Official Title: Pharmacokinetics and pharmacodynamics of anthocyanins after oral cherry juice concentrate in gout patients

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I. SUBJECT CONSENT TO TAKE PART IN A RESEARCH STUDY

TITLE OF STUDY: Pharmacokinetics and pharmacodynamics of anthocyanins after oral cherry juice concentrate in gout patients.

Principal Investigator: Naomi Schlesinger, MD

This consent form is part of an informed consent process for a research study and it will provide information that will help you to decide whether you wish to volunteer for this research study. It will help you to understand what the study is about and what will happen in the course of the Study.

If you have questions at any time during the research study, you should feel free to ask them and should expect to be given answers that you completely understand.

After all of your questions have been answered, if you still wish to take part in the study, you will be asked to sign this informed consent form.

You are not giving up any of your legal rights by volunteering for this research study or by signing this consent form.

Who is conducting this research study?

Dr. Naomi Schlesinger is the Principal Investigator of this research study. A Principal Investigator has the overall responsibility for the conduct of the study. However, there are often other individuals who are part of the research team.

Dr. Naomi Schlesinger may be reached at:

Department of Medicine
Division of Rheumatology Rutgers, The State University of New Jersey
125 Paterson Street, Suite 5200A
New Brunswick, NJ 08901-1962
Tel: 732-235-8378
E-mail: schlesna@rwjms.rutgers.edu

The Principal Investigator or another member of the study team will also be asked to sign this informed consent. You will be given a copy of the signed consent form to keep.

Who will benefit?
You will not receive any direct benefit for participating in this research, but the research may provide scientists with a better understanding of the benefits of tart cherry juice concentrate.

Why is this study being done?
The purpose of this study is to help us understand if tart cherry is absorbed into your body and if it has the potential for health benefits in gout.

Why have you been asked to take part in this study?
We are asking individuals with gout to take part in this study. If you have been approached to participate, it is because you spoke to Dr Schlesinger or responded to an advertisement and met all the criteria to be part of this research study.

Who may take part in this study? And who may not?

Inclusion:
Subjects are eligible for inclusion if they have a diagnosis of gout and are between the ages of 18 and 75 years.

Exclusion:
There are several criteria that would exclude you from eligibility. These criteria are listed below:

- History of allergy to cherries or cherry products
- Active cancer
- Pancreatic disease
- Biliary tract disease
- Hemoglobin of < 10 g/dL
- Liver disease
- Serum creatinine >1.5 mg/dL
- Consumption of tart cherry concentrate or cherries within 14 days of study procedures
    - You may participate if you avoid cherry products for 14 days prior to the study procedure date
- Personal or inherited bleeding disorders or on anticoagulation
- Women who are pregnant or nursing

How long will the study take and how many subjects will participate?
We will enroll 20 subjects in the research study. The duration of study participation includes remaining at the study site (Clinical Research Center at Robert Wood Johnson University Hospital Somerset (RWJS); Suite 1110, 128 Rehill Avenue, Somerville, NJ

08876) or Robert Wood Johnson Medical School (RWJMS) Clinical Research Center (Robert Wood Johnson Medical School; East Tower, 8th Floor; 125 Paterson Street; New Brunswick, NJ 08903) for approximately 9 hours on two separate days. You may select either site based on availability and convenience. There will be at least a 14-day wash-out period between each of the days. Wash-out refers to avoiding cherry products for 14 days.

What will you be asked to do if you take part in this research study?
If you meet the criteria for participation and consent to participate, you will be randomly assigned to consume a single dose of tart cherry concentrate (either 60 mL or 120 mL) at the study center. You will be instructed to avoid any food for a period of 10 hours prior to the study initiation (consumption of tart cherry concentrate at the study site) and will consume a standardized breakfast (high-fat; 750 calories and 35 grams total fat) at the study site 30 minutes prior to when you take tart cherry concentrate. As an example, if the study is scheduled to start at 8:00 a.m., we ask that you avoid eating food at 10:00 p.m. the night before. Following the initial period of the study, you will return to the study set after at least 2 weeks and will receive the alternate dose and the study procedures described below will be repeated. As an example, if you received 60 mL of tart cherry concentrate on day 1 you will receive 120 mL of tart cherry concentrate when you return after 2 weeks.

All women of childbearing age will have a pregnancy test administered prior to administration of tart cherry concentrate. In addition, all subjects will have their hemoglobin checked to make sure they do not have anemia.

Blood samples (about two teaspoons per sample) will be drawn prior to tart cherry concentrate administration. After administration of the tart cherry concentrate, blood samples will be collected at 0.5, 1, 2, 4, and 8 hours after you take your dose at the study site. You will be provided snacks and meals while you are at the study site.

We will draw blood samples from a dedicated temporary intravenous line inserted into your arm to make you as comfortable as possible. This device is called a “saline lock device”. Saline solution will be used to “flush” or clear the line to make sure it stays open. The saline lock will be removed after the 4-hour sample and the last two samples will be drawn from individual needle sticks using a blood collection set. You will not be getting 6 separate “needle-sticks” for each blood sample.

You will also be asked to provide ***optional*** stool samples prior to taking the tart cherry juice or at least 14 days after and then after (1-to-2 days) receiving the tart cherry juice. We will provide additional instructions on how to collect the stool and get it to the laboratory.

What are the risks and/or discomforts you might experience if you take part in this study?
The blood sample draw may be uncomfortable for a short time. When your blood is drawn, there may be a bruise, or bleeding, or infection, at the place where your blood is drawn. However, infection is rare.

While there have been some reports of allergic reaction to tart cherries, they are a commonly consumed food and we expect the risk of allergic reaction to be the same as with any other food.

Tart cherry concentrate is usually well tolerated, but may cause gastrointestinal discomfort, nausea, and/or diarrhea. While these side effects are not expected with one dose, they are possible.

Collection of optional stool samples at home will not have any greater risk compared to the collection of stool samples for usual clinical care. You will be provided with instructions (**Appendix 1**) and supplies to collect the specimens at home without direct physical contact with the stool throughout the process. The stool will be stored in a sealed container, a leak-proof secondary package (e.g. a sealable plastic bag) and an outer package (e.g. a zipped carrier bag). You are not required to store the stool at home; the specimens will be delivered to the research facilities within 1.5 h of collection.

No personal health information will be provided with your blood samples when transported to Rutgers University laboratory. This strategy will reduce the risk of the privacy breach. While study records will be protected within one of the researchers' locked office and on a password protected computer there is risk if the office security is compromised. This event is not likely; however, the possibility exists, therefore complete confidentiality cannot be guaranteed. Patient data will be stored in a secure Research Electronic Data Capture (REDCap™) database. REDCap was designed to protect study subject confidentiality.

Are there any benefits for you if you choose to take part in this research study?

You will not receive any direct benefit for participating in this research, but the research may provide scientists with a better understanding the potential benefits of tart cherry.

What are your alternatives if you don't want to take part in this study?

This is not a treatment study and it is not intended that the research project will treat any health issues that you may be affected by. There are no alternative treatments available. Your alternative is not to take part in this study.

Will there be any cost to you to take part in this study?

There is no cost to you for participating in this research project.

Will you be paid to take part in this study?

We are offering research subjects payment for their time. Payment will be made in the form of a Visa gift card. If you complete the study by remaining at the study site on each of the study days and providing all the requested blood samples the total payment will be $140. This compensation will cover your time and blood samples. If you withdraw prior to study completion your payment will be reduced according to the time

and blood samples you provide. Since each blood sample is timed, we will base your reduced compensation on each blood sample you provide. You will be provided $10 per sample for each sample drawn and an additional $20 if you complete all study procedures (total of $140). You will also be provided breakfast, lunch, and dinner at the study site. For each stool sample you provide you will receive an additional $25. We will request two optional stool samples. (1) Choose either one before receiving tart cherry concentrate or at least 14 days after receiving tart cherry concentrate and (2) also 1-to-2 days after tart cherry is taken.

How will information about you be kept private or confidential?

All efforts will be made to keep your personal information in your research record confidential, but total confidentiality cannot be guaranteed.

This research is confidential. Confidential means that the research records will include some information about you, such as your name, age, gender, medical history, and medications. I/We will keep this information confidential by limiting individual's access to the research data and keeping it in a secure location. The research team, and the Institutional Review Boards at Rutgers University are the only parties that will be allowed to see the data, except as may be required by law. If a report of this study is published, or the results are presented at a professional conference, your identity will not be disclosed.

What will happen if you do not wish to take part in the study or if you later decide not to stay in the study?

Participation in this study is voluntary. You may choose not to participate or you may change your mind at any time.

If you do not want to enter the study or decide to stop participating, your relationship with the study staff will not change, and you may do so without penalty and without loss of benefits to which you are otherwise entitled.

You may also withdraw your consent for the use of data already collected about you, but you must do this in writing to Dr. Naomi Schlesinger. (Address: Department of Medicine, Division of Rheumatology, Rutgers, The State University of New Jersey, 125 Paterson Street, Suite 5200A, New Brunswick, NJ 08901-1962)

Who can you call if you have any questions?

Subjects in this study will be exposed to certain risks of personal injury in addition to those associated with standard forms of treatment, which include: bruising at the site of blood draw, infection at the site of blood draw, or pain. In addition, it is possible that during the course of this study, new adverse effects of tart cherry that result in personal injury may be discovered. The University will make appropriate referrals for medical and/or dental treatment for subjects who sustain personal injuries or illnesses as a direct consequence of participation in the research. The subject's health insurance

carrier or other third-party payer will be billed for the cost of this treatment; provided that the University shall not submit to federally funded programs, e.g., Medicare, Medicaid or CHAMPUS, for reimbursement first if submission to such programs is prohibited by law. No financial compensation will be provided by the University and no other type of assistance is available from the University.

If you have any questions about taking part in this study or if you feel you may have suffered a research related injury, you can call the study coordinator or primary investigator:

Luigi Brunetti, PharmD, MPH
Study Coordinator
908-595-2645

Naomi Schlesinger, MD
Principal Investigator
732-235-8387

If you have any questions about your rights as a research subject, you can call:

Rutgers University IRB Director (732)-235-9806 or Human Subject Protection Program 732-235-8578

What are your rights if you decide to take part in this research study?

You have the right to ask questions about any part of the study at any time. You should not sign this form unless you have had a chance to ask questions and have been given answers to all of your questions.

PERMISSION (Authorization) TO USE OR SHARE HEALTH INFORMATION THAT IDENTIFIES YOU FOR A RESEARCH STUDY

Information about you and your health is personal and private, so this information generally cannot be used in research without your written permission. The next few paragraphs tell you about how researchers want to use and share your health information in this research study. Your information will only be used as described here or as allowed or required by law. Ask questions if you do not understand any part of the research or the use of your health information. If you sign this consent form, you agree to let the researchers use your information in the research and share it with others as described below.

What is the purpose of the research and how will my information be used?
You are being invited to take part in this research study which is described at the beginning of this form. The purpose of collecting and using your health information for this study is to help researchers answer the questions that are being asked in the research.

What information about me will be used?
We will collect your name, age, height, weight, race, gender, medical history, and medication history.

Who may use, share or receive my information?
The research team may use or share your information collected or created for this study with the following people and institutions:

- Rutgers University researchers involved in the study;
- The Rutgers University Institutional Review Board and Compliance Boards
- The Office for Human Research Protections in the U.S. Dept. of Health and Human Services

Those persons or organizations that receive your information may not be required by Federal privacy laws to protect it and may share your information with others without your permission, if permitted by the laws governing them.

Will I be able to review my research record while the research is ongoing?

No. We are not able to share information in the research records with you until the study is over. To ask for this information, please contact the Principal Investigator, the person in charge of this research study.

Do I have to give my permission?

No. You do not have to permit use of your information. But, if you do not give permission, you cannot take part in this research study. (Saying no does not stop you from getting medical care or other benefits you are eligible for outside of this study.)

If I say yes now, can I change my mind and take away my permission later?

Yes. You may change your mind and not allow the continued use of your information (and to stop taking part in the study) at any time. If you take away permission, your information will no longer be used or shared in the study, but we will not be able to take back information that has already been used or shared with others. If you say yes now but change your mind later for use of your information in the research, you must write to the researcher and tell him or her of your decision:

Naomi Schlesinger, MD
Department of Medicine
Division of Rheumatology
Rutgers, The State University of New Jersey
125 Paterson Street, Suite 5200A
New Brunswick, NJ 08901-1962

How long will my permission last?

Your permission for the use and sharing of your health information will last until the end of the research study.

NOTE: SIGNATURE PAGE FOLLOWS IMMEDIATELY.

AGREEMENT TO PARTICIPATE

1. Subject Consent:

I have read this entire form, or it has been read to me, and I believe that I understand what has been discussed. All of my questions about this form or this study have been answered.

_____ **I agree** **OR** _____ **I do not agree** to continue to participate.
(Initial (Initial)

Subject Name:_____

Subject Signature:_____ Date:_____

2. Signature of Investigator/Individual Obtaining Consent:

To the best of my ability, I have explained and discussed the full contents of the study including all of the information contained in this consent form. All questions of the research subject have been accurately answered.

Investigator/Person Obtaining Consent:_____

Signature:_____ Date: _____

Additional consent to provide stool samples follows on the next page.

Additional consent for optional stool sample

AGREEMENT TO PROVIDE STOOL SAMPLES

1. Subject Consent:

I have read this entire form, or it has been read to me, and I believe that I understand what has been discussed. All of my questions about this form or this study have been answered.

_____ **I agree** **OR** _____ **I do not agree** to provide stool samples.
(Initial (Initial)

Subject Name:_____

Subject Signature:_____ Date:_____

2. Signature of Investigator/Individual Obtaining Consent:

To the best of my ability, I have explained and discussed the full contents of the study including all of the information contained in this consent form. All questions of the research subject have been accurately answered.

Investigator/Person Obtaining Consent:_____

Signature:_____ Date: _____