

# Estrogen Metabolism Protocol

Estrogen metabolism and elimination are intimately intertwined with the microbiome. The gut microbiome comprises an estimated average of 39 trillion microbes.<sup>1</sup> It is a diverse group of bacteria, fungi, protozoa, archaea, and viruses.

**The estrobolome is a specific collection of bacteria from the enteric microbiome whose products are capable of influencing estrogens.** It serves to metabolize and modulate the body's circulating estrogen, which in turn affects weight, mood, libido, and accumulation of lifetime exposure to estrogens.<sup>2</sup>

Unfortunately, microbial imbalances (aka dysbiosis) are a common result of contemporary lifestyle and diet choices. Dysbiosis can result in bacterial overgrowth, parasites, impaired digestion, leaky/inflamed tight junctions, elevated  $\beta$ -glucuronidase levels, and hormonal imbalance.

## Estrogen Metabolism

Estrogen metabolizes physiologically in numeric order – Phase 1, Phase 2, Phase 3. But we need to address it in reverse – Phase 3, Phase 2, Phase 1.

### Phase 1: Hydroxylation

This phase occurs in the liver. There, estrogen has three metabolic pathways by which it can be metabolized: CYP1A1, CYP1B1, and CYP3A4. This process results in three forms of hydroxylated estrogens: 2-OH-E1, 4-OH-E1, and 16-OH-E1.<sup>3</sup>

### Phase 2: Conjugation

This step also takes place in the liver. Estrogens become deactivated – specifically through sulfation, glucuronidation, and methylation – before they are eliminated. This process requires certain nutrients and enzymes in the body, namely COMT and MTHFR.<sup>4</sup>

### Phase 3: Elimination

In the final stage, the deactivated estrogens from Phase 2 are packaged up and eliminated from the body through the stool. Bile is also necessary to facilitate this process. Things like inflammation, dysbiosis, and overall intestinal health can all impact how smoothly this process occurs. It is now clear that if Phase 3 is working inefficiently, estrogen metabolism backs up and slows down entirely.

**This explains the importance of addressing Phase 3 first!**

<sup>1</sup>Barko, P., McMichael, M., Swanson, K., & Williams, D. (2017, November 24). The Gastrointestinal Microbiome: A Review. Retrieved August 20, 2021, from <https://onlinelibrary.wiley.com/doi/pdf/10.1111/jvim.14875>

<sup>2</sup>Kho, Z. Y., & Lal, S. K. (2001, January 01). The Human Gut Microbiome – A Potential Controller of Wellness and Disease. Retrieved August 20, 2021, from <https://www.frontiersin.org/articles/10.3389/fmicb.2018.01835/full>

<sup>3</sup>Tsuchiya, Y., Nakajima, M., & Yokoi, T. (2005) Cytochrome P450-mediated metabolism of estrogens and its regulation in human. Cancer letters, 227(2), 115-124. Retrieved September 15, 2021, from <https://pubmed.ncbi.nlm.nih.gov/16112414/>

<sup>4</sup>Yasuda, M.T., Sakakibara, H. & Shimoi, K. Estrogen- and stress-induced DNA damage in breast cancer and chemoprevention with dietary flavonoid. Genes and Environ 39, 10 (2017). <https://doi.org/10.1186/s41021-016-0071-7>



## Gut Dysbiosis and Hormonal Imbalance

The health of the microbiome influences hormonal health in a few ways:

### Suppression of ovarian hormone production

Dysbiosis and its resulting metabolites cause inflammatory damage to the gut lining and increase systemic inflammation, which can suppress hormone production.

### Impaired Phase-3 function

Dysbiosis can result in slowed transit time and/or constipation and reabsorption/recirculation of toxins.

### Elevated $\beta$ -glucuronidase levels

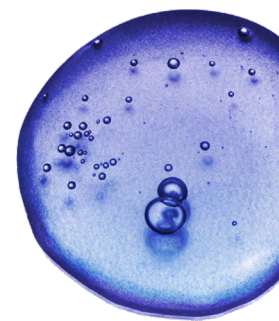
In Phase 3 of estrogen detoxification, the liver and intestines bind toxins and steroid hormones for elimination. These toxins and hormones are bound by glucuronic acid, allowing them to be excreted in the stool.  $\beta$ -glucuronidase is an enzyme that breaks that tight bond between glucuronic acid and toxins and hormones in the intestines.<sup>5</sup> The problem? Elevated  $\beta$ -glucuronidase leads to estrogen excess.<sup>6</sup>

$\beta$ -glucuronidase is produced by intestinal epithelium and certain intestinal bacteria.<sup>7</sup> High levels (detected in most diagnostic stool studies) are not desirable. Higher levels have been associated with higher circulating estrogens and lower excretion in women. Lower levels are currently not of much clinical significance. High levels are commonly seen with an imbalanced microbiome.

#### Common symptoms associated with elevated $\beta$ -glucuronidase:

Heavy periods	Headaches	Anxiety
Clotting	Mood swings	Irregular menses
Cramping	Weight gain	Infertility
Fibrocystic breasts	Fatigue	Brain fog

Biocidin Botanicals® products work to restore healthy balance to the GI tract, supporting Phase 3 – elimination. These products may also reduce the inflammatory load on the liver, liberating nutrients needed for Phases 1 and 2 of estrogen metabolism.



<sup>5</sup>Beta-Glucuronidase; stool. (n.d.). Retrieved August 20, 2021, from <https://www.doctorsdata.com/beta-glucuronidase-stool/>

<sup>6</sup>Briden, D. L. (2020, February 24). How your gut affects your hormones. Retrieved August 20, 2021, from <https://helloclue.com/articles/cycle-a-z/how-your-gut-affects-your-hormones>

<sup>7</sup>Ervin SM; Li H; Lim L; Roberts LR; Liang X; Mani S; Redinbo MR; (n.d.). Gut microbial  $\beta$ -glucuronidases reactivate estrogens as components of the estrobolome that reactivate estrogens. Retrieved August 20, 2021, from <https://pubmed.ncbi.nlm.nih.gov/31636122/>

## Therapeutic Plan Suggestions

Let's review how truly simple it can be to address this complex scenario with your patients.  
We must first rebalance the microbiome!

Estrogen/Hormone Imbalance (resulting from gut dysbiosis) 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 <a href="#">Herxheimer reaction</a> observed/worsens.	
ADDITIONAL SUPPORT		
Proflora™ 4R	1 capsule any time	
Olivirex®	2 capsules 3x/day	
Biotonic®	20 drops 2x/day	
It is essential to maintain a healthy oral and gut microbiome for hormonal balance in the body. Along with supporting the microbiome, the practitioner can support other systems that may be contributing to hormonal imbalance, such as thyroid health.		

## Additional Products

### Calcium-D-Glucarate

Specifically hinders and lowers the enzyme beta-glucuronidase

### Butyrate

If the patient needs specific post-biotic, short-chain fatty acid support

### Liver Nutrients

Methylated B vitamins, amino acids, minerals, N-Acetyl-L-Cysteine, Glutathione

## Questions?

For clinical questions, email [clinical@biocidin.com](mailto:clinical@biocidin.com)  
or call 800-775-4140, x3.



\*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.