Original article

ANTI-INFLAMMATORY AND ANALGESIC EFFECTS OF THE METHANOL EXTRACT FROM *GARCINIA WALLICHII* CHOISY IN ANIMAL MODELS

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Abstract

Pharmacological studies were conducted with the methanol extract from *Garcinia wallichii* Choisy (GW extract) on experimental animals to evaluate anti-inflammatory and analgesic activities. The GW extract was found to exert an inhibitory activity on the acute phase of inflammation, as seen in EPP-induced ear edema as well as carrageenin- and arachidonic acid- induced hind paw edema in rats. The GW extract showed weak inhibitory activity on cotton pellet-induced granuloma formation; a chronic inflammatory model. The extract also showed very strong analgesic activity on both acetic acid-induced writhing response in mice and the tail-flick test in rats. The single high GW extract dose 3,000 mg/kg taken orally did not cause mortality or show any signs of toxicity or changes in the internal organs of rats, indicating the non-toxic nature of the extract. *Chiang Mai Medical Journal* 2009;48(3):105-115.

Keywords: *Garcinia wallichii*, Guttiferae, anti-inflammatory and analgesic effects

*Garcinia wallichii* Choisy belongs to the family; Guttiferae, which includes some economically important species, e.g. mangosteen (*Garcinia mangostana* Linn.), chamuang (*Garcinia cowa* Roxb.) and somkhag (*Gacinia atroviridis* Griff.). The Guttiferae plant family consists of about 50 genera and more than 1,200 species.1,2 The Thai name for *G. wallichii* is “Pawa Som” and it is found in humid mixed or evergreen
forests. Some species of Garcinia are widely used for different types of inflammatory diseases. In Thailand, dry stem bark of *Garcinia* cowa is used as an antipyretic agent, and fresh pericarp of Garcinia mangostana is employed as a topical anti-inflammatory agent. In Thai folklore medicine, gamboge, the reddish-yellow gum resin from the bark of *Garcinia hanburyi* is used externally for infected wounds and systemically for pain and edema. In Ayurvedic medicine, the pericarp of mangosteen-fruit has been widely used against inflammation and diarrhea. The phytochemical studies of the Guttiferae plants have shown that xanthones, antraquinones and tannins are present as major constituents. The xanthones, α- and γ-mangostins, are major bioactive compounds found in the fruit hulls of the mangosteen. As part of our on-going program on the discovery of bioactive compounds from plants, *G. wallichii* was selected for further study, due to the promising biological activities detected in our initial screening assays. The plant has not been investigated previously.

The objectives of the present study are to verify the anti-inflammatory and analgesic activities of GW extract in various animal models in comparison with reference drugs, and determine the toxicity of methanol extract.

**Materials and methods**

**Animals**

Male Swiss albino mice weighing 30-40 g, male Sprague-Dawley rats weighing 40-60 g, 100-120 g, 180-210 g and 180-200 g, and female rats weighing 180-200 g were used. All animals were kept in a room maintained under environmentally controlled conditions of 24±1 °C, relative humidity of 50±10% and a 12 h light – 12 h dark cycle. All animals had free access to water and standard diet. They were acclimatized for at least one week before starting the experiments. All animal experiments were approved by the Animal Ethics Committee, Faculty of Medicine, Chiang Mai University.

**Plant material and plant extract**

*G. wallichii* was collected from Koh Chang, Trat province, Thailand, in March, 2005, and was identified by Narong Nuntasena of the study team. A voucher specimen (BKF. 128221) was deposited at The Forest Herbarium National Park, Wildlife and Plant Conservation Department, Bangkok, Thailand. The methanol extract was prepared as follows: air-dried and finely powdered leaves and twigs of *G. wallichii* (500 g) were extracted with methanol (314 mL) by using accelerated solvent extractor (ASETM, Dionex). The solvent was evaporated to dryness under reduced pressure and the trace of solvent was removed by freeze-drying to give methanol extract (16.5 g).

**Drug administration**

All test drugs were dissolved in distilled water, except in the ear edema model, where they were dissolved in 5%DMSO in acetone. For the anti-inflammatory, analgesic experiments and acute toxicity test, all test drugs were orally administered in an equivalent volume of 0.5 mL/100 g body weight of the rats and 0.1 mL/10 g body weight of the mice. In the tail-flick test in rats, test drugs were intraperitoneally administered, whereas a local application of the test drugs to the outer and the inner surfaces of the ear were performed in the ear edema model.
Anti-inflammatory activity

1. Ethyl phenylpropionate (EPP)-induced ear edema in rats\(^9\)

Male rats weighing 40–60 g were used. Ear edema was induced by topical application of EPP at a dose of 1 mg/20 μL/ear to the inner and outer surface of both ears using an automatic microliter pipette. Test substances, also dissolved in 5% DMSO in acetone, were administered topically (20 μL/ear) just before the inflammogen. The thickness of each ear was measured with digital vernier calipers before and at 15, 30, 60 and 120 min after edema induction. The effect of GW extract on the ear edema was compared with that of a control group, and the percentage inhibition was calculated.

2. Carrageenan- and arachidonic acid-induced hind paw edema in rats

Male rats weighing 100–120 g were used. Paw edema was induced by an intradermal injection of carrageenin (1% in normal saline solution)\(^{10}\) or AA (0.5% in 0.2 M carbonate buffer, pH 8.4)\(^{11}\) into the plantar surface of the right hind paw of the rats, at a volume of 0.05 or 0.1 mL, respectively. The edema volume was determined prior to and 1, 3 and 5 h after carrageenin injection, or 1 h after AA injection using a plethysmometer (model 7150, Ugo Basile, Italy). Test drugs were given 1 h prior to carrageenin or 2 h prior to AA injection. The control group received a vehicle only.

3. Cotton pellet-induced granuloma formation in rats\(^{12}\)

Male rats weighing 180–210 g were used. Test drugs were administered orally in a once daily dosage regimen for 7 days, and the control group received a vehicle. Two sterilized pellets of cotton wool were implanted subcutaneously, one on each side of the animal’s abdomen, under light anesthesia and using a sterile technique. The rats were sacrificed on the eighth day. The implanted pellets were dissected out and recorded for wet weight. Thymuses were also dissected out. Both pellet and thymus were dried at 60 °C for 18 h and the dry weight was recorded. The weight of the transudate and granuloma as well as the percentage granuloma inhibition of the test drugs were calculated. The body weight gain was also recorded.

4. Measurement of alkaline phosphatase activity in the serum\(^{13}\)

After dissecting the pellets and thymus of the animals from the cotton pellet-induced granuloma formation model, blood was collected into a tube by the cardiac puncture technique, for determination of alkaline phosphatase and total protein. The enzyme activity was expressed as units of enzyme per milligram of serum protein.

Analgesic study

1. Acetic acid-induced writhing response in mice\(^{14,15}\)

Male mice weighing 30–40 g were used. A writhing response was induced by an intraperitoneal injection of an aqueous solution of 0.75% acetic acid (0.1 mL/10 g body weight). Five minutes later, the number of writhes (a response consisting of contraction of the abdominal wall, pelvic rotation followed by hind limb extension) was counted for 15 min. Test drugs were administered orally 1 h before acetic acid injection. The control group received a vehicle only.

2. Tail-flick test in rats\(^{16,17}\)

Male rats weighing 180–200 g were used. The rat’s tail was placed to cover a flush mounted photocell window of the tail flick apparatus (model 7360, Ugo Basile, Italy).
Heat was applied by an infrared lamp (50W bulb) mounted in a reflector. The light intensity was adjusted to give a normal reaction time of 2–4 sec. The timer was activated when the lamp was turned on. When the rat felt pain and flicked its tail, the light fell on the photocell and automatically stopped the timer. A cut-off time of 10 sec was the maximum time that an unflicked tail can be exposed to the heat without damage. The control reaction time was determined first. Then test drugs were given 30 min before re-exposure to the heat. The analgesia was quantified as the percentage of maximum possible response time.

**Acute toxicity**<sup>(18)</sup>

Female rats weighing 180-200 g were used. The GW extract, at a dose of 3,000 mg/kg dissolved in distilled water, was given orally to groups of fasted rats. A control group received an equal volume of vehicle. Signs and symptoms observed after the administration of test sample were recorded at 1, 2, 4 and 6 h and then once daily for 14 days. The visual observations included changes in the skin and fur, eyes and mucous membrane, and also respiratory, circulatory, autonomic and central nervous system, as well as somatomotor activity and behavioral pattern. The rats that died during the experimental period were autopsied, and gross pathological changes of the internal organs were recorded. The surviving rats were sacrificed on the 15th day in order to examine any gross pathological changes in the internal organs.

**Statistical analysis**

All data were expressed as mean ± S.E.M. Statistical comparison between groups was analyzed by using one-way analysis of variance (ANOVA) and the post hoc least-significant difference (LSD) test and p values of less than 0.05 were considered significant.

**Drugs and chemicals**

Phenylbutazone, carrageenin, diclofenac, and arachidonic acid were purchased from Sigma (St. Louis, USA); EPP from Fluka Chemicals Co., Ltd. (Japan); prednisolone (Scherisone®, Schering Bangkok Ltd., Nonthaburi, Thailand); and morphine (T.P. Drug Laboratories, Thailand) Soi Sukhumvit 62, Prakanong 10110, Bangkhae, Bangkok.

**Results**

**EPP-induced ear edema in rats**

The ear edema thickness of the rats in the control group increased gradually and peaked at 60 min after EPP application. The edema was maintained for 2 hours of assessment. Phenylbutazone, at a dose of 1 mg/ear, was used as a positive control, and it significantly reduced the edema formation at all assessment times. The GW extract produced significant inhibitory activity at the dose of 1 mg/ear on edema formation at all determination times, with a slightly weaker intensity than phenylbutazone (data not shown).

**Carrageenin-induced hind paw edema in rats**

The results show that diclofenac at the dose of 10 mg/kg also possessed significant inhibitory effect on carrageenin-induced paw edema at all recorded times. Similar to the inhibitory effect that of diclofenac, of the GW extract on the edema formation was seen at a dose of 300 mg/kg at all determination times (Table 1).
Anti-inflammatory and analgesic effects of *Garcinia wallichii*

### Table 1. Effects of the GW extract and diclofenac on carrageenin-induced paw edema in rats

<table>
<thead>
<tr>
<th>Group</th>
<th>Dose (mg/ka)</th>
<th>Edema volume (mL)</th>
<th>% Edema inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>1 h</td>
<td>3 h</td>
</tr>
<tr>
<td>Control</td>
<td>-</td>
<td>0.18±0.01</td>
<td>0.57±0.02</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>10</td>
<td>0.08±0.01*</td>
<td>0.11±0.01*</td>
</tr>
<tr>
<td>GW extract</td>
<td>75</td>
<td>0.14±0.01</td>
<td>0.48±0.02*</td>
</tr>
<tr>
<td>GW extract</td>
<td>150</td>
<td>0.10±0.01</td>
<td>0.36±0.01*</td>
</tr>
<tr>
<td>GW extract</td>
<td>300</td>
<td>0.08±0.01*</td>
<td>0.19±0.04*</td>
</tr>
</tbody>
</table>

Values represent the mean ± S.E.M. (N=6). * Significantly different from the control, actual P-value < 0.05

### Table 2. Effects of the GW extract, diclofenac and prednisolone on AA-induced hind paw edema in rats

<table>
<thead>
<tr>
<th>Group</th>
<th>Dose (mg/kg)</th>
<th>Edema volume (mL)</th>
<th>% Edema inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>-</td>
<td>0.50±0.01</td>
<td>-</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>10</td>
<td>0.47±0.03</td>
<td>6</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>5</td>
<td>0.15±0.01*</td>
<td>70</td>
</tr>
<tr>
<td>GW extract</td>
<td>75</td>
<td>0.41±0.02*</td>
<td>18</td>
</tr>
<tr>
<td>GW extract</td>
<td>150</td>
<td>0.33±0.01*</td>
<td>34</td>
</tr>
<tr>
<td>GW extract</td>
<td>300</td>
<td>0.21±0.04*</td>
<td>58</td>
</tr>
</tbody>
</table>

Values represent the mean S.E.M. (N=6). * Significantly different from the control, actual P-value < 0.05

### AA-induced hind paw edema in rats

The result of the GW extract on AA-induced hind paw edema in rats is shown in Table 2. Diclofenac did not show any inhibitory effect at the dose of 10 mg/kg. By contrast, prednisolone at the dose of 5 mg/kg exhibited significant inhibitory activity on the edema of the rats’ paw when assessment was done 1 h after AA injection. The GW extract at doses of 75, 150 and 300 mg/kg dose-dependently exhibited significant reduction of paw edema.

### Cotton pellet-induced granuloma formation

In this model, GW extract caused significant inhibition of granuloma tissue formation at the dose of 300 mg/kg (Table 3), when compared with the control. Prednisolone and the GW extract markedly reduced the body weight gain and the thymus weight, while diclofenac produced no effect (Table 4). The activity of serum alkaline phosphatase raised in rats in the cotton pellet-induced granuloma model was normalized by the GW extract, similarly to prednisolone (data not shown).
Table 3. Effects of the GW extract, diclofenac and prednisolone on cotton pellet-induced granuloma formation in rats

<table>
<thead>
<tr>
<th>Group</th>
<th>Dose (mg/kg/day)</th>
<th>Granuloma wet weight (mg)</th>
<th>Granuloma dry weight (mg)</th>
<th>Transudative weight (mg)</th>
<th>Granuloma weight (mg/mg cotton)</th>
<th>aGI (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>-</td>
<td>386.92±16.58</td>
<td>71.67±2.75</td>
<td>315.25±17.24</td>
<td>2.59±0.14</td>
<td>-</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>5</td>
<td>178.50±15.26*</td>
<td>40.83±2.20*</td>
<td>137.66±22.14*</td>
<td>1.04±0.11*</td>
<td>60</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>2.5</td>
<td>241.75±33.77*</td>
<td>49.33±5.51*</td>
<td>192.41±22.14*</td>
<td>1.46±0.27*</td>
<td>43</td>
</tr>
<tr>
<td>GW extract</td>
<td>300</td>
<td>243.50±16.02*</td>
<td>52.58±3.67*</td>
<td>190.92±17.24*</td>
<td>1.63±0.18*</td>
<td>37</td>
</tr>
</tbody>
</table>

Values represent the mean ± S.E.M. (N=6).
* Significantly different from the control, actual P-value < 0.05
a Granuloma inhibition

Table 4. Effects of the GW extract, diclofenac and predisolone on boy weight and thymus weight of cotton pellet-induced granuloma formation in rats

<table>
<thead>
<tr>
<th>Group</th>
<th>Dose (mg/kg/day)</th>
<th>Initial</th>
<th>Final</th>
<th>Gain</th>
<th>Dry thymus weight (mg/100 g BW)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>-</td>
<td>199.33±3.63</td>
<td>244.67±3.71</td>
<td>45.33±6.18</td>
<td>49.51±5.31</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>5</td>
<td>190.00±3.93</td>
<td>179.83±12.89</td>
<td>-10.16±9.45*</td>
<td>23.00±2.26*</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>2.5</td>
<td>203.00±4.02</td>
<td>230.66±5.88</td>
<td>27.66±4.33</td>
<td>47.52±2.79</td>
</tr>
<tr>
<td>GW extract</td>
<td>300</td>
<td>195.67±6.20</td>
<td>196.67±7.84*</td>
<td>1.00±2.90*</td>
<td>29.54±1.70*</td>
</tr>
</tbody>
</table>

Values represent the mean ± S.E.M. (N=6).
* Significantly different from the control, actual P-value < 0.05

Acetic acid-induced writhing response in mice

Diclofenac at the oral dose of 10 mg/kg showed marked inhibition of writhes. Similarly, GW extract at doses of 75, 150 and 300 mg/kg significantly exerted inhibitory effect on acetic acid-induced writhing response in mice (Table 5).

Tail-flick test in rats

GW extract, at a dose of 300 mg/kg, and morphine (10 mg/kg) showed marked inhibition on the tail-flick response in rats. In contrast, diclofenac, at a dose of 10 mg/kg, did not show any inhibitory effect on response in the tail-flick test in rats (Table 6).

Acute toxicity

A single oral administration of GW extract, at the high dose of 3,000 mg/kg, did not produce mortality or show any signs of toxicity or changes in general behavior, or other physiological activities when compared with those of the control group.
Table 5. Effect of the GW extract and diclofenac on acetic acid-induced writhing response in mice

<table>
<thead>
<tr>
<th>Group</th>
<th>Dose (mg/kg)</th>
<th>No. of writhes</th>
<th>Inhibition of writhing response (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>-</td>
<td>45.00±3.73</td>
<td>-</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>10</td>
<td>11.00±1.08*</td>
<td>76</td>
</tr>
<tr>
<td>GW extract</td>
<td>75</td>
<td>28.00±0.93*</td>
<td>36</td>
</tr>
<tr>
<td>GW extract</td>
<td>150</td>
<td>21.00±0.80*</td>
<td>53</td>
</tr>
<tr>
<td>GW extract</td>
<td>300</td>
<td>13.00±0.98*</td>
<td>71</td>
</tr>
</tbody>
</table>

Values represent the mean ± S.E.M. (N = 6).
* Significantly different from the control, actual P-value < 0.05

Table 6. Effects of the GW extract and reference drugs on the tail-flick test in rats

<table>
<thead>
<tr>
<th>Group</th>
<th>Dose (mg/kg)</th>
<th>aTb (sec)</th>
<th>bTr (sec)</th>
<th>Inhibition (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>-</td>
<td>2.48±0.18</td>
<td>2.65±0.15</td>
<td>-</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>10</td>
<td>2.46±0.13</td>
<td>3.28±0.08</td>
<td>9</td>
</tr>
<tr>
<td>Morphine</td>
<td>10</td>
<td>2.43±0.09</td>
<td>9.88±0.11*</td>
<td>98</td>
</tr>
<tr>
<td>GW extract</td>
<td>100</td>
<td>2.71±0.14</td>
<td>4.03±0.33*</td>
<td>26</td>
</tr>
<tr>
<td>GW extract</td>
<td>200</td>
<td>2.63±0.09</td>
<td>6.91±0.49*</td>
<td>58</td>
</tr>
<tr>
<td>GW extract</td>
<td>300</td>
<td>2.71±0.08</td>
<td>9.43±0.44*</td>
<td>92</td>
</tr>
</tbody>
</table>

Values were expressed as mean ± S.E.M. (N = 6).
* Significantly different from the control, actual P-value < 0.05
a Baseline reaction time; b Reaction time after injection of test drugs.

Discussion

The results of the present study reveal the anti-inflammatory activity of GW extract in the acute phase of inflammation. Formation of EPP-induced rat ear edema is a useful model for screening and investigating the anti-inflammatory activity of test substances on the acute phase of inflammation. The inflammatory mediators released in this model include histamine, serotonin, bradykinin and prostaglandin (PGs). These mediators are capable of promoting vasodilation and increasing vascular permeability as well as synergistically producing edema. (19) It was found that GW extract significantly elicited inhibitory effect on the edema formation at all assessment times, at the dose of 1 mg/ear similar to that of phenylbutazone. It is suggested that test extracts probably possess anti-inflammatory activity by inhibition of the release or synthesis of various inflammatory mediators. In the carrageenin-induced rat paw edema model, GW extracts showed significant inhibitory effect on the edema formation at the third hour after carrageenin injection. The carrageenin-induced hind paw edema in rats is known to be sensitive to COX inhibitors, but not LOX inhibitors. The local injection of carrageenin-induced inflammatory process in the rat involves three phases by several mediators released in ordinate sequence. (20) The initial phase, during the first 1.5 h, is
caused by the release of histamine and serotonin; the second phase is mediated by bradykinin from 1.5 to 2.5 h and finally, the third phase; the mediator of which is suspected to be PGs, occurs from 2.5 to 6 h after carrageenan injection. This third phase appears to be the most interesting when compared with the two earlier phases. The significant inhibitory effect of the GW extract on carrageenan-induced paw edema at the third hour, suggests that the main mechanism of action of the GW extract may involve PGs biosynthesis.

AA-induced paw edema in rats is a widely used method for evaluating the anti-inflammatory activity of LOX inhibitors and other agents, with a mechanism of action different from the COX inhibitor. It is well known that in AA-induced rat paw edema, products of the LOX pathway of AA metabolism, i.e. leukotrienes (LTs), have an important role and the COX inhibitors show low or no activity. GW extract significantly inhibits paw edema formation in this inflammatory model in a dose-dependent manner. It is therefore possible that the test extract possesses anti-inflammatory activity in part by inhibition of the LOX pathway. The summary of findings from both paw edema models suggests that the mechanism of action in the GW extract may be related to the inhibition of both the COX and LOX pathways, or phospholipase A2.

The cotton pellet induced granuloma model has been employed to assess the transudative and proliferative components of chronic inflammation. Chronic inflammation is a reaction that occurs when the acute response is insufficient to eliminate pro-inflammatory agents. The inflammatory granuloma is a typical feature of established chronic inflammatory reaction. Implanting a foreign body under the skin is used to study the effect of a drug on the proliferative phase. The fluid adsorbed by the pellet greatly influences the wet weight of the granuloma, whereas, the dry weight correlates well with the amount of granulomatous tissue formed. The granuloma formed by day 7 is characterized by the formation of a vascularized fibrous capsule containing fibroblasts and infiltrating mononuclear cells. In this model, GW extract, at the dose of 300 mg/kg, caused significant inhibition of granuloma tissue formation, when compared with the control. Prednisolone and the GW extract markedly reduced the body weight gain and thymus weight, while diclofenac produced no effect. These results reveal similarity in mechanism of the anti-inflammatory action of GW extract and prednisolone. It seems that the anti-inflammatory action may be related to steroidal-like activity. The activity of serum alkaline phosphatase raised in rats in the cotton pellet-induced granuloma model was normalized by the GW extract, similarly to prednisolone. This effect of GW extract may also result from stabilization of the lysosomal membrane and inhibition of the migration of inflammatory cells into the site of inflammation, similar to steroidal drugs.

In the analgesic test, the acetic acid-induced writhing response in mice was used to screen for both peripherally and centrally acting analgesic activity. Acetic acid causes pain by liberating endogeneous substances including serotonin, histamine, PGs, bradykinin and substance P, all of which excite pain nerve endings. PGs are potent hyperalgesic mediators, which modulate multiple sites along the nociceptive pathway and enhance
both transduction (peripheral sensitizing effect) and transmission (central sensitizing effect) of nociceptive information. The results of this model showed that, diclofenac and various doses of the GW extract significantly inhibited the number of writhes induced by acetic acid in a dose-related manner, thus confirming the analgesic effect of GW extract. Although the writhing response test is very sensitive, it has a poor specificity as an analgesic screening test. Therefore, the tail-flick test in rats was conducted to confirm and study the possible analgesic action mechanism of GW extract. The tail-flick test is widely used to investigate centrally acting analgesic activity. The tail-flick response appears to be a spinal reflex, which is modulated by a supraspinal inhibitory mechanism. Opioids exert their action by interfering with pain transmission in the central nervous system (CNS). In this study, morphine and various doses of the GW extract significantly inhibited the tail-flick response in rats, unlike diclofenac, which did not show any effect in this model. It was shown that the GW extract produced anti-nociceptive effects on both the acute and chronic inflammation. It is likely that the extract is a dual inhibitor of arachidonic acid metabolism (both COX and LOX pathways) or an inhibitor of phospholipase A2, similar to corticosteroids. The extract also showed potent analgesic effect. The mechanism of analgesic activity was found to be due to an inhibition of both peripherally and centrally mediated nociception. GW extract seems to be nontoxic, since a single high dose of GW extract at 3,000 mg/kg orally administered did not cause mortality or show any signs of toxicity or changes in the internal organs of rats.

Conclusion
The results obtained in the present study suggest that GW extract possesses anti-inflammatory and analgesic effects. The anti-inflammatory effect of the GW extract was found on both acute and chronic inflammation. It is likely that the extract is a dual inhibitor of arachidonic acid metabolism (both COX and LOX pathways) or an inhibitor of phospholipase A2, similar to corticosteroids. The extract also showed potent analgesic effect. The mechanism of analgesic activity was found to be due to an inhibition of both peripherally and centrally mediated nociception. GW extract seems to be nontoxic, since a single high dose of GW extract at 3,000 mg/kg orally administered did not cause mortality or show any signs of toxicity or changes in the internal organs of rats.

Acknowledgment
Financial support from the Center for Innovation in Chemistry (PERCH-CIC), Commission on Higher Education is gratefully acknowledged.

References
6. Balasubramanian K, Rajagopalan K. Novel xanthones from Garcinia mangostana, structures of
ฤทธิ์ต้านการอักเสบและฤทธิ์ระงับปวดของสารสกัดเมทานอลจากต้นพะวาส้ม (Garcinia wallichii Choisy) ในแบบจำลองสัตว์ทดลอง

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บทคัดย่อ
การศึกษาฤทธิ์ต้านการอักเสบ และฤทธิ์ระงับปวด ของสารสกัดเมทานอลจากพะวาส้ม (GW extract) ในแบบจำลองสัตว์ทดลอง พบว่า สารสกัดพะวาส้ม มีฤทธิ์ต้านการอักเสบเฉียบพลัน ในแบบจำลองการอักเสบเฉียบพลัน ที่ทำให้เกิดการบวมที่ใบหูของหนูขาว โดยใช้เอทิลฟิสิโลโปรปิอเลท และการทำให้เกิดการบวมที่อุ้งเท้าของหนูขาว โดยใช้คาราจีนินและกรดอะร็คิโดนิก สารสกัดพะวาส้มมีฤทธิ์ต้านการอักเสบเฉียบพลันในแบบจำลองการอักเสบเรื้อรัง จากการทำให้เกิดแกลนด์ไดส์โดยการฝังก้อนสัตว์ สารสกัดพะวาส้ม เผยผลให้เห็นว่ามีฤทธิ์ต้านการอักเสบ เฉียบพลัน ที่ทำให้เกิดการบวมที่ใบหูของหนูขาว โดยใช้คาราจีนินและกรดอะร็คิโดนิก นอกจากนี้ สารสกัดพะวาส้มมีฤทธิ์ต้านการระงับการเจ็บปวด ทั้งในแบบจำลองที่เหนี่ยวนำให้เกิดการเจ็บปวด โดยใช้กรดอะซิเตต หรือการเจ็บปวดที่หางของหนูขาวโดยใช้ความร้อนให้เกิดการเจ็บปวด สารสกัดพะวาส้มแสดงให้เห็นว่าไม่มีฤทธิ์ต้านการเจ็บปวดที่เหนี่ยวนำให้เกิดการเจ็บปวด สารสกัดพะวาส้มมีฤทธิ์ต้านการระงับการเจ็บปวดที่หนูขาวโดยใช้กรดอะซิเตต หรือการเจ็บปวดที่หางของหนูขาว โดยใช้ความร้อน สารสกัดพะวาส้มมีฤทธิ์ต้านการระงับการเจ็บปวดที่เหนี่ยวนำให้เกิดการเจ็บปวด ที่หางของหนูขาว โดยใช้ความร้อน สารสกัดพะวาส้มมีฤทธิ์ต้านการระงับการเจ็บปวดที่เหนี่ยวนำให้เกิดการเจ็บปวด ที่หางของหนูขาว โดยใช้ความร้อน สารสกัดพะวาส้มมีฤทธิ์ต้านการระงับการเจ็บปวดที่เหนี่ยวนำให้เกิดการเจ็บปวด ที่หางของหนูขาว โดยใช้ความร้อน สารสกัดพะวาส้มมีฤทธิ์ต้านการระงับการเจ็บปวดที่เหนี่ยวนำให้เกิดการเจ็บปวด ที่หางของหนูขาว โดยใช้ความร้อน สารสกัดพะวาส้มมีฤทธิ์ต้านการระงับการเจ็บปวดที่เหนี่ยวนำให้เกิดการเจ็บปวด ที่หางของหนูขาว โดยใช้ความร้อน สารสกัดพะวาส้มมีฤทธิ์ต้านการระงับการเจ็บปวดที่เหนี่ยวนำให้เกิดการเจ็บปวด ที่หางของหนูขาว โดยใช้ความร้อน สารสกัดพะวาส้มมีฤทธิ์ต้านการระงับการเจ็บปวดที่เหนี่ยวนำให้เกิดการเจ็บปวด ที่หางของหนูขาว โดยใช้ความร้อน สารสกัดพะวาส้มมีฤทธิ์ต้านการระงับการเจ็บปวดที่เหนี่ยวนำให้เกิดการเจ็บปวด ที่หางของหนูขาว โดยใช้ความร้อน สารสกัดพะวาส้มมีฤทธิ์ต้านการระงับการเจ็บปวดที่เหนี่ยวนำให้เกิดการเจ็บปวด ที่หางของหนูขาว โดยใช้ความร้อน สารสกัดพะวาส้มมีฤทธิ์ต้านการระงับการเจ็บปวดที่เหนี่ยวนำให้เกิดการเจ็บปวด ที่หางของหนูขาว โดยใช้ความร้อน สารสกัดพะวาส้มมีฤทธิ์ต้านการระงับการเจ็บปวดที่เหนี่ยวนำให้เกิดการเจ็บปวด ที่หางของหนูขาว โดยใช้ความร้อน สารสกัดพะวาส้มมีฤทธิ์ต้านการระงับการเจ็บปวดที่เหนี่ยวนำให้เกิดการเจ็บปวด ที่หางของหนูขาว โดยใช้ความร้อน สารสกัดพะวาส้มมีฤทธิ์ต้านการระงับการเจ็บปวดที่เหนี่ยวนำให้เกิดการเจ็บปวด ที่หางของหนูขาว โดยใช้ความร้อน สารสกัดพะวาส้มมีฤทธิ์ต้านการระงับการเจ็บปวดที่เหนี่ยวนำให้เกิดการเจ็บปวด ที่หางของหนูขาว โดยใช้ความร้อน สารสกัดพะวาส้มมีฤทธิ์ต้านการระงับการเจ็บปวดที่เหนี่ยวนำให้เกิดการเจ็บปวด ที่หางของหนูขาว โดยใช้ความร้อน สารสกัดพะวาส้มมีฤทธิ์ต้านการระงับการเจ็บปวดที่เหนี่ยวนำให้เกิดการเจ็บปวด ที่หางของหนูขาว โดยใช้ความร้อน สารสกัดพะวาส้มมีฤทธิ์ต้านการระงับการเจ็บปวดที่เหนี่ยวนำให้เกิดการเจ็บปวด ที่หางของหนูขาว โดยใช้ความร้อน สารสกัดพะวาส้มมีฤทธิ์ต้านการระงับการเจ็บปวดที่เหนี่ยวนำให้เกิดการเจ็บปวด ที่หางของหนูขาว โดยใช้ความร้อน

คำสำคัญ: Garcinia wallichii, Guttiferae, ฤทธิ์ต้านการอักเสบ และฤทธิ์ระงับปวด