# Study of the Effects and Mechanisms of Yeast Postbiotics on Persistent Allergic Rhinitis Symptoms

**2025.6.10**

**Study Protocol and Statistical Analysis Plan:**

# Study of the Effects and Mechanisms of Yeast Postbiotics on Persistent Allergic Rhinitis Symptoms

## 1 Background

Allergic rhinitis (AR) is a chronic, non-infectious inflammatory disease of the nasal mucosa mediated by immunoglobulin E (IgE) in atopic individuals following exposure to allergens. Its typical clinical manifestations include paroxysmal sneezing, watery rhinorrhea, nasal itching, and nasal congestion, often accompanied by itchy eyes, tearing, sleep disturbances, and reduced quality of life. AR is one of the most common chronic nasal conditions worldwide, affecting approximately 10%–20% of the global population, and has been recognized by the World Health Organization as a major public health concern. In China, the first nationwide epidemiological survey of adult AR was conducted in 2005. A follow-up telephone-based survey in 18 major cities in 2011 revealed that the self-reported prevalence of adult AR had increased from 11.1% to 17.6%, indicating a rising trend and increasing societal burden. Current standard treatments for AR primarily include antihistamines, intranasal corticosteroids, and allergen-specific immunotherapy. While these can alleviate symptoms, they often show variable efficacy between individuals, have high relapse rates, and suffer from poor long-term adherence, making it difficult to achieve sustained disease control. Therefore, there is an urgent need to explore safe, effective, and mechanistically clear interventions—especially for early prevention and control of AR.

The human gut harbors trillions of microorganisms, which play a critical role in maintaining overall health. At different stages of life, both the composition of the gut microbiota and its interactions with the host significantly influence physiological function and health status. Accumulating evidence from both human and animal studies suggests a potential association between the gut microbiota and allergic diseases. Dysbiosis may be a key indicator of allergic conditions. Postbiotics refer to functional substances composed of inactivated microorganisms and their metabolites, such as short-chain fatty acids (SCFAs), and cell wall components like β-glucans and peptidoglycans. These components have been shown to exert immunomodulatory, antioxidant, and anti-inflammatory effects. Compared with probiotics, postbiotics offer advantages such as

greater stability, no risks associated with live microorganisms, and improved production controllability. Recent studies have demonstrated that β-glucans derived from yeast-based postbiotics may help regulate the Th1/Th2 balance, downregulate IL-4 and IgE expression, and enhance Treg cell function, thus alleviating inflammation in allergic disease models such as asthma and food allergies.

However, clinical research on postbiotic interventions specifically targeting AR remains limited. One 12-week randomized controlled trial found that oral administration of yeast fermentation products significantly reduced nasal congestion (P=0.04) and rhinorrhea (P=0.005), suggesting potential therapeutic benefits. Given the overlap in immunomodulatory mechanisms between postbiotics and probiotics, postbiotics may theoretically improve AR symptoms, reduce recurrence rates, and enhance upper respiratory mucosal defenses through multiple pathways, particularly the gut microbiota–immune axis.

Based on this background, this study aims to conduct a randomized, double-blind, placebo-controlled intervention trial among university students with persistent AR symptoms to evaluate the effects of yeast postbiotics on AR symptoms and related immune and microbial indicators. The goal is to provide scientific evidence supporting the use of postbiotics in the prevention and management of allergic diseases.

## 2 Objectives

(1) To evaluate the effects of yeast postbiotics on improving symptoms of persistent AR.

(2) To explore the potential mechanisms by which yeast postbiotics alleviate persistent AR symptoms through modulation of the gut microbiota.

## 3 Design and Methods

### 3.1 Participants

This study aims to recruit current students at Lanzhou University who have been diagnosed with persistent AR or who present persistent AR-like symptoms as research subjects

#### 3.1.1 Inclusion Criteria:

Participants must meet all of the following conditions:(1) Aged between 18 and 35 years; (2) Meet the diagnostic criteria for persistent AR as defined in the Chinese Guidelines for the Diagnosis and Treatment of Allergic Rhinitis (2022, Revised Edition): ①Symptoms: At least two of the following—paroxysmal sneezing, watery rhinorrhea, nasal itching, and nasal congestion—lasting

or occurring for more than 1 hour per day; may be accompanied by ocular symptoms such as tearing, itchy eyes, and redness; ②Persistent AR: Symptom onset on ≥4 days per week and duration ≥4 consecutive weeks; (3) Have not used probiotics, prebiotics, synbiotics, antihistamines, corticosteroids, or immunosuppressants within one month prior to screening; (4) Willing and able to maintain regular levels of physical activity and dietary patterns throughout the study period; (5) Provide signed informed consent voluntarily.

3.1.2 Exclusion Criteria:

Participants will be excluded if they meet any of the following:(1) Use of antibiotics, osmotic laxatives (e.g., magnesium sulfate, lactulose), anthraquinone-based laxatives (e.g., rhubarb, aloe, senna), or gastrointestinal prokinetic agents (e.g., metoclopramide, domperidone, cisapride) within one month prior to screening; (2) Diagnosis of non-allergic rhinitis (including vasomotor, infectious, hormonal, or drug-induced rhinitis), nasal polyps, severe nasal septum deviation, cerebrospinal fluid rhinorrhea, or aspirin-exacerbated respiratory disease (AERD); (3) Uncontrolled coexisting allergic conditions such as sinusitis, otitis media, allergic asthma, or atopic dermatitis; (4) History of serious gastrointestinal disorders (e.g., chronic diarrhea, inflammatory bowel disease), or gastrointestinal endoscopy within the past month; (5) Presence of congenital genetic disorders, primary immunodeficiency diseases, severe systemic illnesses, or malignant tumors; (6) Pregnant or lactating women, or individuals planning to become pregnant in the near future.

Individuals meeting all inclusion criteria and none of the exclusion criteria will be enrolled as study participants for intervention.

3.2 Study Design

This is a randomized, double-blind, placebo-controlled human intervention trial. All enrolled participants will be stratified based on sex and AR diagnosis status, and then randomly assigned to either the yeast postbiotics group or the control group. During the intervention period, participants in the postbiotics group will take two capsules of yeast postbiotics daily after meals, while the control group will receive two matching placebo capsules. The total duration of the trial is 15 weeks, including a 1-week run-in period, a 12-week intervention period, and a 2-week follow-up period.

3.3 Intervention Protocol

Participants in the intervention group will receive yeast postbiotic capsules, each containing 250 mg of yeast postbiotics, maltodextrin, and a small amount of silicon dioxide. The placebo group

will receive capsules identical in form, taste, appearance, and packaging, composed only of maltodextrin and silicon dioxide. All participants will take two capsules once daily with warm water after meals.

3.4 Safety Assessment of Yeast Postbiotics

The yeast postbiotics used in this study are provided by Angel Yeast Co., Ltd., and have passed a series of toxicological safety assessments, including: acute oral toxicity test, bacterial reverse mutation test (Ames test), mammalian erythrocyte micronucleus test, Chromosomal aberration test in mouse spermatogonia or spermatocytes, and 28-day repeated oral toxicity test. All results confirmed no toxicity or mutagenic risks at the given dosages. Yeast and its derivatives have a long history of safe use in food fermentation and nutritional supplementation, with their safety verified by both population consumption and regulatory evaluations. Therefore, the intervention is considered highly safe. Nevertheless, adverse events (AEs) will be monitored continuously throughout the study, and any serious adverse events will be reported and managed according to ethical requirements.

3.5 Randomization, Blinding, and Unblinding

Stratified randomization will be performed using the blockrand package in R, with fixed block sizes and two stratification factors: sex (male/female) and confirmed AR diagnosis (yes/no, based on self-reported clinical history). Participants will be randomly assigned in a 1:1 ratio to the intervention or control group within each stratum. The randomization sequence will be sealed in opaque envelopes for allocation concealment. After signing informed consent and passing the screening, participants will be assigned ID codes and allocated accordingly.

Double-blinding will be applied to both participants and investigators. Only the study designer will have access to the group allocation. Intervention products and sample labels will be coded to prevent unblinding. If a participant experiences serious adverse effects related to the intervention, unblinding will be performed and the participant withdrawn.

3.6 Sample Size Estimation and Statistical Analysis

The sample size was calculated using the standard formula for randomized controlled trials：

$$N = \frac{2(Z_{1-\alpha} + Z_{1-\beta})^2 \sigma^2}{d^2}$$

Based on the Total Nasal Symptom Score (TNSS) as the primary outcome and parameters α =

0.05, β = 0.1, σ = 1.70, and d = 1.30, the calculated sample size is 36 per group (72 total). Considering a 10% dropout rate, at least 80 participants will be enrolled.

Statistical analysis will be conducted using SAS 9.4. Continuous variables will be expressed as mean ± standard deviation (SD); ordinal variables as rates. group comparisons will use:t-test or Kruskal-Wallis test for continuous variables and Chi-square test or Fisher's exact test for categorical variables. A P-value < 0.05 will be considered statistically significant.

For repeated measures across multiple time points (Weeks 0, 2, 4, and 12), such as TNSS and inflammatory markers, linear mixed-effects models (LMMs) will be constructed to assess the effects of time, group, and their interaction.

3.7 Outcome Measures

3.7.1 Primary Outcome

TNSS: Evaluates four nasal symptoms—itching, sneezing, runny nose, and congestion—each scored 0 to 3. Total score: 0–12, with higher scores indicating greater severity.

3.7.2 Secondary Outcomes

(1) Visual Analogue Scale (VAS): A 0–10 cm line, where 0 = no symptoms and 10 = worst symptoms. Used for assessing subjective severity and frequency of AR symptoms.

(2) Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ): 28 items across 7 domains (daily activity, sleep, nasal/ocular symptoms, emotional status). Each scored 0–6. Higher scores indicate lower quality of life.

(3) Serum Specific IgE (sIgE): Detected using FEIA (e.g., ImmunoCAP). Levels ≥0.35 kU/L indicate sensitization.

(4) Secretory IgA (sIgA): Measured in fecal and saliva samples via ELISA to reflect mucosal immunity.

(5) Inflammatory Cytokines: IFN-γ, IL-4, IL-10, IL-6, TNF-α measured by high-sensitivity ELISA. IFN-γ/IL-4 ratio used to infer Th1/Th2 balance.

(6) Gut Microbiota Composition: Assessed via 16S rRNA gene sequencing from fecal samples to evaluate α/β diversity and dominant genera.

(7) Serum Biochemical Indicators: CRP, ALT/AST, BUN/Cr measured by automated biochemistry analyzers to monitor systemic inflammation, liver, and kidney function.

3.8 Adverse Events

All adverse events (AEs) occurring during or after the intervention period will be recorded, including subjective discomfort, symptom exacerbation, and laboratory abnormalities. Serious adverse events (SAEs) refer to medical incidents that result in death, life-threatening conditions, hospitalization, or significant functional impairment. All AEs will be graded according to the NCI-CTCAE v5.0 criteria. Investigators will assess the causality between each event and the intervention (e.g., definitely related, possibly related, unrelated), and document all findings in the case report form (CRF) for final statistical analysis. In the event of an SAE, the research team will report it in writing to the Ethics Committee and regulatory authority within 24 hours and manage it promptly as per ethical guidance. During the study, participants will be followed up weekly, and investigators will actively inquire about and record any potential adverse events.

3.9 Ethical Considerations

This study has been approved by the Ethics Committee of the School of Public Health, Lanzhou University (Approval No. IRB25041501). All participants will sign written informed consent prior to enrollment. The consent form will include details regarding the study objectives, methods, potential risks and benefits, AE management, and follow-up plan.

Participants are free to withdraw from the study at any time without any reason and without affecting their medical care. All collected data will be anonymized and securely stored for research purposes only, ensuring confidentiality and data protection.

If any adverse events occur due to the intervention, the research team will be responsible for providing appropriate medical support and treatment. The study will be conducted under continuous oversight by the Ethics Committee, in compliance with the *Declaration of Helsinki*, *Good Clinical Practice (GCP)*, and relevant national regulations.

**4 Procedures**

4.1 Participant Recruitment, Informed Consent, and Baseline Survey

Participants will be recruited through advertisements or posters at Lanzhou University. Interested volunteers will be asked to complete a screening questionnaire. Based on predefined inclusion and exclusion criteria, preliminary eligibility will be assessed. Those who pass the initial screening will be invited for a face-to-face interview with the research team, during which the study objectives, procedures, interventions, potential risks, and expected benefits will be fully explained.

Participants who provide written informed consent after understanding the study details will be formally enrolled. A total of approximately 80 participants will be recruited. All participants will be assigned a unique ID code to ensure data confidentiality and for follow-up tracking.

4.2 Baseline Assessments and Sample Collection

Before randomization and intervention, all enrolled participants will complete the following baseline assessments:

(1) Questionnaires: Including demographic information (age, gender, ethnicity, lifestyle habits), allergen exposure, allergic history, medical and family history, TNSS, RQLQ, VAS, and dietary intake assessment.

(2) Anthropometric Measurements: Height, weight, body fat percentage.

(3) Blood Sampling: Used to measure immune indicators, inflammatory cytokines, and sIgE.

(4) Saliva Sampling: Used to measure secretory sIgA levels.

(5) Fecal Sampling: Used to measure secretory sIgA levels and perform 16S rRNA sequencing analysis of the gut microbiota.

4.3 Randomization

This study adopts a stratified randomization method, in which participants are randomly assigned to either the yeast postbiotics group or the placebo group. Stratification factors include:(1) Sex (male/female); (2) Diagnosis of AR (yes/no, based on self-reported clinical history), ensuring balance and comparability between the two groups.

4.4 Intervention

Participants in the yeast postbiotics group will take two capsules of yeast postbiotics daily. Participants in the placebo group will take two placebo capsules daily, which are identical in formulation, taste, appearance, and packaging to the intervention capsules but only contain maltodextrin and a small amount of silicon dioxide. After group assignment, each participant will receive one bottle of the intervention product (90 capsules/bottle). At the 4-week follow-up, remaining capsules will be counted and a second bottle (90 capsules) will be distributed. Throughout the study period, all participants are instructed to avoid any additional intake of probiotics, prebiotics, or synbiotics, and to maintain their usual dietary and physical activity habits. To ensure ethical fairness, participants in the placebo group will be offered yeast postbiotic capsules after the intervention as post-trial nutritional support.

4.5 Follow-up

4.5.1 Follow-up Components:

(1) Scheduled follow-ups: All participants will undergo four scheduled follow-up visits at week 0, week 2, week 4, and week 12 of the intervention. The visits at week 0, week 4, and week 12 include: ① Questionnaire assessments: TNSS (Total Nasal Symptom Score), VAS (Visual Analog Scale), RQLQ (Rhinoconjunctivitis Quality of Life Questionnaire), and dietary survey. ② Physical measurements: height, weight, body fat percentage. ③ Sample collection: blood, urine, saliva, and fecal samples. ④ Adverse events: All reported adverse events will be verified and graded by the study investigator.

At week 2, only saliva samples will be collected.

(2) Daily follow-up: After randomization, all participants will be assigned to three management groups, each overseen by two investigators for daily follow-up. Starting from the first day of intervention, participants must complete an electronic questionnaire daily to record:① TNSS score.② Medication adherence (number of capsules taken, dosage, and time of intake).③ Any adverse events.All participants will receive training before the trial on how to complete the questionnaire accurately to ensure consistent and reliable scoring.

(3) Adherence Monitoring: Each participant is required to take daily photos of their capsule intake and upload them to the study system or designated group. During each scheduled follow-up, investigators will count remaining capsules to calculate the compliance rate. If any participant misses doses or stops the intervention, investigators will conduct follow-up to determine whether the participant should be withdrawn from the study.

4.5.2 Data Collection Procedures:

(1) Basic Information Survey, Physical Measurements, and Sample Collection: All participants will undergo physical measurements, sample collection, and basic information surveys in the morning under fasting conditions before the intervention, and at weeks 4 and 12 of the intervention.

① Basic Information Survey: A structured questionnaire will be administered face-to-face to collect basic demographic and lifestyle data, including name, gender, age, physical activity, smoking and alcohol consumption, medical history, family history, allergen exposure, and allergy-related history (such as AR-related conditions).

② Physical Measurements: Standardized procedures will be used to measure height, weight,

waist circumference, hip circumference, and blood pressure. Body Mass Index (BMI) will be calculated as weight (kg) divided by height squared ($m^2$), with values recorded to two decimal places.

③ Sample Collection:

Blood samples: 10 mL of venous blood will be collected by a qualified nurse. Participants must fast for 10–12 hours before blood collection. After collection, samples will stand at room temperature for 3–5 minutes, followed by centrifugation at 3000 rpm for 10 minutes. The plasma will be separated and transferred into labeled EP tubes and stored at −80°C for future analysis.

Fecal samples: Participants will use sterile cryotubes to collect stool from the central portion to avoid contamination with urine or diarrhea. Samples must be delivered to −80°C storage within 1 hour.

Midstream urine samples: Participants will collect midstream urine in a clean container, then transfer it into EP tubes and store it at −80°C.

Saliva samples: After rinsing the mouth with water and resting for 5–10 minutes, participants will discard the initial saliva. The subsequent saliva will be collected in a clean cup and transferred into EP tubes, then frozen at −80°C.

(2) Dietary Intake: A 3-day consecutive dietary recall will be conducted before the intervention, and again at weeks 4 and 12. Participants will be required to record their complete dietary intake over three consecutive days (including two weekdays and one weekend day), covering all foods and beverages consumed (e.g., breakfast, lunch, dinner, fruits, snacks, and additional meals). Detailed entries must include the food name, ingredients, preparation methods, and portion sizes. For packaged snacks and drinks, the brand name should also be indicated. Prior to data collection, participants will receive standardized training, including a food atlas to assist with accurate portion size estimation. Investigators will collect and review the completed dietary records daily. If any information is missing or unclear, researchers will promptly contact the participant for clarification or supplementation to ensure the accuracy and completeness of the dietary survey.

4.6 Quality Control

To ensure data accuracy and reproducibility, the following quality control (QC) procedures will be implemented:

(1) Questionnaire QC: ①Use of validated and standardized instruments: TNSS, VAS and RQLQ (Chinese versions). ②All investigators will be trained in standardized administration,

scoring, and interview techniques. ③Face-to-face completion or guided interviews will be used. ④All completed questionnaires will be double-checked within 24 hours by a second investigator to identify missing or inconsistent entries. Corrections will be made by contacting the relevant participant.

(2) Blood Samples: ①Fasting blood draws scheduled between 8:00–10:00 AM with prior notice and scheduling. ②Unique ID codes will be assigned to all samples, matched to participant IDs. ③Blood will be drawn by certified nurses using standard vacuum tubes: 5 mL in coagulation tubes and 5 mL in EDTA tubes. ④Plasma/serum will be aliquoted and stored at −80°C. Dry ice will be used for cold chain transport.

(3) Fecal Samples: ① Sterile collection kits with stabilization solution will be used. ② Samples will be delivered to −80°C storage within 4 hours or immediately stored on site. ③ Batch testing will be conducted to minimize inter-assay variability. ④ Sample coding and time-point tracking will be used for consistency.

(4) Data Entry: ① Double data entry will be performed in EpiData by two independent investigators. ② Logic checks will be applied to prevent entry errors. ③ Weekly backups will be maintained on encrypted servers and external drives. ④ Final datasets will be locked prior to statistical analysis and archived for audit

(5) Statistical Analysis: ① All analyses will be conducted using SAS software (version 9.4 or higher). ② Predefined variable libraries, missing data protocols, and sensitivity analyses will be applied. ③ All key results (e.g., effect sizes, p-values) will be double-verified by two statisticians. ④ The final analysis report will be prepared in accordance with CONSORT guidelines.

4.7 Management Policies

(1) Intervention Product Management: Intervention products will be centrally procured and labeled. Distribution will be logged with batch numbers, participant IDs, and intake schedules. Returned and unused products will be counted to ensure traceability.

(2) Participant Management: Participants will receive assigned IDs and follow-up schedules. Weekly reminders via phone or WeChat will ensure compliance. Missing ≥3 consecutive days of intake will be flagged as poor adherence. Reasons for withdrawal will be documented.

(3) Sample Management: All blood and fecal samples will be centrifuged or frozen within 2 hours and stored at −80°C. Samples are for this study only and will be managed in a coded and

traceable system.

(4) Data Management: Data will be entered into an electronic case report form (eCRF), double-entered and validated. All data will be anonymized before analysis and retained for at least 5 years for audit purposes.

4.8 Post-Trial Participant Care

After trial completion, all participants will receive a free health follow-up, including blood routine tests and liver/kidney function assessments. Any abnormalities will be referred to outpatient care. Individual reports will be provided, and those in need will receive continued nutrition consultation services.

**5 Risks and Benefits of the Study**

Participation in this study does not offer you direct benefits, but we hope that the information obtained from your participation will provide important theoretical evidence for developing appropriate dietary recommendations for postbiotics.

The collection of your blood samples will be performed under strict aseptic conditions, and drawing a small amount of blood will not harm your health. However, there may be minor risks associated with sample collection, such as brief pain, localized bruising, or mild dizziness in a small number of individuals.

**6 Costs**

All nutritional supplements and health assessments required for the study will be provided free of charge by the research team. At the conclusion of the study, participants will receive a financial compensation as a token of appreciation for their time and cooperation.

**7 Compensation**

In the unlikely event that you experience harm or injury as a result of participating in this study, you will be provided with appropriate medical treatment and/or financial compensation in accordance with ethical and legal standards.

**8 Confidentiality of Participant Information**

All personal information collected during the study will be kept strictly confidential. For example, your biological samples will be labeled with a numerical code rather than your name. Personally identifiable information will not be disclosed to anyone outside the research team unless you provide written permission to do so.

# Informed Consent Form

**Dear Participant,**

You are invited to participate in a human intervention study conducted by the School of Public Health at Lanzhou University, entitled *"**Study of the Effects and Mechanisms of Yeast Postbiotics on Persistent Allergic Rhinitis Symptoms**"*. This study has been reviewed and approved by the Ethics Committee of the School of Public Health, Lanzhou University, and complies with relevant ethical and scientific research standards. This informed consent form provides you with key information to help you decide whether to participate. Please read it carefully. If you have any questions, feel free to ask the study investigator.

**Purpose of the Study**

Allergic rhinitis (AR) is a chronic, non-infectious inflammatory disease of the nasal mucosa mediated by immunoglobulin E (IgE) in atopic individuals after exposure to allergens. Typical clinical symptoms include paroxysmal sneezing, clear nasal discharge, nasal itching, and nasal congestion, often accompanied by itchy eyes, tearing, sleep disturbances, and reduced quality of life. AR is one of the most common chronic nasal diseases, affecting approximately 10%–20% of the global population, and has been identified by the World Health Organization as a significant public health issue.

Postbiotics are functional substances composed of inactivated microorganisms and their metabolic products, such as short-chain fatty acids and cell wall components (e.g., β-glucan, peptidoglycan). They possess various biological activities, including immunomodulatory, antioxidant, and anti-inflammatory effects. Compared with probiotics, postbiotics offer advantages such as greater stability, no risks associated with live bacteria, and better controllability in production. Previous studies have shown that β-glucan derived from yeast-based postbiotics can regulate the Th1/Th2 balance, downregulate IL-4 and IgE expression, and enhance Treg cell

function. These effects have demonstrated the potential to alleviate inflammatory responses in allergic diseases such as asthma and food allergies in animal models. However, research on postbiotic interventions for AR remains limited.

Based on this background, this study aims to conduct a randomized, double-blind, placebo-controlled intervention trial among college students with persistent AR symptoms to evaluate the effects of yeast postbiotics on AR symptoms and related immunological and microbiota indicators. The goal is to provide scientific evidence supporting the use of postbiotics in the prevention and treatment of allergic diseases.

**Study Procedures**

If you agree to participate in this study, you will be assigned a participant number and randomly allocated to either the yeast postbiotic group or the control group. The study will last for 15 weeks, consisting of a 1-week run-in period, a 12-week intervention period, and a 2-week follow-up period. During the intervention, participants in the intervention group will take two yeast postbiotic capsules daily after meals, while the control group will take an equivalent amount of placebo. At baseline, week 4, and week 12, you will undergo nutritional surveys, physical activity assessments, physical examinations, and collection of biological samples (blood, urine, saliva, and feces). Saliva samples will also be collected at week 2 of the intervention. Two weeks after the intervention ends, a questionnaire will be used to follow up on changes in AR symptoms. A trained nurse will collect 10 mL of venous blood from your arm. Urine, saliva, and stool samples are to be self-collected according to the researchers' instructions and submitted promptly to research staff. Your samples will be used solely for this study.

**Potential Benefits**

There are no direct benefits to you from participating in this study. However, you will receive free health assessments and intervention products. Your participation will help researchers provide scientific evidence for nutritional interventions in AR and similar diseases.

**Risks and Discomforts**

Blood sample collection will be performed under sterile conditions. Risks are minimal and may include slight pain, local bruising, or mild dizziness.

**Confidentiality**

All personal data and information collected during the study will be kept strictly confidential. Your samples and records will be labeled using numeric codes instead of your name. Personally identifiable information will not be shared outside the study team without your consent.

**Costs**

Yeast Postbiotics supplements and health assessments will be provided free of charge. After the trial, the control group will also receive a free 12-week supply of the intervention product. Participants will receive a monetary compensation upon study completion.

**Compensation**

If you suffer injury or harm as a result of participating in this study, you will be entitled to free medical care and/or appropriate compensation.

**Voluntary Participation and Right to Withdraw**

Participation in this study is completely voluntary. You have the right to access information about the study at any time and may choose to withdraw at any point without providing a reason. Withdrawing from the study will not affect your access to medical services. If continuing participation poses a risk to your health, the investigator may decide to withdraw you from the study.

During your participation, we ask that you:

- Follow all study-related instructions.
- Respond truthfully to questions from the investigators.
- Inform the investigator of any discomfort or adverse symptoms.
- Avoid prohibited medications or substances.
- Provide accurate medical history and health information.
- Inform us of any recent or ongoing participation in other studies.

If you fail to follow the study protocol or experience study-related complications, the investigator may terminate your participation.

**Contact Information**

If you have questions about the study, experience discomfort or injury, or have concerns about your rights as a participant, please contact: [Professor/Dr. ] – Phone: [****]

**Consent Signature**

I have read and understood the content of this informed consent form. The investigator [Signature] has explained to me the study's purpose, procedures, risks, and benefits in detail. My questions have been answered to my satisfaction. I voluntarily agree to participate in this study.

Participant Signature: _____ Date: _____ / _____ / _____

Investigator Signature:_____ Date: _____ / _____ / _____

Investigator Contact Number: _____