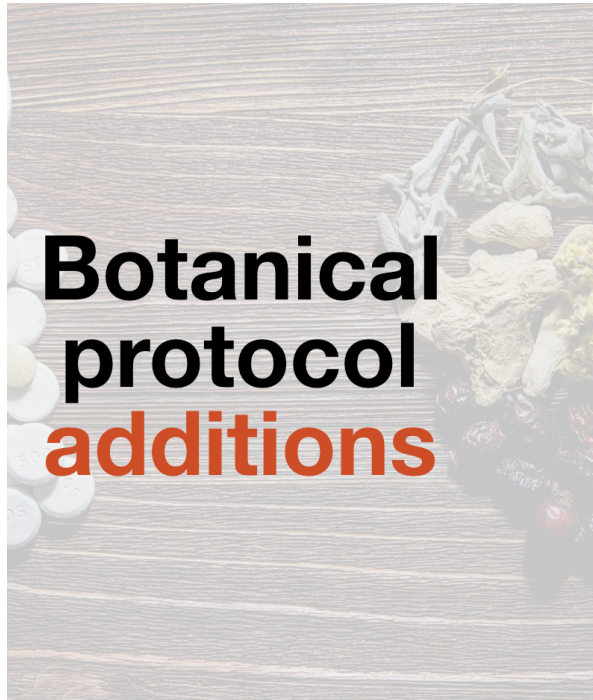


# Gut: Treatment Protocols - SIBO, Part 3



**Iberogast (Tribute Pharmaceuticals in US/ Can.):** prokinetic; contains 9 botanical “bitters” that stimulate bile production and motility

**MotilPro (Pure Encapsulations):** prokinetic containing 5-HTL, acetyl-L-carnitine, B6, and ginger

**Betaine HCL w/pepsin (many brands):** hydrochloric acid supplement with pepsin; HCL and pepsin help with protein digestion, which is often impaired in SIBO patients

**Digestive enzymes (many brands):** help with breakdown of protein, carbs, fat; can be used w/patients with severe gas, bloating, etc.

**PC (Seeking Health/Body Bio):** for patients with fat malabsorption and impaired bile metabolism

Okay, so here are some additions and customizations that you can make to the core botanical protocol that we talked about. And these are all dependent on the patient’s particular presentation. So the first is called Iberogast, and this is a blend of bitters, nine botanical bitters that stimulate bile production and motility. And it’s been used in Europe extensively for 45 years, very well studied and it is a prokinetic, so it improves intestinal motility. So we will tend to use it in patients who have constipation, because constipation is a big risk factor for SIBO recurrence, and I think it can improve the treatment efficacy by possibly stimulating the migrating motor complex, which Dr. Pimentel has argued is deficient in people with SIBO. We also will use it in patients who have significant gas and bloating, because it tends to help a lot with that.

The second supplement is called MotilPro, which is from Pure Encapsulations. It’s a prokinetic, so it also stimulates gut motility, but it does it in a different way than Iberogast. MotilPro contains 5-HTP, which is a precursor to serotonin, and serotonin stimulates gut motility. It’s a neurotransmitter; you’re probably familiar with it from discussions about depression and the idea that depression is caused by a serotonin deficiency, which is, by the way, false. (That’s another discussion for another time.) It also has acetyl-L-carnitine, B6, and ginger, so if the patient’s gut

motility issues are due to low serotonin in the gut, and there's 400 times more serotonin than there is in the brain, then MotilPro can be really helpful, but if their motility issues are not due to serotonin, it really won't do much at all, in our experience. So if I had to choose only one prokinetic to use in a treatment, it would be Iberogast, but some patients do respond very well to MotilPro.

Then we have Betaine hydrochloric acid with pepsin. This is stomach acid, HCl is stomach acid, you know this by now. And pepsin is an enzyme that helps with protein digestion, which is often impaired in SIBO patients, so I don't know that this helps the treatment result, per se, but it can certainly make patients more comfortable and help with their symptoms while they're doing it. Same is true for digestive enzymes; they help with the breakdown of protein, carbohydrates, and fat and can be used with patients with severe gas, bloating, etc., who just need some support while you're doing the treatment.

The last supplement that we might consider adding is phosphatidylcholine, or PC, and this we use for patients with fat malabsorption and impaired bile metabolism, because phosphatidylcholine is a really important nutrient for bile synthesis and metabolism.

So what about the efficacy of this core botanical protocol plus additions? I haven't done any formal studies of it, 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 is as high as 45, 50 percent or more, so when we combine them all together, we would expect a higher efficacy than any single treatment alone. It depends on the patient history and presentation, but I would estimate that we have about 70 to 75 percent efficacy in treating SIBO with this treatment, and it may even be higher since we recently added partially hydrolyzed guar gum.

## Botanical protocol dosages

Nutreaceutical	Dosage
<b>GI Synergy</b>	1 packet BID ( <i>with breakfast and dinner</i> )
<b>Lauricidin</b>	1 scoop TID ( <i>with each meal</i> )
<b>Interfase Plus</b>	3-4 capsules BID ( <i>on empty stomach</i> )
<b>TerraFlora</b>	1 capsule ( <i>with lunch</i> )

Here are the botanical protocol dosages. Don't worry about writing these down. We'll provide you with a handout with the dosages, timing, and detailed instructions. GI Synergy: One packet twice a day with breakfast and dinner. Lauricidin: One scoop three times a day with breakfast, lunch, and dinner. Interfase Plus: Three to four capsules twice a day on an empty stomach. Terraflora: One capsule at lunch time.

## Botanical protocol **additional dosages**

Nutreaceutical	Dosage
<b>Iberogast</b>	20 drops TID just before meals
<b>MotilPro</b>	1-2 caps TID on empty stomach
<b>Betaine HCL with pepsin</b>	1-5 650 mg capsules before meals; sensitive patients can use 200 mg capsules
<b>Digestive enzymes</b>	Depends on manufacturer; take just before meals
<b>Phosphatidylcholine</b>	3,000-6,000 mg per day

With Iberogast, we recommend 20 drops three times a day just before meals. MotilPro, one to three capsules three times a day on an empty stomach, if we use that. Betaine hydrochloric acid, we're going to be talking about HCl protocol, we may have already talked about it, but typically one to five 650 milligram capsules before meals, or more sensitive patients can use 200 milligram capsules. Digestive enzymes, it really depends on the manufacturer, but you can take them just before meals, with meals, and then phosphatidylcholine, we recommend 3,000 to 6,000 milligrams per day.

## Botanical treatment **duration** based on LBT results

H2 @80/90 min	Sum of H2 @80/90 min	Duration
<45 ppm	<160 ppm	<b>4 weeks</b>
45-70 ppm	160–250 ppm	<b>8 weeks</b>
>70 ppm	>250 ppm	<b>12 weeks</b>

As for the duration of the protocol, as we've discussed, it should be based on lactulose breath test results, as that study with rifaximin showed. So this is kind of how we think about as a rough guideline. With mildly positive results of hydrogen below 45 parts per million, or a sum of hydrogen below 160 parts per million, we might do 30 days of the botanical protocol. If hydrogen at 80 or 90 minutes, depending on the lab, some labs report values at 80 minutes and some report at 90, but between 45 parts per million and 70 parts per million, or a sum of 160 to 250 parts per million, we would do eight weeks. And then if hydrogen is over 70 parts per million at 90 minutes, or the sum of hydrogen at 80 to 90 minutes is over 250 parts per million, then we might do 12 weeks duration. And we would always want to retest at the end of the treatment period.

## **Addition of Neomycin to Rifaximin treatment for elevated methane**

<b>Treatment</b>	<b>Clinical Response</b>	<b>Breath Test Normal</b>
<b>Rifaximin alone</b>	<b>56%</b>	<b>28%</b>
<b>Neomycin alone</b>	<b>63%</b>	<b>33%</b>
<b>Rifaximin + Neomycin</b>	<b>85%</b>	<b>87%</b>

Adapted from: Low et al. J Clin Gastroenterol. 2010 Sep;44(8):547-50

So what about methane? In conventional settings, when methane is elevated, neomycin is the drug that's added to rifaximin treatment to make it more effective, and the combination of rifaximin plus neomycin, as you can see here on this slide, is 85 percent effective in terms of clinical response, versus just 56 percent for rifaximin alone, or 63 percent for neomycin alone. And it's 87 percent effective for normalizing the breath test versus much lower 28 percent for rifaximin alone, or 33 percent for neomycin alone. So as you can see, it's very important to customize the treatment if methane is elevated.

If you do a little bit of research with neomycin, you might get scared away from it because you'll see that it's associated with serious adverse events; it has a black box warning for neurotoxicity, including ototoxicity and nephrotoxicity. However, if you dig a little deeper, you'll find that this happens almost exclusively to topical neomycin applied directly to the ear and parenteral neomycin, not oral neomycin. In 25 years of oral neomycin use, there have only been a few cases of ototoxicity, and this is in patients that were taking it long term, for more than six months, and/or had existing kidney problems or serious gastrointestinal inflammation. It doesn't have quite the stellar safety profile that rifaximin has, but overall I believe it's quite safe. It's only 3 percent absorbed in the GI tract. That said, it does have some contraindications that you should be aware of: neomycin is an aminoglycoside which can cross the placenta and cause fetal harm, so it should not be used during pregnancy, and it would be contraindicated in patients with serious inflammatory or ulcerative gastrointestinal disease, like ulcerative colitis or IBD, because of the potential for enhanced gastrointestinal absorption in those cases.

# Atrantil for elevated methane

1

First, *M. balsamea* Willd extract (peppermint) calms the small bowel. This gives Atrantil's two other botanicals the right amount of time to work most effectively.



2

Flavonoids from Quebracho extract (a South American hardwood tree) soak up hydrogen and create an unfriendly environment for the archaeobacteria. They weaken the cell walls—setting the stage for Atrantil's third botanical.



3

Saponin/flavonoid, a natural antibacterial from Conker Tree extract, reducing methane production. It binds to the reductase enzyme in the weakened archaeobacteria—stopping methane production.



What about alternatives to neomycin for methane? One possibility is the supplement called Atrantil created by gastroenterologist, Dr. Kenneth Brown, who was involved in the early rifaximin trials, and he recognized that rifaximin alone doesn't work well for methane-predominant SIBO and even rifaximin plus neomycin or metronidazole does not always work either. So, he studied the literature to find some plant extracts that might have effect against methane.

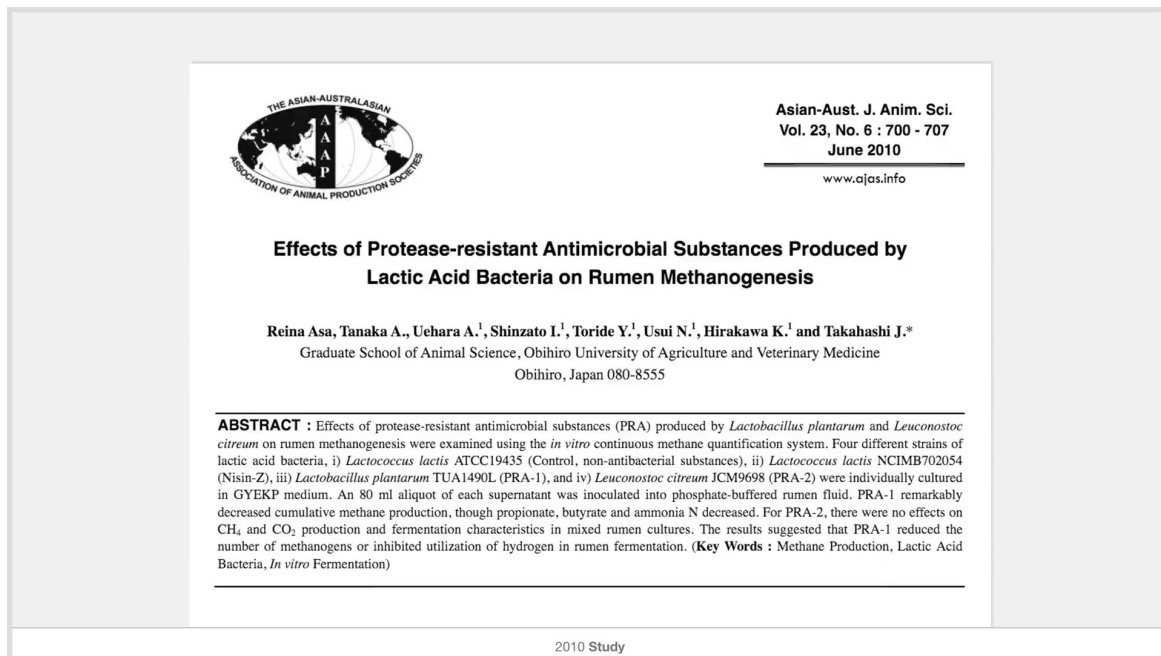
What he came up with was a combination of peppermint, conker tree, and quebracho. Peppermint slightly reduces small bowel mobility and gives the conker tree and quebracho a chance to work. The flavonoids in quebracho soak up the hydrogen produced by bacteria, and remember, the methanogens feed on hydrogen, so anything that reduces hydrogen production will also reduce methane production, and then those flavonoids also create an unfavorable



environment for archaeobacteria. Then, the saponins in conker tree extract bind to the reductase enzyme and the weakened archaeobacteria and stop methane production.

So, the dose for Atrantil is two capsules 3 times a day, although it's often recommended that some patients start with a lower dose if they have sensitivity to supplements where they think they have a Herxheimer or die-off reaction. Some patients in our practice have gone as high as 5 capsules 3 times a day for a temporary period if they respond really well to it.

Atrantil is supported by two peer-reviewed studies which we'll put links to in the resources section. We haven't had a lot of success reversing really high methane levels with Atrantil alone, but adding it to botanical or rifaximin protocol definitely increases its efficacy in our somewhat limited experience so far. Note that Atrantil can be used empirically for IBS with bloating and constipation even when SIBO isn't present and we'll talk about this a little more later. It can also be used at a maintenance dose of 1 capsule 2-3 times a day to prevent recurrence of methane-predominant SIBO, also note that the instructions for Atrantil say "Not to take with probiotics." This comes from an early bias against probiotics in SIBO treatment, but as I've mentioned, the few studies that we do have that looked at probiotic use during SIBO treatment suggest they may improve efficacy. I also did a podcast a while back with Dr. Brown discussing Atrantil in more detail and talking about some of these questions and so we'll put a link for that in the resources section as well.



Another option for methane is *Lactobacillus plantarum*. A study on this side shows that *Lactobacillus plantarum* has a strong activity against methanogens in cows. This is interesting because *Lactobacillus 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 on the market currently that only contains *Lactobacillus plantarum*.

## Length of botanical treatment when methane is elevated

Presentation	Treatment
<25 ppm highest value before 120 min	30 days
25–50 ppm highest value before 120 min	60 days
>50 ppm highest value before 120 min	90 days

There's another option if you are able to prescribe rifaximin, or even just with botanical protocol. The Korean study I mentioned before, which looked at correlating treatment duration with lactulose breath test results, found that in patients who had elevated methane, granted there weren't very many of them in that study because that study was looking at patients with IBS-D, diarrhea, but in the few patients that had elevated methane, 30 days of rifaximin treatment normalized methane in all patients. So it's possible that the standard 10- to 14-day courses of rifaximin aren't effective on their own for methane, but if you use longer courses of rifaximin or longer courses of botanical protocols, they are more effective for methane.

So, considering that, these are the durations of treatment I recommend when methane is elevated for the botanical protocol, and possibly for rifaximin. So this is just empirical, it doesn't come from a study, there haven't been any studies that I'm aware of correlating duration of treatment with breath test results for methane, or even symptoms, but you can combine this with the other chart we saw previously for hydrogen values and how long you should treat. And if either methane or the hydrogen value is exceeded or the highest, then you would then go up to the next level. So, less than 25 parts per million of methane before 120 minutes, the highest value we're talking about here, and obviously not a sum, would be a 30-day treatment. Methane values of 25 to 50 parts per million before 120 minutes would be 60 days, and then any methane value above 50 parts per million before 120 minutes would be a 90-day treatment.