Botanical Strategies for Metabolic Syndrome and Type 2 Diabetes

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Introduction

A survey conducted in 2001 evaluated the most frequently recommended and practiced alternative therapies for patients with type 1 and type 2 diabetes. The results of that survey included solutions such as physical activities, self-help groups, lifestyle, diet, laughter and humor, relaxation therapy, prayer, imagery, visualization, meditation, massage, and music therapy. But one thing that wasn’t included in the survey was botanical medicine. Based on the results of this survey, botanical products are not a frequently recommended solution by diabetes educators, but they have been shown to be quite effective.

In this report, Dr. Tori Hudson, N.D., will discuss several of the botanical solutions that have been shown to be effective in treating patients with metabolic syndrome, type 1 diabetes and type 2 diabetes. This report covers some of the most common botanicals including: cinnamon, fenugreek, bitter melon, gymnema, curcumin, and bilberry.

In addition to discussing the chemical constituents and properties of these botanicals, this report includes information about reported side effects and the recommended dosing amounts. This report also cites research study results, indicating the effectiveness of these botanical solutions in treating patients with type 1 and type 2 diabetes and metabolic syndrome.

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Cinnamon bark
(Cinnamomum species)

Despite the fact that this treatment has been around for centuries, there is often confusion about cinnamon and which tree is actually the cinnamon tree. Most of the modern and historical references to cinnamon may, in fact, be referring to a different cinnamon tree species and what we now call Cassia cinnamon.

Most cinnamon found in the U.S. marketplace is either Cassia cinnamomum or a mixture of Cassia cinnamomum with the Cassia zeylanicum. The cinnamon bark itself contains cinnamaldehyde and other polyphenolic polymers that appear to have glycemic and antioxidant effects that are relevant mechanisms to type 2 diabetes.

Historically, cinnamon wasn’t often used by itself for medicinal purposes. More often, it was used in ancient cultures in combination with other plants.

Research of cinnamon

Research shows that cinnamon appears to have a favorable effect on serum glucose in some, but not all, studies. In one placebo-controlled, randomized clinical trials, 60 type 2 diabetic patients were given 1, 3 or 6 grams of cinnamon per day for 40 days. Patients’ fasting glucose decreased between 18% and 29%, which is a fairly strong result.1

In another randomized, controlled trial, cassia was given at 3g/day for 4 months and diabetics experienced a moderate effect on their fasting glucose but no effect on hemoglobin A1c.2

In a negative study, which was also a randomized and controlled trial, 25 individuals received 1.5 grams of cassia for six weeks and there was no change in fasting glucose.3 This was a relatively short study, and the dosage was lower than other studies where upwards of 3g/day were administered.

Similarly negative results came from a review of five clinical trials that used doses between 1 and 6 grams for type 2 diabetics. In the review of these five studies, there were no signs of any significant changes in hemoglobin A1c, fasting glucose, or lipids.4

In a 2010 clinical trial, 58 individuals with poorly controlled type 2 diabetes were given 2 grams a day of cinnamon or a placebo for 12 weeks. In this study, the mean hemoglobin A1c level modestly decreased from approximately 8.2 down to 7.86, but it was better than the placebo which did not get better, and actually got slightly worse. In this same study, researchers evaluated blood pressure. The systolic blood pressure and the diastolic blood pressure were reduced in the cinnamon group. There was also a small reduction in fasting glucose and body mass index. These results were significant, in that, if doctors can improve insulin sensitivity, there may also be weight loss.5

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In another study, 22 individuals with impaired glucose tolerance and metabolic syndrome were randomly assigned to supplement their diet with either the cinnamon extract of 500 mg a day or a placebo for 12 weeks. At the end of the study, subjects in the cinnamon group had significant decreases in fasting blood glucose averaging a reduction of approximately 8.5%. Similarly, their systolic blood pressure decreased almost 4% and there were increases in their lean mass. All of those results were favorable compared to the placebo. Additionally, when they did this “within group” analysis, they uncovered a small, but statistically significant decrease in body fat in the cinnamon group.6

Based on the research, cinnamon as a single agent for glucose control yields unpredictable results. There is still a considerable amount of research to be done to better understand what form and dosage amounts for cinnamon are needed in order to deliver consistent, positive results.

Women with polycystic ovary syndrome (PCOS) who have impaired glucose tolerance or type 2 diabetes also tend to be overweight—around 50% to 60% of PCOS patients are overweight. These patients are at a high risk for diabetes and cinnamon may be one of many things to help lower insulin resistance and help trigger regular ovulation. One study in women with PCOS, showed a reduction in fasting blood glucose by almost 17% in the cinnamon group, which was statistically significant over the placebo group.7

**Dosage**

Dosages range from 500 mg to 6,000 mg and delivery forms range from pure cinnamon to cinnamon extracts. Above 6 gm/day, patients may encounter side effects, including dizziness and fainting. Cinnamon is likely safe in pregnant women and babies who are being breastfed. No significant or meaningful adverse reactions with the cinnamon bark have been noted in these dosage ranges.

However, cinnamon oil, the essential oil of cinnamon, requires more specific dosing. Some practitioners have found success using cinnamon oil for acute vaginal bleeding, but the dosing is very specific. Cinnamon oil is very different than cinnamon powder or cinnamon capsules.

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Fenugreek seed
(Trigonella foenum-graecum)

Fenugreek is one of the oldest medicinal plants having originated in India and North Africa. In India, fenugreek is commonly used as a condiment. It is also known to be used medicinally as a lactation stimulant.

The chemical constituents of the plant include the saponins, many of which are glycosides of diosgenin. Diosgenin is fairly well known to practitioners as it is extracted from Mexican wild yam in order to make progesterone in the laboratory.

The seeds of fenugreek also contain the alkaloids trigonelline, gentianine, and carpaine compounds. Other components of the seeds include C-glycosides. These seeds are unique because they contain up to 50% of the mucilaginous fiber that affects gastrointestinal (GI) transit and the slowing of glucose absorption. The seeds are the critical component of fenugreek—it is the fiber aspect of the seeds that affects GI transit and slows the glucose absorption.

About 80% of the total content of free amino acid in the seed is present as 4-hydroxyisoleucine, which appears to directly stimulate insulin. It is the mucilaginous fiber aspect and the 4-hydroxyisoleucine that causes the medicinal action for the diabetic population.

Researchers believe fenugreek delays gastric emptying, slows carbohydrate absorption, and inhibits glucose transport. It has also been shown to increase erythrocyte insulin receptors and improve peripheral glucose utilization. There are additional potential pancreatic effects as well.

One of the components in the seeds, fenugreekine, is a steroidal saponin that may have hypoglycemic properties. Another component in the seeds, trigonelline, may exert hypoglycemic effects.

Research of fenugreek

One small, randomized controlled double-blind trial evaluated the effects of fenugreek seeds on glucose control in type 2 diabetics. For this study, one group of type 2 diabetics was given 1 gm/day of an extract of the seeds for a period of two months. The other group was given only dietary and exercise advice. After two months, fasting glucose levels were similarly reduced in both groups, so fenugreek worked as well as the diet and lifestyle advice. The average glucose tolerance tests were also similar in both groups at the end of the study period.8

Another very small, randomized, controlled crossover trial included 10 patients with type 2 diabetes who were given 25 grams a day of fenugreek seeds. This study did not result in a statistically significant mean improvement in the glucose tolerance test scores and the serum clearance rates of glucose.9

Another small study of type 2 diabetics included a higher dosage of 100 grams of fenugreek seed powder. The significant average improvements in fasting glucose levels and the glucose tolerance test (GTT) results were seen clearly in the fenugreek patients. In addition, there was a 64% reduction in the glucose spilling over into their urine.10

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Another study included only 10 patients who were type 1 diabetics on insulin. They were randomized to either placebo or 50 grams of fenugreek defatted seed powder twice a day—a total of 100 grams a day—for 10 days. The study found the mean fasting blood glucose in the fenugreek group decreased from a baseline of 272 down to 196. While these levels are not normal, this is a dramatic reduction using just a single agent. Patients also demonstrated statistically significant decline in their total cholesterol, their triglycerides, and their low-density lipoprotein (LDL) compared to the placebo group. The fenugreek did not appear to have any effect on high-density lipoprotein (HDL), but that is likely attributed to the short duration of this study (10 days). Even in this short duration of time, there were significant changes in lipid and glucose levels.

Finally, one of the largest fenugreek studies was a six-month trial of 60 patients who had inadequately controlled type 2 diabetes. These patients were given 25 gm/day of the fenugreek seed powder. It was administered in two equal doses with lunch and dinner for six months. The average fasting blood glucose decreased from a baseline of 151 to 112, which takes them from clearly abnormal levels to slightly above normal levels. After 24 weeks, the mean one-hour oral glucose tolerance test baseline was 284 compared to 196. The mean two-hour postprandial levels decreased from 257 down to 171 after 24 weeks. These are all very positive results. The mean hemoglobin A1c decreased from a baseline of 9.6 to 8.4 after eight weeks. While this is still not adequate levels—hemoglobin A1c should be around 5.8—this is a good result after just two months using a single agent.

Dosage
There is no proven effective dose of fenugreek in adults. For type 1 diabetes, according to one study referenced earlier, 100 grams a day divided into two equal doses was used. For type 2 diabetes, researchers used between 25 and 50 grams a day. For hyperlipidemia, the dosage was 25 grams of the fenugreek seed powder twice a day and with type 2 diabetics, up to 100 grams.

Side effects
There are some potential adverse reactions, largely because of the fiber, including flatulence and diarrhea. When patients stop taking fenugreek, these symptoms will subside in a few days. If practitioners are aiming to give 50 grams a day, this dosage should be built up over a period of several weeks. There have been hypersensitivity reactions reported such as rhinorrhea, wheezing, even fainting after inhaling the fenugreek seed powder. Also, because it is a member of the legume family, it is theoretically possible for someone with a peanut allergy to react to fenugreek, however, this has not been widely reported. These side effects may occur in infants of nursing mothers who use the substance. Due to the coumarin constituents, practitioners should be careful about fenugreek in patients who are taking anticoagulant therapy. Also, if a patient is on medications, the significant amount of fiber could theoretically cause delayed absorption of those medications because of the high mucilaginous fiber.

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Bitter melon
(Momordica charantia)

Bitter melon or Momordica charantia is a member of the Cucurbitaceae family. It is a perennial, climbing, elongated fruit that actually resembles a cucumber or a gourd. It is sometimes called bitter cucumber or bitter gourd. It is available in some produce sections of specialty Asian markets and often called karela.

The active constituents of bitter melon are not definitively determined, but the plant contains alkaloids, glycoside, peptides, acids, cucurbitins, charantin, cucurbitacins, momordine, momorcharins and proteins. It is thought that the primary constituents responsible for the hypoglycemic properties are charantin, insulin-like peptide, cucurbutanoids, momordicin and oleanolic acids.

The ability of bitter melon to decrease serum glucose levels has been mostly studied in animals and in a small number of human studies. Bitter melon is a plant that has a relatively quick glucose lowering effect, within as few as 30 minutes. The lowest effect seems to occur at about four hours after it’s taken and lasts approximately 12 hours.

Research of bitter melon

One clinical trial included nine type 1 diabetics in the treatment group and 10 type 1 and type 2 diabetics in the placebo group. Patients were given injections of bitter melon extract—the injection was isolated for its crystallized p-insulin component, which resulted in a statistically significant decrease in blood sugar. That effect was noted in the short term, within 30 to 60 minutes after receiving the subcutaneous injection. The study resulted in a 21% drop from baseline glucose and a 28% drop after 12 hours.

It should be noted, the study wasn’t blinded or randomized and the placebo group had a lower average fasting blood glucose than the treatment group.

In a small case series study published in 1981, nine type 2 diabetics took 50 mL of bitter melon juice after a baseline glucose tolerance test (GTT). They took another GTT after drinking the juice and another one 8-11 weeks later after daily ingestion of 0.23 gm of fried bitter melon. The mean drop in glucose was 6% one hour after the fried fruit intake. There was an average drop of 12% one hour after the bitter melon juice and the mean glycosylated hemoglobin dropped by about 8% after eight to 11 weeks of the fried bitter melon. The methodology of this study is fairly weak, with no controls, but the results should not be discounted.

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In another case series, 18 type 2 diabetics were given 100 mL of bitter melon juice 30 minutes before a glucose load and a glucose tolerance test. The results were compared to each patient’s own previous GTT the day before, after drinking just water. Improved glucose tolerance was observed in 13 of the 18 patients.\textsuperscript{17}

Another uncontrolled trial of 12 type 2 diabetics had a study duration of three weeks. Patients were given two preparations: One was a bitter melon water extract and the other was 5 grams of dried fruit powder three times a day. After 21 days, those in the powder group had a 25\% reduction in their mean blood sugar levels. In the aqueous extract group there was a very significant 54\% reduction in mean blood sugar levels and hemoglobin A1c dropped from 8.37 to 6.95. Again, this study shows very promising results, although it is not a controlled trial.\textsuperscript{18}

**Dosage**

Again, dosing with bitter melon is challenging. The powder of dried fruit has been used in a range of 3 to 15 grams a day; the fresh juice, 50 to 100 mL a day; and the aqueous decoction of the fruit 100 to 200 mL a day. The standardized extract dosing ranges from 100 to 200 mg three times a day.

**Side effects**

Bitter melon is considered to be as safe as an oral hypoglycemic agent, but practitioners should monitor blood glucose levels and hemoglobin A1c. Avoid bitter melon in pregnant women, as it may cause miscarriage. This information is based on animal data and there have been historical reports to this effect. Bitter melon seeds contain momorcharin, which has been shown to have some antifertility effects in female mice. In fact, spermatogenesis was actually inhibited in some dogs after being fed the bitter melon fruit extract for a couple of months.

There were two cases of hypoglycemic coma reported in children after bitter melon tea, so it is not recommended to be used in children. Also, avoid giving bitter melon to patients who have a known allergy or hypersensitivity to members of the same family such as gourds and melons, as bitter melon may cause a similar reaction.

In addition, look to use bitter melon along with metformin or various forms of insulin. This can have additional positive effects, but may result in the need to lower the medications. Practitioners must be diligent about monitoring patients and teaching them how to monitor themselves.

Bitter melon seeds should be avoided by those individuals with glucose-6-phosphate dehydrogenase deficiency. Due to its hypoglycemic effects, bitter melon may have additive effects when taken with other blood glucose-lowering agents. Simple familiar testing and monitoring will assure safe use of bitter melon preparations.


\textsuperscript{18} Srivastava Y. Phytother Res 1993;7:285-289
Gymnema (Gymnema sylvestre)

Gymnema is a plant with historical and modern research in the area of lowering serum glucose in both type 1 and type 2 diabetes. The leaves of gymnema have been used for more than 2,000 years in India to treat something referred to as honey urine, which is a condition of glucose spilling into a diabetic’s urine.

Gymnema is often used in people who have glucose and lipid problems. The gymnemic acids seem to reduce intestinal absorption of glucose and may also stimulate pancreatic beta cell growth. There has been research that suggests that constituents of gymnema have a very direct effect on the beta cell function, thus increasing the release of insulin. It seems that it can increase serum C-peptide levels, suggesting an increase in this endogenous insulin secretion.

There is also preliminary human evidence that suggests that gymnema may be effective for the management of the serum glucose levels in both type 1 and type 2 diabetics, especially if used as an adjunct to conventional therapy. It appears to lower serum glucose and lower glycosylated hemoglobin levels following chronic use, but it doesn’t seem to have any significant acute effects. Unfortunately, there are not any high-quality human trials yet in this area of research.

Research of gymnema

There are some animal and human studies that show some effects on glucose levels. One study included type 2 diabetics who were on sulfonylureas, where 22 of them took 400 mg/day of the gymnema capsules in addition to their conventional medication and 25 patients took the placebo and their sulfonylurea for 18 to 20 months. In the gymnema, the mean hemoglobin A1c decreased from a baseline of 11.9 down to 8.48 and the mean fasting glucose seemed to decrease from 174 to 124. Five of the patients were actually able to stop their conventional medication. In this study lipids also decreased significantly and the placebo group had no significant changes on their glucose, their hemoglobin A1c or their lipids.19

Another study looked at type 1 diabetics on insulin. Twenty-seven of them took 200 mg of gymnema capsule twice a day after breakfast and after supper, while 37 of them took insulin. This was over a period of 6 to 30 months. After six to eight months, the average hemoglobin A1c in the gymnema group decreased from 12.8 to 9.5. Over a longer period of time (16 to 18 months), 22 of the patients remaining on the gymnema had a further mean decrease down to 9.0. The most significant results occurred during the six to eight month period versus 16 to 18 months, but at the end of 26 to 30 months, six of the patients who were still on the gymnema had a mean hemoglobin A1c of 8.2%. While still not a normal level, it is a very good result for a single agent. Their average fasting glucose also decreased from baseline of 232 down to 177 after the first few months, and then down to 150 after 16 months. These participants stayed at that level after a couple of years. Patients were able to reduce their average insulin dosing, going from a baseline of 60 down to 45 units a day after the first six to eight months and then down to 30 units a day after 26 to 30 months. The people on the placebo had no significant changes from baseline.20

Side effects

There do not appear to be any adverse reactions reported with gymnema. However, there is not much reliable information on its safety during pregnancy and lactation.

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Curcumin (Curcuma longa)

Curcumin has a wide range of pharmacological activities because of its anti-inflammatory properties, anti-cancer properties, antioxidant effects, wound healing, antimicrobial, etc. The main components are the curcumin, the curcuminoids, and the curcumin oil. In mice, curcumin seems to be effective in lowering glucose levels. In mice who were induced to become obese, the curcumin fed mice were less susceptible to diabetes. While not particularly strong scientific evidence, it does show that curcumin may have a role with diabetes in reducing the risk factors that type 2 diabetics have in terms of heart disease or certain cancers.

Bilberry (Myrtilli folium)

Bilberry is a plant closely related to the blueberry, cranberry and huckleberry. There are two forms of bilberry that are most often used, the dried fruit and the leaf. The leaf is used for diabetes and has a folk medicine history for reducing blood sugar.

The main chemical constituents of bilberry fruits are anthocyanosides, which are flavonoids. These are thought to decrease the vascular permeability and effect of microvascular blood flow, which is so important in diabetics. One of the mechanisms of action might be related to the chromium content in the leaves, not just the flavonoids.

There are not any human trials, but there have been animal studies. The mechanism of action of flavonoids seem to relate to the potential complications of diabetes, especially around visual issues.

Dosage

The best dosing is unclear, but some of the research regarding the visual implications uses 160 mg of the standard extract twice a day.

Side effects

Practitioners should be careful with anticoagulants and careful about the additive effect of bilberry.
Other Botanicals to Consider in Diabetes Treatment

Blueberry
The blueberry leaf contains the phenolic compounds that are involved in optimizing glucose absorption and glucose metabolism. The blueberries themselves have been studied for their impact on insulin sensitivity. This is one of those few fruits that are low on the glycemic index. These berries are a welcome and encouraged part of a diet for someone with metabolic syndrome or diabetes.

A recent double-blind, placebo-controlled study looked at 32 obese, middle-aged non-diabetic and insulin-resistant women and men. They were given either a smoothie that contained blueberries or a smoothie without the blueberries. A dose of the freeze-dried powder of the blueberries was equal to about two cups of fresh, whole blueberries. Researchers used either two cups of fresh blueberries or 22.5 grams of freeze-dried powder. The daily dose of blueberries resulted in significant improvement in patients’ insulin sensitivity, which was about four times greater than the placebo group.21

Berberine
Researchers looked at metformin plus berberine and results showed it worked as well as the metformin in lowering hemoglobin A1c and there was a significant drop when both were taken together. The fasting glucose looked comparable to the metformin.

Metformin and berberine, or metformin and another one of these botanicals can be effective, especially in a patient who has metabolic syndrome or type 2 diabetes. Dosing can be between 500 to 2,000 mg of metformin depending on the agent and we can often end up decreasing their metformin. Practitioners should consider this combination approach.

**Milk thistle**

Milk thistle has been used extensively for many types of hepatic disorders, but it has also been used to attenuate the effects of hepatotoxic medications. It contains silymarin and it may benefit insulin resistance secondary to hepatic damage such as fatty liver. Fatty liver is clearly related to insulin resistance and milk thistle is often appropriate for those patients.

There was a 12-month randomized, open trial with 60 type 2 diabetics with cirrhosis who were all on insulin. One group received 600 mg of silymarin and the other 30 people received placebo for 12 months. The mean fasting glucose declined from 190 to 165 in the silymarin group. After a year, hemoglobin A1c decreased from 7.9 to 7.2. Their daily insulin use decreased from 55 to 42 at 12 months.22

**American ginseng**

American ginseng has been studied in type 2 diabetics. One randomized double-blind placebo controlled study looked at 36 people with type 2 diabetes. They were divided into groups of 12 and given either a placebo, or 100 mg or 200 mg of ginseng for several months. There was a statistically significant decrease, but it was seen only in the 100 mg/day group, indicating that taking more is not any more effective.23

Another study compared American ginseng to placebo. This study group included people with and without diabetes. They were given the oral glucose load with or without 3 grams of the ginseng capsules. They were given ginseng 40 minutes before or with the glucose challenge. There was no significant difference in post prandial glucose when ginseng was taken with the glucose challenge and patients who didn’t have diabetes. However, taking ginseng 40 minutes before the glucose load resulted in a significant reduction in post prandial glucose. Patients with diabetes had significant post prandial glucose whether ginseng was given concomitantly or before the glucose load.24

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22 Velussi M, Cernigoi A, De Monte A, et al. Long-term (12 months) treatment with an anti-oxidant drug (silymarin) is effective on hyperinsulinemia, exogenous insulin need and malondialdehyde levels in cirrhotic diabetic patients. J Hepatol 1997;26:871-879


Case Example 1

A 55-year-old post-menopausal woman, whose average glucose is 115—an impaired glucose tolerance range. Hemoglobin A1c is elevated slightly, she has dyslipidemia and obesity.

The first thing a practitioner should recommend is a total lifestyle change program as well as a combination of herbal support that includes fenugreek, cinnamon and bitter melon. This patient is given a higher end of that combination, two capsules three times a day.

She is also given insulin sensitizing with chromium and fish oil. A robust amount of fish oil should be used, look for products that have at least one-and-a-half times as much eicosapentaenoic acid (EPA) as docosahexaenoic acid (DHA). Because of her dyslipidemia, she should be given a slow-release niacin. During this period, her glucose needs to be watched, both by her practitioner as well as tested on her own.

Her fasting glucose should be tested monthly. Her lipids and hemoglobin A1c should be tested in three months.

Case Example 2

A 60-year-old woman with type 2 diabetes has stage one hypertension with uncontrolled diabetes. She has moderate cognitive impairment and doesn't do well taking her medication or her supplements. Her hemoglobin A1c is not good and her blood pressure is not well controlled.

She is inconsistent about the lifestyle changes, so controlling her blood pressure with lifestyle changes cannot be relied on. It also cannot be controlled with herbs because she can’t be relied on to take things two or three times a day. Therefore, she's on Lisinopril and metformin and insulin. The insulin dose is relatively low, so a focus should be getting her to take bitter melon as much as she can remember. Recall that bitter melon is one of those fast-acting herbs.

In addition, she's on cinnamon and fish oil and alpha-linoleic acid for the bigger picture. At this stage, her blood sugar is down to 120, a reasonable zone. Her hemoglobin A1c is pending, but should be down to around 6.5.
Contributing Author

Dr. Tori Hudson is a naturopathic physician and a graduate of the National College of Naturopathic Medicine. She is currently a clinical professor at NCNM, Southwest College of Naturopathic Medicine, and Bastyr University and has served as medical director, associate academic dean and academic dean for NCNM. She is also the program director for the Institute of Women’s Health and Integrative Medicine. Dr. Hudson also sits on the scientific advisory boards for Gaia Herbs Professional Solutions, Nordic Naturals, Integrative Therapeutics Inc., and Natural Health International.

Dr. Hudson is a nationally recognized author and speaks regularly at conferences and events throughout the country, always trying to elevate the level of knowledge and education throughout the supplement and integrative medicine industry. Dr. Hudson has been in clinical practice for almost 28 years and currently maintains her own practice in Portland, Oregon at A Woman’s Time.