.022>

⁵ Bowler, P., Murphy, C. & Wolcott, R. Biofilm exacerbates antibiotic resistance: Is this a current oversight in antimicrobial stewardship? *Antimicrob Resist Infect Control* 9, 162 (2020). <https://doi.org/10.1186/s13756-020-00830-6>.

⁶ Hernández-Jiménez, Enrique et al. "Biofilm vs. planktonic bacterial mode of growth: which do human macrophages prefer?" *Biochemical and biophysical research communications* vol. 441,4 (2013): 947-52. doi:10.1016/j.bbrc.2013.11.012 <https://pubmed.ncbi.nlm.nih.gov/24239884>

⁷ Petrova, O. E., & Sauer, K. (2012). Sticky situations: key components that control bacterial surface attachment. *Journal of bacteriology*, 194(10), 2413–2425. <https://doi.org/10.1128/JB.00003-12>



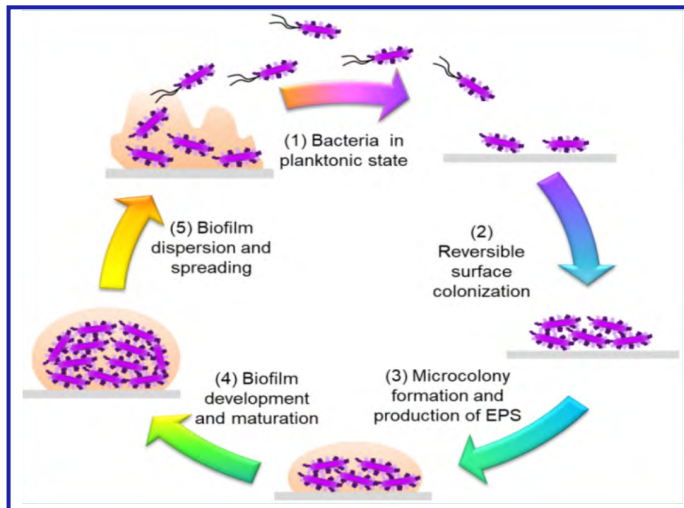


Figure 1. Life cycle of a biofilm

Sahli C, Moya SE, Lomas JS, Gravier-Pelletier C, Briandet R, Hémadi M. Recent advances in nanotechnology for eradicating bacterial biofilm. *Theranostics*. 2022;12(5):2383-2405. Published 2022 Feb 28. doi:10.7150/thno.67296

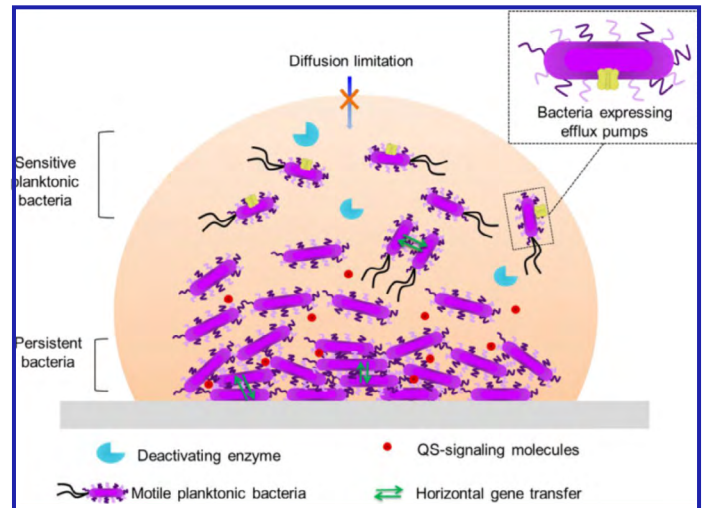


Figure 2. Defense mechanisms of a biofilm

Sahli C, Moya SE, Lomas JS, Gravier-Pelletier C, Briandet R, Hémadi M. Recent advances in nanotechnology for eradicating bacterial biofilm. *Theranostics*. 2022;12(5):2383-2405. Published 2022 Feb 28. doi:10.7150/thno.67296

What is the clinical significance of biofilms?

Problematic biofilms are not isolated to overt, antibiotic-resistant infections. Biofilms are present in everyone, and they are dynamic. They are not always problematic and may house beneficial microorganisms in patients without pathologies.

HOW DO WE KNOW IF BIOFILMS ARE PLAYING A ROLE IN A PATIENT'S ILLNESS?

Testing is not feasible (some tests are available, but their clinical utility is not yet established), so clinical evaluation is essential. Biofilms are more likely to be present for patients with the following presentation:

- Implants
- Prosthetics
- Catheterization
- Oral appliances
- Antibiotic-resistant infections
- Chronic Candida infections

HOW MIGHT THAT LOOK?

- Labs that won't clear
- Labs that change or worsen
- Chronic GI infections unresponsive to treatment
- Patients with refractory illness
- Chronically ill patients

WHAT IS THE CLINICAL SIGNIFICANCE?

- Difficulty resolving infection
- Ongoing toxic exposure
- Disruption of metabolic activity

WHAT MAKES A BIOFILM PATHOLOGICAL?

- Patient health (Is the immune system intact? Are there multiple chronic conditions present?)
- Development stage
 - Physiologic (normal) biofilm: Everyone has these, and they are akin to the “good flora” organisms in the GI tract.
 - Phase 1: Low to normal pathogenicity. These may be normal and can often be addressed by using aromatic herbs in food or a Biocidin® protocol. Addressing biofilms in the early stages can prevent them from becoming a bigger problem.
 - Phase 2: Later stages are universally an obstacle to healing
 - Multiple pathogens are present
 - Requires disruption so that antimicrobials and the immune system can work
 - Can regress to Phase 1 with treatment
 - Bismuth Thiols are recommended as a buster (please see details below)

Biocidin® and biofilms

Dr. Claudia Marques, biofilm researcher at the University of Binghamton, examined the growth inhibition of several pathogens and their biofilms following exposure to Biocidin®. Her results were excellent.

Figure 3. Percent death following exposure to various concentrations of Biocidin® for a period of 4 hours at 37° C with aeration.

		0% Biocidin	25% Biocidin	50% Biocidin	75% Biocidin	100% Biocidin
<i>S. aureus</i>	Biofilms	0%	92.9%	88.4%	95.0%	89.7%
	Planktonic	0%	99.2%	60.0%	91.9%	99.9%
<i>K. pneumonia</i>	Biofilms	0%	90.7%	78.0%	82.7%	99.8%
	Planktonic	0%	99.1%	55.9%	91.0%	99.9%
<i>P. aeruginosa</i>	Biofilms	0%	92.1%	99.9%	99.9%	N/A
	Planktonic	0%	93.3%	99.9%	99.9%	N/A
<i>C. albicans</i>	Biofilms	0%	99.9%	99.9%	99.9%	99.99%
	Planktonic	0%	95.6%	96.3%	95.9%	99.7%

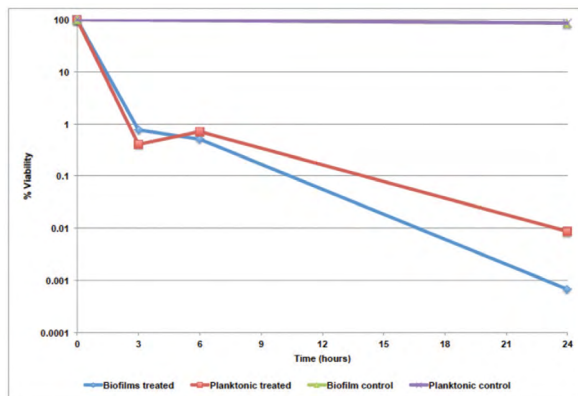


Figure 4. *E. coli* biofilms exposed to 50% Biocidin® for a period of 24 hours. At 24 hrs, most of the biofilm and planktonic populations were eradicated.

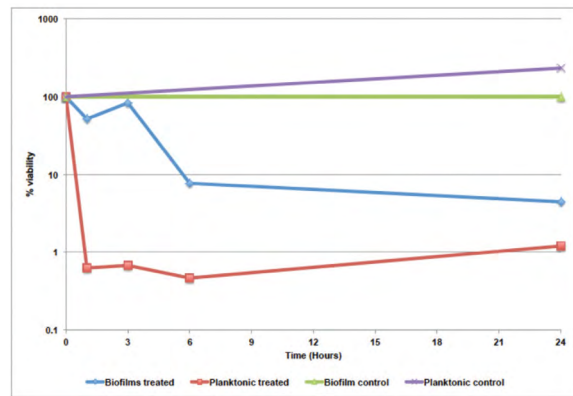


Figure 4. *C. albicans* biofilms exposed to 25% Biocidin® for a period of 24 hours.

Clinical Pearl #1 – Use a Binding Agent

Biofilms harbor bacterial metabolites and toxins. They are so sticky they are used for bioremediation of toxic waste sites. When biofilms are broken down, the metabolites present may cause damage to the surrounding tissues or transient increases in inflammation. This process makes addressing biofilms an imperative part of any detoxification strategy. Include a binder like G.I. Detox™+ to protect the patient from discomfort and improve compliance.

Inflammatory and Toxic Components Found in Biofilms	
Pathogen-Associated Molecular Patterns (PAMPS) such as Lipopolysaccharides (LPS) from gram-negative bacteria and Peptidoglycans from gram-positive bacteria	Heavy Metals
Organophosphates such as pesticides and herbicides	Histamine
Oxalates	Drug Metabolites

Clinical Pearl #2 – Don't Forget the Mouth!

When it comes to considering biofilms, the oral microbiome is often overlooked. A common biofilm in the mouth is dental plaque, aka "fuzzy teeth." Teeth provide a non-shedding surface for biofilms to accumulate. Dental biofilms on the surfaces of the teeth will not go away unless mechanically removed through brushing and cleaning. If left unaddressed, it can lead to the demineralization of the enamel and the formation of dental caries.

Lifestyle Recommendations

- Evaluate lifestyle habits. Smoking, alcohol, simple carbohydrates, and sugar all increase the susceptibility to biofilm formation.
- Consider the Biocidin Botanicals® [Bioclear™ Microbiome Detox Program](#). The booklet accompanying the program includes more comprehensive lifestyle instructions.
- One tablespoon daily of apple cider vinegar can help dissolve biofilms. A quick shot is the best option, but if patients prefer to mix it with water, recommend they drink it with a straw. The acidic pH of apple cider vinegar can erode dental enamel.
- Raw garlic is also a way to dissolve biofilms. 1-2 cloves a couple of times a week is helpful; daily is ideal. Garlic salt and powder do not count!
- To address oral biofilms, Biocidin Botanicals® [Dentalcidin® Oral Care System](#) makes an additional impact. (What grows in the mouth will grow in the gut!)



Therapeutic Plan Suggestions

Gastrointestinal Biofilm Support		
CORE PROTOCOL		
Biocidin® Liquid or Capsules	Titrate to 15 drops 2x/day	Titrate to 2 capsules 2x/day
G.I. Detox™+	2 capsules at bedtime. 1 hour away from food, supplements, and medications. Temporarily increase dose to 2 capsules 2-3x/day if Herxheimer reaction observed/worsens.	
Olivirex®	Titrate to 2 capsules 2-3x/day	
ADDITIONAL SUPPORT		
Proflora™ 4R	1 capsule any time	
Dentalcidin®	2x/day	
Dentalcidin® LS	2 pumps 2x/day	

Oral Biofilm Support	
CORE PROTOCOL	
Dentalcidin®	2x/day
Dentalcidin® LS	2 pumps 2x/day
ADDITIONAL SUPPORT	
Proflora™ 4R	1 capsule any time



Therapeutic Plan Suggestions, continued

Systemic Biofilm Support		
THIS PROTOCOL COMBINES THE GASTROINTESTINAL AND ORAL BIOFILM PROTOCOLS		
CORE PROTOCOL		
Biocidin® Liquid or Capsules	Titrate to 15 drops 2x/day	Titrate to 2 capsules 2x/day
Biocidin® LSF	Titrate to 3 pumps 2x/day	
G.I. Detox™+	2 capsules at bedtime. 1 hour away from food, supplements, and medications. Temporarily increase dose to 2 capsules 2-3x/day if Herxheimer reaction observed/worsens.	
Olivirex®	Titrate to 2 capsules 2x/day	
Proflora™ 4R	1 capsule any time	
Dentalcidin®	2x/day	
Dentalcidin® LS	3 pumps 2x/day	

Additional Considerations by Dr. Paul Anderson

SUPPLEMENTARY THERAPEUTICS

Bismuth Thiol is available in three ways – over the counter (OTC) as a supplement, and as two prescription types, one made by a compounding pharmacy and the other used only in hospitals. Most compounding pharmacies can make it; however, they may not always have ingredients, and prices can vary, so check with the pharmacist first. Please go to [this link](#) for Dr. Anderson’s recommended formula.

1. It is recommended that patients take a multi-mineral supplement with trace minerals during the protocol to offset mineral displacement and increased phase-2 detoxification caused by the ingredients.
2. If abdominal cramping occurs, it is best to stop the dosing for 1 week, double the multi-mineral supplement, and restore hydration.
3. Protocols are recommended for 3 to 12 weeks. Some patients may require longer treatment in which case the dose is reduced to 50% of the original dose. A competent healthcare provider should monitor this.
4. Bismuth Thiol MUST be taken away from food for best efficacy. If absolutely necessary to take with food, then applesauce or other fruit pureés are best. Do not use yogurt or other calcium-containing foods.
5. There are no contraindications and known interactions of taking Bismuth Thiol when taken 1-2 hours away from other medications and antimicrobial treatments.
6. It is good to remember that a normal side effect of bismuth can be black stools.

7. **It is essential to keep supportive therapies in place.** These include lifestyle and dietary habits (please see Lifestyle Recommendations above) and supportive therapies to help patients handle the immunological reactions that begin once the biofilm begins to open up.
8. Therapies include:
 - a. Adrenal support – evaluate the patient’s needs depending on adrenal status. Glandular products may be helpful for those in adrenal exhaustion, while botanicals may be of adequate support for less complex patients.
 - b. Anti-inflammatory herbs
 - c. Immunomodulatory herbs (ex: Turmeric)
 - d. Use of effective dose of binders (like G.I. Detox™+, Diatomaceous earth, even EDTA) combined with fibrous foods that can serve both as binders and as prebiotics.
 - e. NAC
 - f. Enzymes
 - g. Nutrients to support detoxification
8. See protocols below

Bismuth Thiol Protocols For Specific Biofilm Disruption

1. Biofilm disruption for better stool-test sensitivity
 - a. [Biocidin®](#) or Bismuth Thiol (OTC) for 2 weeks prior to stool-sample collection.
 - b. Dose: 1-2 capsules per day away from meals, supplements, and medication. Take with a full glass of water.
2. Protocol for Phase-1 Biofilms
 - a. See [Biocidin®](#) protocol under Therapeutic Plan Suggestions.
3. Protocol for Phase-2 Biofilms
 - a. Bismuth Thiol dose here is with OTC version (Biofilm Phase-2 from Priority One):
 - i. **Week 1:** 1-2 caps in AM on empty stomach with full glass of water. 4 days on and 3 days off in the week.
 - ii. **Week 2-12:** 2-3 caps in AM on empty stomach with a full glass of water. 4 days on and 3 days off in the week. (Increase dose if [Herxheimer](#) or other inflammatory reaction occurs.)

References

1. <https://ndnr.com/gastrointestinal/biofilms-what-have-we-learned-from-the-research/>
2. <https://www.consultdranderson.com/blog/>
3. “Breaking Up With Biofilms,” Webinar recorded 11/9/2022 featuring Dr. Jocelyn Strand, Director of Clinical Education for Biocidin Botanicals®, and Dr. Paul Anderson, NMD. <https://biocidin.com/blogs/webinars>