The effect of Zingiber cassumunar (Phlai capsule) on bronchial hyperresponsiveness in asthmatic patients

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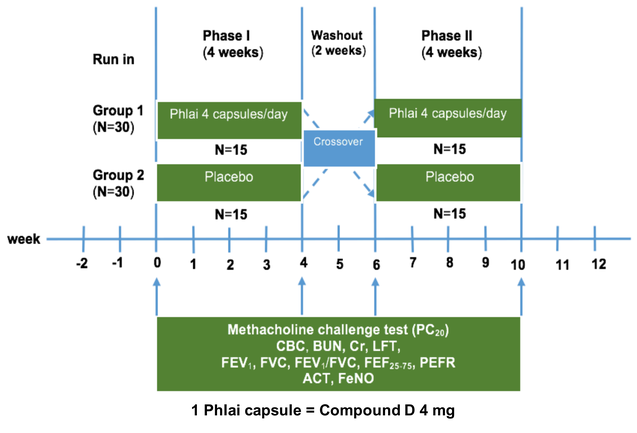
Introduction

Bronchial hyperresponsiveness (BHR) is a key feature of asthma. Compound D (active compound in Phlai) can bind cysteinyl leukotrienes receptors that play role for asthma treatment. This study aimed to determine the effect of Phlai capsules on BHR measured by methacholine challenge tests.

Methods

A randomized, double-blind, placebo-controlled, crossover study was performed between February 2019 - November 2019 at Thammasat University Hospital, Thailand. Asthmatic patients with partly controlled aged at least 18 years were enrolled. Each patient received 4 weeks of treatment with either Phlai or placebo separated by a 2-week washout period. Main outcome was changes in provocative concentration of methacholine causing a 20% drop in FEV_1 (PC_{20}). Fractional exhaled nitric oxide (FeNO), asthma control test (ACT) scores, FEV_1, $FEF_{25-75\%}$,Peak expiratory flow rate (PEFR) were secondary end points. Adverse events were recorded.

Figure 1. Study flow chart



1 Phlai capsule = Compound D 4 mg

Table 1. Baseline characteristics

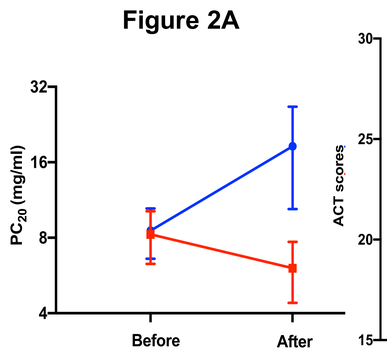
Characteristics		Total N = 30 (%)	Phlai N = 15 (%)	Placebo N = 15 (%)
Age, years		42.9 ± 13.07	45.07 ± 15.40	40.73 ± 10.45
Sex	Male	9 (30)	6 (40)	3 (20)
	Female	21 (70)	9 (60)	12 (80)
BMI, kg/m^2		26.07 ± 4.36	26.76 ± 5.11	25.38 ± 3.48
Smoking history		8 (26.7)	6 (40)	2 (13.3)
Partly controlled asthma		30 (100)	15 (100)	15 (100)
Co-morbidities	Allergic rhinitis	30 (100)	15(100)	15 (100)
	Atopic dermatitis	1 (3.3)	0	1 (6.7)
	Allergic conjunctivitis	3 (10)	1 (6.7)	2 (13.3)
Medications	ICS/LABA	29 (96.7)	15 (100)	14 (93.3)
	INS	28 (93.3)	14 (93.3)	14 (93.3)
BEC, cells/mm^3		281.33 ± 195.67	295.73 ± 219.34	266.9 ± 171.33
ACT scores		21.10 ± 1.73	21.07 ± 1.68	21.13 ± 1.81
FeNO, ppb		37.48 ± 37.06	38.17 ± 42.07	36.80 ± 31.99
Spirometric data	FEV_1, L	2.25 ± 0.59	2.25 ± 0.58	2.25 ± 0.62
	FEV_1/FVC, %	74.71 ± 8.86	75.02 ± 8.79	74.41 ± 9.07
	FEF_{25-75}, %predicted	58.85 ± 22.13	59.97 ± 23.67	57.73 ± 20.80
	PEFR, L/min	399.17 ± 92.27	398.3 ± 95.75	400.33 ± 90.11

P-values are not significant between both groups
Data shown as N (%), mean ± SD
BMI=body mass index, kg/m^2=kilogram per square meter, ACT=asthma control test, ICS/LABA=inhaled corticosteroid plus long-acting β2-agonist, INS=intranasal steroid, BEC=blood eosinophil count, FeNO=fractional exhaled nitric oxide, ppb=part per billion, FEV_1=forced expiratory volume in 1 second, L=liter, FVC=forced vital capacity, FEF_{25-75},forced expiratory flow at 25-75% of FVC, PEFR=peak expiratory flow rate, L/min=liters per minute

Results

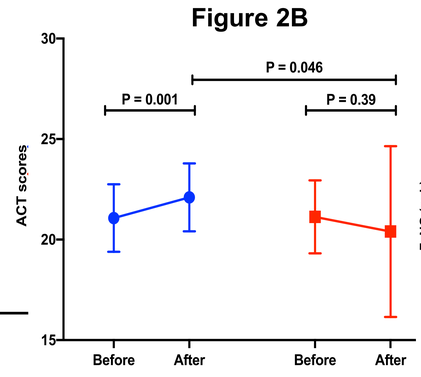
A total of 30 patients were randomly allocated to Phlai or placebo group. All patients had allergic rhinitis (Table1) and 30% with previous history of taking leukotriene receptor antagonist. Four weeks after treatment, mean PC_{20} in Phlai group (18.53 ± 8.12 mg/ml) was higher than placebo (6.05 ± 1.65 mg/ml), p= 0.15 (Figure 2A). The improvement of ACT score in Phlai group was significantly higher than placebo group, p=0.046 (Figure2B). Inflammation parameters (FeNO and blood eosinophil count) decreased after treatment in Phlai group but there was no statistically significant difference between both groups (Figure 2C and Table 2). No change in FEV_1 , FEV_1/FVC , $FEF_{25-75\%}$ and PEFR between both groups (Table 2). All patients in Phlai group were well-tolerated and 30% of patients could reduce rhinitis medications without symptom exacerbation.

Figure 2A



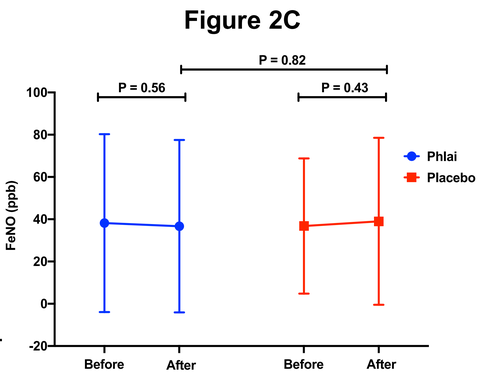
Data shown as mean ± SEM

Figure 2B



Data shown as mean ± SD

Figure 2C



Data shown as mean ± SD

Table 2. Lung function test after 4 weeks of treatments

Data	Phlai				Placebo				Mean difference (95% CI)	P-value
	Before	After	Mean change	P-value	Before	After	Mean change	P-value		
FEV_1, L	2.25 ± 0.58	2.25 ± 0.60	0 (-0.04, 0.04)	0.95	2.25 ± 0.62	2.23 ± 0.63	-0.02 (-0.07, 0.02)	0.33	-0.024 (-0.09 , 0.038)	0.445
FEV_1/FVC, %	75.02 ± 8.80	74.79 ± 9.51	-0.23 (-1.6, 1.13)	0.73	74.41 ± 9.07	74.21 ± 9.69	0.2 (-1.39, 0.99)	0.73	0.03 (-1.73 , 1.80)	0.97
FEF_{25-75}, %predicted	59.97 ± 23.67	60.13 ± 23.84	0.17 (-2.78, 3.11)	0.91	57.73 ± 20.81	56.97 ± 21.53	-0.77 (-3.85, 2.32)	0.61	-0.93 (-5.10 , 3.24)	0.656
PEFR, L/min	398 ± 95.90	410.67 ± 101.64	7.37 (-6.39, 21.12)	0.049*	400.33 ± 90.11	400.67 ± 94.9	0.33 (-14.49, 15.16)	0.96	-7.03 (-26.82 , 12.76)	0.480
BEC, cells/mm^3	295.73 ± 219.33	282.88 ± 166.37	-12.85 (-60.41, 34.71)	0.59	266.89 ± 171.33	271.03 ± 161.41	4.14 (-34.66, 42.94)	0.83	16.99 (-43.13 , 77.11)	0.573

Conclusions

Phlai capsules had a trend to decrease BHR and significantly improve symptom scores. Four weeks after treatment had positive effects on parameters of airway inflammation and could be used as add-on therapy of rhinitis mediations in partly controlled asthmatic patients. The main limitation was small sample size.

Acknowledgement:
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