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Thailand Approves Asian Herb Andrographis to Treat COVID-19

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By [Connor Yearsley \(/resources/herbalgram/authors/yearsley-connor/\)](/resources/herbalgram/authors/yearsley-connor/)

In late December 2020, the government of Thailand approved a pilot study of the use of the southern Asian herb andrographis (*Andrographis paniculata*, Acanthaceae) to treat early symptoms and reduce the severity of COVID-19. Initially, the treatment will be available at five state-owned hospitals in Thailand on a voluntary basis for people 18-60 years old with minor symptoms. It reportedly will be given to patients within 72 hours of symptom onset. This approval comes amid an increase of COVID-19 infections in the country.¹ As of January 28, 2021, Thailand had 16,221 cases of COVID-19 in a total population of about 70 million.²

Called *fah talai jone* in Thai and “the king of bitters,” among other names, andrographis is a small annual plant. In India’s traditional medical system of Ayurveda, the plant’s dried leaves and shoots are used for bronchitis, cough, diarrhea, dyspepsia (indigestion), fever, inflammation, and skin diseases. In traditional Chinese medicine, the plant has been used to treat colitis (inflammatory disease of the colon), cough, dysentery, fever, influenza, and sore throat. Modern studies have focused on andrographis’ potential benefits for respiratory and digestive conditions.³

In late June 2020, *The Nation Thailand* reported that phase 1 of the Thai research initiative on andrographis for COVID-19 had begun at two hospitals in Thailand. In this preliminary trial, patients received andrographis extract capsules* if they were confirmed to be infected with COVID-19 and had mild to moderate symptoms, including fever and coughing, lasting no more than 72 hours. Six subjects reportedly received 60 mg, or three times the normal dose, of andrographis extract capsules three times per day, while another six subjects received 100 mg, or five times the normal dose, three times per day.⁵

In late August 2020, *The Nation Thailand* reported that the lower dose of andrographis showed benefits in the preliminary trial, especially for coughing. Within three days, both cough volume and overall symptom severity reportedly decreased significantly. After five days, other symptoms improved, and real-time polymerase chain reaction (PCR) tests were negative for the COVID-19 virus in two patients. After three weeks, real-time PCR tests were negative in all six subjects, but additional studies were needed to confirm the results.⁶

Phase 2 was scheduled to begin in September 2020 and reportedly included 60 volunteers who were divided into two groups: one that received andrographis and one that received placebo.⁶ Details about the results of this phase are unclear, but in December, when the andrographis extract was approved for the pilot study, the Thai government reportedly claimed that the plant could be used as a safe, effective, less costly treatment alternative for COVID-19 and can reduce inflammation, according to Bloomberg.¹ The plants used in the Thai COVID-19 research initiative are being sourced from Thailand.⁵

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In a study published in November 2020, researchers screened 122 Thai natural products (114 medicinal plant extracts and eight purified compounds) for activity against SARS-CoV-2, the virus that causes COVID-19. Among six selected candidates, andrographis extract had moderate inhibitory activity against the virus in cell cultures, while its purified compound andrographolide exhibited 99.9% inhibitory activity against the virus in cell cultures.⁷

Another in vitro study from Thailand published in December 2020 showed that a 95% ethanol extract of andrographis significantly inhibited the production of SARS-CoV-2 in a human lung cell model. The andrographis material met the criteria of the *Thai Herbal Pharmacopoeia*, and its powder was made into an extract using 95% ethanol at a 4:1 ratio.⁸ It is unclear if these two studies played a part in the government's approval of andrographis for COVID-19.

In an email notice sent by the American Herbal Pharmacopoeia (AHP) on January 4, 2021, about the Thai government's approval of andrographis, Roy Upton, RH (AHG), DipAyu, president of AHP, was quoted as saying: "Mobilizing immune defenses as soon as symptoms arise is critically important for management of any upper respiratory infection.

"It is a strategy employed by Chinese herbal practitioners for centuries and is a formal part of [COVID-19] treatment protocols in China, where more than 90% of COVID patients are treated with herbs," whereas for many COVID-19 patients in the United States, the disease progresses while waiting for the test results.

According to the AHP notice, COVID-19 "patients in the US [may be] at a distinct disadvantage [by] not integrating herbal medicines into the management of COVID-19."

* According to an article published in the Bangkok Post in May 2020, "the Department of Thai Traditional and Alternative Medicine signed an MoU [memorandum of understanding] with the Department of Medical Sciences and the Government Pharmaceutical Organisation (GPO) on Feb. 25 for a laboratory experiment. Under the contract, the Institute of Biological Products conducted the test. It used ground dried leaves of andrographis and andrographis extract produced by Thai Herbal Products Company, an affiliate of GPO."⁴ However, it is not clear if this is the same andrographis preparation used in the human studies.

Other Potential Benefits of Andrographis

Previous studies have found that andrographis may have benefits for other viral infections. A 2004 study that involved 133 children with the common cold compared a preparation of echinacea (*Echinacea purpurea*, Asteraceae) in combination with standard conventional medical treatment, a preparation containing andrographis in combination with standard treatment, and standard treatment only. All three groups experienced improvements in upper respiratory symptoms, but the children who received the preparation containing andrographis recovered from symptoms significantly faster than children in the two other groups.⁹

A 2017 systematic review that included 33 randomized, controlled trials (N = 7,175) suggested that andrographis may have benefits for acute respiratory tract infections (ARTIs). Andrographis improved cough and sore throat compared to placebo and significantly improved overall symptoms of ARTIs compared to placebo and other herbal treatments. The meta-analysis of 12 clinical studies comparing andrographis to usual care (conventional treatment with analgesics, antibiotics, anti-inflammatories, antivirals, corticosteroids, or steroids) indicated a statistically significant reduction in the duration of sore throat and sick leave, but not cough. No major adverse events (AEs) were reported, while minor AEs were mostly gastrointestinal. However, the overall methodological quality of included studies was rated "poor."¹⁰

Andrographis is the main ingredient of the multi-herb formula Nilavembu Kudineer, which is used in Siddha medicine of India and also includes nutgrass (*Cyperus rotundus*, Cyperaceae), threadstem carpetweed (*Mollugo cerviana*, Molluginaceae), black pepper (*Piper nigrum*, Piperaceae), Indian sandalwood (*Santalum album*, Santalaceae), snake gourd (*Trichosanthes cucumerina*, Cucurbitaceae), vetiver (*Vetiveria zizanioides*, Poaceae), and ginger (*Zingiber officinale*, Zingiberaceae). Traditionally, these plants have been used to treat arthralgia (joint pain), arthritis, fever, gastric ulcers, general debility, inflammation, and jaundice. In a 2018 study, an ethanolic extract of Nilavembu Kudineer provided protection against dengue virus (a flavivirus) and chikungunya virus (an alphavirus) during active infection and helped prevent viral infection in

cell cultures that were pre-treated with the formula.¹¹

In a 2018 study, arthritic rats were given andrographolide combined with the conventional drug methotrexate, which can be hepatotoxic. Another group of rats received methotrexate only and another group received andrographolide only. Andrographolide improved the anti-arthritic effect of methotrexate. The combined therapy additively reduced inflammatory symptoms in the rats and significantly alleviated hepatocellular injury induced by methotrexate, according to the authors.¹²

In a 2019 study, pre-treatment with andrographolide sulfonate (AS), a water-soluble form of andrographolide, significantly attenuated lung injury and infiltration of inflammatory cells in mice infected with the bacterium *Klebsiella pneumoniae*, which is a major cause of respiratory infections. Mice treated with AS alone died after six days of infection, while a control group that received only the antibiotic imipenem had a survival rate of 33.3% after 15 days of infection. However, AS combined with imipenem resulted in 100% survival after 15 days of infection. This suggests that AS could synergistically improve the efficacy of imipenem.¹³

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