PREBIOTICS IN WOMEN'S HEALTH AND AGING: THE GUT-BONE CONNECTION

INFORMED CONSENT

MAY 27, 2025

Indiana University Informed Consent Statement for Research

Prebiotics in Women's Health and Aging: The Gut-Bone Connection

IRB #23232

SPONSOR: UNITED STATES DEPARTMENT OF AGRICULTURE

You are being asked to participate in a research study. This consent form will give you information about the study to help you decide whether you want to participate. It is your choice whether or not you want to be in this research study. Please read this form, and ask any questions you have, before agreeing to be in this study.

Important Things to Know:

Previous studies have shown that dietary supplementation with dried plums reduces bone loss in postmenopausal women. Dried plums are also known as prunes. The purpose of this research study is to understand how dried plums work by assessing changes in your immune cells, gut microbes and bone biomarkers. We will also determine if other factors such as your vitamin D status affect your response to dried plums.

As a part of this study, you will complete 5 total visits to the IU Health University Hospital. The first visit will allow us to determine if you qualify for the study by assessing your medical history, height and weight, and the medications and dietary supplements that you take. If you qualify and agree to participate in the study, you will be asked questions about your regular diet and be required to be in another research study entitled "Musculoskeletal Function, Imaging and Tissue (FIT) Core" (IRB study #1707550885). We are using the FIT Core to collect some of the data for our study.

As a part of the FIT Core study, you will receive a separate informed consent that details the study tests and associated risks with that study. In the FIT Core study you will be asked questions about your physical activity, have special imaging tests of your muscles and bones, and be asked to complete tests of your physical abilities, such as how hard you can squeeze your hand (grip strength), how fast you can walk, and how many times you can stand up from a chair in 30 seconds. You will only complete this FIT Core testing one time (at Visit 1).

The primary study is divided into three phases. In one phase, you will consume dried plum (5-6 dried plums) each day for about 4 weeks. Study personnel will provide you with the dried plums. In another phase of the study, you will consume your regular diet (without dried plums) for 4 weeks. Each day you will complete a brief questionnaire about your bowel function and any noticeable gastrointestinal changes. These two phases will be separated by a "washout" or rest period. The order that you complete the two phases will be randomly assigned. You will be in the study for a total of about 14 weeks.

Assessments and sample collection will be performed before and after each phase of the study at your next four visits (Visits 2-5). Prior to these visits you will be provided a kit to collect a fecal stool sample and will be asked to record all of the food and drink that you consume for 3-days prior to the appointment. At these visits, we will record your height and weight, update your medical history form with any changes, ask you questions about your physical activity, diet, sun

exposure, issues with consuming the dried plum and we will draw a blood sample. There may be some discomfort or bruising with the blood draw.

There is no cost to you for participating in this study and you will be paid for participating. As a part of this study, you will receive information about your dietary habits and vitamin D status. You will receive snack packs of dried plum to consume at no charge. Dried plums are rich in nutrients, which can offer many health and nutritional benefits. As a part of the FIT Core study, you will receive a free bone density scan and information about your physical function.

Please review the rest of this document for more details about this study and the things you should know before deciding whether to participate.

Why is This Study Being Done?

Previous studies have shown that supplementing the diet with dried plums reduces bone loss in postmenopausal women. Dried plum's benefits on bone in laboratory animals have been associated with their prebiotic effects on gut microbes and immune function. However, it is not known whether the benefits of dried plum on bone in postmenopausal women are a result of these same prebiotic effects. Also, it is not known if other factors such as a person's vitamin D status influences this response.

This clinical study will investigate how supplementing your diet with dried plums alters your gut microbes, certain immune cells and circulating bone biomarkers. The findings of this study will help us understand how dried plum works and whether your vitamin D status influences this response.

We are asking you if you want to be in this study because you are a postmenopausal woman between the ages of 60-75 yrs who does not have a history of health problems or are on medications or supplements that would interfere with the study.

The study is being conducted by Dr. Brenda Smith, Indiana University Indianapolis, Department of Obstetrics and Gynecology. It is funded by the United States Department of Agriculture, National Institute of Food and Agriculture.

What Will Happen During the Study?

As a part of this study, you will complete 5 visits to the IU Health University Hospital Clinical Research Center (*See Figure 1 next page*). The first visit (Visit 1) will allow us to determine if you qualify for the study by assessing your medical history, height and weight, medications, and dietary supplements. If you qualify for this study**,** you be required to be in another research study entitled the "Musculoskeletal Function, Imaging and Tissue (FIT) Core" (IRB study #1707550885). If you don't want to participate in the FIT Core study, you cannot participate in this study. The reason you must participate in both studies is because certain information collected in the FIT Core study will also be used for this study.

You will receive a separate informed consent that details the study tests and associated risks for the FIT Core study. In brief, it includes measuring how well you perform about 30-45 minutes of tests of your physical abilities including: hand grip strength, how fast you can walk, and how many times you can stand up from a chair in 30 seconds. Data collected in the FIT Core study will be used by other researchers to understand the causes and consequences of different physical function and activity levels across a large population. The main risks of participation in the FIT Core study are the risk of fatigue and falls from the testing. More information about the FIT Core study is in the separate Informed Consent you will receive. You should read the Informed Consent Statement for the FIT study before deciding whether you want to participate in this study.

As part of the FIT Core study you will also be required to undergo a special imaging test of your muscle and bones called a DEXA or bone density test. This test carries a very slight amount of radiation. More information about the radiation risks is included in the FIT study consent. You will only do the FIT Core testing during your first visit in our study. At the end of this visit, we will schedule Visit 2 within 1-3 wks. <u>We anticipate that the first visit will take about 2-2 ½ hrs.</u>

The main study is divided into three phases, with each lasting about 4 weeks (**Figure 1**). In one phase of the study, you will gradually increase your consumption of dried plums over a week to the point that you are consuming 5-6 dried plums (50 grams) each day for 4 weeks. Study personnel will provide the dried plums at no cost. In a separate phase of the study, you will consume your regular diet (without dried plums) for 4 weeks. These two phases will be separated by about 3-4 weeks, a "washout" period. You will be assigned to the order (A or B below) in which you will complete the two test phases by chance. You will be in this study for a total of about 14 weeks (~3 ½ months).

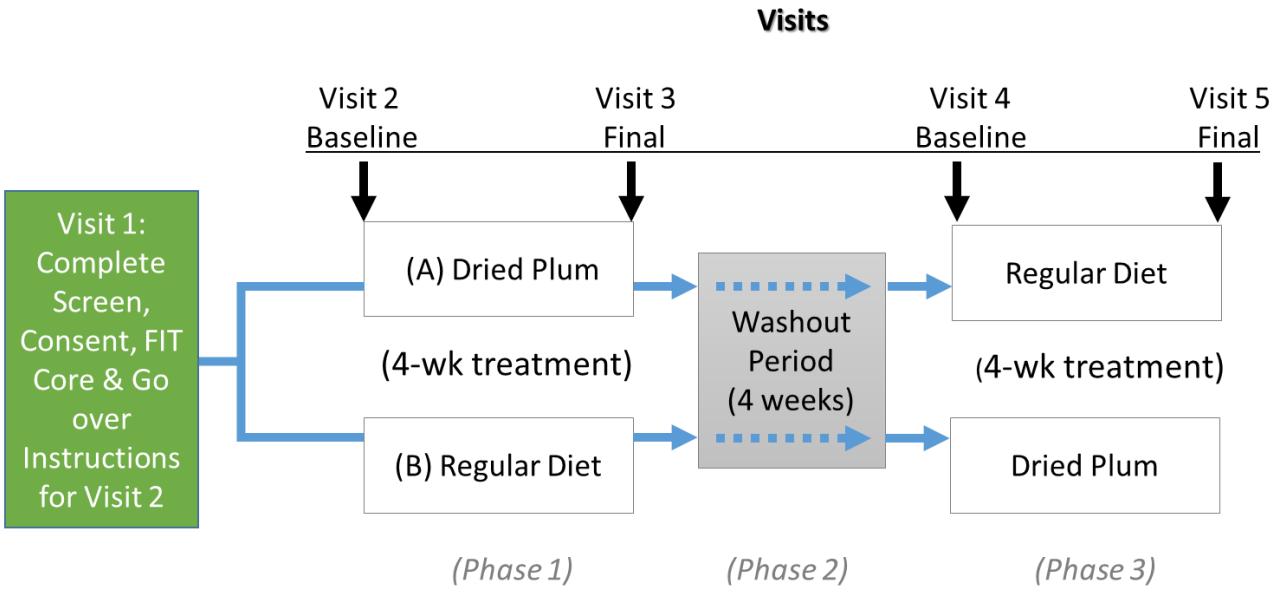

Figure 1. Study Overview. Participants will randomly be assigned to order A or B.

Prior to Visits 2-5, you will be provided a kit with instructions to collect fecal stool samples and will be asked to record all the food and drink that you consume for 3-days prior to the

appointment. You will return your stool sample and diet record at each of these visits. Also at these visits, we will record your height and weight, update your medical history form with any changes that have occurred since your last visit. We will ask you questions about your physical activity, sun exposure, and then draw a fasting blood sample. You should expect that each of the Visits 2-5 will take about 1 hr each. More detailed descriptions of these procedures are provided **Table 1** and in the section that follows.

Table 1. Overview of Timing of Study Procedures

Procedures	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5
Explain the study, answer questions and consent	x				
Medical history questionnaire (form will be updated at Visits 2-5)	x	x	x	x	x
Anthropometric measurements (height & weight)	x	x	x	x	x
FIT Core (bone & muscle imaging, physical function testing, and questionnaires)	x				
Assigned to Group and provided instructions.		x		x	
Complete 3-day Food Record prior to visit		x	x	x	x
Return Stool Sample		x	x	x	x
Physical Activity Questionnaire		x	x	x	x
Sun Exposure Questionnaire		x	x	x	x
Bowel function and gastrointestinal tolerance questionnaires collected			x		x
Fasting Blood Collection		x	x	x	x
Compliance calendar collected			x		x
Honorarium ($50 gift card after each visit is completed)	x	x	x	x	x

- Medical history: A questionnaire will be used to ensure that you do not have any of the medical conditions that prevent you from joining the research study. You will also be asked about medications and supplements that you are currently taking or have taken in the last 12 months and questions related to your lifestyle habits (for example - Do you smoke?). This questionnaire will be completed at Visit 1 and will take about 20 minutes. We will ask if there are any updates to the information at Visits 2-5 (less than 5 minutes).

- Dietary intake: You will be asked to record your dietary intake over 3 days prior to Visits 2-5. At Visit 1, you will be shown how to use an automated tool called the ASA24 that will allow us to assess your dietary intake. This will require that you enter information about everything you eat and drink, and any dietary supplements that you take over the 3-day period. You will be asked to do this during the week prior to Visits 2-5.

- FIT Core: At Visit 1, you will also complete a session at the Indiana Center for Musculoskeletal Health FIT Core (IRB study #1707550885). You will receive a separate informed consent that details the study tests and associated risks for the FIT Core study. We will use the test results data from that study to help answer our research question for this study.

- Physical Activity Questionnaire: A physical activity questionnaire will help us determine how much you exercise and what types of exercise you have done over the past month. This questionnaire will be completed at Visits 2-5.

- Sun Exposure Questionnaire: A brief sun exposure questionnaire will give us information related to your vitamin D status. It will be completed at Visits 2-5.

- Bowel Function and Gastrointestinal Tolerance Questionnaire: During each study period, you will be asked to complete this questionnaire each day. You will be asked to rate your bowel function, any GI symptoms you have experienced (e.g., burping and bloating), as well as the consistency and ease of your bowel movements.

- Blood Sample: For the blood collection, you will have your blood drawn from the vein in the right or left arm by a licensed phlebotomist or a registered nurse. About 2 tablespoons (~26 mL) of blood will be drawn. This will happen 4 times over the course of the study, one time at each of the visits 2-5. The investigators will measure chemicals in your body that provide information about your immune cells, bones, vitamin D, different metabolites and indicators of hormone status. There may be some discomfort or bruising with the blood draw. Blood samples will be labeled with your study number and the date the sample was collected. All samples will be handled by trained study personnel only and will be stored in very cold temperature freezers in the principal investigator's laboratory for up to 10 years.

- Fecal Sample: You will be asked to collect stool samples from two separate bowel movements prior to Visits 2, 3, 4 and 5 using a stool collection kit that will be provided with instructions. You will bring these samples with you when you come in for each of these visits. You will be also asked to rate the consistency of the stool when you collect the samples.

- Daily: Record the date, time, and number of dried plum you ate on the study calendar that is provided. Return any dried plums that you didn't consume to the study personnel at your next visit.

Follow-ups: Study personnel will call, text or email you at times during the study to ask if there are any problems related to your participation in the study and to remind you about sample collections and your next visit.

There is no cost to you for participating in this study and you will be compensated $50 for your time and travel when you complete each visit for a total of $250 by the end of the study. As a benefit of this study, you can receive information about your bone density, physical function abilities, and dietary habits. You will receive snack packs of dried plum to consume at no charge. Dried plums are rich in nutrients, which can offer many health and nutritional benefits.

Because we are receiving this information about your bone health, physical function, and dietary habits, we may learn things about you that could be important to your health or interesting to you. This information likely isn't something that you need to take action on immediately but may be helpful for your health in the future. You will have the option to receive this information at the end of the study and you may want to share this information with your primary care physician. It is your choice whether you receive this information or not. The study team/study will not cover the costs of any follow-up consultations or actions.

What Are the Risks of Taking Part in the Study?

The risk from participating in this study is minimal.

- Allergy: There is a remote possibility that you can develop allergic reaction to consuming dried plums. Plums are related to cherries, peaches, nectarines, and apricots. Should you have an allergy to any of these foods, participation in the study is not recommended unless it is known that no allergy to dried plums exists. The most common allergic reaction is itchy mouth and throat; however more severe reactions such as rash, difficulty breathing, nausea and vomiting, and anaphylactic shock can occur. If you have known allergies to cherries, peaches, nectarines, or apricots, a small sample of dried plums will be provided at the initial visit to monitor the possibility for a reaction.

- Blood draw. The risks of drawing blood might be pain at the needle site, bruising, feeling faint, and slight risk of infection or clotting in the blood vessel may occur. If you get light-headed or feeling faint during any blood draws, you will be asked to lie down and drink juice or eat a light snack, and we will stop the remainder of the blood collections.

- Gastrointestinal symptoms: There is a chance you may experience changes in your bowel habits, the consistency of stools when consuming the dried plum.

- Confidentiality. Someone outside of the research team could get access to your research information from this study.

- Other Risks. As with any research study, there may be additional risks that the researchers don't know about yet. However, the participants will be informed of any such risks if the researchers learn of any.

Who Will Pay for my Treatment if I am Injured?

If you have an injury or illness as a result of participating in the study, you will be responsible for seeking medical care and for the expenses associated with any care received. Any costs not covered by your medical insurance will be your responsibility. We don't have money set aside to pay for these types of injuries. However, signing this form won't take away any of your legal rights if you are injured.

What Are the Benefits of Taking Part in the Study?

As part of this research study, you will have the option of receiving information about your bone density and physical function abilities and dietary habits. For no charge, you will receive the dietary supplements (dried plums) to be consumed daily for about 4 weeks. Dried plums are a rich in nutrients which can offer many health and nutritional benefits. We hope to learn things from your participation in this study that will help other people in the future.

Will I be Paid for Participating?

As a part of this study, you will be compensated $50 for your time and travel after you complete each visit. The total amount for successfully completing all visits is $250 ($50 x 5 visits) by the end of the study.

How Will My Information be Used?

The following individuals and organizations may receive or use your identifiable health information:

- The researchers and research staff conducting the study.
- The Institutional Review Boards (IRB) or its designees that review this study
- Indiana University
    - The Indiana Clinical Research Center (ICRC)
- State and Federal government agencies as permitted by law, including but not limited to:
    - the Office for Human Research Protections (OHRP)

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

How Will My Information be Protected?

We will do our best to keep your personal information private, but we cannot promise complete confidentiality. We will maintain your information related to the study in a secure database called REDCap. We won't share any information that we think could be used to identify you in publications about this study. However, your personal information may be shared outside the research study as described above and/or if required by law.

Who Should I Call with Questions or Problems?

For questions about the study or a research-related problem, contact the researcher, Dr. Brenda Smith, at 317-278-5150 or email bsm14@iu.edu. For questions about your rights as a research participant, to discuss problems, complaints, or concerns about a research study, or to obtain information or to offer input, please contact the IU Human Research Protection Program office at 800-696-2949 or at irb@iu.edu.

What if I Do Not Want to Participate or Change my Mind?

After reviewing this form and having your questions answered, you may decide to participate in the study. Or, you may choose not to participate in the study. This decision is up to you. If you choose not to participate in this study or change your mind after signing this document, it will not affect your relationship with Indiana University or the medical care you receive from IU Health.

If you change your mind and decide to leave the study in the future, the study team will help you withdraw from the study safely. If you decide to withdraw, we ask that you contact the Study Coordinator, Dr. Lily Hernandez at lilphern@iu.edu or (317) 278-0684, or Dr. Brenda Smith at bsm14@iu.edu or (317)278-5150 so that we can collect information related to the reason for and timing of your withdrawal.

Agreement to be Contacted by Text and/or Email

We would like to communicate with you about this study by text message and/or email. We might use text or email to remind you about an upcoming study visits, check on how you are doing, remind you to consume dried plums, or to complete your stool sample collections and your 3-day food records prior to a visit. Text messaging and email are not secure methods of communication. The information sent over text or email, which may include sensitive or personal information, such as protected health information, could be accessed or read by someone other than you. If you would like us to communicate with you via text or email, please initial the lines below and provide the phone number(s) and/or email address(es) you would like us to use.

_____ I authorize the researchers to send me emails related to this research study

Email address for this communication: _____

_____ I authorize the researchers to send me text messages related to this research study

Phone number for this communication: _____

You can still participate in this study even if you do not want us to contact you by text or email.

Participant's Consent

I agree to participate in this research study.

Participant's Printed Name:_____

Participant's Signature:_____**Date:**_____

Printed Name of Person Obtaining Consent:_____

Signature of Person Obtaining Consent: _____**Date:**_____