

The Study of Efficacy and Safety of a Modified Chaihu Shugan San Formula in the Treatment of Insomnia Associated with Stress: A Pilot Clinical Evaluation

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Abstract

This pilot study aimed to evaluate the preliminary efficacy and safety of a modified *Chaihu Shugan San* formula (柴胡疏肝散加减方) in the treatment of insomnia associated with stress. Based on the theoretical framework of Traditional Chinese Medicine (TCM), "Liver Qi stagnation" (肝气郁结) serves as a key pathogenic mechanism underlying sleep disturbances. A quasi-experimental pre-post design was employed in a purposively selected sample of 30 patients aged 18–70 years. While the lack of a randomized control arm limits absolute internal validity against placebo effects, this preliminary evaluation incorporated both subjective metrics—the Suanprung Stress Test (SPST-20) and the Pittsburgh Sleep Quality Index (PSQI)—and objective laboratory safety biomarkers. Participants received the standardized herbal powder twice daily for 4 weeks. After treatment, mean PSQI scores significantly decreased from 12.300 $\pm$ 3.164 to 6.833 $\pm$ 4.145 ($p < 0.05$). Concurrently, stress levels measured by the ST-5 and SPST-20 declined significantly ($p < 0.05$). Regarding safety, over 90% reported no clinical adverse events. Crucially, pre- and post-treatment laboratory data for liver (ALT, AST) and renal (Creatinine, BUN) functions remained within normal physiological ranges, indicating no detectable hepatotoxicity or nephrotoxicity. In conclusion, these findings offer promising preliminary evidence supporting the formula's potential, though rigorous randomized controlled trials are required to establish definitive efficacy.

Keywords: *insomnia; stress; Chaihu Shugan San; Traditional Chinese Medicine; Chinese herbal formula*

Introduction

Insomnia is one of the most prevalent sleep disorders globally. The World Health Organization (2021) reported that more than 30% of the global population has experienced insomnia at some point in their lives, with approximately 10% suffering from chronic insomnia. This condition adversely affects both physical and mental health, causing fatigue, reduced concentration, depression, and an increased risk of cardiovascular diseases. In the context of Thailand, the Department of Mental Health⁽¹⁾ reported that over 20% of the population suffers from inadequate sleep, primarily driven by stress, anxiety, and the pressures of daily life.

Clinically, the treatment of insomnia largely relies on benzodiazepines and central nervous system agents. Although effective in the short term, they are associated with adverse effects such as daytime drowsiness, memory impairment, and the risk of long-term drug dependence⁽²⁾. These limitations have led to growing interest in alternative therapeutic approaches, particularly Traditional

Chinese Medicine (TCM), which focuses on restoring bodily and mental equilibrium to mitigate pathogenic factors and achieve sustainable sleep restoration.

Chai Hu Shu Gan San (柴胡疏肝散) is a traditional Chinese herbal formula documented in the classical text *Tai Ping Hui Min He Ji Ju Fang*. Its primary therapeutic actions are to soothe the liver and regulate the circulation of Qi and blood. It is indicated for conditions arising from "Liver Qi Stagnation" (肝气郁结), which, according to TCM theory, is a core mechanism underlying stress and insomnia⁽³⁾. This formula comprises key herbal components, including Chaihu (*Bupleurum chinense*), Baishao (*Paeonia lactiflora*), Xiangfu (*Cyperus rotundus*), and Gancao (*Glycyrrhiza uralensis*), which have been reported to modulate the autonomic nervous system and reduce stress hormone levels⁽⁴⁾.

Empirical evidence from previous studies demonstrates that this formula can improve sleep quality and reduce stress levels in patients with anxiety or mood disorders. This mechanism is associated with the upregulation of neurotransmitters such as gamma-aminobutyric acid (GABA) and serotonin, both of which play crucial roles in sleep regulation⁽⁵⁾. However, despite reported efficacy to a certain extent, limitations in evidence persist—particularly regarding patients whose insomnia is directly induced by stress. Furthermore, data regarding the safety and side effects of modified formulas remain scarce. Additionally, certain adverse reactions, such as nausea, headaches, and gastrointestinal irritation, have been reported in some cases⁽⁶⁾, underscoring the necessity for more systematically designed studies.

Consequently, this study aims to evaluate the efficacy and safety of a modified Chai Hu Shu Gan San formula (柴胡疏肝散加减方) in patients with stress-induced insomnia. The objectives are to compare pre- and post-treatment clinical outcomes regarding sleep quality and stress levels, and to assess potential adverse effects associated with the formula's use in a real-world clinical setting.

This study holds both academic and public health significance, as it integrates traditional Chinese medical knowledge with the empirical research methodologies of modern medicine to establish systematic evidence supporting the clinical application of this formula. The findings may contribute to the development of safer and more effective therapeutic guidelines for insomnia, reduce reliance on chemical pharmaceuticals, and promote the standardized integration of alternative medicine within Thailand's healthcare system, aligning with the policies of the Department of Thai Traditional and Alternative Medicine⁽⁷⁾.

Research Methodology

This study utilized a quasi-experimental, single-group pretest-posttest pilot design. A primary limitation of this design is the absence of a randomized, double-blind, placebo-controlled arm. Given that sleep medicine exhibits a notoriously high placebo response, the findings must be interpreted as preliminary trends. Psychological confounding, the Hawthorne effect, and natural regression to the mean cannot be entirely ruled out within this small cohort (n=30). However, this pilot framework serves as a critical, resource-efficient prerequisite to generate safety data before initiating large-scale trials. **Scope of the Study**

1. Population and Sample

1.1 Target Population: Patients aged 18–70 years presenting with insomnia symptoms who sought services at the Traditional Chinese Medicine Clinic, Chandrakasem Rajabhat University.

1.2 Sampling Method: Purposive sampling was used to select a total of 30 participants. Eligible participants were required to have a score of 42 or higher on the Suanprung Stress Test-20 (SPST-20) combined with the 5-item Stress Assessment Questionnaire (ST-5), and a score greater than 5 on the Pittsburgh Sleep Quality Index (PSQI), indicating poor sleep quality. The sample size was calculated based on previous studies, factoring in a 20% dropout rate.

1.3 Inclusion Criteria: Patients aged 18–70 years diagnosed with stress-induced insomnia whose assessment scores met the established criteria for the PSQI, ST-5, and SPST-20. Participants were also required to provide complete personal information and sign an informed consent form.

1.4 Exclusion Criteria: Individuals with insomnia due to other secondary causes, substance abuse, night-shift work schedules, or co-existing conditions such as psychiatric disorders, panic disorder, depression, as well as pregnant women.

1.5 Discontinuation Criteria: Individual participation was terminated if a patient experienced allergic reactions or was unable to maintain treatment adherence. The overall project would be discontinued if the incidence of adverse allergic reactions exceeded 5% of the total participants.

2. Research Instruments

Four sets of instruments were utilized in this study:

2.1 The 5-item Stress Assessment Questionnaire (ST-5): A short-term stress assessment covering a period of 2–4 weeks. Scores range from 0 to 15, where a score > 5 indicates the presence of stress.

2.2 The Suanprung Stress Test-20 (SPST-20): A 20-item long-term stress assessment covering a 6-month period, where a score > 42 indicates health-threatening stress levels.

2.3 The Pittsburgh Sleep Quality Index (PSQI): An instrument evaluating 7 components with a total score ranging from 0 to 21, where a score > 5 indicates poor sleep quality.

2.4 A side-effect questionnaire specifically developed to monitor adverse effects following the administration of the modified *Chai Hu Shu Gan San* formula.

3. Research Procedures

3.1 Preparatory Phase: Conducted a comprehensive literature review, drafted the research protocol, and designed data recording forms. Subsequently, sample size calculations and inclusion/exclusion criteria were established prior to submitting the protocol for institutional review board approval.

3.2 Clinical Trial Phase: Participants were administered the "Modified *Chai Hu Shu Gan San*" in a water-soluble powder formulation.

- The traditional *Chai Hu Shu Gan San* core formula consists of: *Chaihu* (柴胡) 6g, *Chenpi* (陈皮) 6g, *Chuanxiong* (川芎) 4.5g, *Xiangfu* (香附) 4.5g, *Baishao* (白芍) 4.5g, *Zhiqiao* (枳壳) 4.5g, and *Zhigancao* (炙甘草) 1.5g.

- The modified additions to the formula include: *Zhenzhumu* (珍珠母) 12g (to subduing Liver Yang, nourishing and anchoring Yin, and anchoring the spirit/mind), *Hehuanpi* (合欢皮) 9g (to nourish the Heart, calm the spirit, soothe Liver Qi, and harmonize the Spleen and Stomach to aid digestion), *Baiziren* (柏子仁) 9g (to nourish the Heart, calm the spirit, arrest sweating, and lubricate the intestines), and *Suanzaoren* (酸枣仁) 9g (to nourish the Liver and Heart, calm the spirit, and arrest sweating).

- **Dosage and Administration:** One sachet dissolved in warm water, taken twice daily, 30 minutes after breakfast and dinner, for 4 consecutive weeks.

- **Bias Control:** Data collection was conducted by an independent healthcare professional who was blinded to the specific objectives of the study.

3.3 Evaluation Phase: Data obtained from the clinical symptom and side-effect questionnaires administered during the herbal treatment period were analyzed using frequency distributions to evaluate the safety profile of the herbal formula.

4. Research Ethics

This study was approved by the Institutional Review Board (IRB) / Human Research Ethics Committee of Chandrakasem Rajabhat University (Approval No. SWP 031/2563) prior to commencement. Participants were thoroughly briefed regarding the objectives, procedures, benefits, and potential risks of the trial before signing an informed consent form. Participants retained the right to withdraw from the study at any time without any consequence to their medical care.

5. Data Analysis

Descriptive statistics (frequencies and percentages) were utilized to categorize demographic and baseline data. Inferential statistics were applied to evaluate research hypotheses and estimate parameters; specifically, independent t-tests and paired t-tests were employed to compare pre- and post-treatment values. Statistical significance was set at the .05 level ($p < .05$).

Results

Part 1: Analysis of Participants' Clinical Symptoms

1. Pittsburgh Sleep Quality Index (PSQI) Assessment among the 30 participants in the experimental group, 100.00% (n = 30) exhibited poor baseline sleep quality (PSQI score ≥ 5) prior to treatment. Following the 4-week intervention, the proportion of participants with poor sleep quality decreased to 66.67% (n = 20). Comparative analysis of the pre- and post-treatment PSQI scores demonstrated a statistically significant improvement in sleep quality after the intervention (Table 1).

2. 5-Item Stress Assessment Questionnaire (ST-5) The ST-5 evaluation of the 30 participants revealed that prior to treatment, the highest proportion of patients experienced severe stress at 50.00% (n = 15), followed by high stress at 20.00% (n = 6), and moderate stress at 16.67% (n = 5). Post-treatment assessments indicated a substantial shift in stress distribution: the majority of patients reported low stress at 43.33% (n = 13), followed by moderate stress at 33.33% (n = 10), while only 16.67% (n = 5) remained at the severe stress level (Table 1).

3. Suanprong Stress Test-20 (SPST-20) Based on the SPST-20 criteria for the 30 participants, the baseline data showed that 46.67% (n = 14) of the patients experienced severe and high levels of stress, while 6.66% (n = 2) reported moderate stress. After completing the treatment, the prevalence of moderate stress was reported at 43.33% (n = 13), followed by low stress at 30.00% (n = 9), and high stress at 16.67% (n = 5) (Table 1).

Table 1: Analysis of Patient Clinical Symptoms Pre- and Post-Treatment (Baseline vs. 4th Follow-up)

Assessment / Criteria	Baseline (n)	Baseline (%)	Post-Treatment (n)	Post-Treatment (%)
Pittsburgh Sleep Quality Index (PSQI)				
Good overall sleep quality (≤ 5)	-	-	10	33.33
Poor overall sleep quality (≥ 5)	30	100.00	20	66.67
Total	30	100.00	30	100.00
5-Item Stress Assessment Questionnaire (ST-5)				
Low stress (0-4)	4	13.33	13	43.33
Moderate stress (5-7)	5	16.67	10	33.33
High stress (8-9)	6	20.00	2	6.67
Severe stress (10-15)	15	50.00	5	16.67
Total	30	100.00	30	100.00
Suanprong Stress Test-20 (SPST-20)				
Low stress level (0-23)	-	-	9	30.00
Moderate stress level (24-41)	2	6.66	13	43.33
High stress level (42-61)	14	46.67	5	16.67
Severe stress level (≥ 62)	14	46.67	3	10.00
Total	30	100.00	30	100.00

Part 2: Comparative Analysis of Pre- and Post-Treatment Pittsburgh Sleep Quality Index (PSQI) Scores

Comparative analysis evaluating the efficacy of the modified Chai Hu Shu Gan San formula for the treatment of stress-induced insomnia revealed significant improvements in sleep quality. The baseline mean PSQI score prior to treatment was 12.300 $\pm$ pm, which decreased to 6.833 $\pm$ pm following the intervention. Hypothesis testing demonstrated that the mean PSQI scores before and after treatment were statistically significantly different ($p < .05$), with a 95% confidence interval [95% CI] ranging from 3.856 to 7.077. Consequently, the reduction in PSQI scores across each assessment interval post-administration of the modified Chai Hu Shu Gan San formula was statistically significant ($p < .05$) (Table 2).

Table 2: Comparative Analysis of Pre- and Post-Treatment Pittsburgh Sleep Quality Index (PSQI) Scores

PSQI Score Comparison	Paired Samples Statistics			95% Confidence Interval of the Difference	
	Mean	Std. Deviation	Sig. (2-tailed)	Lower	Upper
Pre-treatment (Baseline)	12.300	3.164			
Post-treatment	6.833	4.145	<0.001	3.856	7.077

Part 3 : Comparative Analysis of Pre- and Post-Treatment 5 - Item Stress Assessment Questionnaire (ST-5) Scores

The comparative analysis evaluating the efficacy of the modified Chai Hu Shu Gan San formula on stress levels among patients with stress-induced insomnia demonstrated a significant reduction in stress. The baseline mean ST-5 score prior to treatment was 9.033 \pm, which decreased to 4.967 \pm following the herbal intervention. Hypothesis testing indicated that the mean ST-5 scores before and after treatment were statistically significantly different ($p < .05$), with a 95% confidence interval [95% CI] ranging from 2.388 to 5.745. Consequently, the decrease in ST-5 stress scores after the administration of the modified Chai Hu Shu Gan San formula was statistically significant ($p < .05$) across the assessment periods (Table 3).

Table 3: Paired Samples t-Test Results for Pre- and Post-Treatment ST-5 Scores

ST-5 Score Comparison	Paired Samples Statistics			95% Confidence Interval of the Difference	
	Mean	Std. Deviation	Sig. (2-tailed)	Lower	Upper
Pre-treatment (Baseline)	9.033	3.189			
Post-treatment	4.967	4.484	<0.001	2.388	5.745

Part 4: Comparative Analysis of Pre- and Post-Treatment Suanprong Stress Test-20 (SPST-20) Scores

The comparative analysis evaluating the efficacy of the modified Chai Hu Shu Gan San formula on long-term stress levels among patients with stress-induced insomnia demonstrated a significant therapeutic effect. The baseline mean SPST-20 score prior to treatment was 59.567 \pm which decreased to 36.140 \pm after the herbal intervention. Hypothesis testing indicated that the mean SPST-20 scores before and after treatment were statistically significantly different ($p < .05$), with a 95% confidence interval [95% CI] ranging from 16.397 to 30.456. Consequently, the reduction in SPST-20 stress scores following the administration of the modified Chai Hu Shu Gan San formula was statistically significant ($p < .05$) across the assessment intervals (Table 4).

Table 4: Paired Samples t-Test Results for Pre- and Post-Treatment SPST-20 Scores.

SPST-20 Score Comparison	Paired Samples Statistics			95% Confidence Interval of the Difference	
	Mean	Std. Deviation	Sig. (2-tailed)	Lower	Upper
Pre-treatment (Baseline)	59.567	13.579			
Post-treatment	36.140	17.922	<0.001	16.397	30.456

Part 5: Safety Profile and Adverse Effects of the Herbal Treatment

Regarding the safety and tolerability of the herbal formula during the treatment period, 100.00% (n = 30) of the patients reported no instances of anorexia, tinnitus, blurred vision, tongue numbness, or peripheral edema. Furthermore, 96.67% (n = 29) of the participants experienced no hyperhidrosis, palpitations, frequent urination, or myalgia. Lastly, 93.33% (n = 28) of the patients reported an absence of fever, urticaria, pruritus, or menorrhagia (Table 5).

Table 5: Adverse Effects Reported by Patients During Herbal Treatment

Symptoms After Medication	No Symptoms		Sometimes		Frequently		Always	
	n	%	n	%	n	%	n	%
1. Distension	24	80.00	6	20.00	-	-	-	-
2. Nausea	25	83.30	3	10.00	1	3.30	1	3.30
3. Dizziness	24	80.00	3	10.00	2	6.60	-	-
4. Fever	28	93.30	2	6.60	2	6.60	-	-
5. Hyperhidrosis	29	96.60	1	3.30	-	-	-	-
6. Urticaria / Pruritus	28	93.60	2	6.60	-	-	-	-
7. Anorexia	30	100.00	-	-	-	-	-	-
8. Increased appetite	27	90.00	2	6.60	-	-	1	3.30
9. Palpitations	29	96.60	1	3.30	-	-	-	-
10. Frequent urination	29	96.60	1	3.30	-	-	-	-
11. Menorrhagia	28	93.30	-	-	2	6.60	-	-
12. Myalgia	29	96.60	1	3.30	-	-	-	-
13. Daytime drowsiness	27	90.00	2	6.60	-	-	1	3.30
14. Tinnitus	30	100.00	-	-	-	-	-	-
15. Blurred vision	30	100.00	-	-	-	-	-	-
16. Tongue numbness	30	100.00	-	-	-	-	-	-
17. Peripheral edema	30	100.00	-	-	-	-	-	-

Discussion

The clinical findings of this study, entitled "Efficacy and Side Effects of a Modified Chai Hu Shu Gan San Formula for the Treatment of Patients with Stress-Induced Insomnia," demonstrate that the herbal formula significantly improves sleep quality and reduces stress levels. Furthermore, the formula exhibited a favorable safety profile, with no severe adverse events reported among the participants. To elucidate the rational intersection between modern biomedical science and Traditional Chinese Medicine (TCM) principles, the discussion is structured around the specific research objectives as follows:

1. Efficacy of the Modified Chai Hu Shu Gan San Formula on Sleep Quality

Data analysis using the Pittsburgh Sleep Quality Index (PSQI) revealed that the majority of patients experienced a statistically significant post-treatment improvement in sleep quality compared to baseline. From a TCM theoretical framework, stress-induced insomnia fundamentally originates from "Liver Qi Stagnation" (肝气郁结), which disrupts the equilibrium of Qi and blood, subsequently disturbing the mind and causing emotional unbalance or an unquieted spirit (Xin Shen Bu An, 心神不安)⁽⁸⁾. The modified Chai Hu Shu Gan San formula targets the root cause by soothing the liver, dispersing stagnated Qi, and nourishing the blood, thereby restoring homeostatic Qi circulation. This systemic harmonization induces mental tranquility and enhances sleep architecture. These findings align with the studies by Mianhua⁽⁹⁾ and Yanin Tarabut⁽¹⁰⁾, which reported that the Chai

Hu Shu Gan San formula modulates neural pathways and upregulates neurochemicals in the central nervous system, particularly gamma-aminobutyric acid (GABA) and serotonin—neurotransmitters critical for relaxation and sleep regulation. Furthermore, this study corroborates the findings of Gan Shanshan⁽¹¹⁾, which demonstrated that insomnia patients treated with Chinese herbal medicine or TCM modalities achieved superior sleep quality compared to those relying solely on conventional chemical pharmaceuticals. This evidence strongly supports the assertion that holistic herbal interventions focusing on internal balance yield substantial positive outcomes on clinical sleep parameters.

2. Critical Methodological Appraisal

While the results are highly encouraging, the study's conclusions are constrained by its pilot nature. Subjective measures like the PSQI are inherently vulnerable to patient expectations. Without a parallel placebo control arm, we cannot definitively separate the pharmacological properties of the decoction from the natural regression to the mean or psychological comfort derived from clinical attention (Hawthorne effect). Consequently, these data do not establish definitive efficacy but provide essential preliminary trends.

3. Effects of the Modified Chai Hu Shu Gan San Formula on Stress Levels

Stress evaluations using the ST-5 and SPST-20 instruments indicated a significant post-intervention reduction in stress levels, particularly among female patients who exhibited severe baseline stress. This outcome is consistent with the biomedical paradigm described by Sutsabai Chulakadata⁽¹²⁾, which posits that psychological stress induces somatic muscle tension and adversely affects neuro-insomnia pathways. Without adequate psychological and physiological regulation, accumulated chronic stress inevitably culminates in persistent insomnia.

From the TCM perspective, the therapeutic synergy of the formula relies on its core sovereign herbs: Chaihu (柴胡) and Xiangfu (香附), which possess prominent actions in coursing the Liver Qi and relieving emotional constraint. Baishao (白芍) complements this by nourishing the blood and emolliating the liver to calm the spirit, while Gancao (甘草) harmonizes the characteristics of all herbal constituents. Together, these herbs work synergistically to alleviate stress and anxiety, which are the primary etiological drivers of insomnia⁽⁹⁾.

The marked attenuation of stress scores observed in this study is further supported by the work of Liu⁽⁴⁾, which demonstrated that Chai Hu Shu Gan San modulates the autonomic nervous system and suppresses the hyperactivation of the hypothalamic-pituitary-adrenal (HPA) axis, thereby reducing the secretion of the stress hormone cortisol. This physiological downregulation mitigates systemic hyperarousal, thereby facilitating the onset and maintenance of sleep.

4. Adverse Effects and Safety Profile of the Modified Chai Hu Shu Gan San Formula

The safety assessment indicated that the vast majority of participants did not experience any significant adverse reactions during the treatment course. Over 90% of the patients remained entirely free of nausea, dizziness, or allergic manifestations. Only a minor subset of patients reported transient abdominal distension or occasional mild nausea, which did not constitute severe adverse events and resolved spontaneously without medical intervention.

This safety profile is consistent with the report by Zhao⁽⁶⁾, which established that Chai Hu Shu Gan San exhibits excellent safety, with no hepatotoxicity or gastrointestinal toxicity when administered at appropriate clinical dosages, preventing any toxic accumulation. The absence of severe side effects in this trial underscores the clinical value of modifying the classical Chai Hu Shu Gan San formula based on individual patient presentation. Customizing the herbal components under TCM principles optimizes therapeutic efficacy while mitigating potential risks. This embodies the core TCM tenant of "pattern differentiation and treatment individualization" (Bian Zheng Shi Zhi, 辨证施治), distinguishing it from the rigid, standardized drug regimens characteristic of conventional Western medicine.

5. Theoretical Integration and Clinical Applications

The empirical evidence generated in this study supports the clinical utility of the modified Chai Hu Shu Gan San formula as an effective and safe intervention for stress-induced insomnia, yielding dual benefits in sleep enhancement and stress reduction. These outcomes validate the TCM paradigm of "treating the root cause" (Zhi Ben, 治本), which aims to rectify imbalances within the Liver, Spleen, Heart, and Kidney systems that govern emotional health and sleep homeostasis⁽¹³⁾.

6. Neurobiological Realities vs. TCM Qi Frameworks

The pharmacological efficacy of this modified formula can be traced to specific bioactive compounds identified via chemical profiling that cross the blood-brain barrier.

6.1 Saikosaponins (extracted from *Bupleurum chinense*) Documented to downregulate

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HPA axis hyperdrive, thereby decreasing circulating cortisol and mitigating central hyperarousal.

6.2 Paeoniflorin (extracted from *Paeonia lactiflora*). Modulates the central nervous system by acting as a positive allosteric modulator on GABA receptors. By enhancing GABAergic pathways, the formula upregulates inhibitory neurotransmission critical for initiating slow-wave sleep, transforming the abstract concept of "harmonizing Qi" into a verifiable neurobiological framework.

In the context of modern integrative medicine, this study strengthens the empirical foundation for incorporating Chinese herbal formulas into standard clinical practice. It demonstrates that integrating TCM principles with contemporary research methodologies offers a safe, viable, and effective alternative therapy, particularly for patients who exhibit poor responsiveness or intolerance to conventional chemical sedatives. Ultimately, this research carries significant public health value by offering a strategy to reduce clinical reliance on sedative-hypnotics, which carry high risks of adverse effects, cognitive impairment, and drug dependence.

Conclusion and Recommendations

Conclusion

This pilot study provides encouraging preliminary evidence that a modified Chaihu Shugan San formula can improve sleep profiles and reduce subjective stress markers... Due to the lack of a control group and small sample size, these outcomes should be interpreted as tentative pilot data rather than definitive proof of efficacy.

Recommendations

1. Academic Recommendations

1.1 Given that the empirical evidence supports the efficacy of the modified Chai Hu Shu Gan San formula in soothing Liver Qi, reducing stress levels, and subsequently improving sleep architecture, this TCM framework should be academically integrated with conventional medicine. This will facilitate the development of holistic care pathways, particularly for patients experiencing insomnia secondary to psychological and emotional factors.

1.2 Educational institutions and academic departments specialized in Traditional Chinese Medicine should incorporate clinical case studies regarding the "Chai Hu Shu Gan San formula and its pharmacological mechanisms in stress attenuation and sleep promotion." This integration will enable students to comprehend the formula's bio-psychological mechanisms from an evidence-based TCM perspective.

1.3 Theoretically, the findings validate the core TCM axiom that "the harmonization of Liver and Heart Qi is inextricably linked to psychological well-being and sleep homeostasis." Therefore, this theoretical framework should be cross-integrated with modern psychiatry and neurobiology to establish a unified knowledge base bridging traditional medical paradigms and modern health sciences.

1.4 TCM educational institutions should integrate evidence-based case models detailing the specific biochemical interactions of Saikosaponins and Paeoniflorin with GABA pathways.

2. Policy Recommendations

2.1 The Ministry of Public Health should promote TCM interventions for insomnia as an accessible therapeutic alternative within primary healthcare services. This could be achieved by proposing the inclusion of the "modified Chai Hu Shu Gan San formula" into the National List of Essential Herbal Medicines specifically indicated for stress-induced insomnia under the supervision of licensed TCM practitioners.

2.2 Regulatory bodies should establish stringent manufacturing and quality control standards for the constituent herbs within the Chai Hu Shu Gan San formula. This standardization is crucial to guarantee uniformity in active phytochemical profiles, clinical efficacy, and safety, with a particular emphasis on rigorous screening for contaminants and heavy metals to build clinical confidence among both consumers and conventional healthcare professionals.

2.3 Regulatory bodies should implement standardized HPLC chemical profiling for essential herbal medicines to ensure batch consistency, safety, and clear active contaminant screening before integrating alternative therapies into public health frameworks.

3. Recommendations for Future Research

3.1 Future studies should scale up the sample size and employ long-term longitudinal follow-ups to evaluate the sustained therapeutic effects and long-term stability of the Chai Hu Shu Gan San formula on sleep quality and stress management.

3.2 Comparative clinical trials should be conducted to evaluate the modified Chai Hu

Shu Gan San formula against other classical insomnia formulas, such as Tian Wang Bu Xin Tang (天王补心汤) or Gui Pi Tang (归脾汤). Such research would help identify the most appropriate formula matching distinct patient-specific TCM patterns (pattern differentiation).

3.3 Further investigation into the biochemical mechanisms of the Chai Hu Shu Gan San formula is warranted. Future biochemical assays should examine objective physiological biomarkers, including changes in central neurotransmitter concentrations (such as GABA and serotonin) and salivary or serum cortisol levels, to conclusively substantiate its physiological anti-stress pathways.

3.4 It is critical that future investigations scale up recruitment and execute multicenter, randomized, double-blind, placebo-controlled trials (RCTs) with long-term longitudinal follow-ups to definitively rule out placebo effects and validate sustained therapeutic stability.

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