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Application Form of Buddhist Tzu Chi Medical Foundation "Clinical Research on Jingsi Bencao Decoction"

Application number：_____

A. Basic information

Plan name	Chinese	淨斯本草飲濃縮液對長新冠症狀-腸腦軸失調之身心症狀療效-隨機雙盲臨床試驗						
	English	Jing Si Herbal Tea Liquid Packet in the treatment of dyspeptic symptoms and psychophysical burden in patients with disorders of long-COVID gut-brain interaction --a double-blind, randomized, placebo-controlled study						
Principal Investigator Name		Chen, Chien-Lin	Job title	Director of Gastroenterology	Campus	Hualien Tzu Chi Hospital	unit or department	Gastroenterology
Plan execution period		■One year From January 1, 2012 to December 31, 2012, a total of 1 year.						
This year, apply to host various research projects (including pre-approval cases) in the hospital, a total of 1 case. (Co-hosted projects will not be counted) ■ Yes, project name: Exploring the relationship between supragastric belching, physical and mental symptoms, and esophageal acid reflux: clinical application of treatment optimization for gastroesophageal reflux disease. □ No.								
Whether the project has carried out the following related experiments: [If you tick any of the following items, you need to attach the relevant experiment/research consent documents] □ No. ■ Human experiments/human specimens (including human embryos/human embryonic stem cells). **A total of 1 document must be attached.**								
Program Contact		姓名：Chen, Chien-Lin Tel: (public) (03)8561825#13224 (mobile) 0988-282055 E-MAIL：harry.clchen@msa.hinet.net						
Signature and seal of the host of the total plan (please sign in person)		_____，Date:_____Year_____Month_____Day						
Signature and seal of the co-host of the project (please sign in person)		_____，Date:_____Year_____Month_____Day						
Signature and seal of the co-host of the project (please sign in person)		_____，Date:_____Year_____Month_____Day						
Signature and seal of the co-host of the project (please sign in person)		_____，Date:_____Year_____Month_____Day						
Signature and seal of the co-host of the project (please		_____，Date:_____Year_____Month_____Day						

sign in person)	
Signature and seal of the co-host of the project (please sign in person)	_____，Date:_____Year_____Month_____Day
Signature and seal of the co-host of the project (please sign in person)	_____，Date:_____Year_____Month_____Day
Signature and seal of the co-host of the project (please sign in person)	_____，Date:_____Year_____Month_____Day
Signature and seal of the co-host of the project (please sign in person)	_____，Date:_____Year_____Month_____Day
Dean's signature (personal signature or seal)	_____，Date:_____Year_____Month_____Day

Remarks: If there are more than one co-hosts of the plan, please add the column by yourself to facilitate signature

B. Personnel participating in the plan

Category (moderator, co-host, co-host, researcher, etc.)	Name	Current position	The specific nature, project and scope of work undertaken in this research project
Moderator	Chen, Chien-Lin	Director of Gastroenterology	Project progress supervision, research conduct and research plan formulation, data analysis analysis and report writing.
Co-host	Wong, Ming-Wun	Attending Physician of Gastroenterology	Actual case acceptance, case processing, and data collation in the plan.
Co-host	Liu, Tso-Tsai	Director of Endoscopy Department	Actual case acceptance, case processing, and data collation in the plan.
Co-host	Yi, Chih-Hsun	Attending Physician of Gastroenterology	Actual case acceptance, case processing, and data collation in the plan.
Co-host	Lei, Wei-Yi	Attending Physician of Gastroenterology	Actual case acceptance, case processing, and data collation in the plan.
Co-host	Hung, Jui-Sheng	Attending Physician of Gastroenterology	Actual case acceptance, case processing, and data collation in the plan.
Co-host	Liang, Shu-Wei	Attending Physician of Gastroenterology	Actual case acceptance, case processing, and data collation in the plan.
Co-host	Liu, Chin-Hung	Associate Professor	Specimen analysis, data analysis and statistics in the plan.
Co-host	Chen, Chun-Yao	Assistant professor	Specimen analysis, data analysis and statistics in the plan.

Research assistant	Jian, Yu-Xhuan	Research assistant	Organize data, data analysis and statistics and handle administrative affairs.

※If there are not enough fields, please copy by yourself.

C. Implementation of other research projects

In the past three years, the project host, co-hosts, and other research team members must fill in the details of the implementation of the research plan.

Category (moderator, co-host, co-host, researcher, etc.)	Name	Project name	Jobs within the plan	from year to month	Grant agencies
Host	Chen, Chien-Lin	To explore the pathophysiological effects of esophageal contraction, mucosal integrity and acid sensitivity on gastroesophageal reflux disease and the basis for treatment strategies	Host	2020/8/1~ 2023/07/31	Ministry of Science and Technology
Host	Chen, Chien-Lin	Efficacy of Jingsi Bencao Decoction on physical and mental symptoms of functional dyspepsia-a randomized double-blind clinical trial	Host	2022/1/1~ 2022/12/31	Tzu Chi Medical Corporation
Host	Chen, Chien-Lin	Discuss the pathophysiological mechanism of gastroesophageal reflux disease and establish the basis for accurate diagnosis and treatment based on esophageal reflux clearance ability, mucosal integrity and physical and mental characteristics	Host	2022/1/1~ 2022/12/31	Hualien Tzu Chi Hospital
Host	Chen, Chien-Lin	Discussion on the Pathophysiological Mechanism of Laryngopharyngeal Reflux Disease: Clinical Application of Artificial Intelligence Assisted and Accurate Diagnosis and Personalized Treatment Strategies	Co-host	2022/8/1~ 2025/07/31	Ministry of Science and Technology
Host	Chen, Chien-Lin	Discuss the pathophysiological mechanism and treatment strategy of afferent nerve distribution, esophageal peristalsis and drug regulation in gastroesophageal reflux disease	Co-host	2022/8/1~ 2025/07/31	Ministry of Science and Technology
Host	Chen, Chien-Lin	To explore the influence and clinical application of opioid analgesics on the pathophysiological mechanism of esophageal contraction and reflux characteristics	Co-host	2022/1/1~ 2022/12/31	Hualien Tzu Chi Hospital
Host	Chen, Chien-Lin	Analysis of 24-hour esophageal acid-base impedance	Co-host	2022/1/1~ 2022/12/31	Hualien Tzu Chi Hospital

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		examination-technical performance and clinical application of gastroesophageal reflux disease diagnosis with artificial intelligence of supervised learning			
Host	Chen, Chien-Lin	Application of high-resolution impedance pharyngeal function test and Sydney swallowing questionnaire in oropharyngeal dysphagia and voice disorders	Co-host	2022/1/1~ 2022/12/31	Hualien Tzu Chi Hospital
Host	Chen, Chien-Lin	Application of artificial intelligence in high-resolution esophageal function examination - research on unsupervised algorithm model based on deep learning	Co-host	2022/1/1~ 2022/12/31	Hualien Tzu Chi Hospital
Host	Chen, Chien-Lin	To explore the influence of clinical characteristics and intestinal flora in patients with metabolism-related fatty liver under the regulation of diet and exercise	Co-host	2022/1/1~ 2022/12/31	Hualien Tzu Chi Hospital
Host	Chen, Chien-Lin	To explore the role of esophageal microbiota in novel impedance parameters, clinical classification and hypersensitivity in gastroesophageal reflux disease	Host	2021/1/1~ 2021/12/31	Hualien Tzu Chi Hospital
Host	Chen, Chien-Lin	Clinical application of new esophageal impedance basic value supplemented with risk assessment to predict treatment response and recurrence of gastroesophageal reflux disease	Host	2020/1/1~ 2020/12/31	Hualien Tzu Chi Hospital
Co-host	Chen, Chien-Lin	To explore the relationship between esophageal acid sensitivity, second-degree contraction of esophagus and subtypes of gastroesophageal reflux and the pathogenic mechanism	Co-host	2021/1/1~ 2021/12/31	Hualien Tzu Chi Hospital
Co-host	Chen, Chien-Lin	Clinical Application of High-resolution Impedance Pharyngeal Function Examination in Investigating Pharyngeal Dysphagia and Drug Response	Co-host	2021/1/1~ 2021/12/31	Hualien Tzu Chi Hospital
Co-host	Chen, Chien-Lin	Can a cure for hepatitis C improve quality of life?	Co-host	2020/1/1~ 2020/12/31	Hualien Tzu Chi Hospital
Co-host	Chen, Chien-Lin	Improving the quality of fatty liver treatment with cross-group care	Co-host	2020/1/1~ 2020/12/31	Hualien Tzu Chi Hospital
Co-host	Chen, Chien-Lin	Discussion of differences in drug therapy in patients with sensitive esophagus and the role of	Co-host	2020/1/1~ 2020/12/31	Hualien Tzu Chi Hospital

		mucosal afferent innervation in this disease			
Co-host	Chen, Chien-Lin	To explore the pathophysiological role of esophageal mucosal afferent nerve distribution in gastroesophageal reflux disease complicated with esophageal motility dysfunction	Co-host	2020/8/1~ 2022/07/31	Ministry of Science and Technology
Co-host	Chen, Chien-Lin	Improve the diagnosis of laryngopharyngeal reflux disease and establish the indication of hydrogen ion pump blocker by using the average basic mucosal impedance value of the proximal esophagus at night	Co-host	2020/8/1~ 2022/07/31	Ministry of Science and Technology
Host	Wong, Ming-Wun	Discussion on the Pathophysiological Mechanism of Laryngopharyngeal Reflux Disease: Clinical Application of Artificial Intelligence Assisted and Accurate Diagnosis and Personalized Treatment Strategies	Host	2022/8/1~ 2025/07/31	Ministry of Science and Technology
Host	Wong, Ming-Wun	Analysis of 24-hour esophageal acid-base impedance examination-technical performance and clinical application of gastroesophageal reflux disease diagnosis with artificial intelligence of supervised learning	Host	2022/1/1~ 2022/12/31	Hualien Tzu Chi Hospital
Host	Wong, Ming-Wun	Discuss the pathophysiological mechanism of gastroesophageal reflux disease and establish the basis for accurate diagnosis and treatment based on esophageal reflux clearance ability, mucosal integrity and physical and mental characteristics	Co-host	2022/1/1~ 2022/12/31	Hualien Tzu Chi Hospital
Host	Wong, Ming-Wun	To explore the influence and clinical application of opioid analgesics on the pathophysiological mechanism of esophageal contraction and reflux characteristics	Co-host	2022/1/1~ 2022/12/31	Hualien Tzu Chi Hospital
Host	Wong, Ming-Wun	Application of high-resolution impedance pharyngeal function test and Sydney swallowing questionnaire in oropharyngeal dysphagia and voice disorders	Co-host	2022/1/1~ 2022/12/31	Hualien Tzu Chi Hospital
Host	Wong, Ming-Wun	Application of artificial intelligence in high-resolution esophageal function examination - research on unsupervised algorithm model based on deep	Co-host	2022/1/1~ 2022/12/31	Hualien Tzu Chi Hospital

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		learning			
Host	Wong, Ming-Wun	To explore the influence of clinical characteristics and intestinal flora in patients with metabolism-related fatty liver under the regulation of diet and exercise	Co-host	2022/1/1~ 2022/12/31	Hualien Tzu Chi Hospital
Host	Wong, Ming-Wun	Efficacy of Jingsi Bencao Decoction on physical and mental symptoms of functional dyspepsia-a randomized double-blind clinical trial	Co-host	2022/1/1~ 2022/12/31	Tzu Chi Medical Corporation
Host	Wong, Ming-Wun	Improve the diagnosis of laryngopharyngeal reflux disease and establish the indication of hydrogen ion pump blocker by using the average basic mucosal impedance value of the proximal esophagus at night	Host	2020/8/1~ 2022/07/31	Ministry of Science and Technology
Host	Wong, Ming-Wun	To explore the role of esophageal microbiota in novel impedance parameters, clinical classification and hypersensitivity in gastroesophageal reflux disease	Co-host	2021/1/1~ 2021/12/31	Hualien Tzu Chi Hospital
Host	Wong, Ming-Wun	To explore the relationship between esophageal acid sensitivity, second-degree contraction of esophagus and subtypes of gastroesophageal reflux and the pathogenic mechanism	Co-host	2021/1/1~ 2021/12/31	Hualien Tzu Chi Hospital
Host	Wong, Ming-Wun	Clinical Application of High-resolution Impedance Pharyngeal Function Examination in Investigating Pharyngeal Dysphagia and Drug Response	Co-host	2021/1/1~ 2021/12/31	Hualien Tzu Chi Hospital
Host	Wong, Ming-Wun	To explore the pathophysiological effects of esophageal contraction, mucosal integrity and acid sensitivity on gastroesophageal reflux disease and the basis for treatment strategies	Co-host	2020/8/1~ 2023/07/31	Ministry of Science and Technology
Host	Wong, Ming-Wun	Can a cure for hepatitis C improve quality of life?	Co-host	2020/1/1~ 2020/12/31	Hualien Tzu Chi Hospital
Host	Wong, Ming-Wun	Improving the quality of fatty liver treatment with cross-group care	Co-host	2020/1/1~ 2020/12/31	Hualien Tzu Chi Hospital
Host	Wong, Ming-Wun	Clinical application of new esophageal impedance basic value supplemented with risk assessment to predict treatment response and recurrence of gastroesophageal reflux disease	Co-host	2020/1/1~ 2020/12/31	Hualien Tzu Chi Hospital

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Host	Wong, Ming-Wun	Discussion of differences in drug therapy in patients with sensitive esophagus and the role of mucosal afferent innervation in this disease	Co-host	2020/1/1~ 2020/12/31	Hualien Tzu Chi Hospital
Co-host	Yi, Chih-Hsun	Exploring the relationship between esophageal contraction, esophageal mucosal integrity and esophageal mucosal afferent nerves: the mechanism of influence on esophageal dysfunction and gastroesophageal reflux	Co-host	2017/8/1~ 2020/07/31	Ministry of Science and Technology
Co-host	Liu, Tso-Tsai	To explore the influence of clinical characteristics and intestinal flora in patients with metabolism-related fatty liver under the regulation of diet and exercise	Host	2022/1/1~ 2022/12/31	Hualien Tzu Chi Hospital
Co-host	Liu, Tso-Tsai	Discuss the pathophysiological mechanism of gastroesophageal reflux disease and establish the basis for accurate diagnosis and treatment based on esophageal reflux clearance ability, mucosal integrity and physical and mental characteristics	Co-host	2022/1/1~ 2022/12/31	Hualien Tzu Chi Hospital
Co-host	Liu, Tso-Tsai	To explore the influence and clinical application of opioid analgesics on the pathophysiological mechanism of esophageal contraction and reflux characteristics	Co-host	2022/1/1~ 2022/12/31	Hualien Tzu Chi Hospital
Co-host	Liu, Tso-Tsai	Application of high-resolution impedance pharyngeal function test and Sydney swallowing questionnaire in oropharyngeal dysphagia and voice disorders	Co-host	2022/1/1~ 2022/12/31	Hualien Tzu Chi Hospital
Co-host	Liu, Tso-Tsai	Analysis of 24-hour esophageal acid-base impedance examination-technical performance and clinical application of gastroesophageal reflux disease diagnosis with artificial intelligence of supervised learning	Co-host	2022/1/1~ 2022/12/31	Hualien Tzu Chi Hospital
Co-host	Liu, Tso-Tsai	Application of artificial intelligence in high-resolution esophageal function examination - research on unsupervised algorithm model based on deep learning	Co-host	2022/1/1~ 2022/12/31	Hualien Tzu Chi Hospital
Co-host	Liu, Tso-Tsai	Efficacy of Jingsi Bencao Decoction on physical and mental	Co-host	2022/1/1~ 2022/12/31	Tzu Chi Medical

		symptoms of functional dyspepsia-a randomized double-blind clinical trial			Corporation
Co-host	Liu, Tso-Tsai	To explore the role of esophageal microbiota in novel impedance parameters, clinical classification and hypersensitivity in gastroesophageal reflux disease	Co-host	2021/1/1~ 2021/12/31	Hualien Tzu Chi Hospital
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Co-host	Lei, Wei-Yi	Discuss the pathophysiological mechanism and treatment strategy of afferent nerve distribution, esophageal peristalsis and drug regulation in gastroesophageal reflux disease	Host	2022/8/1~ 2025/07/31	Ministry of Science and Technology
Co-host	Lei, Wei-Yi	To explore the influence and clinical application of opioid analgesics on the pathophysiological mechanism of esophageal contraction and reflux characteristics	Host	2022/1/1~ 2022/12/31	Hualien Tzu Chi Hospital

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Co-host	Lei, Wei-Yi	Discuss the pathophysiological mechanism of gastroesophageal reflux disease and establish the basis for accurate diagnosis and treatment based on esophageal reflux clearance ability, mucosal integrity and physical and mental characteristics	Co-host	2022/1/1~ 2022/12/31	Hualien Tzu Chi Hospital
Co-host	Lei, Wei-Yi	Application of high-resolution impedance pharyngeal function test and Sydney swallowing questionnaire in oropharyngeal dysphagia and voice disorders	Co-host	2022/1/1~ 2022/12/31	Hualien Tzu Chi Hospital
Co-host	Lei, Wei-Yi	Application of artificial intelligence in high-resolution esophageal function examination - research on unsupervised algorithm model based on deep learning	Co-host	2022/1/1~ 2022/12/31	Hualien Tzu Chi Hospital
Co-host	Lei, Wei-Yi	Analysis of 24-hour esophageal acid-base impedance examination-technical performance and clinical application of gastroesophageal reflux disease diagnosis with artificial intelligence of supervised learning	Co-host	2022/1/1~ 2022/12/31	Hualien Tzu Chi Hospital
Co-host	Lei, Wei-Yi	To explore the influence of clinical characteristics and intestinal flora in patients with metabolism-related fatty liver under the regulation of diet and exercise	Co-host	2022/1/1~ 2022/12/31	Hualien Tzu Chi Hospital
Co-host	Lei, Wei-Yi	Efficacy of Jingsi Bencao Decoction on physical and mental symptoms of functional dyspepsia-a randomized double-blind clinical trial	Co-host	2022/1/1~ 2022/12/31	Tzu Chi Medical Corporation
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		reflux and the pathogenic mechanism			
Co-host	Lei, Wei-Yi	Clinical Application of High-resolution Impedance Pharyngeal Function Examination in Investigating Pharyngeal Dysphagia and Drug Response	Co-host	2021/1/1~ 2021/12/31	Hualien Tzu Chi Hospital
Co-host	Lei, Wei-Yi	Can a cure for hepatitis C improve quality of life?	Co-host	2020/1/1~ 2020/12/31	Hualien Tzu Chi Hospital
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Co-host	Lei, Wei-Yi	Discussion of differences in drug therapy in patients with sensitive esophagus and the role of mucosal afferent innervation in this disease	Host	2020/1/1~ 2020/12/31	Hualien Tzu Chi Hospital
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Co-host	Lei, Wei-Yi	Exploring the relationship between esophageal contraction, esophageal mucosal integrity and esophageal mucosal afferent nerves: the mechanism of influence on esophageal dysfunction and gastroesophageal reflux	Co-host	2017/8/1~ 2020/07/31	Ministry of Science and Technology
Co-host	Hung, Jui-Sheng	Application of high-resolution impedance pharyngeal function test and Sydney swallowing questionnaire in oropharyngeal dysphagia and voice disorders	Host	2022/1/1~ 2022/12/31	Hualien Tzu Chi Hospital
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Co-host	Hung, Jui-Sheng	To explore the influence and clinical application of opioid analgesics on the pathophysiological mechanism of	Co-host	2022/1/1~ 2022/12/31	Hualien Tzu Chi Hospital

		esophageal contraction and reflux characteristics			
Co-host	Hung, Jui-Sheng	Analysis of 24-hour esophageal acid-base impedance examination-technical performance and clinical application of gastroesophageal reflux disease diagnosis with artificial intelligence of supervised learning	Co-host	2022/1/1~ 2022/12/31	Hualien Tzu Chi Hospital
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Co-host	Hung, Jui-Sheng	Clinical application of new esophageal impedance basic value supplemented with risk assessment to predict treatment response and recurrence of	Co-host	2020/1/1~ 2020/12/31	Hualien Tzu Chi Hospital

		gastroesophageal reflux disease			
Co-host	Hung, Jui-Sheng	Discussion of differences in drug therapy in patients with sensitive esophagus and the role of mucosal afferent innervation in this disease	Co-host	2020/1/1~ 2020/12/31	Hualien Tzu Chi Hospital
Co-host	Hung, Jui-Sheng	Discussion of differences in drug therapy in patients with sensitive esophagus and the role of mucosal afferent innervation in this disease	Co-host	2020/8/1~ 2023/07/31	Ministry of Science and Technology
Co-host	Liang, Shu-Wei	Application of artificial intelligence in high-resolution esophageal function examination - research on unsupervised algorithm model based on deep learning	Host	2022/1/1~ 2022/12/31	Hualien Tzu Chi Hospital
Co-host	Liang, Shu-Wei	Analysis of 24-hour esophageal acid-base impedance examination-technical performance and clinical application of gastroesophageal reflux disease diagnosis with artificial intelligence of supervised learning	Co-host	2022/1/1~ 2022/12/31	Hualien Tzu Chi Hospital
Co-host	Liang, Shu-Wei	Discuss the pathophysiological mechanism of gastroesophageal reflux disease and establish the basis for accurate diagnosis and treatment based on esophageal reflux clearance ability, mucosal integrity and physical and mental characteristics	Co-host	2022/1/1~ 2022/12/31	Hualien Tzu Chi Hospital
Co-host	Liang, Shu-Wei	To explore the influence and clinical application of opioid analgesics on the pathophysiological mechanism of esophageal contraction and reflux characteristics	Co-host	2022/1/1~ 2022/12/31	Hualien Tzu Chi Hospital
Co-host	Liang, Shu-Wei	To explore the influence of clinical characteristics and intestinal flora in patients with metabolism-related fatty liver under the regulation of diet and exercise	Co-host	2022/1/1~ 2022/12/31	Hualien Tzu Chi Hospital
Co-host	Liang, Shu-Wei	Efficacy of Jingsi Bencao Decoction on physical and mental symptoms of functional dyspepsia-a randomized double-blind clinical trial	Co-host	2022/1/1~ 2022/12/31	Tzu Chi Medical Corporation
Co-host	Liang, Shu-Wei	To explore the role of esophageal microbiota in novel impedance parameters, clinical classification	Co-host	2021/1/1~ 2021/12/31	Hualien Tzu Chi Hospital

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		and hypersensitivity in gastroesophageal reflux disease			
Co-host	Liang, Shu-Wei	To explore the relationship between esophageal acid sensitivity, second-degree contraction of esophagus and subtypes of gastroesophageal reflux and the pathogenic mechanism	Co-host	2021/1/1~ 2021/12/31	Hualien Tzu Chi Hospital
Co-host	Liang, Shu-Wei	Clinical Application of High-resolution Impedance Pharyngeal Function Examination in Investigating Pharyngeal Dysphagia and Drug Response	Co-host	2021/1/1~ 2021/12/31	Hualien Tzu Chi Hospital
Co-host	Liu, Chin-Hung	Using bee indicators and geographic information system to assess pesticide exposure in different crops MOST109-2314-B-320-002-MY2	Co-host	2020/08/01~ 2022/07/31	Ministry of Science and Technology
Co-host	Liu, Chin-Hung	Exploring the relationship between cholesterol metabolism pathway and drug insensitivity in oral squamous cell carcinoma TCMRC-P-110011	Host	2022/01/01~ 2022/12/31	慈濟大學
Co-host	Liu, Chin-Hung	Synergistic antitumor effects of statins and SREBP2 inhibitors in oral squamous cell carcinoma: the role of the mevalonate pathway and statin-insensitive features TCMRC-P-109009	Host	2021/01/01~ 2021/12/31	慈濟大學
Co-host	Liu, Chin-Hung	Molecular mechanisms of statins inhibiting the growth of oral squamous cell carcinoma: the role of DNA methyltransferases and the regulation of tumor suppressor gene epigenetics TCMRC-P-108003	Host	2019/10/01~ 2020/09/30	慈濟大學
Co-host	Chen, Chun-Yao	To explore the influence of clinical characteristics and intestinal flora in patients with metabolism-related fatty liver under the regulation of diet and exercise	Co-host	2022/1/1~ 2022/12/31	Hualien Tzu Chi Hospital

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D. Instructions for Expected Use of Funds(Funding will be included in the review and scoring items, please do not make up)

1. Please provide a detailed description of the purpose and annual amount of each expense (including research labor costs, consumables, etc.), if the column is insufficient, please add it yourself.
2. Research manpower expenses shall not be diverted to other business expenses.

[Funds for the first year] (Please copy the form yourself and list the estimated funds year by year)

(New Taiwan dollars)

project name	illustrate	unit price	quantity	total price
1. Research manpower ■Full-time □ concurrently (Please refer to the regulations in the Medical Special Management Measures for relevant insurance premiums)	Full-time staff: (the second year of full-time assistant at the bachelor level) The highest rank of personnel is limited to the ninth level of master's degree, and the items included in the work remuneration, labor and health insurance employer-borne expenses, labor retirement employer-borne expenses and year-end bonuses are handled in accordance with the regulations of the implementing agency (up to 1.5 months as the upper limit).	32,240 2,689 37 1,632 1,998	13 12 12 12 12	419,120 32,268 444 19,584 23,976
	Subtotal			495,392
2. Consumables, items and miscellaneous expenses	Computer peripheral consumables: printer ribbon, toner cartridge, ink cartridge, printer photosensitive drum/roller, special printing paper, etc. Miscellaneous: postage and telecommunications fees, printing fees, photocopying paper, photocopying fees, binding fees, stationery fees, poster production fees, computer data statistics fees, computer data analysis fees, paper submission fees, paper publication fees, etc.	14,608 10,000		14,608 10,000
	Subtotal			24,608
3. Medicine expenses (Jingsi herbal drink concentrate, please fill in the quantity)	Jingsi herbal drink concentrate (2 packs*30 days*150 people) Placebo (2 packs*30 days*150 people)	0 0	9,000 9,000	0 0
	Subtotal			0
4. Subject subsidy	Subject allowance (subsidy)	1,200	150	180,000
	Subtotal			180,000
5. Inspection fee (Please fill in the inspection items and fees)	LC-MS sample processing and analysis, intestinal bacteria analysis	5,000	150	750,000
	Subtotal			750,000
			total	1,450,000

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E. Summary of the plan in Chinese

Please give an overview of the main points of this project within 500 words, and customize keywords according to the nature of this project, and please write in Chinese.

新冠肺炎患者在痊癒後，約 10%患者產生長新冠症狀，長新冠症狀中的腹痛、腹脹、腹瀉及便祕源自於腸腦軸失調，腸腦軸失調包含功能性消化不良和腸躁症，常規檢查無明顯異常，由於原因不明但盛行率高，往往對患者的身心健康影響甚鉅。即使腸腦軸失調目前被認為和胃腸道局部發炎和微生物菌相改變有關，但目前西醫治療療效不佳。有鑑於此，許多研究應用中草藥在功能性消化不良，並且達到不錯的療效。淨斯本草飲濃縮液為取得衛福部外銷專用許可證之食品，其成分為艾葉、魚針草、麥門冬、魚腥草、桔梗、甘草、紫蘇葉、菊花等臺灣本土八種能清潤、散寒、宣肺化痰、利濕清熱的中藥草，在臨床試驗登記立案作為輔助新冠肺炎的治療，目前初步發現亦可改善患者腸胃症狀以及憂焦慮程度。故本研究採雙盲隨機試驗，以淨斯本草飲濃縮液用於客觀檢查皆正常之長新冠症狀-腸腦軸失調患者，評估其治療前後之身心症狀以及腸道菌代謝產物之變化。

關鍵詞：長新冠症狀、腸腦軸失調、淨斯本草飲濃縮液、身心症狀

計畫概述：請概述執行本計畫之目的及可能產生對社會、經濟、學術發展等面向的預期影響性(三百字以內)。

腸腦軸失調(DGBI)包含功能性消化不良和腸躁症為新冠肺炎感染後的腸胃道問題，也是傳統西醫療效值得改善的疾病，淨斯本草飲濃縮液為東部地區研發之中草藥食品，期待淨斯本草飲濃縮液在感染新冠肺炎病毒後改善腸胃道功能以及憂鬱情況的發現能夠用於改善腸腦軸失調(DGBI)之身心症狀。

※此部分內容於獲核定補助後將逕予公開

※If there are not enough fields, please copy by yourself.

Version date：(Version 3, 11/10/2022)

F. Summary of the plan in English

Please provide an overview of the main points of this project within 500 words, and customize keywords according to the nature of this project, and please write in English.

Dyspepsia refers to chronic or recurrent upper gastrointestinal symptoms. According to the Rome IV criteria, functional dyspepsia (FD) symptoms included meal-related fullness, early satiation, epigastric pain or burning which are unexplained after routine investigation. FD causes substantial psychophysical burden because of its unknown etiology and high prevalence. Although FD is currently associated with local inflammation of the gastrointestinal tract and microbiota alteration, current available treatments for FD are of limited effectiveness. In view of this, many studies have applied Chinese herbal medicine in FD and achieved some therapeutic benefit. The Jing Si Herbal Tea Liquid Packet composed of eight native Taiwanese herbs (wormwood, hickory grass, Ophiopogon japonicus, houttuynia cordata, platycodon, licorice, perilla leaves, chrysanthemum) has obtained a special export license from the Ministry of Health and Welfare. The Jing Si Herbal Tea Liquid Packet also has been registered in clinical trials as a complementary treatment for COVID-19. The preliminary data demonstrated that the Jing Si Herbal Tea Liquid Packet may improve gastrointestinal symptoms and anxiety in patients with COVID-19. Therefore, this study aims to investigate the impact of the Jing Si Herbal Tea Liquid Packet on psychophysical burden and metabolites of microbiota in patients with FD through a double-blind randomized manner.

關鍵詞：functional dyspepsia; Jing Si Herbal Tea Liquid Packet; psychophysical burden

※If there are not enough fields, please copy by yourself.

Version date：(Version 3, 11/10/2022)

G. Background and purpose of the research project

Please describe in detail the background, purpose, importance of this research project and the research situation related to this project at home and abroad,
Comments on important references, etc., please write in Chinese format.

Background

Symptoms of the new crown-gut-brain axis disorder (disorders of gut-brain interaction, DGBI)

COVID-19 is raging all over the world. The novel coronavirus recognizes type 2 angiotensin-converting enzyme and infects various cells in the body, including cells in the gastrointestinal tract. About 12%–20% of patients are infected and develop gastrointestinal symptoms. (1, 2) About 10% of patients with COVID-19 will develop symptoms of COVID-19 after recovery, (3) Abdominal pain, bloating, diarrhea and constipation in symptoms of COVID-19 originate from disorders of gut-brain interaction , DGBI). (4) In the upper gastrointestinal tract (upper abdominal pain, abdominal distension), it is called functional dyspepsia, and in the lower gastrointestinal tract (abdominal pain, diarrhea, constipation), it is called irritable bowel syndrome. (5) In a large-scale survey in the United States (more than 100,000 people), it was found that after the COVID-19 epidemic, the incidence of gut-brain axis disorder (DGBI) increased by 75% compared with before the epidemic. (6) Disorders of the gut-brain axis (DGBI) include functional dyspepsia and irritable bowel disorder. At present, there is no clear pathogenesis and standard treatment. The consensus is to use the Roman diagnostic criteria, evaluate by questionnaire, and exclude other organic diseases. disease to diagnose. (5) The possible mechanisms of gut-brain axis disorder (DGBI) include local inflammation of the gastrointestinal tract, infiltration and activation of allergic cells, mucosal defects, changes in microbial flora, and hypersensitivity of viscera. (7) In terms of the microbial flora of the brain-gut axis, the metabolites of intestinal bacteria are regarded as the key to influence, among which short-chain fatty acids (SCFA) are regarded as good metabolizers As a product, when carbohydrates are fermented, anaerobic bacteria will produce many short-chain fatty acids (SCFA) in the distal small intestine and colon, which are composed of 1-6 carbon atoms, and the main three metabolic compounds are acetic acid (Acetate), Propionate and Butyrate. Short-chain fatty acids (SCFA) have been shown in research to have anti-inflammatory, anti-oxidant, anti-diabetic, anti-cancer and antibacterial effects. When the bacterial phase changes, the concentration of short-chain fatty acids may change accordingly and affect human physiological responses. When the intestinal flora is out of balance, a variety of bad metabolites will be produced: Trimethylamine N-oxide, TMAO (derived from L-Carnitine or Choline), indoxyl sulfate (derived from Tryptophan) and p-cresyl sulfate (derived from Tyrosine), etc. (8)

Changes in the bacterial phase of the new crown symptoms

SARS-CoV-2 infection caused significant changes in the intestinal flora of patients. The number of

potential pathogens in the patient's body increases, and the antibiotic treatment also reduces the beneficial bacteria. [9] Hazan et al. (2022) showed reduced gut bacterial diversity in infected individuals, with reduced numbers of Bifidobacterium, Faecalibacterium, and Roseburium. [10] At six months post-infection, the intestinal bacterial diversity of the patients was still significantly low. [11] In addition to reduced diversity, these symptomatic patients had lower numbers of anti-inflammatory bacteria such as Faecalibacterium prausnitzii, Eubacterium rectale, Bifidobacterium adolescentis, and potential pathogens such as Rothia, Erysipelatoclostridium, Ruminococcus gnavus in the gut three months after infection. , Ruminococcus torques, and Bacteroides dorei are more. [12] Su et al. (2022) studied the dysbiosis caused by post-acute COVID-19 syndrome and found that there were more potential pathogens such as Erysipelatoclostridium ramosum and Ruminococcus gnavus, and beneficial bacteria Bifidobacterium adolescentis, B. pseudocatenulatum) decreased. [13] These evidences show that the intestinal flora has not fully recovered from the imbalance during infection, and is still in a state of low diversity and favorable pathogens, which can continue to cause immune responses in the intestine. Functional dyspepsia is also thought to be caused by increased permeability of the intestinal wall of the small intestine, allowing intestinal microbial metabolites to infiltrate the tissues and activate the immune system. [14]

In both functional dyspepsia and irritable bowel disorder, there is marked dysbiosis in the gut. Bacterial changes in patients with functional dyspepsia include decreased numbers of Bacteroidetes (Prevotellaceae) and increased numbers of Proteobacteria, Firmicutes (Streptococcus and Clostridia) and Bifidobacteria. 15 Bacterial changes in IBD included increased Clostridia (increased Ruminococcus but decreased Faecalibacterium), increased Lactobacillus and Streptococcus within the phylum Firmicutes, increased Bacteroides, and decreased Bifidobacteria. 16 After synthesis, it can be seen that the changes in the gut-brain axis disorder are mainly due to the replacement of Bacteroidetes by Firmicutes, while the changes in the number of Proteobacteria and Bifidobacteria are inconsistent.

Jing Si Herbal Tea Liquid Packet

The ingredients of Jing Si Herbal Tea Liquid Packet are mugwort leaves, houttuynia cordata, Ophiopogon japonicus, Houttuynia cordata, Campanulaceae, licorice, perilla leaves, chrysanthemum and other eight native Taiwanese herbs that can clear away moisture, dispel cold, relieve lungs and resolve phlegm, and clear away dampness and heat. Chinese medicinal herb, current research has found that it can block the combination of the new coronavirus and cells, and can also reduce cell penetration and block the virus from penetrating cells, while targeting wild-type and mutant viruses D614G, B.1.1.7, 501Y.V2 Carrying out animal studies, it was found that Jing Si Herbal Tea Liquid Packet can reduce the ability of 60 to 70% of the virus to infect the upper respiratory tract, lung, heart, and intestine of mice and reduce the expression of FKBP51, a protein related to depression, by 40%. The effect of using Jing Si Herbal Tea Liquid Packet to help reduce the amount of virus and systemic anti-inflammatory effect in patients with COVID-19. (9) In our

ongoing clinical study, for functional dyspepsia (FD) patients, Jing Si Herbal Tea Liquid Packet can improve symptoms in 75% of patients, compared with only 33% of placebo.

Purpose

A double-blind randomized trial was conducted to investigate the improvement of Jingsi Bencao decoction concentrate on the physical and mental symptoms of gut-brain axis disorder (DGBI) and the changes in intestinal flora after COVID-19.

Importance

Gut-brain axis disorders (DGBI), including functional dyspepsia and irritable bowel syndrome, are gastrointestinal problems after COVID-19 infection. They are also diseases that are worthy of improvement in the efficacy of traditional Western medicine. The discovery that Jingsi Bencao Drink Concentrate improves gastrointestinal function and depression after infection with the new coronavirus can be used to improve the physical and mental symptoms of gut-brain axis disorder (DGBI).

※If there are not enough fields, please copy by yourself.

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H. Research methods, steps and implementation progress

1. Please describe in detail the research methods and reasons used in this project.
2. Estimated possible difficulties and solutions.
3. If it is a continuous plan, the research progress report or primary data of the previous year should be attached at the same time.
4. Please write in Chinese format.

1. Subject acceptance and exclusion conditions

This study is a prospective study, which is expected to last for one year. It is planned to recruit 150 subjects with gut-brain axis disorder (DGBI) three months after being infected with new coronary pneumonia: 75 of them Functional dyspepsia (FD) subjects and 75 irritable bowel syndrome (IBS) subjects.

Subject inclusion conditions (Inclusion criteria)

1. Age between 20-70 years old.

2. Those who meet the definition of functional dyspepsia (FD).

(Functional dyspepsia (FD) is chronic (once a week, lasting 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, Epigastric pain or burning sensation in the upper abdomen, and no symptoms of gastrointestinal bleeding or significant weight loss, no abnormality after upper gastrointestinal endoscopy).

3. Those who meet the definition of irritable bowel syndrome (IBS).

(Irritable bowel syndrome (IBS) is chronic (once a week, lasting for at least three months) lower gastrointestinal symptoms: abdominal pain combined with diarrhea or constipation, and no symptoms of gastrointestinal bleeding or significant weight loss, no abnormalities after colonoscopy) .

4.Be conscious and willing to sign the subject's consent form.

Subject Exclusions (Exclusion criteria)

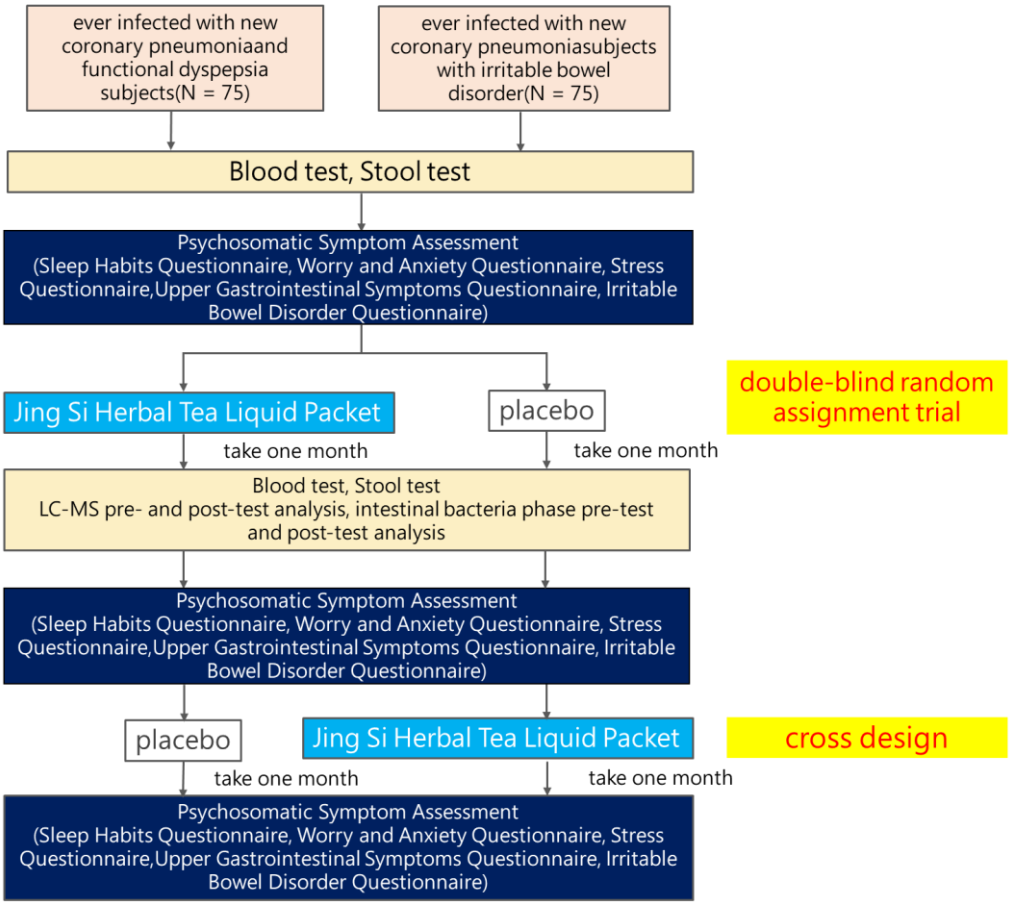
1. Abnormal liver and kidney function;
2. Abnormal blood tests and thyroid abnormalities;
3. Have received surgery on the digestive tract;
4. Abnormal upper gastrointestinal endoscopy;
5. Abnormal colonoscopy;
6. Antibiotics are being used for infectious diseases;
7. Pregnant or breastfeeding women;
8. Suffering from heart, liver, or kidney failure;
9. Physical weakness, allergies, asthenia and cold constitution and chronic diseases.

2. Experimental process

150 subjects with gut-brain axis disorder (DGBI) three months after being infected with new coronary

pneumonia will be recruited in the outpatient department of gastroenterology, including 75 subjects with functional dyspepsia (FD) and 75 subjects with irritable bowel syndrome (IBS)) subjects; qualified subjects will receive blood and feces sampling and complete physical and mental symptom assessment (sleep habits questionnaire, anxiety questionnaire, stress questionnaire, gastrointestinal symptoms questionnaire, and irritable bowel syndrome questionnaire) before treatment , and then according to the double-blind random allocation method, the computer generated garbled characters, and assigned Jing Si Herbal Tea Liquid Packet or placebo according to the coding sequence, and the research assistant gave Jing Si Herbal Tea Liquid Packet or placebo, Host and recipients None of the subjects knew what the content of the assignment was. The experimenters took Jing Si Herbal Tea Liquid Packet or placebo in the first month, and after the end of the month, they received blood and stool tests and complete physical and mental symptom assessment (sleep habits questionnaire, anxiety questionnaire, stress questionnaire) , gastrointestinal symptom questionnaire, and irritable bowel syndrome questionnaire), the laboratory will conduct pre- and post-test analysis of LC-MS and intestinal bacteria, and then conduct a cross-test. The original placebo will take Jing Si Herbal Tea Liquid Packet in the second month, previously taking Jing Si Herbal Tea Liquid Packet will take a placebo in the second month, after the end of the second month, do the third complete physical and mental symptom assessment (sleep habits questionnaire, anxiety questionnaire, stress questionnaire, digestive tract Symptom Questionnaire, Irritable Bowel Disorder Questionnaire), the test is completed.

Research flow chart



3. Questionnaire

The questionnaire items included sleep habits questionnaire, anxiety questionnaire, stress questionnaire, gastrointestinal symptoms questionnaire, and irritable bowel syndrome questionnaire. The details of the questionnaire are attached.

4.Collection, preservation, transportation and DNA extraction of feces

Fix the collection box on the toilet lid, discharge fresh feces into the collection box, then screw the lid tightly and place it in a zipper bag within 4 hours or in a -4℃ refrigerator within 24-48 hours Sent to the laboratory for sub-packaging, and then refrigerated in a -80℃ refrigerator. Thaw when the DNA is extracted, the extraction process includes the following steps sample homogenization, cell lysis, non-DNA material removal and DNA purification.

5.Gut micrtobiota sequencing and community analysis

In this study, 16S rDNA massively parallel sequencing will be used to analyze the composition of gut bacteria. 0.25 g of stool samples were pooled for DNA extraction with the QIAmp PowerFecal Kit (Qiagen, Hilden, Germany). The purified DNA was PCRed with primers for 341F and 805R to amplify the V3-V4 fragments of the 16S rRNA gene, and the barcode was sent to the manufacturer for library building. The Illumina MiSeq platform was used for next-generation pair-end sequencing. Sample 30000 reads. After the sequence obtained by the manufacturer was screened for high-quality fragments by Mothur and Usearch software, the bacterial phase composition and taxonomic status of each sample were calculated. The taxonomic status of each sequence was determined by comparing the Mothur software with the SILVA sequence database. The investigators will use Microbiome Analyst R and other suitable R programming language packages to perform cluster analysis and network analysis of bacterial composition.

6.Stool and Blood LC-MS Analysis

I. Plasma sample collection and preparation：

Whole blood was collected in Vacutainer K2E-EDTA (BD Diagnostics, Franklin Lakes, NJ, USA) blood collection tubes. The collected whole blood samples were then transferred to 15 mL containing Ficoll-paque PLUS medium [whole blood (hall blood)/ Ficoll-paque PLUS medium = 4/3 (volume ratio v/v)] (GE Healthcare Life Sciences, Pittsburgh, PA, USA) and centrifuge (3000 rpm, 30 min) at room temperature. After centrifugation, the plasma (plasma) supernatant that was successfully layered was collected and distributed into sterilized 1.5 mL microcentrifuge tubes (eppendorf), and glacial acetic acid with a concentration of 1 N and a volume of 1% was added.) aqueous solution to prevent the degradation of the analyte in plasma. Plasma is stored in a freezer at -80oC, and the storage period does not exceed 1 year.

II.Previous processing method of Lipophilic Substances：

Thaw the plasma sample at room temperature for 10-20 minutes, then transfer 100 μL of plasma to a new 1.5 mL microcentrifuge tube. Add the internal standard (internal control, 13C-PA) first, then add methanol 3 times the volume of plasma for deproteinization, and let it stand at room temperature for about 15-20 minutes. Then centrifuge the rested microcentrifuge tube (3,000 rpm, 10 min, 4 ℃), and transfer the supernatant to the corresponding small glass test tube. Move the glass test tubes to a nitrogen blowing system, dry the samples through a nitrogen flow, and then add 100 μL of chloroform (Chloroform) to each sample for redissolution. A filtration extraction system was set up, and solid phase extraction columns [Solid phase extraction (SPE) columns (Strata-X-C 33 μm polymeric strong cation 60 mg/3 mL, Phenomenex, Torrance, CA, USA)] were used for extraction. Add 1.0-1.5 mL of n-hexane (hexane) solution to the erected column to activate the column, and use a vacuum pump to pump positive pressure for about 20-30 seconds. Replace the glass test tubes that have been filled with n-hexane solution under the filter extraction system, and then add the samples to the activated column in sequence. Add 1.0-1.5 mL of ethyl acetate (ethyl acetate) for vacuum extraction for about 30-45 seconds, and transfer the sample extracted with ethyl acetate to a nitrogen blowing system to dry it. Redissolve the sample with 100 μL of methanol, and finally transfer the reconstituted sample to a liquid chromatography-mass spectrometer (LC-MS) vial equipped with insert, and prepare for analysis on the machine with an injection volume of 30 μL per needle .

III. Hydrophilic Substances before the processing method：

There are two extraction methods for such compounds, namely traditional methanol extraction (Traditional deproteinized extraction) and SLE column extraction (SLE column extraction). First, place the plasma sample at room temperature to thaw for about 10-20 minutes. After the thawing is complete, take 100 μL to a new 1.5 mL microcentrifuge tube (two tubes of 100 μL are required for each sample). Plasma samples were deproteinized by adding methanol at a volume ratio of 3 times or adding an equal volume of 50 mM sodium phosphate dibasic heptahydrate (Sodium phosphate dibasic heptahydrate) and evenly mixed. Set up the SLE column filtration system and sample test tube, put the sample mixed with 50 mM disodium hydrogen phosphate hydrate into the column, turn on the vacuum pump to filter and extract, wait for about 3 minutes, then add 1.2-1.5 mL of acetic acid Ethyl esters are used for dike flushing. In addition, for the methanol deproteinized group, after waiting for about 20 minutes, they were centrifuged (3,000 rpm, 10 min, 4 ℃), and then the supernatant was taken out into the corresponding glass test tube. The samples with two different treatment methods were put into the nitrogen blowing system for drying and concentration. For the group undergoing deproteinization, add 300 μL of methanol to redissolve, and filter with MILLEX GP 0.45 μM PVDF filter (Millipore), and discharge the liquid into the LC-MS special sample bottle loaded with insert; For the group extracted by the column, 100 μL of methanol was added for back-dissolution and reconstitution, and it was put into the LC-MS special sample bottle loaded with insert, ready for analysis on the machine.

d. LC-MS Analysis Conditions (Liquid Chromatography Mass Spectrometer)：

LC-MS condition I：Used to analyze Lipophilic Substances

LC-MS condition II：Used to analyze Hydrophilic Substances Substances)

Table 1. LC-MS analysis conditions:

LC conditions			
HPLC system	Waters Alliance e2695	**Injection volume**	30 µL
Runtime	60.0 min (I) 18.0 min (II)	**Column**	Phenomenex Luna C18(2) (250 x 4.6 mm, 5 µm)
Flow rate	0.6 mL/min (I) 0.8 mL/min (II)	**Column temp**	35℃ (I) 40℃ (I)
Condiction I (Lipophilic Substances)			
Mobile phase A		**Mobile phase B**	
60:40 Acetonitrile:ddH_2O with 9.2 mM Ammonium acetate ($NH_4CH_3CO_2$) (pH 8.85)		90:10 Isopropanol:Acetonitrile with 9.2 mM Ammonium acetate ($NH_4CH_3CO_2$)	
Time (min)	**%A**	**%B**	**Curve**
Initial	85	15	6
8.0	70	30	6
10.0	52	48	6
44.0	18	82	6
46.0	1	99	6
48.0	1	99	6
48.4	85	15	6
60.0	85	15	6
Condiction II (Hydrophilic Substances)			
Mobile phase A		**Mobile phase B**	
0.1% Formic acid in 99.9% ddH_2O		0.1% Formic acid in 99.9% MeOH	
Time (min)	**%A**	**%B**	**Curve**
0	95	5	6
14	30	70	6
16	30	70	6
18	50	50	6
MS conditions			
Detector	Waters ACQUITY QDa (Performance)		
Ionization mode	ESI Negative (I); ESI Negative and Positive (II)		
Capillary voltage	Default (0.8 kV)		
Probe temp	Default (600℃)		
Cone voltage	20V(I); 15V(II)		
Sampling rate	8 Hz		
Full scan	250-600 *m/z* for Negative (I); 70-600 *m/z* for Negative or Positive		
SIR	See **Table 2** - "Molecular Ions (m/z)"		

e. Method validation：

Including Limits of detection, LOD and Limits of quantitation, LOQ, Calibration curve, Recovery, accuracy and precision, Intra-assay, accuracy and precision and Inter-assay precision and accuracy of each test substance.

Table 2. LC-MS analysis Standard List:

	Molecular ion (*m/z*)	**Ion source mode**

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Lipophilic Substances			
Short Chain Fatty acids (SCFAs)	Acetate (2:0)	42.0+153 (3NPH)	ESI Negative
	Propionate (3:0)	57+153 (3NPH)	ESI Negative
	Butyrate (4:0)	72+153 (3NPH)	ESI Negative
Long Chain Fatty acids	Palmitic acid, PA (16:0)	255.1	ESI Negative
	Stearic Acid, SA (18:0)	283.2	ESI Negative
	Palmitoleic Acid, POA (16:1)	253.2	ESI Negative
	Oleic Acid, OA (18:1)	281.2	ESI Negative
Fatty acid esters of hydroxy fatty acids (FAHFAs)	Palmitoleic Acid Ester of 9-Hydroxystearic Acid (9-POHSA)	535.5	ESI Negative
	Oleic Acid Ester of 9-Hydroxystearic Acid (9-OAHSA)	563.5	ESI Negative
Internal standards			
[$^{13}C_{16}$]- Palmitic acid (IS1)		271.4	ESI Negative
Hydrophilic Substances			
Methionine cycle	*L*-Methionine (*L*-Met)	150.1	ESI Positive
	S-adenosyl-*L*-methionine (SAM)	399.0	ESI Positive
	S-adenosyl-*L*-homocysteine (SAH)	385.0	ESI Positive
	L-Homocysteine (*L*-Hcy)	136.1	ESI Positive
	Methylmalonic acid (MMA)	117.1	ESI Negative
Antioxidants	Ascorbic acid (AA)	174.9	ESI Negative
Nutrition index	3-Methyl-*L*-histidine (3-MH)	170.0	ESI Negative
Fatty acids carrier	*L*-Carnitine (L-Car)	162.1	ESI Positive
	Acetyl-*L*-Carnitine (ALC)	204.0	ESI Positive
	Propionyl-*L*-Carnitine (PLC)	218.0	ESI Positive
Nephrotoxin	Trimethylamine *N*-oxide (TMAO)	76.0	ESI Positive
	Indoxyl Sulfate (InS)	211.9	ESI Negative
	p-Cresyl sulfate (pCS)	187.0	ESI Negative
Internal standards			
d3-*L*-Methionine (d3-*L*-Met) (IS2)		153.1	ESI Positive
d9-Trimethylamine *N*-oxide (d9-TMAO) (IS3)		85.0	ESI Positive

7.Jing Si Herbal Tea Liquid Packet

In this experiment, Jing Si Herbal Tea Liquid Packet was used. Its ingredients are eight kinds of native Taiwan species, such as mugwort leaves, hinoki, Ophiopogon japonicus, Houttuynia cordata, bellflower, licorice, perilla leaves, and chrysanthemum. , Dampness-clearing and heat-clearing herbs, take Jing Si Herbal Tea Liquid Packet 15 ml once a day in the morning and evening.

8.Statistical Analysis

Continuous variables were expressed as mean and standard deviation if they were normally distributed; if they were not normally distributed, they were expressed as median and interquartile range. The treatment effect is presented by the improvement percentage of the sleep habits questionnaire, depression questionnaire, anxiety questionnaire, stress questionnaire, gastrointestinal symptoms questionnaire, and irritable bowel syndrome questionnaire before and after treatment, and the curative effect of Jingsi Bencao Drink Concentrate and placebo is expressed as the chi-square by the improvement percentage Chi-squared test comparison, P value less than 0.05 was considered statistically significant difference, the statistical analysis software used was SPSS 19 for Windows (SPSS, Inc, Chicago, IL, USA).

9. Sample Size Estimation

According to our ongoing research, it is estimated that the efficacy of Jing Si Herbal Tea Liquid Packet for functional dyspepsia (FD) is 75%, while the efficacy of placebo is 33.3%. It is estimated by α-error 0.05; β-error 0.20, at least 100 subjects are required to be admitted, and taking into account that the subjects may withdraw and fail to complete the trial successfully, the estimated number of subjects admitted in this study is 150.

10. Possible difficulties and solutions

Possible difficulties: According to our current research, the effect of placebo on functional dyspepsia (FD) can reach 33.3%, so if the investigators want to prove that Jing Si Herbal Tea Liquid Packet has a positive effect on patients with new coronary pneumonia three months after infection Gut-brain axis dysregulation (DGBI) had to be statistically significantly greater than placebo to have a significant effect.

Solution: This trial adopts a multi-faceted whole-person care model to evaluate the curative effect, not only the symptoms of gut-brain axis disorder (DGBI) three months after being infected with new coronary pneumonia, but also the assessment of physical and mental symptoms, stress, and intestinal flora. Confirm the effect of Jing Si Herbal Tea Liquid Packet on various aspects of gut-brain axis disorder (DGBI).

11. References

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