Biocidin Botanicals®

Non-alcoholic/Metabolic Dysfunction-Associated Fatty Liver Disease Protocol

Introduction

The prevalence of obesity and people who are overweight has never been higher in the United States and presents one of today's most pressing public health challenges. Current statistics paint an alarming picture: One in three adults is considered overweight, while 2 in 5 meet the clinical criteria for obesity.[1] This excess weight burden triggers complex metabolic disruptions throughout the body, substantially increasing the risk of developing serious chronic conditions, including Type 2 diabetes, hypertension, cardiovascular disease, and stroke, among others.[2]

When adipose tissue reaches its storage capacity, excess fatty acids get deposited elsewhere in the body, with the liver serving as a major storage reservoir. This accumulation can lead to what is traditionally known as non-alcoholic fatty liver disease (NAFLD). However, medical terminology has evolved in recent years to better reflect the underlying metabolic dysfunction, leading to this condition's current designation: metabolic dysfunction-associated fatty liver disease (MAFLD).[3] First documented in 1980, MAFLD is now one of the most common diseases in developed nations, with global rates increasing by more than 50% in the past three decades.[4,4a]

Epidemiology

NAFLD/MAFLD affects an estimated 80–100 million people, or approximately 25% of the total adult population in the U.S., and is currently the most common cause of chronic liver disease worldwide.[5] The global prevalence of NAFLD/MAFLD has increased to 34% and is expected to reach 56% by 2030.[6] The incidence and severity of NAFLD/MAFLD increases with advancing age, reaching a peak between 45 and 64 years. Among Caucasian populations, men are more frequently affected than women.[5]

For approximately 30% of patients, NAFLD/MAFLD progresses to a more severe condition called non-alcoholic steatohepatitis (NASH). NASH is characterized by liver tissue inflammation and fibrosis – scarring that ranges from stage F0 (no fibrosis) to F4 (cirrhosis). Currently affecting 1.5-6.5% of U.S. adults, NASH follows an unpredictable course. Some patients may see their condition improve back to simple fatty liver, while others may deteriorate toward cirrhosis or develop hepatocellular carcinoma, a form of liver cancer.[5]

Physiology/Diagnosis/Clinical Relevance

NAFLD/MAFLD is an inflammatory hepatic disorder associated with insulin resistance, central obesity, and metabolic syndrome.[6] It is defined as liver steatosis, or an accumulation of fat in the liver exceeding 5% of the liver's total weight in the absence of significant alcohol consumption.[5]

Fat accumulation comes in the form of triglycerides (TG) deposited in the hepatocytes (liver cells). The primary sources of fatty acids, which are esterified in the liver into TGs, come from the systemic circulation, having originated from lipolysis within the adipose tissue TG, and fatty acids synthesized de novo in the liver from precursors such as carbohydrates (lipogenesis).[5]

NAFLD/MAFLD
Hepatic steatosis with the presence of overweight/obesity OR Type 2 diabetes
At least two of the following metabolic risk factors:[7] • Waist circumference ≥102 cm in men OR ≥88 cm in women OR ≥90/80 cm in individuals of Asian descent • Triglyceride concentration ≥150 mg/dL or treatment for hypertriglyceridemia • High-density lipoprotein concentration <40 mg/dL in men OR <50 mg/dL in women or medication for dyslipidemia • Systolic blood pressure ≥130 mmHg OR diastolic pressure ≥85 mmHg OR treatment for arterial hypertension • HOMA-IR ≥2.5 • CRP concentration >2 mg/L

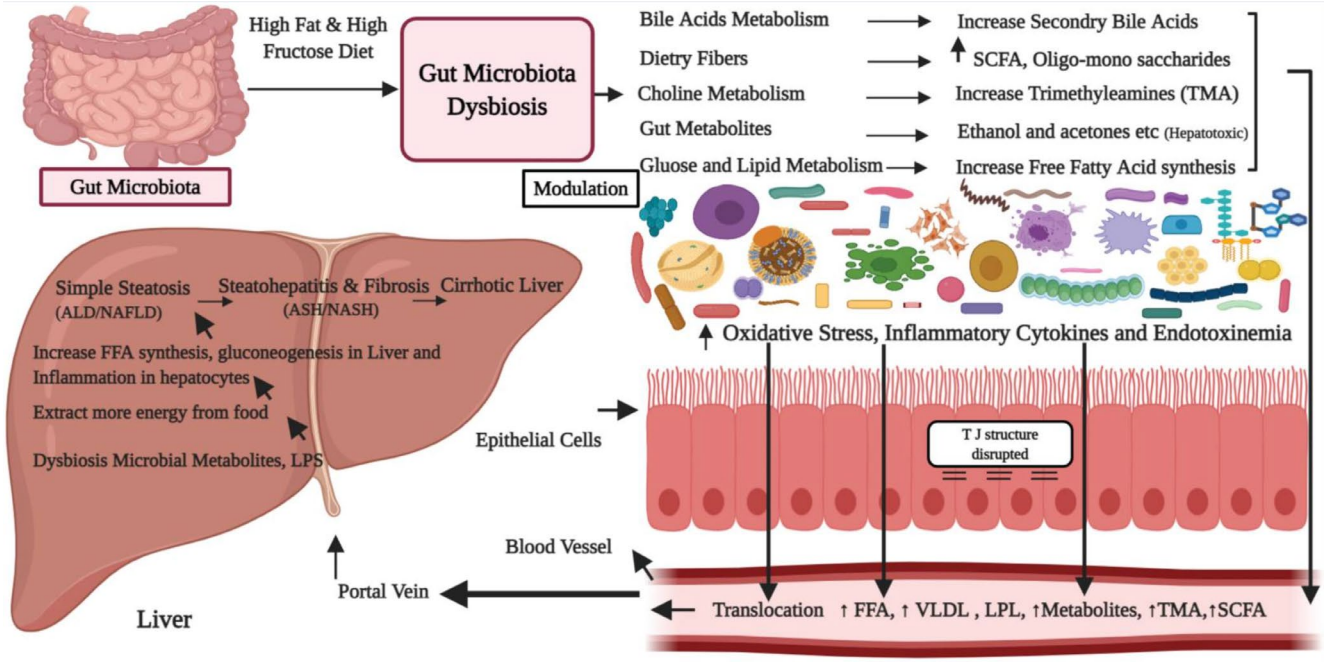
https://pubmed.ncbi.nlm.nih.gov/32278004/

The development and progression of NAFLD/MAFLD is a complex process that is not clearly understood. Without intervention, the condition can advance through increasingly severe stages: from simple fatty liver to NASH, to fibrosis and cirrhosis, and potentially to hepatocellular carcinoma.[4]

Central to this progression is the gut-liver axis (GLA) – a sophisticated bidirectional relationship between the liver, the intestinal tract, and its resident microbiota. This relationship is shaped by dietary, genetic, and environmental factors. The portal vein serves as the primary communication channel, transporting gut-derived substances directly to the liver, while the liver responds through mechanisms such as bile and antibody secretion. The intestinal mucosal and vascular barriers act as critical checkpoints, selectively allowing nutrients to enter circulation while blocking harmful microbes and toxins.[8]

Hepatic inflammation is the primary driver of NAFLD/MAFLD progression and essentially promotes the development of liver fibrosis and cirrhosis.[6] This inflammation can be triggered by a combination of microbes and their metabolites or toxins. For instance, bacterial products such as lipopolysaccharides (LPS) and proinflammatory cytokines can disrupt intestinal tight junction proteins – including zonula occludens-1 (ZO-1) and claudin-1 – leading to increased gut permeability.[6]

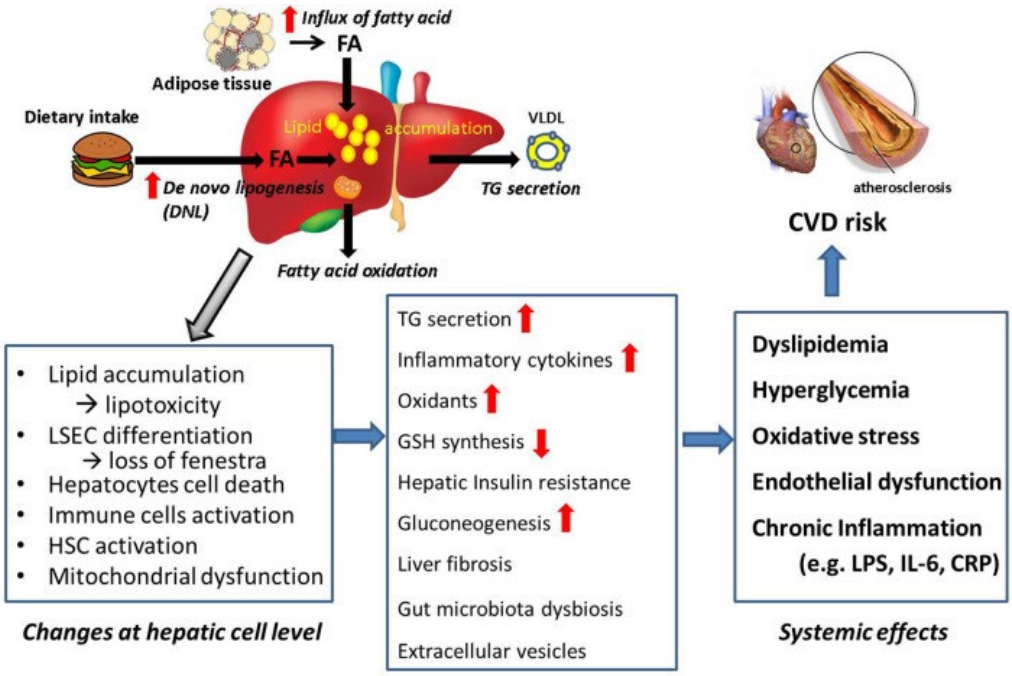
When the gut barrier becomes more permeable, bacteria, toxins, and metabolites can migrate across the epithelial barrier and travel via the portal vein to the liver. This triggers a cascade of inflammatory responses: LPS activates toll-like receptor 4 (TLR4) signaling in macrophages, which in turn activates Nuclear Factor-kappa B (NF-κB) in host cells, generating pro-inflammatory cytokines. These combined processes promote liver inflammation and dyslipidemia, accelerating MAFLD progression.[6]



https://pubmed.ncbi.nlm.nih.gov/33767591/

Figure 1. Influence of diet on the progression of dysbiosis and development of NAFLD/MAFLD[9]

NAFLD/MAFLD has been recognized as an independent risk factor for developing cardiovascular diseases (CVD), including atherosclerosis, hypertension, valvular heart disease, cardiomyopathy, and arrhythmias. In fact, clinical studies suggest that CVD is the primary cause of death in NAFLD/MAFLD patients.[10]



https://pubmed.ncbi.nlm.nih.gov/39411175/

Figure 2. Connections between NAFLD/MAFLD and CVD.[10]

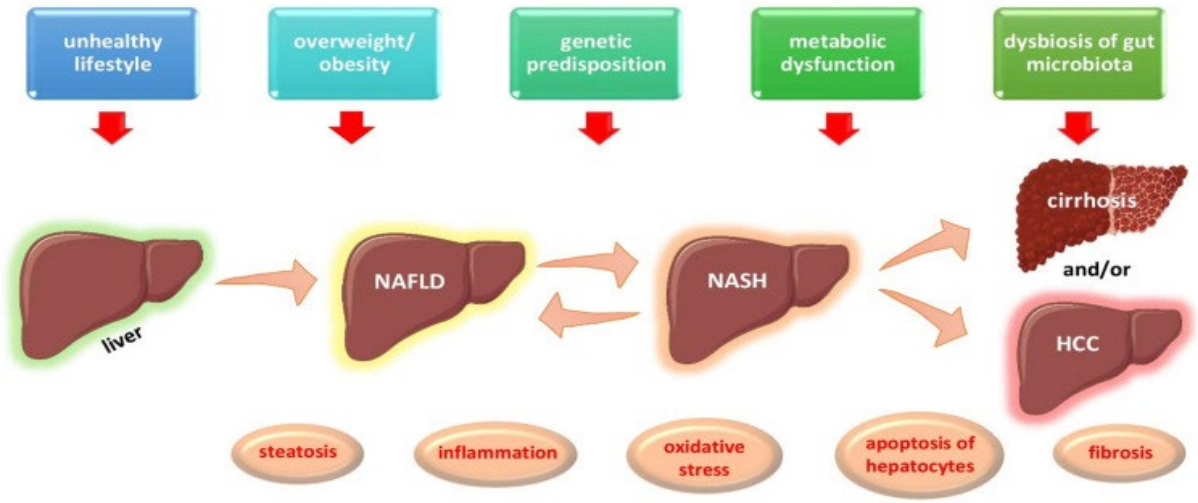
Risk Factors

Factors that contribute to the NAFLD/MAFLD occurrence have been identified, including[4]

- Obesity/overweight
- Metabolic syndrome (MS)
- Highly processed diet (western-type) rich in sugar and saturated fats
- Insufficient physical activity
- Genetic factors (PNPLA3 rs738409 risk genotype (GG))

Insulin resistance (IR) appears to be a central feature linking the metabolic disorders associated with NAFLD/MAFLD. While obesity is the most significant risk factor for hepatic lipid accumulation, a subset of NAFLD/MAFLD patients maintain a normal body weight based on BMI measurements.[4]

The mechanisms underlying IR in lean individuals remain poorly understood. However, several key factors have been identified, including abnormal fat distribution – particularly visceral adiposity – and adipose tissue dysfunction. Recent research has expanded this understanding, suggesting that intestinal inflammation, gut microbiome dysbiosis, and *Helicobacter pylori* infection may also contribute to the development of both IR and NAFLD/MAFLD in lean individuals.[4]



https://pubmed.ncbi.nlm.nih.gov/35053205/

Figure 3. Etiopathogenetic mechanisms of NAFLD/MAFLD progression and staging[5]

Diagnostic Testing

Ultrasound remains the cornerstone of MAFLD diagnosis, valued for its safety, simplicity, cost-effectiveness, and widespread availability. While the traditional ultrasound assessment is subjective, it demonstrates remarkable effectiveness in detecting moderate-to-severe hepatic steatosis (when fat affects more than 20-30% of liver tissue), achieving a sensitivity of 84.8% and specificity of 93.6%.[4]

Technological advances have further enhanced diagnostic capabilities through quantitative ultrasound techniques that analyze the acoustic properties of liver tissue. A notable innovation is the controlled attenuation parameter (CAP), which measures liver steatosis alongside tissue stiffness using vibration-controlled transient elastography (VCTE). This combined assessment, performed with devices such as FibroScan®, has become increasingly central to non-invasive liver evaluation.[4]

The Microbiome Connection

As noted previously, changes in the microbial composition of the intestinal tract and the metabolites they produce can affect the integrity of the intestinal barrier, which can contribute to the development and progression of NAFLD/MAFLD.

Research reveals distinct microbial patterns in NAFLD/MAFLD patients, particularly those with NASH, characterized by an increased abundance of Bacteroidetes and altered *Firmicutes* populations, typically resulting in a decreased *Firmicutes*-to-*Bacteroidetes* ratio. The microbial landscape shows further specific changes: increased presence of *Clostridium*, *Anaerobacter*, *Streptococcus*, *Escherichia*, and *Lactobacillus*, while species like *Oscillibacter*, *Flavonifractor*, *Odoribacter*, and *Alistipes* become less prevalent. NASH patients, specifically, exhibit higher levels of potentially pathogenic bacteria – including Gram-negative *Proteobacteria*, *Enterobacteriaceae*, and *Escherichia* species – alongside reduced populations of beneficial bacteria such as *Faecalibacterium prausnitzii* and *Akkermansia muciniphila*.[5]

Moreover, the gut microbiota in NAFLD/MAFLD patients is enriched with ethanol-producing bacteria like *E. coli*, which generates ethanol under anaerobic conditions. This overrepresentation has been linked to elevated levels of endogenously produced ethanol in the circulation and breath, suggesting that the gut microbiota in these patients produces more ethanol than in healthy controls.[5]

Ethanol exacerbates tissue damage by activating NF-κB signaling pathways, impairing gut barrier function, and increasing portal concentrations of LPS. Furthermore, the liver's detoxification capacity is compromised in NAFLD, leading to increased production of reactive oxygen species (ROS). These ROS can induce oxidative damage to hepatocytes, intensify hepatic inflammation, and ultimately contribute to the progression of NASH.[5]

Clinical Pearl # 1 – Encourage a Diet Rich in Short-Chain Fatty Acids

Encourage a plant-based diet rich in prebiotics and fibers to support the production of short-chain fatty acids (SCFAs). Produced when gut microbiota ferment indigestible carbohydrates, SCFAs are essential energy sources for intestinal epithelial cells. These compounds play multiple protective roles: supporting cell growth and differentiation, maintaining optimal pH levels, enhancing mucus production, and strengthening intestinal barrier integrity. SCFAs demonstrate particular significance in liver health by reducing inflammation and steatosis through their anti-inflammatory properties, promoting energy expenditure, and enhancing lipid oxidation. By strengthening the intestinal barrier, they also help reduce the transfer of harmful bacteria, metabolites, and inflammatory cytokines to the liver.

(Download our Eat Right For Your Microbiome Resource.)

Scan here to view our *Eat Right For Your Microbiome* Resourse

Clinical Pearl # 2 – Support Healthy Bile Production and Secretion

Bile serves several vital roles, most notably involving fat digestion. Bile salts are essential for breaking down fats, making sufficient bile production crucial for fat metabolism and, by extension, weight management. Additionally, bile facilitates the removal of toxins from the liver by transporting them into the feces, ensuring smooth digestion and detoxification. Without a steady bile production and flow, cholesterol stones can form, further disrupting digestive processes.

Bile also helps lubricate the small intestine and aids in stool formation. Insufficient lubrication can lead to constipation, while excessive bile may result in diarrhea. Blockages in bile flow can lead to toxin buildup in the body, contributing to oxidative stress and waste accumulation. When undigested food lingers in the intestine, it ferments, releasing toxic gases that can compromise the intestinal lining and contribute to leaky gut.

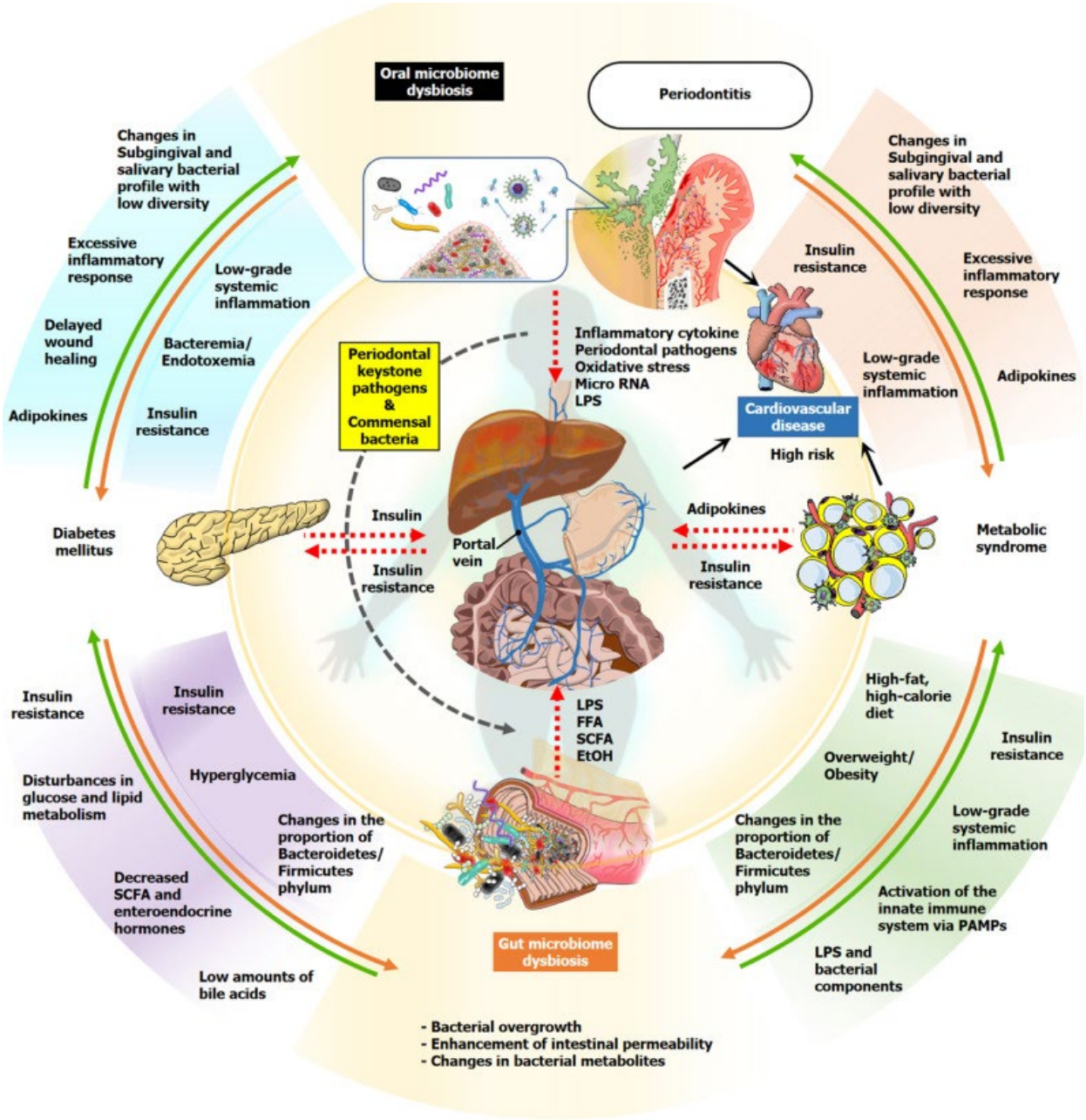
Utilizing botanicals such as artichoke, milk thistle, and turmeric, in addition to the bile acid tauroursodeoxycholic acid (TUDCA), can ensure healthy bile production and secretion. Other supportive herbs like ginger, tangerine peel, and bupleurum offer additional benefits to the liver, gallbladder, and digestive tract and aid in effective digestion, motility, and elimination.

Clinical Pearl #3 – Address Oral Dysbiosis

A growing body of research highlights the significant connection between oral health and liver function. Periodontal disease, characterized by oral inflammation and microbiome disruption, can trigger gut dysbiosis and contribute to NAFLD/MAFLD development.

Be sure to support the oral microbiome by encouraging daily oral hygiene, including flossing, brushing and rinsing, regular dental check-ups, and using oral care products that support healthy oral microbial balance. (See our Periodontal Disease Protocol.)

Scan here to view our Periodontal Disease Protocol



https://pubmed.ncbi.nlm.nih.gov/36844143/

Figure 4. Circular connections between periodontal disease, gut microbiota, diabetes mellitus, and metabolic syndrome in the pathogenesis of nonalcoholic fatty liver disease.[11]

The goal of treating NAFLD/MAFLD is to reduce hepatic steatosis while also treating the components of metabolic syndrome. As IR is a major component of metabolic dysfunction and the development of NAFLD/MAFLD, addressing blood sugar support and insulin signaling is vitally important.

(Please see our Metabolic Syndrome/Insulin Resistance Protocol).

Scan here to go to our Metabolic Syndrome/Insulin Resistance Protocol

Therapeutic Plan Suggestions

Bioclear® Microbiome Detoxification Program contains three products designed to provide a microbial reset. This program acts to remove harmful organisms, bind microbial debris and toxins, and restore beneficial species to the GI tract.

NAFLD/MAFLD Support					
CORE PROTOCOL **Bioclear® Microbiome Detoxification Program**					
Biocidin® Liquid, LSF, or Capsules Choose one	Biocidin® Liquid Titrate to 10 drops 2x/day per booklet instructions	OR	Biocidin® Capsules Titrate to 2 capsules 2x/day per booklet instructions	OR	Biocidin® LSF Titrate to 2 pumps 2x/day per booklet instructions
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.				
Proflora® 4R	1 capsule any time of day				
ADDITIONAL SUPPORT					
Liver GB+™	1 capsule 2x/day				
Biotonic®	20 drops 2x/day				
G.I. InnerCalm®	1 stick pack mixed in water, 1-2 times daily, taken any time				
Dentalcidin®	2x/day				
Dentalcidin® LS	2 pumps 2x/day				
Dentalflora®	Dissolve 1 tablet in mouth daily at bedtime, at least 30 minutes away from other oral care, food, or drinks				

Biocidin Botanicals®

Additional Therapeutic Suggestions

N-acetyl cysteine
Glycine
Taurine
Healthy fats (olives and olive oil, avocados and avocado oil, cold water fatty fish and fish oil, nuts and seeds)
Fiber

Questions?

For clinical questions, email clinical@biocidin.com

References

[1] https://www.niddk.nih.gov/health-information/health-statistics/overweight-obesity (12.05.24)

[2] https://www.niddk.nih.gov/health-information/weight-management/adult-overweight-obesity/health-risks (12.05.24)

[3] https://pmc.ncbi.nlm.nih.gov/articles/PMC7881793/

[4] https://pubmed.ncbi.nlm.nih.gov/36986052/

[4a] https://pubmed.ncbi.nlm.nih.gov/37169151/

[5] https://pubmed.ncbi.nlm.nih.gov/35053205/

[6] https://pubmed.ncbi.nlm.nih.gov/38006804/

[7] https://pubmed.ncbi.nlm.nih.gov/32278004/

[8] https://pubmed.ncbi.nlm.nih.gov/31622696/

[9] https://pubmed.ncbi.nlm.nih.gov/33767591/

[10] https://pubmed.ncbi.nlm.nih.gov/39411175/

[11] https://pubmed.ncbi.nlm.nih.gov/36844143/

*These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.