Research Article

Effects of *Zingiber cassumunar* (Plai cream) in the treatment of delayed onset muscle soreness

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ABSTRACT

OBJECTIVE: To evaluate the effects of *Zingiber cassumunar* (Plai cream) in either 7% or 14% concentration on delayed onset muscle soreness (DOMS).

METHODS: Seventy-five untrained healthy volunteers (28 males and 47 females), performed 4 sets of 25 eccentric repetitions of the dominant quadriceps muscle on an isokinetic dynamometry machine. Participants were then randomized into 3 groups: 14% Plai cream, 7% Plai cream and placebo cream. Two grams of the cream (strips of 5-cm long) were gently rubbed into the quadriceps muscles for 5 min immediately following the exercise and every 8 h thereafter for 7 d in all groups. Muscle soreness, muscle strength, jump height, thigh circumference and creatine kinase were measured before and after eccentric exercise.

RESULTS: Compared to the placebo cream the 14% Plai cream substantially reduced muscle soreness over the 7 d by −82% (95% CI = −155% to −6%, \( P = 0.03 \)), but had similar muscle soreness effects to 7% Plai cream (−34%, −96% to 27%, \( P = 0.2 \)). Compared to the placebo cream the 7% Plai cream resulted in a small non-significant reduction in muscle soreness levels over the following 7 d (−40%, −116% to 36%, \( P = 0.3 \)). Compared to placebo cream there was little effect of Plai cream (7% or 14%) on muscle strength, jump height, thigh circumference or creatine kinase concentration.

CONCLUSION: Using 14% Plai cream over a 7-day period substantially reduced muscle soreness symptoms compared to 7% Plai cream or a placebo cream. The authors suggest that the administration of 14% Plai cream is a useful alternative in the management of DOMS.

TRIAL REGISTRATION: Thai Clinical Trial Registry TCTR20140215001.

Keywords: Plai cream; muscle soreness; muscle strength; creatine kinase

1 Introduction

Delayed onset muscle soreness (DOMS) indicated by muscle pain and tenderness typically occurs after a strenuous workout or undertaking unaccustomed exercise. Eccentric exercise, especially of unfamiliar intensity, has a higher potential to develop muscle injury and DOMS than isometric and concentric exercise[1]. The symptoms of DOMS include pain, loss of strength, swelling and stiffness that generally occur 24–48 h after the exercise and resolve within 10 d[2]. The underlying causes of DOMS are related to exercise-induced muscle damage including sarcomere disruption and the ensuing secondary inflammatory response[3,4]. Inflammatory processes stimulate prostaglandin E2 release which sensitizes type III and IV pain afferents, and leukotrienes to attract neutrophils to produce free radicals that further exacerbate muscle cell damage[5].

DOMS after eccentric exercise may result in reduction of muscle performance of athletes[6]. Numerous methods to prevent and reduce DOMS have been suggested including stretching exercises, massage and nutritional supplementation. Non-steroidal anti-inflammatory drugs (NSAIDs) have been used in an attempt to reduce DOMS by reducing inflammation and pain and improving function. The NSAIDs inhibit cyclooxygenase (COX) activity, resulting in reduction of prostaglandins that are potent vasodilators and pain-producing agents[7]. Baldwin et al[6] revealed that 3 d after eccentric exercise of knee extensors, thigh soreness was 40% lower in participants who received naproxen sodium (220 mg 3 times a day) than the participants who received a placebo treatment. In addition, strength decline associated with DOMS was halved in the naproxen group compared to the placebo group. Rahnama et al[8] showed that muscle soreness and creatine kinase levels 48 h after eccentric exercise were significantly lower in participants who received 2 800 mg ibuprofen (400 mg on 7 occasions) than control subjects who did not receive any treatment. Topical NSAIDs that have minimal systemic absorption are recommended to avoid enteral NSAID adverse effects[8]. Cannavino et al[9] reported that local application of NSAID (transdermal ketoprofen, 1 g of cream applied locally every 8 h) reduced muscle soreness 24 h post-exercise by 37% compared to placebo.

Plai (Zingiber cassumunar Roxb) is a popular herb used for musculoskeletal disorders in Asia. Plai is in the ginger family that contains potent phytochemicals. In animal research Plai extracts reduced edema and inhibited the inflammation process[10–11]. In human use, 14% Plai cream has been used by clinicians to reduce inflammatory processes in musculoskeletal disorders. Laupattarakasem et al[11] concluded that applying 2 g of 14% Plai cream (2 times a day for 7 d) on an ankle sprain reduced pain by 90% on day 5 post-injury and reduced swelling by 55% on day 3 post-injury, compared to placebo. Srirochana[12] showed beneficial effects of applying 14% Plai cream (3 times a day for 4 weeks) over 1% diclofenac gel (reduced pain and improved physical and emotional function in patients with knee osteoarthritis). To the best of the authors’ knowledge, the effect of local application of Plai cream for the treatment of DOMS has not been investigated previously. There are currently two commercially available Plai creams on the market, a lower cost, but lower concentration brand (14%). Little is known about the effectiveness of either cream in the reduction of DOMS. The objective of this study was to evaluate whether application of Plai cream was effective in reducing DOMS and muscle performance loss after eccentric exercise and whether there is a dose-dependent response.

2 Methods

This study was conducted at the Department of Rehabilitation Medicine, Faculty of Medicine, Khon Kaen University, Thailand. Seventy-five healthy untrained volunteers, aged 18–60 years, who gave their written informed consent were included. The exclusion criteria were volunteers who had uncontrolled medical diseases such as diabetes, hypertension and heart disease or uncontrolled psychological problems.

This study has been approved by the Khon Kaen University Ethics Committee for Human Research, reference number HE 561436, and has been registered at Thai Clinical Trial Registry with an identification number TCTR20140215001.

2.1 Exercise-induced DOMS

DOMS was induced by strenuous eccentric exercise of the dominant quadriceps muscles by an isokinetic dynamometer (Primus RS, BTE Technologies, Hanover, MD, USA). Prior to exercise, all subjects completed a warm-up consisting of stretching exercises of the major lower limb muscles for 15 min. The participants were then seated on an adjustable chair with their trunk reclined at 15°. The hip, thigh and non-dominant leg were secured to the chair (via webbing straps) while the dominant leg was strapped to the dynamometer’s attachment with the knee flexion angle of 90°. The rotational axis of knee movement was aligned with the lateral femoral epicondyle. The participants performed 4 sets of 25 maximum eccentric knee extension contractions from flexion (90°) to full knee extension (0°) at a speed of 60°·s⁻¹. A rest period of 10 s was given for recovery between repetitions and a rest period of 3 min was given between each set of contractions. All participants received the same verbal encouragement
throughout the test. The participants were allocated into 3 groups by block randomization (25 participants per group): group 1, 14% Plai cream; group 2, 7% Plai cream; and group 3, placebo (control) (Figure 1). The 3 creams were manufactured by the same company and consisted of the same color, odor and packaging. For all groups a dose of 2 g or approximately a 2.5-cm long strip of cream was gently rubbed into the quadriceps muscles (mid-quadriceps area around 15 cm × 8 cm or 120 cm$^2$) until the cream was not visible (approximately 5 min), immediately following the eccentric exercise. The participants were instructed to apply the cream every 8 h after exercise for 1 week.

The participants were requested not to use other treatments such as an oral NSAID, muscle relaxants, physiotherapy or massage. If the participants received other therapies, all details were recorded. Simple analgesic drugs or paracetamol were allowed for management of severe and intolerant pain, and the number of paracetamol tablets or drugs used per day were recorded. The compliance of cream application was recorded on the daily record checklist. All participants completed the study (Figure 1).

The participants were evaluated at pre-test, and day 1, day 2, day 3 and day 7 post-exercise (Figure 2).

2.2 Plai cream preparation

Plai cream is an ordinary oil in water emulsion technique. Plai oil was extracted by stream distillation from *Zingiber cassumunar* Roxb rhizome. Plai and placebo creams were produced by Bangkok Lab & Cosmetic Co., Ltd., Bangkok, Thailand that has a Good Manufacturing Practice (GMP) standard and manufactures with high quality standards of PIC/S GMP.

2.3 Muscle soreness and swelling

Subjective muscle soreness of the quadriceps was determined by using a visual analogue scale, ranged from 0 to 10 (0 indicating no pain, 10 indicating the worst pain). The visual analogue scale has been widely used as a reliable tool for pain intensity assessment\[14\].

Swelling of the thigh was evaluated by measuring thigh circumference at mid-level (midpoint between inguinal fold and anterior aspect of the patella) in the supine position. The thigh circumferences were measured to the nearest 0.1 cm by using a standard tape (Rollfix, Hoechst mass, Germany). The mean of the two closest thigh circumference measurements was recorded. The research assistant taking the tape measurement was blinded to the participant’s group.

2.4 Muscle strength

Muscle strength was evaluated by 3-second maximal voluntary contraction (MVC) of the dominant quadriceps muscle using isokinetic dynamometry. The dominant leg was secured to the isokinetic attachment with the knee in flexion at 45°. Each subject performed three MVCs, separated by a 2-minute rest. Verbal encouragement was given in order to motivate the subject for the maximal force exertion.

Explosive muscle power was assessed via the countermovement jump test using standard testing equipment (Yardstick, Swift Performance Equipment, New South Wales, Australia). The participants jumped from a standing position and their fingertips reached to the highest level. Participants completed a total of 3 jumps (with a 60-second rest between jumps). The highest jump height of 3 performances was recorded for analysis. Muscle strength and muscle soreness were measured immediately prior to eccentric exercise, and then again at the same time of day on days 1, 2, 3 and 7 post-exercise.

**Figure 1** Flow diagram

**Figure 2** Summary of outcomes measurement in this study

3-s MVC: 3-second maximal voluntary contraction.
2.5 Plasma creatine kinase
A 5-mL blood sample for creatine kinase (CK) was obtained from the median cubital vein by a certified medical technologist at Srinagarind Hospital. The blood CK level was analyzed by an automated analyzer (Cobas® 6000 analyzer; Roche Diagnostics Corp., Indianapolis, IN, USA). Plasma CK was measured at pre-test, and day 1, day 2, day 3 and day 7 post-exercise.

2.6 Statistical analysis
The sample size was calculated based on repeated measures control study. The values were set at significant level for 0.05, power of study for 0.8, difference of mean pain score between two groups for 2, and standard deviation of pain score for 2.8[8]. Therefore, the estimated sample size was 25 participants per group.

Descriptive statistical analysis includes the mean and standard deviation. A generalized linear mixed model was used to analyze repeated measurements of the longitudinal study. Analysis of the statistics indicated the overall effects of treatment and the pattern of change difference of measured time points of muscle soreness score, muscle strength, jump height, thigh circumference and plasma CK among three groups. The analyses were conducted by using STATA program version 13.0. Statistical significant difference was accepted at $P < 0.05$.

3 Results

3.1 Demographic data of participants
There were 75 healthy volunteers enrolled in this study. The characteristics of each group are presented in Table 1.

3.2 Pain score
Subjective pain of the quadriceps muscles was similar in all 3 groups at baseline and increased as a result of the eccentric exercise (Figure 3). Overall, perceived pain levels over the 4 recovery periods were substantially reduced in the 14% Plai group by $–82\%$ ($95\%$ CI = $–155\%$ to $–6\%$, $P = 0.03$) compared to the placebo group. In addition, when analyzing the individual day pain scores, pain was substantially reduced in the 14% Plai group compared to the placebo group on post-exercise day 1 ($–26.8\%$, $–52.4\%$ to $–1.2\%$, $P = 0.04$). The pain levels in the 7% Plai group were not significantly different to the placebo group ($–40\%$, $–116\%$ to $36\%$, $P = 0.3$) and 14% Plai group ($–34\%$, $–96\%$ to $27\%$, $P = 0.2$) throughout the recovery period. No oral analgesic drug was required during the study.

3.3 Muscle strength
The 3-second MVC force of the quadriceps can be seen in Table 2. There was no significant difference in muscle strength at baseline between groups, but all groups showed a substantial decrease in maximal force 24 h after the eccentric exercise bout, and tended to follow a similar recovery pattern over the next 2 d. At 7-day after eccentric exercise, maximal isometric force was substantially higher in the 14% Plai group compared to the placebo group ($22\%$, $0.01\%$ to $43.8\%$, $P = 0.04$).

3.4 CK
Serum CK levels increased significantly in all groups ($P < 0.01$) from baseline (where there were no significant differences between groups) to post-exercise day 1, as a response to the eccentric exercise, and had recovered almost back to baseline levels by post-exercise day 7 (Table 3). There was no overall difference among groups (area under the curve for the 4 measurements) as a result of the separate interventions.

3.5 Jump height and thigh circumference
Finally there was no substantial difference in the countermovement jump height or thigh circumference measures over the period of the study among groups.

4 Discussion
Applying 14% Plai cream over eccentrically worked muscles every 8 h for at least 3 d is likely to have a beneficial effect on DOMS and subsequent recovery of muscle strength, compared to no treatment (placebo). Using 7% Plai cream produced little beneficial effect.

It has been suggested that Plai extracts have anti-inflammatory and analgesic effects. Previous research indicates various phytochemicals that were isolated from Plai including curcumin, cassumunar, and phenylbutenoids (i.e., (E)-4(3′,4′-dimethylphenyl) but-
3-en-I-ol, (E)-1-(3,4-dimethoxyphenyl) but-3-en-2-ol and (E)-1-(3,4-dimethoxyphenyl) butadiene may have beneficial effects on the inflammatory process\[^{10,11,15}\]. Curcumin (diferuloylmethane) has an anti-inflammatory effect in reducing activities of COX-2, lipoxygenase, inducible nitric oxide synthase and inflammatory cytokines\[^{15}\]. Cassumunar extracts have been found to have an anti-inflammatory effect on chemically induced edema of the mouse ear stronger than curcumin\[^{10}\]. In another previous experiment in rats it was revealed that (E)-1-(3,4-dimethoxyphenyl) but-3-en-2-ol reduced edema in induced rat paw edema and inhibited exudate formation, leukocyte accumulation and prostaglandin-like activity of the exudates\[^{11}\]. The anti-inflammation effect of (E)-1-(3,4-dimethoxyphenyl) butadiene has been found through the inhibition of COX, and lipoxygenase pathways\[^{9}\].

The topical Plai preparation can be manufactured in several forms; however, the cream form is the best preparation because a high volume of oil is present as the active ingredient. The cream is easily spread and the patients do not feel greasy and sticky after application. In the balm form, although it has a similar level of active ingredient to the cream, it produces a sticky or tacky feeling especially in a tropical climate. In the gel form, the hydrophilic ingredient is not compatible with a high percentage of Plai oil and therefore the gel has a lower percentage of active ingredient. Topical Plai cream is readily absorbed through the skin and helps reduce inflammation\[^{12,13}\]; however, little research exists on other topical forms.

Previous clinical trials showed that Plai cream reduced musculoskeletal pain in injured individuals. Laupattarakasem et al\[^{12}\] showed Plai cream significantly reduced pain from ankle sprains at days 5 and 6 after treatment and required less analgesic drug at days 1 and 2 than placebo. Sirirochana\[^{13}\] revealed positive effects of Plai cream in treatment of osteoarthritis compared to diclofenac gel after two weeks. The duration of effectiveness may depend on the type and lesion of inflammation. This study showed an acute analgesic effect of 14% Plai cream in reducing muscle soreness 24 h after treatment.

It has been found that topical NSAIDs can help with reducing pain and DOMS\[^{8}\]; however, such drugs also carry the adverse effects of application including dry

### Table 2 Muscle strength of three groups

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Muscle strength (kg)</th>
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<tr>
<td></td>
<td></td>
<td>Baseline</td>
<td>Post-exercise day 1</td>
<td>Post-exercise day 2</td>
<td>Post-exercise day 3</td>
<td>Post-exercise day 7</td>
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<td>Placebo</td>
<td>25</td>
<td>24.5 ± 6.3</td>
<td>23.6 ± 6.9</td>
<td>24.8 ± 6.5</td>
<td>25.6 ± 7.5</td>
<td>25.9 ± 8.4</td>
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<tr>
<td>7% Plai cream</td>
<td>25</td>
<td>25.2 ± 6.7</td>
<td>23.4 ± 5.9</td>
<td>25.1 ± 5.5</td>
<td>25.5 ± 5.4</td>
<td>25.8 ± 6.3</td>
</tr>
<tr>
<td>14% Plai cream</td>
<td>25</td>
<td>25.8 ± 5.6</td>
<td>23.9 ± 5.9</td>
<td>27.4 ± 6.8</td>
<td>28.0 ± 7.9</td>
<td>29.5 ± 6.7</td>
</tr>
</tbody>
</table>

Data are presented as mean ± standard deviation. *P*<0.05, vs placebo group.

### Table 3 Creatine kinase concentration of three groups

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Creatine kinase (mmol/L)</th>
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<tr>
<td></td>
<td></td>
<td>Baseline</td>
<td>Post-exercise day 1</td>
<td>Post-exercise day 2</td>
<td>Post-exercise day 7</td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>25</td>
<td>123.0 ± 49.4</td>
<td>175.0 ± 96.2</td>
<td>180.9 ± 113.7</td>
<td>134.1 ± 53.5</td>
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</tr>
<tr>
<td>7% Plai cream</td>
<td>25</td>
<td>110.4 ± 42.4</td>
<td>167.0 ± 127.7</td>
<td>151.6 ± 80.8</td>
<td>132.2 ± 63.9</td>
<td></td>
</tr>
<tr>
<td>14% Plai cream</td>
<td>25</td>
<td>113.8 ± 51.0</td>
<td>170.6 ± 110.8</td>
<td>154.2 ± 88.4</td>
<td>136.4 ± 64.1</td>
<td></td>
</tr>
</tbody>
</table>

Data are presented as mean ± standard deviation.
skin, rash and pruritus\textsuperscript{[16]}. Additionally, topical NSAIDs have been associated with systemic adverse effects such as dyspepsia or gastritis\textsuperscript{[16]}. The current study found a significant analgesic effect of topical 14\% Plai cream and significant improvement of muscle strength (3-second MVC) at post-exercise day 7 compared to the placebo group. We suggest the topical 14\% Plai cream would be an effective alternative to NSAIDs in DOMS management.

The mechanism of NSAIDs is anti-inflammation resulting in reduced muscle damage. This study, however, did not find any significant difference in CK concentration between 14\% Plai cream and the placebo. The results from the current study indicate that CK concentration was dampened in the Plai groups compared to the control group. It is possible that Plai cream may help reduce the early release of CK; however this will remain speculation until further investigation is conducted with a larger sample size which will help to decrease the effect of the high variability in this parameter.

A secondary objective of this study was to gauge the effect of Plai cream dosage on DOMS and force recovery. Pain scores at days 1, 2 and 3 in participants given the 7\% Plai cream were lower than those in participants given placebo but higher than participants given the 14\% Plai cream. The effect of Plai cream on DOMS may be related to its concentration. It seems that the lower concentration of Plai cream had little effect in either reducing DOMS or helping in the recovery of force production. The dose-related effect of Plai cream may be similar to NSAIDs such as diclofenac or ibuprofen\textsuperscript{[17]}. Taking to our results into consideration we would recommend clinicians to use the 14\% Plai cream as an analgesic.

5 Conclusions

Compared to placebo, 14\% Plai cream reduced DOMS perception at 24, 48 and 72 h after eccentric exercise, but no significant pain reduction was observed with 7\% Plai cream. In addition, those participants who used the 14\% Plai cream showed increased force production recovery compared to the placebo by the end of the 7-day intervention period which was not found in the participants using the 7\% Plai cream. Given these results it is recommended that when using Plai cream as an analgesic the higher concentration (14\%) is likely to be more effective.

6 Acknowledgements

Special thanks to the Thailand Research Fund (TRF) and Khon Kaen University for research funding and facility support. Many thanks to Associate Professor Dr. Bandit Thinkhamrop and Dr. Kaewvaj Thipsubthammarat, Khon Kaen University for statistical analysis.

7 Conflict of interest statement

None declared.

REFERENCES


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**Submission Guide**

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