# Informed Consent Form

# Hesperidin Improves Cognitive Function in Middle-Aged and Older Adults with Overweight or obesity: A Randomized Controlled Trial

**NCT Number: Not yet assigned**

**Document Date: February 17, 2026**

Dear Participant,

Hello!

You are invited to take part in a study funded by the National Natural Science Foundation of China (Grant No. 82304123) and conducted by the School of Public Health, Shanghai Jiao Tong University School of Medicine. Before you decide whether to participate, please read the following information carefully. Feel free to ask the research staff any questions you may have.

**Study title**: Hesperidin Improves Cognitive Function in Middle-Aged and Older Adults with Overweight or Obesity: A Randomized Controlled Trial.

**Background**: According to the China Nutrition and Chronic Disease Status Report (82304023), more than 50% of adults in China are now overweight or obese, and this trend is still rising. Previous studies have shown that obesity is not only closely linked to various metabolic diseases but may also increase the risk of cognitive decline. Hesperidin is a natural flavonoid found in citrus fruits, especially oranges and orange products. Previous research suggests that hesperidin has antioxidant and anti-inflammatory properties and shows potential for helping regulate body weight, blood glucose, blood lipids, and insulin sensitivity. However, its effects on cognitive function in overweight and obese people have not been systematically studied in human populations.

**Purpose**: This study aims to investigate the effects of hesperidin on cognitive function (including executive function, memory, and attention) in overweight or obese middle-aged and older adults. We will also measure changes in gut microbiota and metabolites to explore possible mechanisms, providing scientific evidence for nutritional interventions targeting obesity-related cognitive decline.

**Study procedures**:

Inclusion criteria: Age 55-75 years; BMI $\geq$ 24 kg/m$^2$ or waist circumference $\geq$ 90 cm (men) / $\geq$ 85 cm (women); willing to participate and sign the informed consent form.

Exclusion criteria: Organic neurological disorders (Parkinson's disease, Alzheimer's disease,

etc.); prior stroke or cerebrovascular disease; malignant tumors; severe liver, kidney, or gastrointestinal disease (e.g., severe constipation, ulcerative colitis); major surgery or serious trauma within the past six months; currently using or recently used weight-loss medications (including over-the-counter products or supplements); currently using antidepressants (except statins); strict vegetarians; binge eating disorder; alcohol intake exceeding 14 g/day for women (approximately 350 mL beer (5% vol), 150 mL wine (12% vol), or 45 mL spirits (40% vol, e.g., baijiu, whiskey, vodka)) or 28 g/day for men (approximately 700 mL beer, 300 mL wine, or 90 mL spirits); following a weight-loss plan in the past 3 months; planning to travel, move, or have other arrangements that would interfere with continuous participation in the next six months; participating in another lifestyle or drug intervention study.

If you are eligible and agree to participate, you will be randomly assigned to one of three groups: placebo, medium dose (300 mg hesperidin per day), or high dose (600 mg hesperidin per day). The intervention lasts 10 weeks.

Hesperidin powder is provided by Chengdu Oukang Company, corn starch by Haihua Shunda, and the size 0 capsule shells by Pulu Pharmaceutical, which also handles packaging. All capsules are packaged and stored under uniform conditions, ensuring that each capsule contains the specified amount of hesperidin powder (300 mg) or corn starch (300 mg).

Hesperidin is a natural flavonoid extracted from citrus fruits. Previous human studies have shown it is generally well tolerated. However, like any supplement, it may occasionally cause mild gastrointestinal discomfort or allergic reactions in sensitive individuals. We will monitor your condition closely and stop the intervention immediately if any issues arise.

During the intervention, we will give you a weekly supply of capsules. You will take 2 capsules every morning. We will also provide a nutrition and healthy eating talk once every two weeks. At weeks 2, 4, 6, and 8, you will record your diet, physical activity, and sleep for one day. We will measure your weight, waist circumference, blood pressure, heart rate, skeletal muscle mass, and body fat. You will also provide a urine sample (10 mL) once a week, and stool samples at weeks 2, 4, and 8 (three times in total). Instructions for sample collection are provided below. Before and after the intervention, we will assess your cognitive function (including memory and attention). We will also collect blood (18 mL), urine, and stool samples once each.

To accurately record your daily activities during the study, we will provide you with a free

Huawei Band 10 activity tracker. You will need to wear it every day for the 10-week intervention. The band records your daily step count, activity time, and sleep data. These data will be synced via Bluetooth to a study-dedicated smartphone and used only for this research. After the study ends, all data will be encrypted and stored. If you complete the entire study, the activity tracker is yours to keep as a thank-you gift. If you are unwilling to wear the band, please inform the research staff. We will assess whether complete and reliable daily activity data can still be collected through weekly follow-ups without the band. If we determine that it is possible, we will not provide the band and will instead strengthen weekly observations. If we conclude that data quality cannot be guaranteed without the band, you may not be able to continue in the intervention.

During biological sample collection and biomarker testing, we will strictly protect your privacy and data security. All sample collection and data acquisition will be done only after obtaining your informed consent, following uniform procedures for collection, storage, and transport. Sample storage information will only be known to the research team and used only for the purposes of this study. Any remaining samples after testing will be destroyed at the end of the study.

The study design minimizes risks. The only invasive procedure is blood collection, which will happen twice (before and after the intervention) and will be performed by trained professionals. If you feel any discomfort at any time, please contact the study staff immediately. Thank you for your cooperation and support.

**Participant responsibilities**:

Please truthfully report your medical history (diabetes, hypertension, dyslipidemia, etc.) and all medications and supplements you are currently taking. You must take the capsules daily as instructed and keep record. Try to maintain your usual diet, physical activity, and sleep habits. Complete the scheduled records of diet, activity, sleep, physical measurements, cognitive tests, and sample collections on time. If you experience any discomfort during the study (e.g., digestive issues, dizziness), please notify the research staff immediately. If you need to withdraw from the study, please contact the research staff.

**Risks and discomforts**:

Blood collection may cause a brief needle sting. Collecting urine and stool samples may be inconvenient. Regular follow-ups and tests may take some of your time. If any discomfort or unusual conditions occur during the study, the research staff will promptly assess the situation and provide

necessary medical assistance. You may withdraw from the study at any stage without giving a reason.

**Potential benefits**:

① Four free health checkups, including weight, body fat, waist circumference, blood pressure, etc., with results provided to help you understand your health status.

② Two free biochemical tests (blood glucose, lipids, HbA1c, etc.), with results provided in written or electronic form for your reference.

③ Two cognitive function assessments, with results explained to you.

④ Bi-weekly healthy eating talks to improve your health knowledge and self-management skills.

⑤ A small gift or token of appreciation (approximately 10 RMB in value) each week; after completing the full intervention, you may keep the activity tracker as a gift. You will not be required to upload any further data after the study ends.

⑥ Personalized health guidance to help promote healthy aging.

**Privacy and data protection**:

All your personal information will be coded and used only for this study. Data will be collected and entered using a professional clinical data management platform with dedicated accounts and passwords; only the principal investigator has data export permissions. Data exports require approval from the principal investigator, and all personally identifiable information will be removed before export to ensure your privacy and data security.

All sample and data collection will only occur after obtaining your informed consent, following uniform procedures. Sample storage information is known only to the research team and used only for the purposes of this study. Any remaining samples after testing will be destroyed at the end of the study.

During the study, monitors, auditors, the ethics committee, and relevant regulatory authorities may, within the limits permitted by law and regulations, access your original medical records without infringing on your privacy. Anyone who accesses your information is obligated to keep it strictly confidential and will not use it for any purpose outside this study. Any published results will not contain information that could identify you.

**Voluntary participation**:

Your participation is entirely voluntary. You have the right to withdraw from the study at any

stage, for any reason or no reason, without discrimination or retaliation. Your medical care and rights will not be affected.

**Compensation for study-related injury**:

If you experience an adverse reaction or serious injury related to the study, you will receive prompt, free medical care. The investigator will cover the associated medical costs and provide reasonable financial compensation.

**Costs and compensation**:

You will not be charged for any part of this study. During the study, you will receive an appropriate small gift or token of appreciation each week.

**Contact information**:

If you have any questions about the study, or if you experience discomfort or have concerns about your rights during the study, please contact:

Shiqi Lin, Phone: 18616825727

Ethics committee: Public Health and Nursing Research Ethics Committee, Shanghai Jiao Tong University School of Medicine

Phone: 021-63846590-776499