Safety, tolerability, and pharmacokinetics of an oral *Withania somnifera* product in older adults

NCT06171724

IRB Approval Date: 12.13.2024

OREGON HEALTH & SCIENCE UNIVERSITY

MED. REC. NO. _____
NAME _____
BIRTHDATE _____

STUDY00026055

CLINICAL RESEARCH CONSENT AND AUTHORIZATION SUMMARY OF KEY INFORMATION ABOUT THIS STUDY

TITLE: Safety, tolerability, and pharmacokinetics of an oral *Withania somnifera* product in older adults

PRINCIPAL INVESTIGATOR: Alex Speers, ND, MS | (503) 418-5896

You are being asked to join a research study. This consent form contains important information to help you decide if you want to join the study or not.

PURPOSE: The purpose of the study is to learn more about the absorption of an herbal product called Shoden®, which is an extract of *Withania somnifera* (common name: ashwagandha). Shoden® will be called the "study agent" throughout this form. We want to learn how the active ingredients of the study agent are absorbed and processed in the body. We also want to learn if there are any side effects caused by four weeks use of the study agent at two different doses.

DURATION: Your participation in the study will consist of 8 visits over 3 months. These visits include two baseline visits (13 hours each), a 24 and 48-hour visit after each baseline visit (20 minutes each), and a follow-up visit four weeks after each baseline visit (1 hour each). We will also call you 3 times during the study to check on how you are feeling after taking the study agent.

PROCEDURES: If you decide to take part in this study, we will ask you to take different doses of the study agent daily during two four-week study periods. You will not know which dose you get first or second. We will also ask you to complete surveys about your sleep quality and stress. At baseline visits there will be a blood draw, urine collection, and Electrocardiogram (ECG).

RISKS: During the baseline study visits you will have a catheter (tube) in your vein for about 12 and a half hours at each study visit. You may get an infection where the tube is placed. You may experience temporary digestive symptoms from the study agent such as nausea, gastric reflux/heartburn, diarrhea, and/or vomiting. You may have some side effects we do not expect because we are still learning about the study agent.

BENEFITS: You will not directly benefit from taking part in this research.

CO1450

ALTERNATIVES: You may choose not to participate in this study, or participate in another study if one is available.

This is a voluntary research study. You do not have to join the study. Even if you decide to join now, you can change your mind later. Please ask the Investigator if you have any questions about the study or about this consent form.

END OF CONSENT SUMMARY

OREGON HEALTH & SCIENCE UNIVERSITY

MED. REC. NO. _____
NAME _____
BIRTHDATE _____

STUDY00026055

Clinical Research Consent and Authorization Form

TITLE: Safety, tolerability, and pharmacokinetics of an oral *Withania somnifera* product in older adults

PRINCIPAL INVESTIGATOR:	Alex Speers, ND, MS	503-418-5896
CO-INVESTIGATORS:	Amala Soumyanath, PhD	503-494-6878
	Joseph Quinn, MD	503-494-7231
	Jesus Martinez (Study staff)	
	Katlin Wozniak (Study staff)	

WHO IS PAYING FOR THE STUDY?: National Center for Advancing Translational Sciences

WHO IS PROVIDING SUPPORT FOR THE STUDY?: Arjuna Natural

DO ANY OF THE RESEARCHERS HAVE A CONFLICT OF INTEREST WITH THIS STUDY?: No

WHY IS THIS STUDY BEING DONE?: You have been invited to be in this research study because you are over 65 years old and healthy. The purpose of this study is to learn more about the absorption and possible side effects in older adults of an herbal extract of *Withania somnifera* (common name: ashwagandha) called Shoden®. Shoden® is a commercially available ashwagandha supplement that is available at select health food stores and online retailers without a prescription. Shoden® will be called the "study agent" throughout this form.

Supplements with ashwagandha have been used in herbal medicine systems to help the body adapt to stress. This initial study will add to our current knowledge of ashwagandha and support future research on ashwagandha as a possible treatment for stress and sleep disturbances in older adults. This study will tell us if the active ingredients of the study agent get into the blood stream and will help us decide on a dosage for future human studies in older adults. The use of Shoden® for feelings of stress is experimental. It has not been approved by the FDA for treatment of any medical condition or disease because we do not know enough about it. This study will focus on learning about the safety, tolerability and absorption of ashwagandha in order to add to our understanding of how ashwagandha could be used by older adults in the future.

CO1450

This study requires eight study visits, after an initial screening visit, to OHSU. There are two four-week study periods separated by a two- to four-week period called a "washout" when you will not take the study agent. During each study period, you will attend a 13-hour baseline visit. You will return 24 and 48 hours later for a single blood draw and urine collection. You will then return for a follow-up visit four weeks later. We will call you two weeks after each baseline visit and two weeks after your final study visit to ask about your health and any side effects. The entire study will take about 3 months to complete.

We are asking you to provide blood, urine, and data for a samples and data bank, also called a repository. These samples will be stored indefinitely and may be used and disclosed in the future for research. We will enroll a total of fourteen participants in this study.

WHAT EXAMS, TESTS AND PROCEDURES ARE INVOLVED IN THIS STUDY? This study requires one screening visit and eight study visits at OHSU (see table below). After the screening visit, there will be two four-week study periods with a washout period between them. Every participant will get one of two doses of the study agent at the baseline visit and a 35-day supply for each four-week study period. The investigators will know which dose of the study agent you receive during each study period, but you will not know which dose you receive until the end of the study. This is called a single-blind study. Please ask the investigator if you have any questions about this kind of study.

	Screen	**PK Visit 1**			**2-week f/u**	**4-week f/u**	**Washout Period**	**PK Visit 2**			**2-week f/u**	**4-week f/u**	**Final visit +2 weeks**
Study Period		**1**			**1**	**1**		**2**			**2**	**2**	
Event	Clinic Visit	0 to 12h	24h	48h	Phone visit	Clinic visit		0 to 12h	24h	48h	Phone visit	Clinic visit	Phone visit
Vitals	X	X	X	X		X		X	X	X		X	
Health screening	X												
Safety Labs^	X#	X★	X˚			X		X$	X˚			X	
Electrocardiogram (ECG)	X	X$	X˚			X		X$	X˚			X	
Blood collection	X	X*	X	X		X		X*	X	X		X	
Single dose of study agent		X						X					
Issue 35-day supply of study agent				X						X			
Urine collection	X	X	X	X		X		X	X	X		X	
Symptoms questionnaire		X		X	X	X		X		X	X	X	X
Electronic Surveys		X				X		X				X	
Cognitive screen (MMSE)	X												
Mood screen (GDS)	X	X			X	X		X			X	X	X

f/u – follow-up
^ Safety labs include Complete Blood Count (CBC), Comprehensive Metabolic Panel (CMP), Thyroid-Stimulating Hormone (TSH), Testosterone, and Urinalysis.
# Blood for testosterone testing will not be collected at screening.
$ ECG collected prior to, and 7 hours after, ingestion of study agent
★ CMP collected prior to, and 10 hours after, ingestion of study agent
* At the baseline visits, blood is collected prior to taking the study agent and then at 14 timepoints: 15 minutes, 30 minutes, 45 minutes, 1 hour, 1.5 hours, 2 hours, 2.5 hours, 3 hours, 3.5 hours, 4 hours, 5 hours, 6 hours, 9 hours, and 12 hours
˚An ECG and CMP will be collected at the 24hr visit if the baseline visit was halted prior to the 7hr ECG and CMP being collected.

Screening Visit: During screening we will complete several exams and tests to establish a baseline for your health. You will have an electrocardiogram (ECG) to assess your heart function. A study team member will conduct a screening physical exam and measure your height, weight, pulse rate, temperature, blood pressure, pulse rate, and respiration rate. We will collect three teaspoons of blood and four teaspoons of urine, which will be used to measure blood cell counts, liver and kidney function, and thyroid function. You will complete two questionnaires by answering questions, one will assess your memory and thinking, the other is about and your mood. These questionnaires take 10-15 minutes total. We will review any supplements or drugs you are taking. This screening visit will take 90 minutes in total. After the study team receives your screening results we will contact you to let you know if you qualify for the study.

PHARMACOKINETICS (PK) VISITS: Each PK visit will take place over a 3-day period. You will attend an initial 13-hour baseline visit, followed by 20-minute visits at 24- and 48-hours.

Baseline Visits (0-12 hours): Your first baseline visit will happen about one week after your screening visit. Your second baseline visit will take place at least two weeks after your first 4-week follow-up visit. Each baseline visit will last about 13 hours. To prepare for each baseline visit, you will avoid caffeine, grapefruit juice, poppy-containing foods, and xanthine-containing foods or beverages (e.g., tea, chocolate, caffeine-containing sodas, colas, etc.) The night before each baseline visit, we will ask you to not consume any food or drinks after 9 PM to allow for a 10-12 hour fast. Water is allowed.

You will come to OHSU in the early morning and you will provide a urine sample (four teaspoons). Then, a member of the study team will ask you head-to-toe questions about your health using a symptoms questionnaire. You will complete a five-minute questionnaire about your mood. The study team member will measure your height, weight, pulse rate, temperature and blood pressure and collect an ECG. Next, an IV catheter (tube) will be inserted into a vein in your arm or hand for blood to be collected. An initial six teaspoons of blood will be collected for safety tests (blood cell counts, liver and kidney function, thyroid function, testosterone levels) and an initial sample of your plasma (the liquid base of blood).

You will then ingest two capsules of the study agent on an empty stomach. Blood will be collected at fourteen different time intervals after ingesting the study agent: 15 minutes, 30 minutes, 45 minutes, 1 hour, 1.5 hours, 2 hours, 2.5 hours, 3 hours, 3.5 hours, 4 hours, 5 hours, 6 hours, 9 hours, and 12 hours after taking the study agent. For each blood collection, two teaspoons of blood will be taken through the catheter using a syringe. The total amount of blood collected during the baseline visit will be about 12 tablespoons (~180 ml), a little less than half of what would be collected during a blood donation. You will also collect all your urine over the 12 hours after taking study agent.

If the results of your baseline labs show anemia, blood collection will be halted. We will ask that you stay for 4 hours after ingesting the study agent to assess for side effects. We will ask that you return for the 24-hour visit to collect safety tests (vitals, ECG, and a blood lab to assess liver and kidney function). After the 24-hour visit, you will be withdrawn from the study.

Two hours after taking the study agent, you will be allowed to eat food that follows a special diet (no dairy, grapefruit products, poppy-containing foods, high-fat meals, caffeine, or xanthine-containing foods or beverages) and that won't interfere with the study agent's absorption. All of your meals will be given to you free of charge the day of your baseline study visits. Snacks will be given to you as needed. Seven hours after you ingest the study agent, another EKG and set of vitals (blood pressure, temperature, respiration rate, pulse rate) will be collected. Ten hours after you ingest the study agent, one teaspoon of blood will be collected for liver and kidney function tests.

If we have difficulties collecting blood samples from the catheter, we may choose to halt the baseline visit. We will ask that you stay for 4 hours after ingesting the study agent to assess for side effects and ask that you return for the 24-hour visit to collect safety tests (vitals, ECG, and a blood lab to assess liver and kidney function). You will be allowed to continue on the study if blood collection difficulties were the only reason for ending the baseline visit early.

At the end of the visit, the catheter will be removed, and the area will be wrapped with a compression bandage. A member of the study staff team will ask the same head-to-toe questions about your health that were asked at the beginning of the study visit using a

symptoms questionnaire. Vitals (blood pressure, temperature, respiration rate, pulse rate) will be collected. You will then be allowed to travel home. You will be asked to continue the special diet (no dairy, grapefruit products, poppy-containing foods, high-fat meals, caffeine, or xanthine-containing foods or beverages) until the 24-hour visit the following day.

24- and 48-Hour Visits: After each baseline visit, you will return to OHSU 24 and 48 hours later for a single two teaspoon blood draw and urine collection. Vitals will be collected. A CMP and ECG may be collected at the 24-hour visit if the previous day's baseline visit was halted before 7 hours. At the 48-hour visit, side effects will be assessed using a questionnaire. You will be given a 35-day supply of the study agent at the 48-hour visit and instructed to begin taking two capsules before bed every day for the next four weeks.

Phone Follow-Ups: Two weeks after each baseline visit, a member of the study team will call you to see if you have had any side effects using a head-to-toe questionnaire. Two weeks after the final follow-up visit, a member of the study team will call one more time to see if you had any side effects. You will also complete a five-minute questionnaire about your mood at each phone follow-up visit. Each call should take 10-15 minutes. After the final follow-up call, you are finished with the study.

Follow-Up Visits: Four weeks after each baseline visit, you will return to OHSU for a follow-up visit after fasting for 10-12 hours the night before. A blood sample (four teaspoons) and urine sample (four teaspoons) will be collected to measure how the study agent is absorbed and tests will measure blood cell counts, liver and kidney function, thyroid function, and testosterone levels. You will complete a five-minute questionnaire about your mood. Your height, weight, blood pressure, temperature, and pulse rate will be recorded, and an ECG will be collected. A member of the study team will ask you head-to-toe questions about any potential side effects using a questionnaire. You will return any unused study agent capsules and be asked which dose of the study agent you think you received for the previous four weeks.

Washout Period: After the first four-week follow-up visit, you will stop taking the study product for at least two weeks and not longer than four weeks. If your washout period is longer than 21 days, we will call you at two weeks to assess for any delayed side effects. You will then return to OHSU for the second baseline visit and repeat the previously described study procedures.

Electronic Questionnaires: At four timepoints during the study, you will be emailed two questionnaires to complete on your computer or phone. These questionnaires will take 5-10 minutes to complete. The questionnaires will ask you questions about your stress levels and sleep. You will complete these questionnaires during the week prior to the baseline visit and the week prior to the 4-week follow-up visit for each study period.

In the future, your blood, urine, and information may be given to researchers, for other research studies. These studies may include genetic research. The samples and information will be labeled as described in the **WHO WILL SEE MY PERSONAL INFORMATION?** section.

WILL I RECEIVE RESULTS FROM THE TESTING IN THIS STUDY? We will give you the results of your screening tests to share with your primary care provider. The results will be placed in your medical record. We do not plan to share your research test results with you or your primary care provider; however, if we discover information that is important for your health care, either in this study or in the future, we will contact you and ask if you want to receive the results. If you choose to receive the results, you may need to have additional testing performed that will not be covered by the research study.

WHAT RISKS CAN I EXPECT FROM TAKING PART IN THIS STUDY?: You may have some side effects we do not expect because we are still learning about the study agent. You may not have symptoms for some of these side effects, but you will be monitored by the investigator to check for any changes throughout the study.

Blood Draw: We draw blood from a needle in your arm or hand. You may feel some pain or discomfort when the needle is inserted. There is a small chance the needle will cause bleeding, a bruise, an infection, or fainting.

IV catheter: During the 2 baseline visits you will have a catheter (tube) in your vein for about 12 and a half hours. You may get an infection where the tube is placed. This would cause swelling, redness, and pain. You may bleed, get a bruise, or faint. There is a small chance your blood stream or heart valves might get a serious infection. A piece of the tube could break off in your vein or you may get a blood clot that could go to your lungs, brain, or heart. These risks are very rare. If you have these problems, you will need immediate medical care.

Study Diet: The study diet requires that you avoid any caffeine for 48 hours prior to each baseline visit. If you regularly drink caffeinated beverages like coffee, you may experience symptoms of caffeine withdrawal, including headache, fatigue, decreased energy/activeness, decreased alertness, drowsiness, decreased contentedness, depressed mood, difficulty concentrating, irritability, and feeling foggy/not clearheaded.

Study Agent: Ashwagandha has generally been well-tolerated in clinical trials, with a recent review of 30 ashwagandha trials finding no evidence of serious adverse events or any changes in blood markers or vital signs. Common side effects (>5%) were mild and short-lasting, with the most common being drowsiness and gastrointestinal disturbances. Rare, serious side effects have been reported in isolated cases. Potential risks may include:

Risk	Symptoms	Frequency
Gastrointestinal disturbances	Abdominal pain, loose stools, nausea, dry mouth, acute diarrhea and vomiting	Abdominal pain: up to 9% Loose stools: up to 9% Dry mouth: up to 6% Nausea: up to 3%
Change in energy levels	Drowsiness, hyperactivity	Drowsiness: Up to 21% Hyperactivity: Up to 6%
Body changes	Rash, weight gain	Rash: Up to 6% Weight gain: Up to 6%
Elevated DHEA-S and/or testosterone levels	Excess hair growth, acne, menstrual irregularities, vaginal atrophy, hair loss in women	Increased DHEA-S levels have been observed in one trial of older males. Two trials involving males and females found decreased levels or no effect. Increased testosterone levels have only been observed in males.
Liver toxicity	Fatigue, itching, yellow skin, abdominal pain, loss of appetite, vomiting, diarrhea, fever	Rare: Isolated case reports Not observed in clinical trials
Kidney transplant rejection	Fever, swelling in the hands and feet, tenderness or pain	Rare: Single case report

	over the kidney, decreased urine output, achiness	
Allergic reaction	Itching, rash, difficulty breathing, vomiting, death	Rare: Anecdotal reports of allergy symptoms, possibly related to Nightshade sensitivity or allergy

To assess for liver and renal dysfunction, a blood test (complete metabolic panel) will be collected at baseline and four-week follow-up visits. Blood tests for anemia, thyroid-stimulating hormone, and testosterone will also be collected at baseline and four-week follow-up visits. If abnormalities are present, the clinical investigator will decide whether you should be withdrawn from the study and referred to your PCP for further evaluation.

Please discuss all of your allergies with the study team prior to taking the study agent. If you experience any itching or changes in breathing, please tell the investigator immediately so you may receive immediate medical attention.

There are several drugs (prescription and non-prescription) that may cause problems when taken with the study agent. The investigator will carefully review all of the drugs you are taking before giving you the study agent. If any other health care provider prescribes any new drug(s) for you while you are in this study, please tell the investigator before you take the new drug or continue in the study. That provider can also talk to the investigator before prescribing the new drug. Do not take any new over-the-counter drugs while you are in this study unless you check with the investigator.

Suicidal Thoughts and Behavior: There is no known risk of increased suicidal thoughts and behavior in people taking the study agent. However, suicide rates increase with age and because safety information for the study agent in older adults is limited, we will monitor your mood throughout the study using a 5-minute questionnaire. Depending on your answers, you may be given an additional questionnaire to complete or referred to another clinician as needed.

Pregnancy/risk to fetus: The agents in this study may affect sperm and be present in seminal fluid. You should not cause a pregnancy or donate sperm while you are in this study and for one month following the last dose of the study agent as the effects of ashwagandha in pregnancy are unknown and potentially harmful. If you are sexually active and could cause a pregnancy, you must be sure that your sexual partner(s) are using birth control that works well or you must not have sex. This study may involve risks to an embryo or fetus that are currently unknown. The investigator will talk to you about the types of birth control that are acceptable. If a sexual partner becomes pregnant during the research study, please tell the investigator, and ask your partner to tell her doctor immediately. A records review will be conducted one month after you have completed the study to check for evidence of pregnancy.

Data Confidentiality: Although we have made efforts to protect your identity, there is a small risk of loss of confidentiality. If the results of these studies were to be accidentally released, it might be possible that the information we will gather about you as part of this study could become available to an insurer or an employer, or a relative, or someone else outside the study. Even though there are certain confidentiality protections in both Oregon law and federal law, there is still a small chance that you could be harmed if a release occurred.

WHAT ARE MY CHOICES IF I DECIDE NOT TO TAKE PART IN THIS STUDY?

You may choose not to be in this study.

WHO WILL SEE MY PERSONAL INFORMATION? We will take steps to keep your personal information confidential, but we cannot guarantee total privacy. Your samples and information will be labeled with a unique code number so that you cannot be directly identified from these

materials. We will create and collect health information about you as described in the WHY IS THIS STUDY BEING DONE? and the WHAT EXAMS, TESTS AND PROCEDURES ARE INVOLVED IN THIS STUDY? sections of this form. Health information is private and is protected under federal law and Oregon law. By agreeing to be in this study, you are giving permission (also called authorization) for us to use and disclose your health information as described in this form.

The investigators, study staff, and others at OHSU may use the information we collect and create about you in order to conduct and oversee this research study, store it in a repository, and conduct future research,

We may release this information to others outside of OHSU who are involved in conducting or overseeing research, including:

- The funder of this study, The National Center for Advancing Translational Sciences, and the funder's representatives
- The Food and Drug Administration
- The Office for Human Research Protections, a federal agency that oversees research involving humans

Those listed above may also be permitted to review and copy your records, including your medical records. We may also share your information with other researchers, who may use it for future research studies. Your data, blood, and urine samples will be stored in a repository at OHSU.

We will not release information about you to others not listed above, unless required or permitted by law. We will not use your name or your identity for publication or publicity purposes, unless we have your special permission.

To help us protect your privacy, we have obtained a Certificate of Confidentiality to protect your privacy even from people who try to get your information using a court order. One exception is if you agree that we can give out research information with your name on it. Another exception is information about child or elder abuse or neglect and harm to yourself or others or communicable disease reporting. Note that this doesn't prevent you from releasing the information yourself.

Under Oregon law, suspected child or elder abuse must be reported to appropriate authorities. When we send specimens or information outside of OHSU, they may no longer be protected under federal or Oregon law. In this case, your specimens or information could be used and re-released without your permission.

Data and samples from this study may be shared with other investigators for future research studies. A code number will be assigned to your samples, data, and to the information about you. If samples of your blood and urine, or data are used for future research purposes other investigators may be given the code number which will not identify you, or they may be given the key to the code and other information that could identify you. For example, identifiable information shared could include the dates your samples were collected along with your age and sex. We may provide your medical record number (MRN) with the requested samples/study data (so that future researchers can collect additional data) and this would also identify you. Therefore, your coded blood and urine samples, the key to the code, and other information listed here may be shared with other investigators, but only for scientific research purposes, and only with the appropriate IRB approval.

We may continue to use and disclose your information as described above indefinitely. Some of the information collected and created in this study may be placed in your OHSU medical record.

While the research is in progress, you may or may not have access to this information. After the study is complete, you will be able to access any study information that was added to your OHSU medical record. If you have questions about what study information you will be able to access, and when, ask the investigator.

WILL ANY OF MY INFORMATION OR SAMPLES FROM THIS STUDY BE USED FOR ANY COMMERCIAL PROFIT? Samples and information about you or obtained from you in this research may be used for commercial purposes, such as making a discovery that could, in the future, be patented or licensed to a company, which could result in a possible financial benefit to that company, OHSU, and its researchers. There are no plans to pay you if this happens. You will not have any property rights or ownership or financial interest in or arising from products or data that may result from your participation in this study. Further, you will have no responsibility or liability for any use that may be made of your samples or information.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY? There will be no cost to you or your insurance company to participate in this study. You will receive a prorated payment of $200 for completing the study, $100 after each completed baseline visit. We will request your social security number in order to process any payments for participation. You may receive payment via a debit card. There may be fees (for example, if the card is inactive for more than six months), which will be deducted from the balance on your card. Details on how to use the card and any fees are included in the separate card member agreement and FAQ sheet.

Payment received as compensation for participation in research is considered taxable income for a research subject. If payments are more than $600 in any one calendar year, OHSU is required to report this information to the Internal Revenue Service (IRS). Research subject payments exceeding $600 during any calendar year will result in a 1099 (Miscellaneous Income) from being issued to the research subject and a copy will be sent to the IRS.

WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THIS STUDY?: If you believe you have been injured or harmed as a result of participating in this research and require treatment, contact Dr. Joseph Quinn at 503-494-7231. If you are injured or harmed by the study agent or study procedures, you will be treated. OHSU and the funder do not offer any financial compensation or payment for the cost of treatment if you are injured or harmed as a result of participating in this research. Therefore, any medical treatment you need may be billed to you or your insurance. However, you are not prevented from seeking to collect compensation for injury related to negligence on the part of those involved in the research. Oregon law (Oregon Tort Claims Act (ORS 30.260 through 30.300)) may limit the dollar amount that you may recover from OHSU or its caregivers and researchers for a claim relating to care or research at OHSU, and the time you have to bring a claim.

If you have questions on this subject, please call the OHSU Research Integrity Office at (503) 494-7887.

This federally funded study also does not have the ability to provide compensation for research-related injury. If you are injured or become ill from taking part in this study, it is important to tell your study doctor. Emergency treatment may be available but you or your insurance company will be charged for this treatment.

WHERE CAN I GET MORE INFORMATION? If you have any questions, concerns, or complaints regarding this study now or in the future, contact the Principal Investigator, Alex Speers, ND, MS via phone at (503) 418-5896 or via email speers@ohsu.edu. You can reach or other members of the study team at (herbalPKtrial@ohsu.edu).

This research has been approved and is overseen by an Institutional Review Board ("IRB"), a committee that protects the rights and welfare of research participants. You may talk to the IRB at (503) 494-7887 or irb@ohsu.edu if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.
- You want to get more information or provide input about this research.

You may also submit a report to the OHSU Integrity Hotline online at https://secure.ethicspoint.com/domain/media/en/gui/18915/index.html or by calling toll-free (877) 733-8313 (anonymous and available 24 hours a day, 7 days a week).

WHAT ARE MY RESPONSIBILITIES IN THIS STUDY? We will ask you to complete two 13 hour baseline visits, during which it is important for you to be well-hydrated. We will remind you about hydration prior to the visit and provide water to you during the visit, with an expectation that you will try to drink ~64 ounces of water during the 13 hours. We will ask you to take one capsule of the study agent every night at bedtime for four weeks during both study periods. You should let us know (a) if you experience any significant side effects prior to the 2-week phone call or next scheduled visit and (b) if you start any new prescriptions or over the counter medications during this study.

DO I HAVE TO TAKE PART IN THIS STUDY? Your participation in this study is voluntary. You do not have to join this or any research study. You do not have to allow the use and disclosure of your health information in the study, but if you do not, you cannot be in the study

IF I DECIDE TO TAKE PART IN THIS STUDY, CAN I STOP LATER? If you do join the study and later change your mind, you have the right to quit at any time. This includes the right to withdraw your authorization to use and disclose your health information. If you choose not to join this study, or if you withdraw early from any or all parts of the study, there will be no penalty or loss of benefits to which you are otherwise entitled, including being able to receive health care services or insurance coverage for services. Talk to the investigator if you want to withdraw from the study

If you no longer want your health information to be used and disclosed as described in this form, you must send a written request or email stating that you are revoking your authorization to:

Alex Speers, ND, MS | (503) 418-5896
Oregon Health and Science University
Mail Code OP 32
3181 SW Sam Jackson Park Road
Portland, OR 97239
speers@ohsu.edu

Your request will be effective as of the date we receive it. However, health information collected before your request is received may continue to be used and disclosed to the extent that we have already acted based on your authorization.

If you choose to withdraw before completing the study, you will be requested to do a two-week follow-up phone visit to see if you experienced any delayed side effects from the study agent. We will ask you why you chose to withdraw from the study, which you may choose not to answer. If in the future you decide you no longer want to participate in this research, we will remove your name and any other identifiers from your samples and questionnaires, but the material will not be destroyed, and we will continue to use it for research.

If in the future you decide you no longer want to participate in this research, we will remove your name and any other identifiers from your samples and information, but the material will not be destroyed and we will continue to use it for research.

You may be removed from the study if the investigator or funder stops the study, you become pregnant, you develop serious side effects, or you do not follow study instructions.

We will give you any new information during the course of this research study that might change the way you feel about being in the study.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. law. This web site will not include information that can identify you. At most, the web site will include a summary of the results. You can search this web site at any time.

SIGNATURES:
Your signature below indicates that you have read this entire form and that you agree to be in this study. We will give you a copy of this signed form.

Participant Printed Name	Participant Signature	Date

Person Obtaining Consent Printed Name	Person Obtaining Consent Signature	Date

Use of an Interpreter: Complete if the participant is not fluent in English and an interpreter was used to obtain consent. **Participants who do not read or understand English must not sign this full consent form,** but instead sign the short form translated into their native language. This form should be signed by the investigator and interpreter only. If the interpreter is affiliated with the study team, the signature of an impartial witness is also required.

Print name of interpreter: _____

Signature of interpreter: _____ Date: _____

An oral translation of this document was administered to the participant in _____ (state language) by an individual proficient in English and _____ (state language).

If applicable:

Print name of impartial witness: _____

Signature of impartial witness: _____Date: _____

See the attached short form for documentation.