



Contents lists available at ScienceDirect

Journal of Traditional and Complementary Medicine

journal homepage: <http://www.elsevier.com/locate/jtcm>

Effectiveness of hot herbal compress versus topical diclofenac in treating patients with myofascial pain syndrome

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ARTICLE INFO

Article history:

Received 10 November 2017

Received in revised form

18 May 2018

Accepted 25 May 2018

Available online 1 June 2018

Keywords:

Myofascial pain syndrome (MPS)

Hot herbal compress

Topical diclofenac

ABSTRACT

Myofascial pain syndrome (MPS) is a chronic pain disorder which causes musculoskeletal pain and inflammation in the body's soft tissues. Thai Traditional Medicine uses hot herbal compresses as analgesic and anti-inflammatory treatment. There are no scientifically validated follow-up studies after treatment using hot herbal compresses. Effects of hot herbal compresses as an alternative treatment for MPS in the upper trapezius muscle compared with the standard treatment (diclofenac) were examined. Sixty patients with myofascial pain syndrome in the upper trapezius muscle were randomly divided into two groups and assigned to receive either hot herbal compress or nonsteroidal anti-inflammatory drug (diclofenac) treatment for 2 weeks. Clinical assessments included visual analogue scale (VAS) for pain score, cervical range of motion (CROM) for the neck and pressure pain threshold (PPT) tolerability before and after treatment. Within the groups, all treatments caused significant improvement in VAS and marginally increased effectiveness in PPT; however, only hot herbal compress treatment improved CROM. Hot herbal compress was more effective than diclofenac in all tests. Results provided comparable clinical efficacy between hot herbal compress and diclofenac after 2 weeks of treatment. Hot herbal compress proved to be an effective complementary or alternative treatment for MPS in the upper trapezius muscle.

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1. Introduction

Myofascial pain syndrome (MPS) is a form of myalgia as a chronic pain disorder causing musculoskeletal pain that affects the connective tissues covering the muscles.¹ Simon et al. (1999), categorised MPS using several criteria including the appearance of hyperirritable spots located in a taut band of skeletal muscle with a hypersensitive palpable nodule. Physical examination of this taut band and exquisitely tender nodule gave symptomatic pain under sustained pressure.² Skootsky et al., 1989 suggested that pain from MPS was more likely on the upper body (shoulder and arm region)

than elsewhere.³

The trapezius is a tripartite diamond shaped muscle on the upper back with different fibre directions that perform diverse functions. Paired trapezii form a diamond shape that attaches medially to the superior nuchal line of the occiput (Thoracic 12), reaching anteriorly to include the lateral one-third of the clavicle, laterally to include the acromion and posteriorly throughout the length of the scapular spine. Continuous use of the upper muscles for a long time without rest or relaxation may cause contraction of the trapezius and lead to microscopic muscle injury. This constriction in the trapezius muscle reduces nourishing blood and develops MPS pain or trigger points that may lead to disability. Referred pain arises as often from trigger points in the upper trapezius as in any other muscle of the body. Trigger points in the upper trapezius fibres characteristically refer pain and tenderness along the posterolateral aspect of the neck behind the ear and to the temple. Trigger points in the lower trapezius refer pain and

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Peer review under responsibility of The Center for Food and Biomolecules, National Taiwan University.

Abbreviations

| | |
|--------|--------------------------------------|
| MPS | Myofascial pain syndrome |
| NSAIDs | Nonsteroidal anti-inflammatory drugs |
| COX-1 | Cyclooxygenase-1 |
| COX-2 | Cyclooxygenase-2 |
| VAS | Visual analogue scale |
| CROM | Cervical range of motion |
| PPT | Pressure pain threshold |
| TrP | Trigger point |
| iNOS | Inducible nitric oxide synthase |
| GABA | Gamma-amino butyric acid |
| TRP | Transient receptor potential |

tenderness mainly to the posterior neck and adjacent mastoid area, suprascapular region and interscapular region. The less common middle trapezius trigger points project pain towards the vertebrae and interscapular region.

Pharmacological treatment of MPS may be different depending on the discretion of the doctor with nonsteroidal anti-inflammatory drugs (NSAIDs), the most commonly prescribed medication. Diclofenac is a standard treatment either taken or applied to reduce inflammation and as an analgesic to reduce pain in certain conditions by inhibition of prostaglandin synthesis.⁴ Inhibition of prostaglandin may refer to inhibition of cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) synthesis. The COX-2 inhibitors have an analogous effect to traditional NSAIDs with a relatively more-tolerable side-effect profile. Heat therapy is an alternative treatment which acts by improving circulation and blood flow. Increased temperature at the afflicted area soothes discomfort and increases muscle flexibility.⁵

There are no reports of scientifically validated follow-up studies after treatments using hot herbal compresses.⁶ Effects of hot herbal compresses as an alternative treatment for MPS in the upper trapezius muscle compared with the standard treatment (diclofenac) were examined. The science of Thai Traditional Medicine should be promoted as an alternative therapy for muscle treatment.

2. Materials and methods

2.1. Study designs and ethics

A single-blinded randomised controlled trial was conducted using a simple random sampling method and a regenerated random assignment scheme enclosed in an envelope. This study was approved by the Ethical Committee of Thammasat University, Thailand (No. 224/2559).

2.2. Patient selection

Patients were referred from the Department of Orthopaedics and Applied Thai Traditional Medicine Unit at Thammasat University Hospital. Sixty patients with MPS in the upper trapezius muscle based on clinical diagnosis following the two criteria of nodule tenderness and reproduction of pain based on minimum proposed criteria² were asked to participate. Recruited subjects were assigned into hot herbal compress and topical diclofenac groups using a simple random sampling method and a pre-generated random assignment scheme enclosed in envelopes. Sample size calculation was based on visual analogue scale (VAS) score as the primary endpoint. Sixty patients fell under inclusion criteria from a total of 65 volunteers as 32 women and 28 men. The five dropouts

included one patient with pregnancy and four with hypertension.

2.2.1. Inclusion criteria

- 1 Clinically active MPS on one or both sides of the upper trapezius muscle
- 2 Between 25 and 65 years old
- 3 Had experienced pain for at least 3 months
- 4 Computer literate
- 5 A sign of the trigger point on upper trapezius muscles
- 6 Diagnosis by a physician as shoulder pain following criteria of the Thai Association for The Study of Pain 2009 and Travell JG and Simons DG, 1990^{2,7}
- 7 Local tenderness, taut bands, hyperirritable spot, jump sign and referred pain
- 8 Signed consent form and pleased to cooperate with this research

2.2.2. Exclusion criteria

- 1 Drug allergy especially regarding diclofenac
- 2 Pregnancy
- 3 Broken bones or shoulder injury
- 4 Hyperirritable spot, jump sign and referred pain from neuropathy
- 5 Received steroid or herbal remedies as medications within 2 weeks prior to the programme
- 6 Received treatment for MPS by other methods such as dry needling and acupuncture

2.3. Study interventions

The subjects were allotted into two groups using an envelopment method for random selection. Patients in group 1 received a hot herbal compress using herbal compress balls containing *Zingiber cassumunar* Roxb., *Tamarindus indica* L., *Citrus hystrix* DC., *Curcuma longa* L., *Cymbopogon citratus* (DC.) Stapf., *Acacia concinna* (Willd.) DC., *Blumea balsamifera* (L.) DC. and camphor with alternating 20 min heat and surface temperature $\leq 45^\circ\text{C}$ for 20 min by the same therapist throughout the programme. Herbal compression was performed 6 times from the baseline (once every third day), and follow-up after 2 weeks. Patients in group 2 received nonsteroidal anti-inflammatory drugs self-administered daily as 2 mg of 1% topical diclofenac gel (Difelene™) applied on the trigger point three times a day for 2 weeks with follow-up after 2 weeks (Fig. 1).

2.4. Outcome measures

2.4.1. Visual analogue scale (VAS)

VAS was used as a provocative pain test to evaluate and quantify the pain perceived by the subjects using a 0–10 cm scale. Each patient was instructed to represent their perceived pain as a characteristic or attitude that cannot be directly measured on a continuum of values which ranged from '0' (no pain) to '10' (worst imaginable pain) at the first session and again at the six consecutive sessions.

2.4.2. Cervical range of motion (CROM)

Motion capabilities were measured using a magnetic device to reflect the CROM. The device was placed on the nose bridge and attached externally behind the ears of the patients. A Velcro strap was fastened at the back of the head to enable accurate measurement, re-measurement and rotational movement in an upright position to prevent human errors.

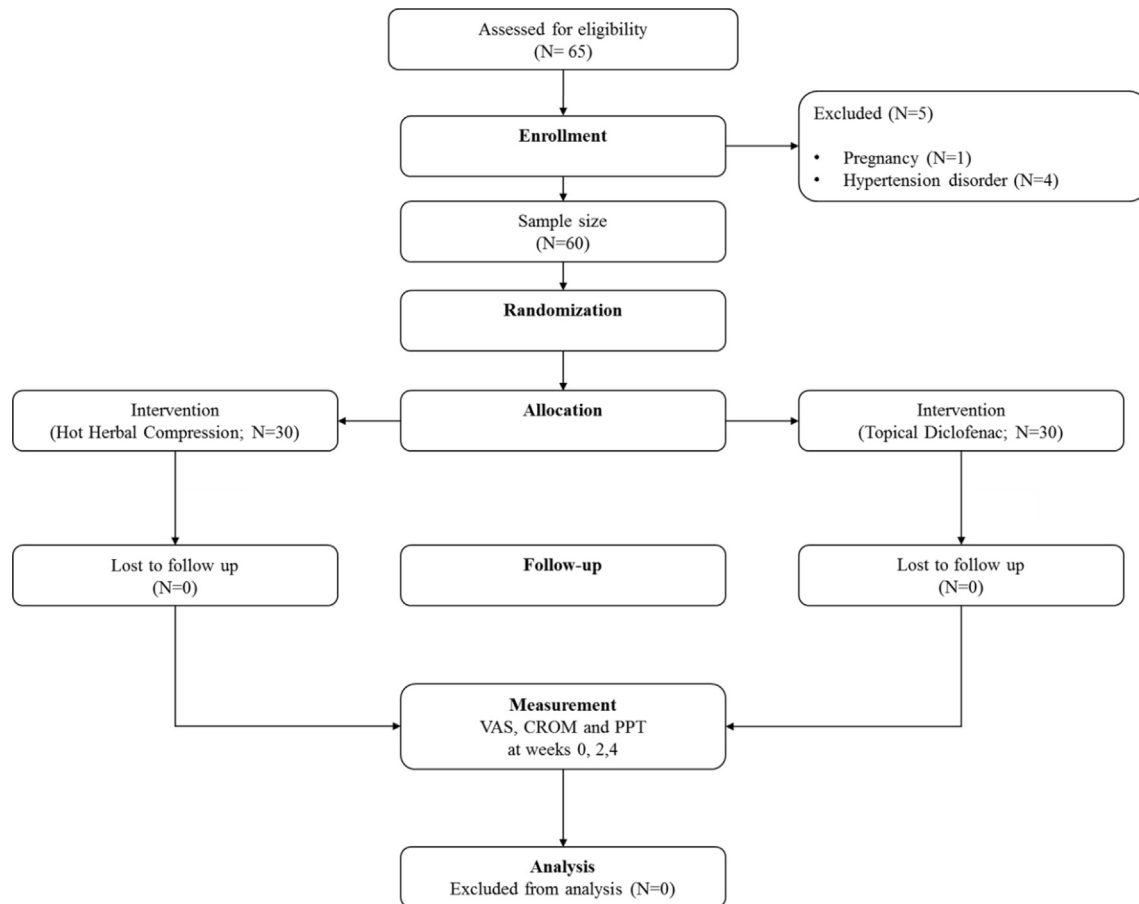


Fig. 1. Diagram showing patient flow.

2.4.3. Pressure pain threshold (PPT)

The minimum force applied which induced pain was examined using PPT following the pressure algometry technique. Measurement precision was determined at 1 kg/cm². A handheld electronic pressure algometry device with surface area at the round tip of 1 cm² was used to gradually increase compression pressure at the rate of approximately 1 kg/s perpendicularly onto the muscle tissue under test. Patients were instructed to indicate when a sensation of pressure turned into a sensation of pain and compression was immediately halted with pressure released. After a 30 s pause, the next measurement was taken. The trigger point (TrP) when the sensation of pressure changed to pain was measured three times and the average value was used for PPT analysis.

2.5. Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics 16. Demographic characteristics were displayed as means \pm SD and percentages. Differences between categorical variables (VAS, CROM and PPT) were also analysed using a Repeated Measures ANOVA with P values < 0.05 considered to be statistically significant.

3. Results

3.1. Demographic characteristics

Subjects (N = 60) were recruited and randomised into Thai

herbal compress and topical diclofenac groups equally with mean ages 36.63 ± 7.68 and 45.40 ± 9.95 years respectively. A total of 86.67% were females. Subjects were required to be computer literate with pain experienced for more than 3 months (Table 1).

3.2. Effectiveness

Hot herbal compress and topical diclofenac treatments showed significant effectiveness in VAS as a primary outcome measurement with CROM and PPT as secondary outcomes. VAS outcome data indicated hot herbal compress to be more potent than topical diclofenac (Table 2). VAS scores for hot herbal compress improved by 59.43% (day 16) and 98.38% (follow-up). Topical diclofenac group scores showed less potency than the herbal compress group with percentage improvement over baseline 46.46% (day 16) and 67.50% (follow-up) ($P < 0.01$).

Functional disability parameters were examined by CROM. Internal comparison of the results indicated that hot herbal compress significantly improved neck motion with right and left lateral flexion more potent than flexion and extension and superior to topical diclofenac ($P < 0.05$) which showed inefficiency in increasing neck movement. Comparison among groups (baseline, day 16 and follow-up day) showed that hot herbal compress significantly improved CROM (Table 3). Treatment tolerability was also investigated and presented as PPT. Tolerability of both groups improved (Table 4) with absence of adverse effects such as overall skin irritation and erythema.

Table 1
Demographic characteristics of patients for both groups.

| Characteristics | Treatment groups | |
|--------------------------------------|------------------------------|-----------------------------|
| | Hot herbal compress (N = 30) | Topical diclofenac (N = 30) |
| Age (Years) ^a | 36.63 ± 7.68 | 45.40 ± 9.95 |
| Sex (F/M) ^b | 26 (86.7)/4 (13.3) | 26 (86.7)/4 (13.3) |
| Weight (Kg) | 60.57 ± 8.20 | 62.23 ± 13.10 |
| Height (Cm) | 161.67 ± 8.20 | 159.97 ± 7.27 |
| Field of job (Computer) ^b | 100.00 | 100.00 |
| Pain period (Months) ^a | 8.13 ± 5.69 | 6.93 ± 4.67 |

^a Mean ± SD.

^b Number (Percentage).

Table 2
Adjusted estimated means of pain intensity measured as Visual Analogue Scale (VAS) scores between the hot herbal compress and topical diclofenac by GLM.

| VAS | Hot herbal compress (N = 30) | | Topical diclofenac (N = 30) | | P-value |
|---------------|------------------------------|------------|-----------------------------|------------|---------|
| | Mean | 95% CI | Mean | 95% CI | |
| VAS Baseline | 5.57 | 5.34, 5.78 | 5.23 | 5.01, 5.45 | 0.053 |
| VAS Day 16 | 2.27 | 2.08, 2.45 | 2.80 | 2.61, 2.98 | 0.000 |
| VAS Follow-up | 0.09 | 0.74, 1.05 | 1.70 | 1.54, 1.85 | 0.000 |

CI = Confidence Interval; GLM = Generalized Linear Model.

4. Discussion

A single-blinded randomised controlled trial was conducted using a simple random sampling method and a regenerated random assignment scheme enclosed in an envelope. MPS is an abnormality in the nociceptor response to stimuli. Topical diclofenac as an overall local pain reliever may have a different action mechanism from hot herbal compress since the herbal ball contains various types of herbs. The trial demonstrated that hot herbal compress reduced pain and increased capabilities of lateral neck motion flexion significantly better than topical diclofenac although pressure pain threshold (minimum force applied which induced pain) marginally increased in both groups. When compared to the inter-group the pain intensity, flexion and right lateral flexion were shown to be significant difference ($P < 0.05$), in addition extension, pressure pain threshold and left lateral flexion were shown to be marginal significant difference ($P > 0.05$). Additionally, hot herbal compress achieved efficacy of symptomatic treatment of MPS and significant improvement of all study parameters consistent with recommendations of pain and function treatment. Topical diclofenac might have a time limitation in terms of treatment and capability for diffusion into the trigger point. Furthermore, topical

Table 4
Adjusted estimate means of the pressure pain threshold (PPT) between the hot herbal compress and topical diclofenac by GLM.

| PPT | Hot herbal compress (N = 30) | | Topical diclofenac (N = 30) | | P-value |
|---------------------|------------------------------|-------------|-----------------------------|------------|---------|
| | Mean | 95% CI | Mean | 95% CI | |
| PPT Baseline RT | 6.50 | 4.81, 8.18 | 4.95 | 3.26, 6.63 | 0.199 |
| Week 2 treatment RT | 8.17 | 6.06, 10.27 | 6.14 | 4.03, 8.24 | 0.178 |
| Week 4 follow-up RT | 9.24 | 6.86, 11.62 | 6.96 | 4.58, 9.34 | 0.180 |
| PPT Baseline LT | 5.75 | 4.04, 7.46 | 5.11 | 3.40, 6.81 | 0.596 |
| Week 2 treatment LT | 7.62 | 5.42, 9.83 | 6.39 | 4.18, 8.59 | 0.432 |
| Week 4 follow-up LT | 8.66 | 6.21, 11.12 | 6.94 | 4.49, 9.40 | 0.326 |

RT = Right; LT = Left; CI = Confidence Interval; GLM = Generalized Linear Model.

diclofenac at this dosage may only transfer into subdermal tissue with limited ability to access interstitial tissue. Hot herbal steam balls containing *Z. cassumunar*, *T. indica*, *C. hystrix*, *C. longa*, *C. citratus*, *A. concinna*, *B. balsamifera* and camphor were shown to be more potent than topical diclofenac for pain reduction.

Heat from hot herbal compression results in dilation of the blood vessels and relaxation of the muscles. Heat therapy is a common alternative treatment to improve circulation and blood flow to a particular area. Furthermore, diverse components of the herbal ball offer various analgesic and anti-inflammatory properties. Complex curcuminoids are active compounds in the herbal ball with *Z. cassumunar* as the main ingredient with well-known analgesic and anti-inflammatory effects. Scientific evidence revealed that *Z. cassumunar* contains cassumunarins which have anti-inflammatory properties induced by 12-*O*-tetradecanoylphorbol 13-acetate. They also contain (E)-1-(3, 4-dimethoxyphenyl) butadiene which is a prostaglandin inhibitor.⁸ Moreover, phenylbutenoids from *Z. cassumunar* have potency on COX-2 inhibition,⁹ while *T. indica* and *C. hystrix* in the herbal ball are acknowledged by traditional medicine practitioners as anti-

Table 3
Adjusted estimate means of the cervical range of motion (CROM) scores between the hot herbal compress and topical diclofenac by GLM.

| CROM | Hot herbal compress (N = 30) | | Topical diclofenac (N = 30) | | P-value |
|---------------------------------|------------------------------|--------------|-----------------------------|--------------|---------|
| | Mean | 95% CI | Mean | 95% CI | |
| Flexion Baseline | 45.50 | 43.64, 47.36 | 46.17 | 44.30, 48.02 | 0.614 |
| Flexion Day 16 | 56.00 | 54.00, 58.00 | 55.50 | 53.50, 57.50 | 0.725 |
| Flexion Follow-up | 66.33 | 64.62, 68.03 | 61.66 | 59.96, 63.37 | 0.000 |
| Extension Baseline | 51.83 | 48.91, 54.75 | 50.66 | 47.74, 53.59 | 0.574 |
| Extension Day 16 | 59.17 | 56.06, 62.27 | 57.00 | 53.89, 60.10 | 0.327 |
| Extension Follow-up | 65.00 | 62.08, 67.91 | 61.33 | 58.41, 64.25 | 0.081 |
| Right Lateral Flexion Baseline | 41.16 | 38.80, 43.52 | 36.16 | 33.80, 38.52 | 0.004 |
| Right Lateral Flexion Day 16 | 46.00 | 43.48, 48.51 | 43.83 | 41.31, 46.35 | 0.228 |
| Right Lateral Flexion Follow-up | 52.50 | 49.83, 55.16 | 48.66 | 46.00, 51.33 | 0.046 |
| Left Lateral Flexion Baseline | 39.50 | 37.27, 41.72 | 36.16 | 33.94, 38.39 | 0.038 |
| Left Lateral Flexion Day 16 | 46.46 | 43.96, 48.99 | 43.63 | 41.10, 46.15 | 0.118 |
| Left Lateral Flexion Follow-up | 51.33 | 48.84, 53.81 | 47.83 | 45.34, 50.31 | 0.051 |

CI = Confidence Interval; GLM = Generalized Linear Model.

inflammatory medicinal plants. Phytochemical screening revealed the presence of certain secondary metabolites such as tannins, alkaloids, saponins, flavonoids and phenol.¹⁰ Flavonoids were substantiated in analgesic and anti-inflammatory activities by potential interaction on prostaglandin cofactor substitution. Flavonoids also inhibit either arachidonic acid lipoxygenation or related enzymes which are active in prostaglandin formation.^{11,12} Moreover, monoterpene hydrocarbons showed advantageous antioxidant properties and their effective potency may be useful for initiating anti-inflammatory activities since oxidation plays a significant role in the pathogenesis of inflammation disorders.¹³ Pino et al., 2002 investigated constituents from *T. indica* leaf and determined limonene and benzyl benzoate as the most predominant compounds.¹⁴ De Sousa et al., 2007 and Amaral et al., 2007 investigated the anti-nociceptive effect of monoterpene. They discovered that both (+)-Limonene and Limonene oxide showed pharmacological activity in various pain *in vivo* models by different routes of administration.^{15,16} Citrus oil from *C. hystrix* was also investigated and found to be a rich source of monoterpene hydrocarbons such as limonene similar to *T. indica* leaf. *C. hystrix* showed potential *in vitro* antioxidant activity in reducing power assay, DPPH, ABTS⁺ and OH radical scavenging capacities and peroxidation inhibition activity which might reflect its analgesic and anti-inflammatory activities. *C. longa* has been scientifically examined for its active components and curcumin is well known for powerful antioxidant and anti-inflammatory properties most likely mediated through its ability to inhibit COX-2, lipoxygenase and inducible nitric oxide synthase (iNOS).¹⁷ The herb *C. citratus* is widely used as a source of ethnomedicines in tropical countries and lemongrass oil constituents of geraniol, neral and myrcene displayed strong analgesic and antipyretic properties with potential as adjuvant therapeutic alternatives in dealing with inflammatory-related diseases.¹⁸ *B. balsamifera* is a remarkable medicinal plant that grows throughout Southeast Asia.¹⁹ The main components of the leaf oil are borneol, carvophyllene and ledol.²⁰ Borneol is a bicyclic monoterpene, historically used as a topical analgesic for millennia and research indicated significant central and peripheral anti-nociceptive and anti-inflammatory activity. Quintans-Júnior et al., 2010 suggested that borneol possessed anticonvulsant and sedative properties due to modulation of gamma-amino butyric acid (GABA) which acts by inhibiting ion channels, a property that contributes to analgesic effects. Borneol was recognised as a GABA mediator which may be responsible for pain states.^{21,22} In Southeastern Asia, camphor is widely used to treat sprains, swellings and inflammation. In Thai Traditional Medicine it was added into the recipe as a pest deterrent and preservative. Camphor, derived from *Cinnamomum camphora* (L.) J. Presl. is an aromatic white crystalline terpenoid. Research in 2005 examined the analgesic mechanism of camphor and results indicated inhibition of several transient receptor potential (TRP) channels which might underlie its analgesic properties.²³

5. Conclusions

A hot herbal compress can be used as an alternative and efficient symptomatic treatment of MPS. Results indicated significant improvement in VAS and CROM with marginal improvement of PPT and scientifically documented that a hot herbal compress can be effectively used as an alternative treatment for MPS as primary health care. Future use of herbs for therapeutic purposes should be encouraged.

Conflicts of interest

None.

Acknowledgements

The authors gratefully acknowledge Thammasat University for funding under TU Scholar Fund (Contract No. 2/40/2560) and also express their appreciation to the Faculty of Medicine, Thammasat University for sponsoring and allowing location use throughout the research.

References

- Ishiki H, Kinkawa J, Watanabe A, et al. Prevalence of myofascial pain syndrome in patients with incurable cancer. *J Bodyw Mov Ther.* 2017.
- Simons DG, Travell JG, Simons LS, Travell JG. *Travell & Simons' Myofascial Pain and Dysfunction: The Trigger point Manual.* second ed. Baltimore: Williams & Wilkins; 1999.
- Skootsky SA, Jaeger B, Oye RK. Prevalence of myofascial pain in general internal medicine practice. *West J Med.* 1989;151(2):157–160.
- Crofford LJ. Use of NSAIDs in treating patients with arthritis. *Arthritis Res Ther.* 2013;15(Suppl. 3):S2.
- Chandler A, Preece J, Lister S. Using heat therapy for pain management. *Nurs Stand.* 2002;17(9):40–42.
- Boonruab J, Niempoo S, Pattaraarchachai J, Palanuvej C, Ruangrunsi N. Effectiveness of the court-type traditional Thai massage versus topical diclofenac in treating patients with myofascial pain syndrome in the upper trapezius. *Indian J Tradit Know.* 2016;15(1):30–34.
- Thai Association for the Study of Pain (TASP). *Clinical Guidance for Acute Pain Management.* vol. 1. Bangkok: Thai Association for the Study of Pain; 2009.
- Jeenapongsa R, Yoovathaworn K, Sriwatanakul KM, Pongprayoon U, Sriwatanakul K. Anti-inflammatory activity of (E)-1-(3,4-dimethoxyphenyl) butadiene from Zingiber cassumunar Roxb. *J Ethnopharmacol.* 2003;87(2–3):143–148.
- Han AR, Kim MS, Jeong YH, Lee SK, Seo EK. Cyclooxygenase-2 inhibitory phenylbutenoids from the rhizomes of Zingiber cassumunar. *Chem Pharm Bull (Tokyo).* 2005;53(11):1466–1468.
- Gupta S, Singh A. Antimicrobial, analgesic and anti-inflammatory activity reported on Tamarindus indica linn root extract. *Phcog J.* 2017;9(3):410–416.
- Baumann J, v. Bruchhausen F, Wurm G. Flavonoids and related compounds as inhibitors of arachidonic acid peroxidation. *Prostaglandins.* 1980;20(4):627–639.
- Hamalainen M, Nieminen R, Asmawi MZ, Vuorela P, Vapaatalo H, Moilanen E. Effects of flavonoids on prostaglandin E2 production and on COX-2 and mPGES-1 expressions in activated macrophages. *Planta Med.* 2011;77(13):1504–1511.
- Geronikaki AA, Gavalas AM. Antioxidants and inflammatory disease: synthetic and natural antioxidants with anti-inflammatory activity. *Comb Chem High Throughput Screen.* 2006;9(6):425–442.
- Pino JA, Escalona JC, Licea I, Pérez R, Aguero J. Leaf oil of Tamarindus indica L. *J Essent Oil Res.* 2002;14(3):187–188.
- de Sousa DP, Junior EV, Oliveira FS, de Almeida RN, Nunes XP, Barbosa-Filho JM. Antinociceptive activity of structural analogues of rotundifolone: structure-activity relationship. *Z Naturforsch C Biosci.* 2007;62(1–2):39–42.
- do Amaral JF, Silva MI, Neto MR, et al. Antinociceptive effect of the monoterpene R-(+)-limonene in mice. *Biol Pharm Bull.* 2007;30(7):1217–1220.
- Menon VP, Sudheer AR. Antioxidant and anti-inflammatory properties of curcumin. *Adv Exp Med Biol.* 2007;595:105–125.
- Gbenou JD, Ahounou JF, Akakpo HB, et al. Phytochemical composition of Cymbopogon citratus and Eucalyptus citriodora essential oils and their anti-inflammatory and analgesic properties on Wistar rats. *Mol Biol Rep.* 2012;40(2):1127–1134.
- Ruangrunsi N, Tantivatana P, Tappayuthpijarn P, Borris RP, Cordell GA. Traditional medicinal plants of Thailand vi. Isolation of cryptomeridiol from Blumea balsamifera. *Sci Asia.* 1985;11(1), 047.
- Bhuiyan MNI, Chowdhury JU, Begum J. Chemical components in volatile oil from Blumea balsamifera (L.) DC. *Bangladesh J Bot.* 2010;38(1).
- Jasmin L, Wu MV, Ohara PT. GABA puts a stop to pain. *Curr Drug Targets - CNS Neurol Disord.* 2004;3(6):487–505.
- Quintans-Júnior LJ, Guimarães AG, Araújo BES, et al. Carvacrol, (-)-borneol and citral reduce convulsant activity in rodents. *Afr J Biotechnol.* 2010;9(39).
- Xu H. Camphor activates and strongly desensitizes the transient receptor potential vanilloid subtype 1 channel in a vanilloid-independent mechanism. *J Neurosci.* 2005;25(39):8924–8937.