Complementary Therapies in Medicine 35 (2017) 70–77

Contents lists available at ScienceDirect

Complementary Therapies in Medicine

journal homepage: www.elsevier.com/locate/ctim

Clinical effects of *Zingiber cassumunar* (Plai): A systematic review

Bunchai Chongmelaxme[a], Rosarin Sruamsiri[a], Piyameth Dilokthornsakul[a,b,*], Teerapon Dhippayom[b], Chuenjid Kongkaew[c,d], Surasak Saokaew[a,e,f], Anchalee Chuthaputti[g], Nathorn Chaiyakunapruk[a,b,e,h,i,**]

[a] Center of Pharmaceutical Outcomes Research, Department of Pharmacy Practice, Faculty of Pharmaceutical Sciences, Naresuan University, Phitsanulok, Thailand
[b] Department of Pharmacy Practice, Faculty of Pharmaceutical Sciences, Naresuan University, Phitsanulok, Thailand
[c] Center for Safety and Quality in Health, Department of Pharmacy Practice, Faculty of Pharmaceutical Sciences, Naresuan University, Thailand
[d] Research Department of Practice and Policy, School of Pharmacy, UCL, UK
[e] School of Pharmacy, Monash University Malaysia, Selangor, Malaysia
[f] Center of Health Outcomes Research and Therapeutic Safety (Cohorts), School of Pharmaceutical Sciences, University of Phayao, Phayao, Thailand
[g] Department for Development of Thai Traditional and Alternative Medicine, Ministry of Public Health, Nonthaburi, Thailand
[h] School of Pharmacy, University of Wisconsin, Madison, USA
[i] Asian Centre for Evidence Synthesis in Population, Implementation and Clinical Outcomes (PICO), Health and Well-being Cluster, Global Asia in the 21st Century (GA21) Platform, Monash University Malaysia, Bandar Sunway, Selangor, Malaysia

ARTICLE INFO

Keywords:
Plai
Zingiber cassumunar
Pain
Systematic review

ABSTRACT

Zingiber cassumunar Roxb. known locally as “Plai” in Thai, has been used for treating bruise, sprain and musculoskeletal pain. Several pre-clinical studies demonstrated the anti-inflammatory effect of Plai. However, current evidence of clinical effects of Plai is still unclear. This study aimed to determine the clinical efficacy and safety of Plai among all identified indications. Of the 808 articles identified by a systematic review, six studies were included. Four studies were randomized controlled trials, while two studies were quasi-experimental studies involving 178 patients in intervention group and 177 patients in control group. Duration of treatment ranged from 7 days to 2 months. Our findings showed that 14% Plai cream had a strong trend of benefits in pain reduction for muscle pain and ankle sprain. However, evidence supporting the effects of Plai on acne vulgaris treatment and anti-histamine effect are still unclear.

1. Introduction

Zingiber cassumunar Roxb. (Family Zingiberaceae) or current scientific name as *Zingiber montanum* (J.Koenig) Link ex A. Dietr., known locally as “Plai” in Thai is a perennial herb, consisting of underground rhizomes. It is used as a single plant or as a component of herbal recipes in Thailand and many Asian countries for the treatment of various conditions, i.e. inflammation, bruise, sprain and strain, rheumatism, musculoskeletal pain, wound, asthma, cough and respiratory problem.[1,2] Furthermore, Plai is also used as a mosquito repellent, carminative, mild laxative as well as anti-dysenteric agent.[1,3] It has been listed in the Thailand’s National List of Essential Medicines (NLEM) in combination with other herbs for internal use (heartburn, menstrual disorders and stomach pain) and external use (bruise, sprain, and musculoskeletal pain).[4]

Previous *in vitro* study.[3] demonstrated that the essential oil of Plai exhibited antimicrobial activity against gram-positive and gram-negative bacteria, dermatophytes and yeasts. Ethanol extraction of Plai indicated a potency as an anti-obesity agent based on in vitro inhibition activity on pancreatic lipase activity [5] In addition, (E)-1-(3,4-dimethoxyphenyl)but-1-ene 2), a compound extracted from the rhizomes of Plai, demonstrated anti-inflammatory activity among carrageenin-induced paw edema in rats as well as analgesic activities among acetic acid-induced vascular permeability and writhing symptoms in mice.[6]

Although Plai has been found among Thailand and other Asian countries, i.e. India, Malaysia and Indonesia, it was extensively used in Thailand.[7] Recently, Plai has been selected as one of the five champion herbal products that have been used and generated income to Thailand

* Corresponding author at: Center of Pharmaceutical Outcomes Research, Department of Pharmacy Practice Faculty of Pharmaceutical Science, Naresuan University, Phitsanulok, 65000, Thailand.
** Corresponding author at: School of Pharmacy, Monash University Malaysia, Jalan Lagoon Selatan, 46150 Bandar Sunway, Selangor, Malaysia.
E-mail addresses: bunchang@hotmail.com (B. Chongmelaxme), kookkai_100@yahoo.com (R. Sruamsiri), piyamethd@gmail.com, piyamethd@nu.ac.th (P. Dilokthornsakul), teerapond@hotmail.com (T. Dhippayom), chuenjid@googlemail.com (C. Kongkaew), saokaew@gmail.com (S. Saokaew), anchaleeuan@gmail.com (A. Chuthaputti), nathorn.chaiyakunapruk@monash.edu (N. Chaiyakunapruk).

http://dx.doi.org/10.1016/j.ctim.2017.09.009
Received 5 July 2017; Accepted 28 September 2017
Available online 07 October 2017

in 2013 and in 2016.[8,9] It is used in combination with *Tamarindus indica*, *Citrus hystrix*, *Curcuma longa*, *Cymbopogon citratus*. and *Acacia concinna*, as an herbal compress for relieving musculoskeletal pain. It could also be used, as a combination product with other herbs, i.e. *Acorus calamus*, *Allium sativum*, and *Piper nigrum*, to treat menstrual disorders and amniotic fluid secretion.

A previous study.[10] demonstrated that 14% Plai cream could reduce pain score among patients with ankle sprain after treating for 4 days. Likewise, 14% Plai showed greater effect than diclofenac gel in a treatment of patients with mild to moderate knee osteoarthritis (OA) [11] However, a recent study.[12] found no effect of 14% Plai cream on pain reduction in patients with muscle strain. The effect of Plai is also used to reduce acne lesions among healthy volunteers who had mild to moderate acne vulgaris [13] Furthermore, the anti-histamine effect of Plai has been evidenced to antagonize the action of histamine on bronchial smooth muscle both in vivo and in vitro studies.[14–16]

Although a number of studies have been conducted to evaluate the efficacy and safety of Plai in a various clinical conditions, efficacy and safety of Plai remain unclear. The objective of this study is, therefore, to systematically review the clinical efficacy and safety of Plai among all identified indications. Our findings would be useful for patients who are considering Plai as an option for treating their symptoms.

2. Results

Initial search result yielded 1234 articles, 426 duplicates were removed because of the duplication. The remaining articles were screened through titles and abstracts, of which 789 articles were excluded because of the irrelevant of Plai or non-human studies. This resulted in 19 articles being full-text reviewed for eligibility. Of those, 13 articles were excluded for the following reasons: study that lacked the outcome reported (n = 1), studies that used Plai in combination with other herbs (n = 6), and abstract and conference poster (n = 6). In summary, a total of 6 articles were included in our systematic review.[10,12,13,17–19] A PRISMA flow diagram is shown in Fig. 1.

All included studies were conducted in Thailand. The majority of them (4/6 studies) were RCTs,[10,12,13,18] while the others,[17,19] were quasi-experimental (QE) studies. Three indications of Plai were found. They were pain reduction [10,12,17,18] acne vulgaris treatment.[13] and anti-histamine effect [19] Since the participants' characteristics and interventions were different across studies, meta-analysis could not be performed, the study characteristic and qualitative summary of evidence was shown in Tables 1 and 2.

2.1. Clinical effects of plai on pain reduction

Among the studies investigating the effect of Plai on pain reduction, one was conducted in patients with ankle sprain,[10] one was conducted in patients with neck and shoulder pain which was caused by working or doing activity in daily living,[17] one was conducted in patients with muscle strain,[12] and the last one was conducted in healthy volunteers who performed quadriceps muscle exercise.[18] Three of the four studies compared Plai cream to placebo,[10,12,18] while another one,[17] study compared Plai oil massage with Thai traditional massage. All of them [10,12,17,18] used visual analogue scale (VAS) to assess pain score.

2.1.1. Muscle pain

Manimmanokorn et al., [18] determined the effect of 7% and 14% Plai cream on delayed onset muscle soreness among 75 healthy volunteers that performed 4 sets of 25 eccentric repetitions of the dominant quadriceps muscles on an isokinetic dynamometry machine. All participants were randomly assigned to receive 7% Plai cream, 14% Plai cream or placebo. They were instructed to apply the interventions on quadriceps muscles every 8 h for 7 days. Results showed that 14% Plai cream could substantially reduce muscle soreness compared to placebo [mean difference (MD) of −82% (95% Confidence Interval, CI: −155%, −6%), $p = 0.03$]. However, 7% Plai cream could not reduce muscle soreness compared to placebo [MD: −40% (95% CI: −116%, 36%), $p = 0.3$].

On the other hand, Cheechareoan et al., [12] reported effect of 14% Plai cream differently. The study was conducted in 140 patients with muscle strain. They were randomly assigned to receive either 14% Plai cream or placebo. Pain score was assessed by VAS after 2 weeks of treatment. The study revealed that the average pain score of patients treating with 14% Plai cream was decreased from baseline by 2.08 ± 1.87, while that of patients treating with placebo was decreased from baseline by 2.11 ± 2.07. However, the difference was not statistically significant ($p = 0.278$).

2.1.2. Ankle sprain

Laupattarakasem et al., [10] investigated the effect of 14% Plai cream in patients with ankle sprain. A total of 21 patients were randomized to receive either 14% Plai cream or placebo. Pain score was assessed by VAS at baseline and every day until 7 days of treatment. Results demonstrated that 14% Plai cream could reduce pain score compared to placebo on day 5 and day 6 ($p < 0.05$) but it was not significant at day 7.

2.1.3. Neck and shoulder pain

A study by Leesiriwatkul et al., [17] was conducted to investigate the effect of Plai oil massage compared to Thai traditional massage in patients with neck and shoulder pain. In this study, the massages were performed at 13 different sitting positions. A total of 60 patients were included and assigned (not randomly) to receive either Plai oil massage or traditional massage. The pain score was assessed by VAS at baseline and 15 min after the massages. Results demonstrated that massage with Plai oil could not statistically reduce pain score compared to traditional massage. The before and after massage pain scores of patients with Plai oil massage were 4.86 ± 2.14 and 1.60 ± 1.37, while those of patients with traditional massage were 4.63 ± 1.47 and 1.80 ± 1.47, respectively. The difference between those massages was not statistically significant ($p > 0.05$).

2.2. Clinical effects of Plai on acne vulgaris

A study by Limwattananon et al., [13] was conducted to investigate the effect of 1% Plai gel on the number of acne lesions in healthy volunteers with mild to moderate acne vulgaris compared to placebo. A total of 60 participants aged 18–25 years with presence of acne vulgaris were included in the study. They were randomly assigned to receive 1% Plai gel or placebo for 8 weeks. The study revealed that 1% Plai was not associated with a reduction of the percentage of total acne lesions a [MD: 0.5 (95% CI: −24.1, 25.1), $p = 0.693$], inflammatory acne lesion [MD: 30.3 (95% CI: −78.9, 18.4), $p = 0.459$], and non-inflammatory acne lesions [MD: 3.9 (95% CI: −19.4, 27.2), $p = 0.905$].

2.3. Anti-inflammatory effect of Plai

A study by Piromrat et al., [19] was conducted to determine the effect of 500 milligrams dried Plai tablet on a reduction of wheal size in children patients with asthma compared to chlorpheniramine 0.1 mg/kilogram. A total of 24 subjects were subcutaneously injected with 0.02 millilitres of 1:100 histamine solution to induce wheal reaction. The subjects were assigned into two groups: (1) receiving 500 mg of dried Plai tablets once and (2) chlorpheniramine 0.1 mg/kilogram once. Both groups were assessed for the reduced size of wheal in terms of diameter at 1.30 h after the treatment. Results indicated that 500 mg dried Plai tablet had less effect than chlorpheniramine ($p < 0.05$). The diameter of wheal reactions in Plai group was 9.6 ± 1.1 millimetres at baseline and 8.6 ± 1.0 millimetres at 1.30 h after the treatment, while that in chlorpheniramine group were 9.6 ± 1.4 millimetres and 7.9 ± 0.9 millimetres, respectively (Table 2).