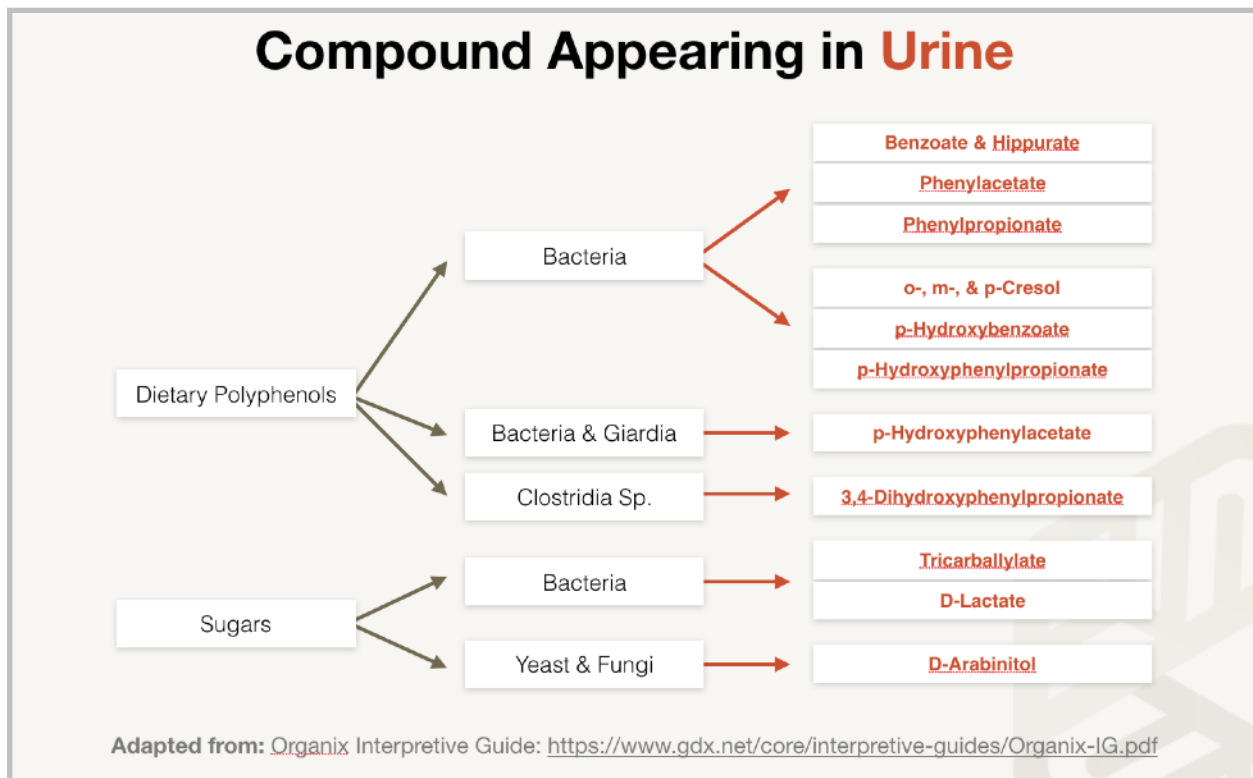


# Gut Diagnosis Organic Acids Review



## MARKERS FOR MICROBIAL OVERGROWTH

- Bacteria and yeast produce metabolites of small molecular weight that can appear in urine.
- These compounds reveal metabolic activities of the microbes that inhabit the mucosal layer and the lumen of the gut.
- Production of organic acids often occurs in the terminal ileum or the ascending colon.
- Therefore, **organic acids testing cannot be used to diagnose SIBO** because this test cannot tell us whether production is in the small intestine or the large intestine.
- However, it may provide supporting evidence when breath test results are equivocal.

Specific compounds that are **generated by each person depend on available substrates and the species of organisms that are present**. Substrates include dietary polyphenols: flavones like parsley, celery, and peppermint; flavonols like cranberries, onions, and peppers; flavanones like citrus; catechins like grapes and plums; anthocyanins like cherries, raspberries, and blueberries; and epicatechins like green and black tea and chocolate. Amino acids and carbohydrates can also serve as substrates for some organic acids.

## CONCERNS REGARDING USING THE ORGANIC ACIDS TESTING IN PRACTICE.

1. Research supporting these markers is not as strong as stool markers or breath testing.
2. We see a lot of variation in test results depending on what the patient is eating. We've seen some strange variation in results across relatively short time periods, without a lot of explanation for why the results vary that much.
3. Uncertainty regarding optimal ranges.

## GENOVA ORGANIX DYSDIOSIS VERSUS GREAT PLAINS LAB MICROBIAL ORGANIC ACIDS TEST (MOAT):

1. Organix uses D-arabinitol instead of arabinose for yeast.
  - a. There is more research behind D-arabinitol as a marker.
  - b. There is not sufficient convincing evidence to support arabinose as a marker for fungal overgrowth, especially if it's the only thing that's elevated on the test, which you'll frequently see with the MOAT test.
2. Organix also measures D-lactate, which is being investigated as an independent marker for SIBO and for leaky gut.
3. Great Plains Lab test has more clostridial markers and more fungal markers overall, including markers that may indicate exposure to mold, which the Organix test does not have,
4. We use Genova Organix more frequently, but we use the Great Plains lab in cases of kids with behavioral or cognitive mood disorders because I think some of the clostridial markers in particular can be helpful in those cases.

Interpretation of benzoate and hippurate patterns			
Benzoate	Hippurate	Other Bacterial Markers	Interpretation
Low	Low	No elevations	Low intake of benzoate; normal intestinal microbes
		Multiple elevations	Low intake of benzoate; microbial overgrowth w/o polyphenol
High	Low	No elevations	Glycine deficiency; high intake benzoate in diet
		Multiple elevations	Glycine deficiency; microbial overgrowth
Low	High	No elevations	Normal Phase II detox; normal intestinal microbes
		Multiple elevations	Normal Phase II detox; microbial overgrowth
High	High	No elevations	High benzoate intake; partial conversion to hippurate
		Multiple elevations	High benzoate intake; microbial overgrowth

Adapted from: Lord, R & Bralley J. Laboratory Evaluations for Functional and Integrative Medicine. Metametrix Institute, Duluth, Georgia, 2008.

## **BENZOATE:**

- Produced by bacterial metabolism of dietary polyphenols.
  - If **elevated with no other markers**, may just indicate **high dietary** intake of **polyphenols**.
- Elevation can be a marker of bacterial overgrowth or impaired phase 2 detox capacity due to glycine and/or pantothenic acid insufficiency.
- High benzoate can also be caused by ingestion of a benzoic acid, which is found in processed and packaged foods like pickles, soda, or lunch meats, or naturally in foods like cranberries.
- Often elevated in conjunction with hippurate, which is a normal byproduct of benzoate metabolism.

## **PHENYLACETATE (PAA)**

- Byproduct of intestinal action on polyphenols, tyrosine, or phenylalanine.
  - Normally present in low concentrations
- Phenylketonuria (PKU), an inherited disorder that leads to accumulated PAA levels.
  - Can lead to neurotoxicity and brain damage
- In most patients there is slight elevation, which is indicative of microbial overgrowth.
  - High levels should be referred to an inherited disease specialist.

## **PHENYLPROPIONATE (PPA)**

- Byproduct of intestinal action on polyphenols and phenylalanine.
- Metabolized by medium-chain acyl-CoA dehydrogenase (MCAD) and normally not in urine.
- Very high levels indicate MCAD deficiency.
- Signs and symptoms (vomiting, lethargy, hypoglycemia) occur early in childhood.
- Mild elevation is a sign of microbial overgrowth.
- Refer out for very high levels.

## **P-HYDROXYBENZOATE**

- From bacterial metabolism of polyphenols and tyrosine.
- Elevations indicate microbial overgrowth, especially E. coli.

### **P-HYDROXYPHENYLACETATE**

- From bacterial metabolism of tyrosine.
- Useful in detecting small bowel disease caused by overgrowth of anaerobes.
- Very high in patients with cystic fibrosis or other conditions that impair amino acid absorption.

### **INDICAN**

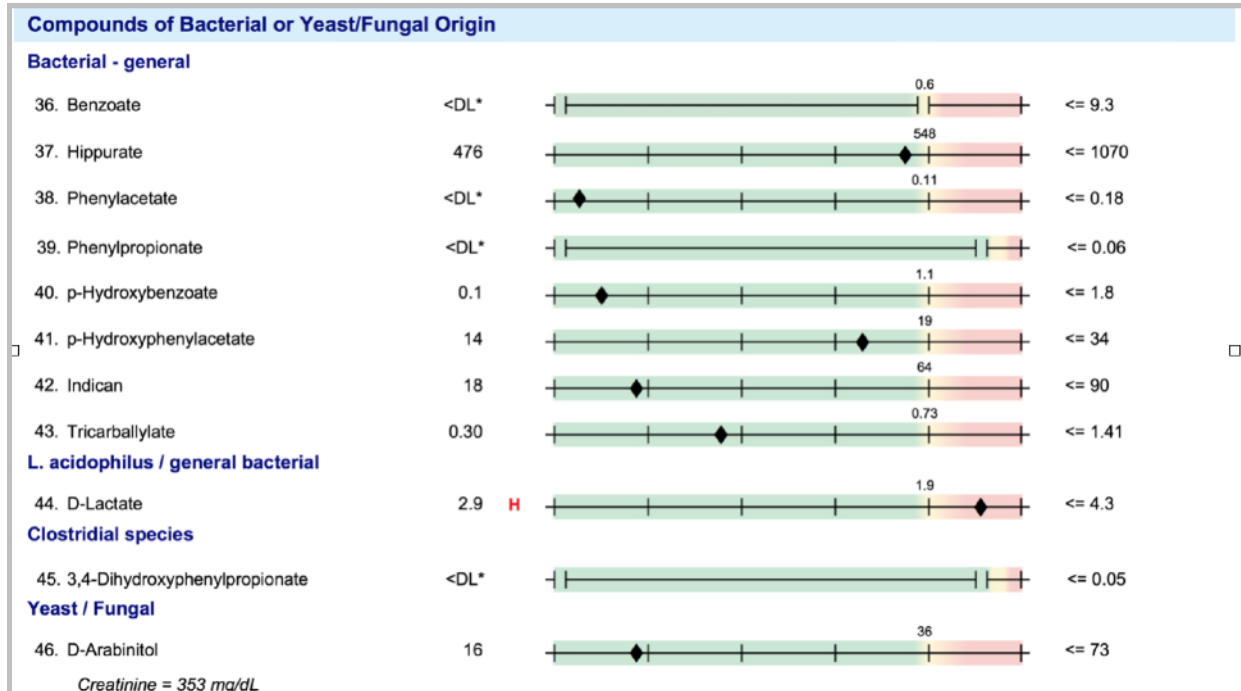
- From bacterial metabolism of tryptophan.
- Elevations indicative of bacterial overgrowth in upper small bowel.
- Can help differentiate pancreatic insufficiency from biliary stasis as a cause of steatorrhea (fatty stools).
  - High indican → pancreatic insufficiency
  - Normal indican → biliary stasis
- Can also signify low stomach acid since incomplete protein digestion can cause elevations.

### **TRICARBALLYLATE**

- Produced by aerobic bacteria.
- Extremely high affinity for magnesium, preventing magnesium absorption.
- When elevated, supplementation with magnesium in addition to gut treatment is necessary.

### **D-LACTATE**

- Major metabolic byproduct of beneficial bacteria species in the gut like *Lactobacillus acidophilus*.
  - Different isomer of lactic acid than the ones produced during exercise.
- Elevated in cases of carbohydrate malabsorption, which allows *L. acidophilus* to flourish.
- *Lactobacillus* species are common in probiotics; best to avoid these when D-lactate is elevated.
  - Red flag for SIBO if patient gets worse with these probiotics.
- Symptoms include GI distress and neurological and cognitive symptoms.



In the example above, D-lactate is high-normal and no other markers are elevated. Would you treat in this case? That depends on the overall presentation of the patient.

This patient was a 30-year-old female with severe and debilitating eczema that migrated all over her body after starting on her neck, arms, hands, and face. She had to be on steroid creams to control it.

Her breath test was equivocally positive for SIBO, and her stool test was unremarkable. In this case, even though there weren't a lot of really strong markers for dysbiosis, microbial overgrowth, or other gut issues, we did decide to do a therapeutic trial of the antimicrobial protocol. Based on my experience and my research, I know that there's a strong connection between the gut and the skin, and the patient also intuitively felt that this was the case for her, and it's a good thing that we did because this patient experienced a 70 percent improvement after doing a round of the antimicrobial protocol. We later discovered in additional follow-up testing that she had high levels of cadmium and arsenic on her blood metals panel, and she got another 20 percent improvement after doing metal detox.

### **3,4-DIHYDROXYPHENYLPROPIONATE (3,4-DHPP)**

- Produced by Clostridia species and elevated in overgrowth.
- Can lead to increased dopamine due to inhibited dopamine metabolism/breakdown.
  - Potential neurologic symptoms, as well as mood and behavioral problems.

### **D-ARABINITOL**

- Metabolite of most pathogenic Candida species.
  - One of the most sensitive markers for invasive candidiasis.
- A better indicator for fungal overgrowth than blood cultures.