นิพนธ์ต้นฉบับ

ผลสัมฤทธิ์ในการรักษาผู้ป่วยติดเชื้อไวรัสโควิด-19 ที่มีอาการไม่รุนแรงด้วยสมุนไพรตามแนวคิดการแพทย์แผนไทย: การศึกษาย้อนหลังจากการทบทวนข้อมูลจากเวชระเบียน

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บทคัดย่อ

การรักษาด้วยสมุนไพรมีบทบาทมากในช่วงการแพร่ระบาดของไวรัสโควิด-19 อย่างไรก็ตามผลวิจัยเชิงประจักษ์ในประสิทธิผลของยาสมุนไพรในการรักษาไวรัสโควิด-19ยังมีจำกัดแม้ว่าวัคซีนและยาต้านไวรัสเป็นมาตรการหลักในการต้านไวรัสยาสมุนไพรยังคงเป็นทางเลือกในการดูแลสุขภาพในการรับมือกับการระบาดของไวรัสอีกในอนาคตการศึกษานี้ใช้กระบวนการวิจัยทบทวนเวชระเบียนย้อนหลังในผู้ป่วย 101 รายที่ได้รับการรักษาด้วยตำรับสมุนไพรเพียงอย่างเดียว ณ คลินิกแพทย์แผนไทย ตำรับที่ใช้เป็นสูตรจากแนวคิดการแพทย์แผนไทยโดยรวมสมุนไพรจากตำรับยาห้ารากประสะเปราะใหญ่และสมุนไพรอื่นรวม 13 ชนิดผลการศึกษาพบว่าตำรับยาที่ใช้มีความปลอดภัยโดยไม่พบอาการไม่พึงประสงค์ที่ร้ายแรงและไม่มีผู้ป่วยที่เสียชีวิตระหว่างการรักษาผู้ป่วยเกือบทุกรายหายจากการติดเชื้อโดยยืนยันด้วยผลการตรวจทางห้องปฏิบัติการภายใน 2 สัปดาห์โดยยกเว้นผู้ป่วยสองรายที่อาการยังไม่ดีขึ้นและขอหยุดการรักษาเพื่อไปรับการรักษาด้วยวิธีอื่นสิ่งที่น่าสนใจคือไม่มีผู้ป่วยรายใดมีพัฒนาการของโรคจนเกิดภาวะปอดอักเสบผลการศึกษานี้แสดงให้เห็นว่าวิธีการรักษาด้วยสมุนไพรตำรับนี้มีความปลอดภัยและช่วยรักษาการติดเชื้อโควิด-19ที่มีอาการไม่รุนแรงได้และเป็นรายงานทางคลินิกในมนุษย์ครั้งแรกของฤทธิ์ต้านไวรัสโควิด-19 ของตำรับที่มีส่วนประกอบสมุนไพรหลักจากตำรับยาห้ารากและประสะเปราะใหญ่ รายงานผลสัมฤทธิ์จากการศึกษานี้แม้จะมีข้อจำกัดที่ไม่สามารถแยกจำนวนผู้ป่วยที่มีอาการไม่รุนแรงและสามารถหายเองได้โดยไม่ต้องได้รับการรักษา แต่คาดหวังที่จะช่วยกระตุ้นการพัฒนาและการวิจัยเพิ่มเติมในประสิทธิภาพและความปลอดภัยของสมุนไพรที่มีคุณสมบัติต้านไวรัสให้มากยิ่งขึ้น

คำสำคัญ: ไวรัสโควิด-19, ยาจากสมุนไพร, การแพทย์แผนไทย

Original Article

Clinical Outcomes of a Treatment for Mild Cases of COVID-19 using a Polyherbal Concoction based on Thai Traditional Medicine: A Retrospective Chart Review

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Abstract

Dating back to the COVID-19 pandemic, herbal medicine gained prominence as a potential means of managing the virus. However, published evidence supporting its efficacy remains limited. Vaccines and antiviral drugs undoubtedly constitute the primary defense against viral threats. However, herbal medicine remains a viable option for management in addressing future viral outbreaks. This study undertakes a retrospective analysis of 101 charts of patients who solely used an herbal concoction based on Thai traditional medicine for COVID-19 treatment in a local clinic. The concoction comprised a combination of 13herbs selected from two distinct formulas, Ya-ha-rak, Prasaporhyai, and other herbs. The findings indicate no fatality or health complications associated with the treatment. Concerning clinical outcome, nearly all patients achieved negative laboratory results for COVID-19 in less than two weeks, except for two individuals whose conditions did not improve within a two-week timeframe. These two patients opted to discontinue the current treatment to pursue alternative therapies. Notably, none exhibited pneumonia symptoms. Thus, this herbal approach seems safe and beneficial for mild COVID-19 cases. This is the first human clinical report on the antiviral properties of a formulation comprising principal medicinal plants sourced from Ya-ha-rak and Prasaporhyai. This study, though constrained by its inability to distinguish between patients who could recover without necessitating medical intervention, was conducted with the aspiration that it will trigger further advancement and investigations into the efficacy and safety of antiviral herbs, thereby enhancing our understanding and utilization of these natural resources.

Keywords: COVID-19, Herbal medicine, Thai traditional medicine

Introduction

The emergence of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in late 2019 has caused a widespread outbreak of an acute respiratory condition known as the novel Coronavirus Disease 2019 (COVID-19). The highly infectious virus has posed a significant and substantial threat to human health and public safety, leading to economic and social repercussions affecting nations globally. In early 2020, Thailand began experiencing a gradual rise in new confirmed COVID-19 cases, starting from January. By mid-March 2020, it had entered its first wave of COVID-19 infections[1,2]. Later in the year, a second wave emerged in December 2020,followed by the third wave in April 2021[1], further challenging the country's efforts to control the spread of the virus. The country initially contained the spread of the virus through strict measures such as travel bans, quarantines, lockdown, and home isolation being implemented in certain areas.

Since the onset and subsequent phases of the COVID-19 pandemic in Thailand, the scarcity of healthcare professionals, limited hospital resources, and challenges associated with accessing in-person healthcare services, some infected individuals resorted to dietary supplements, natural products, plants, and traditional medicine. This complementary approach was adopted with the expectation to mitigate symptoms and boost immune systems. The situation had necessitated researchers and traditional healers to search for alternative approaches to control, prevention, and treatment of the virus. Globally, traditional healers are employing various medicinal plants and concoctions for the management of COVID-19[3]. The use of herbal remedies is found in Traditional Chinese Medicine (TCM), where China has a strong tradition of using herbs to treat illnesses. TCM uses polyherbal decoction formulas, known as Qingfei Paidu Decoction[4,5], Huoxiang Zhengqi, and Lianhua Qingwen[6], either alone or combined with conventional medicines for the treatment of COVID-19. In Thailand, among various plants, ‘Fah Talai Jone’/*Andrographis paniculate* (Burm. f.) Wall. ex Nees and ‘Krachai’ *or* ‘Fingerroot’/*Boesenbergia rotunda* (L.) Mansf.) have gained popularity for treating COVID-19.It has been suggested that the bioactive compounds may interfere with viral replication and exhibit anti-inflammatory effects, which could potentially help in reducing the severity of COVID-19-induced pneumonia symptoms[7]. Later, the Thailand national clinical practice guidelines for the treatment of COVID-19, issued by the Department of Medical Services, recommended Favipiravir and Fah Talai Jone as primary treatment options[8].

The principle of TTM not only aims to treat the cause of the disease but also to restore balance to the body's elements, therefore the basis of treatment is holistic approach. The elements are referred to as the 'Four Elemental Principles' or 'Four Elemental Energies', consisting of Earth (Pathavi), Water (Apo), Fire (Tejo), and Wind(Vayo)[9]. These elements are believed to govern the functioning of the human body and its interactions with the environment. TTM posits that disease affects the four elements and fundamental energies, leading to specific organ imbalances. In the context of COVID-19, TTM practitioners may link specific symptoms or manifestations of the disease, such as excessive mucus in the throat and lungs, to the characteristics identified as So-semha and Ura-semha[9], respectively. This understanding allows traditional healers to tailor treatment approaches that address the imbalances associated with the Doshas[10], the fundamental bioenergetic forces that govern the physiological and psychological aspects of the human body.

Conventional TTM typically employs polyherbal decoction formulas as a treatment approach for fever of unknown origin resulting from infections. This practice can be traced back to TTM scripture known as Taksila[10,11].The Taksila scripture in TTM characterizes a group of illnesses called 'Kai-Pit-Kai-Kan', which is not a specific disease but rather a condition where a patient often experiences a high fever with inflammation in the body, and usually produces rashes on the skin. These diseases are later found to be closely related to, for example, typhoid fever, measles, chickenpox, and dengue fever, which are caused by various pathogens, including bacteria and viruses. One of the recipes in the Taksila mostly used to treat fever of unknown origin and inflammation caused by infection is 'Ya-ha-rak', which combines five roots of medicinal plants. Based on the physiological actions of the recipe and the evidence-based of TTM, there is hope that the 'Five roots medicine' of Ya-ha-rak could be used for COVID-19 treatment. However, at present, there is a lack of substantial clinical evidence supporting the effectiveness of Ya-ha-rak in the treatment of COVID-19.

During the pandemic, Thai traditional practitioners at a local Thai traditional clinic actively engaged in public health campaigns, seeking preventive and supportive measures. amidst medical supply shortages and soaring prices of Fah Talai Jone[12], the primary herbal remedy. Medicinal plants and herbal formulation being considered as possible treatments for COVID-19 were prepared for patients, particularly those with limited access to modern healthcare services or in home isolation. The treatment strategy involved using a TTM herbal mix to manage symptoms and chaotic situations. The formulation, aligning with TTM principles, aimed to alleviate symptoms like fever, inflammation, respiratory issues, and fatigue, while rebalancing the respiratory system, and addressing the body's four elements and energetic systems. Ingredients were chosen based on Thai Traditional scriptures and antipyretic drugs listed in Thailand's National List of Essential Medicines[12]. The formulation comprised dried herbs from two principal TTM recipes, the 'Ya-ha-rak' and 'Prasaporhyai', with additional herbs, total ling thirteen. From Ya-ha-rak, it featured 20g of dried roots from each five plants: 'Chingchi'/*Capparis micracantha* DC., 'Tao-yai-mom'/*Clerodendrum indicum* (L.) Kuntze or *Clerodendrum petasites* S. Moore (often used synonymously), 'Ma-duea-utum-phon'or'clusterfig'/*Ficus racemosa* L., Khonthaa/*Harrisoniaperforata* (Blanco) Merr., and 'Yanang'/*Tiliacoratriandra* (Colebr.) Diels. "Prasaporhyai" contributed'Kot-so'/*Angelica dahurica*(Hoffm.) Benth. & Hook.f. ex Franch. & Sav. (root, 30g), 'Kot-kha-mao'/*Atractylodeslancea* (Thunb.) DC. (rhizome, 30g), 'Prohhom'/*Kaempferia galanga* L. (rhizome, 80g), 'Bua luang' or 'sacred lotus'//*Nelumbo nucifera* Gaertn. (stamens, 30g), 'Pla-lai-phueak'/*Eurycoma longifolia* Jack (root, 10g), 'Cha-em-tet' or 'Liquorice'/*Glycyrrhiza glabra* L., and 'Hanuman-prasan-kai'/*Schefflera leucantha* R. Vig. (leaves, 10g).

In the treatment intervention, the herbal formulation was initially prepared as a decoction but later made available in capsule form to accommodate preferences for convenience in preparation and consumption. The decoction was served in 320-gram servings per food-grade bag, while the powdered herbs were encapsulated in 500 mg vegetable capsules, eliminating the need for boiling. In particular, the decoction form was predominantly prescribed to patients who visited from July to November 2021, and capsule form was predominantly prescribed to patients who visited from December 2021 to April 2022.The recommended dosage was one cup (250 ml) of

decoction three times daily or 3-4 capsules before meals for 10 days. Additionally, for individuals experiencing high fever, a separate tablet formulation named 'Chanthalila' was prescribed, with a recommended dosage of 2-4 tablets every 4 hours. The approach was an interim solution to provide symptomatic relief for patients in anticipation of their access to conventional therapy. The treatment protocol adopted telemedicine and online clinic guidelines announced by "The Medical Council of Thailand"[(14)]. The approach allowed patients to remote consultation with healthcare providers and facilitated virtual clinic visits, providing convenient access to medical care while overcoming barriers of physical proximity and adhering to established guidelines.

Objectives

Concerning the limited clinical evidence supporting herbal-based treatments, this retrospective chart review evaluated the safety and clinical outcomes of an herbal mixture in treating COVID-19 patients who did not undergo concurrent treatments. The assessment focused on clinical outcomes and the time taken until a negative COVID-19 result was achieved post-treatment.

Methodology

The research methodology employed the guideline of are prospective chart review[15].The method involves the examination and analysis of existing patient records, medical charts, and other relevant documents to gather data for research purposes. The study reviewed the charts of 120 patients who sought COVID-19 treatment at Thammathan Thai traditional medical clinic, Nonthaburi, Thailand (clinic license no. 12108001064) between July 2021-November 2021 (Cohort 1) and December 2021-April 2022 (Cohort 2). These time frames corresponded to infections predominantly by the Delta variant and the Omicron variant, respectively[(16)].Out of these, 101 patients' charts met the study criteria, which included, i) laboratory-confirmed positive COVID-19 diagnosis, ascertained either through an Antigen Test Kit (ATK) or Real Time–Polymerase Chain Reaction (Real-Time PCR) prior to treatment, and ii) absence of any concurrent treatment. The exclusion of the 19 patients from the study was due to the absence of laboratory confirmation of COVID-19 before and/or after treatment, discontinued the treatment prematurely(less than 10 days), or voluntarily sought alternative treatment options.

Ethical considerations: The retrospective study was approved by Pathumthani University's institutional Ethics Committee NO. 020/2565.

Statistical analysis: Categorical variables and data were described as frequency, percentages, mean, standard deviation (SD), and range (Min-Max). The statistical difference between two groups was tested using the independent samples t-test or chi-squared statistics, facilitated by Microsoft Excel. The findings were interpreted in a descriptive and exploratory manner.

Results

Patient demographic data

Table 1 presents demographic information pertaining to COVID-19 patients, categorized into two distinct groups based on specific time periods: Cohort 1, and Cohort 2. The dataset categorizes age into three distinct groups: 6-17 years(n=11), 18-25 years (n=9), 26-50 years (n=54) and, over 50 years(n=27). The table also provides details about the mean age, standard deviation (SD) and range of ages (Min-Max) for both cohorts. The average age for Cohort 1 was 38.6±14.4 while for Cohort 2 it was 39.2±17.5. Overall, the average age for both cohorts combined was 39.0±16.3. The range of ages observed in both cohorts varied from young as 7.7 years to old as 74.0 years. Overall, the table indicates that COVID-19 cases spanned a wide range of ages, as reflected in the previously mentioned average ages and age ranges. Additionally, there is no statistically significant difference in the ages of individuals between Cohort 1 and Cohort 2, as indicated by a p-value greater than 0.05.

In addition, medical backgrounds indicated some patients had pre-existing chronic health conditions. Specifically, two participants mentioned having asthma, one had anaemia, and five individuals were dealing with both diabetes and hypertension. Another participant was diagnosed with cardiomegaly. Additionally, two females were pregnant.

Background symptoms of COVID-19 patients before treatment

Table 2 presents comprehensive data pertaining to the symptoms exhibited by patients diagnosed with COVID-19 in the conducted study. The data is reported in terms of the patient count and the corresponding percentage for each symptom, as well as the overall % across all symptoms. The predominant symptom described by the patients was cough, which manifested in 67 individuals, constituting 66.3% of the total patient population. Fever was the second most common symptom, observed in 59 patients, which accounted for 58.4% of all patients. Loss of smell was experienced by 20 patients (50.0%) in Cohort 1 and 3 patients (4.9%) in Cohort 2, making a total of 23 patients (22.8%).

Shortness of breath, the symptom indicating pre- or developing pneumonia, affected around 11patients (27.5%) in Cohort 1 and 8 patients (13.1%) in Cohort 2, resulting in a total of 19 patients (18.8%). Phlegm was reported by 13 patients (32.5%) in Cohort 1 and by 25 patients (41.0%) in Cohort 2, totaling 38 patients (37.6%).

Overall, the table data reveals that cough and fever were the most prevalent symptoms of COVID-19 in both cohorts. Furthermore, the data demonstrates a significant difference in the occurrence of loss of smell between Cohort 1 and Cohort 2, as evidenced by a p-value of less than 0.05. However, there were no significant differences in the prevalence of other symptoms across the two cohorts including phlegm and shortness of breath, the symptoms indicating lung inflammation, as indicated by p-values greater than 0.05.

Safety

Safety assessments were based solely on patient feedback during remote consultations with the medical practitioners. The study found no significant side effects as reported by the patients. Moreover, there were no cases of death associated with the treatment, and the patients

did not encounter any notable lung or cardiovascular issues after recovering from the infection. These findings suggest a favourable safety profile for the treatment employed in the study.

Treatment outcome and Follow-up

Table 3 details the duration of treatment for COVID-19 patients in two cohorts, measured from the start of treatment to the day of a negative test result, confirmed either by ATK or Real-Time PCR tests, and the absence of significant respiratory issues. The data includes recovery days and the percentage of patients in each cohort and overall.

Regarding gender differences, treatment duration was found to be comparable for both males and females across all cohorts, an average duration of being 8.6±2.8 days. A significant variation in treatment duration (p-value < 0.05) was observed among different age groups. Notably, a substantial difference in treatment duration was evident between the youngest age group (6-17 years) and other age groups, as well as between those aged 18-24 years and older groups. Specifically, Cohort 1's 6-17 years age group had a longer average treatment duration compared to Cohort 2. Additionally, the 18-24 years age group recorded the longest average treatment duration, at 10.9±3.7 days. Moreover, the data suggests a statistically significant difference in treatment duration between Cohort 1 and Cohort 2 overall, with Cohort 1 showing a longer average duration (p-value < 0.05).

However, it is important to note that the study did not precisely record the specific recovery dates for each individual symptom. Furthermore, due to delays in obtaining confirmed laboratory results from patients, the actual treatment duration may be shorter than reported. Additionally, the study did not provide detailed information on the exact timeline for the resolution of each symptom.

Discussion

Extensive research has been undertaken during the COVID-19 pandemic to investigate the possible efficacy of various traditional treatments, medicinal herbs, and active chemicals in combating the virus. COVID-19 predominantly affects the respiratory system, leading to lung inflammation, pneumonia, and breathing difficulties, which might result in fatalities. Various medicinal plants and their bioactive compounds have demonstrated encouraging effects, such as antiviral, anti-pyretic, antioxidant, anti-inflammatory and immunomodulatory properties. This growing interest is driven by the historical success of herbal treatments in promoting virus clearance, managing respiratory syndromes, and alleviating related symptoms[3,17,18]. Despite the potential of plant-based medicine as a cost-effective alternative, the clinical evidence for treating COVID-19remains insufficiently established. At present, Fah Talai Jone/*A.paniculata*is the only herbal remedy with established indications for alleviating symptoms in COVID-19 patients with mild symptoms[19]. To intercept into the wisdom of medicine, this research aims to add the growing knowledge regarding alternative remedies for COVID-19. Through this retrospective chart review seeks to provide insights that could complement existing approaches and improve patient outcomes in the ongoing fight against COVID-19 and its potential future strains.

This retrospective chart review included the analysis of 101 patients' charts who met the inclusion criteria of having confirmed COVID-19 infection and not receiving any concurrent treatments. These patients were formerly prescribed a modified polyherbal concoction by Thai traditional practitioners in accordance with government guidelines for telemedicine and online clinics[14]. The primary aim of the concoction was to alleviate clinical symptoms such as fever, cough, while also improving the pulmonary symptoms such as dyspnea. Throughout the treatment period, none of the patients experienced worsening health or mortality. Nearly all patients experienced a full recovery within an average of 8.6±2.8 days. This outcome was observed despite certain patients exhibiting symptoms of pre-existing or emerging pneumonia, characterised by phlegm and shortness of breath. The observed outcomes suggest that the modified concoction, available in both liquid (decoction) and solid (capsule) forms, presents notable therapeutic benefits and safety in the treatment of COVID-19. It appears to be efficient in mitigating respiratory symptoms across all age groups. Nevertheless, it is important to recognize that existing evidence does not preclude the possibility of many individuals with mild symptoms achieving complete recovery independently, without necessitating medical intervention[20].Additionally, the data reveals a statistically significant difference in treatment duration between Cohort 1 and Cohort 2, with the former exhibiting a longer average duration. These findings imply that recovery time following treatment may vary depending on the virulence of the COVID-19 strain. This is illustrated by the shorter recovery observed in Cohort 2, where individuals were suspected to be infected with the Omicron variant, compared to those in Cohort 1, who were believed to be affected by the more virulent Delta variant.

Research findings on the mechanism of action of various plants on COVID-19 are currently under investigation, and the results from these studies are being presented with multiple drug targets. Plant compounds have been shown to interfere with viral entry into cells or directly inhibit viral replication. A molecular docking study identified taraxerol, which is present in *Clerodendrum spp*., as a potential therapeutic candidate against SARS-CoV-2 due to its ability to inhibit viral replication[21].An in silico docking study further suggested that luteolin, an active compound found in *K. galanga*, had the potential to interact with several crucial targets of SARS-CoV-2, including 3CLpro, PLpro, Spro, and RdRp[22]. Glycyrrhizin, an active component found in the root of *G. glabra*, was found to potentially inhibit SARS-CoV-2 replication *in vitro* by targeting the viral main protease M^{pro}[23], which is a crucial component for viral replication. Extract from *T.triandra* showed anti-SARS-CoV-2 activity demonstrated by plaque reduction assay[24]. Quassinoids derived from *E. longifolia,* which serves as an herbal ingredient in both the current formulation and Chanthalila, exhibited inhibition activity against both a common cold human coronavirus and SARS-CoV-2[25].A recent study demonstrated that both Ya-ha-rak, Prasaprohyai, and Chanthalila exhibited the capacity to inhibit the SARS-CoV-2 virus *in vitro* through Angiotensin-Converting Enzyme 2 (ACE2) and Transmembrane Protease (TMPRSS2)[26]. ACE2 is used by the SARS-CoV-2 virus as a receptor to enter human cells[27]. Inhibiting ACE2 might theoretically reduce the virus's ability to enter and infect cells. Further, TMPRSS2 is involved in the activation of the SARS-CoV-2 spike protein, which is necessary for viral entry[27,28]. Inhibiting TMPRSS2 may prevent viral activation and entry. Although, *E. longifolia* was suspected to exert potent SARS-CoV-2 activity[25,26], there is not enough evidence

to conclusively support this hypothesis. The present study also lacks information regarding the specific dosage of Chantilila prescribed to patients with fever and whether individuals adhered to the prescribed doses. Additional research is required to elucidate the potential roles of each formulation and their respective bioactive compounds in combating COVID-19.

Besides the antiviral properties, herbal active compounds have demonstrated potential to combat COVID-19 through multifaceted mechanisms. Certain compounds possess immune-modulatory and anti-inflammatory properties, which are hypothesized to mitigate the excessive inflammation often linked to severe COVID-19 cases. This, in turn, might prevent cytokine storms and alleviate symptoms. Prior studies emphasized the anti-allergic and anti-inflammatory properties of Prasaporhyai, which may be attributed to its ability to reduce nitric oxide levels[29]. The crude extract of Ya-ha-rak was demonstrated to possess antioxidant and anti-inflammatory characteristics[30]. These properties indicate that both Prasaporhyai and Ya-ha-rak may have the potential to alleviate allergy-related symptoms and reduce inflammation caused by COVID-19 infection. Further, quercetin, a bioflavonoid presenting in various plants, demonstrated antioxidant, immune activation, and anti-inflammatory properties through the suppressing of pro-inflammatory enzymes, cyclooxygenase and lipoxygenase[31–33]. Kaempferol and luteolin, bioactive compounds found in *K.galanga* and certain plants, showed protective effects against lung injury in mice by regulating various cellular pathways including NF-kB[34,35], MAPKs[35], and AKT/Nrf2[34]. Atractylenolide, Atractylone, polyethylene alkynes, phytosterols, other sesquiterpene and sesquiterpenoid compounds founds *in A. lancea,* are known for their potential anti-viral, antioxidant, anti-inflammatory, and immunomodulatory effects[36,37].The lipophilic extract from the *A. lancea* rhizome demonstrated potent inhibitory effect against 5-lipoxygenase and cyclooxygenase[38].Additionally, the ethanolic extract from the *A. lancea* rhizome exhibited anti-inflammatory effects by inhibiting the Akt/NF-κBsignaling pathway[39].

Fatigue, headache, discomfort, muscle pain, and cardiovascular issues[40] are significantly common in COVID-19 patients. Herbal bioactive compounds may work additively or synergistically to help alleviate these symptoms. The stamen of sacred lotus (*N. nucifera*) is employed in several traditional medicines or herbal remedies to nourish the heart, anti-arrhythmia effects, improving blood circulation, and boosting the immune system[41,42]. Abundant in bioflavonoids such as kaempferol, myricetin, quercetin, rutin, and a variety of derivatives, it may be responsible for the potential pharmacological activities due to potent antioxidant properties[41–43]. Additionally, Lonicerae Japonicae Flos, the dried bud or flower with initial blooming of *L. japonica,* has a long history in traditional medicine, often used in combination with remedies for purposes such as clearing heat and detoxification, dissipating phlegm, and relieving pain[44]. Chlorogenic acid, a phenolic compound found in *L. japonica,* is known for its antioxidant and anti-inflammatory properties. Chlorogenic acid inhibits the activity of pro-inflammatory enzymes, such as cyclooxygenase-2,by suppressing NF-κB and JNK/AP-1 activation[45]. Iridoids like loganin and sweroside, flavonoids, saponins, and several compounds found in *L. japonica* contribute to their potential anti-viral, anti-inflammatory, and immunomodulatory effects[44]. Furthermore, *S. leucantha* contains various compounds, including triterpenoids, saponins, sesquiterpenes, and lignans[46,47]. The ethno-medicinal uses are for relieving cough, cold, asthma, pains, and improving

blood circulation[46,48]. Saponins are assumed to underlie the bronchodilation properties of *S. leucantha*[47], which could potentially alleviate breathing difficulties in COVID-19 patients.

The clinical evidence of herbal remedies for addressing COVID-19 is constrained by various critical factors. The rapid onset of the pandemic posed significant challenges in conducting rigorous scientific studies on these treatments, with constraints such as limited time, ethical concerns, and the urgent need for effective interventions impeding comprehensive clinical trials. Despite these challenges, herbal remedies have been widely used to mitigate the risk of COVID-19. Thai health authorities have even issued guidelines for incorporating plants, herbs, and traditional Thai medicine in managing COVID-19, including the use of Ya-ha-rak[49]. This retrospective chart review offers supporting evidence for the clinical outcomes of herbal-based treatments in COVID-19 management, albeit with some limitations. One such limitation is the absence of experimental control. Despite these constraints, the study is instrumental in offering preliminary evidence and directing future research into the potential advantages of herbal medicine. Insights from this retrospective analysis could be pivotal in shaping the framework of future prospective studies.

Further, a key limitation of the present study is the lack of comprehensive data, including long-term patient follow-up. Consequently, the study may not capture instances of long COVID-19, where patients continue to experience symptoms after recovering from the acute phase of the illness, or cases where patients passed away at a later stage. Furthermore, the specific recovery dates for each individual symptom were not precisely recorded, limiting the detail available for the resolution of each symptom. Another notable limitation is the absence of information on patients' vaccination status, which could have influenced the treatment results. These constraints are largely attributable to the urgent context of early treatments during the initial phase of the COVID-19 pandemic, when only a small number of patients were vaccinated. Despite the lack of vaccination, the clinical outcomes of the concoction appear to remain intact, evidenced by the positive treatment results seen in unvaccinated patients during the third wave of COVID-19 infections.

As of 2022, Thailand had dispensed millions of doses of the COVID-19 vaccine, resulting in a substantial reduction in the daily count of new cases. The severity of respiratory symptoms caused by the new strain of COVID-19 has also diminished. Through collaborative efforts across multiple sectors, including health, non-health, and the private sector, the outbreak was successfully contained by February 2021[2].Unfortunately, interest in the research and development of herbal solutions to combat COVID-19 has seen a decline. Despite this downturn in interest, the significance of exploring herbal-based treatments for diseases like COVID-19 should not be underestimated. In a world where viruses can rapidly mutate and potentially render existing vaccines less effective, having a diverse array of treatment options is crucial. Herbal medicines have long histories of use in many cultures, and their potential for treating modern diseases is an area ripe for exploration. Moreover, the accessibility and cost-effectiveness of herbal treatments make them especially attractive for developing countries or in regions where healthcare resources are stretched thin. The World Health Organization (WHO) endorses the inclusion of scientifically validated traditional medicine, which encompasses repurposed drugs, traditional medicines, and the development of new therapies, in the quest for potential treatments for COVID-19[50].

Conclusion

One significant factor influencing confidence in using traditional Thai medicine and herbal remedies is the lack of reliable research encompassing safety and efficacy aspects. These results of the retrospective chart review highlight the clinical outcomes of the concoction as a standalone treatment in facilitating the management of COVID-19 infection. Despite some limitations, the current study concludes that the concoction of either traditional decoction or capsules appears to be a safe and efficient treatment option. The utilization of the concoction, grounded in traditional therapeutic medicine theories, with possible pharmacological actions based on modern medicine, has been discussed. This is the first human clinical report on the antiviral properties of a formulation containing herbs from Ya-ha-rak and Prasaporhyai. This study is performed with the aspiration that it will trigger further advancement and investigations into the efficacy, safety of this concoction. Such efforts could provide more alternatives to Fah Talai Jone/*A. paniculata* to substantially contribute to the fight against future viral emerging, especially in the event of more virulent strain mutations. While vaccines and antiviral drugs are certainly the first line of defence, herbal medicines could potentially provide additional support and resilience in the face of viral pandemics. Further research is warranted to investigate whether the formulation has the potential to prevent or mitigate symptoms associated with long COVID-19.

Tables, Figer and Diagrams

Table 1 Patient demographic data

	Cohort 1 (Jul2021–Nov2021)	Cohort 2 (Dec2021-Apr2022)	Total
Sex (number of patients)			
Male	19 (18.8%)	26 (25.7%)	45 (44.6%)
Female	21 (20.8%)	35 (34.7%)	56 (55.4%)
Age range(years)			
6-17	1 (1.0%)	10 (9.9%)	11 (10.9%)
18-25	6 (5.9%)	3 (3.0%)	9 (8.9%)
26-50	25 (24.8%)	29 (28.7%)	54 (53.5%)
> 50	8 (7.9%)	19 (18.8%)	27 (26.7%)
Mean±SD (years)	38.6±14.4	39.2±17.5	39.0±16.3
Min-Max (years)	7.7-74.0	6.4-75.9	6.4-75.9

Table 2 Background symptoms of COVID-19 patients on the first visit for medication

	Number of patients		
	Cohort 1 (Jul2021–Nov2021)	Cohort 2 (Dec2021–Apr2022)	Total
Cough	30 (75.0%)	37 (60.7%)	67 (66.3%)
Fever	23 (57.5%)	36 (59.0%)	59 (58.4%)
Loss of smell	20* (50.0%)	3* (4.9%)	23 (22.8%)
Headache	18 (45.0%)	23 (37.7%)	41 (40.6%)
Sore throat	17 (42.5%)	26 (42.6%)	43 (42.6%)
Shortness of breath	11 (27.5%)	8 (13.1%)	19 (18.8%)
Phlegm	13 (32.5%)	25 (41.0%)	38 (37.6%)
Runny nose	8 (20.0%)	20 (32.8%)	28 (27.7%)
Nausea/Vomiting	4 (10.0%)	9 (14.8%)	13 (12.9%)
Total	**40 (100.0%)**	**61 (100.0%)**	**101 (100.0%)**

*Statistically significant at $p < 0.05$

Table 3 Duration of treatment

	Duration of treatment(days±SD)		
	Cohort 1 (Jul2021–Nov2021)	**Cohort 2 (Dec2021–Apr2022)**	**Total (days)**
Sex			
Male	10.1±2.9	7.3±1.6	8.6±2.7
Female	10.6±3.7	7.6±1.8	8.7±3.0
Age range(year)			
6-17	12.0±0.0*	6.9±1.8*	7.4±2.3*
18-24	12.2±3.8	8.3±2.3	10.9±3.7*
25-50	9.8±2.9	7.2±1.4	8.4±2.6
> 50	9.6±4.0	8.0±1.9	8.5±2.7
Total(days)	10.2±3.3*	7.5±1.7*	8.6±2.8

*Statistically significant at $p < 0.05$

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