

ประสิทธิผลและความปลอดภัยของยาประสะเปราะใหญ่เปรียบเทียบกับลอราทาดีนในผู้ป่วยโรค จมูกอักเสบจากภูมิแพ้

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บทนำ: ยาประสะเปราะใหญ่** ถูกใช้เพื่อรักษาอาการหวัดและไข้ แต่ยังไม่มีรายงานประสิทธิผลและความปลอดภัย ดังนั้น วัตถุประสงค์ของการศึกษานี้คือเพื่อเปรียบเทียบประสิทธิผลและความปลอดภัยของยาผงประสะเปราะใหญ่ และ ยาลอราทาดีน ในผู้ป่วยโรคจมูกอักเสบจากภูมิแพ้อาการน้อย

วิธีการ: การออกแบบการศึกษาเป็นการทดลองแบบสุ่มที่มีกลุ่มควบคุมและปิดบังสองชั้น อาสาสมัครโรคจมูกอักเสบจากภูมิแพ้จำนวน 63 คนถูกแบ่งออกเป็นสองกลุ่มแบบสุ่ม กลุ่มหนึ่งรับประทานยาผงประสะเปราะใหญ่ ในปริมาณ 1,000 มิลลิกรัม วันละ 3 ครั้งก่อนอาหาร และอีกกลุ่มรับประทาน ยาลอราทาดีน ในปริมาณ 10 มิลลิกรัม วันละ 3 ครั้งก่อนอาหาร และได้รับยาหลอกเพื่อรักษาภาวะปิดบังสองชั้นเป็นเวลา 6 สัปดาห์ อาสาสมัครทั้งหมดได้รับการติดตามในสัปดาห์ที่สามและสัปดาห์ที่หกเพื่อประเมินประสิทธิผลและความปลอดภัยของยา

สรุป: ยาผงประสะเปราะใหญ่ เพิ่มพื้นที่หน้าตัดในโพรงจมูก ในสัปดาห์ที่หก ยาผงประสะเปราะใหญ่ และ ยาลอราทาดีน สามารถบรรเทาอาการจาม น้ำมูกไหล คัดจมูก คันจมูก อาการทางจมูกทั่วไป และช่วยยกระดับคุณภาพชีวิตได้ ผลข้างเคียงของ ยาผงประสะเปราะใหญ่ คือ เรอเปรี้ยว และผลข้างเคียงของ ยาลอราทาดีน คือ ง่วงนอน หลังจากรับประทานยาผงประสะเปราะใหญ่ ไม่มีผลข้างเคียงต่อการทำงานของไตหรือตับ ดังนั้นยาผงประสะเปราะใหญ่ จึงมีความปลอดภัยและมีประสิทธิภาพ เทียบเท่ากับการรักษาด้วย ยาลอราทาดีน และอาจเป็นทางเลือกในการรักษาโรคจมูกอักเสบจากภูมิแพ้อาการน้อยได้

คำสำคัญ: โรคจมูกอักเสบจากภูมิแพ้ ยาผงประสะเปราะใหญ่

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ตำรับยาประสะเปราะใหญ่ เป็นตำรับยาการแพทย์แผนไทยลักษณะเป็นผงนำมาบรรจุเป็นแคปซูล จัดทำโดยฝ่ายวิจัย สถานการณ์แพทย์แผนไทยประยุกต์ คณะแพทยศาสตร์ มหาวิทยาลัยธรรมศาสตร์ (ศูนย์รังสิต)

Efficacy and Safety of Prasaprophyai Remedy, a Thai traditional remedy compared to Loratadine in Allergic Rhinitis Patients

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Background: Prasaprophyai remedy (PSPR) has been used to treat common cold and fever, but there is no report of efficacy and safety. Thus, the objectives of this study are to compare the efficacy and safety of PSPR powder and Loratadine in mild symptoms of allergic rhinitis.

Methods: The study design was a double-blind, randomized controlled trial. Sixty-three allergic rhinitis volunteers were divided into two random groups. One took PSPR remedy powder at a dose of 1,000 mg three times a day before meals, and the other took Loratadine at a dose of 10 mg once daily before meals and received a placebo to maintain double-blind conditions for six weeks. All volunteers were followed up in the third week and the sixth week to evaluate the efficacy and safety of the medicines.

Conclusion: PSPR increased the minimal cross section area (MCA) in the sixth week. PSPR and Loratadine were able to relieve the symptoms of sneezing, running nose, stuffy nose, itchy nose, total nasal symptoms, and to raise quality of life ($p < 0.05$). A side effect of PSPR is eructate (23.3%) and a side effect of Loratadine is drowsiness (13.3%). After taking PSPR, there was no adverse effect on either renal or liver function. Then PSPR appears to be as safe and effective as Loratadine treatment and could be a potential choice for the treatment in mild symptoms of allergic rhinitis.

Keywords: Allergic rhinitis, Prasaprophyai remedy, Kaempferia galanga L.

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Prasaprap Yai medicine recipe is a traditional Thai medicine recipe in the form of powder packed into capsules. It was created by the Research Division, Applied Thai Traditional Medicine Institute, Faculty of Medicine, Thammasat University (Rangsit Center).

Introduction

Allergic rhinitis (AR) is a common disease in Thailand. The patients suffer from nasal obstruction, rhinorrhea, sneezing, excessive sputum, post-nasal drip, and a reduction of smell sensation. Although not life-threatening, the disease significantly interferes with the patient's quality of life. It has an effect on sleep quality.¹ AR also aggravates obstructive sleep apnea in some patients². Furthermore, allergic rhinitis is considered to be a risk factor for asthma.³

Prasaprophyai remedy (PSPR), which is in the Thai National List of Essential Medicines (NLEM) since 2011, but no studies the mechanism. Prasaprophyai remedy consists of 21 herbal species. The major component of PSPR is *Kaempferia galanga* L. (rhizome) with the remaining 20 species being: *Amomum testaceum* Ridl. (fruit), *Anethum graveolens* L. (fruit), *Angelica dahurica* Benth. (root), *Angelica sinensis* (Oliv.) Diels (root), *Artemisia annua* L. (all parts), *Atractylodes lancea* (Thunb.) DC. (rhizome), *Cuminum cyminum* L. (fruit), *Dracaena loureiri* Gagnep. (stem), *Foeniculum vulgare* Mill. var. *dulce* (Mill.) Thell. (fruit), *Lepidium sativum* L. (seed), *Ligusticum sinense* Olive. Cv. Chuanxiong (rhizome), *Mammea siamensis* Kosterm.

(flower), *Mesua ferrea* L. (flower), *Mimusops elengi* L. (flower), *Myristica fragrans* Houtt. (aril, nutmeg and stem), *Nelumbo nucifera* Gaertn. (pollen), *Nigella sativa* L. (seed) and *Syzygium aromaticum* (L.) Merr. et Perry (flower-bud) in equal weight each. The Thai National List of Essential Medicines suggests taking Prasaprophyai at a dose of 1.0-1.5 g/meal to treat the common cold and fever. Ethyl p-methoxycinnamate from PSPR as an active anti-allergic and anti-inflammatory agent is stable under accelerated condition. This result can conclude that PSPR ethanolic extract is stable regarding the chemical content and both activities, as it can be kept in a tight container protected from light and heat for two years at room temperature⁴. but there is no report on efficacy of PSPR in clinical study research. Thus, the objectives of this study are to compare the safety and efficacy of PSPR powder and Loratadine, which is an antihistamine drug in mild symptoms of allergic rhinitis.

Methods

Drug preparation

Prasaprophyai remedy (PSPR) consists of 21 herbal species. The major component of PSPR is *Kaempferia galanga* L. while the

remaining 20 species are present in equal weight each. Medicinal plants were collected from many parts of Thailand or imported from other countries. They were ground and

sieved to a particle size number 80. The powder was mixed according to the formulation (Table 1).

Table 1 Medicinal plants in Prasapraohyai remedy formulations (For 1,000 g. of powder drug)

Scientific name	Family	Voucher specimen	Part used	Weight (g)	Collected from	Ethno-medicinal knowledge
<i>Amomum testaceum</i> Ridl.	ZINGIBERACEAE	SKP 206011101	Fruit	25	Chantaburi, Thailand	Cough drug and Carminative drug
<i>Anethum graveolens</i> L.	UMBELLIFERAE	SKP 199010701	Fruit	25	India	Carminative drug
<i>Angelica dahurica</i> Benth.	UMBELLIFERAE	SKP 199010401	Root	25	China	Expectorant drug
<i>Angelica sinensis</i> (Oliv.) Diels	UMBELLIFERAE	SKP 199010901	Root	25	China	Cough drug
<i>Artemisia annua</i> L.	COMPOSITAE	SKP 051010101	All part	25	China	Asthma drug and cough drug
<i>Atractylodes lancea</i> (Thunb.) DC.	COMPOSITAE	SKP 051011201	Rhizome	25	China	Asthma drug
<i>Cuminum cyminum</i> L.	UMBELLIFERAE	SKP 199030301	Fruit	25	India	Carminative drug
<i>Dracaena loureiri</i> Gagnep.	DRACAENACEAE	SKP 065041201	Stem	25	Chantaburi, Thailand	Cough drug
<i>Foeniculum vulgare</i> Mill. var. <i>dulce</i> (Mill.) Thell.	UMBELLIFERAE	SKP 199062201	Fruit	25	India	Carminative drug and tonic drug
<i>Kaempferia galanga</i> L.	ZINGIBERACEAE	SKP 206110701	Rhizome	500	Kanchanaburi,	Cold drug and Carminative drug
<i>Lepidium sativum</i> L.	BRASSICACEAE	SKP 057121901	Seed	25	India	Expectorant drug
<i>Ligusticum sinense</i> Olive. Cv. Chuanxiong	UMBELLIFERAE	SKP 199121901	Rhizome	25	China	Carminative drug
<i>Mammea siamensis</i> Kosterm.	GUITTIFERAE	SKP 083131901	Flower	25	Ratchaburi, Thailand	Antipyretic drugs
<i>Mesua ferrea</i> L.	GUITTIFERAE	SKP 08313060	Flower	25	Ratchaburi, Thailand	Tonic drug
<i>Mimusops elengi</i> L.	SAPOTACEAE	SKP 171130501	Flower	25	Ratchaburi, Thailand	Hematinic drug
<i>Myristica fragrans</i> Houtt.	MYRISTICACEAE	SKP 121130601	Aril	25	Chumphon, Thailand	Carminative drug
<i>Myristica fragrans</i> Houtt.	MYRISTICACEAE	SKP 121130601	Seed	25	Chumphon, Thailand	Carminative drug
<i>Myristica fragrans</i> Houtt.	MYRISTICACEAE	SKP 121130601	Stem	25	Chantaburi, Thailand	Antipyretic drugs
<i>Nelumbo nucifera</i> Gaertn.	NELUMBOCEAE	SKP 125141401	Pollen	25	NakornPathom, Thailand	Expectorant drug
<i>Nigella sativa</i> L.	RANUNCULACEAE	SKP 160141901	Seed	25	India	Carminative drug
<i>Syzygium aromaticum</i> (L.) Merr. et Perry	MYRISTICACEAE	SKP 123190101	Flower-bud	25	Chantaburi, Thailand	Carminative drug

PSPR passed standard quality control following the Thai Pharmacopoeia protocol including weight deviation, total ash and acid insoluble ash, loss on drying, dissolution test, heavy metals contamination, bacteria and yeast contamination, and stability in accelerated conditions testing. Moreover, PSPR has anti-allergic activity control and stability in accelerated conditions testing

And also biological activity control accompanied by an anti-allergic activity testing by inhibiting β -hexosaminidase release. PSPR has a stable anti-allergic shelf-life of 2 years. All the ingredients were filled into size 0 capsules (500mg). Loratadine 10 mg tablets (Clarityne®), as a long-acting, non-sedating antihistamine drug from Schering-Plough and lactose monohydrate, were filled into size 0 capsules (500 mg), and Lactose monohydrate was used as placebo, filled into size 0 capsules (500 mg).

Participants

This research was approved by the Human Research Ethics Committee of Thammasat University (Faculty of Medicine) registry number MTU-EC-TM-6-090/55. Patients were recruited as volunteers from the out-patient department of Ear Nose

Throat, Thammasat University Hospital between August 8, 2014 - November 5, 2015

The inclusion criteria of patients: age in range 20 - 80 years old, mild symptoms of allergic rhinitis (classified followed ARIA criteria) by clinical diagnosis, stop using antihistamine at least 7 days before participating. The patients who used nasal spray, had nasal polyp, were pregnant or lactating, had nasal septum perforations or had sinus surgery, patients with serious medical conditions such as congestive heart disease, liver and renal dysfunction, uncontrolled hypertension, severe asthma, tuberculosis, HIV were excluded. The patients who were eligible for the study first obtained an informed consent before starting treatment.

Study design

The study design was a double-blind, randomized controlled trial. A computer generated random numbers for each of 63 volunteers on the list. The data for 60 patients could be completely collected and evaluated. All of them were divided into two random groups: the treatment group and the control group. The first group took PSPR powder at a dose of 1,000 mg three times a day before a meals (reference dose followed

NLEM 2011) . The second group took Loratadine 10 mg once daily before meal (breakfast) and took placebos twice a day before lunch and dinner for six weeks. Each patient's treatment code had the same outward appearance as all the others and was accessed only in the medical emergency conditions. The masking was successfully achieved until opened after data analysis. All volunteers were followed up in the third week and the sixth week in order to evaluate the efficacy and safety of the medicines by using standard equipment, acoustic rhinometry and assessment forms covering severe nasal symptoms, quality of life assessment, and global assessment. Safety was evaluated via physical examination, renal and liver function tests, and a hematology test.

Efficacy and safety evaluation instruments

Acoustic Rhinometry (ARM) : Acoustic rhinometry (SRE2000 Rhinometrics) was chosen to express the degree of mucosal edema, as this method directly measures the minimum cross-sectional area (MCA) or volume of the nasal cavity (Vol) . Thus, changes in these values within weeks or months will reflect changes in thickness of the nasal mucosa. In the present study

parameters were recorded: between 0.0-2.2 cm. and between 2.2-5.4 cm. from the nostril. All rhinometric measurements were made bilaterally and in triplicate by the same operator. Rhinometry is a quick, painless, noninvasive, reliable method which is easily performed with minimal patient invasiveness.⁵

Assessment: Severe nasal symptoms and a global assessment were used as assessment forms in order to collect volunteer information. A visual analog scale (VAS) consisted of a 10 cm. line. The assessments of symptoms were related to the length along the scale where 0 cm. = no symptom, 10 cm. = unbearably severe. All assessment was executed by patients themselves.

Assessment of quality of life

This parameter consisted of a 10 cm. line which was related to the severity of effect. The severest affect = 0 cm. The least severe effect = 10 cm. The assessment of quality of life was executed by patients themselves.

Hematology: Hematology tests were administered to evaluate the white blood cells such as leukocytes, neutrophil, lymphocyte, monocyte, eosinophil and basophil count in serum and to evaluate of

safety via physical examination and laboratory investigations.

Statistical Analysis

The data gathered was evaluated using statistical software. The results are in the form of mean $\pm$ standard deviation. Baseline characteristic data was evaluated by Student's t-test or Mann Whitney U test. The repeated measured ANOVA or Friedman's test in order to evaluate the differences between groups, accompanied by using paired t-test or Wilcoxon's test in order to evaluate differences within groups. A

significance level of $p < 0.05$ was considered statistically significant.

Results

Patient Characteristics

A total of 63 patients were assessed for eligibility and randomly divided into two groups. At follow-up PSPR group lost 1 patient and the Loratadine group lost 2 patients. At the end of the study, there were 30 patients in each group. There were no significant differences in their baseline characteristics, except ALP level and right (Vol_R) as shown in **Table 2**.

Table2: Baseline characteristic of patient

Characteristic	PSPR Mean (SD)	Loratadine Mean (SD)	p-value
Demographics:			
age (years)	32.80 (13.84)	36.90 (13.99)	0.960
height (cm.)	160.58 (12.13)	163.32 (10.34)	0.259
weight (kg)	61.16 (20.14)	61.34 (12.80)	0.352
No (%) of women (N (%))	23 (76.67)	18(60)	0.165
Nasal symptom severity:			
Sneezing	3.58 (1.64)	3.44 (1.81)	0.755
Runny nose	3.97 (1.83)	3.94 (2.21)	0.939
Congestion	4.02 (2.07)	4.33 (1.94)	0.552
Itchy nose	3.59 (2.14)	3.14 (1.85)	0.394
Post nasal drip	2.76 (1.32)	2.81 (2.43)	0.935
Total nasal symptom	4.25 (1.88)	4.37 (1.67)	0.806
Quality of life:	4.90 (2.47)	5.43 (1.63)	0.427
Global assessment:	2.65 (2.09)	2.08 (1.96)	0.962
Acoustic rhinometry:			
MCA_L (cm ²)	0.33 (0.13)	0.34 (0.11)	0.810
MCA_R (cm ²)	0.44 (0.38)	0.41 (0.40)	0.717
Vol_L (cm ³)	2.09 (1.27)	2.22 (1.09)	0.249
Vol_R(cm ³)	3.05 (1.73)	2.22 (1.01)	0.029
Laboratory data:			
Hematology test			
WBC (K/cum)	6.13 (1.92)	6.26 (1.79)	0.785
Neutrophil (%)	52.13 (12.52)	55.14 (9.75)	0.302

Characteristic	PSPR Mean (SD)	Loratadine Mean (SD)	p-value
Lymphocyte (%)	38.20 (11.11)	35.92 (7.98)	0.365
Monocyte (%)	4.31 (2.05)	4.59 (3.57)	0.970
Eosinophil (%)	4.88 (4.52)	3.74 (2.58)	0.469
Basophil (%)	0.48 (0.36)	0.60 (0.34)	0.205
Liver function test			
AST (U/L)	24.80 (19.91)	25.23 (27.20)	0.652
ALT (U/L)	45.40 (40.81)	40.47 (24.31)	0.491
ALP (U/L)	77.07 (13.48)	88.83 (22.34)	0.017
Renal function test			
BUN (mg/dL)	10.63 (3.28)	11.63 (3.06)	0.227
Creatinine (mg/dL)	0.75 (0.15)	0.77 (0.16)	0.560

Efficacy

Acoustic Rhinometry: PSPR increased minimal-cross section area (MCA_L) in the sixth week ($p < 0.05$) but the Loratadine group

was not different at the statistical level (Table 3). However, there was no significant difference in MCA value and nasal volume between the two groups.

Table 3: The minimal crosssectional area of nasal cavity and nasal volume as determined by acoustic rhinometry

Data	Follow-up	Treatment (mean±SD)		P-value
		PSPR	Loratadine	
MCA_L	Week0	0.33 (0.13)	0.34 (0.11)	0.280
	Week3	0.35 (0.16)	0.33 (0.12)	
	Week6	0.40* (0.13)	0.35 (0.16)	
MCA_R	Week0	0.44 (0.38)	0.41 (0.40)	0.657
	Week3	0.38 (0.14)	0.35 (0.16)	
	Week6	0.50 (0.44)	0.40 (0.18)	
Vol_L	Week0	2.09 (1.27)	2.22 (1.09)	0.532
	Week3	1.83 (1.16)	2.06 (1.11)	
	Week6	2.01 (1.32)	1.90 (0.90)	
Vol_R	Week0	3.05 (1.73)	2.22 (1.01)	0.860
	Week3	2.87 (1.69)	2.26 (1.14)	
	Week6	2.67 (1.61)	2.35 (1.21)	

* Significant different from Week0 within group ($p < 0.05$)

Nasal symptoms: Both groups showed alleviation of symptoms of sneezing, runny nose, congestion, itchy nose, and total nasal symptoms. All symptoms were relieved in week 3, except that sneezing in the PSPR

group and itchy nose in Loratadine group were relieved in week 6. However, there was no significant difference between the PSPR group and the Loratadine group except post-nasal drip. PSPR has more efficacy than

Loratadine (**Table 4**). The post-nasal drip in week 3, but not different at a statistical level in week 6. PSPR group decreased in the third and sixth week, but the Loratadine group decreased in

Table 4: Assessment of nasal symptom severity (no symptom = 0 cm, 10 cm. = unbearably severe)

Data	Follow-up	Treatment (Mean±SD)		P-value
		PSPR	Loratadine	
Sneezing (0-10)	Week0	3.58 (1.64)	3.44 (1.81)	0.742
	Week3	2.94 (1.49)	2.37* (1.39)	
	Week6	2.17* (1.52)	1.91* (1.98)	
Runny nose (0-10)	Week0	3.97 (1.83)	3.94 (2.21)	0.397
	Week3	2.67* (1.88)	2.84* (2.09)	
	Week6	2.14* (1.37)	1.99* (1.90)	
Congestion (0-10)	Week0	4.02 (2.07)	4.33 (1.94)	0.159
	Week3	2.85* (1.83)	2.79* (1.91)	
	Week6	2.56* (1.97)	1.94* (1.84)	
Itchy nose (0-10)	Week0	3.59 (2.14)	3.14 (1.85)	0.638
	Week3	2.68* (1.80)	2.62 (1.94)	
	Week6	2.02* (1.58)	2.08* (1.62)	
Post nasal drip (0-10)	Week0	2.76 (1.32)	2.81 (2.43)	<0.001 ^b
	Week3	1.58* (1.69)	1.76* (1.57)	
	Week6	1.56* (1.68)	2.05 (1.90)	
Total nasal symptom (0-10)	Week0	4.25 (1.88)	4.37 (1.67)	0.910
	Week3	2.78* (1.63)	2.98* (1.76)	
	Week6	2.31* (1.77)	2.65* (1.57)	

* Significant different from Week 0 within group (p < 0.05)

^b significant difference between group (p < 0.05)

Effects on quality of life

There was no significant difference between the PSPR and Loratadine groups after 6 weeks. When compared within groups, the quality of life of PSPR volunteers had

increased in week 3 and 6 from baseline (p = 0.001). Conversely, the Loratadine group had increased quality of life in week 3 but there was no significant change in week 6 (**Table 5**).

Table 5: Quality of life (severest effect = 0 cm, the least severe effect = 10 cm.)

Quality of life (0-10)	PSPR	Loratadine	p-value
	Mean (SD)	Mean (SD)	
Week 0	4.90 (2.47)	5.43 (1.63)	0.226
Week 3	6.66* (1.80)	6.63* (1.83)	
Week 6	6.75* (2.05)	6.09 (1.95)	

* Significant different from Week 0 within group (p < 0.05)

Hematology test

There were no significant differences in WBC, neutrophil, lymphocyte, monocyte and basophil, except for the eosinophil count.

The mean of eosinophil count in PSPR group decreased in Week 6, while the Loratadine group increased in mean Eosinophil count in week 6 (**Table6**).

Table 6: Laboratory test of liver function, renal function and hematology test

Data	Follow-up	Treatment (mean ± SD)		P-value
		PSPR	Loratadine	
Liver function				
AST (15-37U/L)	Week0	24.80 (19.91)	25.23 (27.20)	0.746
	Week3	24.47 (29.25)	22.17 (17.86)	
	Week6	18.73 [*] (9.68)	24.13 (24.73)	
ALT (30-65U/L)	Week0	45.40 (40.81)	40.47 (24.31)	0.124
	Week3	40.40 (27.63)	40.97 (19.35)	
	Week6	37.53 (15.09)	41.30 (21.41)	
ALP (50-136U/L)	Week0	77.07 (13.48)	88.83 (22.34)	0.02 ^b
	Week3	81.43 [*] (12.14)	87.97 (20.23)	
	Week6	78.77 (13.02)	88.50 (20.91)	
Renal function				
BUN (5-23 mg/dL)	Week0	10.63 (3.28)	11.63 (3.06)	0.966
	Week3	10.64 (2.82)	11.57 (2.63)	
	Week6	10.78 (3.06)	11.89 (3.12)	
Creatinine (0.6-1.4 mg/dL)	Week0	0.75 (0.15)	0.77 (0.16)	0.030 ^b
	Week3	0.77 (0.16)	0.82 [*] (0.13)	
	Week6	0.75 (0.17)	0.82 [*] (0.16)	
Hematology test				
WBC (4-11K/cumm.)	Week0	6.13 (1.92)	6.26 (1.79)	0.144
	Week3	6.20 (1.94)	6.29 (1.65)	
	Week6	6.21 (1.66)	5.81 [*] (1.31)	
Neutrophil (45-75%)	Week0	52.13 (12.52)	55.14 (9.75)	0.212
	Week3	53.04 (9.62)	55.39 (8.39)	
	Week6	56.31 [*] (8.24)	55.47 (6.51)	
Lymphocyte (20-45%)	Week0	38.20 (11.11)	35.92 (7.98)	0.559
	Week3	36.98 (9.77)	35.07 (7.04)	
	Week6	35.77 (7.38)	35.29 (5.59)	
Monocyte (2-10%)	Week0	4.31 (2.05)	4.59 (3.57)	0.534
	Week3	4.45 (2.07)	4.55 (1.63)	
	Week6	3.51 [*] (1.20)	4.87 (1.71)	
Eosinophil (4-6%)	Week0	4.88 (4.52)	3.74 (2.58)	0.005 ^b
	Week3	5.02 (4.65)	4.43 [*] (3.38)	
	Week6	4.23 (4.63)	3.82 (2.66)	
Basophil (0-1%)	Week0	0.48 (0.36)	0.60 (0.34)	0.578
	Week3	0.51 (0.25)	0.56 (0.27)	
	Week6	0.52 (0.16)	0.55 (0.20)	

* Significant different from Week 0 within group ($p < 0.05$)

^b Significant different between group ($p < 0.05$)

Safety

After taking the drugs for 6 weeks, there was no significant difference in AST, ALT and BUN levels in both groups, except for ALP and creatinine levels. PSPR group was significantly increased in ALP level in week 3 but within normal limits and returned to baseline level by week 6 while the Loratadine group showed no significant difference changes. The creatinine level in the Loratadine group significantly increased in the third and sixth week from baseline but within normal limits while the PSPR group showed no significant difference changes (**Table 6**).

Adverse effect

Adverse effects from PSPR exist, such as eructate (n=7, 23.3%), nausea (n=4, 13.3%), increased appetite (n=2, 6.7%), anorexia, dizzy, drowsiness and dry mouth (n=1, 3.3%). Conversely, side effects of Loratadine are drowsiness (n=4, 13.3%), nausea, dry nose and parched throat (n=2, 6.7%), diarrhea, increased appetite, anorexia, dizziness, dry mouth (n=1, 3.3%). All symptoms were mild (grade 1).

Discussion

In order to prove that the Prasaprophyai remedy is an effective and safe treatment for mild symptoms of allergic rhinitis, its efficacy was compared to that of Loratadine. The acoustic rhinometry machine measured morphology change in the nasal cavity. It indicated whether there was any nasal obstruction. Acoustic rhinometry measured the minimum cross-sectional areas (MCA) and nasal volume (Vol). It is a sensitive and objective method of assessment of nasal obstruction. Acoustic rhinometry was chosen to express the degree of mucosal edema. The relationship between MCA and severity of reaction against the antigen in allergic rhinitis patients was statistically significant⁶. The results of this study showed that the PSPR increased minimum- cross section area (MCA_L) in the sixth week. Increasing MCA was an indicator of the drug's efficacy. PSPR has the ability to reduce nasal obstruction and severity of nasal symptoms.

In vitro research show that PSPR can inhibit releasing of histamine (determine by measured inhibits β -hexosaminidase release; IC₅₀ in range of 12.83 – 25.11 μ g/ml). Histamine is released in the late phase response in allergic reaction, which results in the

prolongation of symptoms. According to this study, PSPR was able to relieve the severity of nasal symptoms such as sneezing, running nose, congestion, itchy nose, and total nasal symptoms. PSPR worked as well as the antihistamine drug (Loratadine) at a statistically significant level, except post-nasal drip symptom.

Allergic rhinitis also triggers a systemic inflammation besides local inflammation, which can in turn augment inflammation in both the upper and lower airways and explains the link to asthma. PSPR can inhibit the pro-inflammatory mediator, Nitric oxide. PSPR has good anti-inflammatory activity ($IC_{50}=18.40\pm0.43\mu\text{g/ml}$).⁴

In reviewing research on PSPR's chemical components of volatile oil, the researchers used gas chromatography and mass spectrometry (GC-MS). The main chemical compound is ethyl-p-methoxycinnamate, which is the main chemical component in *Kaempferia galanga* L.⁷ and Oleic acid ethyl ester, Ethyl linolelaidateliquid, Octadecanoic acid, Austrobailignan- 6, Ethyl myristate, ethyl cinnamate, eugenol, Dill- apiol, Ethyl 3- (4-ethoxy- 3- methoxyphenyl) acrylate, Pentadecane, Eicosanoic acid, Ethyl 3, 7, 11, 15- tetramethyl- 2- hexadecenoate, Ethyl 9-

hexadecenoate, Hexadecane, Docosanoic acid (CAS), Eugenol acetate, Elemicin, Valencene, Methoxyeugenol and Allyl phenoxyacetate are chemical constituents. *In vitro* and *in vivo* researchers found that Eugenol had an anti-allergic effect.⁸ Moreover, ethyl-p-methoxycinnamate, which is the main chemical compound, can inhibit inflammation by suppressing interleukin- 1 and tumor necrosis factor- α using both in *in vivo* and *in vitro* experiment.⁹ However, there is no report on active compounds of PSPR having an anti-allergic effect. Further investigations would reveal more.

In all the laboratory examinations, the AST, ALT and BUN levels were not significantly different between both groups, but the PSPR group was significantly increased in ALP level in week 3 but returned to baseline level by week 6. By contrast, the Loratadine group showed no change in the ALP over the whole research period. The creatinine level in the Loratadine group significantly increased in week 3 and 6 from baseline. However, increasing of ALP in the PSPR group and increasing creatinine level in the Loratadine group did not exceed the standard ranges for ALP and creatinine. Moreover, in a previous study, no kidney injury was reported after taking Loratadine.^{10, 11} Thus, after taking PSPR

remedy and Loratadine for 6 weeks, it was found that there was no effect on renal and liver function.

Eructate (n=7, 23.3%) was the most common symptom as a side effect of PSPR because of major components which were carminative herbs, such as *Kaempferia galanga* L., *Ligusticum sinense* Oliv. cv. Chuanxiong, *Atractylodes lancea* (Thunb.) DC., *Anethum graveolens* L., *Cuminum cyminum* L., *Foeniculum vulgare* Mill. var. *dulce* (Mill.) Thell., *Nigella sativa* L., *Myristica fragrans* Houtt (aril and nutmeg), *Amomum testaceum* Ridl and *Syzygium aromaticum* (L.) Merr. et Perry. In 1 hour after taking PSPR, eructate disappeared.

Drowsiness was the most common side effect of Loratadine. It is a side effect of antihistamine drugs, although being a second-generation antihistamine drug. Loratadine was a non-*sedating* antihistamine drug, but it still caused drowsiness in a few people.¹² PSPR rarely experienced drowsiness (n=1, 3.3%). Finally, PSPR was a good choice for allergic rhinitis patients who did not need medicines that caused drowsiness.

This research is the first report which did clinical trial in allergic rhinitis patients and compared PSPR with Loratadine. As a logical

next step, further studies on a larger number of patients will be needed to consolidate and verify these results, accompanied by isolation of and research on active compounds together with their mechanism of action. The limitation of this research is small number of participants and short time. A long term study period and large scale are needed to completely evaluate the efficacy and safety of PSPR. In addition, the followed of symptoms of AR are recurrent is important. Therefore, future studies should be followed up after the participants stopped the drug and recurrent symptoms.

Conclusions

PSPR is as safe and effective as Loratadine treatment. It is able to relieve nasal symptoms with equal effectiveness to Loratadine treatment, except for post nasal drip. PSPR has more efficacy than Loratadine. Prasaprophyai is safe. However, ALP value increased in the PSPR group in week 3 but returned to baseline level in week 6; increasing of ALP in the PSPR group did not exceed the standard ranges for ALP. Side effects of PSPR are eructate (n=7, 23.3%). It rarely produced drowsiness. PSPR appears to be as safe and effective as Loratadine

treatment and could be a potential choice for the treatment of mild symptoms of allergic rhinitis.

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Conflicts of interest

The authors declare no conflict of interest.

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