Buddhist Tzu Chi Medical Foundation Hualien Tzu Chi Hospital
Consent Form for Clinical Trial Subjects

Only with the stamp of this committee will it be valid

Revised version of Research Ethics Committee meeting 23 February 2021

Project name English：Jing Si Herbal Tea in the treatment of dyspeptic symptoms and psychophysical burden in patients with functional dyspepsia--a double-blind, randomized, placebo-controlled study	
Test agency: Buddhist Tzu Chi Medical Foundation Hualien Tzu Chi Hospital Gastroenterology	Entrusting unit/pharmaceutical factory: None Research funding source: Hualien Tzu Chi Hospital
Trial Host: Dr. Chen, Chien-Lin Unit/ Title: Division of Gastroenterology / Director Co-host: Dr. Wong, Ming-Wun Unit / Title: Division of Gastroenterology / Attending Physician Co-host: Dr. Yi, Chih-Hsun Unit / Title: Division of Gastroenterology / Attending Physician Co-host: Dr. Liu, Tso-Tsai Unit/ Title: Gastrointestinal Examination Room/Director Co-host: Dr. Lei, Wei-Yi Unit/ Title: Division of Gastroenterology / Attending Physician Co-host: Dr. Hung, Jui-Sheng Unit / Title: Division of Gastroenterology / Attending Physician Co-host: Dr. Liang, Shu-Wei Unit / Title: Integrative Medicine/ Resident Physician Co-host: Liu, Chin-Hung Unit / Title: Department of Pharmacology, College of Medicine, Tzu Chi University / Associate professor	
24-hour emergency contact person: Dr. Chen, Chien-Lin Tel: 0988-282055	
Subject name:	Medical record number:
Before your questions are answered satisfactorily , please do not sign this consent form. **You do not have to decide immediately whether to participate in this trial, please sign after careful consideration.** You must sign a consent form to participate in this trial. If you wish to participate in this trial, this document will be considered a record of your consent. **Even with your consent, you can withdraw from the trial at any time without giving any reason.**	
A. Purpose of the test： This trial is a clinical trial in a single center in Taiwan, and it is expected to enroll 300 people. This test is a double-blind randomized test, the purpose of which is to investigate the improvement degree of **Jing Si Herbal Tea** on the physical and mental symptoms of **functional**	

dyspepsia (FD) . Functional dyspepsia (FD) is a common disease, but the effect of traditional western medicine is worthy of improvement. **Jing Si Herbal Tea** is a Chinese herbal food developed locally. This study adopts a double-blind randomized trial. **Jing Si Herbal Tea** is normal in the objective examination For patients with functional dyspepsia, evaluate their physical and mental symptoms before and after treatment, as well as changes in intestinal bacterial metabolites.

Any treatment has risks, and clinical trials are no exception. Please consider carefully before deciding whether to participate in this trial.

B. Research background or product status :

Jing Si Herbal Tea

The ingredients of Jing si Herbal Tea are eight kinds of Chinese herbal medicines in Taiwan, such as Artemisia argyi, Houttuynia cordata, Ophiopogon japonicus, Houttuynia cordata, Platycodon grandiflorum, Licorice root, Perilla leaf, Chrysanthemum, etc. , the current study found that it can block the combination of the new coronavirus and the cell, and can also reduce the cell penetration, and block the virus from penetrating the cell, and the wild type and the mutant virus D614G, B.1.1.7, 501Y.V2 were tested in animals Studies have found that Jing Si Herbal Tea can reduce the ability of 60-70% of the virus to infect the upper respiratory tract, lungs, heart, and intestines of mice and reduce the expression of the protein FKBP51 related to depression by 40%. Currently, clinical trials have been registered (ClinicalTrials.gov Identifier : NCT04967755) for COVID-19 patients using Jing Si Herbal Tea to help reduce the amount of virus.

C. The main inclusion and exclusion conditions of the trial:

Physicians or related researchers who carry out this research project will discuss with you the necessary conditions for participating in this research. Please cooperate and honestly tell us your past health conditions. If you are not eligible to participate in this study, you will not be able to participate in this study.

1. Inclusion conditions (conditions for participating in this study):
   (1) Age limit 20 to 79 years old.
   (2) Those who meet the definition of chronic dyspepsia (FD).
   (Functional dyspepsia (FD) is chronic (once a week , lasting for at least three months, at least six months before the first symptom) upper gastrointestinal symptoms (any of the following) : abdominal distension after meals, easy to feel full , epigastric pain or burning sensation in the upper abdomen, and no symptoms of gastrointestinal bleeding or significant weight loss, and no abnormality after upper gastrointestinal endoscopy.)
   (3) Clear consciousness and willing to sign the subject's consent form.

2. Exclusions (if you have any of the following conditions , you will not be able to participate in this study):
   (1) Abnormal liver and kidney function;
   (2) Abnormal blood test, abnormal thyroid gland;
   (3) Have undergone esophageal or gastric surgery;
   (4) Abnormal upper gastrointestinal endoscopy;
   (5) Have gastric pylori infection;
   (6) Antibiotics are being used for infectious diseases;
   (7) Pregnant or breastfeeding women;
   (8) Suffer from heart, liver, kidney failure.
   (9) Weakness, allergies, coldness , chronic diseases, poor kidney function, infants under three years old, children, pregnancy, breastfeeding, menstrual period.

D. The test method and related procedures:

This study is a prospective study, which is expected to last for 1 year. It is planned to recruit 300 functional dyspepsia (FD) subjects from the Department of Gastroenterology and Hepatobiliary Medicine. Functional dyspepsia (FD) is chronic (once a week , lasting for at least three months, at least six months before the first symptom) upper gastrointestinal symptoms (any of the following) : postprandial abdominal distension, easy to feel full, If you have epigastric pain or burning sensation in the upper abdomen, and have no symptoms of gastrointestinal bleeding or significant weight loss, and there is no abnormality in upper gastrointestinal endoscopy, if you meet the definition of chronic dyspepsia (FD), you decide to join this study and sign this After the consent form, eligible subjects received blood tests and complete physical and mental symptom assessments (PSQI, TDQ, PSS-10, STAI, PAGI-SYM) before treatment, and then randomized according to double - blind The method is to generate garbled codes by computer, and 150 of them are included in the Jing Si Herbal Tea group , and the other 150 are included in the placebo group according to the coding sequence. After grouping, the research assistant gave Jing Si Herbal Tea or placebo, and neither the host nor the subjects knew which group to assign. The period of taking Jing Si Herbal Tea or placebo lasted for a total of two months. At the end of the first month, blood test (LC-MS pre- and post-test analysis) and complete physical and mental symptom assessment (PSQI, TDQ, PSS-10, STAI, PAGI-SYM) were accepted again. In the next month, the Jing Si Herbal Tea group and the placebo group were cross-tested. The original placebo group was changed to Jing Si Herbal Tea, and the Jing Si Herbal Tea group was changed to placebo. At the end of the course of treatment, the third complete physical and mental symptom assessment was accepted. (PSQI, TDQ, PSS-10, STAI, PAGI-SYM).

Research Program Map:

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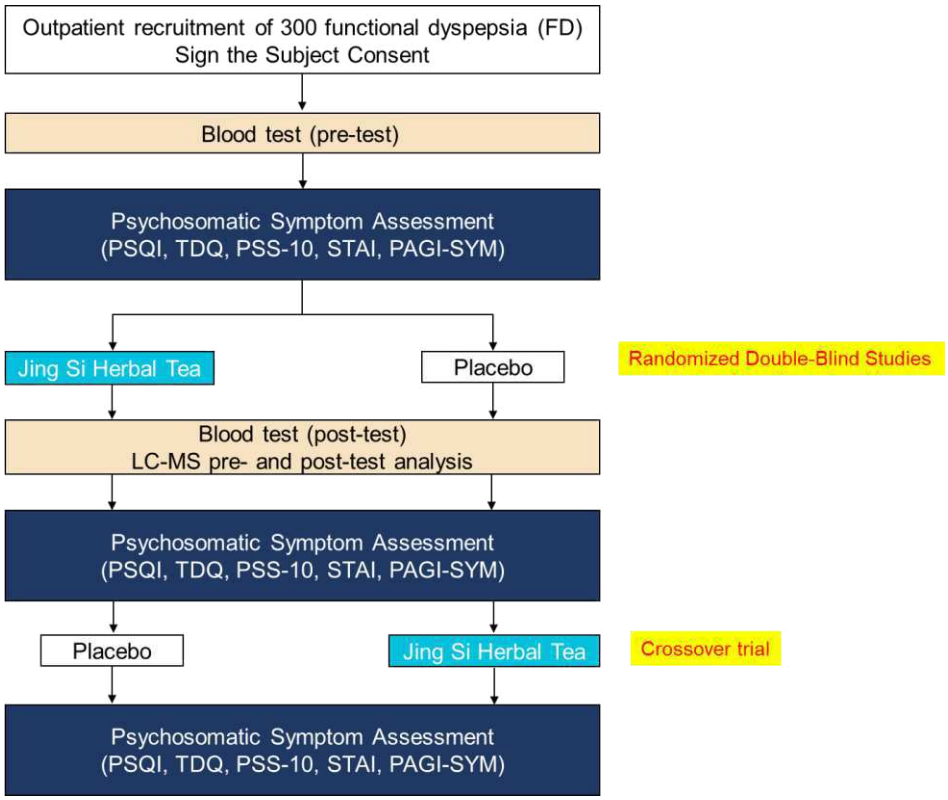

Jing Si Herbal Tea

In this experiment , Jing Si Herbal Tea Concentrated Liquid is used. Its ingredients are eight kinds of Taiwanese local ingredients, such as mugwort leaves , houttuynia cordata, Ophiopogon japonicus, Houttuynia cordata, Bellflower, licorice, perilla leaves, and chrysanthemum. , Dampness-clearing and heat-clearing Chinese herbal medicine, take 15 ml of **Jing Si Herbal Tea concentrate** once a day .

E. Possible risks and their incidence and treatment methods:

※Jing Si Herbal Tea and placebo are suitable for ordinary people; people with infirmity, allergies, coldness , chronic diseases, poor kidney function, infants under three years old, children, pregnancy, breastfeeding, and menstrual period, please use with caution; if you feel unwell, please stop using. Do not drink before going to bed to avoid frequent urination at night and affect sleep.

If you feel uncomfortable physically and mentally due to the long time of filling out the questionnaire, please inform the research host or other researchers at any time. If you want to withdraw from this study, we will respect your wishes.

You will be monitored regularly for side effects while you are in the trial by the trial physician and other trial staff. Additional visits and tests will be scheduled as necessary. If you have side effects, please inform the trial physician and other trial personnel, and the trial physician will decide to give appropriate treatment according to your situation.

If you have any of these serious or dangerous side effects you should as soon as possible:

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1. Call the 24-hour emergency contact.
2. Go to the nearest emergency room if necessary.

F. Other Alternative Remedies & Instructions:

You are not obliged to participate in the study. If you do not participate in the study, the doctor will check your symptoms through routine examination and give appropriate drug treatment.

G. Expected benefits of the trial:

At present , Jing Si Herbal Tea has been observed in animal experiments to block the combination of the new coronavirus and cells, and can also reduce cell penetration and block the virus from penetrating cells. 501Y.V2 conducted animal research and found that Jing Si Herbal Tea can reduce the ability of the upper respiratory tract, lungs, heart, and intestines of mice infected with the virus by 60-70% and reduce the expression of FKBP51, a protein related to depression, by 40%. Clinical trials have been registered (ClinicalTrials.gov Identifier: NCT04967755) The effect of using Jing Si Herbal Tea to help reduce the amount of virus in patients with COVID-19. In this study, Jing Si Herbal Tea was used to drink functional dyspepsia patients with normal objective examinations, and the changes of their physical and mental symptoms and intestinal bacterial metabolites were evaluated before and after treatment.

Even with the above information, there is still no guarantee that participating in this trial will improve your condition or bring you other direct benefits, but the results of the trial may be helpful to the entrusting unit and/or the trial host, and will also be used in the future. May benefit other patients with the same disease.

H. Contraindications, restrictions and matters that should be cooperated by the subjects during the trial:

When you participate in this test , for your safety, please cooperate with the following

-Provide your past medical history, medical records and correct information about your current condition.

- Use Jing Si Herbal Tea correctly according to the instructions .

-Do not give Jing Si Herbal Tea to others. Please keep Jing Si Herbal Tea (storage method: room temperature, refrigerated, etc.) and make sure it is out of reach of children.

- For your safety, please inform the trial physician of any uncomfortable symptoms you experience.

- If you have any questions, please feel free to ask the test personnel (physician, nurse) directly.

- If you have been hospitalized or your medical condition has changed between two visits, or if you want to stop using Jing Si Herbal Tea (or have already stopped using it), please notify the trial physician.

I. Confidentiality of personal data of subjects:

Hualien Tzu Chi Hospital will treat any identifiable records and personal privacy information as

confidential according to law and will not make them public. The researchers will identify you with a research code, which will not reveal your name, national ID number, address and other identifiable information. If the trial results are published, your identity will remain confidential. You also understand that if you sign the consent form, you agree that your original medical records can be directly reviewed by monitors, auditors, Hualien Tzu Chi Hospital Research Ethics Committee and competent authorities to ensure that the clinical trial process and data comply with relevant laws and regulations. personnel and undertake not to violate the confidentiality of your identity. In addition to the above-mentioned agencies having the right to review according to law, we will carefully safeguard your privacy.

J. Withdrawal and suspension of the test:

You are free to decide whether to participate in this trial; you can withdraw or suspend your consent at any time during the trial, and you can withdraw from the trial without any reason, and it will not cause any discomfort or affect the medical care of your doctor in the future.

When there is important new information during the execution of the trial (referring to your rights or affecting your willingness to continue participating), you will be notified and further explained. Please reconsider whether to continue participating. You can decide freely and will not cause any discomfort. Or affect their future physicians to your medical care.

The program director may also suspend the entire experiment if necessary.

K. Damage Compensation and Insurance:

Trials are bound to be risky. In order to ensure the possible protection for your damage due to adverse reactions during participation in the trial, please be sure to read this description carefully:

1. Hualien Tzu Chi Hospital shall be responsible for compensation for damages caused by adverse reactions in accordance with the clinical trial plan formulated by this study . However, the expected adverse reactions recorded in the subject's consent form will not be compensated.
2. If adverse reactions or damages occur due to the clinical trial plan formulated in this study, the hospital is willing to provide professional medical care and medical consultation. You do not have to pay for medically necessary treatment of adverse reactions or damages.
3. Except for the first two items of compensation and medical care, this research does not provide other forms of compensation. If you are unwilling to accept the risk, do not take part in the trial.
4. You will not lose any legal rights by signing this agreement.
5. Liability insurance for human trials was not insured for this study .
6. The test food has been insured for product insurance. (The insured is Dajiang Biomedical Co., Ltd.; policy number: 150110CG01568 ; product name: Jing Si Herbal Tea, Jing si Herbal Dettol .)

If you do suffer damage caused by adverse reactions due to your participation in this trial, the

aforementioned compensation includes reasonable medical expenses, but the following conditions should be met: you use the trial drug according to the instructions of the trial doctor; your damage is not caused intentionally; you obey the trial doctor medical advice.

L. Preservation, use and reuse of subjects' samples (including their derivatives) and personal data

1. Specimen (including its derivatives), preservation and use of personal data

The specimens and related materials you provided will be used in this test plan and stored in the laboratory of Professor Liu,Chin-Hung , Department of Pharmacology, Faculty of Medicine, Hualien Tzu Chi University until **December 31, 2024.** When the storage period expires, they will be destroyed according to law. In order to protect your personal privacy, we will replace your name and related personal information with a test number to confirm that your specimen and related information are kept completely confidential.

If you have doubts about the use of specimens and related materials, or have any need to destroy specimens or data, please contact us immediately (Contact Person: Dr. Chen, Chien-Lin; Tel: 0988-282055; Contact Unit: Gastrointestinal Examination Room ; Tel: 03-8561825 ext. 13224; Address: No. 707, Section 3, Zhongyang Road, Hualien City) , and we will destroy your specimen and related information. You can also contact the Research Ethics Committee of Hualien Tzu Chi Hospital (Tel: 03-8561825 ext. 12124) to assist you in resolving any disputes over the use of specimens and personal data in research.

2. Storage and reuse of remaining specimens

This test does not save the remaining samples for reuse, and your samples will be destroyed after the storage period expires.

3. Storage and use of personal data

The personal information and related information you provide will be used in this trial project and stored in the gastrointestinal examination room of Hualien Tzu Chi Hospital until **December 31, 2024.** When the storage period expires, it will be destroyed according to law. In order to protect your personal privacy, we will replace your name and related personal information with a test number to confirm that your relevant information is kept completely confidential.

If you have doubts about the use of relevant materials, or have any need to destroy the data, please contact us immediately (Contact Person: Dr. Chen, Chien-Lin; Tel: 0988-282055; Contact Unit: Gastrointestinal Examination Room; Tel: 03-8561825 Ext. 13224; address: No. 707, Section 3, Zhongyang Road, Hualien City) , and we will destroy your relevant information. You can also contact the Research Ethics Committee of Hualien Tzu Chi Hospital (Tel: 03-8561825 ext. 12124) to assist you in resolving any disputes over the use of personal data in research.

M. Subject rights:

1. If you have doubts about the nature of the trial work during the trial, have opinions on the rights and interests of patients, or suspect that you have been victimized by

participating in the research, you can contact the Research Ethics Committee of Hualien Tzu Chi Hospital for consultation. Tel: 03-8561825 ext. 12124 .

2. During the trial, any major findings related to your health or disease that may affect your willingness to continue to accept the clinical trial will be provided to you immediately. If you decide to withdraw, your physician will arrange for you to continue receiving medical care. If you decide to continue in the trial, you may be required to sign an updated consent form.
3. In order to carry out the experimental work, you must be under the care of Dr. Chen, Chien-Lin. If you have any questions or conditions now or during the trial, please feel free to contact Dr. Chen, Chien-Lin from the Gastroenterology Department of Hualien Tzu Chi Hospital (24-hour contact number: 0988-282055) .
4. This consent form is in duplicate, and the trial host or his authorized personnel has given you a copy of the consent form , and has fully explained the nature and purpose of this research. Physicians have answered your questions about drugs and research.
5. The subsidy for participating in the experimental research plan, in order to compensate you for the transportation and time spent on participating in the experiment, you will receive a subsidy of NT$300 after signing the agreement, and a subsidy of NT$300 after the experiment is completed, a total subsidy of NT$600.
6. If after the trial is over, there are unexpected safety concerns that directly affect you, you will also be notified.

N. The commercial benefits that may be derived from this research are expected:

Information obtained from this trial may lead to the discovery, invention, or development of commercial products, and all such rights belong to the commissioner. You and your family will not receive any financial benefit or monetary compensation for the research and development results, inventions or other discoveries in this information, or have the ownership of the results of the above inventions.

O. Instructions for signing the consent form:

1. **The consent form should be signed and dated after the research director or his authorized personnel explain the research content to the research subjects and answer all the questions of the research subjects; then ask the research subjects or their related persons to sign after consideration.**
2. **Timing of signing by legal representative/person with consent/guardian/assistant:**

∗ Article 79 of the Medical Act/Article 12 of the Human Research Act/Article 5 of Good Clinical Practice Guidelines for Drugs/Article 6 of Precautions for Collection of Human Specimens for Research/Articles 13 and 15 of the Civil Code:

(1) Subjects who are incapacitated (minors under the age of seven or persons declared

under guardianship) shall be acted by their legal representatives; persons under guardianship declaration shall have their guardians act as their legal representatives.

(2) The subject is a person with limited behavioral capacity (a minor over the age of seven, or due to a mental disorder or other mental defect, the ability to express or accept the expression of intention, or to recognize the effect of the expression of intention is obviously insufficient, and Those who have been assisted by the court) shall obtain the consent of the person himself and his legal representative or assistant.

(3) Although the subject is not incapacitated or limited in capacity, but is unable to communicate and judge effectively due to confusion or mental and intellectual impairment, a person with the right to consent shall do so. The person with the right to consent is the spouse and relatives living together.

(4) When the research object is a fetus, the consent of the mother should be obtained.

(5) The provision of autopsy should be subject to the written consent of the person's closest relative or the person himself before his death.

3. **Witness signing timing:**

＊ Article 21 of the Good Clinical Practice Guidelines for Pharmaceuticals / Article 3 of the Civil Code:

(1) When the subject, legal representative, or consenting person cannot read it, witnesses should be present to participate in all discussions about the subject's consent form. Witnesses should read the consent form of the subject and provide any other written information of the subject to witness that the research director or the person designated by him or her has accurately delivered the content to the subject, legal representative or person with consent explain, and make sure they fully understand the content of all materials.

(2) The subject, legal representative or person with the right to consent shall still sign and date the subject's consent form. However, fingerprints can be used instead of signatures.

(3) After the witness completes the oral statement and confirms that the consent of the subject, legal representative or person with the right to consent is completely free of his own will, he shall sign and date the subject's consent form.

(4) No one involved in the research may be a witness.

(5) If a fingerprint , cross or other symbol is used to sign the document, the two signatures on the document will also have the same effect as the signature.

4. **Instructions for the order of signatures of those with the right to consent:**

＊ Article 12 of the Human Body Research Act: Except for fetuses or corpses, research objects are limited to adults with meaningful abilities. However, this does not apply to those who are obviously beneficial to a specific population group or cannot be replaced by other research objects. When the research object is an adult with the proviso of the preceding paragraph, the consent of the related person shall be obtained in the following order:

1. spouse.

2. adult children.
3. parents.
4. brothers and sisters.
5. grandparents.

According to the written consent of the related party in the preceding paragraph, the written consent can be carried out by one person; if the related parties express disagreement, the order of each item in the preceding paragraph shall be determined. For persons in the same order as mentioned in the preceding paragraph, those who are close relatives take precedence; for those who are on the same level of kinship, the cohabiting relatives take precedence; for those without cohabiting relatives, the elders take precedence.

P. Sign

1. The trial host, or the co-host or its authorized personnel has explained in detail the nature and purpose of the above-mentioned research methods in this research plan, as well as the possible dangers and benefits.

   Trial host/co-host signature: _____

   Date: _____

   Signatures of other researchers who participated in the presentation and discussion during the consent process: _____

   Date: _____

2. After the explanation, I have a detailed understanding of the above-mentioned research methods and possible risks and benefits, and I have also received detailed explanations about the questions about this experimental plan. I agree to accept and voluntarily participate in this study and will have a copy of the consent form.

   Subject signature:_____Date: _____

   Telephone:

∗ **When the subject of the case meets the item (2) of [Signing Instructions for Consent Letter], the signature in this field must be completed.**

3. Signature of legal representative/person with consent:_____

   Date: _____

Relationship with subject (please circle) :

self, spouse, father, mother, son, daughter, others: _____

Telephone:

∗ **The subject of the case meets the item (3) of [Signing Instructions for Consent Letter] , the signature in this field must be completed.**

4. Witness 1 Signature: _____ Date: _____

Telephone:

Witness 2 Signature: _____ Date: _____

Telephone: