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Exploring the Efficacy of Herbal & Medicinal Plants Native to China and Thailand as a Complementary & Alternative Treatment in Mitigating Mild-to-Moderate COVID-19 Symptoms

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**Exploring the Efficacy of Herbal & Medicinal Plants Native to China and Thailand as a
Complementary & Alternative Treatment in
Mitigating Mild-to-Moderate
COVID-19 Symptoms**

By

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NURS 4500: Nursing Research and Senior Thesis

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Abstract

Background

In December 2019, the World Health Organization (WHO) was informed of an outbreak of an unknown cause of pneumonia-like symptoms in residents concentrated in Wuhan, China; this marked the start of China's epidemic, which transformed into a pandemic affecting all continents of the world. The cause of the pneumonia-like symptoms was found to be due to the growth and development of the virus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which spreads through an infected person's respiratory droplets through activities such as talking, coughing, and sneezing. With COVID-19 vaccine manufacturers available worldwide, even the economically and technologically forward countries such as Thailand and China contain pockets of residents without access to the COVID-19 vaccine to this day.

Objective

This paper will examine the potential use of herbal and medicinal plants as a form of treatment in mitigating mild to moderate COVID-19 symptoms in diagnosed COVID-19 positive residents in Thailand and China.

Methods

A comprehensive literature review was performed using PubMed and references cited in UpToDate. Seven articles that focused on the topic were chosen for a narrative review. Based upon the research literature, a proposal for further mixed-method study is presented.

Keywords: Epidemic, pandemic, COVID-19, SARS-CoV-2, China, Thailand, complementary and alternative medicine, mild to moderate symptoms

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Introduction

In December 2019, the World Health Organization (WHO) was informed of an outbreak of an unknown cause of pneumonia-like symptoms in Wuhan, China residents; this marked the start of China's epidemic, which in the blink of an eye transformed into a pandemic affecting all continents of the world (McIntosh et al., 2021). The cause of the pneumonia-like symptoms was due to the severe acute respiratory syndrome coronavirus 2 virus (SARS-CoV-2) which spreads through an infected person's respiratory droplets through activities such as talking, coughing, and sneezing. With these droplets being viable for up to a few days, the WHO emphasized the importance of maintaining a physical distance of at least six feet, wearing a facial covering over the nose and mouth, and strict hand hygiene as crucial steps in preventing the spread of coronavirus disease of 2019 (COVID-19).

Although a handful of vaccine manufacturers worldwide have surpassed the research and development phase and produced their formulated vaccine to combat the rapid spread of COVID-19, even the economically and technologically forward countries such as Thailand and China to this day contain pockets of residents without access to the COVID-19 vaccine. Therefore, the purpose of this literature review and proposal for further study is to explore the potential for Chinese and Thai herbal therapies to manage mild to moderate COVID-19 symptoms.

The research question is:

What is the efficacy of native Thai and Chinese herbal and medicinal plants as a nonpharmacological intervention in mitigating mild-to-moderate COVID-19 symptoms for patients in China compared to Thailand?

Literature Review

In this narrative literature review, seven articles were obtained from databases such as PubMed and UpToDate. The objective of this process is to identify articles demonstrating the efficacy of herbal and medicinal plants native to China and Thailand in mitigating mild to moderate COVID-19 symptoms. The articles found were narrowed by the year of publication, type of research the literature was categorized as, and region the literature is concentrating on. The acceptable time range of published studies needed to fall within December 2019 (start of the COVID-19 widespread) until the current day (November 2021). The last search strategy used pertains to the studied region, which for this particular literature review is focused on Thailand and China.

The search terms used included terms such as herbal plants, medicinal plants, COVID-19, traditional Eastern medicine, Thailand, China, SARS-CoV-2, antiviral, treatment, prevention, herbal, traditional Chinese medicine, ethnobotany, mild COVID-19 symptoms, mild to moderate COVID-19 symptoms, moderate COVID-19 symptoms, meta-analysis, systematic review, coronavirus, and anti- SARS-CoV-2. An example of a search entry used on PubMed was COVID-19 [OR] SARS-CoV-2 [AND] China [OR] Thailand [AND] herbal plants [OR] medicinal plants [AND] treatment.

In the process of sifting through the databases available through Dominican University of California's library webpage, PubMed, UpToDate, Cochrane Library, and the US National Library of Medicine National Institute of Health (PMC) yielded the most relevant information regarding the proposed topic. Seven articles selected by the mentioned criteria were chosen to support the research questions posed regarding the efficacy of herbal and medicinal plants native to China and Thailand in relieving mild to moderate COVID-19 symptoms are organized into

three categories: herbal and medicinal plants used to mitigate mild to moderate COVID-19 symptoms in Thailand, China, and studies of adaptations made to traditional Chinese medicine used for COVID-19 patients.

The Use of Herbal and Medicinal Plants Native to Thailand for Mitigating Mild to Moderate COVID-19 Symptoms

From January 3, 2020, to October 18, 2021, COVID-19 cases in Thailand ranks 24 of 223, and 69.8 million people in 2020, there were 1,793,812 reported positive COVID-19 cases, 1,668,250 recoveries, 18,336 deaths, and 10,111 daily new cases (*Thailand: Who coronavirus disease (covid-19) dashboard with vaccination data*, n.d.). In terms of COVID-19 vaccination status, although 59,258,667 vaccine doses have been administered, 35,462,170 people have been vaccinated with at least one dose and 23,796,497 are considered as fully vaccinated (dependent on the vaccine manufacturer). Three articles were chosen to demonstrate the use of herbal and medicinal plants in Thailand by identifying which species of plants contain anti-SARS-CoV-2 mechanisms, which parts of the plant have the highest antiviral effect, and uses among Thai Karen and Hmong residents.

The article titled, “High-content screening of Thai medicinal plants reveals *Boesenbergia rotunda* extract and its component Panduratin A as anti-SARS-CoV-2 agents” details the extensive work to develop a high-content screening method for potential antiviral plants (Kanjanasirirat et al., 2020). The researchers used SARS-CoV-2 nucleoprotein detection to measure the amount of plaque reduction assay and dose-response analysis to indicate the effectiveness of the identified herbal and medicinal plants in viral suppression. With a sample size of 122 Thai medicinal plants, the researchers developed a quantitative experimental research design using a two-step approach: pre-entry and post-infectious treatments. The pre-entry

approach of the quantitative experiment was described as pre-incubating each of the Thai herbal plants' natural extracts with the SARS-CoV-2 virus strain into a test tube before being inoculated. The post-infectious portion of their experiment was carried out by introducing the natural extracts to the cell culture after viral infection in which the effectiveness of the viral suppression activity was observed for the duration of the experiment.

Of the three plant extracts experimented on, Panduratin A (extract named *B. rotunda*) demonstrated the highest inhibitory concentration against the SARS-CoV-2 virus during both the pre-entry and post-infection phase as well as successfully suppressing viral growth when exposed to extracted human's airway epithelial cells in a controlled manner. Three main strengths were identified: the results from their study were thoroughly performed and collected as they measure the outcome of the chosen medicinal plants through both dose-response relationship and plaque assay reduction, a large study sample of one hundred twenty-two potential native Thai medicinal plants to be tested were studied in detail in preparation for their experiment, and beyond testing the impact of the *B. rotunda* extract from the Panduratin A plant on the post-infection phase, the researchers expanded their study and tested whether the two components would have an effect for pre-entry treatment which also showed successful results. One major limitation the authors stated about their product was, "it has prompted us to develop, for the first time, a high-content screening platform" which indicates a possible lack of credibility with the results found as their same study has not been able to be replicated by others in a way to obtain the same experimental results (Kanjanasirirat et al., 2020, pg. 2).

The next article to be included in this comprehensive literature review is "Rapid selection of *Andrographis paniculata* medicinal plant materials based on major bioactive using near-infrared spectroscopy" which is a quantitative study focusing on developing experimental

research that determines the efficacy of the *Andrographis paniculata* Thai medicinal plant on its antiviral activity against SARS-CoV-2. For this study, one hundred and seventy samples (collected from ten provinces of Thailand including Bangkok, Nakhon Pathom, Nonthaburi, Praeeenburi, Phetchaburi, Phetchabun, Mahasarakham, Suphanburi, and Sa Kaeo) of the plant were obtained over two years which were categorized into four groups: aerial, stems, leaves, and stems mixed with leaves (Kasemsumran et al., 2021). Fresh samples of the *Andrographis paniculata* plant were made into a powder form being dried at 50 degrees Celsius for ten hours and then mechanically ground, then placed into their respective test tube for near-infrared spectrophotometer (NIR) testing.

The NIR technique was chosen by the researchers as the plants did not have to be extracted prior and had the lowest risk of destroying or tampering with the sample in the process. Additionally, because of the difficulty in distinguishing the parts of the plant after thorough grinding, this was another reason which prompted the researchers to create an experiment to quantify the contents with the NIR banding method. The Partial Least Squares-Discriminant Analysis method (PLS-DA) showed success in classifying the results in the controlled and experimental test tubes. From the different plant parts included in the experiment, the leaves only test tubes were found to yield the highest content of bioactive compounds as well as andrographolide (AP1) whereas in the test tubes which contained a mixture of the *Andrographis paniculate* leaves and arterial parts contained the highest amount of dehydroandrographolide (AP3). AP1 is a chemical compound that interferes with the reproduction of malignant cells such as those replicated by the SARS-CoV-2 virus, while AP3 is found to be an anti-inflammatory and antiviral agent.

The last article which magnifies the use of native Thai herbal and medicinal plants in mitigating mild COVID-19 symptoms is “Medicinal Plants Used for Treating Mild Covid-19 Symptoms Among Thai Karen and Hmong”. This study includes a compiled literature review and qualitative study executed in the form of field interviews with a total of 1,230 use reports of medicinal plants among residents in the Thai Karen (555 reports) and Hmong (675 reports) communities with mild COVID-19 symptoms (Phumthum et al., 2021). Additionally, sixteen local healers were included in this study as they primarily use medicinal herbs and ethnobotany practices to treat the symptoms experienced. Four hundred ninety-one plant species were identified among the Thai Karen and Hmong communities to alleviate symptoms of fever (commonly *Acorus calamus*, *Strobilanthes cusia*, and *Melicope glomerata*), cough (commonly *Zingiber officinale*, *Blumea balsamifera*, and *Elephantopus scaber*), and diarrhea (*Psidium guajava* and *Zingiber ottensii*) labeled as mild COVID-19 symptoms by the World Health Organization (WHO).

With the rapid spread of COVID-19 worldwide, identification of these plants native to Thailand provides significant information which could alleviate the strain on healthcare workers, institutions, as well as benefit residents in Thailand who may be isolated due to living situations or access to healthcare and the COVID-19 vaccine.

Using Traditional Chinese Medicine Alongside Western Medicine

Examining the Use of Integrative Medicine: Using Traditional Chinese Medicine Alongside Western Medicine

From January 3, 2020, to October 18, 2021, China ranks 133 of 223 as there have been a total of 125,254 confirmed cases, 5,695 deaths, and a total of 2,228,305,003 vaccine doses administered (1,014,573,856 people being fully vaccinated) (*China: Who coronavirus disease (covid-19) dashboard with vaccination data*, n.d.). To examine the use of integrative medicine

using traditional Chinese medicine (TCM) alongside conventional Western medicine (CWM), two primary articles demonstrate the benefits of using both practices concurrently for better outcomes in patients diagnosed with COVID-19.

“Chinese herbal medicine for coronavirus disease 2019: A systematic review and meta-analysis” summarizes the results of eighteen randomized controlled trials on 2,275 COVID-19 positive patients using traditional Chinese herbal medicine in mainland China (Xiong et al., 2020). Two groups were studied: the control group receiving conventional Western medicine and/or a combination of Chinese herbal medicine placebo while the treatment (experimental) group was treated by Chinese herbal medicine and/or alongside conventional Western medicine. To ensure continuity in the interventions between the two groups, the medication used for the Western medicine practice was given by the same dosage, route of administration, and usage. The experimental results were primarily monitored in the form of multiple lung CT scans throughout the study period and measuring the clinical cure rate, length of hospital stay, and pertinent inflammatory biomarkers which snapshot the patient’s recovery such as white blood cells, lymphocytes, C-reactive protein, and neutrophils.

From this experiment, the risk reduction (RR) for lung CT improvement among 749 the experimental Chinese herbal medicine (CHM) and 653 controlled conventional Western medicine (CWM) participants was 1.23, death in 256 CHM and 207 CWM showed a RR of 0.34 or indicating very little difference, and clinical symptoms (including sore throat, dry throat, chest tightness, fever, and fatigue) were shown to be significantly improved through the use of scoring the individual’s clinical symptoms. To gain a deeper understanding of the use of integrative medicine, the risk reduction rate was compared between the CHM (experimental) and CWM (controlled) groups that showed significant improvement in cough among 240 CHM and 182

CWM participants of an RR value of 1.50, fever being significantly reduced within 433 patients with a weight mean difference of -0.60, fatigue reduction among 167 patients in CHM and 140 in CWM with a RR value of 1.73, TCM syndrome reduction within 141 CHM participants with a weight mean difference of -6.60. In terms of the laboratory markers monitored throughout the study, although there were no significant differences in the two groups in improving white blood cell and lymphocyte count, in six trials the C-reactive protein showed a significant reduction in the experimental group with a weight mean distribution of -8.91. Lastly, for participants to be considered for discharge from the hospital, the clinical cure rate which includes four sub criteria must be completed: significantly improved respiratory symptoms, completing two COVID-19 tests at least one day apart from each other which showed negative results, stabilizing and return of body temperature within normal limits for at least three days, and results from the CT scan which showed decreased inflammation of the pulmonary system. Of 1,523 participants, including 760 from the CHM and 763 from the CWM group, yielded a risk reduction rate of 1.18 in those receiving the combination of traditional Chinese medicine alongside conventional Western medical interventions.

The second article demonstrating adaptations made to TCM is titled, “Efficacy and safety of Integrated Traditional Chinese and Western medicine for Coronavirus disease 2019 (COVID-19): A systematic review and meta-analysis” (Liu et al., 2020). The purpose of the study was to determine the efficacy and safety of using Traditional Chinese Medicine alongside Western Medicine for COVID-19 patients also known as “integrative medicine”. For this study, 982 participants (ages 18 or older and clinically diagnosed with COVID-19) were included in the control and experimental groups with studies ranging from 5 to 30 days with an average of 13.55

days. Due to the ranging treatment time frames, this potentially hinders the results obtained as the participants did not receive the treatment for an equal duration of time.

Four of the studies were randomized controlled trials and seven were case-control studies which were assessed using the Cochrane Risk of Bias tool and Newcastle-Ottawa Scale respectively. Patented Chinese medicine used for this trial includes Shufeng Jiedu Capsule, Lianhua Qingwen granules, and QingFei TouXie FuZhengFang. The practices of Western medicine incorporated in this study include respiratory assisted ventilation, antiviral agents such as lopinavir and abidol, supportive care, and glucocorticoid therapy to inhibit inflammation. Participants in the control group only received modern Western treatments for COVID-19 symptoms, while the experimental group received the integrated medicine practice of combining TCM and Western medicine.

In terms of quantitative-wise, the risk ratio value (RR) was used for testing factors which fell into the dichotomous data category of having two categories of outcomes, while the weighted mean difference (WMD) was used for continuous testing factors such as the hospital stay which could result in a large range of outcomes such as a couple of days to years. Participants in the experimental group who received the integrated medicine treatment had an overall better outcome than the control group for the following categories: response (RR= 1.230), severity of illness (RR=0.350), cure (RR=1.604), and hospital stay rate (WMD= -1.991). About interpreting the risk ratio, the cure rate which resulted in a score of 1.604 means the odds of the outcome in participants receiving the integrated medicine treatment are 1.604 times the odds of the outcome happening in the controlled group (those who received a placebo) to be cured of COVID-19. The use of integrated medicine for this particular group of patients showed the ability to mitigate symptoms of cough, fatigue, anorexia, fever, fatigue time, chest tightness,

and sputum production from the lungs or throat from coughing. Although clinical symptoms which are deemed as subjective data were collected from the participants, other objective data indicators were included such as measuring the C-reactive protein count, white blood cell, lymphocyte percentage, and tumor necrosis factor-alpha. This study is the beginning of many potential research topics regarding integrated medicine for diagnosed COVID-19 patients.

Overall, these two studies demonstrated the positive outcome of integrated medicine as opposed to solely Western medicine in the treatment regimen for COVID-19 positive patients in relieving the category of symptoms mentioned earlier such as fever and cough along with improving the patient's laboratory indicators, specifically the lymphocyte percentage and interferon-alpha levels back to within normal limit ranges.

Adaptations to Traditional Chinese Herbal Medicine for Use to Improve COVID-19 Patient Outcomes

Two articles were chosen to demonstrate the adaptations to the use of traditional Chinese herbal medicine which has been thoroughly studied to improve COVID-19 patient outcomes. The adaptations made to Eastern medicine include providing the herbal and medicinal plants native to China in a form of an injectable treatment while examining the potential treatment for COVID-19 symptoms by providing a dual treatment of Chinese herbal medicine alongside Western medicine.

In the article, “A real-world study on adverse drug reactions to Xuebijing Injection: Hospital intensive monitoring based on 93 hospitals (31,913 cases)” the authors determined the efficacy and safety of traditional Chinese medicine injections on patients located in China diagnosed with community-acquired pneumonia, regardless of age and gender (Zheng et al., 2019). Although their population of interest seems to be very broad, they narrowed down the participants who would qualify to take part in this study by having either of the criteria listed.

For example, to be declared as a “critically severe patient” they have to either have one of the listed: respiratory failure requiring mechanical ventilation, shock, or organ failure needing intensive care unit monitoring and treatment. Although this paper focuses on the effects of COVID-19 on patients, it is important to note the significant correlation between those with COVID-19 (experiencing mild to moderate respiratory symptoms) have a higher risk of developing pneumonia and can even experience severe complications diagnosed as pneumonia.

With randomized controlled trials being conducted, 31,913 participants from 93 hospitals (within August 2013 to August 2016) were divided into three groups: those who received no treatment, a placebo, or were given an injection as the active treatment. The TCM injections used in reducing community- acquired pneumonia symptoms include the Xiyanping, Xuebijing, Reduning, Tanreqing, Xingnaojing, Shenfu, Shengmai, and Shenmai injection. From their study, 34 community-acquired pneumonia patients treated with the Chinese traditional injectable medicine alongside receiving Western medicine before admission showed better recovery outcomes. A major finding was that the Xuebijing injectable in particular enabled absorption of pulmonary lesions and decreased the risk of patients with pneumonia from experiencing a septic shock. Although the Xuebijing injectable yielded many positive results, there has not been any research on whether it is effective on inflammation reduction and negative transformation of nucleic acid as well as having a total of 96 adverse reaction cases to the Xuebijing injection which equates to 0.3% of their total sample size.

Another article that focuses on determining the effectiveness of the Xuebijing injection for diagnosed COVID-19 patients is named, “Effect of Xuebijing Injection on Inflammatory Markers and Disease Outcome of Coronavirus Disease 2019” (Wen et al., 2020). Sixty clinically diagnosed COVID-19 patients in severe conditions admitted to the Changsha Public Health

Treatment Center in Changsha, China between January and March 2020 were divided into three groups for this study. Before taking part in the study, the chosen participants had their blood work taken to measure the pre- and post-treatment (taken eight days after the treatment course) levels of C-reactive protein, acute physiology and chronic health evaluation II (APACHE II) score, erythrocyte sedimentation rate, and COVID-19 test. The sixty participants were evenly divided into three groups (each with twenty participants): the control group who received the routine treatment for COVID-19, Xuebijing 50mL injection, and Xuebijing 100mL injection. Across the three groups, after the treatment period was completed, a decrease in C-reactive protein and erythrocyte sedimentation rate was observed, while the lymphocyte and white blood cell count increased. Overall, participants receiving the Xuebijing 100mL injection had more significantly improved results in the laboratory indicators mentioned above as well as their APACHE II score which was lower than the control and Xuebijing 50mL participants.

Summarizing the Findings

Each of the studies included in this literature review has demonstrated positive and promising results regarding the use of herbal and medicinal plants native to China and Thailand to mitigate mild to moderate COVID-19 symptoms experienced in the qualified participants. Beyond confirming the efficacy of Chinese and Thai herbal plants in diagnosed COVID-19 patients, a few studies have shown even better results when combining the practice with Western medicine. The findings summarized can be used to further healthcare practices, although further research would need to be conducted as many of the screening components used in the studies published have been the first to be produced in the field to detect the safety and efficacy of the Thai and Chinese herbal plants among COVID-19 patients. This creates a major limitation in the results gained from the literature sources as many studies were unable to be replicated to obtain

the same results due to time restraints and this matter being a recent topic of discussion in the healthcare field. For further information regarding the articles used, please refer to Appendix A for the summary of each literature review.

Proposal for Further Study

Although an immense amount of information was gained from the literature that was reviewed, there are apparent gaps in the research. The use of herbal and medicinal plants for mitigating COVID-19 symptoms is a fairly recent topic of discussion in the healthcare field. However, the majority of research in the review focused on the patient in the hospital setting. Therefore, a study is proposed to determine the efficacy of the native Chinese and Thai medicinal plants for mitigating COVID-19 respiratory symptoms among residents of rural areas of China and Thailand. The main research questions are:

- How do specific species of medicinal plants, native to China and Thailand, perform in terms of mitigating mild respiratory symptoms, specific COVID-19, when used by residents of China and Thailand who live in rural areas?
- How do the Chinese and Thai herbs compare to each other in regard to mitigating patients' mild COVID-19 respiratory symptoms?

Theoretical Framework

The proposed study will expand based on the germ theory, a theory brought up by Robert Koch which structured the research carried out by Louis Pasteur (*A Theory of Germs*, 2004). The four Koch postulates describe the relationship of microscopic organisms as the cause of disease in the host: (1) The microorganism must be found in diseased but not healthy individuals; (2) The microorganism must be cultured from the diseased individual; (3) Inoculation of a healthy individual with the cultured microorganism must recapitulate the disease; and (4) The microorganism must be re-isolated from the inoculated, diseased individual and matched to the original microorganism (Segre, 2013, pg. 2141-2142). In relation to COVID-19, the germ theory provides an excellent foundation demonstrating how the SARS-CoV-2 virus is responsible for

the COVID-19 disease. Additionally, the SARS-CoV-2 virus spreads through airborne particles from an infected person's respiratory droplets through the body of healthy and susceptible hosts creating manifestations such as respiratory distress, fever, chills, sore throat, and new loss of taste and/or smell.

This theory follows under the Western or biomedical system (as opposed to the magicoreligious and naturalistic health systems) which describes the cause of disease as being a result of abnormalities in the function of organs and body systems due to invasion of germs. Interestingly, people in rural China and Thailand, may not identify the changes in health that they experience with the SARS-CoV-2 virus as a communicable disease and not acknowledge that there is a world-wide pandemic.

Primary Research Aims

The primary research aim for this proposed quasi experimental study (to be approved by the Institutional Review Board [IRB]) is to determine the efficacy rates of native Thai and Chinese medicinal plants in mitigating respiratory-specific COVID-19 symptoms. Other aims of this study are to identify the benefits of herbal and medicinal plants as a practice in treating COVID-19 positive patients residing in rural Thailand and China areas where medical resources are limited and isolated.

Ethical Considerations

Interested participants will be informed by an IRB approved designee regarding the study's purpose, risks, benefits, research approach, and alternatives to participation concerning the use of medicinal plants as a form of treatment for mild COVID-19 respiratory symptoms. Potential participants will then be provided sufficient time to ask the researchers questions related to the study and consider involvement prior to signing an informed consent which can be

removed at any time of the study and will not hinder them in any way. As this study engages with a vulnerable population group, participants will be informed of the risk and benefits and protective measures will be taken to ensure the adverse risk is low through implementing interventions which strictly follow the research design approved by the IRB to minimize unnecessarily exposing participants to risk, while promoting beneficence, nonmaleficence, and the participant's autonomy throughout the study.

To establish the confidentiality of our participants, study identifiers will be used throughout the preparation and duration of the experiment. A master document of the participant's name and their respective study identifiers will be secured on a password-protected computer. To ensure the security of the documents used for this study, all files will be locked with a password and documents will be encrypted when embedded into emails. Additionally, only researchers in direct contact and working with the study participants will be discussing the inputs, outputs, outcome, and goal for this study, while also ensuring that researcher bias is minimized by strictly following the research plan and implementing parameters to reduce bias (such as the triangulation method to increase validity and credibility of the research findings).

Research Method

Research Design

The design of this proposed research study will be carried out in a mixed manner, having components of qualitative and quantitative study.

Research Population and Sample Size

A total of 1,500 participants will be recruited throughout rural China (750 residents) and Thailand (750 residents) to be included in the study. The criteria to be used are as follows:

between the ages of 18 and 65 years old, clinically diagnosed with COVID-19, and residing in a geographically determined rural area in either Thailand or China, without any limitations on nationality and gender.

Strategy for Recruitment

As this study is aimed to work with residents in rural areas of China and Thailand, they tend to have limited resources and are isolated from hospitals and local clinics. The strategies used for the recruitment of participants will be through snowball sampling. The researchers will form a healthcare team and partner with a mobile clinic that travels throughout the countryside and local public health nurses to inform the residents they are supporting when visiting their homes for health check-ups or providing COVID-19 testing.

Statistical Analysis for Quantitative Research

A randomized controlled trial will be used to categorize the qualified participants into one of three groups (each consisting of 500 participants): a controlled group of participants receiving the placebo treatment, an experimental group receiving a Thai medicinal herb, and another experimental group receiving a Chinese medicinal herb to test the efficacy of the specified herbal plants as a form of treatment in mitigating respiratory specific COVID-19 symptoms among residents in rural areas of China and Thailand.

A mobile clinic with a healthcare team will be used in each country to visit the rural communities targeted for participation. The mobile health clinic trailer will contain x-ray and CT imaging equipment. The primary pre- and post-experimental indicators used to determine and compare treatments in this study include a chest x-ray and/or lung CT scan to determine initial lung damage, real-time polymerase chain reaction (PCR) diagnostic panel, a complete blood

count panel, and other laboratory values such as white blood cell count, erythrocyte sedimentation rate, prothrombin time. With data collected from the three groups, an analysis of variance (ANOVA) will be used to compare the statistics obtained. Each arm of the study (Control, Chinese Herb, and Thai Herb) is expected to run from seven to 30 days and participants will be completing a daily survey ranking the intensity of their dyspnea, pain, and tiredness on a numerical rating scale of 0 to 10 (ordinal data) to be analyzed using ANOVA.

Content Analysis for Qualitative Research

Pre- and post-study semi-structured interviews through focus groups (5-8 participants) will be conducted by researchers working directly with this experiment to document the participant's own experiences, biases, and concerns. Before the interviews, participants will be asked for consent to use information obtained and transcribed into a transcript to be included as study data. Examples of the questions to be included in the interview are as follows:

1. Where is the closest clinic or hospital located? How many minutes away is the site?
2. What do you call this "health change" (i.e. the COVID-19 pandemic)?
3. How would members of your culture treat this condition (i.e. treat symptoms related to the virus)?
4. What symptoms are you feeling and how long have you been experiencing them?
5. How has your experience with the use of herbal and medicinal plants compared to your usual practices?

In terms of the content analysis for qualitative research, the researchers will search for similar words and phrases throughout all of the focus groups to be organized into categories and subunits to identify common themes (Fain, 2021, pg. 212).

Conclusion

The use of native herbal and medicinal plants from China and Thailand as a means of treating community-acquired pneumonia and mitigating mild-to-moderate COVID-19 symptoms are shown to be a safe practice that yields successful results. The seven literature sources provide a foundation for further research that could be the basis of evidence-based practice interventions implemented in medical settings. The proposed research will advance the profession of nursing by understanding the substantial significance of nonpharmacological interventions using herbal and medicinal plants. Implementing this practice in rural areas eliminates the challenges of being isolated and having inaccessible medical resources, while potentially reducing the morbidity and mortality rate of these residents (especially those unvaccinated) which would otherwise lead to rapid health deterioration.

Beyond the knowledge acquired, important next steps in this process would be to determine the safety and efficacy rates of native Thai herbal plants used alongside Western medicine in mitigating COVID-19 symptoms, use of this practice among vulnerable populations such as children, geriatrics population, and pregnant women, and how these medicinal plants will be distributed to those who need them.

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Wen, L., Zhou, Z., Jiang, D., & Huang, K. (2020). *Zhonghua wei zhong bing ji jiu yi xue*, 32(4), 426–429. <https://doi.org/10.3760/cma.j.cn121430-20200406-00386>

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Xiong, X., Wang, P., Su, K., Cho, W. C., & Xing, Y. (2020). Chinese herbal medicine for coronavirus disease 2019: A systematic review and meta-analysis. *Pharmacological research*, 160, 105056. <https://doi.org/10.1016/j.phrs.2020.105056>

Zheng, R., Wang, H., Liu, Z., Wang, X., Li, J., Lei, X., Fan, Y., Liu, S., Feng, Z., & Shang, H. (2019). A real-world study on adverse drug reactions to Xuebijing injection: hospital intensive monitoring based on 93 hospitals (31,913 cases). *Annals of translational medicine*, 7(6), 117. <https://doi.org/10.21037/atm.2018.09.26>

Appendix A: Literature Review Table

Authors/Citation	Purpose/Objective of Study	Sample - Population of interest, sample size	Study Design	Study Methods	Major Finding(s)	Strengths	Limitations
Kanjanasirirat, P., Suksatu, A., Manopwisedjaroen, S., Munyoo, B., Tuchinda, P., Jearawuttanakul, K., Seemakhan, S., Charoensuththivarakul, S., Wongtrakongate, P., Rangkasenee, N., Pitiporn, S., Waranuch, N., Chabang, N., Khemawoot, P., Sa-Ngiamsumtom, K., Pewkliang, Y., Thongsri, P., Chutipongtanate, S., Hongeng, S., Borwornpinyo, S., ... Thitithanyanont, A. (2020). High-content screening of Thai medicinal plants reveals <i>Boesenbergia rotunda</i> extract and its component	The purpose of their study was to develop a high-content screening for potential antiviral plants using the SARS-CoV-2 nucleoprotein detection in Vero E6 cells by measuring the amount of plaque reduction assay and dose-response analysis which indicated the viral suppression.	Their sample tested 122 Thai medicinal plants and their efficacy in suppressing SARS-CoV-2 infectivity.	Quantitative-Experimental Research uses two approaches: pre-entry and post-infectious treatments. Pre-entry approach: The natural extracts were pre-incubated with the virus before inoculation of the concoction with the cells. Post-infectious: Natural extracts were introduced to the cell culture after viral infection and throughout the experiment.	From the 122 Thai medicinal plants, three plants (extracts and purified compounds) were chosen to be tested further for their antiviral properties. From the extracts, two-fold cell dilutions were added into a cell culture after two hours of viral adsorption and the cell culture remained for 48 hours. The cells were then stained with anti-SARS-CoV NP mAB and Alexa Fluor 488-labeled secondary antibody to be observed for their dose-response relationship.	Panduratin A (extracted <i>B. rotunda</i>) has inhibitory effects against SARS-CoV-2 infection during the pre-entry and post-infection phases. Treatments involving Panduratin A and <i>B. rotunda</i> extract successfully suppressed viral growth in human airway epithelial cells.	The results from their study were thoroughly performed and collected as they measured the outcome of the chosen medicinal plants through two ways: dose-response relationship and plaque assay reduction. A large study sample of 122 potential medicinal plants to be tested was studied in preparation for their study. Besides testing the impact of <i>B. rotunda</i> extract and the panduratin A on the post-infection phase, they expanded the study and tested whether the two	The authors stated that the rapid spread of COVID-19, “it has prompted us to develop, for the first time, a high-content screening platform” which has only been used with their study indicating a possible lack of credibility behind their discovery.

Authors/Citation	Purpose/Objective of Study	Sample - Population of interest, sample size	Study Design	Study Methods	Major Finding(s)	Strengths	Limitations
Panduratin A as anti-SARS-CoV-2 agents. <i>Scientific reports</i> , 10(1), 19963. https://doi.org/10.1038/s41598-020-77003-3 .						components would have an effect on pre-entry treatment which also showed successful results.	
Kasemsumran, S., Apiwatanapiwat, W., Ngowsuwan, K., & Jungtheerapanich, S. (2021). Rapid selection of <i>Andrographis paniculata</i> medicinal plant materials based on major bioactive using near-infrared spectroscopy. <i>Chemicke zvesti</i> , 1–12. Advance online publication. https://doi.org/10.1007/s11696-021-01746-0	Determining the efficacy of <i>Andrographis paniculate</i> medicinal plant on antiviral activity against SARS-CoV-2.	The <i>Andrographis paniculate</i> plant was used for this study. For this study, 170 samples of the plant were obtained over two years which were categorized into four groups: aerial, stems, leaves, and stems mixed with leaves. The samples were collected from ten provinces of Thailand: Bangkok, Nakhon Pathom, Nonthaburi, Prajeenburi, Phetchaburi, Phetchabun, Mahasarakham,	Quantitative study-experimental research	This quantitative study to identify the effectiveness of the <i>Andrographis paniculate</i> plant was carried out using near-infrared spectroscopy. Fresh samples were made into a powder form being dried at 50 degrees Celsius over a period of ten hours and then mechanically grinded. Each of the powdered samples was then placed into their respective test tube for a near-infrared spectrophotometer.	Commercial samples from the study may have been harvested during the vegetative period, but not more than 50% of the flowering. The leaves had the highest yield of API whereas the leaf and arterial parts contained the highest amount of AP3. The Partial Least Squares-Discriminant Analysis method (PLS-DA) showed success in classifying results in none and pretreatment patients.	Their study consisted of a large sample size of 120 plant samples. The NIR technique can be used when running a sample as it does not require the sample to be extracted and does not run the risk of destroying or tampering with the sample either.	A limited amount of research was performed and gained as the duration needed to run these samples took hours to weeks to finalize, some of their samples were destroyed due to the use of chemical substances and were costly due to the extensive types of equipment needed to successfully run their samples. Difficulty distinguishing the parts of the plants after thorough grinding prompted

Authors/Citation	Purpose/Objective of Study	Sample - Population of interest, sample size	Study Design	Study Methods	Major Finding(s)	Strengths	Limitations
		Suphanburi, and Sa Kaeo.			The leaf of the plant yielded the highest content of bioactive compounds.		the researchers to create a method to quantify the contents with the NIR spectroscopy method.
Liu, M., Gao, Y., Yuan, Y., Yang, K., Shi, S., Zhang, J., & Tian, J. (2020). Efficacy and Safety of Integrated Traditional Chinese and Western Medicine for Corona Virus Disease 2019 (COVID-19): a systematic review and meta-analysis. <i>Pharmacological research</i> , 158, 104896. https://doi.org/10.1016/j.phrs.2020.104896	The purpose of this study is to determine the efficacy and safety of using Traditional Chinese Medicine alongside Western Medicine for COVID-19 patients also known as “integrated medicine”.	For this study, a total of 982 participants were included in the control and experimental groups. The treatment duration ranged from 5 to 30 days with an average of 13.55 days. Two main qualifications were created for interested participants including having to be 18 years of age or older and having to be diagnosed positive with COVID-19 by the laboratory.	Quantitative experimental research performed	From their intensive literature review search through six Chinese and English-based databases regarding the use of integrated medicine on COVID-19 positive patients, the researchers narrowed the information down to a total of 11 studies. Four of the studies were randomized controlled trials and seven were case-control studies which were assessed with the Cochrane Risk of Bias tool and Newcastle-Ottawa Scale respectively.	In terms of quantitative-wise, the risk ratio (RR) was used for testing factors which fell into the dichotomous data category of having two categories of outcomes, while the weighted mean difference (WMD) was used for continuous testing factors such as the hospital stay which could result in a large range of outcomes such as a couple of days to years. Participants in the experimental group who received the integrated medicine	To obtain the most relevant and reliable information from their literature review search, the authors narrowed the articles used from December 01, 2019, to March 24, 2020, which marked the discovery and peak of the spread of the SARS-CoV-2 virus. Although clinical symptoms which are deemed as subjective data were collected from the participants, other objective data indicators were included such as measuring the C-reactive protein count, white blood	This study is the beginning of many potential research topics regarding integrated medicine for diagnosed COVID-19 patients. Due to the ranging treatment time frames, this could hinder their results as the participants did not receive the treatment for an equal duration of time which could have yielded varying results.

Authors/Citation	Purpose/Objective of Study	Sample - Population of interest, sample size	Study Design	Study Methods	Major Finding(s)	Strengths	Limitations
				<p>As for the traditional Chinese medicine used for this trial, this included patented Chinese medicine such as the Shufeng Jiedu Capsule, Lianhua Qingwen granules as well as Chinese medicine compound drugs such as the QingFei TouXie FuZhengFang.</p> <p>The practices of Western medicine incorporated in this study include respiratory assisted ventilation, antiviral agents such as lopinavir and abidol, supportive care, and glucocorticoid therapy primarily to inhibit inflammation.</p> <p>Participants randomly selected to</p>	<p>treatment had an overall better outcome than the control group for the following categories: response (RR= 1.230), severity illness (RR=0.350), cure (RR=1.604), and hospital stay rate (WMD= -1.991).</p> <p>Moreover, the use of integrated medicine for this particular group of patients showed the ability to mitigate symptoms of cough, fatigue, anorexia, fever, fatigue time, chest tightness, and expectoration (sputum production from the lungs or throat from coughing).</p>	<p>cell, lymphocyte percentage, and tumor necrosis factor-alpha.</p>	

Authors/Citation	Purpose/Objective of Study	Sample - Population of interest, sample size	Study Design	Study Methods	Major Finding(s)	Strengths	Limitations
				be included in the control group received only modern Western treatments for COVID-19 symptoms, while the experimental group received the integrated medicine practice of combining TCM and Western medicine.			
Phumthum, M., Nguanchoo, V., & Balslev, H. (2021). Medicinal Plants Used for Treating Mild Covid-19 Symptoms Among Thai Karen and Hmong. <i>Frontiers in pharmacology</i> , 12, 699897. https://doi.org/10.3389/fphar.2021.699897	The purpose of this study is to identify which medicinal plants commonly used by the Thai Karen and Hmong community can also be used to treat mild symptoms of COVID-19.	A total of 491 plant species were identified by both the Thai Karen and Hmong communities to alleviate symptoms of cough, diarrhea, sore throat, headache, and a rash which are labeled as mild symptoms by the WHO. Information regarding the use of ethnobotany was also obtained through literature review	Literature review and qualitative study performed. Sixteen key respondents with roles as local healers in the communities primarily using medicinal plants were interviewed and obtained others through a snowball sampling.	The study was conducted through literature reviews as well as field interviews of the residents in the Thai Karen and Hmong communities with mild COVID-19 symptoms.	From the medicinal plants identified in their study, fever was the most commonly treated symptom, then cough, diarrhea, muscle pain, skin rash, headache, then sore throat (in that order). Treatment of conjunctivitis received the lowest reports among the Hmong and Karen communities.	Because the authors used articles in their literature review which dated back to 1999, they decided to obtain more relevant data about mild symptoms in the Hmong and Karen community in 2020. They used both previously published data and their data to strengthen the use of medicinal plants in mitigating the mild COVID-19 symptoms.	When performing field interviews, when asking regarding signs and symptoms of mild COVID-19, this is subjective data being obtained as everyone may have their definition of their condition “improving, stabilizing, or worsening.” The researchers and authors only identified medicinal

Authors/Citation	Purpose/Objective of Study	Sample - Population of interest, sample size	Study Design	Study Methods	Major Finding(s)	Strengths	Limitations
		from thirty-one Karen and nineteen Hmong villages as well as six new Hmong villages as well as 1230 overall respondents (675 Hmong and 555 Karen residents).					plants which were used to treat fever, cough, diarrhea, muscle pain, rash, headache, conjunctivitis, and sore throat, meaning other mild COVID-19 sign and symptoms (such as respiratory) identified by the WHO were not included in their study.
Wen, L., Zhou, Z., Jiang, D., & Huang, K. (2020). <i>Zhonghua wei zhong bing ji jiu yi xue</i> , 32(4), 426–429. https://doi.org/10.3760/cmaj.cn121430-20200406-00386	Determine the efficacy of Xuebijing injections in severe COVID-19 patients (controlled, 50mL, and 100mL dosages).	Sixty clinically diagnosed COVID-19 patients in severe conditions were admitted to the Changsha Public Health Treatment Center in Changsha, China between January and March 2020	Quantitative research study	The sixty participants were evenly divided into three groups, each with twenty participants, of those who received the routine protocol and treatment for COVID-19, Xuebijing 50mL injection, and Xuebijing 100mL injections.	Across the three groups after the treatment period was completed, a decrease in C-reactive protein and erythrocyte sedimentation rate was observed, while the lymphocyte and white blood cell count increased.	Participants receiving the Xuebijing 100mL injection had more significantly improved results in the laboratory indicators mentioned above as well as their APACHE II score which was lower than the control and	The study did not indicate the results (improved) by category and rather in a manner which talks about all three groups.

Authors/Citation	Purpose/Objective of Study	Sample - Population of interest, sample size	Study Design	Study Methods	Major Finding(s)	Strengths	Limitations
				The study was conducted over seven days, with those in the experimental group receiving their respective dosage of Xuebijing injection twice a day.		Xuebijing 50mL participants.	
Xiong, X., Wang, P., Su, K., Cho, W. C., & Xing, Y. (2020). Chinese herbal medicine for coronavirus disease 2019: A systematic review and meta-analysis. <i>Pharmacological research</i> , 160, 105056. https://doi.org/10.1016/j.phrs.2020.105056	This systematic review and meta-analysis depict the use of traditional Chinese medicine, in particular Chinese herbal medicine, to treat COVID-19 positive patients in mainland China.	A total of eighteen randomized controlled trials were run with a total of 2,275 participants throughout China. The only qualification required to be a participant in their study is to be diagnosed with COVID-19 without any limitations on nationality, gender, and age.	A quantitative study was performed	The study was conducted in the manner of a quantitative study of a randomized controlled trial with two groups: the control group receiving conventional Western medicine and/or a combination of Chinese herbal medicine placebo while the treatment (experimental) group was treated by Chinese herbal medicine and/or alongside conventional Western medicine.	the risk reduction rate was compared between the CHM (experimental) and CWM (controlled) groups which showed significant improvement in cough among 240 CHM and 182 CWM participants of an RR value of 1.50, fever being significantly reduced within 433 patients with a weight mean difference of -0.60, fatigue reduction among 167 patients in CHM and 140 in CWM with a RR value of 1.73, TCM syndrome reduction	Experiment results success was measured in the form of a lung CT as well as other measures such as clinical symptoms, inflammatory markers	This study is the beginning of many potential research topics regarding integrated medicine for diagnosed COVID-19 patients.

Authors/Citation	Purpose/Objective of Study	Sample - Population of interest, sample size	Study Design	Study Methods	Major Finding(s)	Strengths	Limitations
					within 141 CHM participants with a weight mean difference of -6.60		
Zheng, R., Wang, H., Liu, Z., Wang, X., Li, J., Lei, X., Fan, Y., Liu, S., Feng, Z., & Shang, H. (2019). A real-world study on adverse drug reactions to Xuebijing injection: hospital intensive monitoring based on 93 hospitals (31,913 cases). <i>Annals of translational medicine</i> , 7(6), 117. https://doi.org/10.21037/atm.2018.09.26	The purpose of this study is to determine the efficacy and safety level of using traditional Chinese medicine injections on those with community-acquired pneumonia.	The population of interest is those patients currently diagnosed with community-acquired pneumonia., regardless of age and gender. Although their population description seems to be very broad, they narrowed down the participants who would qualify to take part in this study by having either of the criteria listed. For example, to be declared as a “critically severe patient” they have to either have one of the listed: respiratory failure requiring mechanical	Qualitative (literature reviews from various databases such as PubMed, Wang Fang Database, and Cochran Library) and quantitative study (randomized controlled trials and nonrandomized studies)	Interventions: Chinese traditional medicine injections reported in the guideline, ^[4] including Xiyanning injection, Xuebijing injection, Reduning injection, Tanreqing injection, Xingnaojing injection, Shenfu injection, Shengmai injection, and Shenmai injection. 2. Controls: Include no treatment, placebo, or other active treatment recommended by the guideline. 3. Outcomes: We provide the following results to reflect the efficacy and safety of	From various studies, there has been research showing that 34 community-acquired pneumonia patients treated with Chinese traditional injectable medicine alongside Western medicine prior to admission showed better recovery outcomes. Additionally, the use of the Xuebijing injectable has promoted the absorption of pulmonary lesions and reduced the risk of septic shock.	There has not been any systematic reviews or meta-analysis which compiled information regarding the safety and effectiveness of Chinese traditional injectable medicine for community-acquired pneumonia patients. Their study aims to look at the topic on a holistic level including researching the effective rate, all-cause mortality clinical recovery time, and negative time of novel coronavirus nucleic acid which is aimed to provide information for	Although the Xuebijing injectable yielded many positive results, there has not been any research on whether it is effective on inflammation reduction and negative transformation of nucleic acid. There were 96 cases of adverse reactions to the Xuebijing injection which equates to 0.3% of the total sample size.

Authors/Citation	Purpose/Objective of Study	Sample - Population of interest, sample size	Study Design	Study Methods	Major Finding(s)	Strengths	Limitations
		ventilation, shock, or organ failure needing intensive care unit monitoring and treatment.		<p>traditional Chinese medicine injection.</p> <p>4. Main results: effective rate and all-cause mortality.</p> <p>5. Secondary results: clinical recovery time, negative time of novel coronavirus nucleic acid, mechanical ventilation time, intensive care unit length of stay, dose-response of injection, and adverse event rate.</p>		evidence-based practice studies and treatment.	