Study title: High-protein Oral Supplement With Liposomal Curcumin in Adults Undergoing Hemodialysis

NCT: NCT06381076

Date: 08/28/2024

Study time: 12 weeks

Study location: UF Dialysis Clinic, Gainesville

Investigators:

Principal Investigator: Jeanette Andrade PhD, RDN/LDN, FAND

Study coordinator: Sofia Acevedo BS

Background

Chronic Kidney Disease (CKD) is a prevalent and progressive condition characterized by the gradual loss of kidney function over time. It is classified into stages based on the level of kidney function, commonly measured by the glomerular filtration rate (GFR). CKD stages range from mild (Stage 1) to severe (Stage 5), also known as end-stage kidney disease, where individuals may require dialysis or kidney transplantation. This categorization not only guides clinical assessments but also shapes the therapeutic approach to mitigate the consequences of CKD[1]. The intricate interplay between inflammation and kidney damage becomes a key aspect in the understanding of CKD progression. Inflammation not only accelerates the deterioration of renal function but also becomes a precursor to complications such as cardiovascular disease and anemia, further exacerbating the burden on adults undergoing hemodialysis[2]. A comprehensive understanding of the inflammatory pathways can target the interventions to slow down or even halt the progression of CKD. Research on protein post-dialysis interventions contributes to refining nutritional guidelines for adults undergoing hemodialysis and identifies optimal protein levels and sources that can significantly impact the quality of life[3]. Protein post-dialysis is vital for adults undergoing hemodialysis to maintain proper protein levels and overall health, and the role of protein intervention post-dialysis in CKD patients is crucial to managing nutritional status and supporting their recovery and overall well-being[4]. When targeting inflammatory pathways, nutritional interventions such as incorporating spices may help leverage the effect of protein in lowering inflammation and ultimately improving quality of life for this population. Turmeric, a spice known for its anti-inflammatory properties, contains curcumin - a bioactive compound known for its antioxidant and anti-inflammatory effects[5]. Incorporating curcumin, specifically in nano-encapsulated form, into the diet of adults undergoing hemodialysis might have a beneficial impact on reducing inflammation and oxidative stress[4]. As we delve into the interconnection of CKD, inflammation, protein dynamics, and the therapeutic potential of turmeric, the combination of these elements becomes central in shaping a holistic approach to the management of this intricate condition. This exploration not only adds depth to our comprehension of CKD but also paves the way for innovative and targeted interventions that can redefine the landscape of patient care in the realm of chronic kidney disease.

Objectives

Objective 1: To examine the effect of nano-encapsulated curcumin in a high-protein beverage on inflammation and oxidative stress of adults on hemodialysis over the course of 12 weeks.

- Primary outcome: Serum C-reactive protein (CRP) differences at baseline, 8 and 12-weeks.
- Secondary outcomes:
    - Changes in serum NF-*k*B at baseline, 8-, and 12-weeks.
    - Changes in oxidative stress markers (advanced glycation end products and fatty acid oxidation byproducts - 4-hydroxynon-enal, malondialdehyde, and 8-F2isoprostanes) at baseline, 8-, and 12-weeks.

Objective 2: Evaluate the impact of nano-encapsulated curcumin in a high-protein beverage on quality of life for adults on hemodialysis over 12 weeks.

- Primary outcome: Changes in quality of life as assessed by the 36-item Kidney Disease Quality of Life instrument at baseline, 8- and 12-weeks.

Additional information collected to avoid cofounding errors:

- Informal semiquantitative food frequency questionnaire (FFQ), and a spice frequency questionnaire at baseline and at the end of the 8-week intervention
- Adverse events
- Compliance
    - Reported intake of oral supplement
    - Normalized protein catabolic rate (nPCR)

Study Design

This is an 8-week double-blind randomized controlled trial to evaluate the impact of nano-encapsulated curcumin in a liquid protein supplement on inflammation and oxidative stress for adults undergoing hemodialysis. Inflammation and oxidative stress markers will be assessed from monthly blood samples using validated Elisa kits. Quality of life will be measured using the standard 36-item kidney disease quality of life instrument to detect differences over the intervention. There will be a 2-month recruitment period prior to the start of the trial to ensure the potential participants are familiarized with the clinical trial. After the recruitment period has finished, eligible participants will sign the consent form to participate in the study. Once the expected number of participants has been reached, they will be randomized 1:1 using block randomization through a computer-generated program. The block randomization will be based on the variable of liquid protein supplement (LPS) consumption for those participants who have been consuming LPS for 1 or more months prior to the study.

The intervention will take place over an 8-week period. Participants will have their blood drawn at the beginning of the study by the dialysis practitioner and start receiving the product on their next scheduled dialysis appointment. Participants will receive the supplement three times a week in accordance with their dialysis schedule (M-W-F or T-Th-S), for a total of 24 times. The product will be given to participants within 2.5 hours of when the dialysis session was initiated, following the current protocols of the clinic. Blood will be collected at baseline, at the end of the study and a month after to assess any carryover effects. Additionally, participants will complete a semi-quantitative food frequency questionnaire, a spice-consumption survey, and a quality-of-life assessment at the beginning and end of the study.

Patient characteristics

Adults undergoing hemodialysis will be recruited from UF Health Dialysis Clinic.

Inclusion criteria

The adults that are eligible for the study must be:

- 18 years old or older
- diagnosed with stage 5 CKD.
- receiving hemodialysis at least three months before the trial start date
- All participants can provide signed informed consent, have no dietary restrictions, no food allergies, nor chewing/swallowing difficulties.

The medical director will ensure the patients are eligible for the study and the study coordinator (Acevedo) will consent them.

Exclusion criteria

Additional criteria for a potential participant to be excluded to participate from the study:

- Adults with CKD stages 1-4.
- Adults undergoing peritoneal dialysis.
- Pregnant and/or lactating for the duration of the study as confirmed by the dialysis medical staff.
- Use of other protein supplements (not the LPS product) within 3 months of the initiation of the study.

Recruitment

Potential participants will be identified by clinical nurse managers and informed about the study. The PI and/or study coordinator will meet with the potential participants at their earliest convenience and the study will be described to the potential study participants using the approved script and the inclusion/exclusion criteria will be read. Potential participants will be directed to listen to the criteria and state “yes” or “no” after each criterion is read, and then decide whether

they would like to continue with study procedures. If they agree to the aspects of the study and meet all criteria, they will sign the consent form.

Consent

Participants who agree to participate will sign the consent form. Participants will receive a total of $60 for participating in the study, $20 for each blood draw.

Withdrawal Criteria

Participants are free to withdraw from the study at any point and for any reason as will be discussed when signing the informed consent. If participants feel comfortable, they will share with the study team the reason for withdrawal. No follow-up other than recovery of the Investigational Product (IP) will be done for the participants who decide to end their participation except if the withdrawal was due to medical reasons that may be related to the study. In this event, participants will be followed-up until recovery. If a participant withdraws from the study, information collected up until the withdrawal point can be used unless the participant requests otherwise. The principal investigator and medical director can withdraw a participant from the study before the end of the study if instructions given were not followed (e.g. the oral supplement was not consumed for 3 consecutive times, appointments were missed or if the participant did not complete questionnaires).

Investigational Product (IP)

The investigational product (IP) is LPS that will be administered at a total volume of 85 g (3 ounces) as a gelatin form. It contains 25.5 g of total protein, 52.5 mg of potassium, and 1.5 mg of phosphorus per serving. A total of 7 ml (1.5 tsp) of curcumin will be added to half of the products. The protein supplement will be modified and prepared in a food-grade facility in the Food Science and Human Nutrition Department by the study coordinator. Using a LPS of whey and collagen from ND labs (which is used in the dialysis clinic), the researchers will create a 3 oz gelatin product with 1.5 teaspoon of Knox unflavored gelatin mixed with 3 tablespoons of boiling water and then mixed with 1.5 oz of the mango peach LPS and 7 mL (1.5 tsp) of liposomal curcumin (Manna, vitamins evolved) to the intervention supplements. This *will be done at the beginning of the week for all the participants.* With permission of the medical staff at the dialysis clinic, the product will be labeled with a 3-digit code that aligns with the participants in the respective groups and distributed on dialysis days to the participants.

Nutrition Facts

1 servings per container

Serving size	**3 oz (85g)**
Amount Per Serving	
Calories	**200**
	% Daily Value*
Total Fat 1g	**1%**
Saturated Fat 0g	**0%**
Trans Fat 0g	
Cholesterol 0mg	**0%**
Sodium 50mg	**2%**
Total Carbohydrate 19g	**7%**
Dietary Fiber 0g	**0%**
Total Sugars 0g	
Includes 0g Added Sugars	**0%**
Protein 26g	
Vitamin D 0mcg	0%
Calcium 0mg	0%
Iron 0mg	0%
Potassium 52.5mg	2%
Phosphorus	0%

*The % Daily Value (DV) tells you how much a nutrient in a serving of food contributes to a daily diet. 2,000 calories a day is used for general nutrition advice.

Testing outcomes and measures.

Participants will complete an initial survey and provide blood samples, as described below.

Blood samples: Collection of whole blood (6 mL) for determination of inflammation and oxidative stress markers at the start of the dialysis session.

Upon collection of the whole blood samples, samples will be transported to the PI's bio-safety level facility for extraction of serum. Samples will be spun in a centrifuge at 1600 ´g for 10 minutes for separation of the serum. If serum is not separated, the speed will be increased to 1600 ´g for 10 minutes. Serum will be aliquoted and immediately transported to a -80°C freezer until ready for analysis. For the analysis of the inflammation markers, the Abcam™ High-Sensitivity Human C-Reactive Protein enzyme-linked immunosorbent assay (ELISA) Kit will be used to detect serum hs-CRP. This kit is used for human serum samples and both inter-assay and intra-assay precision was at 1.4% (Abcam, ab260058). The average sample recovery for this plate was 92.34% (Abcam, ab100646). For analysis of the NF-kB, the Abcam transcription factor assay kit will be used. For measurement of oxidative stress makers, standard analyses that are validated will be used.

Food Frequency Questionnaire: At baseline participants will complete a food frequency questionnaire, the CKD short food frequency questionnaire (CKD-SFFQ), with a total of 49 food/beverage items and follow up questions [6].

Spice Frequency Questionnaire: At baseline participants will complete a validated 50-item questionnaire regarding their frequency and amount of 25 spices consumed over the past 30-days with 9 frequency choices of never to 6 or more servings per day. This will be repeated at the end of the intervention period and at the 4-week follow-up.

Demographic Questionnaire: At baseline, participants will complete a demographic questionnaire that includes questions related to sex, race/ethnicity, and Body Mass Index (as determined by height and weight).

Quality of life Questionnaire: The 36-item validated Kidney Disease Quality of Life instrument will be used to detect symptoms, effects, and burden with kidney disease along with work status, cognitive function, quality of social interaction, sexual function, sleep, social support, and patient satisfaction[7].

*Normalized Protein Catabolic Rate (nPCR): N*ormalized protein catabolic rate (nPCR) (g/kg/day) will be calculated from dialysis kinetic modeling and the following equation:

PCR = 0.262 x (G urea + 54)/BW post

Where urea generation rate (G urea) is provided by the clinic.

Statistical Design:

A sample size of 30 (n=15 per group) based on a priori power analysis considering an alpha of 0.05, power of 0.80, effect size of 0.563, and considering a multiple linear regression with 2 variables and 2 cofounders, time of day receiving the supplement and compliance. Differences in CRP will be evaluated through a multiple linear regression accounting for the time of the day the supplement is being received and participant compliance, with the significance level of $p<0.05$. All data will be analyzed using SAS JMP v15 with statistical significance detected at $p<0.05$. Assuming a dropout rate of 20%, as identified in clinical trials and what has been observed in the PIs clinical trials, a total of 34 participants will be initially enrolled and randomized. However, it is anticipated that we will need to recruit at least 60 participants as some individuals will not qualify.

Clinicaltrials.gov

The study will be registered and updated on ClinicalTrials.gov in accordance with US Public Law 110-85 (a Protocol Record must be updated and reviewed every 6 months). The registration number is pending. The Informed Consent Form will include the following, "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 study participants. At most, the Web site will include a summary of the results. You can search this Web site at any time".

Data Management Plan

Data Storage, Security, and De-identification Plan

Data and files will be secured in locked filling cabinets and office space. Paper questionnaires will only include date and research study assigned participant number. Data that is originally captured as hardcopy/paper (e.g. questionnaires) will be transcribed to encrypted electronic files.

Following the completion of the study, any potential identifiers will be removed from data to meet HIPAA de-identification standards (According to the October 2002 Privacy Rule § 164.514.(b).2. the indicated information/will be removed from all study records).

Potential Discomforts and Risks

Protein supplements are safe for consumption for children and adults when consumed appropriately via the FDA. Although rare, possible side effects of consuming high doses of protein supplements include increased bowel movement, nausea, thirst, bloating, cramps, reduced appetite, fatigue, and headache. Therefore, to avoid potential discomfort and risks the daily dose the participant will receive in the duration of the study is below 0.8 g of protein per Kg of bodyweight.

Informed consent forms given to all participants specify that the PI, Dr. Andrade as the contact in the case of issues or questions arising during the study. In the case that a professional intervention is necessary due to an adverse effect on the study subjects, Dr. Andrade will contact the appropriate authority or organization pertinent to the circumstance of the event. Serious adverse events will be reported to the sponsor within 24 h of the PI being notified. In the event of a data safety breach, Dr. Andrade and the appropriate University of Florida personnel will contact participants to inform them of this breach, as well as notify the Institutional Review Board of the University of Florida.

Adverse Events and Serious Adverse Events

Adverse Events (AEs) are defined as any undesirable experience occurring to a participant during a clinical trial, whether related to the IP. A serious adverse event (SAE) is any adverse event that results in any of the following outcomes such as death, life-threatening adverse event, permanent or severe disability/incapacity, inpatient hospitalization or prolonging existing hospitalization, congenital abnormality/birth defect, cancer or medication overload. AEs and SAEs will be reported per UF IRB guidelines. All adverse events reported spontaneously by the participants or observed by the study team should be recorded.

Adverse Events (AEs) are defined as any undesirable experience occurring to a participant during a clinical trial, whether or not it is related to the investigational products. AEs and SAEs will be reported per UF IRB guidelines. All adverse events reported spontaneously by the participants or observed by the study team should be recorded.

Potential Benefits

Participants will not experience benefits directly.

Conflict of Interest

The investigators may benefit professionally by publishing and presenting the results of this study. The findings may be shared with International Flavors & Fragrances (IFF), Inc. if requested.

Compensation

Participants will receive a total of $60 for participating in the study. They will receive $20 for each sample resulting in $20 at baseline, $20 at the end of the intervention, and $20 after the 4-week follow-up.

References

1. Kopyt, N.P. Chronic Kidney Disease: The New Silent Killer. *Journal of the American Osteopathic Association* 2006, *106*, 133–136.
2. Cobo, G.; Lindholm, B.; Stenvinkel, P. Chronic Inflammation in End-Stage Renal Disease and Dialysis. *Nephrology Dialysis Transplantation* **2018**, *33*, iii35–iii40, doi:10.1093/ndt/gfy175.
3. Kalantar-Zadeh, K.; Stenvinkel, P.; Pillon, L.; Kopple, J.D. Inflammation and Nutrition in Renal Insufficiency. **2003**, doi:10.1053/j.arrt.2003.08.008.
4. Kalantar-Zadeh, K.; Moore, L.W. Does Kidney Longevity Mean Healthy Vegan Food and Less Meat or Is Any Low-Protein Diet Good Enough? *Journal of Renal Nutrition* 2019, *29*, 79–81.
5. Alp Ikizler, T.; Burrowes, J.D.; Byham-Gray, L.D.; Campbell, K.L.; Carrero, J.-J.; Chan, W.; Fouque, D.; Friedman, A.N.; Ghaddar, S.; Jordi Goldstein-Fuchs, D.; et al. *KDOQI CLINICAL PRACTICE GUIDELINE FOR NUTRITION IN CKD: 2020 UPDATE*; 2020; Vol. 76;.

UF | Institutional Review Board
UNIVERSITY of FLORIDA

INFORMED CONSENT FORM
to Participate in Research, and
AUTHORIZATION
to Collect, Use, and Disclose Protected Health Information (PHI)

INTRODUCTION

Name of person seeking your consent:_____

Place of employment & position:_____

GENERAL INFORMATION ABOUT THIS STUDY

1. Name of Participant ("Study Subject")

_____

2. What is the title of this research study (this "Research Study")?

Examining the impact of high-protein oral supplement with liposomal curcumin on inflammation markers and oxidative stress in adults undergoing hemodialysis.

3. Whom do you call if you have questions about this Research Study (the "Study Team")?

Principal Investigator: Dr. Jeanette Andrade, PhD, RDN, FAND, 352-294-2975
Study Coordinator: Sofia Acevedo, 352-294-3975

4. Who is paying for this Research Study?

The sponsor of this study is the University of Florida.

5. In general, what do you need to know about this Research Study?

Agreeing to become involved in any research is always voluntary. By signing this form, you are not waiving any of your legal rights. If you decide not to participate in this research, you will not be penalized in any way and you will not lose any benefits to which you are entitled. If you have questions about your rights as a research subject, please call the University of Florida Institutional Review Board (IRB) office at (352) 273-9600.

a) In general, what is the purpose of the research? How long will you be involved?

The purpose of this research is to see if curcumin, a natural ingredient found in turmeric, in a food supplement reduces markers of inflammation. Inflammation is the body's natural response to infection or injury and usually it shows swelling, redness, and pain in tissues. Curcumin itself has a slightly bitter, earthy taste that may be similar to ground mustard or curry powder. If you agree to participate in this study, you are expected to participate for 12 weeks.

b) What is involved with your participation, and what are the procedures to be followed in the research?

If you decide to take part in this study, you will be randomly assigned, much like the flip of a coin, to receive either the protein supplement that is normally given during your dialysis session or the protein supplement with added curcumin. This will be a single blind study, meaning you will not be made aware of what group you are assigned to, but the research team and the doctor will know. You will only know which group you were in if the blinding had to be broken. You are expected to eat/drink 2.5 oz (1/3 cup) of the supplement after dialysis (3 days per week) for 8 weeks. You are also expected to fill out a 24-hour recall and spice intake survey before you get the protein with or without curcumin, after 8 weeks, and 4 weeks after the end of the study. We will draw an extra 1 tsp of blood at the beginning of the study, at 8 weeks, and 4 weeks after you complete the study.

c) What are the likely risks or discomforts to you?

Possible side effects from consuming the protein with curcumin includes

- Potential teeth staining

Rare side effects may include:

- Nausea or gastric upset or vomiting
- Jaundice
- Cardiac issues

d) What are the likely benefits to you or to others from the research?

Potential direct benefits: You may experience a reduction in your body's markers of inflammation (as measured through bloodwork), which may or may not have a direct benefit to you. This study's results may help researchers better understand how curcumin can affect inflammation.

Potential indirect benefits: This research will advance our scientific understanding of

curcumin's therapeutic potential and its mechanisms of action. Positive findings could lead to broader clinical use of curcumin, improving public health outcomes. Furthermore, the study results could inspire future research into curcumin-based treatments and studies.

e) What are the appropriate alternative procedures or courses of treatment, if any, that might be helpful to you?

This study is not a treatment study and it is not meant to treat swelling, redness, and/or pain. Please talk with your doctor if you are seeking that information. The alternative course is to not participate in the study, receive your regular dialysis schedule, and protein supplementation as the dietitian deems necessary.

Additional and more detailed information is provided within the remainder of this Informed Consent form. Please read before deciding if you wish to participate in this 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.

WHAT CAN YOU EXPECT IF YOU PARTICIPATE IN THIS STUDY?

6. What will be done as part of your normal clinical care (even if you did not participate in this Research Study)?

As part of your normal care, you will receive the liquid protein supplement.

7. What will be done only because you are in this Research Study?

If you decide to take part in this study, you will be randomly assigned (much like the flip of a coin) to receive a protein supplement (total volume: 2.5 oz or 1/3 cup) that has the curcumin (treatment) or placebo. A placebo is a substance that looks like and is given in the same way as an experimental treatment but does not contain anything, for example the protein supplement with no curcumin. A placebo is used in research studies to show what effect a treatment has compared with taking nothing at all. If you are assigned to receive the placebo, you will not receive the benefits of the curcumin, if there are any, nor will you be exposed to its risks, which are described below under "What are the possible discomforts and risks?" Studies have shown that about 1 in 3 persons who take a placebo do improve, if only for a short time. You, the doctor, and other persons doing the study will not know whether you are receiving placebo or treatment, but that information is available if it is needed. You will have a 50% chance of receiving treatment and a 50%

chance of receiving the placebo. In the remainder of the description of what will be done, both the curcumin supplement and the placebo will be called "study treatment." These supplements will be provided two hours after dialysis treatment started for three days each week for 8 weeks. A portion, 6mls or 1 tsp, of extra blood will be taken and given to the researchers to analyze them for inflammation and oxidative stress.

Blood samples, 6 mL or 1 tsp will be drawn at baseline, at weeks 8, and 4 weeks after the end of the study for follow-up. You will complete a 3-day 24-hour recalls (2 non-dialysis days and 1 dialysis day), a spice intake survey, demographic questionnaire at baseline. The 24-hour recalls and spice questionnaire will be done again at the end of the 8-week study, and 4 weeks after the end of the study. The study team does not expect you to change your dietary habits during the duration of the study.

If you have any questions now or at any time during the study, please contact someone who is listed in question 3 of this form.

If any identifiable information is collected as part of this research, it is possible that your research information with all personally identifiable information removed, could be used for future research studies, or distributed to another investigator for future research studies without additional informed consent from you or your legally authorized representative.

If you have any questions now or at any time during this Research Study, please contact one of the Research Team members listed in question 3 of this form.

8. What identifiable health information will be collected about you and how will it be used?

The Research Team will collect:
- Demographic information
- Blood samples
- Lab results from your medical chart
- Dietary recalls
-Spice intake

The Research Team listed in question 3 above will use or share your health information as described below to carry out this research study. A review of your medical chart to obtain pre-post blood urea nitrogen to calculate protein intake will be collected during the study.

9. With whom will this health information be shared?

This health information may be shared with:
- the study sponsor (listed in Question 4 of this form)

- United States governmental agencies that are responsible for overseeing research, such as the Food and Drug Administration, the Department of Health and Human Services, and the Office of Human Research Protections.
- government agencies that are responsible for overseeing public health concerns, such as the Centers for Disease Control and federal, state, and local health departments,
- the IRB that reviewed this Research Study and ensures your rights as a Study Subject are protected.

Otherwise, your identifiable health information will not be shared without your permission unless required by law or a court order. Once your health information is shared with those listed above, it is possible that they could share it without your permission because it would no longer be protected by federal privacy law.

10. How long will you be in this Research Study?

3 months (12 weeks)

This Authorization to use and share your health information expires at the end of the study unless you revoke it (take it back) sooner.

11. How many people are expected to take part in this Research Study?

30 participants are expected to complete this study, where a total of 10 additional participants will be enrolled/included in this study but may discontinue due to various reasons and with 20 participants not meeting the screening criteria. Thus, a total of 60 participants are anticipated.

WHAT ARE THE RISKS AND BENEFITS OF THIS STUDY AND WHAT ARE YOUR OPTIONS?

12. What are the possible discomforts and risks of taking part in this Research Study?

If you are consuming the protein supplement with curcumin, you may experience:

- teeth staining

In rare cases, you may experience:

- nausea or gastric discomfort or vomiting with the doses used for this study
- Jaundice
- Cardiac issues

If you only receive the protein supplement, you should not experience the above issues.

This Research Study may also include risks that are unknown at this time.

Please note that participating in more than one research study or project may further increase the risks to you. If you are already enrolled in a research study, please inform one of the Research Team members listed in question 3 of this form or the person reviewing this consent with you before enrolling in this or any other research study or project.

During the study, the Research Team will notify you of new information that may become available and might affect your decision to remain in the study.

The University of Florida is required by law to protect your health information. Your health information will be stored in locked filing cabinets or on computer servers with secure passwords, or encrypted electronic storage devices, as required by university policy. However, there is a slight risk that information about you could be released inappropriately or accidentally. Depending on the type of information, a release could upset or embarrass you, or possibly affect your ability to get insurance or a job.

If you wish to discuss the information above or any discomforts you may experience, please ask questions now or call one of the Research Team members listed in question 3 in this form.

13a. What are the potential benefits to you for taking part in this Research Study?

Potential direct benefits: You may experience a reduction in your body's markers of inflammation (as measured through bloodwork), which may or may not have a direct benefit to you. This study's results may help researchers better understand how curcumin can affect inflammation.

13b. How could others possibly benefit from this Research Study?

Potential indirect benefits: This research will advance our scientific understanding of curcumin’s therapeutic potential and its mechanisms of action. Positive findings could lead to broader clinical use of curcumin, improving public health outcomes. Furthermore, the study results could inspire future research into curcumin-based treatments and studies.

13c. How could the Research Team members benefit from this Research Study?

In general, this study's results may help researchers better understand how curcumin can affect inflammation.

14. What other choices do you have if you do not want to be in this study?

If you prefer not to participate in the study, you will still receive your standard of care in the dialysis unit which includes the liquid protein supplement.

You may also refuse to authorize the use of your health information, but if you refuse, you may not be allowed to be in this research study or receive any research-related treatment that is only available in this research study. However, your decision not to sign this Authorization will not affect any other treatment you may be eligible to receive.

15a. Can you withdraw from this study?

You may withdraw your consent and stop participating in this Research Study at any time. If you do withdraw your consent, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. If you decide to withdraw your consent to participate in this Research Study for any reason, please contact the Research Team listed in question 3 of this form. They will tell you how to safely stop your participation.

You can also change your mind and take back this Authorization at any time by sending a written notice to the Research Team listed in question 3 of this form to let them know your decision. If you take back this Authorization, the Research Team may only use and disclose your health information already collected for this research study. No additional health information about you will be collected or disclosed to the Research Team. However, if you take back this Authorization, you may not be able to continue in this study. Please discuss this with a member of the Research Team listed in question #3.

15b. Can the Principal Investigator withdraw you from this Research Study?

You may be withdrawn from this Research Study without your consent for the following reasons:

• Adverse reaction to the ingredients within the product
• Gastrointestinal distress and/or condition
- Failure to follow the instructions such as not consuming the supplement 3 times in a row.
- 3 Appointments were missed.
- Not wanting to complete the dietary recalls and/or spice intake survey.

WHAT ARE THE FINANCIAL ISSUES IF YOU PARTICIPATE?

16. If you choose to take part in this Research Study, will it cost you anything?

The Sponsor will pay for all study related clinical services that you receive as part of your participation in this study that are not considered routine clinical services, also called standard-of-care services. All standard of care clinical services will be billed to you or your insurance company as usual. You will be responsible for paying any deductible, co-insurance, co-payments, for those standard of care clinical services, and for any non-covered or out-of-network services. Some insurance companies may not cover the cost of routine clinical services if they are associated with research studies.

The study coordinator can help you work with UF Health to answer any financial questions you have about your participation in this study.

17. Will you be paid for taking part in this Research Study?

You will receive $20 US dollars after the completion of each blood draw. A total of 3 blood draws will be collected for the total duration of this research study therefore, the total compensation you may receive for this research study is $60 US dollars.

Your payment for participation in this research study is handled through the University of Florida's Research Participant Payments (RPP) Program. Your information which will include your name, address, date of birth, and SSN (depending on amount of money you are paid) is protected. Access to the (RPP) Program site is limited to certain staff with the assigned security role. You will be randomly assigned a specific identification (ID) number to protect your identity.
If you have any problems regarding your payment, contact the study coordinator.

18. What if you are injured while in this Research Study?

It is important that you promptly tell any member of the research team if you experience an injury or have questions about any discomforts that you experience while participating in this study. If you are injured, you will be treated or referred for treatment.

If you are injured while you are participating in this study, the cost of the diagnosis and/or treatment may be covered by the University of Florida or the study sponsor or billed to you or your insurer just like other medical cost, depending on a number of factors, such as if the injury was the result of the study, or the way in which the study was conducted. The University of Florida and the study sponsor do not normally provide any other form of compensation for injury. The principal investigator and others involved in the study may be University of Florida employees. As employees of the University, they are protected under state law, which limits financial recovery for negligence.

Please contact one of the Research Team members listed in question 3 of this form if you experience an injury or have questions about any discomforts that you experience while participating in this Research Study.

SIGNATURES

As an investigator or the investigator's representative, I have explained to the participant the purpose, the procedures, the possible benefits, and the risks of this Research Study; the alternative to being in the study; and how the participant's protected health information will be collected, used, and shared with others:

_____ _____

Signature of Person Obtaining Consent and Authorization Date

You have been informed about this study's purpose, procedures, possible benefits, and risks; the alternatives to being in the study; and how your protected health information will be collected, used and shared with others. You have received a copy of this form. You have been given the opportunity to ask questions before you sign, and you have been told that you can ask questions at any time.

You voluntarily agree to participate in this study. You hereby authorize the collection, use and sharing of your protected health information as described above. By signing this form, you are not waiving any of your legal rights.

_____ _____

Signature of Person Consenting and Authorizing Date