

Traditional Thai herbal medicine for treating COVID-19

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ABSTRACT

Traditional Thai herbs, especially their phytochemicals, are believed to have a wide range of antimicrobial, anti-inflammatory, antioxidant, and antiviral properties. This review focuses on traditional Thai herbs for the potential treatment of coronavirus disease 2019 (COVID-19). Thai herbal therapies, including traditional Thai medicines, have been studied, investigated, and used to advance scientific knowledge. Specifically, Thai herbs, including *Andrographis paniculata*, *Boesenbergia rotunda*, *Phyllanthus amarus*, *Phyllanthus emblica* L., *Citrus medica*, *Zingiber officinale*, *Rheum officinale* Baill., and Kerra capsule, have been documented and used in the treatment of severe acute respiratory syndrome (SARS)-CoV-2. Traditional Thai herbs are believed to have various antiviral properties, and these herbs show promise as defense mechanisms against SARS-CoV-2. The focus of this review is on the traditional Thai herbs that have anti-viral properties and may have an impact on COVID-19.

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic is still a concern. According to the Status Report of COVID-19, there are 263,248,748 cases of infection and 5,237,114 fatalities worldwide. There are 171,978 cases in Thailand, including 4,886 new cases, 2,120,758 confirmed cases, and 20,812 deaths (Status Report of COVID-19. Retrieved 8 December 2021). For instance, the Department of Disease Control has undertaken measures to prevent and control the spread of COVID-19. However, the spread of COVID-19 and deaths have continued due to a virus mutation, resulting in thousands of daily infections and overwhelming government hospitals. The guidelines for patients with COVID-19

at home (home isolation) have been developed under a monitoring system to solve this problem. Treatment guidelines, as recommended by the Ministry of Public Health, Thailand, for patients with COVID-19 vary according to the severity of the disease and the appearance of symptoms. For COVID-19 treatment, favipiravir is a therapy option in some circumstances. However, it has several adverse effects, including the possibility of teratogenicity and an increase in uric acid levels. In particular, pregnant women and patients with impaired liver function should be cautious when using this medication (Shang *et al.*, 2022).

Therefore, medicinal herbs are another option for treating COVID-19 in asymptomatic or mildly symptomatic patients. Thai traditional herbs, particularly their phytochemicals, have been reported to have broad-spectrum antimicrobial, anti-inflammatory, antioxidant, and antiviral properties (Chotchoungchatchai *et al.*, 2012; Chusri *et al.*, 2015; Lumlerdkij *et al.*, 2018; Sangkitporn *et al.*, 2005). These herbs point to their suitability as anti-severe acute respiratory syndrome (SARS)-CoV-2 candidates. This review aims to focus on traditional Thai herbs, which may potentially affect COVID-19.

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TRADITIONAL THAI HERBS FOR TREATING COVID-19

Commercial antivirals are frequently restricted to usage in hospitals and in severe instances. Therefore, several herbal therapies, including Thai traditional medicines, were studied, examined, and used to advance our scientific understanding. In particular, Thai herbal plants, including *Andrographis paniculata*, *Boesenbergia rotunda*, *Phyllanthus amarus*, *Phyllanthus emblica* L., *Citrus medica*, *Zingiber officinale*, *Rheum officinale* Baill., and Kerra capsule, have been documented and used in the treatment of COVID-19 (Table 1).

Andrographis paniculata

Andrographis paniculata (*A. paniculata*) leaves were used to treat fever and sore throat, as documented in Thailand's National List of Essential Drugs. In addition, numerous investigations indicated that it possessed antibacterial action, and andrographolide is the primary constituent. Earlier research suggested that andrographolide inhibited virus proliferation and infection in various viruses, including the chikungunya virus, influenza virus, HIV, dengue virus, and herpes simplex virus type 1 (Chen *et al.*, 2009; Panraksa *et al.*, 2017; Seubsasana *et al.*, 2011; Uttekar *et al.*, 2012; Wintachai *et al.*, 2015).

An *in silico* docking analysis revealed that 15 phytochemicals from *A. paniculata* had an affinity for and interacted with S-protein, virus C-terminal cleavage, and virus polyprotein N-terminal cleavage of SARS-CoV-2 (Hiremath *et al.*, 2021). Additionally, *A. paniculata* (*Andrographis*) is a widely used herbal product for various indications (Sa-Ngiamsumtorn *et al.*, 2021). The anti-SARS-CoV-2 efficacy of *A. paniculata* extract (the active ingredient is andrographolide) was determined *in vitro* in a study of herbal medicine (Sa-Ngiamsumtorn *et al.*, 2021). *In vitro* studies indicated that the *A. paniculata* ethanolic extract (andrographolide) suppressed viral multiplication following infection of Calu-3 cells with SARS-CoV-2 (IC₅₀ = 9.54 and 1.68 M, respectively) (Sa-Ngiamsumtorn *et al.*, 2021). This study demonstrates the efficacy of *A. paniculata* in inhibiting viral replication, but its utility in a clinical investigation remains unknown. One trial has already demonstrated a reduction in pneumonia symptoms in patients receiving 94.3% pure *A. paniculata* ethanolic extract and a decrease in the need for mechanical ventilation (Benjaponthak *et al.*, 2021).

Another study (Benjapolphithak *et al.*, 2021) reported the usage of *A. paniculata* to treat COVID-19 and discovered that it could help avoid COVID-19 symptoms. The trial enrolled 526 patients who did not receive *A. paniculata* and 309 patients who did get *A. paniculata* in combination with 180 mg/day of andrographolide. It was shown that individuals who did not get andrographolide progressed more rapidly, developing pneumonia or requiring intubation. Only three patients (0.97%) had severe symptoms, which implied that the number needed for a treatment equals 7.32, indicating that administering *A. paniculata* to every eight patients with COVID-19 can prevent one case of pneumonia. *Andrographis paniculata* can significantly reduce the incidence of pneumonia by 94.3% (Benjapolphithak *et al.*, 2021). However, long-term use of *A. paniculata* can result in various adverse effects. There are also some restrictions, including the prohibition

of use in pregnant women, breastfeeding women, patients with liver disease, and patients with renal disease (Shang *et al.*, 2022).

Furthermore, patients receiving *A. paniculata* have reported experiencing hypersensitivity, and healthcare practitioners should be aware of this potential risk. Hypersensitivity reactions should be handled when utilizing products from *A. paniculata* (Suwankesawong *et al.*, 2014).

Boesenbergia rotunda

Boesenbergia rotunda (*B. rotunda*) is a perennial herb known locally in Thailand as "Krachai." It is botanically classified as a tiny herbaceous plant with short, fleshy, or slender rhizomes. Fresh rhizomes have a distinctive scent and a mildly spicy flavor (Sudwan *et al.*, 2007; Tuchinda *et al.*, 2002) and are widely used in Southeast Asia as food spices or condiments (Isa *et al.*, 2012) and in folk medicine. For centuries, traditional healers have used this plant to treat inflammation, aphthous ulcers, dry mouth, stomach pain, dysentery, leukorrhea, oral ailments, cancer, and kidney issues (Morikawa *et al.*, 2008). Moreover, this plant and panduratin A were discovered to inhibit HIV-1 protease and to have antinociceptive properties in thermal and mechanical pain models (Cheenpracha *et al.*, 2006). In particular, this pharmacodynamic impact reduces the body warmth and nociception associated with a viral infection. The ethanolic extract possessed anti-inflammatory, antibacterial, anti-foot and mouth disease virus, and anti-dengue viral properties. Furthermore, it inhibits the pathogens *Staphylococcus aureus* and *Klebsiella pneumoniae* (Suknasang *et al.*, 2017). Thus, the ethanolic extract of this plant may be utilized to treat COVID-19 since it is capable of eradicating SARS-CoV-2 and alleviating the associated symptoms, particularly pneumonia.

Boesenbergia rotunda extract and its phytochemical component, panduratin A, were also found to have anti-SARS-CoV-2 action (Kanjanasirirat *et al.*, 2020) when antiviral medication candidates were screened utilizing a high-content screening technology. The fluorescence-based approach was applied to infect a coronavirus-resistant cell line. A total of 122 extracts were examined and purified for the chemicals produced from Thai medicinal plants. The extracts and compounds with the most excellent antiviral activity were subsequently investigated using dose-response and plaque-reduction assays. In addition, the selected compound was tested for efficacy in the human airway, and the anti-SARS-CoV-2 capability of the compound was evaluated in human lung epithelial cells using a high-content imaging technique compared to remdesivir, the first COVID-19 medication licensed by the Food and Drug Administration (FDA). Finally, the investigation established that extracts of *B. rotunda* (fingerroot) and panduratin A, its phytochemical component, were viable candidates for a novel COVID-19 treatment (Kanjanasirirat *et al.*, 2020).

Citrus medica and *Z. officinale*

Citrus medica (Manoa-Kwai in Thai) and other *Citrus* species have a high amount of vitamin C. They have mucolytic effects and can help reduce coughing and fever. *Citrus* spp. peel includes coumarin chemicals that have anticoagulant characteristics and can aid in blood circulation improvement. In Thai traditional medicine, *Z. officinale* is used to treat air cavity disorders such as allergic rhinitis, nausea, sore throat, lung cancer,

Table 1. A summary of Thai herbal medicine's active ingredients, SARS-CoV-2 antiviral activity, and side effects.

Herbal medicine	<i>Boesenbergia rotunda</i>	<i>Phyllanthus amarus</i>	<i>Phyllanthus emblica</i>	<i>Andrographis paniculata</i>	<i>Rheum officinale</i> Baill	<i>Citrus medica</i> , and <i>Zingiber officinale</i>	Kerra capsules
Active ingredients	Panduratin A	Flavonoid compounds (astragalin, kaempferol, quercetin, quercetin-3-O-glucoside, and quercetin) Tannins (corilagin, furosin, and geraniin)	(2S)-Eriodictyol 7-O-(6'-Ogalloyl)-D-glucopyranoside (EBDGp)	Andrographolide	Emodin	Rhoifolin, naringin, neohesperidin, apigenin 6,8-di-C-glucoside, adenine, hesperidin, 6-gingerol Z, and xanthine	Kaen Chan Daeng (<i>D. laureiroi</i>) Kaen Chan Khao (<i>T. hoensis</i> , Calathea (<i>S. dichotomus</i>) Gac Root (<i>M. cochinchinensis</i>), Lemon root (<i>C. auratifolia</i>) Sakae root (<i>C. quadrangulare</i>) Kra Tung Root (<i>D. Volubilis</i>) Bai-ya-nang (<i>T. triandra</i>), <i>T. cordifolia</i> (<i>T. crispa</i>)
Antiviral activities	Physically binds and inhibits the viral protease	Inhibits SARS-CoV replication by inhibiting two proteins (RdRp)	High affinity for binding to RdRp	Interaction with S-protein, virus C-terminal cleavage, and virus polyprotein N-terminal cleavage of SARS-CoV-2	Inhibits the infection of VeroE6 cells by S-protein-pseudotyped retrovirus	Reducing viral load and shedding of SARS-CoV-2	Inhibition of the SARS-CoV-2 main protease and the SARS-CoV-2 RdRp, anti-inflammatory activity, reducing intracellular viral activity
Side effects	Analgesic and antipyretic effects	Vasculogenic effect on the kidney blood vessels	No information on side effects	A range of side effects, such as hypersensitivity and renal impairment This drug should not be used by pregnant women, nursing mothers, patients with liver disease, and patients with renal impairment, or hypersensitivity	Stomach pain, diarrhea, nausea, vomiting, and cramps	<i>Citrus medica</i> : nausea, vomiting, diarrhea. heartburn stomach cramps or bloating fatigue and sleepiness, or sometimes insomnia, headache, and skin flushing	Diarrhea, one incidence of dizziness, and one case of black stool
							<i>Z. officinale</i> : heartburn, diarrhea, burping, and general stomach discomfort

Continued

Herbal medicine	<i>Boesenbergia rotunda</i>	<i>Phyllanthus amarus</i>	<i>Phyllanthus emblica</i>	<i>Andrographis paniculata</i>	<i>Rheum officinale</i> Baill	<i>Citrus medica</i> , and <i>Zingiber officinale</i>	Kerra capsules
	Cheenpracha <i>et al.</i> (2006)	Hiremath <i>et al.</i> (2021)		Benjapolphithak <i>et al.</i> (2021).	Ho <i>et al.</i> (2007)	Haridas <i>et al.</i> (2021)	Seetaha <i>et al.</i> (2022)
References	Panthong <i>et al.</i> (1989)	Eweka <i>et al.</i> (2011)	Pandey <i>et al.</i> (2021)	Shang <i>et al.</i> (2022)			Srathong <i>et al.</i> (2022)

and viral infections of the respiratory system (Itharat *et al.*, 2021). Moreover, *Z. officinale* (Ginger, Khing in Thai) was also examined for antiviral activity against respiratory tract viruses, demonstrating that hot water infused with fresh ginger also had antiviral activity against the human respiratory syncytial virus (HRSV) in human respiratory tract cell lines by inducing HRSV plaque formation on airway epithelium and by inhibiting viral attachment and internalization (Chang *et al.*, 2013). This investigation discovered that fresh ginger has superior antiviral efficacy to dried ginger. *Zingiber officinale* extract prevented *Pseudomonas aeruginosa*-induced acute pneumonia, a symptom of COVID-19 (Chakotiya *et al.*, 2018). Additionally, *Z. officinale* has been associated with numerous studies of its anti-inflammatory effect, which aids in reducing lung tissue damage. Its major constituents, gingerol and shogaol, also demonstrated significant acute and chronic anti-inflammatory effects (Kuropakornpong *et al.*, 2020). *Citrus medica* and *Z. officinale* were recently determined for the spike protein and other proteins on SARS-CoV-2 using *in silico* analysis. The efficacy of the rhoifolin, naringin, neohesperidin, apigenin 6,8-di-C-glucoside, adenine, hesperidin, 6-geringol Z, and xanthine components to the spike protein and other proteins on SARS-CoV-2 were determined (Haridas *et al.*, 2021). *In silico* studies indicate that the phytochemicals in *C. medica* and *Z. officinale* may have a significant potential for reducing viral load and shedding SARS-CoV-2. Further research is suggested to determine its effectiveness in decreasing COVID-19 transmission (Haridas *et al.*, 2021). Thus, ginger and *Citrus* spp. (lime, lemon) should be studied further for their potential to treat COVID-19 symptoms and antiviral activity.

Phyllanthus amarus and *P. emblica*

Phyllanthus amarus (Makhm-Pom in Thai) is a widely distributed tropical, medicinal plant that is utilized as an antipyretic in Thai traditional medicine. It possesses a broad range of medicinal properties, including antibacterial, antiviral, antimalarial, anti-inflammatory, anticancer, and antioxidant properties (Sarin *et al.*, 2014; Yeo *et al.*, 2015). *Phyllanthus amarus* has been tested for its antiviral efficacy against SARS-CoV-2 infection. A previous study of *P. amarus*'s interaction with RNA-dependent RNA polymerase (RdRp) and papain-like protease on SARS-CoV-2 demonstrated its flavonoid compounds (astragalin, kaempferol, quercetin, quercetin-3-O-glucoside, and quercetin) and tannins (corilagin, furosin, and geraniin) have a higher affinity for binding. It has been reported that *P. amarus* inhibits SARS-CoV replication by inhibiting two proteins (RdRp) (Hiremath *et al.*, 2021). Moreover, as indicated previously, *P. amarus* was discovered to possess antiviral efficacy against HIV-1 (Notka *et al.*, 2004). Meanwhile, an *in silico* model revealed that (2S)-eriodictyol 7-O-(6"-Ogalloyl)-D-glucopyranoside (EBDGp), a compound of *P. emblica* has a high affinity for binding to RdRp (-23.32 kcal/mol) and hence inhibits viral replication (Pandey *et al.*, 2021). However, *P. emblica* was discovered to have antiviral action against HIV-1 when used as a traditional Thai treatment Triphala component (Mishra *et al.*, 2018; Pandey *et al.*, 2021). The isolated glochicoccinoside D exhibited significant action against influenza A virus strain H3N2 and hand, foot, and mouth virus strain EV71, with IC₅₀ values of 4.5, 0.6, and 2.6 0.7 g/ml, respectively (Lv *et al.*, 2015). *Phyllanthus emblica* fruits have

been shown in numerous previous trials to have adjuvant qualities for COVID-19 treatment, including immunological, anti-allergy, antitussive, and laxative actions (Zhang *et al.*, 2021). These activities may alleviate such symptoms in persons infected with COVID-19. However, additional research is necessary.

***Rheum officinale* Baill.**

Rheum officinale Baill. (Rhubarb or Kod Num Taow in Thai) was extracted for the emodin, an anthraquinone group compound isolated from the root tubers. The extract was reported to inhibit the infection of VeroE6 cells by S-protein-pseudotyped retrovirus (Ho *et al.*, 2007). These data suggested that emodin could be a viable lead therapy drug for SARS. Previously, emodin was shown to exhibit specific anti-inflammatory action in a noninfectious mice model of asthma. Emodin suppressed ovalbumin (OVA)-induced increases in eosinophil count; interleukin- (IL-) 4, IL-5, and IL-13 levels were regained in bronchoalveolar lavage fluid, and serum levels of OVA-specific IgE, IgG, and IgG1 were decreased. Emodin significantly decreased OVA-induced eosinophilia in lung tissue and mucus hypersecretion by goblet cells in the airway, as evidenced by histological examinations. Furthermore, pretreatment with emodin resulted in a significant decrease in the mRNA expression of acidic mammalian chitinase, chitinase 3-like protein 4 (Ym2), and Muc5ac in lung tissues, as well as an increase in methacholine-induced airway hyperresponsiveness. These data imply that emodin may effectively postpone the progression of airway inflammation and may be used to treat allergic airway inflammation in patients. Emodin has been reported in *Cassia* species, including *Cassia siamea* Lam. (Khe-lhek in Thai), *Cassia alata* (L.) Roxb. (Chum-Hed-Thet in Thai), and *Cassia Angustifolia* M. Vahl (Makham-Kak). All of these plants exhibit laxative effects. In Thai traditional medicine, it has laxative properties.

Recently, emodin has been shown to inhibit the interaction between the SARS-CoV spike protein and angiotensin-converting enzyme-2 via an inhibitory effect on the infectivity of S-protein-pseudotyped retrovirus in VeroE6 cells. (Ho *et al.*, 2007). Emodin, an anthraquinone molecule originating from the species *Rheum* and *Polygonum*, dose-dependently inhibited the S-protein-ACE2 interaction.

Kerra capsules

Taksila formula is an herbal medicine recipe that Thai people have used to treat epidemic ailments since ancient times. It consists of herbal formulations (Kerra capsules). Kerra capsules comprise nine major herbal constituents and have been registered with the FDA and the Ministry of Public Health under the registration number G 40/57 for use in traditional medicine formulae to treat fevers. The herbal recipe aids in the reduction of heat, fever, cough, headache, and phlegm, while also nourishing the lymphatic system, boosting the immune system, alleviating restlessness, reducing inflammation, discomfort, and swelling, and improving heart and blood circulation (Singthong *et al.*, 2014; Sun *et al.*, 2019). Therefore, utilizing traditional herbal medicines as a treatment can help minimize the cost of COVID-19 treatment.

Interestingly, the Kerra capsule is a potential herbal remedy. Kerra capsule is a traditional Thai herbal formula from the Taksila texts in King Rama V's royal medical handbook

(Chitsanucha, 2021). The recipes call for the use of a variety of herbs, including Kaen Chan Daeng (*Dracaena loureiroi*), Kaen Chan Khao (*Tarenna hoaensis*), *Calathea* (*Schumannianthus dichotomus*), Gac Root (*Momordica cochinchinensis*), lemon root (*Citrus aurantifolia*), Sakae root (*Combretum quadrangulare*), Kra Tung Root (*Dregea volubilis*), Bai-ya-nang (*Tiliacora triandra*), and *Tinospora cordifolia* (*Tinospora crispa*).

There are several medicinal properties in each herb. First, *D. loureiroi* helps relieve a fever, cough, restlessness, inflammation, pain, and swelling, as well as helps nourish the heart and blood circulation. According to various studies, several species of plants in the *Dracaena* family consist of phenol, flavonoid, and oligomer. These substances are anti-free radicals that help inhibit inflammation and prevent infection and microorganisms. It also helps prevent cardiovascular and related cerebrovascular disorders and inflammation in various conditions (Sun *et al.*, 2019). Second, *T. hoaensis* is an herb that helps with appetite, thirst, nourishing, fatigue, dizziness, headache, nausea, and strength and helps heal the nervous system. The extract of their components is rich in glucosides, glycosides, and saponins, which contain antioxidant activity and can help inhibit inflammation (Yang *et al.*, 2007). Third, *S. dichotomus* have some properties that help reduce fever and relieve thirst and inhibit inflammation within the body. In ancient times, the head was often used as a drug to treat fever poisonings such as hay fever, jaundice, typhus, smallpox, and chickenpox (Maneenoon *et al.*, 2015). Fourth, *M. cochinchinensis* has its root with outstanding properties in reducing fever, relieving aches and pains, expelling phlegm, and helping boost the body's immune system. The roots are rich in active pharmaceutical ingredients, more than 60 substances such as calendulosides, saponins, and triterpene glycosides such as mocochoinosides A and B, which contain properties to reduce inflammation through inhibition of the formation of nitric oxide (NO) by macrophages (Huang *et al.*, 2021), thereby reducing fever symptoms and the likelihood of a cytokine storm, which is often a consequence when the body becomes infected. Another study found that chymotrypsin-specific inhibitors (MCoCl), a type of squash root, have a stimulating effect on cell division and white blood cell embryos in the spinal cord and larynx and help reduce the generation of radicals independent of different types of white blood cells, which causes the cells to be injured (Tsoi *et al.*, 2006). The extract from the squash root helps regulate the function of the immune system so that it can respond to pathogens. Moreover, studies have found that glycosides and saponins in the guava root may inhibit thrombosis by preventing the aggregation of fibrinogen and platelets. However, this mechanism is still being studied (Lichota *et al.*, 2020). Fifth, *C. aurantifolia*, the extracts derived from *citrus* plants, including lemon roots, are often rich in nutrients with antioxidants such as terpenoids, flavonoids, polysaccharides, and polyphenols, which help prevent inflammation and cell damage in various conditions. Furthermore, lemon roots also contain naringin and hesperidin, which inhibit COX-2, IL-1 β , and IL-6, a cytokine-stimulating inflammation secreted by macrophages (Liu *et al.*, 2022), indicating that the use of lemon juice for the treatment of infectious diseases will help reduce the risk of cytokine storms, which can cause severe inflammation all over the body. Sixth, *C. quadrangulare*, the extracts of Sakae root, are rich in flavonoids and many triterpenes, such as combretic acids, combretanones, and quadrantids, which qualify outstanding in protecting liver cells by inhibiting inflammation and

cell death (Banskota *et al.*, 2000). Furthermore, Sakae extracts also reduced the production of IgE cytokines and various chemokines of white blood cells such as IL-6, IL-13, and TARC at the mRNA level by regulating Mitogen-activated protein kinase signaling pathways properties to help suppress inflammation predominantly expressed on the skin (Biswas *et al.*, 2010; Park *et al.*, 2020). Seventh, the root extract of *D. volubilis* has many properties. This herb contains many essential substances, such as pregnane glycosides and polyoxypregnane glycosides, which affect the free radicals in cells by inhibiting the lipid oxidation process and reducing the sensitivity of various types of free radicals such as NO and superoxide anion, thereby reducing the injury of organ tissues (Biswas *et al.*, 2010). Eight, in terms of *T. triandra*, current research also revealed that the extract from yanang has properties related to reducing sugar and fat in the blood, including helping stimulate the functioning of the nervous system and brain. In the leaves and vines, yanang is rich in antioxidants of the phenol group, which has an anti-inflammatory effect on the body, prevents clot formation of blood clots, and has high stability even in capsule form (Singthong *et al.*, 2014). Several studies of various herbs in Thailand have found that the vine has properties preventing various pathogens, such as bacteria, *Candida* fungi, and the porcine reproductive and respiratory syndrome virus, which cause disease in the respiratory system (Arjin *et al.*, 2020). However, the activities related to inhibiting the virus that causes human disease still need further study. Ninth, for *T. crispa*, different parts of the plant contain antioxidants such as alkaloids and flavonoids and a very high glycoside content (Jaric *et al.*, 2015). In terms of infectious disease prevention and mitigation properties, previous work research has found that *T. crispa* extract will help stimulate the cell function of macrophages in response (chemotaxis) and ingestion (phagocytosis) (Ahmad *et al.*, 2018).

Furthermore, a recent study has reported that *T. cordifolia*'s extract contains alkaloids, steroids, and terpenoid lignans, which have medicinal properties against SARS-CoV-2, which causes COVID-19. These substances inhibit the binding between the S-protein of the SARS-CoV-2 virus and the ACE2 receptor in human cells, thus preventing virus from getting into cells (Jena *et al.*, 2021). Another study found that tinocordiside in *T. crispa* can bind to the main protease enzyme of SARS-CoV-2 with a force greater than 8 kcal/mol, resulting in changes in the enzyme molecules to the point where the virus can no longer use it to continue to increase the number of diagonals (Shree *et al.*, 2022). Other studies have also found that the active ingredients in *T. cordifolia*, such as glycosides, triterpenoids, and lactones, modulate cell balance in the immune system together in response to pathogens accurately without inducing severe inflammation or cytokine storms. Therefore, wormwood may help reduce the severity of COVID-19 in some patients (Khan and Rathi, 2020) and may help prevent infection and transmission of SARS-CoV-2, which can cause COVID-19.

All of the above-mentioned herbs aid in the reduction of heat, fever, and cough; the elimination of phlegm; the nourishment of lymph; the stimulation of the immune system; the reduction of restlessness; the reduction of inflammation, pain, and swelling; the improvement of heart and blood circulation (Singthong *et al.*, 2014; Sun *et al.*, 2019).

Previous *in vitro* research examined the efficiency of the Kerra extract in inhibiting the COVID-19 main protease of SARS-

CoV-2. It revealed that Kerra extract could inhibit both the SARS-CoV-2 main protease and the SARS-CoV-2 RdRp (Seetaha *et al.*, 2022). Furthermore, Kerra extract may affect macrophages' anti-inflammatory activities (Seetaha *et al.*, 2022). Moreover, Kerra extract has decreased intracellular viral activity in Crandell-Rees feline kidney cells (Seetaha *et al.*, 2022). There were no significant adverse reactions such as diarrhea or dizziness during the cytotoxicity test, owing to the very few or no poisonous chemicals identified by the Thai Herbal Pharmacopoeia 2018 criteria, and the acute toxicity of Kerra capsules examined in rats is extremely low. This indicates that the Kerra capsules are safe and may potentially reduce the severity of COVID-19 infection and mortality rates.

A previous article examined the effect of traditional herbal therapy (Kerra capsules) on the clinical characteristics of patients with COVID-19 isolated at home during July and August 2021. Moreover, another retrospective study was conducted on 2,476 COVID-19-positive patients in Pathum Thani Province who were treated with medicinal herbs (Kerra capsules) and then self-isolated under the supervision of Prachathipat Hospital (Srathong *et al.*, 2022). The findings indicated that most patients (60.33%) had a cough before obtaining the herbal medicine and drank the Kerra capsules alone (96.04%) during home isolation. Most patients (62.8%) recovered between 1 and 7 days after getting the herbal remedy. No adverse events were reported in 99.68% of patients, and this trial did not result in any referrals or deaths. As a result, Kerra is a candidate for COVID-19 medication treatment that is safe and cost-effective (Srathong *et al.*, 2022).

CONCLUSION

Several herbal remedies, including Thai traditional medicine, have been studied, analyzed, and used to advance scientific knowledge. Primarily, Thai medicinal herbs such as *A. paniculata*, *B. rotunda*, *P. amarus*, *P. emblica* L., *C. medica*, *Z. officinale*, *R. officinale* Baill., and Kerra capsules have been used in the treatment of COVID-19. These medicinal herbs are other alternatives for treating COVID-19 in patients with little or no symptoms. Traditional Thai plants, especially their secondary plant compounds, are believed to have broad-spectrum antiviral, anti-inflammatory, antioxidant, and antibacterial effects. These plants show their potential as anti-SARS-CoV-2 candidates. This review focuses on traditional Thai herbs that may affect COVID-19.

AUTHOR CONTRIBUTIONS

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work. All the authors are eligible to be an author as per the international committee of medical journal editors (ICMJE) requirements/guidelines.

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DATA AVAILABILITY

All data generated and analyzed are included in this research article.

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