Buddhist Tzu Chi Medical Foundation Taipei Tzu Chi Hospital Human Experiment Review Committee

Research Participant Consent Form

You are invited to participate in this study and this form provides you with information about the study. Before you agree to participate in this study, the research moderator or researcher will explain the research content to you and answer any questions you have. Please read this consent form in detail and sign it before you can participate in this study.
The study protocol was approved by the Ethics Committee of Taipei Tzu Chi Hospital (IRB number 10-XD-132).

Project Chinese name	淨斯本草飲在呼吸系統疾病的研究		
Project English name	Comprehensive Research on Jing-Si-Herbal-Tea in Respiratory System Diseases		
Institution	Taipei Tzu Chi Hospital	Date	20230101

Research Team Information

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Research Participant Name: Gender:

Date of Birth: (Year /Month /Day) (Over 20 years old □ Yes □ No)

Address:

Contact Phone Number:

Name of Legal Guardian/Consenting Person:

Relationship with Research Participant (Please tick):

☐ (1) Spouse ☐ (2) Adult Children ☐ (3) Parents ☐ (4) Siblings ☐ (5) Grandparents

ID Number:

Address:

Contact Phone Number:

Introduction	Jing-Si-Herbal-Tea (JSHT) is currently sold in Jingsi Hall. It contains eight kinds of traditional Chinese medicine ingredients, namely Ophiopogon japonicus, Houttuynia cordata, Platycodon grandiflorum, fish needle grass, licorice, mugwort leaf, perilla leaf, and chrysanthemum. Ophiopogon japonicus has the effect of moistening the lungs and relieving coughs, mainly targeting coughs, dry coughs, hemoptysis and other symptoms caused by yin deficiency and dryness of the lungs caused by insufficient lung yin. Houttuynia cordata has a significant inhibitory effect on a variety of pathogenic microorganisms, strengthens immune function, relaxes bronchial smooth muscle, and achieves antitussive and asthmatic effects. Platycodon has the effect of draining pus, relieving coughs and removing phlegm. It is often used for various coughs and phlegm syndromes. It is also very effective for those with sore throat and hoarseness. Fish needle grass is a commonly used medicinal herb, mainly used to treat colds and fever, vomiting and abdominal pain, gastric pain, skin eczema, etc. Licorice is a traditional Chinese medicinal material that has pharmacological effects such as relieving coughs and moisturizing the lungs. Mugwort can treat cold cough and asthma, and has the functions of relieving cough, eliminating phlegm and relieving asthma. Perilla is often used to treat colds, colds and coughs, and has a certain effect in treating allergies. Chrysanthemum has the effect of clearing away heat and detoxifying, which can help relieve the discomfort of throat inflammation and oral ulcers. It can also improve body fever, headache, thirst, cough with yellow phlegm, sore throat, yellow and thick nasal discharge, etc. These Chinese medicinal materials have anti-inflammatory effects. For example, Houttuynia Cordata can enhance the phagocytosis function of macrophages and has also been proven to have anti-inflammatory effects. Some studies have found that it can inhibit tumor necrosis factor-α (TNF-α) in sepsis, interleukin-1β (IL-1β) production and toll-like receptor 4 (TLR4) expression. In addition, Houttuynia cordata also has antioxidant effects and can relieve peroxidative stress.

Methods	Research purposes: COPD is a disease caused by long-term inflammation of the respiratory tract or interstitium of the lungs, resulting in respiratory obstruction, which prevents gas from flowing in and out of the respiratory tract smoothly, or interstitial pulmonary fibrosis that prevents gas exchange. These patients suffer from poor pulmonary gas exchange function, symptoms of chest tightness, wheezing and coughing often occur. In addition, these patients are more likely to be accompanied by other comorbidities, such as cardiovascular disease, osteoporosis, diabetes, lung cancer, etc. These diseases have a huge impact on the patient's quality of life and life safety. Research is very important for the control of respiratory diseases. Although some drugs are currently used to treat these diseases, the therapeutic effect is limited. JSHT has anti-inflammatory and antioxidant effects, which can inhibit the inflammatory response of respiratory diseases. We aim to study the effect of JSHT in COPD.
	The main inclusion and exclusion conditions of the study: Inclusion criteria: (1) Outpatients: patients with chronic stable respiratory diseases (COPD, asthma, bronchiectasis, pulmonary fibrosis, interstitial pulmonary disease, sarcoidosis) (2) Hospitalized patients: patients hospitalized due to acute attacks of respiratory diseases (COPD, asthma, bronchiectasis, pulmonary fibrosis, interstitial pulmonary disease, sarcoidosis) (3) Severe patients: Respiratory failure due to acute attack of respiratory diseases (COPD, asthma, bronchiectasis, pulmonary fibrosis, interstitial lung disease, sarcoidosis) using invasive or non-invasive respirators and admitted to intensive care patients in ward Exclusion criteria: 1. Under legal age 2. Those who are unwilling to join 3. Those with severe liver function abnormalities 4. People with severe renal dysfunction 5. Have a history of allergies to JSHT

	Research Methods and Procedures: This study comprises two parts, focusing on patients with COPD acute exacerbation (COPDAE). In the COPDAE part, the control group received standard treatment including intravenous steroids, inhaled butanyl and ipratropium, and parenteral antibiotics for secondary infections. Placebo mimics of JSHT were administered to the control group. The JSHT group received standard COPDAE treatment plus JSHT for one week. Baseline and post-treatment HRQL were assessed using the COPD assessment test (CAT), along with blood tests including white blood cells (WBCs), percentages of different types of WBCs (neutrophils, lymphocytes, monocytes, eosinophils, basophils), hemoglobin (Hb), hematocrit (Hct), platelets (PLT), blood urea nitrogen (BUN), creatinine (Cr), uric acid (UA), liver enzymes (aspartate aminotransferase, alanine aminotransferase), electrolytes (sodium, potassium), C-reactive protein (CRP), and pro-brain natriuretic peptide (pPro-BNP). For patients with stable COPD, the control group received standard inhaled medications according to the GOLD guidelines. Placebo mimics of JSHT were administered to the control group. The JSHT group additionally received JSHT daily for three months. Baseline and post-treatment HRQL assessments, blood tests, and pulmonary function tests (PFT). The study protocol was approved by the Ethics Committee of Taipei Tzu Chi Hospital (IRB number 10-XD-132). Informed consent was obtained from all participants. HRQL The Taiwan Society of Pulmonary and Critical Care Medicine offers the Chinese version of the COPD Assessment Test (CAT) on the website. This test consists of eight items designed to evaluate COPD symptoms. These symptoms include cough, phlegm production, chest tightness, breathlessness, limitations in daily activities, confidence in leaving the house, sleep disturbances, and energy levels. Each symptom is rated on a scale from 0 to 5, culminating in a total CAT score ranging from 0 to 40. A higher score reflects more severe COPD symptoms. A score of 10 or higher is indicative of a significant symptom burden. The Modified Medical Research Council (mMRC) scale was used to evaluate dyspnea. This scale, comprising a 5-point grading system ranging from 0 to 4, measures dyspnea severity. A score of 0 indicates dyspnea only during intense exercise, while a sore of 4 represents breathlessness at rest. The 5-item Brief Symptom Rating Scale (BSRS-5) was used to assess psychological distress. It consists of five items: feeling tense, being easily angered, feeling depressed, feeling inferior to others, difficulty with sleep, and suicidal thoughts. The scale is a 5-point scale ranging from 0 (not at all) to 4 (extremely), with higher scores indicating more severe symptoms. Pulmonary function tests

	PFT were conducted using a spirometer following the guidelines set by the American Thoracic Society. Cellular study for assessing the effects of JSHT on Inflammation In the cellular study conducted on A549 cells, five groups were analyzed to evaluate the effects of JSHT. The groups were: Control group: did not receive treatment; lipopolysaccharide (LPS) group: treated with LPS for 16 hours to induce inflammation; JSHT group: treated with JSHT for 12 hours; Pre-JSHT+LPS group: cells were pre-treated with JSHT for 1 hour, then LPS treatment for 16 hours; Post-JSHT+LPS group: cells were exposed to LPS for 16 hours followed by JSHT for 12 hours. Measurements were performed for DAMPs such as high mobility group box 1 (HMGB1), formyl peptide receptor 1 (FPR1), and extracellular adenosine triphosphate (ATP); transcription factor nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB); phosphorylated mitogen-activated protein kinase (p-MAPK) and c-Jun N-terminal kinase (p-JNK); apoptotic marker cleaved Caspase 3 (cCaspase 3); and pro-inflammatory cytokines, including interleukin-1 (IL-1), interleukin-6 (IL-6), interleukin-8 (IL-8), and tumor necrosis factor-alpha (TNF-α). Measurement of DAMPs A549 cells were cultured in a 6-well plate and incubated at 37°C for 24 h in a humidified incubator. Afterward, the cells were cultured under the conditions of the five experimental groups; the medium was collected and centrifuged, and then the supernatant was stored at -80°C. Commercial enzyme-linked immunosorbent assay (ELISA) kits were used to measure the expression levels of DAMP, including HMGB1, FPR1, and extracellular ATP, in the medium, following the manufacturer's instructions. The absorbance was measured at a specified wavelength using an Infinite 200 PRO microplate reader. Measurement of cCaspase-3, NF-kB, p-MAPK, and p-JNK The cells were collected and lysed in cold Radioimmunoprecipitation Assay buffer containing protein and phosphatase inhibitors. Proteins were dispensed into each well and subjected to electrophoresis on a Sodium Dodecyl Sulfate-Polyacrylamide Gel Electrophoresis at 140 volts for one hour, followed by the transfer of proteins onto Polyvinylidene Difluoride (PVDF) membranes at 200 mA for two hours. The membranes were blocked with TOOLSpeed Blocking Reagent and incubated with cCaspase-3, NF-kB, p-MAPK, and p-JNK primary antibodies overnight at 4°C, then with secondary antibodies for an additional hour. The protein bands were visualized using enhanced chemiluminescence reagents and radiographic films. The intensities of the reactive bands were analyzed using the Bio-Rad ChemiDoc XRS+ system. Cytokines ELISA A549 cells were cultured in a 6-well plate in a humidified incubator for 24

	hours at 37°C. Following culture, the cells were subjected to the conditions of the five experimental groups. The culture medium of each experimental treatment group was collected and stored at -80°C. The cytokines were quantified utilizing ELISA kits, following the protocols provided by the manufacturer.
	During the study, participants with contraindications such as severe liver dysfunction, severe renal dysfunction, or a history of allergy to JSHT are excluded from enrollment based on the exclusion criteria at the time of enrollment. The only requirement for participants is to adhere to the study protocol regarding the consumption of JSHT and undergoing tests.
	Expected Benefits of the Study: The pathogenesis of COPD involves inflammation and oxidative reactions. The anti-inflammatory and antioxidant effects of JSHT make it suitable for treating acute exacerbations of respiratory diseases. For stable-phase patients, we anticipate that JSHT may provide better control of their condition. The benefits for patients include disease management, while from a medical perspective, understanding the therapeutic effects of JSHT can help benefit more patients.
	Participants' Rights and Obligations: 1. Participation in the study is voluntary and does not involve any financial compensation. 2. Participants will not incur any expenses related to the study. **3.** This study has been reviewed and approved by the Institutional Review Board (IRB) of Taipei Tzu Chi Hospital, including assessment of research benefits and risks, protection of participants' rights and personal data. If participants have any concerns about their rights as research participants or believe they have been harmed by participating in the study, they can contact the IRB of Taipei Tzu Chi Hospital for consultation at 02-66289779 ext. 5706.
	Personal Data Protection: 1. Participants consent to the review of their personal data by the executing institution, research contracting unit, Institutional Review Board, and regulatory authorities to ensure compliance with relevant laws and regulations. The Principal Investigator and related research personnel pledge to maintain the confidentiality of participants' identities. **2.** Even if the research results are published, your identity will remain confidential**.**
	Withdrawal of Consent for the Study: You are free to decide whether to participate in this study. You may also

	withdraw your consent and discontinue participation in the study at any time during the research process, without providing any reason. None of these actions will cause any discomfort or affect your legitimate rights and interests. The Principal Investigator or the contracting unit may also suspend or terminate the study if necessary.
	Foreseeable Risks: Blood tests and cardiopulmonary function tests are routine examinations for these patients and do not pose additional risks. (Please appropriately explain any anticipated risks or inconveniences that participating in the study may pose to the research participants, particularly clear explanations regarding potential risks to embryos, infants, or breastfeeding infants. Also, please explain the potential impacts of participating in the study on the physical, psychological, personal privacy, or information obtained from research specimens on the donors and their relatives or ethnic groups.)
	Storage of Human Specimens or Personal Data: The biological specimens provided by you, their derivatives, or personal data will be stored during the trial at the Department of Pulmonary Medicine, Taipei Tzu Chi Hospital, located at No. 289, Jianguo Road, Xindian District, New Taipei City, Republic of China. The person in charge of storage is Dr. Lan Chou-Chin.
	Utilization Plan for Research Materials at the End of the Study or Upon Expiry of the Storage Period: Research materials other than the specimens provided by you will be kept until the termination or completion of the study, or continued storage for 10 years, after which they will be destroyed. **If there are remaining specimens, their continued storage and future use require the consent of the participant.** **Upon your agreement, the Division of Pulmonary Medicine Laboratory at Taipei Tzu Chi Hospital (No. 289, Jianguo Road, Xindian District, New Taipei City, Republic of China) will continue to store the biological specimens or their derivatives until December 31, 2031, for future research on chest diseases (please provide detailed project descriptions). Upon expiry, they will be destroyed. All new research projects involving these specimens will need approval from the Institutional Review Board of Taipei Tzu Chi Hospital. Your provided research materials will be protected according to the terms stated in this agreement.** **If you have any concerns regarding the use of remaining specimens or their derivatives, or if you wish to request the destruction of remaining specimens or their derivatives, please contact us immediately (Contact Person: Li-Ling Yang, Department: Department of Chest Medicine, Phone: 0927686972). You may also contact the Institutional Review Board of Taipei Tzu Chi Hospital for assistance in resolving any disputes regarding the use of remaining specimens or their derivatives in research.**

	Participant's Signature: _____, **Date: Year ____ Month ____ Day**
	Agreement on Potential Commercial Benefits and Their Application: It is anticipated that this study will not generate patents or other commercial benefits. Any outcomes from this study, such as academic publications, intellectual property, or other tangible benefits, will be utilized by Taipei Tzu Chi Hospital for medical purposes including disease prevention, diagnosis, treatment, and research.
	Compensation and Insurance: 1. According to the clinical trial protocol established by this study, in the event of adverse reactions or damages, the executing institution and the principal investigator are willing to provide professional medical care and consultation. You will not be responsible for the necessary medical expenses incurred in treating adverse reactions or injuries. 2. Apart from the aforementioned compensation and medical care, this study does not offer any other form of compensation. If you are unwilling to accept such risks, please do not participate in this trial. 3. Signing this consent form will not result in the forfeiture of any legal rights you may have.
	Signature: The principal investigator or their research staff has thoroughly explained the nature, methodology, and purpose of this study, as well as the potential risks and benefits, and other relevant matters. They have also addressed any questions you may have had regarding the study. If you agree to participate in this research, please sign the Participant Consent Form. Two copies of this consent form will be provided, and one signed copy will be given to you before the commencement of the study. Signature of Principal Investigator/Co-Principal Investigator/Associate Investigator:_____Date:_____ [Year] [Month] [Day] Signature of Person Providing Execution Instructions:_____ Date:_____ [Year] [Month] [Day]
The research participant has understood the aforementioned study and its potential risks and benefits. Any questions regarding the study protocol have been thoroughly explained by the principal investigator or research staff. I hereby consent to participate as a research participant in this study.	

Participant's Signature: _____ Date:_____	