

National Taiwan University Hospital Clinical Trial Research Protocol and Statistical Analysis Plan

Project Title: To evaluate the influence of LUA probiotics on uric acid

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National Taiwan University Hospital Clinical Trial Protocol

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☐ Drug ☐ Medical Device ☐ Medical Technology ☒ Other: This study does not involve drugs, medical technology, or medical devices.

I. Project Title

To evaluate the influence of LUA probiotics on uric acid.

II. Principal Investigator

Dr. Jyh-Ming Liou, Department of Internal Medicine, National Taiwan University Hospital

Co-Investigators:

Dr. Chien-Chuan Chen

Dr. Chieh-Chang Chen

Dr. Mei-Chih Chen

III. Study Topic

This study aims to evaluate whether consuming the lactic acid bacteria “LUA probiotics” can lower serum uric acid levels to help prevent the onset of gout symptoms, thereby avoiding the need for long-term medication through the use of dietary supplements.

IV. Abstract

Hyperuricemia refers to an abnormally high concentration of uric acid in the serum. Chronic hyperuricemia is a major factor in the development of gout and is also associated with various diseases. Therefore, the prevention and treatment of hyperuricemia are receiving increasing attention. Recent studies, including

cellular and animal experiments, suggest that lactic acid bacteria (LAB) may reduce uric acid levels. However, rigorous clinical observational studies are lacking to further investigate LAB's effects on uric acid.

The product "LUA Probiotics" is developed and produced by Grape King Bio Ltd. Longtan Plant. Its main ingredients include *Lactobacillus reuteri*, beta-carotene, silicon dioxide, and magnesium stearate. This product is not yet available on the market.

V. Objective

To evaluate whether "LUA probiotics" can reduce serum uric acid levels and serve as a preventive health supplement before the onset of gout symptoms, thereby avoiding the need for medication.

VI. Materials and Methods

Site: National Taiwan University Hospital

Inclusion Criteria:

1. 20 participants, male or female, aged 20 or above.
2. Mentally competent, voluntarily participating, and signed informed consent.
3. Patients with hyperuricemia (uric acid ≥ 7.5 mg/dL) not on uric acid-lowering medication, or those with a history of gout not currently on such medication.

Exclusion Criteria:

1. Patients diagnosed with catastrophic illnesses per National Health Insurance regulations.
2. Pregnant or planning pregnancy within 6 months.
3. Abnormal liver function (AST/ALT > 2 x upper limit).
4. Renal impairment (serum creatinine > 1.5 mg/dL).

5. Gastrointestinal disorders (e.g., surgeries, chronic diarrhea).
6. Long-term use of antibiotics, H2-blockers, PPIs, antioxidants, probiotics, or laxatives.
7. Serious complications in the past 6 months (e.g., stroke, myocardial infarction, major trauma or surgery).
8. Allergy to *Lactobacillus*.
9. Inability to give informed consent.
10. Irregular diet or inability to comply with the study protocol.
11. Poor compliance with medical advice.

Study Design and Procedure

1. Confirm eligibility based on criteria.
2. Recruit 20 eligible patients with hyperuricemia or gout not on uric acid-lowering drugs.
3. If eligible, complete informed consent and a gastrointestinal questionnaire (~20 mins).
4. Study has 2 phases:
 - **Phase 1:** 2 weeks, take 2 capsules of Test Material A (Placebo) (500 mg/cap) daily after dinner.
 - **Phase 2:** 4 weeks, take 2 capsules of Test Material B (Test article) (500 mg/cap) daily after dinner.
5. Blood sampling schedule: Week 0, Week 2, and Week 6.
6. At each timepoint, collect 20 c.c. of fasting blood to test uric acid and the following: CBC, fasting glucose, TG, TC, HDL, LDL.
7. Additionally, analyze serum levels of IL-1 β , IL-6, IL-10, IL-13, IL-17, IL-18, TNF- α , IFN- γ .
8. **Statistical Analysis:** All data will be shown in the form of Mean $\pm$ S.D., using SPSS 16.0 and Student's *t*-test. Statistical significance at $p < 0.05$.

LUA Probiotics Composition

- **Active ingredients:** *Lactobacillus reuteri*, beta-carotene, silicon dioxide, magnesium stearate
- **Dosage form:** 500 mg/capsule, 60 capsules/bottle

Placebo Composition

- **Ingredients:** Dextrin, beta-carotene, silicon dioxide, magnesium stearate
- **Dosage form:** 500 mg/capsule, 60 capsules/bottle

VII. Outcome Assessment

Evaluate whether taking “LUA probiotics” reduces serum uric acid levels in participants.

VIII. Clinical Adverse Reactions and Management

Uric acid > 7 mg/dL is classified as hyperuricemia; medication is typically prescribed at $\geq 9 \sim 10$ mg/dL. For patients with gout attacks but uric acid < 9 mg/dL, lifestyle and hydration are advised. Probiotics are generally safe, but some may experience diarrhea, nausea, abdominal pain, or constipation. Discontinue use if serious discomfort occurs.

IX–XVII. Additional Sections (Summarized)

- Investigator qualifications and training (Appendix)
- Informed consent format (Appendix)
- No prior preclinical trials or foreign regulatory approvals
- No known psychological, physical, or financial risks or benefits
- No conflict of interest
- No additional data

XVIII. Research Staff & Responsibilities

Principal Investigator – Dr. Jyh-Ming Liou:

1. Study design
2. Subject recruitment
3. Data analysis
4. Report writing
5. Data management

Co-Investigators – Drs. Chien-Chuan Chen, Chieh-Chang Chen, Mei-Chih Chen:

1. Subject recruitment
2. Data management

XIX. Budget

XX. Research Outcomes – Ownership and Use

This study is initiated by the sponsoring company. All rights to patents and commercial applications derived from this study belong to Grape King Bio Ltd., Longtan Plant.