

Botanical Strategies to Support Metabolic Issues in Midlife Women



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Table of Contents

Introduction	1
Metabolic Issues in Midlife Women	2
Hypothyroid.....	2
Adrenal dysregulation.....	2
Perimenopause.....	2
Menopause.....	3
Insulin resistance	4
Type 2 diabetes.....	4
Obesity in women.....	5
Slowed metabolism.....	5
Investigating Botanical Solutions	6
Adaptogens.....	6
Botanical Adaptogens:	7
• Rhodiola rosea	7
• Schisandra chinensis.....	9
• Ashwagandha (Withania somnifera).....	10
• Other Botanical Adaptogens.....	11
Contributing author	12

Introduction

This report investigates many of the metabolic changes that occur in women beginning in their 40s and 50s. Dr. Tori Hudson, N.D., covers a range of metabolic issues including thyroid, adrenal dysregulation, insulin resistance, diabetes, obesity and metabolism during perimenopause and menopause stages; and offers several botanical solutions that address some of these issues and their related symptoms. Throughout the report, Dr. Hudson cites multiple research and case studies proving the effectiveness of botanical solutions for metabolic issues, and suggests proper dosages for each adaptogen discussed: *Rhodiola rosea*, *Schisandra chinensis* and *Withania Somnifera*.

This report is based on a webinar presented by Gaia Herbs Professional Solutions and hosted by Integrative Practitioner in October 2011.

Metabolic Issues in Midlife Women

Hypothyroid

When discussing thyroid issues, it's not always apparent how common it is for women over the age of 50 to begin having issues with their thyroid. There are about 11 million Americans today who have been diagnosed with thyroid issues. By the age of 60, about 17 percent of women and 9 percent of men have been diagnosed with hypothyroid.

One of the biggest problems, however, is the large number of thyroid conditions that go undiagnosed. It is estimated that one-in-71 women over the age of 50 go undiagnosed, despite the fact that we have many basic screening tools, including physical exams and laboratory diagnosis, to identify people who suffer from thyroid problems.

Adrenal Dysregulation

"Adrenal dysregulation", which refers to women who don't have Addison's (at one end of the spectrum) and women who don't have Cushing's (at the other end of the spectrum) is used throughout this report to describe the area in between the two. Some doctors use the term "adrenal fatigue," others call it "adrenal fatigue syndrome" and then some improperly refer to it as "adrenal failure".

After other conditions have been ruled out, often using salivary cortisol testing, it is determined that patients have some kind of abnormal adrenal function based on the four-point cortisol test. These patients often have fatigue, insomnia, anxiety, depression, and are often overweight. It is these people who fall into the category of adrenal dysregulation.

Chronic fatigue syndrome is most commonly seen between the ages of 20 and 40. The majority of people at particular risk for acquiring chronic fatigue syndrome and suffering from the condition are middle-class women working in the service industry. There are chronically abnormal cortisol levels with chronic fatigue syndrome and thus with adrenal dysregulation as well.

Women also have hormonal influences of the premenstrual syndrome, postpartum states, perimenopause and menopause, which adds an additional layer of complexity and confusion that is unique to women and their adrenal functions.

Perimenopause

Perimenopause, the period of time leading up to menopause, often begins in the 40s. The average onset for 95 percent of women is between the ages of 39-51 and lasts for 5-7 years, on average (2-8 years for 95 percent of women). During perimenopause there are a lot of biological changes occurring. The number of oocytes has reached very low numbers, the menstrual cycle begins to vary, and there is less frequent ovulation.

With less frequent ovulation there is a lack of cyclic progesterone production during those months when women aren't ovulating. There is also an increase in the FSH, even though a woman's cycle may still be regular. However, the FSH isn't always a great test since a woman's cycle might be irregular and she might be experiencing perimenopause symptoms, but still test normal levels of the FSH on that day.

Additionally, the ovarian production of estradiol and progesterone and testosterone levels decrease. The total blood levels decrease. Eventually, the lower level of estrogen secretion is no longer adequate to cause the buildup of the uterine lining and consequently there's not enough tissue to produce a menstrual cycle. Women become menopausal once they haven't had a period for 12 consecutive months.

Menopause

Shortly after the onset of menopause, which occurs at an average age of 51, doctors can safely say there are no remaining ovarian follicles. Eventually, there is a significant increase in FSH, a ten- to twenty-fold increase, and about a three-fold increase in Luteinizing hormone (LH). Luteinizing hormone reaches its maximum increase at about one to three years after menopause, followed by - oddly enough - a gradual, but slight, decline in both of the gonadotropins. The postmenopausal ovary secretes androstenedione and testosterone, but after menopause that circulating level of androstenedione is about one-half of what it used to be prior to menopause, and most of that postmenopausal androstenedione is derived from the adrenal glands, with only a small amount secreted from the ovary.

Other hormones that decline markedly with aging are the two hormones that originate in the adrenal gland: DHEA and DHEA sulfate. Ten years after menopause the circulating levels of DHEA are approximately 70 percent less and the DHEA sulfate is approximately 74 percent less, than their levels at younger ages.

Testosterone production decreases by approximately 25 percent after menopause. Even though the postmenopausal ovary doesn't secrete less testosterone than the premenopausal ovary, the total testosterone in the blood decreases because the amount of the primary source, which is the peripheral conversion of androstenedione to testosterone, is reduced.

The circulating estradiol after menopause drops off to 10–20 pg/mL, and most of that is derived from the peripheral conversion of estrone, which, in turn, is derived mainly from the peripheral conversion of androstenedione.

In the postmenopausal woman, her circulating level of estrone is at approximately about 30–70 pg, higher than her level of estradiol which hovers near 10–20 pg. That androgen-estrogen ratio changes drastically after menopause because of the marked decline in estrogen. This is why we might see hair thinning in postmenopausal women and facial hair and acne. It's not because there's more testosterone—there's less—but the ratio of androgens to estrogen changes, so hair follicles and skin glands are more susceptible to testosterone. Women experience more testosterone because there's less estrogen to oppose it.

Insulin Resistance

The connection between menopause and insulin resistance is interesting. With menopause, there appears to be an association between a decrease in pancreatic insulin secretion and increased insulin resistance. These two changes are thought to contribute to an increased risk for developing type 2 diabetes after menopause. However, it is not known whether this is due to the postmenopausal lowered estrogen status or due to aging itself. The two big studies, the HERS study and the WHI study, suggest that estrogen alone, or when estrogen is combined with a progestogen, actually can reduce the instance of new-onset diabetes. These concepts are often used in the selection of treatment, including hormone-replacement therapy for women who have impaired glucose tolerance or metabolic syndrome already. If women have moderate menopause symptoms, doctors might be more likely to lean towards hormone-replacement therapy than botanicals.

This connection between estrogen and insulin resistance in type 2 diabetes is further strengthened by one meta-analysis that quantified the effects of hormone therapy on metabolic syndrome in postmenopausal women. In the meta-analysis, they found that exogenous hormone therapy in peri- and postmenopausal women did indeed improve insulin resistance and fasting glucose in women with diabetes. At the same time it improved insulin resistance, lipids, blood pressure and abdominal obesity in women without diabetes. Therefore, the studies in analysis ended up strongly suggesting that the normal endogenous low estrogen level in menopause does indeed influence the development of insulin resistance and metabolic syndrome and type 2 diabetes.

These metabolic changes that are related to a loss of estrogen in the postmenopausal women can impact a woman's future health. Along with the loss of estrogen a woman faces increased central body fat, increased low-density lipoproteins, increased triglycerides, decreased HDLs, increased glucose and increased insulin resistance, which can substantially increase her risk for cardiovascular disease. When doctors think about treating women in this situation, treatments shouldn't focus on just optimizing glucose control and insulin sensitivity. Doctors need to also focus treatments on supporting a woman's endogenous hormones and being very strategic with preventing cardiovascular disease or treating it if it already exists. Therefore, simply tightening glycemic control in a woman with type 2 diabetes is not enough to reduce her cardiovascular risk.

Type 2 Diabetes

Type 2 diabetes affects an estimated 24 million individuals in the U.S., which is about 8 percent of the population. More than nine million of those with type 2 diabetes in the U.S. are women and nearly a third of those women remain undiagnosed. As men and women age, the incidence of diabetes increases and by the time people are 65 or older, about a fifth of men and women in the U.S. will have type 2 diabetes. As people are living longer, the number of women who acquire diabetes will be greater, those at risk will be greater, and therefore, those who will have cardiovascular disease will also be greater.

Obesity in Women

Another big metabolic change in midlife women is obesity. The age-adjusted percentage of adults age 20 years or older who are obese, from 2003 to 2006, varied by race and ethnicity among women. The highest is 53 percent for non-Hispanic black women, 42 percent for Mexican-American women, and 31 percent for non-Hispanic white women. Interestingly enough, the obesity levels are closer together for men amongst those three groups, but there's a significant disparity amongst women.

In terms of weight gain in general, for midlife women, weight gain and obesity are associated with menstrual cycle alterations and ovulatory cycles. Often women don't feel good because they're having hot flashes, aren't sleeping properly, or are having aches and pains, which generally lead to poor lifestyle habits that cause weight gain. Women tend to gain weight in the abdominal region and their body composition often changes to an apple-shaped body. These changes seem to be related not only to aging and a general slowing of metabolism, but also to the lower estrogen status and other unknown factors.

Metabolism

There are also some interesting metabolism changes that occur as women age. One thing that affects metabolism is damage caused by dieting—the low protein, the high protein, the yo-yo dieting, the fasting, even excessive exercise and chronic stress—all those things can damage metabolism. Women should consider healing this damage to their metabolism before engaging in a weight-loss plan. Working on healing the metabolism through building muscle tissue, restoring sleep, moderating reactions to stress and normalizing glucose tolerance will allow for greater gains in weight-loss efforts.

Between the ages of 20 and 40, women also experience approximately a 50 percent drop in DHEA levels. Since DHEA is one of the major androgen precursors, that becomes extremely relevant. The other factor is that ATP production is dropping, which will affect not only metabolism, but will also affect weight.

Investigating Botanical Solutions

Adaptogens

There are many different definitions of adaptogens. One definition is that adaptogens are “herbal preparations that increase attention and endurance in fatigue, and reduce stress-induced impairments and disorders related to the neuro-endocrine and immune systems.” Historic definitions state that adaptogens produce a non-specific response. However, there has been some research to show very specific organ and metabolic responses. Adaptogens help the body adapt better to stress and therefore help our numerous body systems to recover.

Here’s another definition: “Substances which elicit a state of raised resistance to stress.” A word that comes up often in these historical definitions is “normalizer.” Adaptogens are thought to normalize, balance and restore homeostasis—this is very common language in traditional herbal medicine. It doesn’t matter if the state of the individual being treated has hyperfunctioning signs and symptoms, or hypofunctioning signs and symptoms—most adaptogens can be used in either of those states. There is a bimodal action to it, which is good because there are many people who can’t be diagnosed by usual means, and adaptogens can fill in that niche and be a foundational part of the treatment approach.

Adaptogens also don’t overstimulate, are non-toxic and have relatively no side effects. It’s not that there are never any side effects, but very few side effects have been associated with something that helps us adapt to stress, essentially something that is a tonic or a normalizer/balancer.

Another common way to describe the impact of adaptogens is that it helps the body regulate itself as a metabolic regulator. Consider adaptogens as a stimulator for an individual who is worn down because her life involves a lot of stressors. These stresses could be severe, acute stress; prolonged, milder stress; or it could be prolonged, more severe stress. This woman is not hypothyroid and she doesn’t have dysglycemia, or an infection, and she doesn’t have anemia. This woman also doesn’t have Addison’s disease—she has adrenal dysregulation.

A good example of this scenario can be equated to finances. It’s similar to when a person has spent the cash in their pocket, then they’ve spent the money in their checking account, then they dipped into their savings account and spent that, and now they’re going into their investments. The solution is not just to replenish the cash in their pocket every day—there is not enough there to fund all that is required—so they’ve dipped into the reserve and reserve and reserve, such that the whole supply line is less and they have less to draw on and fewer reserves. Those reserves need to be slowly built up. Now, if someone were just to be given a stimulant, that would be like sticking cash in this person’s pocket, but they are going to go through it quickly. While some people need that cash in their pocket—we all need the cash in our pockets—we need the reserves, the backup, the checking accounts, the savings and investments to pull us through day after day and to handle the 40-hour work week, plus the kids at home, plus the cooking, plus the laundry, plus the fact that a kid is sick, plus a husband that lost his job, etc. People need that whole supply line.

Now taking that example back to the general stimulatory effect of adaptogens, what’s appealing about adaptogens is that you get that stimulation without any depletion of their nutrient stores or their energy stores. In addition, there is no addiction potential and rarely any side effects.

Botanical Adaptogens

Adaptogens reduce stress-induced generation of nitric oxide, which prevents a shortage in ATP production in stress, resulting in increased performance and endurance. It's thought that you can use adaptogens to prevent ATP depletion. If a shortage of ATP is prevented then an individual will have more fuel to go exercise, handle a long workday, enhance performance, enhance our stamina, etc. Adaptogens can also decrease lactic acid buildup.

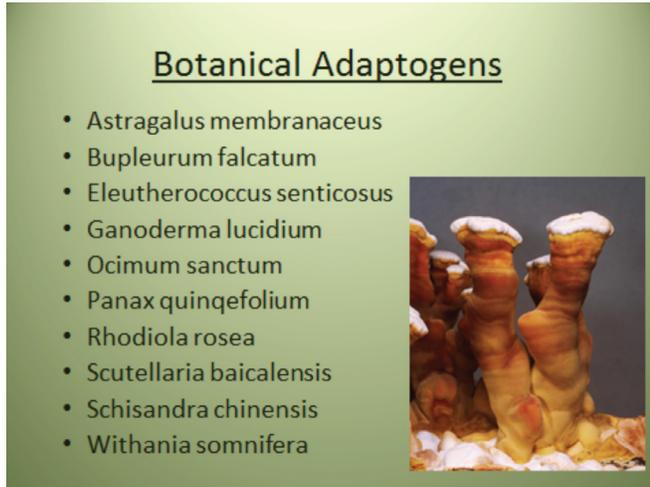


Figure 1: Examples of botanical adaptogens

Rhodiola rosea

Rhodiola rosea, also called rose root or arctic root, has not been available in the U.S. marketplace for very long. Rhodiola is native to the northern regions of Canada, Scandinavia and Siberia and high elevations in the Alps and the Pyrenees. An interesting commonality amongst many adaptogens is that they often grow in fairly stressed environments. Many adaptogens have adapted to their environment in high altitudes, cold weather, and rugged mountain regions.



Figure 2: Rhodiola rosea

The part of the Rhodiola plant that's used medicinally is the rhizome, a fleshy underground stem. Rhodiola rosea is dioecious—having separate female and male plants. Some of the active constituents are:

- Rosavin, rosin, rosarin, salidroside, rhodiolide, tyrosol, flavonoids (rodiolin, rodionin), phenolic antioxidants, including proanthocyanidins, quercetin, gallic acid, chlorogenic acid and kaempferol

There is some evidence that Tyrosol, one of the active principles of Rhodiola, can increase the phosphorylation of nitric oxide and FOXO3a, a fork head transcription factor that controls synthesis of proteins involved in stress resistance, detoxification, and longevity. This tyrosol also can act to alleviate the depletion of brain catecholamines in the alarm phase of the stress adaptation cycle. By doing so, it reduces fatigue.

In addition, anxiety, depression/moodiness, and enhancing performance are also indications for Rhodiola. There is some data on high-altitude sickness. Rhodiola also has been shown to enhance memory, and it is in many mild cognitive impairment formulas, which is also a very common condition in perimenopause and menopausal women, again due to that changing hormone bath in the brain. Sleep disturbances and insomnia are also things that have shown up as a theme for Rhodiola.

Some of the mood-regulating effects are potentially due to the ability of Rhodiola to optimize serotonin and dopamine, and it does that by monoamine oxidase inhibition and its influence on opioid peptides such as beta-endorphins.

Research

In a small study using the classic Hamilton Depression Scale¹ the group that took Rhodiola did have improvement in their overall depression, which was mild to moderate depression. Subjects even improved their sleep and mood as well. There was one group that had 340 mg/day and one group that had 680 mg/day and one placebo group. Both those doses of Rhodiola had the positive results in mild to moderate depression.

Another study² showed that Rhodiola, at a dose of 288 mg/twice a day or placebo for a month, resulted in a significant reduction in functional fatigue, some improvement in cognitive performance, improvement in attention to detail and recall.

Dosage

- 4-8 ml/d liquid extract
- 200-600mg/d dried root
- 100 mg of extract standardized to 3 percent rosavins and 0.8-1 percent salidroside, as the naturally occurring ratio of these compounds is approximately 3:1
- A high dose-daily intakes of 1,000 mg
- Mild – Moderate Depression: 170 mg or 340 mg twice daily/placebo for 6 weeks¹
- Anti-fatigue: 200 mg three times a day
- Insomnia: 600mg dose²

¹ Darbinyan V, Aslanyan G, et al Clinical trial of Rhodiola rosea L. extract SHR-5 in the treatment of mild to moderate depression, Nord J Psychiatry (2007) 61(5):343-8 ISSN: 0803-9488

² Olsson, E.M.G.; von Schéele, B.; Panossian, A.G. A randomized double-blind placebo controlled parallel group study of SHR-5 extract of Rhodiola rosea roots as treatment for patients with stress related fatigue. Planta Med. 2009, 75,105–112

Schisandra chinensis

Schisandra chinensis is a fruit and seed native to forests of Northern China and the Russian Far East. It is often thought of as a tonic that has a calming effect. Schisandra aids in enhancing mental performance, improving physical endurance, handling stress better, and generally being more resistant to stress. There are some anti-inflammatory properties and it is shown to inhibit nuclear factor of activated T cells (NFAT), which plays a role in the autoimmune process. It is also shown to inhibit leukotriene biosynthesis inhibiting release of arachidonic acid.

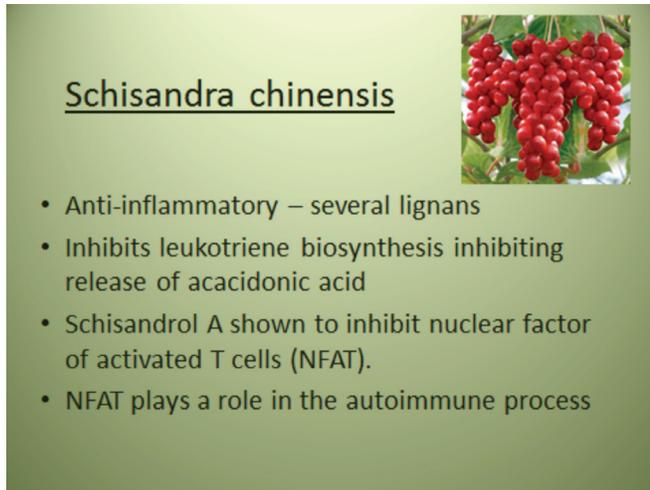


Figure 3: Properties of Schisandra chinensis

Schisandra also helps to decrease fatigue, improve the general mood, and possibly even improve appetite. It can even be used with tranquilizers or antidepressants in such a way that it helps eliminate the side effects of those drugs, which therefore allows patients to take those drugs in more therapeutic doses³.

Dosage

- 3-10 mls/day 1:3 liquid extract
- 2-6 g/day dry fruit
- Avoid in pregnancy
- No negative effects were observed on the somatic state of patients

³ Darbinyan, V. et al; A. Clinical trial of Rhodiola rosea L. extract SHR-5 in the treatment of mild to moderate depression. Nord. J. Psychiatry 2007, 61, 2343–2348

Ashwagandha (*Withania somnifera*)

The traditional description of Ashwagandha is as a tonic, improving the ability of the body and the organism to adapt to its surroundings. Amphoteric is one of the actions of Ashwagandha, which is a substance that normalizes functions of an organ or system within the body. Ashwagandha is not just adaptogenic, but it has a broad spectrum of activity including anti-inflammatory properties, blood-sugar regulating properties, general immune support, anti-oxidant, anti-anemic, anti-tumor, hypoglycemic agent, neuroendocrine tonic, regulates HPA axis, and as a general tonic.

There are many therapeutic uses, especially for depression, exhaustion, chronic fatigue, hypothyroidism, adrenal insufficiency and even infertility. There have been some clinic trials and animal research that support the use of Ashwagandha for anxiety, for cognitive disorders, inflammation and even Parkinson's disease. It is often used as an adjunct for patients undergoing chemotherapy or radiation. Patients using Ashwagandha during therapy tend to maintain a higher level of energy than people who don't take it.

There is also some thyroid impact of Ashwagandha as well as a role in metabolic syndrome and in type 2 diabetes because it supports blood sugar stabilization. Ashwagandha—and most of these adaptogens—can be thought of as an orchestra conductor, regulating the hypothalamic-pituitary-adrenal axis. That's important in perimenopausal women when that HPA axis is discombobulated and erratic. There have been some in vitro studies which show a decrease in oxidative stress load, reduction in lipid peroxidation, increase in SOD and catalase, regulation of serum T3 & T4 levels, and regulation of thyroid hormone conversion.⁴

Research

A double-blind, randomized, placebo-controlled 60-day trial assessed men and women aged 18 to 60 years and assessed blood pressure, resting heart rate, reflexes, and neurological and psychological status and used a questionnaire assessing the severity of their stress symptoms⁵.

They were assayed for serum concentrations of cortisol, dehydroepiandrosterone sulfate (DHEAS), C-reactive protein, fasting blood glucose, total cholesterol, triglycerides, low-density lipoprotein cholesterol, very low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and hemoglobin. It was found that a dosage of up to 250 mg twice a day reduced their stress, reduced their anxiety, reduced their elevated cortisol levels, and reduced their C-reactive protein, regulated their pulse, their blood pressure, and enhanced their production of DHEA sulfate.

⁴ Panossian A and Wikman G, Effects of Adaptogens on the CNS and the Molecular Mechanisms Associated with Their Stress-Protective Activity, *Pharmaceuticals* 2010, 3,188-224; doi:10.3390/ph3010188

⁵ Panossian A and Wikman G, Effects of Adaptogens on the Central Nervous System and Molecular Mechanisms Associated with Their Stress—Protective Activity, *Pharmaceuticals* 2010, 3,188-224; doi:10.3390/ph3010188

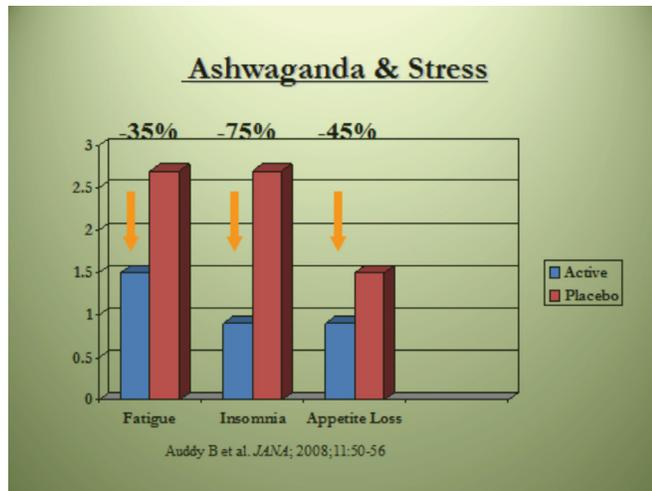


Figure 4: Results of Withania Clinical Trial

The results of this study show that Ashwagandha achieved a 35 percent reduction in fatigue, 75 percent reduction in insomnia, and improvement of patient's appetite.

Dosage

- 3-6 grams daily of the dried root
- 6-15ml of a 1:2 fluid extract per day
- 300-500 mg of an extract standardized to contain 1.5 percent withanolides
- 125mg-250mg/d WSE- CVS/ Glucose regulation*
- 125mg-500mg/d WSE for stress reducing effects*
- It's generally safe, large doses have been shown to cause gastrointestinal upset, diarrhea, and vomiting.

Other Botanical Adaptogens

Three plants to consider for thyroid support include Forskolin, Ashwagandha and Guggul. Forskolin (from *Coleus forskohlii*) mimics the effects of thyrotropin and is a general adenylatecyclase activator and seems to induce the secretion of T3 and T4. Ashwagandha also increases T3 and T4, although that's just an in vitro study, and contraindicated in hyperthyroid. Guggul (gum resin of *Commiphora mukul*) is also thought to stimulate thyroid hormone synthesis, specifically T3.

Contributors

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 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. Hudson also sits on the scientific advisory boards for Gaia Herbs Professional Solutions, Nordic Naturals, Integrative Therapeutics Inc., and Natural Health International.

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 maintains her own practice in Portland, Oregon.