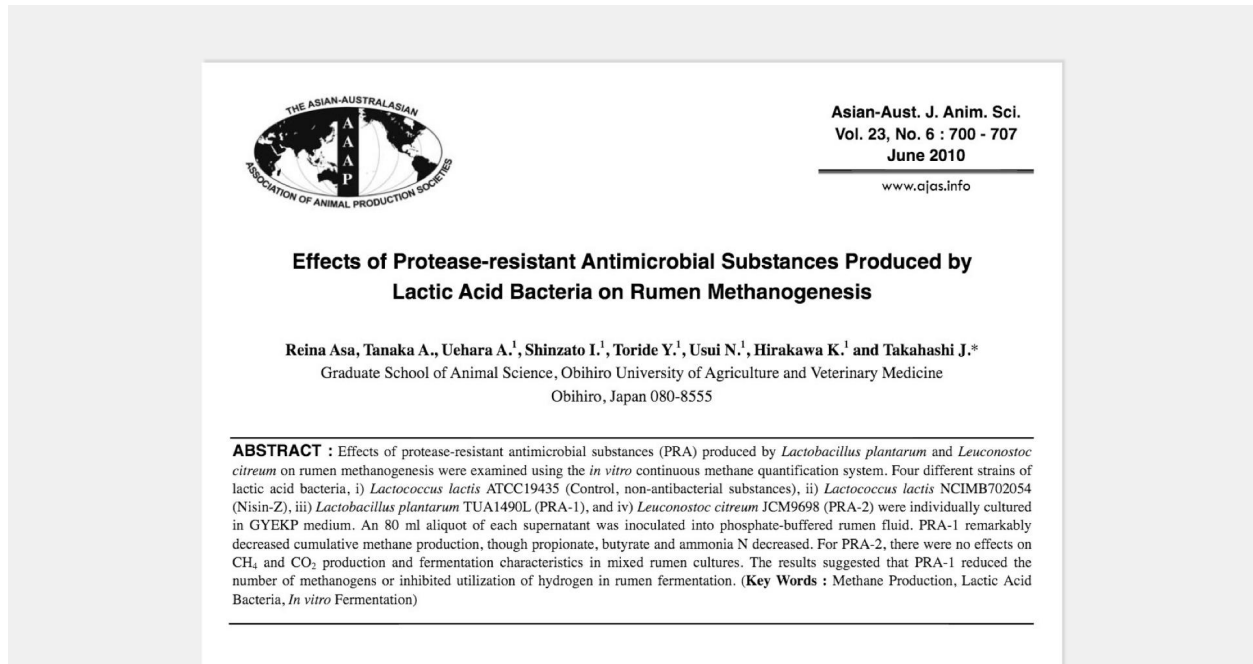


# Gut Treatment Protocols: SIBO, Part 4



2010 Study

A study on this slide shows that *L. plantarum* has strong activity against methanogens in cows. This is interesting because *L. plantarum* is one of the few probiotics that does seem to work for constipation. So perhaps it's working by reducing methane production. The recommended dose is 10 billion CFU per day. Jarrow Ideal Bowel Support is one of the few products in the market currently that only contains *L. plantarum*.

## Effect of *Lactobacillus reuteri* (DSM 17938) on methane production in patients affected by functional constipation: a retrospective study

V. OJETTI<sup>1</sup>, C. PETRUZZIELLO<sup>1</sup>, A. MIGNECO<sup>1</sup>, M. GNARRA<sup>2</sup>,  
A. GASBARRINI<sup>1</sup>, F. FRANCESCHI<sup>1</sup>

<sup>1</sup>Department of Medical Sciences, Division of Gastroenterology, Catholic University of the Sacred Heart, Rome, Italy

<sup>2</sup>Dermatology Unit, Columbia University Medical Center, NYC, NY, USA

**Abstract. – OBJECTIVE:** Constipation is a common symptom affecting up to 30% of the Western population and is strongly associated with the presence of intestinal methanogens, which may directly inhibit motor activity. Two recent studies performed on adult and children af-

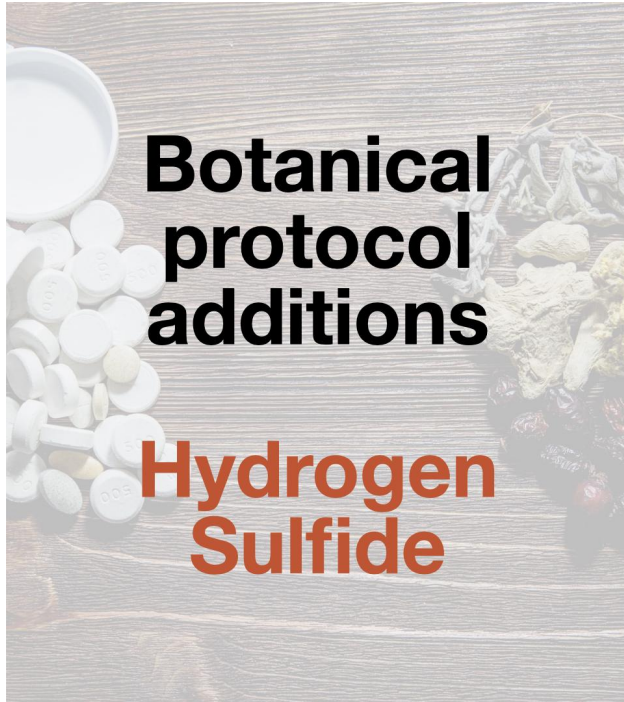
### Introduction

Constipation is defined by Rome III criteria (Table I) as less than three defecations in a week, often with hard stools, excessive straining, and/

2017 Study

The study on this slide shows *L. reuteri* improved chronic constipation via a significant decrease in methane production in adults using [the] lactulose breath test. [The] recommended dose is 10 billion CFU per day. BioGaia Gastrus by Everidis Health Sciences is our preferred brand product.

I think we are still just beginning to understand what is driving the overproduction of hydrogen sulfide and the mechanisms [at] play for H<sub>2</sub>S excess SIBO. I've listed some of the botanical protocol add-ons that target H<sub>2</sub>S excess at different places in the metabolic pathway. Some are cofactors essential for the sulfate reduction pathway, and others help to reduce the impact of [H<sub>2</sub>S] excess. A reminder that a lot of these patients have trouble tolerating alcohol, have trouble sleeping, [and have a reaction] to eggs and potentially a good list of other foods.



**Molybdenum (Mo-Zyme Forte by Biotics Research):** cofactor for sulfite oxidase enzyme and essential for the breakdown of sulfite to sulfate.

**Hydroxocobalamin (Hydroxo B12 lozenge by Seeking Health):** binds to H<sub>2</sub>S and reduces the biologic activity of H<sub>2</sub>S.

**Bismuth (Pepto Bismol, Bio-HPF):** reduces H<sub>2</sub>S-producing/sulfate-reducing bacteria.

**Zinc acetate (many brands):** binds to H<sub>2</sub>S and replaces potential loss as a result of environmental toxin burden (like glyphosate).

**Activated charcoal (many brands):** binder for endotoxins and H<sub>2</sub>S.

**Korean Red Ginseng (Pure Encapsulations):** suppresses activity of CBS and CSE enzymes, reducing H<sub>2</sub>S production internally.

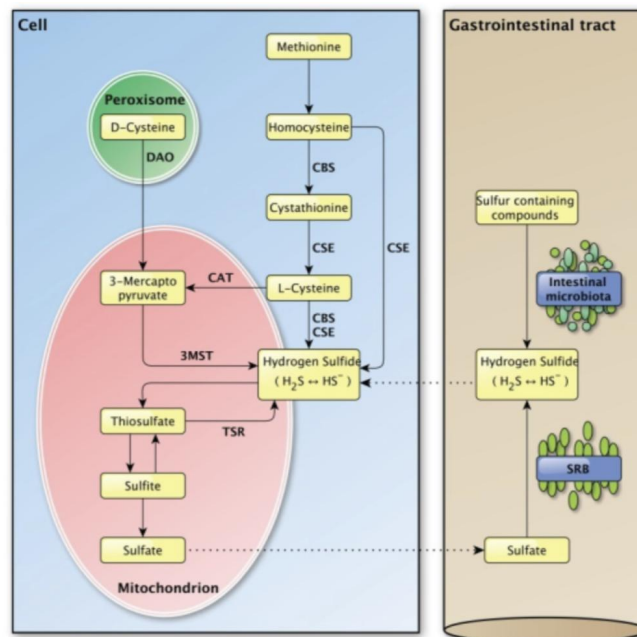
Molybdenum is a trace mineral. We just need a small amount of it every day because it is only used by a few processes in the body. One of those processes is turning sulfite, thought to be the more problematic form, into sulfate, the end product used for beneficial processes. If there isn't enough molybdenum around, then the enzyme making this conversion slows down, leading to excess sulfite, which can cause more symptoms and problems. The typical dosing for this is 150 micrograms twice daily.

Hydroxy B12, [a] form of [vitamin] B12, lowers the level of hydrogen sulfide in the blood by binding to H<sub>2</sub>S and rendering it less biologically active. I have used it both intramuscularly and orally, but I have used it sublingually mostly in my practice—a few thousand micrograms daily.

Using bismuth in [gastrointestinal] (GI) disorders is not [a] new concept. Many studies have shown the combination of bismuth with antibiotics to increase [the] effectiveness of treatment. More specifically, studies show bismuth reduces H<sub>2</sub>S production or sulfate-reducing bacteria. The typical dose is 400 to 500 milligrams, three to four times daily. We'll talk a little bit more about duration and treatment as we go through the presentation.

Zinc is two-fold here. Studies have shown that zinc binds to H<sub>2</sub>S, therefore reducing levels, and glyphosate also strongly chelates zinc, reducing levels in the body. So if glyphosate is playing a role in impaired sulfur metabolism and zinc levels are low, then replacing zinc makes sense on

multiple levels. To be honest, I haven't been able to find the suggested dosing for this. Often, it just says hefty doses. I've generally been using about 60 to 75 milligrams per day and continuing to monitor levels. Activated charcoal can be used as a binder for endotoxins and hydrogen sulfide, and Korean ginseng has been shown to suppress activity in the CBS and CSE enzyme, thus reducing H<sub>2</sub>S production internally. It seems to work pretty well for patients [who] also present with fatigue and brain fog.



© Perridon, B., Leuvenink, H., Hillebrands, J., van Goor, H. and Bos, E. (2016). The role of hydrogen sulfide in aging and age-related pathologies. *Aging*, 8(10), pp.2264-2289.

Like I mentioned, when it comes to [H<sub>2</sub>S] excess, I think we're still just beginning to understand what is driving the overproduction of [H<sub>2</sub>S] and causing symptoms in some people. At the time of this recording, there are a handful of different camps and theories. So I'm just going to do my best to give you a brief overview of those things. [There are] many roles for sulfur in the body. First, sulfation occurs in the liver to help detox and excrete molecules in the urine. Second, it helps with the production of collagen, which is a substance that forms connective tissues, cell structure, and artery walls. And third is protein synthesis. Additionally, it's part of keratin, giving strength to hair, skin, and nails. And sulfur in the body [is] dietary, and it's converted from sulfur to sulfate, partly through bacteria or through a series of oxidative steps and enzymatic actions. Inside the cell cystathionine beta-synthase (CBS) and cystathionine gamma-lyase (CSE), transsulfuration enzyme pathways use substrates like homocysteine, cystathionine, or cysteine to generate hydrogen sulfide. You might be familiar with this pathway because it's important in glutathione production. This pathway can be upregulated or downregulated, depending on

different genetic variants. In the gut, hydrogen sulfide can be produced by a variety of bacteria. The sulfate-reducing bacteria are ubiquitous in the gut and are predominantly *Desulfovibrio*, *Desulfobacter*, *Desulfobulbus*, [and] *Desulfotomaculum* genera. They are sulfate and sulfide to fuel metabolism with hydrogen sulfate as a byproduct. They use hydrogen as an electron donor, hence why we often see low levels of hydrogen on the breath test where the hydrogen sulfide excess is present.

The second source of hydrogen sulfide in the gut comes from the enzymatic conversion of the amino acid cysteine. This can be performed either by the colonic tissues or by specific anaerobic bacteria such as [*Escherichia coli*, *Salmonella enterica*, Clostridia, and *Enterobacter*. Additionally, *H. pylori* [have] been shown to generate hydrogen sulfide, while other gut bacteria like *E. coli*, *Klebsiella*, *Bacillus*, *Staphylococcus*, *Coryne*, and *Rhodococcus* can also generate the gas by a similar sulfate reduction, via sulfite reductase, actually. Researchers have suggested that the majority of hydrogen sulfide production occurs in the upper digestive tract, the stomach and small intestine, rather than the colon. Studies suggest that physiological levels of hydrogen sulfide may play important roles in maintaining the gut–blood barrier, modulating the inflammatory response, modulating vascular and circulatory homeostasis, and promoting colonic mucus production. However, excess levels have actually also been implicated in the pathogenesis of chronic inflammation, IBS symptoms, [inflammatory bowel disease] (IBD), and bowel cancer. So sulfide is an intermediate in the sulfur metabolism, but it can also be ingested via dietary sources. Sulfide is extremely toxic and can lead to significant oxidative damage, so it's important that the body can rapidly convert it to sulfate. The sulfide to sulfate conversion relies on an enzyme called sulfite oxidase (SUOX), which uses molybdenum as a cofactor. This results in [a] buildup of sulfite and sulfate deficiency. When we discuss theories of hydrogen sulfide excess or impaired sulfur metabolism, the leading theories are environmental toxin exposures, deficiency in nutrient cofactors, and/or some sort of genetic play. Some scientists and medical professionals, like Dr. Nye, feel that CBS mutations may be heavily involved in this process. The CBS enzyme drives the recycling of sulfur-containing compounds, and with heterozygous mutations, you may have a buildup of unstable sulfur and not enough usable sulfur. Then there [are] also the imbalances that impact enzymatic activity of sulfide oxidase. [These] imbalances [include] molybdenum deficiency, glyphosate substitution for glycine and protein synthesis, mercury and lead toxicity interfering with enzyme activity, and sulfide oxidation genetic polymorphisms.

In this scenario, it is suspected that the overproduction of hydrogen sulfide by microbes is a compensatory mechanism in the body to find another way to dispose of sulfide buildup in the gut. So [this is] helpful in the setting of someone who has sulfur metabolism issues, but is the presence of hydrogen sulfide excess also problematic?

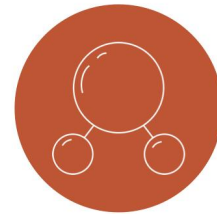
## Hydrogen sulfide SIBO treatment



Core SIBO  
protocol



Detox support



Sulfur  
metabolism  
support

When we're looking at hydrogen sulfide SIBO protocol treatments, we should consider both the impacts of hydrogen sulfide gas levels and what may be actually driving the overproduction. Some symptoms [that] impair sulfur metabolism include red hot symptoms like flushing, eczema, hives, other skin symptoms similar to that, alcohol intolerance, [and] sensitivities or reactions to sulfur-containing foods like eggs, garlic, onion[s], leeks, and cruciferous vegetables. This may sound very similar to histamine intolerance or mast cells, so it could be a little tricky to differentiate. But you may also see headaches, fast heart rate, or arrhythmias when you have something that's a little bit closer to histamine intolerance that you don't really see with hydrogen sulfide excess.

For hydrogen sulfide excess, we often use portions of the core SIBO protocol, plus some detox support and support for sulfur metabolism. I also generally test for urine glyphosate or, at the very least, talk about ways to reduce glyphosate exposure and its role in inhibiting sulfate production with a displacement of cofactors like molybdenum. In some cases, I will also test for the CBS variants using 23andMe or Genova's methylation plus genomic add-on panel. I think most of you know this, but it feels important to mention I don't really prescribe to the idea that you can create diets and supplement protocols and treatment plans based [on] a genetic report alone. I think genetic reports can be helpful; [they're] super fascinating, but it all really has to be interpreted together, combining labs, symptoms, [and] genetics to get the whole picture so that you can design a treatment plan and guide a patient with the most comprehensive information possible.



So what about the efficacy of the core botanical protocol, plus the additions we spoke about? We haven't really done any formal studies, but we're using several evidence-based treatments, as you can see. Every component in the treatment is evidence-based, and they have confirmed efficacy, and the efficacy of some of the individual components of the treatment are as high as 45 to 50 percent or more.

# 70-75%

When we combine them all together, we would expect a higher efficacy than any single treatment alone. I know that's not always the case, but generally, we do see that. And it depend[s] on the patient's history and presentation, but I would probably estimate that we have about 70 to 75 percent efficacy in treating SIBO with the core protocol. Some caveats to this, though, [are] that one, with the ability now to test for hydrogen sulfide SIBO, we have just started treating hydrogen sulfide excess SIBO aggressively, so we don't have as much to report back on it just yet. But so far, what we have seen is comparable to the above 70 to 75 percent efficacy. Second, as we will discuss in more detail later in the presentation, SIBO can be pretty tricky and recalcitrant, and I think, at this point, most Functional Medicine practitioners that have been treating SIBO for some time realize that this is likely because of either undiagnosed or untreated imbalances and burdens that allow for the overgrowth to occur.