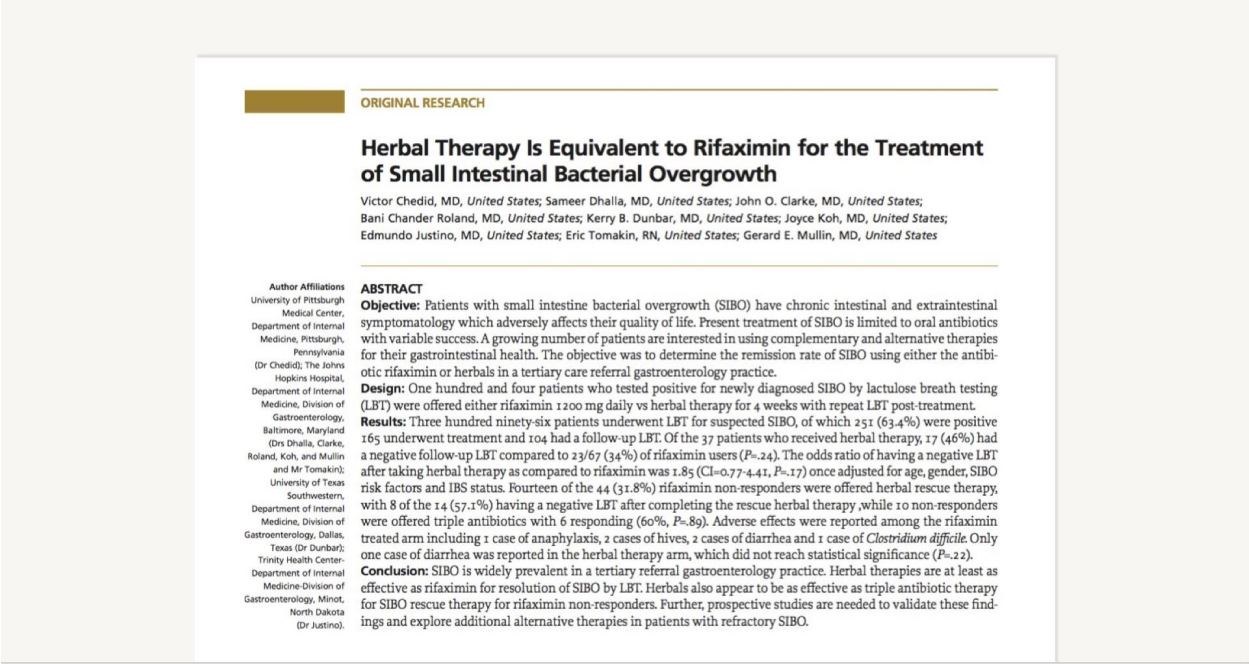
KRESSER INSTITUTE FOR FUNCTIONAL AND EVOLUTIONARY MEDICINE

Gut Treatment Protocols: SIBO, Part 2

or some combination of these three

The second principle is that treatment should be based on whether hydrogen is elevated, methane is elevated, or hydrogen sulfide is elevated, or some combination of the three. We previously discussed the typical patterns we see based [on] the competitive gas model. But there are different combinations that are possible. I think this is important for both botanical and prescription treatment options when considering what to do. And with botanical treatments, there [are] a little less changes to be made because we're able to use base protocols with adjustments vs. with prescriptions, [for] which we may use a different treatment altogether. Retesting after treatment is absolutely essential. Without it, you really have no idea what's going on. So if the patient doesn't feel better, it could be because the treatment wasn't successful, or it could be that SIBO wasn't causing their symptoms, and without retesting, you can't know the answer to this question for sure. You need to explain to patients upfront that retesting is a crucial part of the treatment protocol, prepare them for it in advance, and let them know that they may need multiple retests, depending on the success of the treatment.

Let's move on to talking about antimicrobials. I'm going to start with the botanical treatment. A study in 2014 compared botanical therapy to treatment with rifaximin, which is the drug of choice, and this was an open-label trial.



ORIGINAL RESEARCH

Herbal Therapy Is Equivalent to Rifaximin for the Treatment of Small Intestinal Bacterial Overgrowth

Victor Chedid, MD, *United States*; Sameer Dhalla, MD, *United States*; John O. Clarke, MD, *United States*; Bani Chander Roland, MD, *United States*; Kerry B. Dunbar, MD, *United States*; Joyce Koh, MD, *United States*; Edmundo Justino, MD, *United States*; Eric Tomakin, RN, *United States*; Gerard E. Mullin, MD, *United States*

Author Affiliations
University of Pittsburgh Medical Center, Department of Internal Medicine, Pittsburgh, Pennsylvania (Dr Chedid); The Johns Hopkins Hospital, Department of Internal Medicine, Division of Gastroenterology, Baltimore, Maryland (Drs Dhalla, Clarke, Roland, Koh, and Mullin and Mr Tomakin); University of Texas Southwestern, Department of Internal Medicine, Division of Gastroenterology, Dallas, Texas (Dr Dunbar); Trinity Health Center-Department of Internal Medicine-Division of Gastroenterology, Minot, North Dakota (Dr Justino).

ABSTRACT

Objective: Patients with small intestine bacterial overgrowth (SIBO) have chronic intestinal and extraintestinal symptomatology which adversely affects their quality of life. Present treatment of SIBO is limited to oral antibiotics with variable success. A growing number of patients are interested in using complementary and alternative therapies for their gastrointestinal health. The objective was to determine the remission rate of SIBO using either the antibiotic rifaximin or herbals in a tertiary care referral gastroenterology practice.

Design: One hundred and four patients who tested positive for newly diagnosed SIBO by lactulose breath testing (LBT) were offered either rifaximin 1200 mg daily vs herbal therapy for 4 weeks with repeat LBT post-treatment.

Results: Three hundred ninety-six patients underwent LBT for suspected SIBO, of which 251 (63.4%) were positive 165 underwent treatment and 104 had a follow-up LBT. Of the 37 patients who received herbal therapy, 17 (46%) had a negative follow-up LBT compared to 23/67 (34%) of rifaximin users (P=.24). The odds ratio of having a negative LBT after taking herbal therapy as compared to rifaximin was 1.85 (CI=0.77-4.41, P=.17) once adjusted for age, gender, SIBO risk factors and IBS status. Fourteen of the 44 (31.8%) rifaximin non-responders were offered herbal rescue therapy, with 8 of the 14 (57.1%) having a negative LBT after completing the rescue herbal therapy ,while 10 non-responders were offered triple antibiotics with 6 responding (60%, P=.89). Adverse effects were reported among the rifaximin treated arm including 1 case of anaphylaxis, 2 cases of hives, 2 cases of diarrhea and 1 case of *Clostridium difficile*. Only one case of diarrhea was reported in the herbal therapy arm, which did not reach statistical significance (P=.22).

Conclusion: SIBO is widely prevalent in a tertiary referral gastroenterology practice. Herbal therapies are at least as effective as rifaximin for resolution of SIBO by LBT. Herbals also appear to be as effective as triple antibiotic therapy for SIBO rescue therapy for rifaximin non-responders. Further, prospective studies are needed to validate these findings and explore additional alternative therapies in patients with refractory SIBO.

2014 **Study**

Subjects were given the option of rifaximin at 1,200 milligrams per day, which is less than the current dose recommended by Dr. [Mark] Pimentel. They were given this option of rifaximin 1,200 milligrams per day for 30 days or two capsules each day of four different botanical formulas for 30 days. At the end of the 30-day period, 46 percent of people who were taking the botanicals had a normal lactulose breath test vs. 34 percent of [people who were taking] rifaximin. So the botanical protocol was 85 percent more likely to produce normal lactulose breath test results, although that was not statistically significant. Fourteen of 44 rifaximin non-responders were offered the botanical protocol at that point, and 57 percent of those non-responders had a normal lactulose breath test after that.

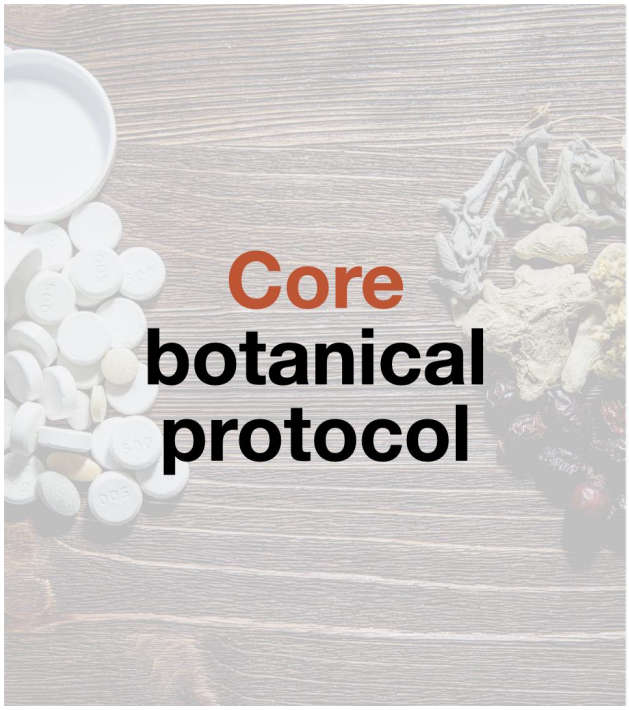
Ten of the non-responders were then reported in the rifaximin arm, but none were reported in the botanical arm. So this is a really remarkable study, and it shows us, essentially, that botanical protocols are equivalent or better than rifaximin treatment, or at least of the 1,200 milligrams [per] day. And we've definitely seen this in our practice where patients come to us having already done rifaximin, and they're doubtful that botanicals will help because they perceive drugs to be more effective. But we explain the study to them, and in some cases, they go ahead and do the botanicals, and they have better results. You'll also note, as I mentioned at the end there, that the adverse effects were not noted at all with the botanical protocols, though they were with rifaximin. So our main experience with that is a little bit different. We do definitely see some adverse effects in both cases, but I think they're more related to Herx die-off reaction than they are to a typical adverse effect of the medication themselves. As you can see, botanical therapy's

at least as effective and maybe more effective with fewer side effects. Rifaximin efficacy was low in that study, and I'm not sure why, but the overall efficacy of rifaximin in meta-analysis is about 50 percent. That's obviously not super great. It's kind of a flip of a coin. But this may be because the dose and duration of rifaximin treatment [were] not high enough and not matched with the severity of the lactulose breath test results in those patients.

Rifaximin isn't approved by the [U.S. Food and Drug Administration] (FDA) for treatment of SIBO, so it's only approved for hepatic encephalopathy and [irritable bowel syndrome] with diarrhea (IBS-D). A one-month supply of rifaximin [that] is paid out of pocket at 1,200 milligrams at a typical pharmacy is over $1,200. However, there [are] cash pay options for ordering rifaximin direct from Australia, as I mentioned at the Center for Digestive Disorders. It's still expensive, but it's about a third of the cost of [what] the patient would have to pay at a local pharmacy. I think it probably ranges [from] about three to four hundred dollars for a two-week supply. It's important to note that [at] the time of this recording, they only accept prescriptions from MDs and DOs, not from nurse practitioners or physician's assistants, so you might have to work that out with your patient.

Also, SIBO tends to be a recurrent issue in a subset of patients. So this means that they may need treatment more than once. And taking botanicals repeatedly over time, I think, is probably safer than taking rifaximin repeatedly, even though it's relatively safe as an antibiotic and doesn't seem to impact the rest of the microbiome and does seem to be effective as multiple treatments as some of Dr. Pimentel['s] studies have shown. Finally, another benefit of the botanical protocol is that we can use roughly the same protocol with minor tweaks for elevated hydrogen, methane, and even suspected or confirmed hydrogen sulfide excess.

Here's the core or foundation of the antimicrobial protocol we've used for many years with some adjustments and variations, of course. We're often updating and tweaking this as we go. This is the current protocol at the time of this recording.



GI Synergy (Apex Energetics): broad spectrum of anti-bacterial, anti-fungal, and anti-parasitic botanicals

Lauricidin (Lauricidin): monolaurin, an extract of lauric acid, with activity against fungi, viruses, bacteria, and biofilm

Interfase Plus (Klaire Labs): a preparation of systemic enzymes that disrupt biofilm

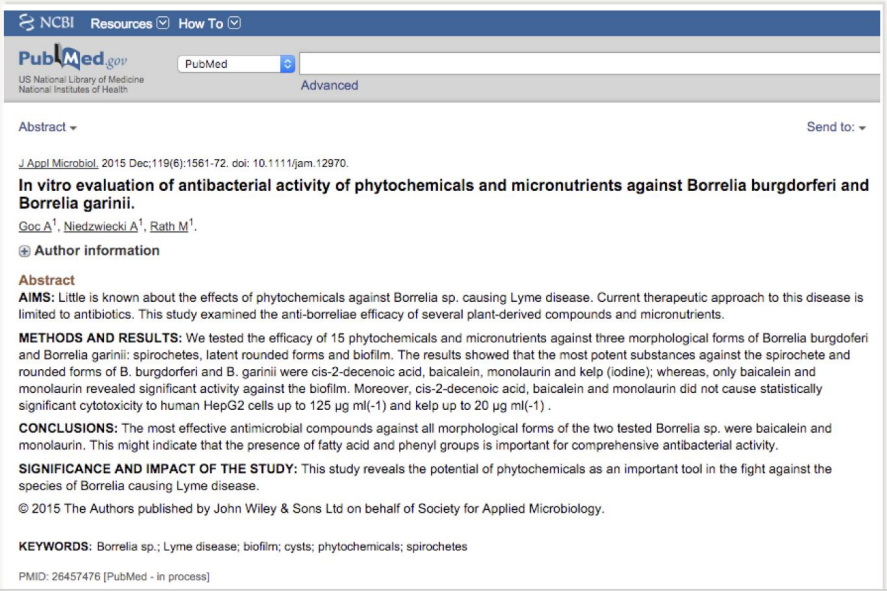
TerraFlora or SEED probiotics with antimicrobial properties **(optional if tolerated)**

We've gone back and forth with adding a prebiotic fiber, such as partially hydrolyzed guar gum (PHGG), to the botanical protocols. Some compelling research was released on this that suggested that adding a prebiotic to the treatment protocol increases its efficacy. This is based on a fundamental principle in microbiology, which is you have to feed them to kill them, which means if you're starving the bacteria and not providing them with a food source by doing a very-low-FODMAP diet and lowering fiber intake, then they'll go into a dormant state and they'll be even harder to kill with antibiotics. However, after a couple of years of doing this in the clinic, we found that we had typically worse results when we added [PHGG] into the protocol. Many patients with SIBO are simply just not able to tolerate it. So we've decided to take that out of our core protocol despite that one very positive study that showed a pretty significant increase in the efficacy of rifaximin with PHGG added to the protocol. Now, instead of it being part of the core protocol, we will add this in when appropriate.

Let's talk about each component in a little bit more detail. GI-Synergy, which I would look at as the antimicrobial portion of the core protocol, is a product from Apex Energetics that has a combination of three of their products. One of the ingredients is H-PLR, which is [a blend of] antibacterial herbs. The other is Yeastonil, which is an antifungal herb, and then the other is Parastonil, which has antiparasitic properties and is an antiparasitic herb. But those are just rough ideas or rough categories because botanicals don't have [a] black and white distinction like medication. So it's really just this combination of several different antimicrobial herbs in a

convenient delivery package for patients, and we found it to work exceptionally well. Lauricidin is monolaurin. It's [a particular] form of monolaurin, which is an extract of lauric acid found in coconut oils and mother's milk. And it's what's responsible for the antimicrobial qualities of coconut oil and mother's milk, at least in part. There are other antimicrobials in mother's milk like lactoferrin that can help make up for some of that, as well. Lauricidin has activity against yeast, viruses, and bacteria and also has some activity against biofilm.

A study tested the activity of 15 phytochemicals against *Borrelia burgdorferi*, the bacterium that causes Lyme disease, which is extremely difficult to treat, I'm sure you know, and monolaurin was actually one of the four most effective botanical compounds but only one of two that had [an] effect against *Borrelia* biofilm.



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J Appl Microbiol. 2015 Dec;119(6):1561-72. doi: 10.1111/jam.12970.

In vitro evaluation of antibacterial activity of phytochemicals and micronutrients against Borrelia burgdorferi and Borrelia garinii.

Goc A[1], Niedzwiecki A[1], Rath M[1].

Author information

Abstract

AIMS: Little is known about the effects of phytochemicals against Borrelia sp. causing Lyme disease. Current therapeutic approach to this disease is limited to antibiotics. This study examined the anti-borreliae efficacy of several plant-derived compounds and micronutrients.

METHODS AND RESULTS: We tested the efficacy of 15 phytochemicals and micronutrients against three morphological forms of Borrelia burgdoferi and Borrelia garinii: spirochetes, latent rounded forms and biofilm. The results showed that the most potent substances against the spirochete and rounded forms of B. burgdorferi and B. garinii were cis-2-decenoic acid, baicalein, monolaurin and kelp (iodine); whereas, only baicalein and monolaurin revealed significant activity against the biofilm. Moreover, cis-2-decenoic acid, baicalein and monolaurin did not cause statistically significant cytotoxicity to human HepG2 cells up to 125 μg ml(-1) and kelp up to 20 μg ml(-1) .

CONCLUSIONS: The most effective antimicrobial compounds against all morphological forms of the two tested Borrelia sp. were baicalein and monolaurin. This might indicate that the presence of fatty acid and phenyl groups is important for comprehensive antibacterial activity.

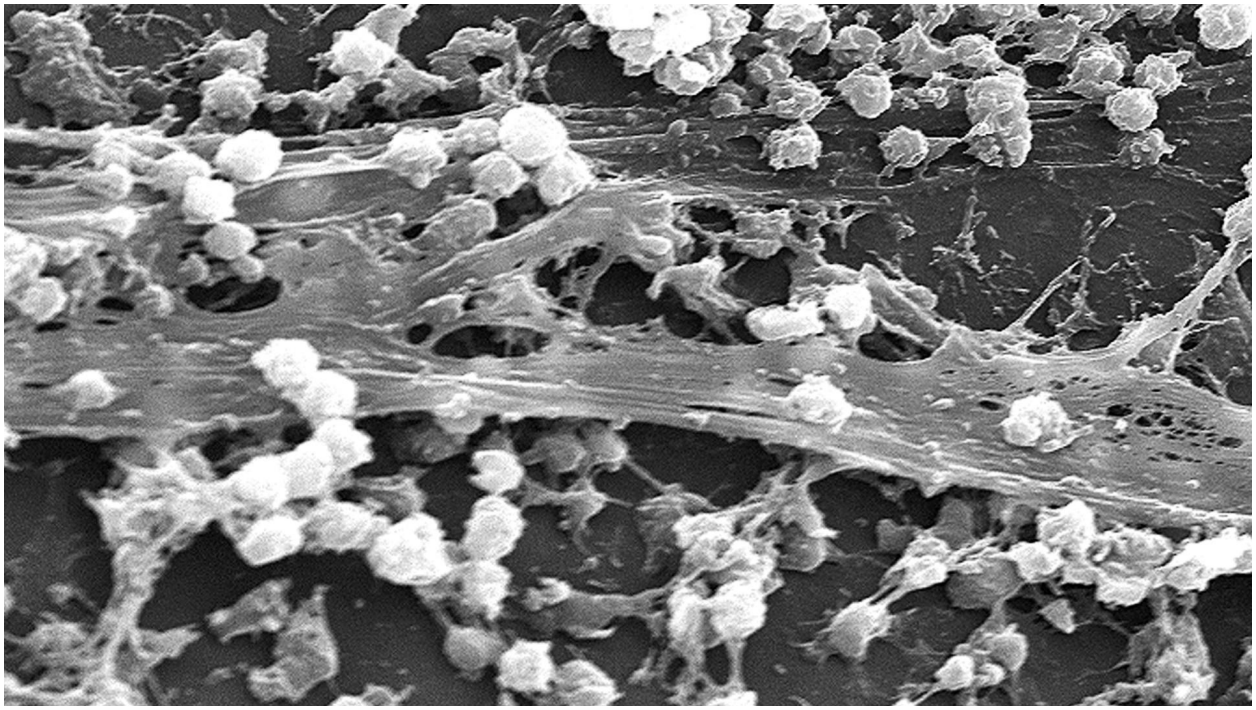
SIGNIFICANCE AND IMPACT OF THE STUDY: This study reveals the potential of phytochemicals as an important tool in the fight against the species of Borrelia causing Lyme disease.

KEYWORDS: Borrelia sp.; Lyme disease; biofilm; cysts; phytochemicals; spirochetes

PMID: 26457476 [PubMed - in process]

2015 **Study**

Importantly, it did not cause toxicity to human cells. We found it to be really effective and, most importantly, really well-tolerated. I believe it's relatively safe to take for a long term or even take repeatedly, so that's pretty important for patients who have recurrent problems. Interfase Plus is a biofilm disrupter. So what's a biofilm? If you're not sure yet, it's any group of microorganisms in which cells stick to each other on a surface. And in this case, we're talking about the gut lining.



Cells are embedded in this extracellular matrix, which protects the microbes from antimicrobials in our immune system. And some studies show that antibiotics are hundreds or even thousands of times less effective against biofilm. Interfase Plus and Lauricidin in this protocol helped to break up biofilm and increase the efficacy of the treatment. I should mention that it does contain lysozyme from egg white, and while I think it is generally well-tolerated and is not a problem for most people who have egg issues, I do use a different biofilm disrupter for those patients who have [an] egg allergy to err on the side of caution. I also have some patients [who] are very sensitive to eggs and will ask to avoid this or anything with eggs, for that matter. So [I] just want to say something about that and to be aware of this product; we do have substitute options available in the preferred supplement list for reference.

Terraflora's a broad spectrum symbiotic that's formulated with the combination of spore-form probiotics and advanced food-based ancient prebiotics. These are often referred to as soil-based organisms, but technically, they're transient gut commensal organisms that use an environment vector soil—in this case, to gain exposure to the host. They spend about 21 to 27 days in the gut. They don't colonize the gut, typically, and they perform a variety of important functions. One of these is [the] secretion of antimicrobial peptides, which, of course, have an antibiotic effect. The one advantage of Terraflora is that it's shelf-stable and it is generally well-tolerated, even by people who have SIBO and don't typically tolerate other probiotics very well. So for this reason, we use it in the protocol for most patients. I will say in practice that they can generally tolerate it. I

will hold off on introducing probiotics until the patient is stable on the first three products, maybe two or three weeks, and then slowly introduce the probiotics, especially if someone has had trouble with probiotics in the past.

Image credits: https://shop.enviromedica.com/Terraflora-Broad-Spectrum-Synbiotic, https://seed.com/daily-synbiotic

The other symbiotic we're using regularly in practice is Seed Daily Symbiotic, a broad spectrum, 24-strain probiotic plus prebiotic formulated for systemic health. And their via cap two-and-one nested capsule safeguards the viability through digestion so that you can have delivery of an average up to 100 percent of that probiotic species with that starting dose happening in the colon. The outer capsule serves as [a] barrier to oxygen, moisture, and heat. The nice thing is there's no refrigeration necessary either. I really like this product, and it's pretty well-tolerated for most patients. The only caveat is that it is a subscription-based model, but it's super easy to move your monthly shipping date around if you don't end up meeting it every month, and I usually just give patients a heads up.