วารสารการแพทย์แผนไทยและการแพทย์ทางเลือก Journal of Thai Traditional & Alternative Medicine
ปีที่ ๕ ฉบับที่ ๓ กันยายน-ธันวาคม ๒๕๕๐ Vol. 5 No. 3 September-December 2007

Original Article

The Efficacy of *Andrographis paniculata* (Burm. f.) Wall. ex Nees for the Relief of the Symptoms of Influenza

Anchalee Chuthaputti*
Virul Pornpatkul†
Udomlug Suwankiri‡

Abstract

Tablets or capsules of the dried aerial part of *Andrographis paniculata* (Burm.f.) Wall. ex Nees comprise a single herbal medicine selected for inclusion in the National List of Essential Drugs in Thailand for the relief of the symptoms of the common cold; however, there is no clinical evidence yet to support its similar use for influenza. Therefore, this study was conducted to determine if *A. paniculata* could also relieve the symptoms of influenza as it does in the common cold. A multi-center, randomized controlled open-label study was carried out in health-service centers and a hospital under the Nonthaburi Provincial Public Health Office in patients having a fever of 38˚C or higher, respiratory and constitutional symptoms for no longer than 36 hours, and laboratory-confirmed as having influenza. Patients were randomly divided into two groups: Group I received paracetamol tablets at the dose of 1 gram every 6 hours for fever, headache and myalgia; and Group II received the same dose of paracetamol and *A. paniculata* capsules at the dose of 1.6 grams 4 times daily. Body temperatures were recorded and the severity of the symptoms of influenza, namely nasal congestion/runny nose, sore throat, cough, headache, malaise, myalgia, fatigue, chill, and overall symptoms were determined by the Visual Analog Scale on the day of enrollment (Day 0) and on Days 2, 4 and 6 of the treatment. At the end of the study there were 10 patients in Group I and 15 patients in the Group II. It was found that in Group II, from Day 2 of the treatment, body temperature, the severity of overall symptoms and almost all the other symptoms of influenza, except for cough, were significantly improved compared with those of Day 0. Meanwhile, for Group I, on Day 2 only the body temperature, overall symptoms and malaise were significantly lower than the values on Day 0. When comparing the two groups, it was found that the severity of cough, fatigue, and overall symptoms of the group treated with paracetamol and *A. paniculata* was significantly lower than that of the group treated with paracetamol alone from Day 4 of the treatment. Eighty percent of the patients in Group II would choose the same medications again the next time they have influenza, while only 20 percent of the patients in Group I would do so. The numbers of patients who would choose the previously prescribed medications or new medication were statistically significantly different between the two groups. In conclusion, the present study showed that *Andrographis paniculata*, when given together with paracetamol, could significantly reduce the severity of the overall symptoms of influenza and induce a more rapid improvement of various symptoms of influenza better than paracetamol alone did. This finding warrants a recommendation for using *Andrographis paniculata* for influenza in primary health care and inclusion on the National List of Essential Drugs as well as further study in a larger group of patients in the future.

Key words: ***Andrographis paniculata*, influenza, symptom**

**Institute of Thai Traditional Medicine, Department for the Development of Thai Traditional and Alternative Medicine*
†Narathiwat Rajanakarin Hospital, Narathiwat province
‡Nonthaburi Provincial Public Health Office

Background and Rationale

Influenza or "flu" and the common cold are both respiratory diseases but they are caused by different viruses. Even though the symptoms of influenza and the common cold are similar and sometimes difficult to tell apart, influenza is generally much worse than the common cold. Symptoms such as fever, body aches, extreme tiredness, and dry cough are more common and intense in influenza. Generally, these symptoms will improve within 5 days after a person becomes ill; patients should recover and become normal within 7-14 days. However, in the elderly, children, or patients with other chronic diseases or weakened immune system, the flu may cause severe illness and life-threatening complications such as bronchitis or pneumonia.[1-2]

In Thailand, influenza can be found throughout the year but the incidence is highest during the rainy season (June-September).[3] The numbers of reported cases of influenza appears to have decreased during the past 6 years, from more than 39,000 cases during the period 2001-2002 to over 19,000 cases in the period 2004-2005; in 2006 the reported cases of influenza totaled 16,146.[4] In 2004, it was calculated that the economic cost of seasonal influenza in Thailand ranged from about 928 million to 2,360 million baht. Of this amount, the cost of medical care accounted for 384 million-842 million baht; transportation 80 million-300 million baht; and productivity losses 464 million-1,230 million baht. Overall, the economic cost of seasonal influenza was about 992-2,417 baht per case.[5]

The treatment of influenza is generally symptomatic. Patients are advised to take some rest, drink a lot of fluid, and use paracetamol to reduce fever and relieve muscle ache. An antitussive, expectorant, nasal decongestant may also be taken, if necessary. Currently, antiviral agents, e.g., oseltamivir, amantadine or rimantadine, can relieve the symptoms of influenza and help patients to recover sooner, but the medication must be taken within 48 hours after the symptoms first develop. For persons in the high-risk group, influenza can be fatal; thus, flu vaccine should be administered as a preventive measure.[2]

Andrographis paniculata is an herb that has a long history of use in Ayurvedic medicine and traditional Chinese medicine.[6-7] In India, *A. paniculata* is useful in liver disorders, jaundice, dysentery, cholera, diabetes, influenza, bronchitis, hemorrhoids and gonorrhea.[6] According to the Pharmacopoeia of the People's Republic of China, this herb is indicated for influenza with fever, sore throat, ulcers in the mouth or on the tongue, acute or chronic cough, colitis, dysentery, urinary tract infection with difficult or painful urination, carbuncles, sores, and venomous snakebite.[7] In Thailand, *A. paniculata* is officially listed in the Thai Herbal Pharmacopoeia[8] and it was included in the National List of Essential Drugs (Herbal Medicinal Products) for the relief of the symptoms of the common cold and non-infectious diarrhea.[9] Similarly, WHO also selected this herb for the prophylaxis and symptomatic treatment of upper respiratory infections, such as the common cold and uncomplicated sinusitis, bronchitis and pharyngotonsillitis, lower urinary tract infections and acute diarrhoea.[10] Various kinds of lactones, e.g., andrographolide, neoandrographolide, deoxyandrographolide and deoxy-didehydroandrographolide, are the active principles of *A. paniculata.*[10] According to the standard specification of *A. paniculata* in the Thai Herbal Pharmacopoeia, the aerial part of the herb must contain not less than 6 percent of the total lactones calculated as andrographolide[8]. *In vitro* studies and *in vivo* studies in experimental animals have shown that extracts of this herb and/or its latones possess various pharmacological activities, e.g., anti-inflammatory, antipyretic, immonomodulatory, antioxidant, and antidiarrheal activities, which could account for its therapeutic efficacy.[10]

There are several clinical reports on the efficacy of *A. paniculata* in patients with upper respiratory tract infection.[11-17] The first report was a multi-center study, conducted in Thailand by Thamlikitkul *et al.*, which showed that *A. paniculata* at the dose of 6 g per day in 4 divided doses was effective for the relief of fever and pharyngotonsillitis.[11] Standardized extract of *A. paniculata* was later found to be effective for relieving the intensity of the symptoms of the

common cold, e.g., cough, phlegm, nasal secretion, headache, tiredness, earache, sleeplessness, and sore throat.[12-14]

Later on clinical studies were conducted on the product of Swedish Herbal Institute called Kan Jang®, a fixed combination of SHA-10 standardized *A. paniculata* extract and SHE-3 standardized extract of *Eleutherococcus senticosus*, which was found to be effective in the treatment of uncomplicated upper respiratory tract infection including sinusitis.[15-17] In addition, it was shown that, when taken as an adjuvant at the early stage of uncomplicated commnon colds in children, Kan Jang® was more effective than Immunal®(standardized extract of *Echinacea purpurea*) in accelerating the recovery time and lessening the severity of the common cold, especially the amount of nasal secretion and nasal congestion.[17] Two systematic reviews later confirmed the therapeutic efficacy of *A. paniculata* in the treatment of uncomplicated acute upper respiratory tract infection.[18-19] However, there has been no study on the efficacy of this herb in influenza reported so far.

This study was therefore conducted to determine whether *A. paniculata* capsules, which is already an herbal medicine in Thailand's National List of Essential Drugs for the common cold, would also be effective for the relief of the symptoms of influenza. If that is proven to be the case, its indication in the National List of Essential Drugs could then be expanded to cover influenza as well, and the herb should then be promoted for use in the common cold and influenza in the primary health care. The use of *A. paniculata* in such cases will promote the self-reliance of the country's pharmaceutical industry with regard to the production of medicine to replace imported and expensive antiviral agent against influenza virus as well as to help reduce the economic cost of seasonal influenza of the country.

Methodology

The clinical trial proposal was approved by the Ethics Committee on the Study in Human Subjects in the Fields of Thai Traditional and Alternative Medicine, Ministry of Public Health. This research project was a randomized controlled open-label study conducted in 15 health service centers and 1 hospital under the Nonthaburi Provincial Public Health Office during the period October 2004 - March 2006.

The **inclusion criteria** for the study subjects were (1) male or female aged 18-65 years of age, (2) having a febrile influenza-like illness for no longer than 36 hours, with a fever of 38°C or higher, (3) having at least one respiratory symptom, i.e., nasal congestion/runny nose, cough, or sore throat, (4) having at least one of the constitutional symptoms, i.e., headache, malaise, myalgia, sweating/chill or fatigue, which had occurred for no longer than 36 hours, (5) positive results of the Quick Vue Influenza Test of nasal secretion specimens, indicating laboratory-confirmed influenza, (6) ability to use the visual analog scale (VAS) to rate the severity of the symptoms, and (7) agreement to avoid drinking alcohol or taking other medications.

The **exclusion criteria** were (1) received influenza vaccine within the previous 12 months, (2) had the following symptoms, i.e., pneumonia, otitis media, bronchitis, severe bacterial pharyngitis or previous history of *Streptococcus* group A infection, (3) respiratory rate > 20/minute and crepitation of the lung, (4) took antibiotic, antihistamine, cough and cold medications prior to the study, (5) hypersensitive to paracetamol or *A. paniculata*, (6) alcoholic or drug addict, and (7) pregnant or nursing mother.

Patients would be discontinued from the study if they no longer wanted to participate in the study, their symptoms become much worse, or their respiratory diseases were later diagnosed as being something other than influenza, or they were allergic to the medications used in the study.

A. paniculata capsules purchased from Chaophaya Abhaibhubejhr Hospital contained 400 mg of the aerial part of *A. paniculata* per capsule. The content of total lactones of the AP capsules calculated as andrographolide, as analyzed by the Medicinal Plant Research Institute, Department of Medical Sciences, was 9 percent, which was higher than the standard specification set at not less than 6 percent by the

Thai Herbal Pharmacopoeia.[8]

Patients with a body temperature of 38°C or higher, having at least one respiratory symptoms and at least one of the constitutional symptoms described above for no longer than 36 hours, were laboratory confirmed for influenza by testing their nasal secretions with the Quick Vue Influenza test (Quidel Cooperation, USA) which could screen for both Influenza A and B. Patients with laboratory-confirmed influenza were then informed about the study project and those who were willing to participate in the study were then asked to give their consent and they were randomly assigned to the paracetamol group or the paracetamol + *A. paniculata* (AP) group.

Patients in the paracetamol group were prescribed a 7-day supply of 500 mg paracetamol tablets (Government Pharmaceutical Organization) to be taken at the dose of 2 tablets (1 g) every 6 hours if they still had fever, headache and/or myalgia. Patients in the paracetamol + AP group received a 7-day supply of the same dose of paracetamol plus 400 mg. *A. paniculata* capsules to be taken at the dose of 4 capsules (1.6 g) 4 times daily, after meals and at bedtime if they still had the symptoms. Patients were asked to come back every other day for three follow-up visits to the same health service centers where they received the treatment.

The efficacy of the two treatments was evaluated by taking the patients' body temperature and asking them to rate their symptoms prior to the treatment (Day 0) and at the three follow-up visits (Days 2, 4, 6) using the VAS of 0 (no symptom) to 10 (most severe symptoms). The symptoms evaluated were overall symptoms; respiratory symptoms, i.e. nasal congestion and runny nose, sore throat, and cough; and constitutional symptoms, i.e., headache, malaise, myalgia, fatigue, and sweating/chill. Any possible side effects and patient's level of satisfaction with the study medications were also assessed. The data were analyzed by unpaired t-test, repeated one-way ANOVA, or Chi-square test, where appropriate, using the SPSS program for Windows. The p value of < 0.05 was considered to be statistically significant.

Results

Of the 15 health service centers and one hospital in Nonthaburi Province that took part in the study during the period October 2004-March 2006, only 7 health service centers had laboratory-confirmed cases of influenza and could recruit patients into the study. At the end of the study, there were 25 patients participating in the study, 10 in the paracetamol group and 15 patients in the paracetamol + AP group. Tables 1 and 2 showed that prior to the treatment (Day 0), the body temperature, and the severity of the overall symptoms, the respiratory and constitutional symptoms of the patients in both groups were not significantly different.

For patients in the paracetamol group, it was found that body temperature, the severity of the overall symptoms, and malaise had become significantly lower than the pre-treatment values from Day 2 of the treatment, while headache, myalgia, fatigue and chill were significantly improved on Day 4 and sore throat on Day 6 (Table 1). Even though the severity of nasal congestion/runny nose and cough appeared to be better on Day 6, the symptom scores were not statistically significant different from those of Day 0 (Table 1).

For patients taking paracetamol and *A. paniculata*, the body temperature, the overall symptoms, and almost all of the other symptoms, i.e., nasal congestion/runny nose, sore throat, headache, malaise, myalgia, fatigue, and chill, were significantly improved from Day 2 of the treatment, while coughing was significantly better on Day 6 (Table 2).

When the symptom scores on Days 2, 4, and 6 of the two groups were compared, it was found that the overall symptoms, and the severity of cough and fatigue of the paracetamol + AP group were significantly lower than those of the paracetamol group from Day 4 of the treatment (Table 3). Meanwhile, body temperatures and the scores for the other symptoms of influenza on Days 2, 4 and 6 (i.e., nasal congestion/runny nose, sore throat, malaise, myalgia, and chill) were not significantly different between the two groups.

Table 1 Symptom scores on Days 0, 2, 4 and 6 of the paracetamol group (n=10)

Symptoms	Day 0	Day 2	Day 4	Day 6
Body temperature	38.37 ± 0.42	37.51 ± 0.37* (p=0.000)	36.95 ± 0.35* (p=0.000)	36.85± 0.22* (p=0.000)
Overall symptoms	6.50 ± 1.72	4.50± 1.51* (p=0.035)	3.60 ± 1.90* (p=0.012)	2.00± 1.15* (p=0.000)
Nasal congestion/runny nose	4.40 ± 2.67	4.60 ± 2.37 (p=1.000)	3.70 ± 2.95 (p=1.000)	2.00 ± 2.31 (p=0.339)
Sore throat	5.70 ± 2.98	3.70 ± 3.47 (p=0.492)	3.20 ± 3.05 (p=0.344)	1.50 ± 1.96* (p=0.017)
Cough	4.80 ± 2.74	5.30 ± 2.58 (p=1.000)	4.10 ± 2.38 (p=1.000)	2.80 ± 2.44 (p=0.542)
Headache	6.10 ± 2.96	3.60 ± 2.50 (p=0.119)	2.10 ± 1.79* (p=0.008)	0.90 ± 1.10* (p=0.001)
Malaise	7.20 ± 2.15	4.50 ± 2.17* (p=0.017)	2.10 ± 1.52* (p=0.000)	1.00 ± 1.25* (p=0.000)
Myalgia	7.10 ± 2.51	4.20 ± 2.20 (p=0.077)	2.30 ± 1.57* (p=0.002)	0.80 ± 0.92* (p=0.000)
Fatigue	6.60 ± 3.03	5.20 ± 2.70 (p=0.206)	2.30 ± 1.25* (p=0.004)	1.20 ± 1.03* (p=0.000)
Chill	5.40 ± 2.88	2.30 ± 2.26 (p=0.058)	1.10 ± 1.59* (p=0.013)	0.50 ± 0.97* (p=0.001)

The numbers indicate the mean ± SD.

* indicated p-value < 0.05 as compared with the scores on Day 0.

Table 2 Symptom scores on Days 0, 2, 4 and 6 of the Paracetamol + AP group (n=15)

Symptoms	Day 0	Day 2	Day 4	Day 6
Body temperature	38.60 ± 0.49	37.25 ± 0.50* (p=0.000)	37.02 ± 0.39* (p=0.000)	36.83 ± 0.32* (p=0.000)
Overall symptoms	6.80 ± 0.86	3.27 ± 1.71* (p=0.000)	2.00 ± 1.31* (p=0.000)	0.53 ± 0.64* (p=0.000)
Nasal congestion/runny nose	5.33 ± 2.41	3.20 ± 2.34* (p=0.014)	1.73 ± 1.94* (p=0.001)	0.67 ± 1.05* (p=0.000)
Sore throat	6.00 ± 2.70	2.87 ± 2.07* (p=0.002)	1.13 ± 1.25* (p=0.000)	0.20 ± 0.41* (p=0.000)
Cough	4.67 ± 2.79	4.20 ± 2.11 (p=1.000)	2.40 ± 1.59 (p=0.081)	0.87 ± 1.41* (p=0.002)
Headache	6.87 ± 2.26	2.67 ± 2.53* (p=0.000)	1.27 ± 1.71* (p=0.000)	0.13 ± 0.35* (p=0.000)
Malaise	8.00 ± 1.89	3.33 ± 2.89* (p=0.000)	1.93 ± 2.09* (p=0.000)	0.53 ± 1.06* (p=0.000)
Myalgia	7.67±1.68	2.93 ± 2.60* (p=0.000)	1.47 ± 1.51* (p=0.000)	0.13 ± 0.35* (p=0.000)
Fatigue	6.80 ± 1.78	2.40 ± 2.10* (p=0.000)	0.93 ± 0.96* (p=0.000)	0.53 ± 0.74* (p=0.000)
Chill	4.40 ± 3.04	0.87 ± 1.46* (p=0.001)	0.27 ± 0.80* (p=0.001)	0.00 ± 0.00* (p=0.000)

The numbers indicate the mean ± SD.

* indicated p-value < 0.05 as compared with the scores on Day 0.

Table 3 Comparison of the symptom scores of the paracetamol group and paracetamol + AP group on Days 2, 4 and 6.

Symptoms	Treatment group	Day 2	Day 4	Day 6
Body temperature	Paracetamol	37.51 ± 0.37	36.95 ± 0.35	36.85 ± 0.22
	Paracetamol + AP	37.24 ± 0.50	37.02 ± 0.38	36.82 ± 0.32
		(p=0.172)	(p=0.619)	(p=0.844)
Overall symptoms	Paracetamol	4.50 ± 1.50	3.60 ± 1.89	2.00 ± 1.15
	Paracetamol + AP	3.27 ± 1.71	2.00 ± 1.30*	0.53 ± 0.64*
		(p=0.077)	(p=0.020)	(p=0.003)
Nasal congestion/runny nose	Paracetamol	4.60 ± 2.36	3.70 ± 2.94	2.00 ± 2.30
	Paracetamol + AP	3.20 ± 2.33	1.73 ± 1.94	0.67 ± 1.04
		(p=0.158)	(p=0.055)	(p=0.061)
Sore throat	Paracetamol	3.70 ± 3.46	3.20 ± 3.04	1.50 ± 1.95
	Paracetamol + AP	2.87 ± 2.06	1.13 ± 1.24	0.20 ± 0.41
		(p=0.506)	(p=0.067)	(p=0.067)
Cough	Paracetamol	5.30 ± 2.58	4.10 ± 2.37	2.80 ± 2.44
	Paracetamol + AP	4.20 ± 2.11	2.40 ± 1.59*	0.87 ± 1.40*
		(p=0.255)	(p=0.043)	(p=0.041)
Headache	Paracetamol	3.60 ± 2.50	2.10 ± 1.79	0.90 ± 1.10
	Paracetamol + AP	2.67 ± 2.52	1.27 ± 1.71	0.13 ± 0.35
		(p=0.373)	(p=0.253)	(p=0.058)
Malaise	Paracetamol	4.50 ± 2.17	2.10 ± 1.52	1.00±1.24
	Paracetamol + AP	3.33 ± 2.89	1.93 ± 2.08	0.53 ± 1.06
		(p=0.290)	(p=0.831)	(p=0.325)
Myalgia	Paracetamol	4.20 ± 2.20	2.30 ± 1.56	0.86 ± 0.91
	Paracetamol + AP	2.93 ± 2.60	1.47±1.50	0.13 ± 0.35
		(p=0.219)	(p=0.195)	(p=0.051)
Fatigue	Paracetamol	5.20 ± 2.70	2.30 ± 1.25	1.20 ± 1.03
	Paracetamol + AP	2.40 ± 2.09*	0.93 ± 0.96*	0.53 ± 0.74*
		(p=0.008)	(p=0.005)	(p=0.003)
Chill	Paracetamol	2.30 ± 2.26	1.10 ± 1.59	0.50 ± 0.97
	Paracetamol + AP	0.87 ± 1.45	0.27 ± 0.79	0.00 ± 0.00
		(p=0.098)	(p=0.096)	(p=0.138)

The numbers show the mean ± SD.

*indicated p–value < 0.05 as compared with the scores with the the paracetamol group on the same day.

Regarding the satisfaction of the patients with the treatment received, it was found that 80 percent (8/10) of the patients in the paracetamol group were moderately satisfied and 20 percent (2/10) were very satisfied with the medication received. Meanwhile, 46.7 percent (7/15) of the patients in the paracetamol + AP group were moderately satisfied and 53.3 percent (8/15) were very satisfied with the medications prescribed. The levels of satisfaction with the treatments received were not significantly different between the two groups ($p > 0.05$).

Patients were also asked that, if they contracted influenza again in the future, would they like to take the same medication they had been prescribed or would they the prefer a new medication. It was found that only 20 percent (2/10) of the patients in the paracetamol group would like to take paracetamol again, while 80 percent (8/10) would rather receive a new medication. In contrast, 80 percent (12/15) of the patients in the paracetamol + AP group would choose the same medications again, while only 20 percent (3/15) would rather have a new medication.

The numbers of patients who would choose the previously prescribed medication or a new medication were significantly different between the two groups ($p < 0.05$).

Discussion

According to the Weekly Epidemiological Surveillance Report of the Bureau of Epidemiology, Department of Disease Control, in 2006 there were 16,146 reported cases of influenza with no death in Thailand and there were 88,841 reported cases of pneumonia that required hospitalization and 765 deaths, 20 percent of which were caused by the influenza virus.[4] In 2007, up to the 48th week (November 25-December 1, 2007), there were 15,179 reported cases of influenza and 7 deaths and 78,140 admitted cases of pneumonia and 757 deaths.[20] These figures indicate that influenza is still one of several health problems in Thailand that can cost the nation up to a thousand million baht or more in of medical care costs and productivity losses.

As the treatment of influenza is symptomatic, some modern medicines, e.g., antipyretics, antitussives, expectorants, antihistamines and nasal decongestants, may be taken for symptomatic relief, if necessary. In addition, some antiviral agents, e.g., oseltamivir, amantadine or rimantadine, may also be taken within the first 48 hours in order to reduce the severity of the symptoms and help patients the recover quicker. However, these medications must be imported from overseas and some are expensive and not easily accessible by the public. Therefore, if *Andrographis paniculata*, an indigenous medicinal plant of Thailand, can help influenza patients to recover sooner, it would significantly help the country to save on medical-care costs and prevent productivity loss as a results of influenza.

Beneficial effect of *A. paniculata* was noted in this study as it was found that in the paracetamol group, only three parameters, i.e., body temperature, the severity of malaise and the overall symptoms, were significantly lower than those of Day 0 from Day 2 of the treatment. However, when *A. paniculata* was concomitantly given, additional therapeutic effects were observed from Day 2 of the treatment, i.e., nasal congestion/runny nose, sore throat, headache, myalgia, fatigue, and chill were also significantly less severe than those of Day 0, while coughing was significantly better on Day 6 (Table 2). For the paracetamol group, it took longer than 2 days for headache, myalgia, fatigue, and sore throat to be significantly less severe than those of Day 0, while nasal congestion/runny nose and cough did not significantly improve even on Day 6 (Table 1).

When comparing the two groups, it was found that the severity of cough, fatigue, and overall symptoms of the group receiving both paracetamol and *A. paniculata* was significantly less than those of the paracetamol group since Day 4 of the treatment. The therapeutic efficacy of *A. paniculata* was also evident in terms of patient satisfaction, as 80 percent of the patients receiving *A. paniculata* together with paracetamol said that they would choose the same medications again next time they have influenza, while only 20 percent of the patients in the paracetamol group would choose paracetamol again if they get influenza. However, there were some patients complaining that the number of capsules of *A. paniculata* to be taken were too many. Hence, to increase public acceptance and compliance in the future, this herbal medicine should be made in the form of standardized extract instead.

The results of the present study therefore support the use of *A. paniculata* to help reduce certain respiratory and constitutional symptoms of influenza and help patients to recover sooner, which is similar to its traditional use in cases of influenza by Chinese and Indian people.[6-7] The efficacy of *A. paniculata* in relieving various respiratory and constitutional symptoms of influenza is similar to its previously reported efficacy in common cold[12-14] suggesting that the herb's active constituents, total lactones, are effective not only for milder symptoms of the common cold but also for more severe symptoms of influenza. The pharmacological activities that account for its therapeutic efficacy in the common cold and influenza are likely due to its immunomodulating effect, antipyretic activity and anti-inflammatory action.[9-10]

The drawback of the present study was that, even though 15 health service centers and 1 hospital joined in the study and the data were collected over an 18-month period, only 25 patients could be recruited into the study. There were three main reasons that explained why the number of patients participated in this study was rather low. First, during the study period, cases of avian influenza were reported in several provinces of Thailand, including Nonthaburi province. Therefore, when patients suspected of having influenza visited the study sites and the test of their nasal secretions showed a positive result for influenza, there was the possibility that the patients might have avian influenza. Therefore, the health officials were reluctant to recruit such patients into the study for fear that, if they really had avian influenza, they would not receive proper treatment and it would be harmful to their health and well-being. Therefore, we could not recruit patients into the study for a considerable period of time. Second, before visiting the study sites, a number of influenza patients had already taken some over-the-counter cold medications, and thus could not be included in the study. Thirdly, some health service centers had no case of influenza at all and as many as 80 suspected case were tested negative for influenza. This was probably because Nonthaburi province previously did not have many reported cases of influenza. Therefore, if there is going to be a further study in the future, other provinces with history of high numer of reported cases, such as southern provinces, Kanchanaburi, or Chantaburi[3,4] should be selected as study sites instead.

In conclusion, the present study shows an additional beneficial effect of *Andrographis paniculata* (6.4 g/day) when it is given with paracetamol (4 g/day): it reduces the severity of overall symptoms of influenza, cough, and fatigue better than paracetamol alone and helps influenza patients to recover from various respiratory and constitutional symptoms sooner than they otherwise would. This finding supports the recommended use of this herbal medicine in influenza in primary health care and for its inclusion on the National List of Essential Drugs. However, further study in a larger group of influenza patients may be helpful for building stronger evidence to support such therapeutic use.

Acknowledgements

The authors would like to express their gratitude to Dr. Paijit Warachit, Director-General of the Department of Medical Sciences; Dr. Pathom Sawanpanyalert, Director of the National Institute of Health, Department of Medical Sciences; and Pol. Capt. Dr. Rungrueng Kijphati for kindly providing us with 400 Quick Vue influenza test kits for the study. We are also thankful to the Chaophaya Abhaibhubejhr Hospital Foundation for providing us with Andrographis paniculata capsules at a special price and the staff of the Herbal Quality Assurance Center, Department of Medical Sciences for their assistance on the quality analysis of the herbal medicine. We are also thankful to Mrs. Pranee Chavalittumrong, Director of the Medicinal Plant Research Institute, Department of Medical Sciences, for her suggestions and help on the statistical analysis of the data, and to Miss Kritiya Yamnium for her help in the research project. We would also likes to express our thanks to the officers and staff of the Bang Kruai Hospital and the 15 health service centers under the Nonthaburi Provincial Public Health Office who contributed to the study: the health service centers of Bang Srimuang, Wat Sai Ma, Tasai, Talard Quan, Tansamrit, Tumbon Bang Kruai, Tumbon Sao Thong Hin, Wihan Pracha, Tumbon Bang Lane, Wat Rajniyom, Klaung Pra Udom, Bang Pood, Wat Lad Pladook, Moo 3 Bang Kurat, and Bangrak Yai.

References

1. Centers for Disease Control and Prevention. Cold versus Flu. [cited 2007 Oct 27]. Available from: http://www.cdc.gov/flu/about/qa/coldflu.htm
2. American Lung Association. Guidelines for the prevention and treatment of influenza and the common cold. [cited 2007 Oct 27]. Available from: http://www.lungusa.org/site/pp.asp?c=dvLUK9O0E&b=23161.
3. Phatinawin L. Influenza: 2006 Annual report. [cited 2007 Nov 3]. Available from: http:/203.157.15.4/Annual/Annual49/Part1/29_Influenza.doc.
4. Weekly Epidemiological Surveillance Report. [cited 2007 Nov 3]. Available from: http://203.157.15.4/wesr/file/F47534.pdf, http://203.157.15.4/wesr/file/F48524.pdf, http://203.157.15.4/wesr/file/

F49525.pdf.

5. Influenza Foundation (Thailand). Economic cost of influenza. [cited 2007 Oct 20]. Available from: http://www.ift2004.org/IFTNEWS/proceeding/IFT4/iftnews4_5.asp
6. Sharma PC, Yelne MB, Dennis TJ, Joshi A, Prabhune YS, Khade K, Rawat MS. Database on Medicinal Plants Used in Ayurveda. Vol. 4. New Delhi: Central Council for Research in Ayurveda & Siddha. 2002. p. 34-60.
7. Chinese Pharmacopoeia Commission. Pharmacopoeia of the People's Republic of China. Vol. I. English edition. Beijing: People's Medical Publishing House. 2005. p. 121.
8. Department of Medical Sciences. Thai Herbal Pharmacopoeia. Vol. 1. Bangkok: Prachachon Co., Ltd. 1995. p. 24-31.
9. National Drug Committee. List of Herbal Medicinal Products A.D. 2006. Bangkok: Agricultural Cooperative Community of Thailand Publishing. 2006. p. 40-52.
10. WHO Monographs on Selected Medicinal Plants. Vol. II. Geneva: World Health Organization. 2002. p. 12-24.
11. Thamlikitkul V, Dechatiwongse T, Theerapong S, Chantrakul C, Booroj P, Punkrut W, Ekpalakorn W, Boontaeng N, Taechaiya S, Petcharoen S, Orn-Chom-Jan T, Riewpaiboon W, Pradipasena S, Riewpaiboon A, Timsard S, Tenambergen ED. Efficacy of *Andrographis paniculata* Nees for pharyngotonsillitis in adults. J Med Assoc Thai 1991;74:433-42.
12. Hancke J, Burgos R, Caceres D, Wikman G. A double-blind study with a new monodrug Kan Jang: Decrease of symptoms and improvement in the recovery from common cold. Phytother Res 1995;9:559-62.
13. Caceres DD, Hancke JL, Burgos RA, Sandberg F, Wikman GK. Use of visual analogue scale measurement (VAS) to assess the effectiveness of standardized *Andrographis paniculata* extract SHA-10 in reducing the symptoms of common cold. A randomized double blind-placebo study. Phytomedicine 1999;64:217-23.
14. Caceres DD, Hancke JL, Burgos RA, Wikman GK. Prevention of common colds with *Andrographis paniculata* dried extract. A pilot double-blind study. Phytomedicine 1997;4:101-4.
15. Melchior J, Spasov AA, Ostrovskij OV, Bulanov AE, Wikman G. Double-blind, placebo-controlled pilot and phase III study of activity of standardized *Andrographis paniculata* Herba Nees extract fixed combination (Kan Jang) in the treatment of uncomplicated upper-respiratory tract infection. Phytomedicine 2000;7:341-50.
16. Gabrielian ES, Shukarian AK, Goukasova GI, Chandanian GL, Panossian AG, Wikman G, Wagner H. A double-blind, placebo-controlled study of *Andrographis paniculata* fixed combination Kan Jang in the treatment of acute upper respiraory tract infections including sinusitis. Phytomedicine 2002;9:589-97.
17. Spasov AA, Ostrovskij OV, Chernikov MV, Wikman G. Comparative controlled study of *Andrographis paniculata* fixed combination, Kan Jang and an Echinacea preparation as adjuvant, in the treatment of uncomplicated respiratory disease in children. Phytother Res 2004; 18:47-53.
18. Coon JT, Ernst E. *Andrographis paniculata* in the treatment of upper respiratory tract infections: a systematic review of safety and efficacy. Planta Med 2000;70:293-8.
19. Poolsup N, Suthisisang C, Prathanturarug S, Asawamekin A, Chachareon U. *Andrographis paniculata* in the symptomatic treatment of uncomplicated upper respiratory tract infection: systematic review of randomized controlled trials. J Clin Pharm Ther 2004; 29: 37-45.
20. Bureau of Epidemiology, Department of Disease Control. Reported cases and deaths of diseases under surveillance by province, Thailand, Week 48, 2007 (Nov 25, 2007- Dec 1, 2007). [cited 2007 Dec 6]. Available from: http://203.157.15.4/weekly/w_2550/wk50_48/wk48.xls

บทคัดย่อ

ประสิทธิผลของฟ้าทะลายโจรในการบรรเทาอาการของโรคไข้หวัดใหญ่

อัญชลี จูฑะพุทธิ*, วิรุฬห์ พรพัฒน์กุล†, อุดมลักษณ์ สุวรรณคีรี‡

**สถาบันการแพทย์แผนไทย, กรมพัฒนาการแพทย์แผนไทยและการแพทย์ทางเลือก กระทรวงสาธารณสุข นนทบุรี ๑๑๐๐๐*

†โรงพยาบาลนราธิวาส ราชนครินทร์ จังหวัดนราธิวาส ๙๖๐๐๐

‡สำนักงานสาธารณสุขจังหวัดนนทบุรี นนทบุรี ๑๑๐๐๐

ยาเม็ดและแคปซูลฟ้าทะลายโจรเป็นยาจากสมุนไพรที่บรรจุในบัญชียาหลักแห่งชาติเพื่อใช้บรรเทาอาการโรคหวัด. อย่างไรก็ตาม ยังไม่มีรายงานการวิจัยทางเวชกรรมเพื่อแสดงประสิทธิผลของยานี้ในโรคไข้หวัดใหญ่. ดังนั้น จึงได้ดำเนินการวิจัยทางเวชกรรมเพื่อศึกษาว่าฟ้าทะลายโจรจะสามารถบรรเทาอาการของโรคไข้หวัดใหญ่เช่นเดียวกับในโรคหวัดหรือไม่. งานวิจัยนี้เป็นการศึกษาควบคุมแบบสุ่มเปิดฉลากในหลายศูนย์ที่ดำเนินการในสถานบริการสาธารณสุขและโรงพยาบาลในสังกัดสำนักงานสาธารณสุขจังหวัดนนทบุรี ในผู้ป่วยที่มีไข้ ๓๘ องศาเซลเซียสหรือสูงกว่า, มีอาการทางระบบการหายใจและมีอาการหลักอื่นมาไม่เกิน ๓๖ ชั่วโมง, และผลการตรวจทางห้องปฏิบัติการยืนยันว่าติดเชื้อไวรัสไข้หวัดใหญ่. จากนั้นแบ่งผู้ป่วยแบบสุ่มออกเป็น ๒ กลุ่ม: กลุ่มที่ ๑ ได้รับยาพาราเซตะมอลขนาด ๑ กรัม ทุก ๖ ชั่วโมง หากมีอาการไข้ ปวดศีรษะหรือปวดเมื่อยกล้ามเนื้อ. กลุ่มที่ ๒ ได้รับยาพาราเซตะมอลขนาดเท่ากันร่วมกับแคปซูลฟ้าทะลายโจรในขนาด ๑.๖ กรัม วันละ ๔ เวลา เมื่อมีอาการ. บันทึกอุณหภูมิร่างกาย และความรุนแรงของอาการของโรคไข้หวัดใหญ่ได้แก่ คัดจมูก/น้ำมูกไหล, เจ็บคอ, ไอ, ปวดศีรษะ, รู้สึกไม่สบาย, ปวดเมื่อยตัว, อ่อนเพลีย, รู้สึกหนาว รวมทั้งอาการโดยรวม ในวันแรกที่เข้าร่วมโครงการ วันที่ ๒, ๔ และ ๖ ของการรักษา โดยใช้ visual analog scale. เมื่อจบการศึกษา มีผู้ป่วยที่ร่วมโครงการวิจัยในกลุ่มที่ ๑ จำนวน ๑๐ คน กลุ่มที่ ๒ จำนวน ๑๕ คน. ผู้ป่วยในกลุ่มที่ ๒ มีอุณหภูมิร่างกาย, ความรุนแรงของอาการโดยรวม และความรุนแรงของอาการเกือบทุกอาการยกเว้นอาการไอ น้อยลงกว่าเมื่อวันแรกอย่างมีนัยสำคัญ ตั้งแต่วันที่ ๒ ของการรักษา, ขณะที่ผู้ป่วยกลุ่มที่ ๑ ในวันที่ ๒ ของการรักษา เฉพาะอุณหภูมิร่างกาย อาการโดยรวม และความรู้สึกไม่สบายเท่านั้นที่น้อยกว่าวันแรกอย่างมีนัยสำคัญ. เมื่อเปรียบเทียบระหว่างทั้ง ๒ กลุ่ม พบว่าความรุนแรงของอาการไอ อ่อนเพลีย และอาการโดยรวมของกลุ่มที่ได้รับทั้งพาราเซตะมอลและฟ้าทะลายโจรน้อยกว่ากลุ่มที่ได้รับพาราเซตะมอลอย่างเดียวอย่างมีนัยสำคัญตั้งแต่วันที่ ๔ ของการรักษา. ร้อยละ ๘๐ ของผู้ป่วยกลุ่มที่ ๒ เลือกที่จะใช้ยาเดิม หากป่วยเป็นไข้หวัดใหญ่อีก ขณะที่เพียงร้อยละ ๒๐ ของผู้ป่วยกลุ่มที่ ๑ จะใช้ยาเดิม. จำนวนผู้ป่วยที่เลือกใช้ยาเดิมและที่เลือกใช้ยาใหม่ของทั้งสองกลุ่มแตกต่างกันอย่างมีนัยสำคัญ. สรุปได้ว่า การศึกษานี้แสดงว่าเมื่อให้ฟ้าทะลายโจรร่วมกับยาพาราเซตะมอลสามารถลดความรุนแรงของอาการโดยรวมของไข้หวัดใหญ่และช่วยให้อาการหลายอย่างของไข้หวัดใหญ่ทุเลาลงได้เร็วกว่าเมื่อได้รับยาพาราเซตะมอลอย่างเดียว. ผลการวิจัยนี้ได้ช่วยสนับสนุนการแนะนำให้ใช้ฟ้าทะลายโจรสำหรับไข้หวัดใหญ่ในสาธารณสุขมูลฐานและในบัญชียาหลักแห่งชาติและสนับสนุนการศึกษาวิจัยในกลุ่มผู้ป่วยที่จำนวนมากขึ้นต่อไป.

คำสำคัญ: **ฟ้าทะลายโจร, ไข้หวัดใหญ่, อาการโรค**