Brief Report

DOI: 10.5582/ddt.2023.01053

Efficacy of *Andrographis paniculata* spray in acute pharyngitis: A randomized controlled trial

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SUMMARY Acute viral pharyngitis is a self-limited disease but the symptoms, a sore throat in particular, can affect one's quality of life. Medicine for symptom relief is the main treatment. Recently, many studies have shown that *Andrographis paniculata* was efficacious in treating many diseases, including upper respiratory infections. However, adverse reactions to systemic intake are a concern. Therefore, *A. paniculata* spray is intended to reduce systemic adverse reactions and provide patients with more comfort as its local use. This randomized, double-blind study enrolled 60 adult patients with acute viral pharyngitis. All patients were asked to score the severity of symptoms including a sore throat, difficulty swallowing, and coughing using an 11-point numeric rating scale from 0 to 10. A physical examination was performed to score the severity of erythematous and swollen mucosa using a 0-3 score (0 = no, 1 = mild, 2 = moderate, and 3 = severe). The patients were randomized to receive treatment with either an *A. paniculata* spray or a positive control chamomile spray. Results revealed a significant reduction in the severity of all signs and symptoms in both groups ($p < 0.05$). The duration of treatment response in the *A. paniculata* spray group was 1.9 ± 0.7 days compared to 2.5 ± 1.2 days in the chamomile spray group ($p = 0.049$). No adverse events were noted in either group. *A. paniculata* spray is safe and highly efficacious in treating acute viral pharyngitis and can reduce symptoms more rapidly than a positive control spray.

Keywords *Andrographis paniculata*, acute viral pharyngitis, sore throat, plant extract, spray

1. Introduction

Acute pharyngitis is the inflammation of the mucous membrane of the oropharynx located in the upper part of the respiratory system. It is mostly caused by viruses and bacteria (*1*). Other less common causes of pharyngitis are allergies, trauma, cancer, reflux, and certain toxins (*2*). Patients with acute pharyngitis have a sore throat, cough, and difficulty swallowing. The disease can progress rapidly and may cause severe throat edema leading to dyspnea and suffocation. In adults, approximately 80%-90% of pharyngitis cases are caused by viruses (*3*) and in children, up to about 95% of cases of an acute sore throat are associated with viral infection (*4*). This indicates that the primary cause of acute pharyngitis is viruses. Even though viral pharyngitis can self-resolve in less than a week (*5*), many patients suffer from a severe sore throat that affects their quality of life. Thus far, there are no specific drugs for the treatment of viral pharyngitis. However, antibiotics are sometimes prescribed without being indicated. A point that must be emphasized is that excessive and inappropriate use of antibiotics can lead to the development of new resistant strains of microorganisms (*6*). Therefore, treatment or medication to relieve symptoms and avoid unnecessary use of antibiotics might be the best alternative. Many herbs have been used for centuries as remedies for human diseases. Recently, interest in searching for high efficacious and safe, new bioactive components from plants has increased. Many types of plants have been reported to have various pharmacological activities (*7–9*).

Andrographis paniculata, known as Fah Talay Jone (in Thai), is an annual herb in the family Acanthaceae. The plant is commonly found in many countries in Asia, and particularly India, China, and Thailand. It is one of the principal herbs in traditional medicinal remedies for the treatment of acute upper respiratory tract infection and diarrhea in India, China, and Thailand (*10*). It has been reported to have medicinal and pharmacological properties and to be effective for the treatment of various

diseases such as cancer, diabetes, high blood pressure, ulcer, leprosy, bronchitis, skin diseases, flatulence, colic, influenza, dysentery, dyspepsia, and malaria (*11*). The anti-inflammatory and antimicrobial activities of this plant have been reported (*12,13*). Its extract was prescribed in oral form to treat upper respiratory infections, including acute pharyngitis, during the coronavirus disease 2019 (COVID-19) pandemic (*14*). However, adverse reactions have been reported after systemic administration (*15*). Therefore, local administration using throat spray containing *A. paniculata* extract has been considered.

In many countries including Thailand, the herbal sprays that are commercially available are those containing chamomile extract. Due to its anti-inflammatory action, chamomile extract has been reported to relieve symptoms in patients with acute nasopharyngitis (*16*). Since the COVID-19 outbreak, the sprays have been used more widely and are in short supply. *A. paniculata* extract has therefore been put forward as a local herb that can help to relieve COVID-19 symptoms. To the extent known, no study has reported on *A. paniculata* extract spray to treat pharyngitis. Therefore, this pilot study was conducted with the aim of highlighting the first ever report on the efficacy of *A. paniculata* spray in acute pharyngitis. The clinical effectiveness and safety of *A. paniculata* spray in relieving symptoms of acute pharyngitis were investigated in comparison to chamomile spray.

2. Materials and Methods

2.1. Materials

A. paniculata extract was kindly provided by the Chao Phya Abhaibhubejhr Hospital Foundation, Prachinburi Province, Thailand. All chemicals and solvents used were of the highest pharmaceutical grade available. A commercial herbal spray containing mainly 37% chamomile extract, namely chamomile spray, was used as a positive control and purchased from a drug store in Thailand.

2.2. Preparation of *A. paniculata* spray

A. paniculata spray was prepared by the Chao Phraya Abhaibhubejhr Hospital Foundation using a cosolvent method. The formula contains 0.3% of *A. paniculata* extract, glycerine, ethanol, and flavoring agents. The mixture was gently mixed until a homogeneous solution formed. The resulting solution was adjusted to volume with sterile water and gently shaken to avoid air bubbles. The final solution was transferred into a light-protected container with a spray nozzle.

2.3. Study design and sample size

This study was approved by Chiang Rai Prachanukroh Hospital's Ethics Committee in Human Research (No. CR 0033.102/EC.66-025). All study procedures were in accordance with the provisions of the Declaration of Helsinki. The study protocol was registered with the Thai Clinical Trials Registry (TCTR 20230915005).

A randomized, double-blind study was conducted by the Department of Otolaryngology at Chiang Rai Prachanukroh Hospital in Thailand from February 1 to April 30, 2023. Sample sizes were calculated using the ANCOVA method and based on a previous study (*17*). The estimated sample sizes for two groups with repeated measures were used. From this calculation, the sample size (n) with an alpha error of 5% and a power of 80% is 28 patients/group. To compensate for unexpected loss during follow-up, 30 patients were included in each group. Therefore, a total of 60 patients were recruited.

2.4. Participant selection and eligibility criteria

Adult patients (aged from 18 years old) treated at Chiang Rai Hospital with an acute sore throat for less than 4 days were enrolled. Patients with a pain score greater than 5 out of 10 and a diagnosis of acute pharyngitis confirmed by an otolaryngologist were included in this study. The exclusion criteria were a positive COVID-19 test, a history of allergies, intolerance or sensitivity to any of the study medications, pregnant or lactating women, and patients who had taken antibiotics or corticosteroids less than 14 days prior.

2.5. Randomization and blinding

The patients in each group were randomized using a computer-generated blocked randomization schedule. Both groups received throat spray bottles and were blinded to treatment. Both sprays were packaged in bottles with the same appearance labeled as either A or B. Codes A and B were announced as either *A. paniculata* spray or chamomile spray after the end of the study analysis.

2.6. Study assessment

On the first day of study participation (day 0), the patients were asked to rate the severity of their symptoms, including a sore throat, difficulty swallowing, and coughing using an 11-point numeric rating scale from 0 to 10 (0 = no symptoms and 10 = the worst symptom that you can imagine). An otolaryngologist then performed a physical examination to assess the throat mucosa and score the severity of erythema of the pharyngeal mucosa (0 = no, 1 = mild, 2 = moderate, and 3 = severe erythema) and swelling of the pharyngeal mucosa (0 = no, 1 = mild, 2 = moderate and 3 = severe swelling). After the history was taken and a physical examination was performed, the patients were advised to spray the throat 2 spritzes/time and 3 times a day for

5 days. Symptoms were assessed for another 5 days (day 1 to day 5 = 1 to 5 days after using the sprays). The patients were asked to record the severity of their daily symptoms. These included a sore throat, difficulty swallowing, and coughing on an 11-point numeric rating scale from 0 to 10. A 20% or greater reduction in symptoms from the pretreatment score was considered acceptable (*18*). In addition, the patients were examined twice by an otolaryngologist on day 3 and day 5 of the study. All patients were asked to score their satisfaction with the received spray at the end of day 5.

2.7. Safety assessment

Adverse events were monitored throughout the study. All participants were asked to promptly report any severe adverse events or adverse reactions that occurred. They would then be asked to discontinue the study and receive immediate medical treatment from an expert physician.

2.8. Statistical analysis

Baseline demographic characteristics were described using descriptive statistics. Scores from the numeric rating scale and evaluations of the pharyngeal mucosa were expressed as the mean ± S.D. Differences between groups were assessed using the Chi-squared test for categorical variables and the Mann-Whitney *U* test for continuous variables. The level of statistical significance was set at $p < 0.05$.

3. Results and Discussion

The aim of the current study was to investigate the efficacy of the developed throat spray containing an extract of *A. paniculata* in patients with acute viral pharyngitis. A commercial herbal spray, namely chamomile spray, was used as a positive control. Although acute viral pharyngitis can resolve by itself, supportive treatment is also an important option for relieving a sore throat (*5*). Many studies have proven that *A. paniculata* extract has the potential to inhibit inflammation of the upper respiratory tract (URI) including pharyngitis (*19,20*). However, some systemic adverse effects, *e.g.*, induction of acute renal injury (*15*) and gastrointestinal disorders (*21*) after parenteral and oral administration, have been reported. In the current study, local administration of the developed *A. paniculata* spray was used to reduce systemic adverse reactions. A total of 60 patients were enrolled and remained in the

Table 1. Patient demographics and clinical characteristics

Items	*A. paniculata* spray		Chamomile spray		*p*-value
	n	%	*n*	%	
Gender					0.596
Female	17	56.67	20	66.67	
Male	13	43.33	10	33.33	
Age (years)	42.6 ± 13.9*		44.1 ± 15.2*		0.685
Occupation					0.638
None	2	6.67	0	0.00	
Government employee	5	16.67	6	20.00	
Office worker	3	10.00	4	13.33	
Company employee	2	6.67	2	6.67	
Farmer	1	3.33	4	13.33	
Nurse	2	6.67	2	6.67	
Housewife	3	10.00	6	20.00	
Freelance	8	26.67	4	13.33	
Other	4	13.33	2	6.67	
Underlying illness	16	53.33	3	36.67	0.299
Currently using medication	12	40.00	9	30.00	0.589
Duration of sore throat (days)	2.4 ± 1.1*		2.6 ± 0.9*		0.508
Difficulty swallowing	21	70.00	25	83.33	0.360
Cough	22	73.33	26	86.67	0.333
Fever	1	3.33	3	10.00	0.612
Headache	3	10.00	3	10.00	1.000
Hoarseness	6	20.00	7	23.33	1.000
Dyspnea	1	3.33	0	0.00	1.000
Nasal congestion/rhinorrhea	13	43.33	17	56.67	0.439
Otalgia	1	3.33	1	3.33	1.000
Throat soreness score (0-10)	5.7 ± 0.9*		6.5 ± 1.7*		0.148
Difficulty swallowing scale (0-10)	4.6 ± 1.9*		5.5 ± 2.1*		0.202
Cough severity (VAS 0-10)	4.0 ± 3.0*		5.1 ± 2.7*		0.065
Body temperature (°C)	36.41 ± 0.17*		36.42 ± 0.24*		0.759
Erythematous of the pharynx (0-3)	2.4 ± 0.7*		2.3 ± 0.7*		0.469
Swollen mucosa of the pharynx (0-3)	2.0 ± 0.5*		2.1 ± 0.6*		0.812

* Data express the mean ± S.D.

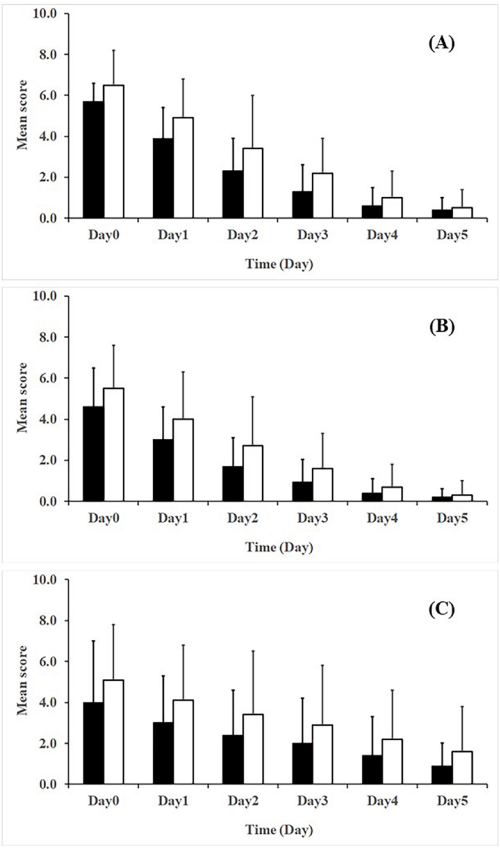

Figure 1. Mean score for the severity, as determined by patients using an 11-point numeric rating scale from 0 to 10, of throat pain (A), difficulty swallowing (B), and coughing (C) after using *A. paniculata* spray (black column) and chamomile spray (white column).

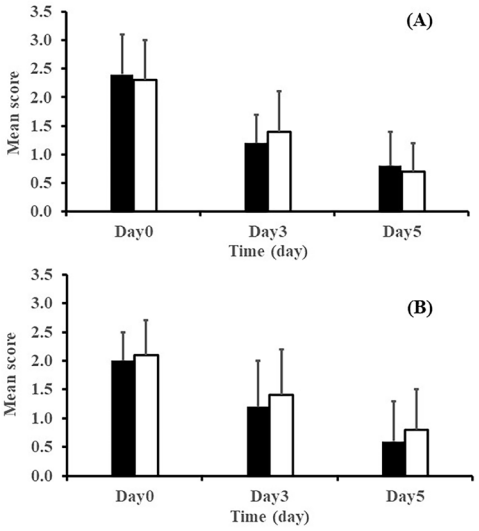

Figure 2. Mean score for the severity, as determined by otolaryngologists, of erythema (A) and swelling (B) of the pharyngeal mucosa after using *A. paniculata* spray (black column) and chamomile spray (white column).

final analysis (*A. paniculata* spray: $n = 30$, chamomile spray: $n = 30$). The two groups did not differ in baseline demographics and clinical characteristics as shown in Table 1. The mean duration of the clinical sore throat was 2.4 days in the *A. paniculata* spray group and 2.6 days in chamomile spray group. Common comorbid symptoms for each group were difficulty swallowing and coughing. The baseline signs and symptoms of pharyngeal inflammation did not differ significantly between the two groups.

Results indicated that the severity of a sore throat, difficulty swallowing, and coughing decreased significantly from day 1 after use of the spray in both groups and the score continued to decrease to nearly 0 at the end of the assessment as shown in Figure 1. The percentage of responders on day 1 was 80% in the *A. paniculata* spray group and 66.7% in the chamomile spray group. The mean (± SD) of the response duration was 1.9 (± 0.7) days and 2.5 (± 1.2) days in the *A. paniculata* spray group and chamomile spray groups, respectively ($p = 0.049$). Twenty-two patients in each group (73.3%) had no sore throat (score = 0) at the end of the study. The mean (± SD) duration to absence of pain was 3.4 (± 1.1) days and 3.7 (± 1.1) days in the *A. paniculata* spray and chamomile spray groups, respectively ($p = 0.468$). There was no difference in the overall satisfaction of using sprays between the two groups. In addition, there were no adverse events during this study. Other assessments scored by an otolaryngologist including erythema and swelling of the pharyngeal mucosa also decreased significantly in both groups as shown in Figure 2. Daily symptom scores between the two groups were compared, revealing no statistical difference.

The current results indicate that the sprays significantly alleviated clinical symptoms. Most patients were pain-free after less than 5 days of using the sprays, while the disease resolved on its own within 10 days. The duration to becoming pain-free did not differ between groups, but the duration of a clinical response differed. The *A. paniculata* group had a slightly faster recovery than the chamomile group. The current results on the effectiveness of an *A. paniculata* spray in reducing the severity of a sore throat are consistent with those reported by other studies involving *A. paniculata* in tablet form (*22-24*). However, the use of tablets results in significantly more adverse reactions than a topical spray. Adverse effects from an *A. paniculata* extract as reported earlier were mostly mild gastrointestinal symptoms such as constipation, nausea, vomiting, diarrhea, or dyspeptic symptoms (*25*). In contrast, there were no adverse events during the current study. This confirms that that topical application of an *A. paniculata* spray can be highly efficacious without causing systemic adverse reactions and that the study objective was achieved. The *A. paniculata* spray had anti-inflammatory action in terms of reducing pain without causing adverse reactions in this study, but the medicine should only be recommended when appropriate as determined by a physician.

Most patients were similarly satisfied with each

spray, but some participants mentioned the intense taste of the *A. paniculata* spray. Patients complaining about the taste of pharmaceutical products is one of the most important problems. *A. paniculata* is known as the king of bitters (*11*), so a challenge for further development is to use pharmaceutical technology to mask or minimize the bitter taste of an *A. paniculata* spray while maintaining its powerful anti-inflammatory action. In addition, the current work is a pilot study. The sample size for this study was calculated based on previous studies, assuming similar efficiency of the spray. Further studies with larger populations will help with the use of an *A. paniculata* spray in the future.

4. Conclusion

The current study yielded positive results with an *A. paniculata* spray that can be used as an alternative treatment to relieve the symptoms of pharyngitis while causing fewer systemic adverse reactions. It is a safe and convenient form of administration that capitalizes on the beneficial properties of Asian herbs. It has anti-inflammatory action in patients with acute viral pharyngitis. It can effectively relieve symptoms faster than a chamomile extract spray.

Acknowledgements

The authors wish to thank Chao Phraya Abhaibhubejhr Hospital for its financial support. The authors would also like to thank Dr. Patchara Ruangwongroj from the Department of Rehabilitation Medicine in Chiang Rai Prachanukroh Hospital for her advice on statistical analysis. The authors would also like to thank the Center of Excellence in Pharmaceutical Nanotechnology, Chiang Mai University, for the extent of its support.

Funding: None.

Conflict of Interest: The authors have no conflicts of interest to disclose.

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Received July 27, 2023; Revised September 16, 2023; Accepted September 21, 2023.

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Released online in J-STAGE as advance publication October 11, 2023.