Original Article

Clinical Trial Phase I of Prasaprohyai Extract Capsules

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Background: Prasaprohyai remedy (PSPR) is a Thai traditional medicine that has long been used to treat the common cold and fever. Previous studies revealed that PSPR powder can relieve allergic rhinitis symptoms as effectively as Loratadine. The usual dose was 3,000 mg/day; however, if the extract could be used it may be possible to reduce the dosage. Therefore, it is necessary to find out if the administration of PSPR ethanolic extract to healthy volunteers is safe.

Objective: To study the safety of PSPR ethanolic extract in healthy volunteers.

Materials and Methods: The present study was a randomized, open-labelled, trial for safety assessments in 24 healthy volunteers. The volunteers were divided into two groups, one group receiving 3x100 mg/day and the other group receiving 3x200 mg/day before meal for 6 weeks. The blocked randomization was done by a computer program with equal distribution of genders. The experiment with group 2 started after finishing with group 1. There was a wash-out period after week 6th. All volunteers were followed-up in the 3rd week, 6th week and 8th week to evaluate the safety of the medicine.

Results: There was no toxicity of PSPR to the liver and kidney. The results on blood glucose, lipid profile and complete blood count were normal.

Conclusion: The PSPR remedy ethanolic extract capsules at 300 and 600 mg/day were safe to use in healthy volunteers for 6 weeks, with mild side effects. Oral administration was recommended after meals.

Keywords: Prasaprohyai remedy, Safety, Complementary medicine, Herbal extract

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Prasaprohyai remedy (PSPR), a Thai traditional medicine, has long been used to treat the common cold and fever[1]. It consists of 21 herbs. The major component of PSPR is the rhizome of *K. galanga* L. (KG) with the remaining 20 herbs in equal weights. A previous phytochemical study showed that ethyl-*p*-methoxycinnamate (EPMC) and eugenol were the two main chemical components of PSPR detected by GC-MS[2]. EPMC and eugenol were identified as markers for anti-allergic activity[3]. Previous studies showed that the 95% ethanolic extract of PSPR had notable anti-allergic effects on RBL-2H3 cell line model (IC_{50} = 16.59±1.68 µg/ml)[4]. The extract has been reported to have anti-inflammatory effect by inhibiting nitric oxide release (IC_{50} = 18.40±0.43 µg/ml)[5]. Other reported biological activities of PSPR were analgesic[6], antibacterial[7], anticancer[6], antimalarial[8], antipyretic[6] antioxidant[5] and cytotoxic activities[9]. A previous clinical study comparing the efficacy and safety of PSPR capsules and Loratadine in allergic rhinitis patients showed PSPR to be as safe and effective as Loratadine. In this study patients receive PSPR powder (3x1,000 mg/day) for six weeks. The patients showed improvement of total nasal symptoms. Its inhancement of quality of life was as effective as the treatment with Loratadine[10].

The usual dose of PSPR was 3,000 mg/day; however, if the extract could be use instead of powdered PSPR the dose could be reduced. Therefore, it was necessary to find out if the administration of PRPR extract to healthy volunteers was safe.

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Materials and Methods

Volunteer subjects

The US food and drug administration (FDA) suggests a minimum group of 20 healthy volunteers for study in clinical trial phase I[11]. Allowing a 20% drop out rate, therefore, a total of 24 persons were required.

The criteria for recruitment were: age 20 to 60 years old, healthy, or without serious medical conditions, and able to follow the instructions for 8 weeks. The criteria for exclusion were allergic reactions to PSPR, receive other medication, pregnant, lactating women or participate in other study.

Volunteers should take all of the PSPR extract

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capsules, refrain from taking supplementary food or vitamins, smoking and drinking alcohol. The volunteers who failed to follow the instructions were discarded.

Study design

The present study was a randomized, open-labeled, trial for safety assessments in 24 healthy volunteers.

The study was approved by the Medical Ethics Committee of the Faculty of Medicine, Thammasat University which was accredited by the Thai FDA (Registry# MTU-EC-TM-4-137/59) and posted on www.clinicaltrial.gov (Registry #NCT 03077282).

Procedure

The volunteers were divided into two groups, one group receiving 3x100 mg/day and the other group receiving 3x200 mg/day before meals for 6 weeks. The blocked randomization was done by a computer program with equal distribution of genders. The experiment with group 2 started after ending the experiment with group 1. There was a wash-out period after week 6th. All volunteers were followed-up in the third week, sixth week and eighth week to evaluate the safety of the medicine (Figure 1). The researcher recorded data such as age, career, BMI, vital signs, health signs and symptoms. Safety to the volunteers was monitored by full blood analysis including liver and renal function tests, lipid profile, blood sugar and complete blood counts.

Plant materials

All PSPR plant components were bought from various sources. The plant parts were identified by the botanist at the Herbarium of Southern Center of Thai Medicinal Plants at Faculty of Pharmaceutical Science, Prince of Songkla University, Songkhla province, Thailand. The voucher specimen number of each plant material is shown in Table 1.

Drug preparation

Each plant material was cleaned, cut into small pieces, and dried at 50°C for 24 h. Dried plant material was powdered using an electric grinder (40 mesh). The powdered plant materials were weighed according to their proportions described in Table 1 and were homogenously mixed. The mixed powder was macerated with 95% ethanol (2: 1) for 3 days. Then filtered with Whatman number 1 paper. The residue of PSPR was remacerated twice and the same treatment was applied. These three filtrates were combined and the

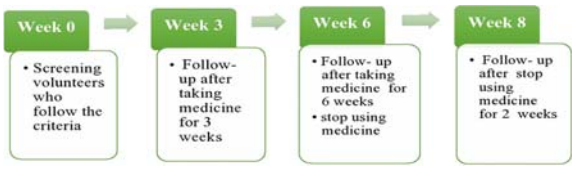

Figure 1. Study design.

Table 1. Medicinal plant ingredients in Prasapraohyai remedy (PSPR) formulation (for 1,000 g. of powder drug)

Scientific name	Family	Voucher specimen	Part used	Weight (g)	From
Amomum testaceum Ridl.	Zingiberaceae	SKP206011101	Fruit	25	Chantaburi, Thailand
Anethum graveolens L.	Umbelliferae	SKP199010701	Fruit	25	India
Angelica dahurica Benth.	Umbelliferae	SKP199010401	Root	25	China
Angelica sinensis (Oliv.) Diels	Umbelliferae	SKP199010901	Root	25	China
Artemisia annua L.	Compositae	SKP051010101	All parts	25	China
Atractylodes lancea (Thunb.) DC.	Compositae	SKP051011201	Rhizome	25	China
Cuminum cyminum L.	Umbelliferae	SKP199030301	Fruit	25	India
Dracaena loureiri Gagnep.	Dracaenaceae	SKP065041201	Hart wood	25	Chantaburi, Thailand
Foeniculum vulgare Mill. var. dulce (Mill.) Thell.	Umbelliferae	SKP199062201	Fruit	25	India
Kaempferia galanga L.	Zingiberaceae	SKP206110701	Rhizome	500	Sukhothai, Thailand
Lepidium sativum L.	Brassicaceae	SKP057121901	Seed	25	India
Ligusticum sinense Olive. Cv. Chuanxiong	Umbelliferae	SKP199121901	Rhizome	25	China
Mammea siamensis Kosterm.	Guittiferae	SKP083131901	Flower	25	Ratchaburi, Thailand
Mesua ferrea L.	Guittiferae	SKP08313060	Flower	25	Ratchaburi, Thailand
Mimusops elengi L.	Sapotaceae	SKP171130501	Flower	25	Ratchaburi, Thailand
Myristica fragrans Houtt.	Myristicaceae	SKP121130601	Nutmeg/aril	25	Chumphon, Thailand
Myristica fragrans Houtt.	Myristicaceae	SKP121130601	Seed	25	Chumphon, Thailand
Myristica fragrans Houtt.	Myristicaceae	SKP121130601	Hart wood	25	Chantaburi, Thailand
Nelumbo nucifera Gaertn.	Nelumboceae	SKP125141401	Pollen	25	Nakhon Pathom, Thailand
Nigella sativa L.	Ranunculaceae	SKP160141901	Seed	25	India
Syzygium aromaticum (L.) Merr. et Perry	Myristicaceae	SKP123190101	Flower-bud	25	Chantaburi, Thailand

Table 2. Quality control of PSPR ethanolic extract capsules

	PSPR results	Requirement	Result
Average weight (g)*[13]	0.612 gram	0.551 to 0.673 gram	Pass
Loss on drying (%)[13]	7.76±1.50%	<10%	Pass
Disintegration time (min)[13]	10 min	<30 min	Pass
Contamination**[13]			
Aerobic microbial count	<10 CFU/g	<5x10^3 CFU/g	Pass
Yeasts and moulds count	<10 CFU/g	<5x10^2 CFU/g	Pass
Heavy metal contents[13]			
Arsenic (As)	0.237	<4 ppm	Pass
Lead (Pb)	ND	<10 ppm	Pass
Cadmium (Cd)	ND	<0.3 ppm	Pass
PSPR extract			
Ethyl-*p*-methoxycinnamate (EPMC)	227.1 mg/g	-	-
eugenol	52.9 mg/g	-	-

* The average weight by more than the percentage deviation of 10 percent and none deviates by more than twice that percentage.
** Plate-Count Methods
ND = Not detected (Detection limit : As = 0.001 ppm, Pb =0.002 ppm, Cd = 0.035 ppm)

solvent removed using a rotary evaporator under reduced pressure at 40°C to obtain dry ethanolic extract. The extract was dried to constant weight in a hot air oven at 45±5°C and kept at -20°C until use. The extractive yield was 5.05% (w/w).

A 100 mg of extract and other ingradients were filled into a capsule size 0 in a capsule blister pack and sealed with aluminum foil. PSPR extract capsules were tested for contamination, weight variation, loss on drying, heavy metals contamination and disintegration (Table 2).

Outcome assessment

As indicator parameters, the participant profiles of interest were: 1) age 2) Hemodynamic profiles: pulse rate and systolic blood pressure; 3) Biochemical profiles: renal and liver function tests, glucose, lipid profile; 4) Hematology: Complete blood count (CBC).

Statistical analysis

The data were evaluated using a statistical software. The results were reported as mean ± standard deviation. The data were tested for normality and homogeneity in order to select a proper statistical test. The study was planned as Independent Sample t-test or Man Whitney U test in order to evaluate differences between groups, accompanied by 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

Quality control

The PSPR extract capsules passed the requirements of quality standard including average weight, loss on drying, disintegration time and contaminant test. The analysis of the markers performed by HPLC yielded, 227.1 mg/g EPMC and 52.9 mg/g eugenol (Table 2).

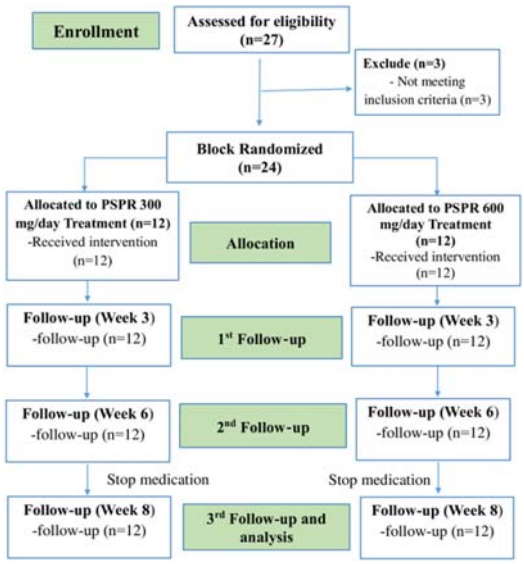

Figure 2. CONSORT flow diagram.

Volunteers

Healthy volunteers were recruited between August and November of 2017 from Thammasat University, Rangsit Campus. Eligible healthy volunteers were men and women who met the recruitment criteria. A total of 27 participants were enrolled in the study and 3 participants were later excluded (Hypertension = 1, High AST = 2). Twenty-four eligible participants were block randomized to take PSPR 300 mg/day or 600 mg/day.

All participants were followed-up in the third week, sixth week and eighth week to evaluate the safety of the medicine. All participants complied with the study design (Figure 2).

Baseline characteristics of healthy volunteers

There were no significant differences in indicator parameters between group1 and group2 before starting the experiment (Table 3).

Vital signs

There was no significant difference between the two groups in vital signs during the experiment and after washout period (Table 4).

Laboratory tests

Renal and liver function tests

There was no significant difference between the two treated groups in BUN, creatinine, total protein, albumin, globulin, total bilirubin, direct bilirubin, AST, ALT, and ALP levels. There was significant difference within group on BUN, total protein, total bilirubin, and AST level only in group 1. There was no significant difference within-group 2 in renal and liver function tests. All results of the renal and liver function tests were in normal range (Table 5).

Glucose and lipid profile

There was no significant difference between two groups in glucose, HDL-cholesterol, total cholesterol, LDL-cholesterol, and triglyceride levels. There was

Table 3. Baseline characteristics of healthy volunteers in the two groups

Data	PSPR 300 mg/day Mean (SD)	PSPR 600 mg/day Mean (SD)	*p*-value[T]
Demographics			
Age (year)	30.25	34.08	0.315[M]
BMI (kg/m^2)	22.29	22.10	0.865
Hemodynamics			
Pulse (/min)	75.25 (11.32)	71.42 (5.43)	0.385[M]
SBP (mmHg)	107.00 (8.68)	111.25 (9.56)	0.267
DBP (mmHg)	73.83 (6.46)	72.92 (8.11)	0.762

[T] Independent sample t-test, [M] Mann Whitney U-test

Table 4. Comparison of the vital signs between group 1 and group 2

Vital signs	Time of experiment	PSPR treatment, mean (SD)		*p*-value[B]
		Group 1[W] (n = 12)	Group 2[W] (n = 12)	
Temperature (°C)	Week 0	36.26 (0.22)	36.26 (0.41)	1.000
	Week 3	36.30 (0.42)	36.31 (0.33)	0.958
	Week 6	36.18 (0.45)	36.19 (0.35)	0.96
	Week 8	36.17 (0.43)	36.35 (0.26)	0.224
Pulse (beats per minute)	Week 0	75.25 (11.32)	71.42 (5.43)	0.410
	Week 3	74.08 (9.46)	75.00 (8.80)	0.977
	Week 6	78.42 (8.48)	82.17 (8.92)	0.319
	Week 8	75.25 (11.32)	76.08 (6.61)	0.478
Respiratory rate (breaths/minute)	Week 0	14.25 (3.25)	16.58 (3.03)	0.089
	Week 3	15.33 (4.44)	16.92 (2.15)	0.630
	Week 6	15.17 (3.35)	16.50 (3.09)	0.347
	Week 8	16.50 (2.84)	18.00 (2.55)	0.319
Systolic (mmHg)	Week 0	107.00 (8.68)	111.25 (9.56)	0.267
	Week 3	106.25 (11.51)	108.33 (12.11)	0.670
	Week 6	105.83 (10.84)	107.50 (11.38)	0.717
	Week 8	106.50 (11.97)	106.25 (11.89)	0.960
Diastolic (mmHg)	Week 0	73.83 (6.46)	72.92 (8.11)	0.762
	Week 3	71.17 (8.17)	73.17 (9.00)	0.575
	Week 6	72.50 (8.66)	73.75 (5.69)	1.000
	Week 8	72.33 (9.34)	73.75 (5.69)	0.659

[B] Comparison between-group: Independent-samples t-test or Mann Whitney U-test, [W] Comparison within-group from week 0: Wilcoxon sign rank test

* Statistically significant (p<0.05)

Table 5. Comparison of the renal and liver function test in orally-administered PSPR ethanolic extract capsules between dose 300 mg/day (group1) and 600 mg/day (group2)

Laboratory test (male and female normal range)	Time of experiment	Treatment; mean (SD)		*p*-value[B]
		Group 1 [W] (n = 12)	Group 2 [W] (n = 12)	
BUN (7 to 18 mg/dL)	Week 0	10.71 (3.49)	11.70 (3.72)	0.508
	Week 3	12.81 (4.08)*	12.26 (4.67)	0.761
	Week 6	12.18 (3.47)	11.48 (2.56)	0.584
	Week 8	12.84 (3.30)*	12.11 (4.75)	0.664
Creatinine (M: 0.67 to 1.17, F: 0.51 to 0.95 mg/dL)	Week 0	0.78 (0.17)	0.86 (0.17)	0.262
	Week 3	0.76 (0.18)	0.87 (0.18)	0.123
	Week 6	0.80 (0.17)	0.86 (0.17)	0.406
	Week 8	0.79 (0.14)	0.85 (0.17)	0.312
Total protein (6.4 to 8.2 mg/dL)	Week 0	7.74 (0.41)	7.79 (0.32)	0.742
	Week 3	7.90 (0.46)*	7.71 (0.34)	0.255
	Week 6	7.93 (0.58)*	7.75 (0.46)	0.397
	Week 8	7.93 (0.48)*	7.67 (0.41)	0.169
Albumin (3.4 to 5.0 mg/dL)	Week 0	4.20 (0.24)	4.16 (0.36)	0.740
	Week 3	4.19 (0.25)	4.13 (0.28)	0.594
	Week 6	4.23 (0.20)	4.12 (0.38)	0.356
	Week 8	4.22 (0.26)	4.13 (0.34)	0.508
Globulin (1.5 to 3.5 mg/dL)	Week 0	3.53 (0.43)	3.67 (0.40)	0.440
	Week 3	3.71 (0.55)	3.57 (0.48)	0.510
	Week 6	3.70 (0.61)	3.63 (0.51)	0.747
	Week 8	3.71 (0.50)	3.53 (0.54)	0.418
Total bilirubin (0.2 to 1.0 mg/dL)	Week 0	0.49 (0.17)	0.58 (0.29)	0.590
	Week 3	0.73 (0.28)*	0.68 (0.23)	0.551
	Week 6	0.48 (0.19)	0.54 (0.27)	0.671
	Week 8	0.53 (0.22)	0.54 (0.26)	0.977
Direct bilirubin (0.0 to 0.2 mg/dL)	Week 0	0.13 (0.05)	0.13 (0.05)	0.755
	Week 3	0.12 (0.04)	0.13 (0.05)	0.514
	Week 6	0.13 (0.05)	0.13 (0.05)	1.000
	Week 8	0.12 (0.04)	0.13 (0.05)	0.633
AST (15 to 37 U/L)	Week 0	15.17 (7.40)	22.17 (12.79)	0.115
	Week 3	15.58 (5.50)	23.58 (12.08)	0.054
	Week 6	22.67 (9.98)*	19.67 (5.02)	0.362
	Week 8	20.50 (5.92)*	19.00 (5.39)	0.523
ALT (M: 16 to 63 U/L, F: 14 to 59 U/L)	Week 0	24.00 (8.22)	29.00 (15.46)	0.378
	Week 3	23.50 (7.18)	32.92 (25.66)	0.630
	Week 6	27.25 (12.55)	25.92 (10.79)	0.977
	Week 8	25.42 (8.77)	27.92 (10.89)	0.755
ALP (50 to 136 U/L)	Week 0	66.67 (26.35)	63.92 (27.17)	0.804
	Week 3	65.42 (26.15)	62.75 (27.29)	0.809
	Week 6	66.50 (29.01)	63.00 (28.54)	0.769
	Week 8	65.17 (28.92)	62.92 (26.68)	0.845

[B] Comparison between-group: Independent-samples t-test or Mann Whitney U-test, [W] Comparison within-group from week 0: Wilcoxon sign rank test
* Statistically significant ($p<0.05$)

significant difference within-group in glucose and HDL-cholesterol level. However, the increase of glucose and decrease of HDL-cholesterol level did not exceed the normal range (Table 6).

Hematology test

There was no significant difference between the two groups in complete blood count. WBC and eosinophil showed some variation during the experiment but all values were in normal range (Table 7).

Adverse events

Groups 1 and 2 experienced minor adverse events during the experiment, such as: eructation at week 3 (25 to 33.3%), burning sensation in the stomach (25 %) and stomachache (16%).

Table 6. Comparison of glucose and lipid profiles in orally-administered PSPR ethanolic extract capsules of dose 300 mg/day and 600 mg/day

Laboratory test (male and female normal range)	Time of experiment	Treatment; mean (SD)		*p*-value[B]
		Group 1[W] (n = 12)	Group 2[W] (n = 12)	
Glucose (74 to 106 mg/dL)	Week 0	88.08 (3.92)	86.50 (6.08)	0.456
	Week 3	98.08 (5.20)*	92.58 (8.23)*	0.063
	Week 6	88.42 (3.37)	88.00 (5.15)	0.817
	Week 8	89.08 (7.80)	86.08 (4.78)	0.268
HDL-cholesterol (40 to 60 mg/dL)	Week 0	66.33 (16.04)	57.17 (16.53)	0.182
	Week 3	57.08 (14.75)*	57.58 (16.13)	0.938
	Week 6	56.83 (14.46)*	63.42 (18.18)	0.337
	Week 8	56.92 (15.08)*	59.58 (16.29)	0.681
Total cholesterol (0 to 200 mg/dL)	Week 0	204.17 (31.71)	207.67 (34.64)	0.799
	Week 3	210.00 (28.66)	212.33 (33.89)	0.857
	Week 6	212.25 (28.11)	216.75 (28.83)	0.702
	Week 8	208.67 (25.26)	216.17 (36.68)	0.566
LDL-cholesterol (0 to 100 mg/dL)	Week 0	129.58 (31.70)	131.08 (27.83)	0.843
	Week 3	135.75 (30.86)	131.25 (29.21)	0.671
	Week 6	133.17 (30.04)	136.58 (29.12)	0.799
	Week 8	131.42 (23.78)	135.25 (32.44)	0.977
Triglycerides (0 to 150 mg/dL)	Week 0	81.00 (57.79)	122.42 (95.87)	0.443
	Week 3	90.83 (87.43)	110.42 (94.04)	0.242
	Week 6	105.00 (103.66)	108.17 (57.23)	0.266
	Week 8	87.0 (66.93)	110.42 (65.49)	0.219

[B] Comparison between-group: Independent-samples t-test or Mann Whitney U-test, [W] Comparison within-group from week 0: Wilcoxon sign rank test
* Statistically significant (p<0.05)

Discussion

The PSPR extract capsules were made according to Thai Herbal Pharmacopoeia (THP) requirments. Our results provided as a guidance for PSPR specifications as shown in Table 2. The analyses of the anti-allergic markers, EPMC and eugenol, done by HPLC[3], revealed their contents to be 227.1 and 52.9 mg/g, respectively.

The results of our study showed that treatment with PSPR extract at the doses of 3x100 mg/day and 2x200 mg/day had no toxicity to the liver and kidney. There was no difference in glucose, lipid profile and complete blood count as compared to the values at the beginning of the experiment. A previous an *in vivo* study in rat also showed that PSPR extract at a dose of 1,000 mg/kg/day had no toxicity to liver or kidney[12].

Moreover, allergic rhinitis patients who received powdered PSPR at a dose of 3x1,000 mg/day for 6 weeks did not show abnormal results in liver and renal function tests, glucose, lipid profile and CBC[10].

Upon examination of WBC, the number of eosinophil counts in healthy volunteers showed gradual reduction. Previous experiment on allergic rhinitis patients also showed the same reduction pattern of eosinophil after taking PSPR powder[10]. Normally eosinophil increase in patients with allergic disease[14]. Therefore, the reduction in the number of eosinophil may suggest reduction of allergy.

There were minor adverse events such as eructation, burning sensation in the stomach and mild stomachache. The symptoms of eructation diminished after 3 weeks. Due to the persistence of burning sensation in the stomach (25%) and mild stomachache (16%) throughout the experiment, we suggest an oral administration of PSPR extract capsules after meals to reduce the sensation of burning. Patients with severe peptic ulcer must use the drug with caution.

Eugenol, a pungent compound, might be the reason for the adverse events. A previous study showed that eugenol was an agonist of transient receptor potential vanilloid 1 (TRPV-1)[15], a heat sensor[16] found in the stomach and duodenum[17]. This may be the reason why volunteers felt a burning sensation in the stomach.

Conclusion

The PSPR remedy ethanolic extract capsules at 300 and 600 mg/day were safe to use in healthy volunteers for 6 weeks without renal and liver toxicity, with mild side effects. We suggest that a minimal dose of 3x100 mg/day of PSPR extract is preferable, taken after meals.

What is already known on this topic?

Traditionally, the powdered PSPR was used to treat AR patients. It was shown that PSPR had no difference on efficacy and safety when compare with Loratadine. *In vitro* study showed that the PSPR ethanolic extract had good anti-allergic and anti-inflammatory activities. The PSPR

Table 7. Comparison of the complete blood count (CBC) in group 1 (300 mg/day) and group 2 (600 mg/day)

Laboratory test (male and female normal ranges)	Time of experiment	Treatment; mean (SD)		*p*-value[B]
		Group 1[W] (n = 12)	Group 2[W] (n = 12)	
WBC (4 to 11 K/cumm)	Week 0	5.21 (1.60)	5.63 (1.22)	0.480
	Week 3	5.30 (1.41)	5.91 (1.32)	0.290
	Week 6	5.37 (1.61)	6.47 (1.14)	0.065
	Week 8	5.11 (1.39)	6.38 (1.22)	0.027*
Neutrophil (45 to 75%)	Week 0	55.88 (9.94)	50.81 (8.69)	0.197
	Week 3	54.06 (7.66)	46.00 (12.36)	0.068
	Week 6	52.88 (8.39)	55.14 (10.70)	0.571
	Week 8	54.63 (6.95)	55.11 (5.77)	0.855
Lymphocyte (20 to 45%)	Week 0	35.41 (9.34)	39.01 (7.95)	0.320
	Week 3	38.72 (7.29)	45.72 (13.30)	0.124
	Week 6	38.31 (8.64)	36.87 (9.69)	0.704
	Week 8	37.48 (6.76)	35.96 (5.94)	0.563
Monocyte (2 to 10%)	Week 0	3.97 (1.93)	4.43 (1.29)	0.502
	Week 3	2.90 (0.86)	3.23 (1.35)*	0.480
	Week 6	4.97 (2.50)	3.51 (1.12)*	0.078
	Week 8	4.39 (1.62)	3.23 (1.26)*	0.062
Eosinophils (4 to 6%)	Week 0	4.33 (2.62)	5.20 (2.38)	0.406
	Week 3	3.90 (2.26)	4.58 (1.48)	0.395
	Week 6	3.13 (2.45)	3.92 (2.51)*	0.443
	Week 8	3.03 (2.04)*	5.25 (2.63)	0.030*
Basophils (0 to 1%)	Week 0	0.41 (0.22)	0.56 (0.24)	0.089
	Week 3	0.43 (0.23)	0.48 (0.42)	0.799
	Week 6	0.72 (0.22)*	0.57 (0.49)	0.078
	Week 8	0.48 (0.26)	0.46 (0.35)	0.671
RBC (M: 4.5 to 6.0, F: 4.0 to 5.5 x10^6/cumm)	Week 0	4.76 (0.57)	4.94 (0.78)	0.509
	Week 3	4.76 (0.55)	4.90 (0.71)	0.613
	Week 6	4.77 (0.61)	4.90 (0.69)	0.639
	Week 8	4.76 (0.56)	4.87 (0.75)	0.697
Hb (M: 14 to 18 gm/dL, F: 12 to 16 gm/dL)	Week 0	12.46 (1.36)	12.68 (1.08)	0.658
	Week 3	12.45 (1.49)	12.63 (1.03)	0.730
	Week 6	12.46 (1.56)	12.72 (1.27)	0.662
	Week 8	12.47 (1.53)	12.59 (1.38)	0.835
Hct (M: 41 to 51%, F: 35 to 45%)	Week 0	38.20 (3.16)	38.75 (3.39)	0.685
	Week 3	38.03 (3.69)	38.00 (2.90)	0.985
	Week 6	38.33 (3.96)	38.24 (3.32)	0.952
	Week 8	38.22 (3.45)	38.50 (4.08)	0.856
MCV (82 to 96 fl)	Week 0	81.06 (8.65)	79.40 (8.33)	0.637
	Week 3	80.58 (9.08)	78.50 (8.42)*	0.567
	Week 6	81.01 (9.23)	78.89 (8.26)*	0.560
	Week 8	80.96 (9.00)	80.06 (8.85)	0.807
MCH (27 to 32 pg)	Week 0	26.44 (3.64)	26.04 (3.29)	0.780
	Week 3	26.39 (3.73)	26.15 (3.16)	0.866
	Week 6	26.38 (3.90)	26.23 (3.24)	0.919
	Week 8	26.43 (3.81)	26.19 (3.17)	0.867
MCHC (32 to 36 g/dL)	Week 0	32.53 (1.32)	32.74 (1.17)	0.687
	Week 3	32.67 (1.20)	33.25 (0.99)*	0.207
	Week 6	32.44 (1.35)	33.21 (1.04)*	0.133
	Week 8	32.54 (1.52)	32.68 (0.92)	0.797
RDW (11.5 to 14.5%)	Week 0	12.98 (1.81)	12.92 (0.74)	0.919
	Week 3	12.77 (1.70)*	12.67 (0.76)*	0.857
	Week 6	12.80 (1.55)	12.64 (0.84)*	0.758
	Week 8	12.85 (1.66)	12.82 (0.72)	0.950
Platelet (150 to 400 K/cumm)	Week 0	252.33 (47.93)	278.08 (64.11)	0.277
	Week 3	275.92 (63.81)	275.92 (63.81)	0.614
	Week 6	258.33 (44.67)	287.75 (58.94)	0.182
	Week 8	272.75 (49.74)*	279.67 (60.96)	0.764

[B] Comparison between-group: Independent-samples t-test or Mann Whitney U-test,[W] Comparison within-group from week 0: Wilcoxon sign rank test

* Statistically significant ($p<0.05$)

extract showed no chronic toxicity in rat.

What this study adds?

The results of this study proved that the ethanolic extract of PSPR is safe to use in healthy volunteers at the dose of 3x100 to 200 mg/day after meals.

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Potential conflicts of interest

The authors declare no conflicts of interest.

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การศึกษาวิจัยทางคลินิกระยะที่ 1 ของแคปซูลสารสกัดเอทานอลของตำรับประสะเปราะใหญ่

ณิชมน มุขสมบัติ, ไวพจน์ จันทร์วิเมลือง, อรุณพร อิฐรัตน์, กมล บุษบา, บัญชา อุไรกุล

ภูมิหลัง: ตำรับยาประสะเปราะใหญ่ เป็นตำรับสมุนไพรไทยที่ใช้ในการรักษาอาการหวัดและเป็นไข้ จากการศึกษาวิจัยก่อนหน้าพบว่ายาประสะเปราะใหญ่ สามารถบรรเทาอาการจมูกอักเสบจากการแพ้ได้ประสิทธิผลเช่นเดียวกับยาลอราทาดีน โดยขนาดปกติที่รับประทานคือ 3,000 มิลลิกรัม/วัน อย่างไรก็ตามหากสามารถใช้สารสกัดยาประสะเปราะใหญ่ได้จะสามารถลดขนาดรับประทานได้ ดังนั้นจึงมีความจำเป็นในการศึกษาความปลอดภัยของการรับประทานยาสารสกัดตำรับประสะเปราะใหญ่ในอาสาสมัครสุขภาพดี

วัตถุประสงค์: เพื่อศึกษาความปลอดภัยของสารสกัดตำรับประสะเปราะใหญ่ในอาสาสมัครสุขภาพดี

วัสดุและวิธีการ: การศึกษาวิจัยโดยมีการสุ่ม และเปิดเผยกลุ่มศึกษา โดยประเมินความปลอดภัยของอาสาสมัครสุขภาพดี 24 ราย อาสาสมัครถูกแบ่งออกเป็น 2 กลุ่ม กลุ่มแรกรับประทานยา 3x100 มิลลิกรัม/วัน และกลุ่มที่ 2 รับประทานยาขนาด 3x200 มิลลิกรัม/วัน ก่อนอาหารเป็นระยะเวลา 6 สัปดาห์ การสุ่มทำโดยการใช้โปรแกรมคอมพิวเตอร์โดยสุ่มให้มีจำนวนเพศหญิงและชายเท่ากัน โดยกลุ่มที่ 2 เริ่มทำการศึกษา หลังจากมีการประเมินผลของอาสาสมัครกลุ่มที่ 1 เรียบร้อยแล้ว หลังการรับประทานยา 6 สัปดาห์จะเป็นช่วงหยุดยา (wash-out period) ซึ่งอาสาสมัครทุกคนต้องมาติดตามผลในสัปดาห์ที่ 3, 6 และ 8 เพื่อติดตามความปลอดภัยของยา

ผลการศึกษา: ไม่พบความเป็นพิษต่อตับและไต ไม่มีผลต่อระดับน้ำตาลในเลือด ไขมันในเลือด และความสมบูรณ์ของเลือด

สรุป: สารสกัดประสะเปราะใหญ่ขนาด 300 และ 600 มิลลิกรัม/วัน มีความปลอดภัยในการใช้ในอาสาสมัครสุขภาพดีเป็นเวลา 6 สัปดาห์ โดยมีผลข้างเคียงเล็กน้อย จึงแนะนำให้รับประทานหลังอาหาร